VHIO

VALL D'HEBRON
Institute
of Oncology

Advancing cancer care through transformative team science

SCIENTIFIC REPORT **2022**

EXCELENCIA SEVERO OCHOA
2022 - 2026

CERCA
Centres de Recerca de Catalunya

AT A GLANCE 2022

VHIO talents:
accelerating cancer discovery through team science

600
PROFESSIONALS

28
RESEARCH GROUPS

13
MULTIDISCIPLINARY TASK FORCES

7
TRANSVERSAL CLINICAL TRIAL CORE SERVICES/ UNITS

300
ONGOING RESEARCH PROJECTS

4 INSTITUTIONAL PROGRAMS:

"la Caixa" Foundation
CaixaResearch Advanced Oncology Research Program

Fundación BBVA
BBVA Foundation Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI)

fundación fero
Molecular prescreening powered by our Advanced Molecular Diagnostics Program (DIAMAV)

EXCELENCIA SEVERO OCHOA
Center of Excellence Severo Ochoa

Our preclinical and clinical researchers, oncologists, nursing staff and research support professionals, located at VHIO and the Vall d'Hebron University Hospital, work as closely connected teams to develop and advance new diagnostic tools and more effective therapeutics against cancer

Scientific productivity 2022

412 PUBLISHED RESEARCH ARTICLES

MEDIAN IMPACT FACTOR **19,14**

68% of publications in the first quartile

50% of publications in the first and second decile

VHIO VALL D'HEBRON Institute of Oncology

Clinical trials at VHIO

+1500 patients included each year in **+700** active clinical trials.

50% clinical trials are early phase studies at our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch.

Active clinical trials in oncology, hematology, and radiotherapy in 2022:

3	262	33	186	211	1
phase 0	phase I	baskets	phase II	phase III	medical device

- Since our Institute was established in 2006 our teams have contributed in **40** new drug indications.
- **1513** patients enrolled in 2022.
- **230** new trials initiated including **14** post-authorization and rollover studies in 2022.

Technology transfer to-date, development of new therapies & technologies in precision oncology

31 PATENT FAMILIES

4 SPIN-OFF COMPANIES:

Mosaic Biomedicals

Mosaic Anti-LIF antibody MSC-1 acquired by AstraZeneca, now AZD0171, is being evaluated in a phase II trial

PEPTOMYC

MYC inhibitor OMO-103 has finalized a first-in-human phase I trial.

REVEAL GENOMICS®

HER2DX® assay launched as a new diagnostic tool for early-stage HER2+ breast cancer and recognized by TIME Magazine as one of the best inventions in 2022.

ONIRIA THERAPEUTICS

First-in-class TET2 modulator ONR-001 in preclinical development.

80 M€
RAISED BY VHIO'S SPIN-OFF.

30 JOBS GENERATED BY VHIO'S SPIN-OFF.

+90
PATIENTS TREATED WITH VHIO DERIVED THERAPIES.

2
ADVANCED THERAPIES DEVELOPED IN-HOUSE: p95HER2 CAR-T and NextGen-TIL-ACT.

RAD51 predict

Co-developed with third parties RAD51 predict as a new assay to identify patients who could benefit from PARP inhibitors, now used in a prospective clinical trial.

VHIO 360

- Liquid biopsy test based on Guardant360® technology
- Comprehensive genomic profiling of 74 cancer-associated genes
- First test in Europe based on this cutting-edge technology

Cross-border consortia & partnerships of excellence

+40
European and international consortia, collaborations, and alliances of excellence in oncology (co) led by VHIO investigators.

Education and training 2022*

26 VHIO - CAIXARESEARCH SCIENTIFIC SEMINARS IN 2022.

This educational program is supported by the "la Caixa" Foundation and welcomes internationally renowned researchers and clinical investigators to VHIO to share, discuss and debate latest insights, discovery, and next directions in oncology.

VHIO ACADEMY

In addition to coordinating the VHIO – CaixaResearch Scientific Seminars in 2022, the VHIO Academy, which is part of our Scientific Management Area, also organized:

5	12	11	2
academic programs	scientific and transferable skills trainings	workshops on professional development skills for clinicians	Cancer Core Europe (CCE) educational activities

The VHIO Academy encompasses all educational programs at our Institute to attract young talent globally and provide state-of-the-art training and career development activities.

13 BENCHSTORMINGS IN 2022

Our annual series of preclinical, translational and clinical Benchstorming Seminars represent an excellent educational opportunity for VHIO faculty VHIO to present and exchange on and around their respective research areas.

19 AD-HOC EVENTS IN 2022

We also share our expertise, learn from eminent guest speakers, discuss, and debate our latest findings through the organization of VHIO ad-hoc courses, workshops, observerships and preceptorships.

*Some of these events took place remotely online due to the COVID-19 pandemic.

Recognition through accreditation

ISO 9001 IN RESEARCH MANAGEMENT

ISO 15189 FOR ALL PROCEDURES AND TESTS IN CANCER GENOMICS & MOLECULAR ONCOLOGY

Generalitat de Catalunya

VHIO continues to meet the high standards in quality and procedures in the audit of our Clinical Trials Units, carried out by the Generalitat de Catalunya (Government of Catalonia).

European Neuroendocrine Tumor Society (ENETS) certification as a Center of Excellence for treating neuroendocrine tumors in 2020. VHIO was the first in Spain to achieve this certification, which provides joint recognition for the Vall d'Hebron University Hospital and VHIO.

CERCA Centres de Recerca de Catalunya

In 2022 VHIO underwent evaluation for accreditation of the Institució CERCA– Centres de Recerca de Catalunya (CERCA Institute of Research Centres of Catalonia) for the period 2017–2021, and was awarded an A grading.

EXCELENCIA SEVERO OCHOA 2022 - 2026

VHIO is accredited as a Severo Ochoa Center of Excellence 2022-2026, the most outstanding recognition that the Spanish Ministry of Science confers to research centers in Spain.

Patient engagement events, fundraising, and public outreach activities

+35 VHIO (co) organized/hosted patient engagement events, fundraising and public outreach activities in 2022.

Directed by Josep Tabernero, our Principal Investigators, Heads of our Transversal Clinical Trials Core Services, Units and Programs, lead transformative team science to advance cancer care. We work in close connectivity and in partnership with many other investigators across the globe to expedite the translation of laboratory discoveries into novel, more effective cancer therapies and improved outcomes for patients.


María Abad

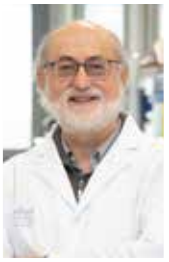

Susana Aguilar


Joaquín Arribas


Judith Balmaña


Marta Beltrán


Francesc Bosch


Francesc Canals


Joan Carles


Cristina Casal


Isabel Cidoncha


Rodrigo Dienstmann


Imma Falero

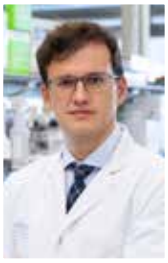

Enriqueta Felip

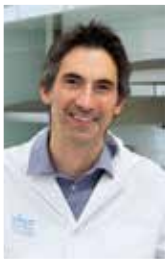

Elena Garralda


Jordi Giralt


Alena Gros


Teresa Macarulla


Joaquin Mateo


Mate Maus


Susana Muñoz


Lara Nonell


Paolo G. Nuciforo


Ana Oaknin


Héctor G. Palmer


Ángeles Peñuelas


Raquel Perez-Lopez


Alejandro Piris


Gemma Sala


Cristina Saura


Joan Seoane


Jose A. Seoane


Violeta Serra


César Serrano


Laura Soucek


Josep Tabernero


Josep Villanueva


Ana Vivancos

mobile version

scan to visit

Vall d'Hebron Institute of Oncology (VHIO)
CELLEX CENTER – C/Natzaret, 115 – 117 – 08035 Barcelona, Spain
Tel. +34 93 254 34 50 – **www.vhio.net**

Direction: Amanda Wren
Photography: Katherin Wermke
Design: parra estudio

INDEX

VALL D'HEBRON INSTITUTE OF ONCOLOGY (VHIO)
SCIENTIFIC REPORT 2022

Foreword

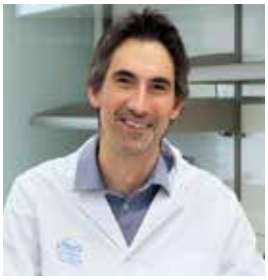
Josep Tabernero
Director
Vall d'Hebron Institute
of Oncology (VHIO)

2022: Advancing cancer care through transformative team science

Established in 2006, the Vall d'Hebron Institute of Oncology (VHIO) is a reference center for personalized medicine in oncology. Thanks to our pioneering model of multidisciplinary and translational research, as well as participation in consortia and projects with other prestigious centers around the world, VHIO is among the leading comprehensive centers in Europe.

We believe that advancing cancer care as rapidly as possible is only achievable through transformative team science, spurred by our various groups who work in close connectivity as well as through partnerships of excellence across borders.

Based on our strategic priorities and to further strengthen these efforts, throughout this past year we have been preparing for the incorporation of new talents to establish and lead new groups. This will help us expand our current research priorities and pursue emerging areas of translational cancer science and clinical research.



Mate Maus, Principal Investigator of our newly established Aging and Cancer Group.

In October, Mate Maus joined our Preclinical and Translational Research Program -- co-directed by Joan Seoane and Laura Soucek -- to head VHIO's Aging and Cancer Group. His team focuses on novel paradigms that can quantify and modulate the processes of cellular senescence, immunosenescence, and organismal aging; evaluating each in the context of oncology and longevity.

Illustrative of his research efforts this year, results of a study [1] posted on the *bioRxiv* preprint server showed that iron accumulation can play an important part in several of these processes with important implications for the pathobiology of aging and cancer. This work was co-led by Mate and Manuel Serrano, an ICREA Research Professor and Head of the Cellular Plasticity and Disease Group at the Institute for Research in Biomedicine (IRB Barcelona). In this context, he is now exploring the function and diagnostic and therapeutic potential of age-associated iron accumulation in longevity and cancer.

As this Scientific Report goes to print, I am delighted to note that Marcus Malumbres will be joining us in January 2023 to direct our newly created Cancer Cell Cycle Group. His team focuses on deciphering the mechanisms that drive tumor cell proliferation, with a patient-focused perspective, and identifying therapeutic opportunities of inhibiting the activity of critical cell cycle regulators in cancer.

To be celebrated in next year's report, several other leading investigators will also be joining VHIO throughout 2023 to spearhead new groups. We will also be announcing a number of well- deserved promotions of VHIO researchers and clinical investigators as leaders of newly established groups across our programs. Watch this space!

Advancing cancer discovery and precision oncology

In reviewing the array of peer-review articles published by our clinicians and researchers over the past year, I am once more humbled by the talent, dedication, and commitment of my colleagues. Their efforts continue to make a difference in our ongoing battle against cancer.

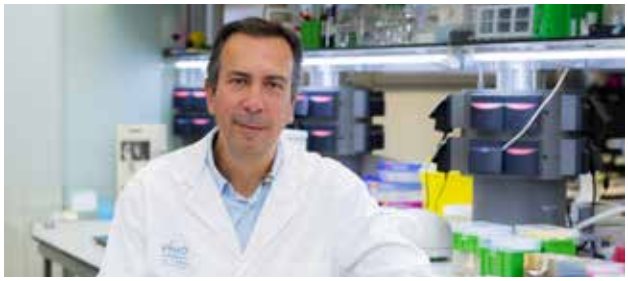
In collaboration with many other leading research centers and groups, both nationally and internationally, VHIO teams and talents published 412 scientific articles, including many in the most prestigious scientific and medical journals, as corresponding, senior or co-authors in 2022.

I cannot possibly do justice to all of our contributions to translational cancer science and clinical research over the past 12 months, but here are a few that have particularly caught my eye.

Novel treatment approaches and the development of anti-cancer therapies

Our co-Directors of Preclinical and Translational Research, Joan Seoane and Laura Soucek, both reported exciting advances in targeted therapies.

Novel T cell bispecific antibody shows promising anti-tumor activity in preclinical models of EGFRvIII-positive glioblastoma



Joan Seoane, co-Director of our Preclinical and Translational Research Program, Principal Investigator of VHIO's Gene Expression and Cancer Group, an ICREA Research Professor, and co-founder of VHIO-born spin-off Mosaic Biomedicals.

Results of a study directed by Joan Seoane, published in the journal *Molecular Cancer Therapy* [2] , showed the striking anti-tumor activity of a novel EGFRvIII-T cell bispecific antibody in preclinical, patient-derived models of glioblastoma. The investigators reported that this bispecific antibody induced T cell recruitment and infiltration resulting in tumor regression and an anti-tumor response in intracranial tumors. This showed for the first time that immunotherapy could work in cold solid tumors (always recalcitrant to immunotherapy) such as glioblastoma.

These preclinical data provided the rationale for a first-in-human clinical trial to assess this bispecific compound as monotherapy in newly diagnosed or recurrent EGFRvIII-positive glioblastoma. This multi-center, international study is currently recruiting patients across several cancer centers, including VHIO.

MYC inhibition halts metastatic breast cancer progression

Laura Soucek, co-Director of our Preclinical and Translational Research Program, Principal Investigator of VHIO's Models of Cancer Therapies Group, an ICREA Research Professor, and co-founder and CEO of VHIO-born spin-off Peptomyc.

Led by Laura Soucek, results of study published in *Cancer Research Communications* [3] showed important advances in the study of the first-in-class MYC inhibitor Omomyc, developed by Laura's team and researchers at Peptomyc, in treating metastatic breast cancer.

For the first time, the investigators showed that MYC inhibition by Omomyc dramatically reduces both primary and metastatic growth in breast cancer. By demonstrating the applicability of Omomyc against metastatic breast cancer (especially the triple-negative subtype), these results challenge the controversial notion that MYC inhibition could induce tumor cell invasion and metastasis. Their results promise new therapeutic opportunities for patients suffering from triple-negative breast cancer.

The early clinical promise of the MSC-1 (AZD0171) monoclonal antibody

Left to right: VHIO's Director Josep Tabernero, co-Principal Investigator of the phase I study of MSC-1, Elena Garralda, co-Director of our Clinical Research Program, Principal Investigator of Early Clinical Drug Development at VHIO, and Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch.

Illustrative of our collaborative early clinical drug development efforts led by Elena Garralda, results of a phase I first-in-human clinical trial show that MSC-1 -- now AZD0171*, a monoclonal antibody developed by Joan Seoane's team and VHIO-born spin-off Mosaic Biomedicals -- is safe and well tolerated in patients with advanced solid tumors.

This study, which I co-led with Erkut Borazanci, Deputy Director of Oncology, HonorHealth in Scottsdale, Arizona, and co-authored by other colleagues at VHIO including Elena Garralda and Joan Seoane, enrolled 41 patients treated at our Vall d'Hebron University Hospital (HUVH), the Memorial Sloan Kettering Cancer Center (MSKCC), New York, and the Princess Margaret Cancer Center in Toronto.

Published in the journal *ESMO Open*, [4] these promising results also showed preliminary evidence of immunoactivating activity, with biomarkers of immune activation identified in the tumor microenvironment of patients' biopsies. In combination with immunotherapy, the drug is progressing to a phase II trial in patients with metastatic pancreatic cancer.

---

* Mosaic Biomedicals was acquired by Medimmune/Astrazeneca in 2020.

Final analysis of the POLO trial: PARPi olaparib in BRCA-mutated metastatic pancreatic cancer

Teresa Macarulla, Principal Investigator of our Gastrointestinal and Endocrine Tumors Group.

In a multi-center study led by Hedy L. Kindler, Medical Director of Gastrointestinal Oncology at the University of Chicago (USA), published in the *Journal of Clinical Oncology* [5], VHIO's Teresa Macarulla and colleagues from centers in Europe, USA, Israel and South Korea reported results of the final analysis of overall survival form the phase III POLO trial in patients with *BRCA*-mutated metastatic pancreatic cancer.

This study enrolled 154 patients who were randomly assigned to receive treatment with PARP inhibitor olaparib or placebo, and previously showed significant progression-free survival for active PARPi maintenance therapy versus placebo. Although the investigators saw no statistically significant benefit in overall survival, olaparib confers some clinical benefits including increased time off chemotherapy and long-term survival in a subset of patients.

Triplet therapy points to a new standard of care in metastatic prostate cancer

Joan Carles, Principal Investigator of our Genitourinary, CNS Tumors, Sarcoma and Cancer of Unknown Primary Site Group.

The phase III PEACE-1 study led by Karim Fizazi, Head of the Department of Cancer Medicine, Institut Gustave Roussy in Villejuif, Paris, enrolled more than 1,100 patients at 77 hospitals across Belgium, France, Ireland, Italy, Romania, Spain, and Switzerland to evaluate the efficacy and safety of abiraterone plus prednisone, with or without radiotherapy, in addition to standard of care.

Published in *The Lancet*, [6] the PEACE-1 investigators, including Joan Carles, reported that triplet therapy with androgen deprivation therapy, docetaxel, and abiraterone in *de novo* metastatic castration-sensitive prostate cancer improved both overall survival and radiographic progression-free survival. This combined approach could become a new standard of care for these patients.

Determining the optimal duration of androgen deprivation therapy combined

Xavier Maldonado, a Radiation Oncologist of VHIO's Radiation Oncology Group directed by Jordi Giralt.

The multi-center DART 01/05 phase III clinical led by Almudena Zapatero, a Senior Consultant, Radiation Oncology Department at the Hospital Universitario de la Princesa in Madrid, was carried out at ten Spanish hospitals including Vall d'Hebron. This study was designed to determine whether long-term adjuvant androgen deprivation (LTAD) is superior to short-term androgen deprivation when combined with high-dose radiotherapy in prostate cancer.

The 5-year results reported that 2 years of LTAD plus high-dose radiotherapy significantly improved outcomes and overall survival in patients with localized prostate cancer, especially in those with high-risk disease. After an extended 10-year follow up, the investigators, including VHIO's Xavier Maldonado, published the final results of this trial in *The Lancet Oncology* [7]. While the same significant benefits of LTAD after 5 years were not observed, the magnitude of benefit was clinically relevant in high-risk patients. Patients with intermediate-risk disease did not benefit from LTAD plus high-dose radiotherapy.

The promise of precision cancer medicine in practice

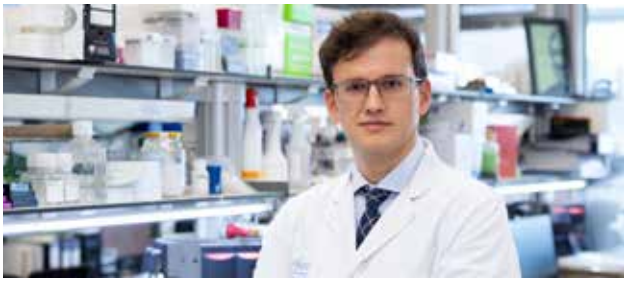
The ESMO ESCAT scale: driving targeted treatment in patients with cholangiocarcinoma

Also led by Teresa Macarulla, in collaboration with colleagues of our Molecular Prescreening Program and other VHIO investigators, a study published in *Clinical Cancer Research* [8] assessed the use of the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT) to guide clinicians in fine-tuning the use of molecular profiling data to select matched targeted therapies in patients with advanced cholangiocarcinoma.

Using this ranking of genomic alterations as targets for precision medicine, the investigators compared survival in patients harboring targetable alterations versus outcomes

in patients with nonactionable alterations. Data showed that targeted treatment administered per alteration according to ESCAT, associated with improved survival in cholangiocarcinoma.

Extending the promise of personalized medicine in oncology: current challenges and next directions



Joaquin Mateo, Principal Investigator of our Prostate Cancer Translational Research Group.

While more effective and targeted cancer treatments continue to be developed and approved, the implementation of precision oncology in the clinic falls short. A review article published in *Nature Medicine* [9] explored some of the major challenges that currently hamper patient access to advanced diagnostics and precision medicine in oncology.

Several experts in oncology, including lead author Joaquin Mateo and VHIO's Elena Garralda, set out future directions toward extending the promise of personalized medicine to an increasing number of cancer patients. These included facilitating equal access to genomics tests, providing more robust data for new medicines and technologies, and enabling physicians to interpret genomic-driven data. The authors also underlined the necessity of empowering patients in shared decision-making, as well as promoting a multi-stakeholder approach to translate research advances into clinical benefits for cancer patients globally.

The Molecular Tumor Board Portal: a support system to guide clinical decision making in precision oncology

First authored by David Tamborero, a Senior Scientist at the Karolinska Institute in Stockholm, and published in *Nature Cancer* [10], members of the Cancer Core Europe consortium (CCE), including VHIO investigators, reported on the promise and the obstacles of implementing CCE's Molecular Tumor Board Portal (MTBP) as an academic, digital support system to guide clinical decision making at the point of care and facilitate automated reporting in precision oncology.

This MTBP aims to provide the infrastructure to systematically gather and store molecular and clinical data in a biorepository to accelerate biomarker discovery and generate insights for future clinical trial designs. But deploying the MTBP across the CCE network posed several challenges, underpinning the challenging task ahead in delivering biomarker-driven oncology at scale. The authors concluded that the success of these scientific and technological platforms will require long-term investment and expertise in areas including medical software regulation, cybersecurity, and front-end development.

Application of novel biomarkers of clinical outcome

Novel microprotein as a regulator of epithelial cell identity with tumor suppressor activity

Maria Abad, Principal Investigator of VHIO's Cellular Plasticity and Cancer Group.

Adding to mounting evidence exposing the microproteome as a valuable source of new regulators of cell identity relevant for cancer, a study led by VHIO's María Abad, in collaboration with other VHIO teams and investigators, identified a new microprotein, pTINCR, as a driver of epithelial differentiation with tumor suppressor activity.

Published in *Nature Communications*, [11] the investigators reported that various epithelial tumors lose pTINCR expression to dedifferentiate and acquire malignant properties, and that forcing pTINCR expression in PDX models reduces tumor growth and could represent a novel therapeutic target for these tumor types.

Their data also showed that the expression level of pTINCR correlates with survival in patients with different tumor types including pancreatic and lung cancer. This new microprotein could serve as a novel prognostic biomarker.

RNF43 mutations as a new biomarker of response to anti-BRAF/EGFR combinatory therapies in metastatic colorectal cancer

Left to right: Elena Élez, a Senior Investigator of VHIO's Gastrointestinal and Endocrine Tumors Group, and Rodrigo A. Toledo, a Translational Investigator of the same group.

In another VHIO-led study, published in *Nature Medicine*, [12] co-corresponding authors Elena Élez and Rodrigo A. Toledo, and colleagues at three Italian hospitals, reported a promising new predictive biomarker of response to anti-BRAF/EGFR combination therapy in patients with microsatellite *BRAF*^{V600E} metastatic colorectal cancer. Mutations in the *RNF43* show promise as a marker of clinical outcomes in this patient population to help guide clinical decision making and refine treatment strategies.

By performing extensive genomic analysis of more than 20,000 genes, analyzing data from 166 patients, their analysis showed that patients with tumors harboring loss-of-function mutations in the *RNF43* tumor suppressor gene had a better response to treatment, longer progression-free and overall survival with dual *BRAF*/EGFR blockade.

While these results promise a much-needed biomarker of response in this setting, the authors suggest that further research should incorporate this candidate biomarker in routine testing along with BRAF and MSS/MSI status and evaluate their integration with other transcriptomic, microbiome or microenvironmental indicators to help guide clinical decision making and refine treatment strategies.

Diagnostic tissue biopsy: informing biomarker-driven clinical decision making in advanced prostate cancer

Another study co-led by VHIO's Joaquin Mateo, alongside Amado J. Zurita-Saavedra, Professor, Department of Genitourinary Medical Oncology at the University of Texas MD Anderson Cancer Center, explored the impact of standard-of-care hormonal therapies on metastatic prostate cancer (mPC) clinical genomic profiles in real-world practice, with a focus on homologous recombination-repair (HRR) genes.

The integration of genomic biomarkers into the clinical management of these patients is limited to highly selected populations. Extending the promise of personalized medicine to an increasing number of mPC patients in routine practice requires more diverse, real-world data sets from larger cohorts and the generation and application of novel clinical genomic insights.

In this retrospective study, the investigators analyzed data from a large cohort of more than 1,300 patients who had undergone tumor genomic profiling in routine clinical care. By integrating genomics and clinical data, they compared the prevalence of clinically relevant genomic biomarkers in primary and metastatic biopsies across the mPC disease spectrum and exposure to androgen-targeting therapies and assessed clinical and genomic variables associated with high genomic loss of heterozygosity (gLOH) scores.

Published in *JCO Precision Oncology*, [13] this work showed that the frequency of some genetic alterations increased with disease progression, while others remained stable. The investigators discovered that the prevalence of mutations in *BRCA* and other *HRR* genes remained stable during disease evolution. These observations are particularly relevant for the stratification of patients for treatment with approved PARP inhibitors. Results verified the use of diagnostic archival tissue biopsies to match patients to PARPi therapy based on HRR status, irrespective of subsequent lines of treatment, and proposed higher gLOH scores as a biomarker for resistance to hormone-basted treatments, independently of individual HRR gene mutation status.

Advancing insights into T cell biology and extending the promise of immunotherapy against cancer

New biomarkers of antitumor T cells associate with improved prognosis in endometrial cancer

Alena Gros, Principal Investigator of VHIO's Tumor Immunology and Immunotherapy Group.

Published in the *Journal of ImmunoTherapy of Cancer*,[14] results of a multi-center study led by Alena Gros reported important findings in characterizing the role of tumor infiltrating lymphocytes (TILs) in endometrial cancer. They identified biomarkers of tumor-reactive CD4+ and CD8+ TILs associated with improved prognosis in patients with endometrial cancer.

Results have advanced insights into the biology of tumor-reactive T cells infiltrating this disease and provided tools to dissect the antitumor CD8+ and CD4+ T cell response infiltrating human tumors that could be extrapolated to other tumor types.

They reported that CD4+ and CD8+ TILs that recognize and kill cancer cells are characterized by expression of PD-1, CD39 and CXCL13 in CD8+ cells; and expression of CXCL13 and high levels of PD-1 in CD4+ cells. The authors suggest that these markers could be used to select and enrich diverse populations of these tumor-reactive T cells for the development of adoptive cellular therapy and advancing personalized medicine, and that the predictive value of these biomarkers in immunotherapy warrants further investigation.

Practice-changing: immunotherapy in combination improves event-free survival in patients with resectable non-small-cell lung cancer

Enriqueta Felip, co-Director of our Clinical Research Program, Principal Investigator of VHIO's Thoracic Tumors & Head and Neck Cancer Group.

Directed by Patrick M. Forde, Director, Division of Upper Aerodigestive Malignancies at Johns Hopkins in Baltimore, results of the phase III international CheckMate-816 clinical trial, co-authored by VHIO's Enriqueta Felip alongside the CheckMate 816 Investigators, showed great promise in improving outcomes for patients with resectable non-small-cell lung cancer (NSCLC).

Data published in *The New England Journal of Medicine* [15] demonstrated that neoadjuvant treatment with nivolumab immunotherapy plus chemotherapy prior to surgery, followed by resection, improved event-free survival and long-term complete pathological response. The addition of nivolumab to chemotherapy did not increase the incidence of adverse events or impede the feasibility of surgery.

This combined strategy was approved by the U.S. Food and Drug Administration (FDA) in March 2022 and is expected to also open up a new preoperative treatment avenue for patients in Europe.

Expanding immunotherapy to recurrent or metastatic cervical cancer

Ana Oaknin, Principal Investigator of our Gynecological Malignancies Group.

Co-led by VHIO's Ana Oaknin and Krishnansu S. Tewari, Chief of the Division of Gynecologic Oncology at the University of California, Irvine (USA), the landmark multi-center phase III EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9 trial assessed the efficacy of PD-1 inhibitor cemiplimab as monotherapy for the treatment of patients with recurrent or metastatic cervical cancer that has progressed on or after first-line platinum-based chemotherapy.

Published in *The New England Journal of Medicine* [16], the practice-changing data showed significant survival benefit, with cemiplimab reducing the risk of death by 31% compared to chemotherapy during the study, which led to the European Commission's approval in November 2022 of cemiplimab as the first second-line immunotherapy for this patient population.

Antibody-drug conjugate: a hotspot for targeted cancer therapy

The power of two: potentiating HER2-targeting ADC

Joaquín Arribas, Principal Investigator of VHIO's Growth Factors Group and an ICREA Research Professor.

A preclinical study published in *Cancer Research* [17], directed by Joaquín Arribas and other VHIO investigators, showed that the addition of therapy-induced senescence with CDK4/6 inhibitors boosted the efficacy of a novel HER2-targeted antibody-drug conjugate (ADC) trastuzumab duocarmazine (SYD985) in HER2-positive breast cancer.

Exploring the effect of ADCs on cells previously treated with standard-of-care senescence-inducing therapies the investigators discovered that this combined strategy could improve their efficacy by facilitating a bystander effect against antigen-negative tumor cells. In breast cancer patient-derived xenograft (PDX) models they showed that treatment with CDK4/6 blockade plus SYD985 showed improved antitumor effects over either therapy alone.

Results support the strategy of combining next-generation ADCs against HER2 with senescence-triggering therapies against tumors with heterogeneous and low HER2 expression.

ADC in HER2-low breast cancer: groundbreaking results, practice-changing data

Cristina Saura, Principal Investigator of VHIO's Breast Cancer & Melanoma Group.

In clinical research, Cristina Saura was a co-author of the major multi-center phase III DESTINY-Breast04 study published in the *New England Journal of Medicine*

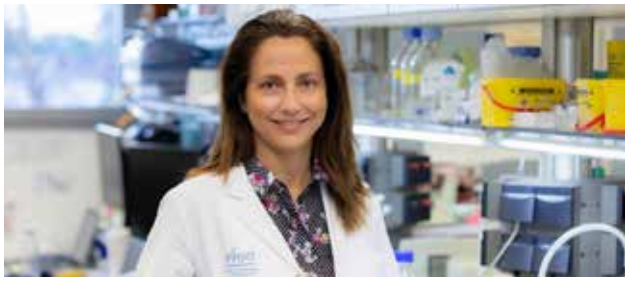
[18]. Led by corresponding author Shanu Modi, Medical Oncologist and Attending Physician at the Memorial Sloan Kettering Cancer Center (MSKCC), New York, the investigators analyzed more than 500 patients with HER2-low metastatic breast cancer with hormone receptor (HR)-positive or HR-negative disease and showed that treatment with the antibody-drug conjugate trastuzumab deruxtecan results in significant improvements in overall survival than the standard chemotherapy.

This drug lowered the risk of disease progression or death by 50% versus physician's choice chemotherapy. Median progression-free survival was 9.9 months in the trastuzumab deruxtecan group and 5.1 months in the physician's choice group. The median overall survival was 23.4 months and 16.8 months, respectively.

These striking results, presented by Shanu Modi at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting, led to the U.S. Food and Drug Administration (FDA) approval of trastuzumab deruxtecan in August 2022 for subsets of patients with unresectable HER2-low breast cancer. As this Scientific Report goes print, the European Commission approved this antibody-drug conjugate in January 2023.

Predictive science: a critical component of cancer care

RAD51 test for identifying homologous recombination-deficient tumors and patient stratification



Violeta Serra, Principal Investigator of our Experimental Therapeutics Group.

Based on DNA repair functionality, the RAD51 assay, pioneered and developed in-house by VHIO's Experimental Therapeutic Group, has been proven to complement genetic testing in clinical studies. Writing in the journal *Cancer Research* [19], Violeta Serra in collaboration with several other VHIO investigators and teams, sought to validate the sensitivity of this test in predicting response to platinum-based chemotherapy or PARP inhibitors in PDX models recapitulating patient homologous recombination deficient status and treatment response.

The investigators preclinically validated the RAD51 score cut-off, confirmed this assay as a more robust predictor of response to PARPi compared to other detection methods, and showed that RAD51 can also capture dynamic changes in homologous recombination repair status upon acquisition of PARPi resistance. These findings support the future incorporation of RAD51 in the clinic. For example, RAD51 is now being used in a prospective clinical trial to predict olaparib sensitivity in patients with metastatic HER2-negative breast cancer, co-led by Judith Balmaña, Principal Investigator of our Hereditary Cancer Genetics Group, and Aleix Prat, Head of the Medical Oncology Department at the Hospital Clinic Barcelona.

New gene classifier predicts risk of recurrence or progression of early pre-cancers in breast

José A. Seoane, Principal Investigator of VHIO's Cancer Computational Biology Group.

Reported in *Cancer Cell* [20], research directed by Robert B. West and colleagues at the Stanford University School of Medicine has revealed a new gene classifier to help predict clinical outcomes in ductal carcinoma *in situ* (DCIS). This research, co-authored by José A. Seoane, has advanced insights into the spectrum of molecular events in DCIS, identified the tumor and stromal predictors of subsequent events, and exposed the factors that underlie progression to invasive disease.

The investigators identified 812 genes associated with cancer recurrence within five years from treatment and developed a new gene classifier to predict DCIS recurrence and progression. Data showed that disease progression is promoted by interactions between invasive DCIS cells and specific features of the tumor environment.

The majority of DCIS cancers studied were identified to be at low risk of cancer progression or recurrence, illuminating the need for an accurate predictive test. Results of this study could ultimately help guide treatment decision making based on individual risk of disease progression and avoid overtreatment of a subgroup of patients without compromising clinical outcomes.

Novel gene expression assay to predict disease progression in blood cancer

Francesc Bosch, Principal Investigator of our Experimental Hematology Group.

Several gene expression profiles with a robust correlation with clinical outcomes in patients with chronic lymphocytic leukemia (CLL) have previously been described but their application as biomarkers in clinical practice has been somewhat limited.

Researchers from our Experimental Hematology Group directed by Francesc Bosch, devised a gene expression profile based on a 15-gene signature (CLL15) that that is associated with the time to first treatment in patients with CLL. Reported in *Blood Advances* [21] by investigators including corresponding author Pau Abrisqueta, Clinical Research Coordinator of the same group, this panel shows great promise in routine diagnostic settings.

Developing new platforms, technologies, and diagnostic tools in precision oncology

Paolo Nuciforo, Director of Core Technologies at VHIO, and Principal Investigator of our Molecular Oncology Group.

Under the direction of Paolo Nuciforo, our Core Technologies Program accelerates cancer discovery and precision medicine in oncology by developing and validating novel tumor biomarkers, implementing transformative technologies, and advancing the treatment and care of cancer patients through dynamic approaches, new diagnostic tools, and state-of-the-art genomics platforms.

Serving as core facilities as well as independent research groups, VHIO's Bioinformatics, Cancer Genomics, Molecular Oncology, Proteomics teams, led by Lara Nonell, Ana Vivancos, Paolo Nuciforo, Francesc Canals, respectively, as well as our VHIOTECA headed by Susana Aguilar, epitomize team science of excellence.

Driving important progress in combating cancer, let me highlight just some of the many developments in 2022

Expanding VHIO's suite of cutting-edge technologies: Guardant Health's liquid biopsy now operational

Ana Vivancos, Principal Investigator of our Cancer Genomics Group.

Since VHIO incorporated in-house BEAMing liquid biopsy RAS biomarker technology in 2015, the first academic test center to do so, our teams have made important progress in validating and developing liquid biopsy technologies for the more effective, less invasive 'policing' of cancer over time, in real time.

In 2021, Ana Vivancos and her team incorporated the Guardant Health liquid biopsy at VHIO. As the first cancer research center to do so in Europe, this avant-garde platform provides complete genomic results in all solid tumors from a simple blood test in seven days and with therefore help to overcome the limitations associated with traditional tissue biopsy.

Ana and her group have since performed extensive in-house validation of this assay, attaining very high levels of sensitivity and specificity, and implemented and validated the VHIO360 test for liquid biopsy; technology transfer of the Guardant 360® DX test.

Also illustrative of our leading expertise in liquid biopsy technology, Ana and I were invited to author a News & Views article in *Nature Medicine* [22] on the prognostic potential of circulating tumor DNA in advanced non-small-cell lung cancer, to discuss the results of an international cohort study that sought to validate the utility of ctDNA as a genomic biomarker to help guide treatment decision making and explored its association with impact on survival [23].

HER2DX®: the world's first genomic tool for patients with HER2+ breast cancer

REVEAL GENOMICS®

REVEAL GENOMICS S.L. is a spin-off company of the Hospital Clínic de Barcelona, August Pi I Sunyer Biomedical Research Institute (IDIBAPS), University of Barcelona (UB), and VHIO. Committed to bringing new scientific knowledge and technology to the clinic, this biotechnology start-up develops innovative diagnostic tools to help define optimal therapeutic strategies for cancer patients.

Directed by CEO and co-founder Patricia Villagras and Aleix Prat, CSO and co-founder of the company, REVEAL GENOMICS also counts on the leading expertise of its Board members Joel S. Parker and Charles M. Perou, from the Lineberger Comprehensive Cancer Center in North Carolina, and VHIO's Ana Vivancos.

As the first genomic tool for patients with HER2+ early-stage breast cancer, one of the most aggressive types of breast cancer, HER2DX® is a sophisticated tool that reveals long-term relapse risk, probability of therapy response, and tumor expression levels. This assay measures the expression of 27 genes and evaluates the biological processes of immune infiltration, luminal differentiation, tumor cell proliferation, and HER amplicon expression. The biological data from these signatures is combined with clinical data including tumor stage and nodal stage.

Brought to market this year, HER2DX® featured among *TIME* magazine's listing of Best Inventions of 2022 under the category of Medical Care.

In our exploration of novel immuno-oncology biomarkers for patient selection across our phase I clinical trials, I must also mention our VIGex immune gene expression signature. Based on our Nanostring and RNA-seq technologies for the detection of an immune signature, this tool has been developed in-house thanks to the close collaboration and teamwork between investigators at our Research Unit for Molecular Therapy of Cancer (UITM) – Caixa Research directed by Elena Garralda, and VHIO's Cancer Genomics Group led Ana Vivancos.

In collaboration with investigators at the Princess Margaret Cancer Centre in Toronto, we continue to further validate VIGex as a novel predictive biomarker for immune checkpoint treatment in patients with advanced solid tumors. This tool, combined with ctDNA analysis by liquid biopsy, holds promise in identifying responders to cancer immunotherapy.

The power of cross-border collaborative team science

Illustrative of the theme of this year's Scientific Report, we continue to identify, develop and (co-) lead important collaborations and partnerships with other leading research centers and investigators a national and international level. These strong alliances are key in our collective efforts aimed at solving cancer sooner. In 2022, we celebrated the launch of 12 new consortia, in addition to our many other muti-center ongoing projects (pages 185-199), detailed as a dedicated section in this report.

In addition to advancing care through transformative team science, our continued progress in beating cancer can and will only happen through dedicated priority setting, the necessary infrastructures and support mechanisms in place, and careful planning. For this reason, I take this opportunity to highlight the EU UNderstand CANcer project.

Aimed at implementing the European Union's Europe's Beating Cancer Plan and the Horizon Europe Mission on Cancer, the UNderstand CANcer (UNCAN.eu) project is dedicated to addressing the many urgent and critical scientific and medical challenges in cancer prevention, early diagnosis, treatment and survival, in men, women and children.

UNCAN.eu is one of the 13 specific objectives of the Mission, and its Coordination and Support Action (CSA), 4.UNCAN.eu [24], is coordinated by Eric Solary, Institut Gustave Roussy in Villejuif, France. Aimed at drafting a blueprint for UNCAN.eu, this CSA will provide crucial insights into the shaping and strengthening of oncopolicy as well as addressing the unacceptable regional inequalities in cancer research, access to optimal treatment and care, and disease prevention in Europe.

Core partners from Spain are VHIO and the Biomedical Research Networking Center (CIBER), and I lead one of the six work packages to identify cancer research challenges to address future EU priorities and research policies.

The UNCAN.eu initiative receives funding from the European Union's Horizon Europe and innovation programme HORIZON-MISS-2021-UNCAN-01-01 under grant agreement No. 101069496.

Honoring the life and legacy of José Baselga

José Baselga, MD, PhD (1959-2021): a visionary leader in translational science and precision oncology.

The untimely passing of José Baselga, VHIO's first and Founding Director and Founder and late Honorary President of one of our Institutional Supporters and Patrons Fundación FERO, continues to represent an unfillable void in cancer research treatment and care, he leaves a tremendous legacy for the scientific community: one that will continue to inspire present and future generations of cancer researchers and clinical investigators.

Marking the first anniversary of his death and to honor his exceptional career and contributions to cancer science and clinical oncology, as well as his final appointment as Executive Vice President of Oncology R&D at AstraZeneca in Boston, VHIO and AstraZeneca co-organized a commemorative event: Challenges in Oncology Research. A tribute to José Baselga.

We paid homage to José and warmly welcomed special guests including José's wife Silvia Garriga, and speakers from AstraZeneca in Boston and Madrid. From Boston, Susan Galbraith, Executive Vice President of Oncology R&D; Maurizio Scaltriti, Vice President, Translational Medicine, Early Oncology, Oncology R&D; and Jorge Zeron-Medina, Senior Medical Director, Early Clinical Oncology, and from Madrid, Rick R. Suárez, Country President Spain, and Ramón Mel Cadahía, Country Head Oncology from Madrid. The many other guests and speakers included VHIO investigators and other researchers who have also had the privilege of working José and knowing him as an extraordinary person impassioned by everything he did.

To further honor José's incredible legacy, we announced the launch of the VHIO - AstraZeneca José Baselga Innovative Disruption (J-BID) Program, in collaboration with his family. Starting next year, the main objectives of this program are to spur the development of pioneering preclinical and translational research projects, attract and retain research talents, and support young investigators in Spain.

Left to right: Josep Tabernero and Rick R. Suárez at the signing of the VHIO - AstraZeneca J-BID program agreement.

Institutional programs, platforms and recognition

Supported by three of VHIO's Institutional Supporters and Patrons, our trio of Institutional Programs, the Fundación FERO Institutional Advanced Molecular Diagnostics Program (DIAMAV), CaixaResearch Advanced Oncology Research Program, and the Fundación BBVA Comprehensive Program of Cancer Immunotherapy and Immunology (CAIMI), further enable us to make important progress in advancing precision medicine in oncology (pages 126-128).

As I advanced in last year's report, VHIO received Excelencia Severo Ochoa accreditation in 2021, and is now recognized as a Severo Ochoa Center of Excellence (2022-2026). This accolade recognizes national research centers demonstrating scientific leadership of excellence and impact at a global level. This fourth Institutional Program at VHIO (page 129) further strengthens our various research programs and teams in driving important advances against cancer.

In addition to these programs, as well as the tremendous support we receive from our other two Institutional Supporters and Patrons, Generalitat de Catalunya and Fundació Privada CELLEX (pages 17 and 18), VHIO was awarded by the Asociación Española Contra el Cáncer – AECC, another longstanding supporter of several of our groups and investigators.

Announced at the end of December and set to launch as our fifth Institutional Program, our Institute has been awarded by AECC's Excellence Program - Advanced Therapies Accelerator Program. We aim to establish VHIO as an international reference in the rapidly emerging field of gene and cellular therapies. To boost the development of academic gene and cellular therapy products and associated translational research, we plan to construct a Clean Room laboratory, provide our teams with the necessary training, foster and develop national and international collaborations, and establish an optimal program governance structure. These actions will enable us to develop new gene and cellular therapy products and improve existing ones in our pipeline.

In addition to all of these programs, I am delighted to announce the launch of a new platform this year. The UNIQUE - UNderstanding cancer through sIngle cell seQUEncing initiative is supported by the "la Caixa" Foundation and represents a valuable tool that will help us to generate insights into complex biological processes (including intra- and inter-tumor heterogeneity), through state-of-the-art single cell sequencing technologies. The implementation of this platform will also lead to new research collaborations as well as further strengthen innovation and technology transfer at VHIO.

I am also pleased to report that in 2022 we received renewed Institució CERCA–Centres de Recerca de Catalunya accreditation. In recognition of our progress, knowledge transfer activities and management of excellence, VHIO was awarded the maximum qualification of an A grading.

In addition to these developments, just some of the many other research highlights, programs, activities, and initiatives that shaped our year can be found in the pages that follow. I invite you to come on in and discover more!

The Last Word

As VHIO's Director, I am privileged to lead and work with our many research talents and dedicated healthcare professionals in oncology. Our multidisciplinary, preclinical, translational and clinical teams, also In collaboration with many other investigators and partners across the globe, work together to improve outcomes for cancer patients.

Our intense desire to reduce the devastating burden that this disease has on society is also shared by our amazing Institutional Supporters and Patrons – Generalitat de Catalunya, Fundació Privada CELLEX, Fundación FERO, "la Caixa" Foundation, and the Fundación BBVA (pages 17-21), as well as the Excelencia Severo Ochoa (page 129) and the AECC Excellence (page 38) programs, in addition to VHIO's many other supporters, funding entities, agencies, and individuals (pages 182-184).

Illustrated by the many research highlights and developments chaptered in the pages that follow, we continue to drive important advances against cancer and do so through team science of excellence at national and international level.

Spurred by the planned expansion of our research programs, groups, and facilities, I believe that we will report bigger success in more effectively targeting and defeating this disease through 2023 and beyond.

We can, and will, do even better.

References

1. Maus M, López-Polo V, Lafarga M, Aguilera M, De Lama E, Meyer K, Manonelles A, Sola A, Lopez Martinez C, López-Alonso I, Hernandez-Gonzales F, Chaib S, Rovira M, Sanchez M, Faner R, Agusti A, Prats N, Albaiceta G, Cruzado JM, Serrano M. Iron accumulation drives fibrosis, senescence and the senescence associated secretory phenotype. *bioRxiv* 2022.07.29.501953; doi: https://doi.org/10.1101/2022.07.29.501953.

2. Iurlaro R, Waldhauer I, Planas-Rigol E, Bonfill-Teixidor E, Arias A, Nicolini V, Freimoser-Grundschober A, Cuartas I, Martínez-Moreno A, Martínez-Ricarte F, Cordero E, Cicuendez M, Casalino S, Guardia-Reyes X, Fahrni L, Pöschinger T, Steinhart V, Richard M, Briner S, Mueller J, Osl F, Sam J, Colombetti S, Bacac M, Klein C, Pineda E, Reyes-Figueroa L, Di Somma A, González J, Nuciforo P, Carles J, Vieito M, Tabernero J, Umaña P, Seoane J. A Novel EGFRvIII T-Cell Bispecific Antibody for the Treatment of Glioblastoma. *Mol Cancer Ther*. 2022 Oct 7;21(10):1499-1509.

3. Massó-Vallés D, Beaulieu ME, Jauset T, Giuntini F, Zacarías-Fluck MF, Foradada L, Martínez-Martín S, Serrano E, Martín-Fernández G, Casacuberta-Serra S, Castillo Cano V, Kaur J, López-Estévez S, Morcillo MÁ, Alzrigat M, Mahmoud L, Luque-García A, Escorihuela M, Guzman M, Arribas J, Serra V, Larsson LG, Whitfield JR, Soucek L. MYC Inhibition Halts Metastatic Breast Cancer Progression by Blocking Growth, Invasion, and Seeding. *Cancer Res Commun*. 2022 Feb 21;2(2):110-130.

4. Borazanci E, Schram AM, Garralda E, Brana I, Vieito Villar M, Spreafico A, Oliva M, Lakhani NJ, Hoffman K, Hallett RM, Maetzel D, Hua F, Hilbert J, Giblin P, Anido J, Kelly A, Vickers PJ, Wasserman R, Seoane J, Siu LL, Hyman DM, Hoff DV, Tabernero J. Phase I, first-in-human study of MSC-1 (AZD0171), a humanized anti-leukemia inhibitory factor monoclonal antibody, for advanced solid tumors. *ESMO Open*. 2022 Aug;7(4):100530.

5. Kindler HL, Hammel P, Reni M, Van Cutsem E, Macarulla T, Hall MJ, Park JO, Hochhauser D, Arnold D, Oh DY, Reinacher-Schick A, Tortora G, Algül H, O'Reilly EM, Bordia S, McGuinness D, Cui K, Locker GY, Golan T. Overall Survival Results From the POLO Trial: A Phase III Study of Active Maintenance Olaparib Versus Placebo for Germline BRCA-Mutated Metastatic Pancreatic Cancer. *J Clin Oncol*. 2022 Dec 1;40(34):3929-3939.

6. Fizazi K, Foulon S, Carles J, Roubaud G, McDermott R, Fléchon A, Tombal B, Supiot S, Berthold D, Ronchin P, Kacso G, Gravis G, Calabro F, Berdah JF, Hasbini A, Silva M, Thiery-Vuillemin A, Latorzeff I, Mourey L, Laguerre B, Abadie-Lacourtoisie S, Martin E, El Kouri C, Escande A, Rosello A, Magne N, Schlurmann F, Priou F, Chand-Fouche ME, Freixa SV, Jamaluddin M, Rieger I, Bossi A; PEACE-1 investigators. Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2×2 factorial design. *Lancet*. 2022 Apr 30;399(10336):1695-1707.

7. Zapatero A, Guerrero A, Maldonado X, Álvarez A, San-Segundo CG, Rodríguez MÁC, Solé JM, Olivé AP, Casas F, Boladeras A, de Vidales CM, de la Torre MLV, Vara S, Sanz JL, Calvo FA. High-dose radiotherapy and risk-adapted androgen deprivation in localised prostate cancer (DART 01/05): 10-year results of a phase 3 randomised, controlled trial. *Lancet Oncol*. 2022 May;23(5):671-681.

8. Verdaguer H, Saurí T, Acosta DA, Guardiola M, Sierra A, Hernando J, Nuciforo P, Miquel JM, Molero C, Peiró S, Serra-Camprubí Q, Villacampa G, Aguilar S, Vivancos A, Tabernero J, Dienstmann R, Macarulla T. ESMO Scale for Clinical Actionability of Molecular Targets Driving Targeted Treatment in Patients with Cholangiocarcinoma. *Clin Cancer Res*. 2022 Apr 14;28(8):1662-1671.

9. Mateo J, Steuten L, Aftimos P, André F, Davies M, Garralda E, Geissler J, Husereau D, Martinez-Lopez I, Normanno N, Reis-Filho JS, Stefani S, Thomas DM, Westphalen CB, Voest E. Delivering precision oncology to patients with cancer. *Nat Med*. 2022 Apr;28(4):658-665.

10. Tamborero D, Dienstmann R, Rachid MH, Boekel J, Lopez-Fernandez A, Jonsson M, Razzak A, Braña I, De Petris L, Yachnin J, Baird RD, Loriot Y, Massard C, Martin-Romano P, Opdam F, Schlenk RF, Vernieri C, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium; Balmaña J, Apolone G, Caldas C, Bergh J, Ernberg I, Fröhling S, Garralda E, Karlsson C, Tabernero J, Voest E, Rodon J, Lehtiö J. The Molecular Tumor Board Portal supports clinical decisions and automated reporting for precision oncology. *Nat Cancer*. 2022 Feb;3(2):251-261.

11. Boix O, Martinez M, Vidal S, Giménez-Alejandre M, Palenzuela L, Lorenzo-Sanz L, Quevedo L, Moscoso O, Ruiz-Orera J, Ximénez-Embún P, Ciriaco N, Nuciforo P, Stephan-Otto Attolini C, Albà MM, Muñoz J, Tian TV, Varela I, Vivancos A, Ramón Y Cajal S, Muñoz P, Rivas C, Abad M. pTINCR microprotein promotes epithelial differentiation and suppresses tumor growth through CDC42 SUMOylation and activation. *Nat Commun*. 2022 Nov 11;13(1):6840.

12. Elez E, Ros J, Fernández J, Villacampa G, Moreno-Cárdenas AB, Arenillas C, Bernatowicz K, Comas R, Li S, Kodack DP, Fasani R, Garcia A, Gonzalo-Ruiz J, Piris-Gimenez A, Nuciforo P, Kerr G, Intini R, Montagna A, Germani MM, Randon G, Vivancos A, Smits R, Graus D, Perez-Lopez R, Cremolini C, Lonardi S, Pietrantonio F, Dienstmann R, Tabernero J, Toledo RA. RNF43 mutations predict response to anti-BRAF/EGFR combinatory therapies in BRAFV600E metastatic colorectal cancer. *Nat Med*. 2022 Oct;28(10):2162-2170.

13. Zurita AJ, Graf RP, Villacampa G, Raskina K, Sokol E, Jin D, Antonarakis ES, Li G, Huang RSP, Casanova-Salas I, Vivancos A, Carles J, Ross JS, Schrock AB, Oxnard GR, Mateo J. Genomic Biomarkers and Genome-Wide Loss-of-Heterozygosity Scores in Metastatic Prostate Cancer Following Progression on Androgen-Targeting Therapies. *JCO Precis Oncol*. 2022 Jul;6:e2200195.

14. Palomero J, Panisello C, Lozano-Rabella M, Tirtakasuma R, Díaz-Gómez J, Grases D, Pasamar H, Arregui L, Dorca Duch E, Guerra Fernández E, Vivancos A, de Andrea CE, Melero I, Ponce J, Vidal A, Piulats JM, Matias-Guiu X, Gros A. Biomarkers of tumor-reactive CD4+ and CD8+ TILs associate with improved prognosis in endometrial cancer. *J Immunother Cancer*. 2022 Dec;10(12):e005443.

15. Forde PM, Spicer J, Lu S, Provencio M, Mitsudomi T, Awad MM, Felip E, Broderick SR, Brahmer JR, Swanson SJ, Kerr K, Wang C, Ciuleanu TE, Saylors GB, Tanaka F, Ito H, Chen KN, Liberman M, Vokes EE, Taube JM, Dorange C, Cai J, Fiore J, Jarkowski A, Balli D, Sausen M, Pandya D, Calvet CY, Girard N; CheckMate 816 Investigators. Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. *N Engl J Med*. 2022 May 26;386(21):1973-1985.

16. Tewari KS, Monk BJ, Vergote I, Miller A, de Melo AC, Kim HS, Kim YM, Lisyanskaya A, Samouëlian V, Lorusso D, Damian F, Chang CL, Gotovkin EA, Takahashi S, Ramone D, Pikiel J, Mańkowiak-Matejczyk B, Guerra Alía EM, Colombo N, Makarova Y, Rischin D, Lheureux S, Hasegawa K, Fujiwara K, Li J, Jamil S, Jankovic V, Chen CI, Seebach F, Weinreich DM, Yancopoulos GD, Lowy I, Mathias M, Fury MG, Oaknin A; Investigators for GOG Protocol 3016 and ENGOT Protocol En-Cx9. Survival with Cemiplimab in Recurrent Cervical Cancer. *N Engl J Med*. 2022 Feb 10;386(6):544-555.

17. Duro-Sánchez S, Nadal-Serrano M, Lalinde-Gutiérrez M, Arenas EJ, Bernadó Morales C, Morancho B, Escorihuela M, Pérez-Ramos S, Escrivá-de-Romaní S, Gandullo-Sánchez L, Pandiella A, Esteve-Codina A, Rodilla V, Dijcks FA, Dokter WHA, Cortés J, Saura C, Arribas J. Therapy-Induced Senescence Enhances the Efficacy of HER2-Targeted Antibody-Drug Conjugates in Breast Cancer. *Cancer Res*. 2022 Dec 16;82(24):4670-4679.

18. Modi S, Jacot W, Yamashita T, Sohn J, Vidal M, Tokunaga E, Tsurutani J, Ueno NT, Prat A, Chae YS, Lee KS, Niikura N, Park YH, Xu B, Wang X, Gil-Gil M, Li W, Pierga JY, Im SA, Moore HCF, Rugo HS, Yerushalmi R, Zagouri F, Gombos A, Kim SB, Liu Q, Luo T, Saura C, Schmid P, Sun T, Gambhire D, Yung L, Wang Y, Singh J, Vitazka P, Meinhardt G, Harbeck N, Cameron DA; DESTINY-Breast04 Trial Investigators. Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer. *N Engl J Med*. 2022 Jul 7;387(1):9-20.

19. Pellegrino B, Herencia-Ropero A, Llop-Guevara A, Pedretti F, Moles-Fernández A, Viaplana C, Villacampa G, Guzmán M, Rodríguez O, Grueso J, Jiménez J, Arenas EJ, Degasperi A, Dias JML, Forment JV, O'Connor MJ, Déas O, Cairo S, Zhou Y, Musolino A, Caldas C, Nik-Zainal S, Clarke RB, Nuciforo P, Díez O, Serres-Créixams X, Peg V, Espinosa-Bravo M, Macarulla T, Oaknin A, Mateo J, Arribas J, Dienstmann R, Bellet M, Oliveira M, Saura C, Gutiérrez-Enríquez S, Balmaña J, Serra V. Preclinical In Vivo Validation of the RAD51 Test for Identification of Homologous Recombination-Deficient Tumors and Patient Stratification. *Cancer Res*. 2022 Apr 15;82(8):1646-1657.

20. Strand SH, Rivero-Gutiérrez B, Houlahan KE, Seoane JA, King LM, Risom T, Simpson LA, Vennam S, Khan A, Cisneros L, Hardman T, Harmon B, Couch F, Gallagher K, Kilgore M, Wei S, DeMichele A, King T, McAuliffe PF, Nangia J, Lee J, Tseng J, Storniolo AM, Thompson AM, Gupta GP, Burns R, Veis DJ, DeSchryver K, Zhu C, Matusiak M, Wang J, Zhu SX, Tappenden J, Ding DY, Zhang D, Luo J, Jiang S, Varma S, Anderson L, Straub C, Srivastava S, Curtis C, Tibshirani R, Angelo RM, Hall A, Owzar K, Polyak K, Maley C, Marks JR, Colditz GA, Hwang ES, West RB. Molecular classification and biomarkers of clinical outcome in breast ductal carcinoma in situ: Analysis of TBCRC 038 and RAHBT cohorts. *Cancer Cell*. 2022 Dec 12;40(12):1521-1536.e7.

21. Abrisqueta P, Medina D, Villacampa G, Lu J, Alcoceba M, Carabia J, Boix J, Tazón-Vega B, Iacoboni G, Bobillo S, Marín-Niebla A, González M, Zenz T, Crespo M, Bosch F. A gene expression assay based on chronic lymphocytic leukemia activation in the microenvironment to predict progression. *Blood Adv*. 2022 Nov 8;6(21):5763-5773.

22. Vivancos A, Tabernero J. Circulating tumor DNA as a novel prognostic indicator. *Nat Med*. 2022 Nov;28(11):2255-2256.

23. Jee J, Lebow ES, Yeh R, Das JP, Namakydoust A, Paik PK, Chaft JE, Jayakumaran G, Rose Brannon A, Benayed R, Zehir A, Donoghue M, Schultz N, Chakravarty D, Kundra R, Madupuri R, Murciano-Goroff YR, Tu HY, Xu CR, Martinez A, Wilhelm C, Galle J, Daly B, Yu HA, Offin M, Hellmann MD, Lito P, Arbour KC, Zauderer MG, Kris MG, Ng KK, Eng J, Preeshagul I, Victoria Lai W, Fiore JJ, Iqbal A, Molena D, Rocco G, Park BJ, Lim LP, Li M, Tong-Li C, De Silva M, Chan DL, Diakos CI, Itchins M, Clarke S, Pavlakis N, Lee A, Rekhtman N, Chang J, Travis WD, Riely GJ, Solit DB, Gonen M, Rusch VW, Rimner A, Gomez D, Drilon A, Scher HI, Shah SP, Berger MF, Arcila ME, Ladanyi M, Levine RL, Shen R, Razavi P, Reis-Filho JS, Jones DR, Rudin CM, Isbell JM, Li BT. Overall survival with circulating tumor DNA-guided therapy in advanced non-small-cell lung cancer. *Nat Med*. 2022 Nov;28(11):2353-2363.

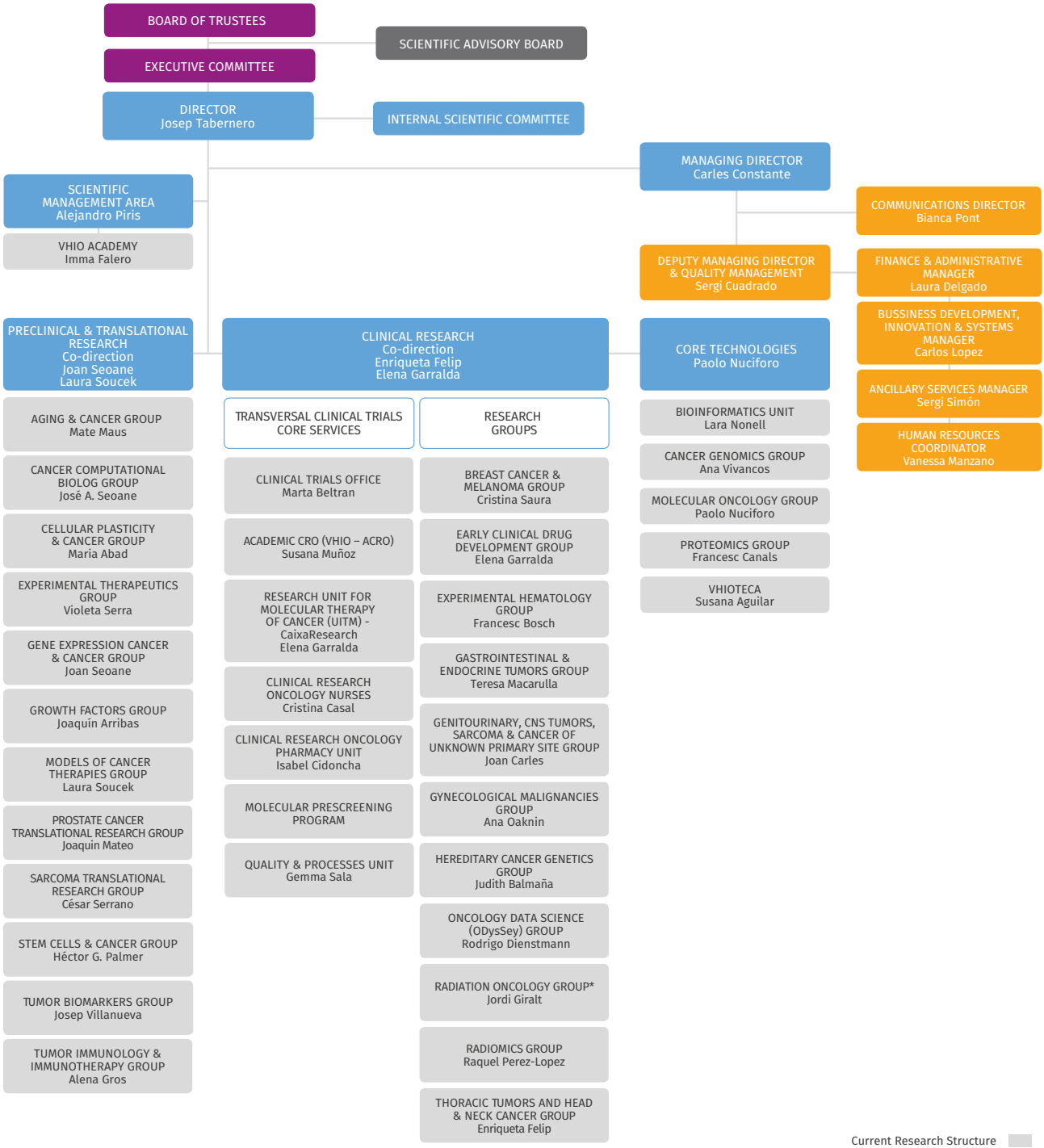
24. Drafting a Blueprint for European Cancer Research. *Cancer Discov*. 2022 Nov 2;12(11):OF1.

Who we are and what we do

VHIO's Organigram 2022

In order to translate cancer discovery into real benefits for an increasing number of our patients, we adopt a purely translational, multidisciplinary research model. Organized into three main programs – Preclinical & Translational, Clinical, and Core Technologies, our research focuses on achieving a deeper understanding of the fundamental biology of human cancer, from cellular and molecular biology and genetics through to therapeutics.

Our optimal organizational structure enables VHIO's research talents to anticipate and tackle the many unresolved questions that currently hamper efforts aimed at solving cancer sooner.



VHIO in 2022: Advancing cancer care through transformative team science

Josep Tabernero, VHIO's Director and Head of the Medical Oncology Department, Vall d'Hebron University Hospital – HUVH (Vall d'Hebron Barcelona Hospital Campus).

Under the leadership of Josep Tabernero, the Vall d'Hebron Institute of Oncology (VHIO) has established itself as a comprehensive cancer center of proven excellence internationally and continues to grow from strength to strength. It is thanks to VHIO's optimal organizational structure and multidisciplinary, translational research model that we continue to anticipate and tackle the many challenges posed by this multifaceted, heterogeneous and hugely complex disease.

This transformative approach was pioneered by José Baselga, our Institute's founder and first director, who very sadly passed away from Creutzfeldt-Jakob disease (CJD), a rapidly progressing, neurodegenerative disease, at the age of 61 on 21 March, 2021.

From the outset, José had one guiding principle for VHIO. Namely, to seamlessly bridge preclinical and clinical research in order to foster a continuous virtuous cycle of knowledge from bench to bedside and back. This translational approach continues to be at the very core of VHIO's philosophy and is passionately pursued by our multidisciplinary teams and research talents.

In honor of José Baselga's incredible legacy, we collectively strive to apply the same dedication and fight in beating cancer, each and every day.

Without the generous support we receive from our Institutional Supporters, public funding, private institutions, companies, and individuals, as well as through International and National Competitive Grants, our Institute would simply cease to exist.

We are also truly grateful for the tremendous backing that we continue to receive from our dedicated patrons: the Generalitat de Catalunya, Fundació Privada CELLEX, Fundación FERO, "la Caixa" Foundation, and the Fundación BBVA.

Just some of their many contributions include the following:

Generalitat de Catalunya

Our public Patron, the Generalitat de Catalunya (Government of Catalonia) – together with the Vall d'Hebron University Hospital (HUVH) – represented by its Departament de Salut (Department of Health), and Departament de Empresa i Coneixement (Department of Industry and Knowledge), has from the very outset been a dedicated supporter of VHIO's cancer science and medicine.

As a devoted ambassador of VHIO and our various research programs and projects, it has been institutionally and financially supporting us from the very start, with the Catalan Minister of Health as the President of our Board of Trustees.

VHIO's translational and multidisciplinary approach to cancer research is greatly facilitated through the connectivity and tremendous collaboration we have with the entire spectrum of oncology professionals at the Vall d'Hebron University Hospital (HUVH), the Vall d'Hebron Barcelona Hospital Campus, and the rest of the Catalan Public Health System.

The Departament de Salut has played an essential role in integrating VHIO's research activity into the Catalan Health System, through the Institut Català de la Salut – ICS

(Catalan Institute of Health), representing a successful example of how the public and private sectors can work closely together for the benefit of science, patients and society.

As an active member of the Institució CERCA–Centres de Recerca de Catalunya (CERCA Institute of Research Centers of Catalonia), this collaboration affords us access to the Catalan Research System and the fiscal and legal benefits that this represents. The financial support it has provided has consequently contributed majorly to VHIO's structural overheads, allowing us to center our efforts on our core research activities. Additionally, our groups also receive funding from various calls promoted and supported by the Generalitat de Catalunya.

In 2022, the recipients of the ICS Research Awards (page 34) included Enriqueta Felip, co-Director of VHIO's Clinical Research Program and Principal Investigator of our Thoracic Tumors & Head and Neck Cancer Group, and Raquel Perez-Lopez, Principal Investigator of our Radiomics Group.

Enriqueta Felip received the ICS Research Career Prize. This recognition honors investigators at hospitals belonging to ICS who have made exceptional contributions to biomedicine. Raquel Perez-Lopez received this year's ICS Young Investigator Prize for her research focused on the application of imaging biomarkers in radiomics for the detection of cancer and the development of precision imaging techniques toward improving patient outcomes.

Fundació Privada CELLEX

It is thanks to one of our private patrons, the Fundació Privada CELLEX (CELLEX Private Foundation), that we have been able to build new facilities that have subsequently spurred our efforts aimed at advancing precision oncology and providing optimal patient treatment and care.

As a first example, it is thanks to this Foundation that the Vall d'Hebron University Hospital's Oncology Department's Oncology Day Hospital and Outpatients Facility opened its adjoining doors in 2008, with a subsequent and final phase of reforms in 2012. This carefully planned expansion and integration of various units and services, resulted in uniting all specialties and disciplines involved in the treatment and care of our patients in the same place and in so doing, helps to spur purely translational and multidisciplinary research for which VHIO is famed.

The CELLEX CENTER: the home and hub of translational & transformative research at VHIO.

The Fundació Privada CELLEX also financed the construction and infrastructures of our state-of-the-art building – the CELLEX CENTER – that was completed back in 2015. Marking a new chapter at VHIO, our then new premises provided the necessary space and amenities for us to expand our research activities and further foster our multidisciplinary connectivity and exchange by bringing all VHIO research teams together under the same roof.

Providing our teams with the valuable space through which to grow, the CELLEX CENTER has not only enhanced collaborations and accelerated our dedicated efforts to combat

cancer, it has also allowed us to strengthen our teams, pursue and develop new emerging research areas, and strengthen our research structure.

As importantly, thanks to this Foundation, our cutting-edge Animal Facility that we share with other colleagues across the Vall d'Hebron Barcelona Hospital Campus, enables our investigators to further develop and finely-tune our predictive cancer models. Incorporating the latest platforms and technologies, this facility has helped to establish VHIO as a reference in preclinical cancer modelling.

Fundació Privada CELLEX's continued support of our building and infrastructures enables our teams to work together in close connectivity to drive scientific advances in cancer discovery and precision oncology.

Support received from the Fundación FERO (FERO Foundation), has from the very outset promoted science of excellence at VHIO and supported the careers of up-and-coming talents in oncology through its annual research grants and fellowships.

As examples, Josep Villanueva, PI of our Tumor Biomarkers Group, Laura Soucek, PI of VHIO's Mouse Models of Cancer Therapies Group and ICREA Research Professor, Violeta Serra, PI of VHIO's Experimental Therapeutics Group, Joaquín Arribas, PI of our Growth Factors Group, also an ICREA Research Professor, Sandra Peiró, formerly a PI of VHIO's previous Chromatin Dynamics Group, and César Serrano, PI of our Sarcoma and Translational Research Group, have all been able to grow their labs, groups and advance their pioneering research lines thanks to FERO.

FERO has also contributed to the expansion of our facilities. As an example, this Foundation was a sponsor of our Breast Cancer Center *Endavant i de Cara*, along with a personal donation received from Maria Àngels Sanahuja.

One of our three Institutional Programs, FERO's Institutional Advanced Molecular Diagnostics Program (DIAMAV), page 126, catalyzes precision medicine at VHIO by supporting our Molecular Prescreening Program (page 146). Serving as a core VHIO platform, our expert team focuses on the clinical implementation of advanced molecular diagnostics to optimize the selection of therapies for patients being considered for enrolment in clinical trials, as well as continued medical education on emerging cancer biomarkers for precision cancer therapy.

Our investigators perform molecular profiling in over 1,100 patients each year as potential candidates for inclusion in our phase I clinical trials at our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, directed by Elena Garralda (page 138). Patients' suitability for enrolment in a particular clinical study is assessed based on their respective, individual genomic profile and pathologic features.

Regarding FERO's Annual Awards for Translational Research in Oncology, a total of sixteen of our investigators have been prized to date: Laura Soucek (2011), Héctor G. Palmer (2012), Ibrahim Yasir – formerly an investigator of VHIO's Experimental Therapeutics Group directed by Violeta Serra (2013), César Serrano (2015), Beatriz Morancho (2016), María Abad (2017), Alena Gros (2018), Joaquin Mateo, Violeta Serra and Judith Balmaña through the first FERO-ghd funded project (2019), Raquel Perez-Lopez, Cristina Saura and Miriam Sansó – the second annual FERO-ghd award (2020), Nicolás Herranz (2021), and José A. Seoane and Tian Tian (2022).

This year, Tian Tian, Senior Researcher Preclinical Team Leader of our recently established Upper Gastrointestinal Cancer Translational Research Group directed by Teresa Macarulla, received the XXII FERO Award for Translational Research in Oncology, supported by the Fundación Ramón Areces. His two-year project will explore epigenetic features hidden in the plasma of cholangiocarcinoma patients by liquid biopsy.

The IV FERO-ghd Award for Breast Cancer Research, sponsored by the ghd hair styling product company, was presented to José A. Seoane, Principal Investigator of our Cancer Computational Biology Group, for his two-year project focused on the epigenetic differences associated with hormone treatment resistant breast cancer heterogeneity. For more details please see page 35 of this report.

Thanks to the support received from the "la Caixa" Foundation, VHIO's Research Unit for Molecular Therapies of Cancer (UITM) – CaixaResearch (page 138), opened its doors in 2010 to pioneer early drug discovery and clinical studies tailored to the specificities of patients. Research at this Unit has contributed to the development of several targeted therapies including trastuzumab, pertuzumab, cetuximab, panitumumab, ramucirumab, trifluridine/tipiracil, gefitinib, osimertinib, ceritinib, crizotinib, loratinib and everolimus, among others. Current focus also centers on the early drug development of immune-based treatment strategies including new cytokines, bispecific antibodies, intratumoral agents, immunomodulatory checkpoint inhibitors, and combinatorial treatment approaches.

The UITM – CaixaResearch, under the direction of Elena Garralda, co-Director of VHIO's Clinical Research Program and Principal Investigator of our Early Clinical Drug Development Group (page 92), has subsequently established itself as a leading reference in developing novel therapies based on the molecular profile of each tumor and optimizing treatment strategies using combinations of new agents with already existing ones. It also pioneers the design and development of novel, adaptive clinical studies including multi-modular basket studies and umbrella trials. Elena's team is dedicated to studying the efficacy of treatment approaches and anti-cancer medicines by allowing for the 'real time' and necessary adaptation in tune with the rapid pace of cancer discovery - especially in the academic setting.

Our portfolio of early phase clinical studies continues to expand, with 86 new studies opened in 2022. To sustain this continued growth and continue to provide optimal quality care to our patients, in 2022 we increased our treatment room facilities as well as space for the processing of patient samples.

By advancing clinical trial study design, VHIO continues to make important progress in tackling the current challenges in oncology including the globalization of clinical research and the implementation of emerging health technologies in the clinical setting. One major development in this direction, was the launch of the EU-funded, multi-site project, Cancer Core Europe Building Data Rich Clinical Trials - CCE-DART (page 185), which is coordinated by Elena Garralda.

In addition to various grants supporting several VHIO groups and projects, "la Caixa" Foundation also supports one of VHIO's four major Institutional Programs. Our CaixaResearch Advanced Oncology Research Program 2020-2023 (page 127), enables our teams to accelerate the development of novel, more effective anti-cancer medicines, fortify existing research lines as well as initiate new projects to lead frontier research in some of the most relevant and rapidly emerging fields in precision oncology.

Aimed at delivering on the true promise of personalized medicine for an increasing number of patients and within the scope of this program, our teams have performed several clinical trials with patients selected based on molecular alterations: mutations in *AKT1, EGFR, IDH1, ALK, ROS1, BRAF, NRAS, KRAS, FGFR1* and *2, MET, HER2, HER3, RET; ATM; BRCA*, amplifications in *HER2, AKT 1, 2,* and *3, FGFR1, MET, NOTCH1-4,* rearrangements of *NTRK1-3 ROS1, ALK, BRAF, RSPO2/3, RET, NRG* and *FGFR1-3*.

2022 marked the launch of a new platform: The UNIQUE - UNderstanding cancer through sIngle cell sequencing (page 23). Also supported by the "la Caixa" Foundation, this initiative represents a valuable tool that will help us to generate insights into complex biological processes (including intra- and inter-tumor heterogeneity), through state-of-the-art single cell sequencing technologies. The implementation of this platform will also lead to new research collaborations as well as further strengthen innovation and technology transfer at VHIO.

It is also thanks to the "la Caixa" Foundation that VHIO's Clinical Research Oncology Pharmacy Unit's (page 144) new home was completed in 2019. Providing the much-needed additional space and equipped with the very latest technologies, the Molecular Therapy of Cancer (UITM) – CaixaResearch Clinical Research Onco-Hematology Unit enables Isabel Cidoncha's team to provide even higher quality pharmaceutical care and services, as well as continue to meet all the regulatory requirements.

Two new VHIO projects received funding from the "la Caixa" Foundation in 2022. Francesco Grussu, a Postdoctoral Fellow of our Radiomics Group, received a Junior

Group Leader Grant for his project, *New-generation oncological MRI (New-OncoMRI): development, validation and application*, under the mentorship of Raquel-Perez Lopez.

Under the scope of the "la Caixa" Predoctoral InPhinit Retaining program, Cayetano Galera, a Graduate Student of VHIO's Gene Expression and Cancer group, received funding to study the molecular mechanisms underlying the tumor microenvironment in bone metastasis to identify novel therapeutic targets, to be mentored by Joan Seoane.

Finally, through our VHIO – CaixaResearch Scientific Seminars Series (page 31-33) we continue to welcome internationally renowned researchers and clinical investigators to VHIO to share, discuss and debate latest insights, discovery and next directions in oncology with our students, postdocs and senior faculty from our preclinical, translational and clinical research groups. In 2022, a total of 26 seminars took place, some of which took place remotely online due to the COVID-19 pandemic.

Fundación BBVA

Driving programs to spur VHIO's avant-garde translational research in precision oncology, the Fundación BBVA financed our Tumor Biomarkers Research Program back in 2011. This five-year framework agreement supported collaborative science to develop personalized therapies for cancer patients through biomarker research.

Building on the successes of this very first program, our second BBVA-VHIO Institutional Program: Fundación BBVA Comprehensive Program of Cancer Immunotherapy & Immunology – CAIMI (page 128), focuses on developing therapies that inhibit checkpoint regulation of the immune system, advancing insights into mechanisms of resistance and response to immune-based strategies, and prioritizes the early clinical development of the most promising novel therapies. It also supports various research lines across other VHIO groups.

CAIMI counts on the expertise of VHIO's Elena Garralda, co-Director of Clinical Research at VHIO, Principal Investigator of our Early Clinical Drug Development Group, and Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, who heads up the program's clinical research. Alena Gros, Principal Investigator of our Tumor Immunology and Immunotherapy Group, leads CAIMI's translational research. This work is also carried out in collaboration with VHIO's Molecular Prescreening Program (page 146), supported by the Fundación FERO's Advanced Molecular Diagnostics Program – DIAMAV.

Main objectives of CAIMI include achieving a deeper understanding of naturally occurring T-cell response to cancer and establishing novel ways to exploit these anti-cancer responses to develop more effective, powerful, and personalized immune-based strategies against several tumor types. In 2022 this program continued to expand with various translational projects linked to the early clinical development phases of immunotherapy underway.

Just some research areas include the characterization of hyperprogressive disease with immunotherapy to advance insights into this phenomenon, led by Elena Garralda, and the validation of a radiomic signature to predict response to immunotherapy and the correlation of the results with the genomic evolution observed in patients. This work is carried out in collaboration with Raquel Perez-Lopez, Principal Investigator of our Radiomics Group (page 108).

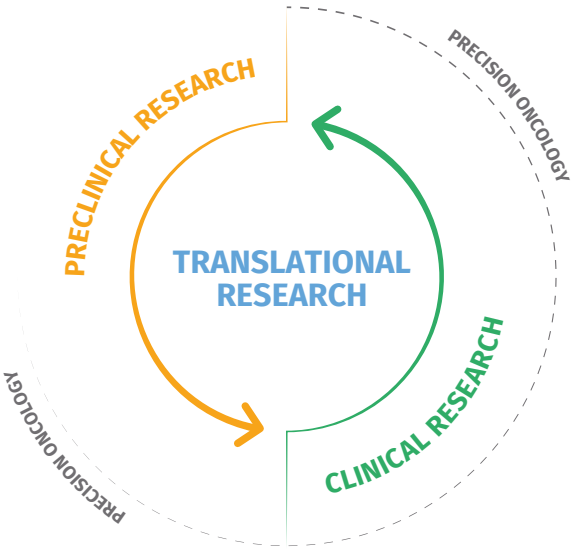
Importantly, also thanks to the funding received through CAIMI, Elena Garralda's team and Alena Gros' group worked together to finalize the clinical grade validations of tumor-infiltrating lymphocytes (TILs) expansion for the treatment of different tumor types at the Vall d'Hebron University Hospital (HUVH). This work was carried out in collaboration with the Banc de Sang i Teixits - BST (Blood and Tissue Bank), a public agency of the Catalan Department of Health.

The NEXTGEN-TIL phase I trial at our Institute is now recruiting patients to assess the safety and tolerability of neoantigen-selected TIL therapy in advanced epithelial tumors and solid tumors, in patients with metastatic or unresectable epithelial tumors and immune checkpoint blockade resistant solid tumors.

A little more on how we did it in 2022

Located within the Vall d'Hebron Barcelona Hospital Campus, our researchers and clinical investigators work together as multidisciplinary teams. Also carried out in collaboration with physician-scientists and other professionals as well as disciplines in oncology at our Vall d'Hebron University Hospital – HUVH (page 25), our preclinical, translational, and clinical research investigators advance cancer care through transformative team science.

This privileged environment affords VHIO direct access to patients as well as the entire spectrum of oncology professionals who care for them, and a second-to-none appreciation of how cancer science can translate into more powerful, targeted treatments to improve patient outcomes. We also firmly believe in combining strengths through cross-border collaborations and national and international consortia of excellence (pages 185-199). These partnerships continue to further spur advances against cancer drug resistance, disease progression and recurrence.



VHIO's multidisciplinary and translational model: the seamless, unrestricted flow of discovery in oncology.

Preclinical Research

From the preclinical side, results from the laboratory are rapidly applied to patients.

Translational Research

Translational research is the fastest route to offering effective alternative treatments to patients. This type of research is only possible thanks to the coexistence of researchers from two distinct areas: clinical research, closely involved with the patients and their treatments; and basic research, carried out in laboratories.

Clinical Research

From the clinical side, samples from patients are analyzed and studied in the laboratory.

Main focus areas of research at VHIO:

- Precision oncology.
- Development of sophisticated preclinical humanized models.
- Mechanisms/signatures of sensitivity, primary and secondary resistance to oncology treatments.
- Big data (molecular, clinical, RWD). of sensitivity, and primary and acquired resistance.
- Early drug development/clinical trials with innovative agents.
- Immune therapeutics (including cell therapies), radiomics, microbiome, machine learning-AI, single-cell sequencing studies, cell dormancy, senescence, computational biology, etc.

Advancing cancer care through transformative team science

The Fundació Privada CELLEX, one of VHIO's Patrons and Institutional Supporters, financed the construction of our state-of-the-art building – the CELLEX CENTER – that was completed back in 2015. Also supporting our infrastructures, the CELLEX Foundation enables us to advance translational cancer science through our purely multidisciplinary research model and interconnected facilities and platforms.

In 2022, 412 scientific articles were published by VHIO researchers as corresponding, senior or co-authors (pages 156-181). To read about some of these contributions that made headlines this year, please turn to our Director's Foreword, pages 4-13. For a selection of some of the most relevant articles by VHIO researchers published this year please see pages 49-59.

To view each Principal Investigator's Paper Pick 2022 (highlighting a maximum of four selected contributions in 2022), please refer to their corresponding group pages.

The development and application of cutting-edge platforms and empowering technologies in precision oncology

VHIO's Core Technologies Program, led by Paolo Nuciforo, Principal Investigator of our Molecular Oncology Group (page 118), accelerates progress against cancer by

developing and validating novel tumor biomarkers, implementing transformative technologies and advancing the treatment and care of cancer patients through dynamic approaches and novel diagnostic tools.

Our Institute was the first academic test center to incorporate in-house BEAMing liquid biopsy RAS biomarker technology in 2015. As highlighted throughout this scientific report, our multidisciplinary teams - in collaboration with our Cancer Genomics Group (page 116) directed by Ana Vivancos and Paolo Nuciforo's Molecular Oncology Group - continue to make important progress in developing liquid biopsy technologies for the less invasive capturing and tracking of tumor evolution and clinical outcomes during cancer therapy.

In 2022, Ana's lab completed the technology transfer of the U.S. Food and Drug Administration (FDA) approved Guardant360® CDx liquid biopsy test for comprehensive genomic profiling. With this test, VHIO360, our Institute is the first cancer research center in Europe to have a laboratory equipped with this cutting-edge platform. Aimed at overcoming some limitations and challenges of traditional tissue biopsies, this technology provides complete genomic results in solid tumors from a simple blood draw in seven days.

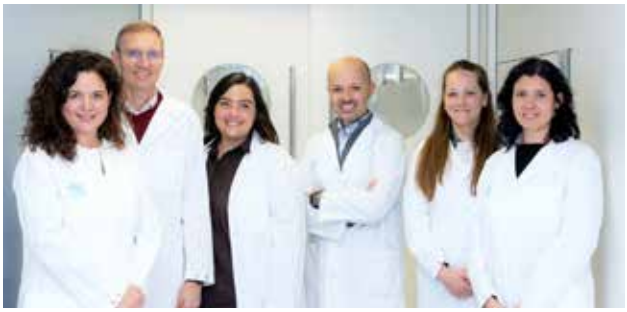
We continue to validate our VIGex immune gene expression signature. Based on our Nanostring and RNA-seq technologies for the detection of an immune signature to help guide patient selection across our phase I clinical trials, this tool has been developed in-house thanks to great teamwork between investigators at our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch directed by Elena Garralda (page 138), and Ana's Group, in collaboration with researchers at the Princess Margaret Cancer Centre in Toronto.

As already highlighted by our Director Josep Tabernero in his Foreword, REVEAL GENOMICS S.L., a spin-off company of the Hospital Clínic de Barcelona, August Pi I Sunyer Biomedical Research Institute (IDIBAPS), University of Barcelona (UB), and VHIO, brought the HER2DX® assay to market. Featuring among *TIME* magazine's listing of Best Inventions of 2022 under the category of Medical Care, this is the first genomic tool for patients with HER2-positive early-stage breast cancer. For more details see page 11.

"la Caixa" Foundation

Announced this year, the UNIQUE - UNderstanding cancer through sIngle cell seQUEncing platform is supported by the "la Caixa" Foundation (page 20). This platform represents a valuable tool that will help us to generate insights into complex biological processes (including intra- and inter-tumor heterogeneity), through state-of-the-art single cell sequencing technologies. The implementation of UNIQUE will also lead to new research collaborations as well as further strengthen innovation and technology transfer at VHIO. See page 27 of this Scientific Report to discover more about this exciting new initiative.

Prescreening at VHIO: driving the clinical implementation of emerging molecular biomarkers in oncology



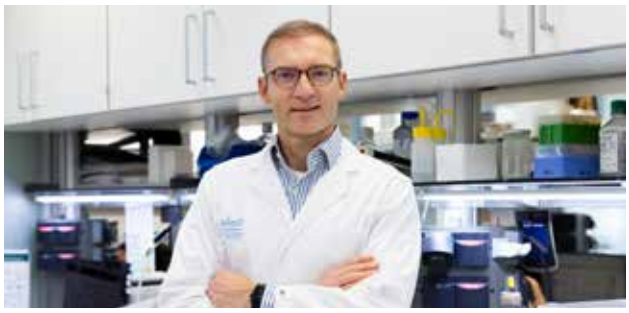
VHIO's Molecular Prescreening team. Left to right: Elena Garralda, Rodrigo Dienstmann, Ana Vivancos, Paolo Nuciforo, Jenifer González and Susana Aguilar.

Thanks to the support received from one of our Institutional Supporters and Patrons, Fundación FERO (page 19), VHIO's Molecular Prescreening Program (page 146) is powered by one of our Institutional Programs, the FERO Foundation Institutional Advanced Molecular Diagnostics Program – DIAMAV (page 126). Over the past decade, this program has provided access to advanced molecular diagnostics to over 1,100 patients each year, establishing our Institute as one of the few centers in Europe to run such a comprehensive program.

These efforts are co-led by Ana Vivancos, Principal Investigator of our Cancer Genomics Group, Elena Garralda, co-Director of Clinical Research at VHIO and Director of our Research Unit for Molecular Therapy of Cancer (UITM) – Caixa Research, Paolo Nuciforo, Principal Investigator of our Molecular Oncology Group, and Rodrigo Dienstmann, Principal Investigator of VHIO's Oncology Data Science (ODysSey) Group. This program is coordinated by Susana Aguilar, Head of VHIO's VHIOTECA (page 122), in collaboration with Jenifer González, a Research Support Technician of our Cancer Genomics Group.

The main objective of molecular prescreening at VHIO is to facilitate the clinical implementation of emerging cancer biomarkers that help to optimize the selection of therapies for patient enrolment in our clinical trials. This program helps to guide clinicians in selecting both standard-of-care and investigational anti-cancer therapies, and accelerates clinical-molecular correlative research at our Institute. We also develop and validate diagnostic tests in-house for the cost effective and streamlined identification of tumor molecular alterations of major interest in drug development.

Our cancer researchers and genomicists participate in weekly tumor board meetings with VHIO's medical oncologists to provide guidance on the interpretation of next-generation sequencing results. During these meetings, our teams also discuss new markers for clinical testing in patients eligible for inclusion in matched early phase clinical studies performed at our UITM – CaixaResearch.



Rodrigo Dienstmann, Principal Investigator of VHIO's Oncology Data Science (ODySey) Group, leads VHIO's participation in AACR's Project GENIE.

We continue to extend our efforts to an increasing number of patients through collaborations with many other research institutes and international projects. As an example, VHIO participates in the American Association for Cancer Research (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE). This program catalyzes the sharing of integrated genomic and clinical datasets across multiple cancer centers worldwide.

AACR Project GENIE® brings together twenty participating institutions and two informatics partners. Our Institute is the only partner from Spain. This project serves as a global precision medicine knowledge base of increasing impact to inform clinical decision-making and bring together cancer researchers internationally.

The first set of cancer genomic data aggregated through this project was available to the global oncology community in January 2017. As this Scientific Report goes to print the thirteenth data set, GENIE 13.0-public, was released in January 2023. The registry now contains more than 167,000 sequenced samples from 148,000+ patients, making the AACR Project GENIE registry among the largest fully public cancer genomic data sets released to date.

VHIO was invited to join AACR Project GENIE® in 2018 and our participation is led by Rodrigo Dienstmann, Principal Investigator of our Oncology Data Science (ODysSey) Group (page 104).

VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch: pioneering early clinical drug development and dynamic studies in precision oncology

Led by Elena Garralda (left), the UITM-CaixaResearch is the heart and hub of our early clinical drug development.

Thanks to the support we receive from one of our Institutional Supporters and Patrons, "la Caixa" Foundation (page 20), VHIO continues to establish itself as a leading reference in advancing drug development and targeted therapies against cancer. Established in 2010, our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138), has rapidly become one of the few comprehensive facilities in Europe to translate latest discovery into improved outcomes for patients, as rapidly as possible.

Headed by Elena Garralda, co-Director of VHIO's Clinical Research Program, it has been able to do so through the bridging and close connectivity between health care professionals, VHIO researchers and clinical investigators, and by identifying novel predictive markers of response to anti-cancer therapies and markers of primary resistance (de novo) and secondary treatment.

Research at this Unit is driven by Elena Garralda's Early Clinical Drug Development Group (page 92). Her group focuses on the development of new drugs based on the molecular profile of each tumor as well as the optimization of treatment regimens using combinations of novel agents with those that already exist. These efforts have contributed to the development of several tumor cell targeted agents including trastuzumab, pertuzumab, cetuximab, panitumumab, ramucirumab, trifluridine/tipiracil, gefitinib, osimertinib, ceritinib, crizotinib, loratinib and everolimus, among others. As a result of the clinical studies conducted at our UITM-CaixaResearch, more than 30 anti-cancer agents by either the U.S. Food and Drug Administration (FDA), or the European Medicines Agency (EMA), or both.

Current research also centers on accelerating and advancing immuno-oncology against cancer. Illustrative of these efforts are our studies evaluating various different agents, mostly in combination. Just some of these include atezolizumab, nivolumab, ipilimumab,

and pembrolizumab. This Unit's Task Force in early drug development of immunotherapeutics and cell signaling focuses on second generation immunotherapies including new cytokines, bispecific antibodies, intratumoral agents, combination immunomodulation for checkpoint inhibitors, as well as translational research in immuno-oncology carried out in collaboration with several VHIO groups including Alena Gros' Tumor Immunology & Immunotherapy Group (page 86).

Our portfolio of early phase clinical studies continues to expand. In 2022 we opened 86 new studies. This year, we conducted 239 ongoing phase I clinical trials, 29 of which are Basket studies, as well as 3 phase 0 trials, with a total of 651 patients enrolled. We have treated over 1,400 patients throughout the year, with a median of 400 patients per month. In order to sustain this continued growth and continue to provide optimal quality care to our patients, we have also increased our treatment room facilities as well as space for patient sample processing.

The design and development of next generation adaptive studies in oncology

Our UITM-CaixaResearch facilities, coupled with VHIO's CaixaResearch Advanced Oncology Research Program - 2020-2023 (page 127), enable us to continuously expand our broad range of early phase studies including complex trials such as basket studies. We also lead the design and development of next generation clinical trials in oncology.

Illustrated by the above-mentioned numbers, we are ardently committed to delivering on the true promise of personalized medicine for an increasing number of our patients. In collaboration with our Molecular Prescreening Program (page 146), our teams have performed several clinical trials with patients selected based on the identified molecular alterations. These include mutations in *AKT1, EGFR, IDH1, ALK, ROS1, BRAF, NRAS, KRAS, FGFR1* and *2, MET, HER2, HER3, RET; ATM; BRCA*, amplifications in *HER2, AKT 1, 2, and 3, FGFR1, MET, NOTCH1-4*, rearrangements of *NTRK1-3 ROS1, ALK, BRAF, RSPO2/3, RET, NRG*, and *FGFR1-3*.

Our participation in several ongoing European and international projects include the Cancer Core Europe (CCE)-developed Basket of Baskets (BoB) investigator-initiated adaptive trial, and the EU-funded Cancer Core Europe Consortium – Building Data Rich Clinical Trials - CCE-DART (page 185). These projects facilitate the optimization of biomarker-drug co-development to more precisely match tailored therapies to each disease setting, each individual patient. These 'smarter' study designs seek to more effectively identify the optimal treatment for the right patient, at the right time. They also promise to overcome the rigidity and limitations associated with more traditional clinical trial designs.

Alongside several other investigators at VHIO and in partnership with other CCE members and participating research centers of excellence, both of these studies are led by Elena Garralda.

VHIO's Clinical Trials Office directed by Marta Beltran (page 134), is also located in the patient environment of the Vall d'Hebron University Hospital (HUVH). Her team coordinates our phase I and Basket studies as well as a large portfolio of phase II & III clinical trials.

In oncology and hematology, our Clinical Trials Office managed a total of 3 phase 0 trials, 262 phase I trials, 33 basket studies, 186 phase II trials, 209 phase III clinical trials, and 1 medical device study in 2022. Patient enrolment across all of these studies totaled at 1,503. Marta's team also managed 2 phase III studies and 1 post-authorization trial in radiotherapy with a total of 10 patients included.

230 new trials were initiated in 2022, including 14 post-authorization trials and rollover studies. In addition, our Clinical Trials Office follows up patients who were recruited in studies prior to 2022 and are still enrolled and receiving study treatment (1,180 patients in total, and 2,087 in follow-up).

In 2022 a total number of 1,328 patients were enrolled across the 542 actively recruiting trials in oncology. In addition, 321 patients were included in a total of 38 post authorization and rollover studies. Across the 152 actively recruiting clinical studies in hematology, a total of 175 patients were included, with an additional 32 patients enrolled in 26 post authorization and rollover trials.

VHIO's direct access to cancer patients: at the center of our purely translational research model

The Vall d'Hebron University Hospital (HUVH): the largest hospital complex in Catalonia and one of the most important in Spain.

VHIO is located within the Vall d'Hebron Barcelona Hospital Campus, which is also home to our Vall d'Hebron University Hospital (HUVH) and two other research institutes of international reference; the Vall d'Hebron Institute of Research (VHIR), and the Multiple Sclerosis Centre of Catalonia (Cemcat). Our hospital affords VHIO

direct access to patients as well as the entire spectrum of oncology professionals who care for them.

Organized into multidisciplinary and integrated teams, our researchers closely collaborate and interact with physician-scientists at Vall d'Hebron. Translational science and clinical research are therefore tightly connected, accelerating the bench-bedside-bed cycle of knowledge.

VHIO's Institutional Programs: driving the development of novel therapies and treatment strategies against cancer

We are indebted to our Patrons and Institutional Supporters: the Generalitat de Catalunya, Fundació Privada CELLEX, Fundación FERO, "la Caixa" Foundation, and the Fundación BBVA (pages 17-21). In addition to their invaluable support, their shared backing and belief in our research and collective fight against cancer, we also advance precision oncology through our four Institutional Programs (three of which are supported by VHIO Patrons):

Our FERO Advanced Molecular Diagnostics Program – DIAMAV (page 126). This program supports molecular prescreening at VHIO and performs molecular profiling in patients to more effectively match personalized treatment strategies based on the genomic or pathologic profile of each individual patient and the molecular makeup of their disease. Our investigators work together to identify specific molecular risk factors to better predict the potential efficacy of specific agents tailored to each particular tumor, advance insights into the more precise and less invasive tracking of disease by liquid biopsy, and develop cancer diagnostics for the early detection of disease.

CaixaResearch Advanced Oncology Research Program (page 127). Building on the successes of the two previous VHIO – "la Caixa" institutional three-year programs, the CaixaResearch program - 2020-2023, enables VHIO teams to accelerate the development of more potent and targeted anti-cancer medicines, strengthen existing research lines as well as initiate new projects to lead frontier research in some of the most relevant and emerging fields in precision oncology; those areas showing particular promise in solving the multiple questions that currently stand in the way of more effectively combating cancer.

Fundación BBVA Comprehensive Program of Cancer Immunotherapy & Immunology – CAIMI (page 128). As a result of the achievements of the very first VHIO – BBVA Foundation Program on Tumor Biomarkers Research, the BBVA Foundation officially launched this second four-year program in 2018 to advance agents that inhibit checkpoint regulation of the immune system, achieve a deeper understanding of mechanisms of resistance and response to these therapies, and prioritize the early development of promising novel therapies in immuno-oncology.

Center of Excellence Severo Ochoa (page 129). VHIO received Excelencia Severo Ochoa accreditation in 2021 and is awarded as a Severo Ochoa Center of Excellence, 2022- 2026. This accolade recognizes national research centers demonstrating scientific leadership of excellence and impact at a global level. This fourth Institutional Program at VHIO further strengthens our various research programs and teams in driving important advances in cancer discovery and precision medicine in oncology.

New in 2022

Announced in December 2022 and set to launch as our fifth Institutional Program, we have received additional institutional support through the Asociación Española Contra el Cáncer – AECC (Spanish Association Against Cancer) Excellence Program - Advanced Therapies Accelerator Program. We aim to establish VHIO as an international reference in the rapidly emerging field of gene and cellular therapies and contribute to the expansion of Europe's product development in this area.

To boost the development of academic gene and cellular therapy products and associated translational research, we plan to construct a Clean Room laboratory, provide our teams with the necessary training, foster and develop national and international collaborations, and establish an optimal program governance structure. These actions will enable us to develop new gene and cellular therapy products and advance existing ones in our pipeline.

We look forward to updating on this exciting new program in next year's Scientific Report.

We also take this opportunity to thank the AECC for its longstanding support of several VHIO groups and researchers. In 2022 three of our investigators were awarded across two of AECC's funding programs.

For further details please see page 38 of this Scientific Report.

"la Caixa" Foundation

UNIQUE - UNderstanding cancer through sIngle cell seQUEncing platform is also supported by the "la Caixa" Foundation (page 20). This project represents a valuable tool that will help us to generate insights into complex biological processes (including intra- and inter-tumor heterogeneity), through state-of-the-art single cell sequencing technologies. UNIQUE will synergize with our existing core technologies, strengthen our capacity for centralized data generation, analysis and storage, and lead to increased scientific productivity and impact of our investigators.

The integration of this platform will provide new opportunities for advancing the clinical management of cancer patients, ultimately consolidate VHIO as a reference hub in single-cell analysis, lead to new research collaborations, as well as further strengthen innovation and technology transfer at VHIO.

Consortia and partnerships of excellence across borders

National and international consortia, partnerships and alliances: empowering collaborative team science.

At VHIO we are dedicated to fostering, developing and (co) leading multi-center collaborations that combine the necessary expertise and resources to accelerate research against cancer. These national and international partnerships enable us to collectively advance cancer care through transformative team science.

We currently (co) lead and participate in thirty-seven national and international consortia of excellence (pages 185-198). Among these, twelve new projects launched in 2022. In addition to the European UNderstand CANcer – UNCAN.eu, featured in our Director's Foreword to this year's Scientific Report (page 12), we take this opportunity to highlight a few more of these important initiatives.

PCM4EU

The PCM4EU – Personalised Cancer Medicine for all EU Citizens is funded by the European Union under the Europe's Beating Cancer Plan by EU4Health. This consortium connects partners from fifteen countries across Europe including VHIO, and aims to facilitate the implementation of molecular cancer diagnostics for precision oncology including clinical studies such as Drug Rediscovery Protocol (DRUP) trials.

Coordinated by Hans Gelderblom, Head of the Department of Medical Oncology at the Leiden University Medical Centre (LUMC) in the Netherlands, PCM4EU is divided into six workpackages (WPs): WP2 focuses on mapping and facilitating use of molecular cancer diagnostics and WP3 centers on precision oncology and promoting more national DRUP-like clinical trials in European countries. WP4 will seek to implement precision oncology and standards for use in diagnostics and molecular tumour boards (MTBs) in European countries. WP5 focuses on facilitating equitable and cross-border access, and WP6 is tasked with identifying training opportunities for the next generation of oncologists.

PCM4EU has also incorporated a patient engagement strategy to ensure access to molecular-based clinical trials and will build a data aggregation platform. Our investigators are participating in WPs 2, 3 and 5.

Funded by the European Union

The PCM4EU project receives funding from the European Union's Horizon Europe and innovation programme HORIZON-HLTH-2021-CARE-05 under grant agreement No. 101057091.

ODELIA

Co-coordinated by Daniel Truhn, an AI Researcher and Radiologist at the Department of Diagnostic and Interventional Radiology, the University Hospital Aachen in Germany, and Jakob N. Kather, Head of the Department of Clinical Artificial Intelligence at the Else Kroener Fresenius Center for Digital Health in Dresden, Germany, the EU-funded ODELIA Open Consortium for Decentralized Medical Artificial Intelligence will develop and implement a pan-European swarm learning (SL) network that enables privacy-preserving and democratic training of medical AI algorithms.

Focused on breast cancer detection in MRI screenings, this five-year project aims to demonstrate the power of SL and its potential application in various clinical

settings. Bringing together experts from twelve academic institutions and industry partners from across Europe, ODELIA aims to serve as a hub for the exponential growth of the SL network and extend this data privacy-preserving framework to a multitude of medical applications. This will provide patients, healthcare providers, and citizens in Europe with a digital infrastructure that facilitates the development of expert-level AI tools for big data analytics without compromising data safety and data privacy.

VHIO's Radiomics and Breast Cancer Groups (pages 108, 90), led by Raquel Perez-Lopez and Cristina Saura respectively, are participating in this project to help develop an SL model for improving breast cancer screening. Our investigators will also provide support for all the logistical and ethical local requirements and provide feedback and technical expertise in the front-end-software development.

Funded by the European Union

The ODELIA project receives funding from the European Union's Horizon Europe and innovation programme HORIZON-HLTH-2021-CARE-05 under grant agreement No. 101057091.

CGI-Clinics
Cancer Genome Interpreter

Coordinated by Núria López-Bigas, an ICREA Research Professor and Group Leader in Biomedical Genomics at IRB Barcelona, the EU-funded CGI-Clinics Cancer Genome Interpreter is a five-year community-driven project that brings together 17 project partners including organizations representing patients, clinicians, and researchers, that aims to improve precision medicine in oncology.

Analysis of a patient's tumor genome offers great possibilities for personalized treatment, but the interpretation of this data is complex, time-consuming and relies on having the right experts at the patient's hospital. CGI-Clinics aims to provide a one-stop shop solution that systematizes tumor genome interpretation to support physicians in choosing the most effective treatment for each patient.

The Cancer Genome Interpreter (CGI), which Núria López-Bigas and colleagues have been developing for over five years, has immense potential in precision oncology. This platform uses machine-learning and other computational methods to systematically extract information from mutations observed in thousands of tumors to improve the interpretation of the variants observed in each patient.

Project partners will aim to optimize this platform for its use in hospitals and healthcare centers to support clinical decision-making by oncologists. CGI-Clinics will build a new CGI and nine hospitals and healthcare research centers from four European countries, including VHIO, will be the first to implement this platform.

This project will also set up virtual molecular tumor boards including international experts with whom medical doctors can consult and discuss the reports produced by the CGI.

A key pillar of this project is the involvement of people with cancer. The Asociación Española Contra el Cáncer (AECC - Spanish Association Against Cancer) and the European Cancer Patient Coalition (ECPC) will represent society and patients.

Funded by the European Union

This project has received funding from the European Union's Horizon program HORIZON-HLTH-2021-CARE-05-02 under grant agreement No.101057509.

To discover more about VHIO's participation in ongoing and newly launched consortia, read about these projects as well as other collaborative partnerships and initiatives, please refer to pages 185-199 of this Scientific Report.

Technology transfer, development of new therapies & technologies in precision oncology

VHIO's spin-off successes

PEPTOMYC

Laura Soucek, co-Director of VHIO's Preclinical and Translational Research Program, Principal Investigator of our Models of Cancer Therapies Group, an ICREA Research Professor, and co-Founder & Chief Executive Officer of VHIO-born spin-off Peptomyc S.L.

Co-founded back in 2014 by Laura Soucek, co-Director of Preclinical and Translational Research at VHIO, the VHIO-born spin-off Peptomyc received approval in 2021 to initiate the first-in-human Phase I/IIa clinical trial with its first Omomyc-derived compound (OMO-103), a disruptive MYC inhibitor.

OMO-103 successfully completed the Phase I part of the study in October 2022. This part of the study, sponsored by Peptomyc, was conducted at three Spanish hospitals including the Vall d'Hebron University Hospital (HUVH), and led by VHIO's Elena Garralda, co-Director of Clinical Research at VHIO, Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch and Principal Investigator of our Early Clinical Drug Development Group.

Building on the proven preclinical efficacy and safety of their Omomyc cell-penetrating mini-protein in mouse models and Peptomyc's development of anti-MYC peptides for the treatment of several tumor types, this development represents a greatly anticipated leap into the clinical research setting and an important step forward in becoming the first ever clinically viable and direct inhibitor of MYC – a protein implicated in the formation of most tumor types.

At the preclinical level, results of a study published this year* reported important advances in evaluating Omomyc for the treatment of metastatic breast cancer.

---

* Massó-Vallés D, Beaulieu ME, Jauset T, Giuntini F, Zacarías-Fluck MF, Foradada L, Martínez-Martín S, Serrano E, MartínFernández G, Casacuberta-Serra S, Castillo Cano V, Kaur J, López-Estévez S, Morcillo MÁ, Alzrigat M, Mahmoud L, LuqueGarcía A, Escorihuela M, Guzman M, Arribas J, Serra V, Larsson LG, Whitfield JR, Soucek L. MYC Inhibition Halts Metastatic Breast Cancer Progression by Blocking Growth, Invasion, and Seeding. *Cancer Res Commun*. 2022 Feb 21;2(2):110-130.

Mosaic Biomedicals

Joan Seoane, co-Director of VHIO's Preclinical and Translational Research Program, Principal Investigator of our Gene Expression & Cancer Group, an ICREA Research Professor, and co-Founder of Mosaic Biomedicals.

VHIO's Joan Seoane and his Gene Expression and Cancer Group previously established the role of LIF in oncogenesis as a promoter of cancer progression by regulating the tumor microenvironment and inducing self-renewal in tumor-initiating cells. This research culminated in the development of MSC-1, a therapeutic LIF neutralizing antibody.

Joan Seoane, co-Director of VHIO's Preclinical and Translational Research Program, co-founded VHIO-born spin-off Mosaic Biomedicals in 2012 for the design and development of this novel compound. In 2016, Mosaic merged with Northern Biologics Inc. (Toronto, Canada), and Northern-Mosaic announced the global acquisition of clinical-stage MSC-1 (now AZD0171) by MedImmune/ AstraZeneca in 2020.

MSC-1's transition to the clinic and translation into benefits for cancer patients promises an important addition to the current arsenal of powerful anti-cancer weaponry. Published this year ahead of print, results of a study* directed by Joan have described this drug's mechanism of action.

Also reported this year**, results of the phase I first-in-human clinical trial of MSC-1 (AZD0171) conducted at our Vall d'Hebron University Hospital, the Memorial Sloan Kettering Cancer Center (MSKCC), New York, and the Princess Margaret Cancer Center in Toronto, show that this novel monoclonal antibody is safe and well tolerated in patients with advanced solid tumors.

This study was co-led by VHIO's Director Josep Tabernero, and co-authored by other VHIO investigators including Joan Seoane and Elena Garralda, Principal Investigator of Early Clinical Drug Development at VHIO, and Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch

A phase II clinical trial of AZD0171 in combination with durvalumab and chemotherapy in solid tumors initiated patient recruitment in 2021 and is now underway.

---

* Hallett R, Bonfill-Teixidor E, Iurlaro R, Arias A, Raman S, Bayliss PE, Egorova O, Neva-Alejo A, McGray AR, Lau E, Bosch A, Beilschmidt M, Maetzel D, Fransson J, Huber-Ruano I, Anido J, Julien JP, Giblin PA, Seoane J. Therapeutic targeting of LIF overcomes macrophage mediated immunosuppression of the local tumor microenvironment. *Clin Cancer Res*. Epub 2022 Nov 28:CCR-21-1888.

** Borazanci E, Schram AM, Garralda E, Brana I, Vieito Villar M, Spreafico A, Oliva M, Lakhani NJ, Hoffman K, Hallett RM, Maetzel D, Hua F, Hilbert J, Giblin P, Anido J, Kelly A, Vickers PJ, Wasserman R, Seoane J, Siu LL, Hyman DM, Hoff DV, Tabernero J. Phase I, first-in-human study of MSC-1 (AZD0171), a humanized anti-leukemia inhibitory factor monoclonal antibody, for advanced solid tumors. *ESMO Open*. 2022 Aug;7(4):100530.

ONIRIA THERAPEUTICS

Héctor G. Palmer, Principal Investigator of VHIO's Stem Cells & Cancer Group, co-Founder and Chief Scientific Officer of ONIRIA Therapeutics.

Created in 2021 and officially launched this year, ONIRIA Therapeutics was co-founded by VHIO, the Universidad de Barcelona (UB),and the ICREA Catalan Institution for Research, and had been mainly funded by the "la Caixa" Foundation (page 20), Asociación Española Contra el Cáncer – AECC (Spanish Association Against Cancer), and the Instituto de Salud Carlos III – ISCIII (Institute of Health Carlos III), prior to its incorporation.

By modulating cell dormancy to overcome cancer persistence, this spin-off is developing new anti-cancer armory to counteract resistance and prevent disease relapse in patients. Among various ongoing projects, ONIRIA's most advanced agent is a first-in-class molecule, ONR-001, that allosterically activates the TET2 master

epigenetic enzyme causing tumor cells to enter a dormant state and even die.

ONIRIA has already secured patent protection for its TET2 modulators and demonstrated efficacy in preclinical animal models by showing that ONR-001 promotes and sustains cancer cell dormancy and even causes cell death upon prolonged treatment with high tolerability in mice. The investigators are now evaluating the efficacy of ONR-001 in several hematologic and solid cancers and its targeting of hypermethylated tumors as a consequence of TET2 loss-of-function.

This project has also been possible thanks to the additional support received from the Agència de Gestió d'Ajuts Universitaris i de Recerca – AGAUR (Agency for Management of University and Research Grants), Fundación FERO (page 19), and the Fundació Privada CELLEX (page 18). Since it was officially established, ONIRIA has also received support from the Torres y Quevedo Program – Ministerio de Ciencia e Innovación (Spanish Ministry of Science and Innovation), and a Start-Up Capital Grant from the Agencia para la Competitividad de la Empresa - ACCIÓ (Catalan Regional Government's Agency for Business Competitiveness).

In addition to these important developments, REVEAL GENOMICS S.L., a spin-off company of the Hospital Clínic de Barcelona, August Pi I Sunyer Biomedical Research Institute (IDIBAPS), University of Barcelona (UB), and VHIO, launched its HER2DX® assay as a new diagnostic tool for early-stage HER2-positive breast cancer. Brought to market this year, HER2DX® featured among *TIME* magazine's listing of Best Inventions of 2022 under the category of Medical Care. To discover more, please see page 11 of our Director's Foreword to this Scientific Report.

Our RAD51 predict test to identify patients who could benefit from treatment with PARP inhibitors is now being used in a prospective clinical trial to predict olaparib sensitivity in patients with metastatic HER2-negative breast cancer. For more details, please see page 10 of the Foreword to this Scientific Report.

We have also completed the technology transfer of the U.S. Food and Drug Administration (FDA) approved Guardant360® CDx liquid biopsy test for comprehensive genomic profiling. With this test, VHIO360, our Institute is the first cancer research center in Europe to have a laboratory equipped with this cutting-edge platform. Aimed at overcoming some limitations and challenges associated with traditional tissue biopsies, this technology provides complete genomic results in solid tumors from a simple blood draw in seven days. More information can be found on page 11.

Based on VHIO's Nanostring and RNA-seq technologies for the detection of an immune signature to help guide patient selection across our phase I clinical trials, VHIO invesgitators continue to validate our VIGex immune gene expression signature – see page 12 to discover more.

VHIO ACADEMY

The VHIO Academy: promoting educational programs, trainings and career development activities.

Launched in 2021 and headed by Imma Falero, the VHIO Academy encompasses all educational programs at our Institute to attract young talent globally and provide state-of-the-art training and career development activities. These learning opportunities aim to equip and empower VHIO fellows to reach their full potential.

Organizing a broad portfolio of complementary courses ranging from scientific to vocational training, the Academy's educational activities further promote professional growth and assist fellows to make informed decisions about their next career steps.

In addition to coordinating the VHIO – CaixaResearch Scientific Seminars (page 31-33), the Academy organized five academic programs, twelve scientific and transferable skills trainings, eleven workshops focused on professional development skills for clinicians, and two Cancer Core Europe – CCE (page 185) educational activities in 2022.

To discover more about our VHIO Academy and highlights this year, please refer to page 154 of this Scientific Report.

GREEN VHIO

Green VHIO in action: 'Greenform' trainings and 'Into the Green' outdoor environmental activities.

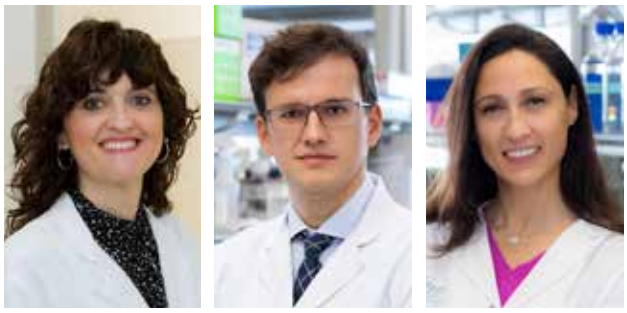
Green VHIO launched in 2021 in support of the European Climate Pact. The Green VHIO team is championed by VHIO's Climate Pact Ambassador Kinga Bernatowicz, a Postdoctoral Fellow of our Radiomics Group, alongside several other VHIO investigators and administrative personnel.

This program seeks to raise awareness about the urgency of climate change as well as the importance of environmental protection in cancer prevention, take action to contribute to the transition to climate neutrality, and report on sustainable research practices.

Green VHIO aims to fulfil these objectives through five dedicated action areas: Greenform (providing information, seminars); Green enVHIOment (creating an even stronger health-conscious environment at VHIO; Green commute (transport-related actions); Green labs (informing on sustainable research practices); and Into the Green (outdoor environmental activities).

VHIO-organized events: the sharing and exchange of latest advances in cancer discovery and precision oncology

VHIO is dedicated to organizing events to present and debate the very latest in cancer discovery – from the bench to bedside and back. These educational opportunities often lead to new research collaborations that continue to accelerate our collective efforts aimed at solving cancer sooner.



Scientific co-Chairs (left to right): Elena Élez, Medical Oncologist and Senior Clinical Investigator of VHIO's Gastrointestinal and Endocrine Tumors Group, Joaquin Mateo, Principal Investigator of our Prostate Cancer Translational Research Group, and Laura Soucek, co-Director of VHIO's Preclinical and Translational Research Program and Principal Investigator of VHIO's Models of Cancer Therapies Group.

Launched back in 2019 and supported by the "la Caixa" Foundation (page 20), our VHIO – CaixaResearch Scientific Seminars Series educational program welcomes internationally renowned researchers and clinical investigators to VHIO to share, discuss and debate latest insights, discovery and next directions in oncology with our students, postdocs and senior faculty from our preclinical, translational and clinical research groups.

These sessions, coordinated by the VHIO Academy (page 154), take place in VHIO's CELLEX CENTER Auditorium, although some were hosted virtually in 2022 due to the COVID-19 pandemic. Chaired by each respective VHIO host, these seminars typically consist of a 30-45 minute talk followed by a Q&A round with the audience.

In 2022, a total of 26 VHIO - CaixaResearch Scientific Seminars took place:

Speaker: Francesco Nicassio, Principal Investigator and Coordinator of the Center of Genomic Science (CGS-IIT@SEMM), Genova, Genomic Science, Italy

Talk title: New insights into miRNA biology and human cancer

Date: 14 January

VHIO Host: Paolo Nuciforo, PI, Molecular Oncology Group

Speaker: Jason Carroll, Professor of Molecular Oncology, University of Cambridge, and Senior Group Leader, Cancer Research UK (CRUK), Cambridge, UK

Talk title: Mechanisms of estrogen receptor transcriptional activity in breast cancer

Date: 28 January

VHIO Host: Violeta Serra, PI, Experimental Therapeutics Group

Speaker: Maria Rescigno, Vice Rector and Delegate for research, and Professor of General Pathology, Humanitas University, Milan, Italy

Talk title: The microbiota in host-immune interactions

Date: 11 February

VHIO Host: Paolo Nuciforo, PI, Molecular Oncology Group

Speaker: Mark J Nieuwenhuijsen, Research Professor and Director of Urban Planning, Environment and Health Initiative, ISGlobal, Barcelona, Spain

Talk title: Urban and transport planning pathways to carbon neutral, liveable and healthy cities

Date: 25 February

VHIO Host: Kinga Bernatowicz, Postdoctoral Fellow, Radiomics Group

Speaker: David Cortéz, Associate Director of Basic Science Research and Co-Leader, Genome Maintenance Research Program, Vanderbilt-Ingram Cancer Center, Vanderbilt University, Nashville, USA

Talk title: Overcoming replication stress: mechanisms and regulation to maintain genome stability

Date: 10 March

VHIO Host: Violeta Serra, PI, Experimental Therapeutics Group

Speaker: Sean Morrison, Director, Children's Medical Center Research Institute, UT Southwestern Medical Center, and Investigator, Howard Hughes Medical Institute (HHMI), Maryland, USA

Talk title: The regulation of melanoma metastasis

Date: 25 March

VHIO Host: María Abad, PI, Cellular Plasticity and Cancer Group

Speaker: Sara Sdelci, Group Leader, Centre for Genomic Regulation (CRG), Barcelona, Spain

Talk title: LOXL2 aids the formation of BRD4S and MED1 transcriptional foci to control cell cycle gene expression in triple-negative breast cancer

Date: 08 April

VHIO Host: Tian Tian, Senior Researcher, Preclinical Team Leader, Gastrointestinal & Endocrine Tumors Group

Speaker: Justin Odegaard, Adjunct Clinical Professor of Pathology, Stanford University, and Vice President of Clinical Development at Guardant Health, California, USA

Talk title: Current and future applications of liquid biopsy

Date: 03 May

VHIO Host: Josep Tabernero, VHIO's Director

Speaker: Carlos Arteaga, Director, Simmons Comprehensive Cancer Center, and Associate Dean of Oncology Programs, UT Southwestern Medical Center, Dallas, USA

Talk title: FGFR Pathway as a Mechanism of Resistance to Endocrine Therapy in Breast Cancer

Date: 16 May

VHIO Host: Josep Tabernero, VHIO's Director

Speaker: Robert Schreiber, Director of the Andrew M. and Jane M. Bursky Center for Human Immunology and Immunotherapy Programs, Washington University School of Medicine in St. Louis (WUSTL), USA

Talk title: Neoantigens as probes and targets of tumor specific immune responses

Date: 26 May

VHIO Host: Ricardo Pujol, Scientific Advisor

Speaker: Ugo Cavallaro, Director of the Program of Gynecological Oncology and Department of Experimental Oncology, European Institute of Oncology (IEO), Milan, Italy

Talk title: Cancer stem cells: shedding light on the dark side of ovarian carcinoma

Date: 27 May

VHIO Host: Paolo Nuciforo, PI, Molecular Oncology Group

Speaker: Oskar Marin, Senior Postdoc in P-CMRC, Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain

Talk title: Drug resistance mechanisms and cancer cell vulnerabilities

Date: 10 June

VHIO Host: María Abad, PI, Cellular Plasticity and Cancer Group

Speaker: I-Mei Siu, Senior Editor, *Cancer Discovery*, Maryland, USA

Talk title: An Introduction to *Cancer Discovery*

Date: 23 June

VHIO Hosts: Javier Carmona, Senior Project Manager, Scientific Management Area, and César Serrano, PI, Sarcoma Translational Research Group

Speaker: Direna Alonso-Curbelo, Junior Group Leader, Inflammation, Tissue Plasticity & Cancer Group, Institute for Research in Biomedicine (IRB), Barcelona, Spain

Talk title: Epigenetic licensing of tumor-promoting inflammation in pancreatic cancer

Date: 05 July

VHIO Host: Tian Tian, Senior Researcher, Preclinical Team Leader, Gastrointestinal & Endocrine Tumors Group

Speaker: Antonio Agudo, Head, Nutrition and Cancer Unit, Cancer Epidemiology Research Program, Institut Català d'Oncologia (ICO), Barcelona, Spain

Talk title: Does population health mean planetary health? Sustainable diet and cancer prevention

Date: 22 July

VHIO Host: Kinga Bernatowicz, Postdoctoral Fellow, Radiomics Group

Speaker: Laura Fouassier, Researcher, French Institute of Health and Medical Research (INSERM), and Head, Cholangiocarcinoma Research Group, Saint-Antoine Research Center (CRSA), Paris, France

Talk title: Pleotropic functions of EGFR in cholangiocarcinoma

Date: 08 September

VHIO Host: Tian Tian, Senior Researcher, Preclinical Team Leader, Gastrointestinal & Endocrine Tumors Group

Speaker: Francisco Barriga, Cancer Biology & Genetics Program, The Scott Lowe Lab, Memorial Sloan Kettering Cancer Center (MSKCC), Sloan Kettering Institute, New York, USA

Talk title: Dissecting the function of copy number alterations in cancer

Date: 20 September

VHIO Host: Javier Carmona, Senior Project Manager, Scientific Management Area

Speaker: Jose Javier Bravo-Cordero, Associate Professor, Tisch Cancer Institute, Division of Hematology/Medical Oncology, New York, USA

Talk title: High-resolution intravital microscopy reveals the plastic behavior of disseminated dormant cells and their niches

Date: 23 September

VHIO Host: Héctor G. Palmer, PI, Stem Cells and Cancer Group

Speaker: Francisco Martínez-Jiménez, Center for Molecular Medicine and Oncode Institute, University Medical Center Utrecht, Hartwig Medical Foundation – Amsterdam, The Netherlands

Talk title: Understanding tumor evolution and its interplay with the immune system

Date: 04 October

VHIO Host: Javier Carmona, Senior Project Manager, Scientific Management Area

Speaker: Alejo Efeyan, Group Leader, Metabolism and Cell Signaling, Spanish National Cancer Research Center (CNIO), Madrid, Spain

Talk title: The nutrient – Rag GTPase signaling as a driver of cancer and aging

Date: 14 October

VHIO Host: María Abad, PI, Cellular Plasticity and Cancer Group

Speaker: Mate Maus, PI, VHIO's newly established Aging and Cancer Group, Barcelona, Spain

Talk title: From age-associated remodeling of cells and tissues to cancer: exploring the connections between aging and cancer

Date: 24 October

VHIO Host: Javier Carmona, Senior Project Manager, Scientific Management Area

Speaker: Francesca Demichelis, Group Leader, Computational and Functional Oncology Lab Department of Cellular, Computational and Integrative Biology University of Trento (UNITN), Italy

Talk title: Interrogation of multiple analytes in serial liquid biopsy samples to monitor metastatic prostate cancer patient disease state

Date: 11 November

VHIO Host: Joaquín Mateo, PI, Prostate Cancer Translational Research Group

Speaker: Iván Ballesteros, Ramon y Cajal Fellow, Spanish National Centre for Cardiovascular Research (CNIC), Madrid, Spain

Talk title: Functional organization of innate immunity

Date: 14 November

VHIO Host: Alejandro Piris, Chief Scientific Officer, Scientific Management Area

Speaker: Manolis Kogevinas, Severo Ochoa Scientific Director, Barcelona Institute for Global Health (ISGlobal), Barcelona, Spain

Talk title: Sleep, food, light-at-night and cancer: why circadian rhythms matter.

Date: 25 November

VHIO Host: Jonathan R. Whitfield, Senior Investigator, Models of Cancer Therapies Group

Speaker: Lucas Pontel, Josep Carreras Leukemia Research Institute (IJC-Barcelona), PCI Fellow, Biomedicine Institute of Buenos Aires – Partnership of the Max Planck Society (IBioBA-MPSP (Buenos Aires, Argentina) Group Leader

Talk title: Exploiting Metabolic Vulnerabilities in Resilient Tumors

Date: 28 November

VHIO Host: Alejandro Piris, Chief Scientific Officer, Scientific Management Area

Speaker: Bruno Di Stefano, Group Leader, CPRIT Scholar in Cancer Research Assistant Professor in Molecular and Cellular Biology, Stem Cells and Regenerative Medicine Center & Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, USA

Talk title: Defining the Role of RNA Sequestration in Oncogenesis

Date: 15 December

VHIO Host: Tian Tian, Senior Researcher, Preclinical Team Leader, Gastrointestinal & Endocrine Tumors Group

Our Benchstorming Seminars co-Chairs. Left to right: Chiara Bellio, Associate Researcher of VHIO's Tumor Biomarkers Group, Fabio Giutini, PhD Student of our Models of Cancer Therapies Group, and Sara Simonetti, Attending Physician of VHIO's Molecular Oncology Group.

Established in 2016, our annual series of Benchstorming Seminars represent an excellent educational opportunity for junior faculty at VHIO to both present and exchange on and around their respective research interests across VHIO's various research programs.

Not only do our young researchers learn more about their other colleagues and research lines currently underway, they can also express their ideas surrounding a given topic presented at each seminar; the specially crafted informal format favors free thought, flow, and interaction between the speakers and participants.

Reflective of VHIO's purely translational and multidisciplinary research model, our Benchstorming co-Chairs also organize clinical seminars that count on the participation and expertise of our Clinical Investigators and Medical Oncologists.

In 2022, 13 Benchstorming Sessions took place - some of which were organized remotely online due to the COVID-19 pandemic - and each invited VHIO investigator(s) discussed and 'benchstormed' their respective research areas and activities.

Ad-hoc courses, workshops, perceptorships and observerships

Based on specific lines and research areas that continue to position VHIO as a leading international reference, we share our expertise, learn from eminent guest speakers, discuss, and debate our latest findings through the organization of VHIO ad-hoc courses and workshops.

Exchanging latest discovery in cancer science and medicine, 19 courses, workshops, observerships and perceptorships took place in 2022, some of which were organized remotely online due to the COVID-19 pandemic.

Recognitions and prized research in 2022

In addition to all our newly funded research lines and programs in 2022 (pages 201-210) - also driven through the backing received each year from our Institutional Supporters, and public and private national, European, and international funding sources and entities - VHIO investigators and teams have also been recognized through several prizes, honors and accolades, including institutional recognitions.

We take this opportunity to highlight just some of these in 2022:

Reflective of their exceptional contributions to cancer science, VHIO's Josep Tabernero and Enriqueta Felip were recognized once again as Highly Cited Researchers in 2022.

Published in November, Clarivate® revealed its annual list of Highly Cited Researchers 2022. Featuring among the world's elite scientists at academic research institutes and commercial organizations are VHIO's Director Josep Tabernero and Enriqueta Felip, co-Director of Clinical Research at VHIO, and Principal Investigator of our Thoracic Tumors & Head and Neck Cancer Group.

Powered by Web of Science™ data and InCites™ metrics provided by Clarivate, and using both quantitative and qualitative analysis, the list of Highly Cited Researchers 2022 included 6,938 individuals who have demonstrated a significant and broad influence in their field(s) of research across the 22 broad disciplines used by Essential Science Indicators (ESI).

Josep Tabernero, also Head of the Vall d'Hebron University Hospital's (HUVH) Medical Oncology Department, was selected for the seventh consecutive year for significantly advancing cancer research under the category of Clinical Medicine that included total of 466 named leaders in 2022. VHIO's Enriqueta Felip, also Head of the Thoracic Cancer Unit at HUVH and President of the Spanish Society of Medical Oncology (SEOM), was also recognized in this same field for a fifth year running.

Javier Cortés, an Associate Translational Investigator at VHIO, also featured as a Highly Cited Researcher 2022 under the same category for a second year running.

Institut Català de la Salut

21 November 2022: the ICS Research Awards ceremony.

Celebrated during the Institut Català de la Salut (Catalan Health Institute - ICS) 13th Annual Conference on research developments at ICS, the recipients of the 2022 ICS Research Awards included Enriqueta Felip, co-Director of VHO's Clinical Research Program and Principal Investigator of VHIO's Thoracic Tumors & Head and Neck Cancer Group, and Raquel Perez-Lopez, Principal Investigator of our Radiomics Group.

Enriqueta Felip, Head of Vall d'Hebron's Thoracic Cancer Unit and President of the Spanish Society of Medical Oncology (SEOM), and Ferran Barbé, Regional Clinical Director of Chronic Respiratory Diseases at the Arnau de Vilanova University Hospital of Lleida (HUAV), Catalonia, and Director of the CIBERES Biomedical Research Network of Respiratory Diseases in Madrid, were equally awarded as recipients of the ICS Research Career Prize which honors renowned investigators at hospitals belonging to ICS who have made exceptional contributions to biomedicine.

VHIO's Raquel Perez-Lopez received this year's ICS Young Investigator Prize for her research focused on the

application of imaging biomarkers in radiomics for the detection of cancer and the development of precision imaging techniques toward improving patient outcomes.

16 May 2022: XXII Fundación FERO Award Ceremony, Museo Nacional d'Art de Cataluña (MNAC).

One of our Patrons and Institutional Supporters, Fundación FERO (page 19), presided by Sol Daurella, celebrated its Annual Award Ceremony and fundraising gala dinner at the Museo Nacional de Arte de Cataluña (MNAC) in May 2022. These prestigious accolades include the FERO Awards for Translational Research, FERO-ghd Awards for Breast Cancer Research, and launched this year, the Dr. Baselga Award in honor of José Baselga, Founder and late Honorary President of FERO and VHIO's founder and first director, who tragically passed away in 2021.

Two VHIO-led projects were prized by FERO in 2022:

Tian Tian, Senior Researcher Preclinical Team Leader of our recently established Upper Gastrointestinal Cancer Translational Research Group directed by Teresa Macarulla, received the XXII FERO Award for Translational Research supported by the Fundación Ramón Areces.

His two-year project seeks to decipher epigenetic features hidden in the plasma of cholangiocarcinoma patients by liquid biopsy and assess the utility of this technology in gene expression profiling, the detection of minimal residual disease following curative surgery, and the tracking of treatment response and identification of mechanisms of resistance.

The IV FERO-ghd Award for Breast Cancer Research sponsored by the ghd hair styling product company, was presented to José A. Seoane, Principal Investigator of our Cancer Computational Biology Group, for his two-year project focused on the epigenetic differences associated with hormone treatment resistant breast cancer heterogeneity.

This research aims to characterize the epigenetic profile of breast tumors treated with hormone therapy - both before and after treatment- to achieve a deeper understanding of the mechanisms of resistance to endocrine therapy in hormone receptor-positive breast cancer. These insights could help to predict disease relapse and enable the monitoring of patients by liquid biopsy before metastases are detected in the clinical setting.

Alongside Tian Tian and José A. Seoane, María Casanova-Acebes, Head of the Cancer Immunity Group at the Spanish National Cancer Research Center – CNIO (Madrid, Spain), was also awarded with a XXII FERO Award supported by the Fundació Bosch Aymerich. Her awarded project aims to advance insights into mechanisms of resistance to immunotherapy.

Dr. Baselga Award 2022

José Baselga, MD, PhD (1959-2021): a visionary leader in translational science and precision oncology.

The Dr. Baselga Award supports translational research of excellence carried out at research institutes in Spain by consolidated investigators of any nationality.

The first annual Award, including a trophy designed by Barcelona artist Jaume Plensa, was presented during this year's Award Ceremony to Ignacio Melero, co-Director of the Department of Immunology and Immunotherapy, Cima Universidad de Navarra Research Center (Pamplona), by José Baselga's wife Silvia Garriga and daughter Clara Baselga. This grant will support research aimed advancing insights into antigen cross-presentation and T-cell cross-priming in cancer immunology and immunotherapy.

FERO Award recipients 2022. Left to right: Ignacio Melero, María Casanova-Acebes, José A. Seoane and Tian Tian.

03 May 2022: VHIO's Enriqueta Felip presented with the first prize XI Premio Vanguardia de la Ciencia by Germán Ramón-Cortés, President of the Fundación Catalunya La Pedrera.

The Preimo Vanguardia de la Ciencia, a joint initiative of the Spanish periodical *La Vanguardia* and the Fundación Catalunya La Pedrera (Catalunya La Pedrera Foundation), recognizes some of the most pioneering science published from institutions of excellence throughout Spain. This recognition launched in 2011 to give more visibility to national research of excellence.

Now in its 11th annual edition, VHIO's Enriqueta Felip, Principal Investigator of our Thoracic Tumors & Head and Neck Cancer Group and Head of the Thoracic Cancer Unit at Vall d'Hebron, was voted by *La Vanguardia* readers as the recipient of the first prize this year for the landmark IMpower010 study. This research compared the efficacy and safety of an immune checkpoint inhibitor, atezolizumab, versus best supportive care as adjuvant therapy in patients with stage IB-stage IIIA non-small cell lung cancer (NSCLC), following resection and adjuvant chemotherapy.

First authored by Enriqueta, results of exploratory analyses of sites of disease relapse and subsequent therapy with atezolizumab compared with best supportive care showed significantly less disease recurrence and improved disease-free survival, particularly in those patients whose tumors expressed PD-L1. These findings, published in *The Lancet**, pointed to a potential paradigm shift in the treatment of patients with resected, early-stage NSCLC.

---

*Felip E, Altorki N, Zhou C, Csőszi T, Vynnychenko I, Goloborodko O, Luft A, Akopov A, Martinez-Marti A, Kenmotsu H, Chen YM, Chella A, Sugawara S, Voong D, Wu F, Yi J, Deng Y, McCleland M, Bennett E, Gitlitz B, Wakelee H; IMpower010 Investigators. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial. *Lancet*. 2021 Oct 9;398(10308):1344-1357.

30 November 2022: our Director Josep Tabernero (left) was presented with the XII *ABC* Prize for Best Physician of the Year by Enrique Ruiz Escudero, Cabinet Minister of Health of Madrid.

Awarded by the Spanish periodical *ABC*, *ABC Salud*'s annual prizes recognize the outstanding work of healthcare professionals and entities in Spain as well as important contributions to research.

Among the awarded individuals and healthcare entities under the categories of best public hospital, private hospital, medication, nursing program, healthcare technology, pharmacy, and foundation, VHIO's Director Josep Tabernero received the 2022 prize for Mejor Médico del Año (Best Physician of the Year). This prize recognizes his clinical research of excellence against gastrointestinal and endocrine tumors, his development of more effective targeted anti-cancer therapies, and his numerous contributions to advancing precision medicine in oncology.

Premios M. Chiara Giorgetti
PROYECTO GANADOR

IV Premios Chiara Giorgetti Award Winners 2022: Laura Soucek (left) and Meritxell Bellet (right).

Announced at the end of 2022, Laura Soucek, co-Director of our Preclinical and Translational Research Program, and Meritxell Bellet, a Clinical Investigator of VHIO's Breast Cancer Group and a Medical Oncologist at Vall d'Hebron, were among the recipients of this year's annual Premios Chiara Giorgetti.

ICREA Research Professor Laura Soucek was awarded with the top prize for her project that will combine MYC and PARP inhibitors as a novel therapeutic strategy against triple-negative breast cancer (TNBC). Led by Laura and carried out by Fabio Giuntini, a PhD Student of her Models of Cancer Therapies Group at VHIO, this research is based on their preliminary data suggesting that MYC inhibition in TNBC could potentiate the efficacy of PARP inhibitors to overcome cancer drug resistance.

The investigators will evaluate their first Omomyc-derived compound, OMO-103, that successfully completed the phase I part of the phase I/IIa clinical trial in 2022 (page 28), combined with PARPi.

Meritxell Bellet received one of the two Metarpremios this year. Her prized project will seek to clinically and molecularly characterize oligometastasic breast cancer. This research will be carried out in collaboration with co-Principal Investigator of this study, Juan Miguel

Cejalvo, an Investigator and Medical Oncologist, INCLIVA Biomedical Research Institute and Hospital Clínico Unversitatrio (Valencia, Spain), and colleagues at four other Spanish hospitals: ICO-Hospitalet, ICO-Badalona, Hospital Clínic de Barcelona (Catalonia), and the Hospital 12 de Octubre (Madrid).

20 June 2022: our Director Josep Tabernero was presented with the Fundación Lilly Prize for Biomedical Research under the category of Clinical Biomedical Research.

Established in 2001, the Fundación Lilly annual Prizes for Biomedical Research recognize leading Spanish preclinical and clinical investigators who have significantly advanced biomedicine and health science.

In 2022 our Director Josep Tabernero was prized under the category of Clinical Biomedical Research in recognition of his outstanding career and contributions to precision oncology. These include the discovery of new mechanisms driving tumor growth, the early clinical drug development of more effective, targeted anti-cancer medicines with particular focus on gastrointestinal tumors, pioneering novel immune-based strategies against cancer, the implementation and development of liquid biopsy and advancing insights into the gut microbiome and its role in colorectal cancer, among many others.

Salvador Aznar Benitah, Senior Group Leader at the Institute for Research in Biomedicine – IRB (Barcelona), Head of IRB's Aging and Metabolism Group, and an ICREA Research Professor, received this year's prize for preclinical research for his discoveries in aging and cancer, stem cells and cancer, and the interplay between diet, circadian rhythm and cancer.

12 December 2022: VHIO's Laura Palomo (center) awarded by La Fundación AstraZeneca with a Premio Jóven Investigador (Young Investigator Prize).

Celebrating the 6th annual edition of the Fundación AstraZeneca Premios Jóvenes Investigadores (Young Investigator Prizes), in collaboration with the Instituto de Salud Carlos III (ISCIII), Laura Palomo, a Postdoctoral Scientist of VHIO's Experimental Hematology Group, was presented with a prize under the newly created category that awards research jointly carried out by different groups across Spain based on identified synergies and to connect expertise toward accelerating scientific discovery.

Under the category of Oncology, Precision Medicine and Immunotherapy, Laura was awarded alongside the other investigators for their project entitled: *Germline predisposition to myelodysplastic syndromes in adults: expanding diagnostic accuracy and evidence of pathogenicity*.

This collaborative study will be coordinated by Andrés Jerez, Principal Investigator of Hematology and Clinical-Experimental Medical Oncology, Instituto Murciano de Investigación Biosanitaria Pascual Parrilla (IMIB), and counts on the collaboration of four other co-principal investigators including Laura Palomo. They are: Mónica del Rey, an investigator of the Genetics in Oncohematology Group at the Salamanca Cancer Center (CIC) – Institute for Biomedical Research of Salamanca (IBSAL); Adrián Mosquera, Lead Researcher of Computational and Genomic Hematology at the Health Research Institute of Santiago de Compostela (IDIS); and Ana Alfonso, Attending Physician and Clinical Investigator in Hematology, the Centre for Applied Biomedical Research (CIMA), Clínica Universidad de Navarra.

30 November: Vall d'Hebron Barcelona Hospital Campus awarded by *Gaceta Médica* for excellence in healthcare and oncology research.

For the second consecutive year VHIO was recognized by the Spanish specialized healthcare publication *Gaceta Médica*. Our Director and Head of the Vall d'Hebron University Hospital's Medical Oncology Department Josep Tabernero received the Best in Class (BiC) prize for research in oncology.

Pere Barba, a Hematologist and Lead Investigator of our Experimental Hematology Group, and physician at Vall d'Hebron's Hematology Service was honored for Vall d'Hebron's CAR T-cell therapy program. Celebrating the 17th annual edition of BiC, these prizes award the best national public and private healthcare services, units and programs across disciplines and specialties.

In addition to VHIO, other entities and units at our Vall d'Hebron Barcelona Hospital Campus were also awarded

this year. The Multiple Sclerosis Centre of Catalonia (Cemcat), directed by Xaiver Montalbán, received the Best-in-Class prize under the category of multiple sclerosis; Patricia Pozo, Head of Section of the Neurology Service at Vall d'Hebron, Head of the Headache and Neurological Pain Group at the Vall d'Hebron Research Institute (VHIR), and Director of the Migraine Adaptive Brain Center at Vall d'Hebron, received the Best-in-Class prize for the best headache unit; and Maria Josep Carreras, Head of Vall d'Hebron's Oncohematology Pharmacy Unit, received the prize for the best Unit in hospital oncology pharmacy.

"la Caixa" Foundation

The "la Caixa" Foundation is one of our Institutional Supporters and Patrons (page 20) that supports several VHIO programs, facilities and initiatives including our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138), Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch Clinical Research Onco-Hematology Unit (page 144), CaixaResearch Advanced Oncology Research Program 2020-2023 (page 127), and a new program - UNderstanding cancer through sIngle cell seQUEncing: the UNIQUE platform (page 27).

In 2022, it also awarded two new VHIO research projects. Francesco Grussu, a Postdoctoral Fellow of our Radiomics Group led by Raquel Perez Lopez, received a Junior Group Leader Award to lead a project on the development, validation, and application of new-generation oncological MRI. Mentored by Raquel, this research aims to boost the sensitivity and biological specificity of diffusion MRI in cancer using artificial intelligence and computer simulations guided by histology.

Cayetano Galera, a Graduate Student of VHIO's Gene Expression & Cancer Group led by Joan Seoane, received predoctoral funding through an InPhinit Retaining grant. Directed by Joan, Cayetano's research will focus on the tumor microenvironment and molecular mechanisms involved in bone metastasis to identify novel therapeutic targets.

asociación española contra el cáncer

The Asociación Española Contra el Cáncer – AECC (Spanish Association Against Cancer), is a longstanding supporter of several VHIO groups and researchers. We take this opportunity to salute and applaud AECC's invaluable contribution to promoting cancer discovery and translational research of excellence, as well as the essential backing that it provides to countless investigators and teams across Spain and beyond.

Three additional VHIO researchers were awarded this year across two of AECC's many funding programs. César Serrano, Principal Investigator of our Sarcoma Translational Research Group, received funding through an AECC National Consortium clinical research grant for his project on the centralization of pathological diagnosis and implementation of precision medicine strategies in sarcoma.

Through the ERA-NET: Sustained collaboration of national and regional programmes in cancer research, the AECC and the Instituto de Salud Carlos III – ISCIII (Carlos III Health Institute) granted two new VHIO projects in 2022, within the scope of the phase two part of the TRANSCAN-3 program funded by the EU's Horizon Europe framework programme.

Joan Seoane, co-Director of VHIO's Preclinical and Translational Research Program and Principal Investigator of our Gene Expression and Cancer Group, will lead the iParaCyts project to evaluate the therapeutic potential of immunosuppressive paracrine cytokines in the tumor microenvironment of metastatic lesions. The second TRANSCAN-3-funded project, directed by Raquel-Perez Lopez, Principal Investigator of our Radiomics Group, will explore artificial-intelligence-based end-to-end prediction of cancer immunotherapy response (TANGERINE). For more information about these two VHIO TRANSCAN-3 projects please see page 192.

At the end of 2022, we received institutional support through AECC's Excellence Program - Advanced Therapies Accelerator Program. We aim to establish VHIO as an international reference in the rapidly emerging field of gene and cellular therapies and contribute to the expansion of Europe's product development in this area.

To boost the development of academic gene and cellular therapy products and associated translational research, we plan to construct a Clean Room laboratory, provide our teams with the necessary training, foster and develop national and international collaborations, and establish an optimal program governance structure. These actions will enable us to develop new gene and cellular therapy products and advance existing ones in our pipeline.

We look forward to reporting on this exciting new Institutional Program in next year's Scientific Report.

SEOM Sociedad Española de Oncología Médica

VHIO recipients of SEOM awards and prizes in 2022 (left to right): Cristina Suarez, Meritxell Bellet, Iosune Baraibar and Nadia Saoudi.

In 2022, four of our investigators were awarded with research grants and prizes from the Sociedad Española

de Oncología Médica – SEOM (Spanish Society of Medical Oncology).

Cristina Suarez received a SEOM-BMS grant for translational research projects in immuno-oncology to validate the predictive value of the VIGex immune gene expression signature (see page 12), to enrich patient selection in immuno-oncology phase I renal cancer clinical trials.

Developed in-house by VHIO investigators including Alberto Hernando-Calvo, formerly a phase I investigator at VHIO, Elena Garralda, co-Director of our Clinical Research Program, Principal Investigator of VHIO's Early Clinical Drug Development Group, and Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, and Ana Vivancos, Principal Investigator of our Cancer Genomics Group, Cristina will use this tool in metastatic renal cancer, in patients treated with first-line immune-based combinations.

Meritxell Bellet, a Clinical Investigator of VHIO's Breast Cancer Group and a Medical Oncologist at Vall d'Hebron, received a SEOM/FECMA grant for the LABEL study. This study aims to redefine the prognosis of invasive lobular carcinoma in early-stage breast cancer, and validate a new cutoff point for Ki67 - a protein that is associated with cell proliferation in tumors and an important prognostic and predictive marker in cancer.

Iosune Baraibar, a Clinical Investigator of our Gastrointestinal & Endocrine Tumors Group and a Medical Oncologist at Vall d'Hebron, received the Premio SEOM for the best doctoral thesis, and Nadia Saoudi, a Clinical Investigator and Medical Oncologist of the same group, received one of the two SEOM-MERCK "Somos futuro" prizes.

In addition, Alberto Hernando-Calvo received funding through a SEOM-Fundación CRIS contra el Cáncer grant for returning young investigators that will enable him to return to our Institute in 2023 when he completes his stay (2021-2022) at the Princess Margaret Cancer Centre in Toronto (Canada). His current Fellowship was also funded through a SEOM – Fundación CRIS contra el Cáncer grant that supports visits in centers of excellence in oncology overseas.

Oriol Mirallas received a travel grant to participate in the clinical rotation program (two month stay) at the University of Texas MD Anderson Cancer Center (USA).

Institutional support and accreditation 2022

EXCELENCIA SEVERO OCHOA 2022 - 2026

Our Institute received Excelencia Severo Ochoa accreditation in 2021 and is now recognized as a Severo Ochoa Center of Excellence (2022-2026); VHIO's fourth Institutional Program. Granted under the subprogram of the Spanish Institutional Strengthening of the State Plan for Scientific and Technical Research and Innovation, this accolade recognizes national research centers demonstrating scientific leadership of excellence and impact at a global level.

This distinction not only reflects VHIO's important contributions to cancer science and precision medicine in oncology, but also confirms our capacity to advance frontier research, generate high-impact results, as well as attract and retain research talent. Set within the Vall d'Hebron Barcelona Hospital Campus, VHIO is the first research center closely linked to one of the Spanish National Healthcare System's Hospitals to have been endorsed by this prestigious seal of excellence. For more details see page 129 of this report.

CERCA Centres de Recerca de Catalunya

In 2022 VHIO underwent evaluation for renewed accreditation of the Institució CERCA–Centres de Recerca de Catalunya (CERCA Institute of Research Centres of Catalonia) for the period 2017–2021.

In recognition of VHIO's progress, performance in knowledge transfer activities and management of excellence, VHIO was awarded the maximum qualification of an A grading. This achievement recognizes the excellence and quality of work carried out by all individuals, teams, and groups at our Institute.

For a full listing of accreditations please see page 200 of this Scientific Report.

VHIO's patient engagement events, fundraising, and public outreach activities

VHIO supports and organizes activities to increase public interest in cancer research and promote the important advances reported by our scientists and clinical investigators. These efforts are aimed at patients and non-specialized audiences to enrich scientific culture as well as promote science as a stimulating career path for young people – the future of our research.

Importantly, some of these initiatives have resulted in considerable funding for research at VHIO, as documented in this section of our Scientific Report. We will continue to seek out, lead and participate in all these precious initiatives and launch new ones based on identified opportunities.

Illustrative of these efforts, we take this opportunity to mention just some of the many highlights and activities in 2022:

Connecting and conversing with cancer patients, their families and friends outside of the clinic

8th edition of our annual breast cancer workshops (October 2021 – June 2022).

HUVH-VHIO's annual breast cancer workshops for our cancer patients, their families and friends, as well as the general public.

Timed to coincide with World Breast Cancer Day, 19 October, the 8th edition of our annual breast cancer workshops ran from October 2021 – June 2022 and took place remotely online due to the COVID-19 pandemic. Coordinated by Lucía Sanz, a Medical Oncologist and Clinical Investigator of VHIO's Breast Cancer Group, directed by Cristina Saura, these workshops cover a broad range of topics relating to the physical, emotional and social aspects of this disease as well as survivorship.

Launched back in 2015, these events are organized in collaboration with the Vall d'Hebron University Hospital's (HUVH) Breast Cancer Unit, also led by Cristian Saura, and other expert teams across the Vall d'Hebroun Barcelona Hospital Campus. Open to patients, their loved ones and friends, these events provide opportunity for debate and two-way exchange with our physician-scientists, cancer researchers and other professionals in oncology, and are supported by Pfizer and iCROM Clinical Research Office Management, in collaboration with the Asociación Endavant Chic@s.

The 9th annual edition of these workshops, also supported by Pfizer in collaboration with Asociación Endavant Chic@s, launched in October 2022 and have now resumed as in-person workshops at VHIO's CELLEX Building.

Online workshops for cancer patients.

Our series of online, monthly workshops are designed for cancer patients, their families, as well as the general public. Counting on the participaton of VHIO investigators and other expert professionals in oncology at the Vall d'Hebron University Hospital (HUVH), Vall d'Hebron Barcelona Hospital Campus, this educational resource covers a broad range of topics and different tumor types, as well as current directions in cancer research, treatment and care. A total of eight workshops took place in 2022.

Supported by IPSEN, our first workshop aimed at cancer patient associations took place at VHIO to update on just some of our current lines of research. This initiative aims at strengthening communication between our Insitute and patient associations, organizatons and advocates and inform on the latest developments in cancer research.

Jorge Hernando, a Clinical Investigator of VHIO's Gastrointestinal & Endocrine Tumors Group and Medical Oncologist at Vall d'Hebron, leading the conversation at our first workshop for patient organizations held at VHIO's CELLEX Building.

Public fundraising in support of cancer research

el paseíco de la mama
10º aniversario

El Paseíco de la Mama (loosely translated as strolling for breast cancer) began to take shape when Inés Gasén was diagnosed with breast cancer during her pregnancy – not only provoking fear and uncertainty but also raising many questions and doubts concerning the health and the future ahead for her baby.

Bringing a positive out of the then challenging times, Inés and her family organized the first El Paseíco de la Mama

7.5 km sponsored walk along Zaragoza's canal in 2011 to support breast cancer research directed by Cristina Saura, Principal Investigator of our Breast Cancer Group and Head of the Vall d'Hebron University Hospital's (HUVH) Breast Cancer Unit.

While 2021's sponsored 7.5 km walk had once again to adapt to the restrictions imposed during the COVID-19 pandemic, this did not deter the fundraising efforts. This event raised an incredible 40,148€, presented by Inés Gasén to VHIO's Cristina Saura and Lucía Sanz in January this year.

Left to right: Cristina Saura, Inés Gasén and Lucía Sanz.

This support will fund research led by Lucía Sanz, a Medical Oncologist and Clinical Investigator of Cristina's research group and the Breast Cancer Unit at Vall d'Hebron, aimed at improving the staging of breast cancer in pregnant women.

Detecting breast cancer early during pregnancy is challenging and is often diagnosed at a later stage compared to women who are not pregnant, and the risk of metastasis is thus higher. Imaging techniques including nuclear magnetic resonance, that do not use ionizing radiation or require intravenous contrast, promise more precise data regarding the location and stage of disease.

Lucía's research will evaluate if this approach can increase sensitivity and specificity for the detection of liver, lung, and bone metastases, and better guide treatment decision making.

Now in its 12th annual edition, funds raised from this year's sponsored walk 2022 will support research led by Mara Cruellas, also a Clinical Investigator and Medical Oncologist of Cristina Saura's team. She will study the efficacy of CDK4/6 inhibitor therapy in a cohort of patients with hormone receptor-positive metastatic breast cancer with a *BRCA1/2* mutation

15 October 2022: raising funds for breast cancer research at the 12th annual El Paseíco de la Mama.

Left to right: Judith Balmaña, Cristina Saura and Luisa Vázquez.

Shortly after Luisa Vázquez's first cancer diagnosis in one breast, a second tumor was detected in her other breast. Luisa underwent a double mastectomy, but her liver was also affected, and she needed a transplant.

During her cancer journey Luisa discovered that some patients go through breast cancer without the necessary support to help them at such a crucial time in their lives, and she consequently decided to create the voluntary Asociación Endavant Chic@s. Supported by the guidance of Eva Muñoz, a Medical Oncologist and Clinical Investigator of Cristina Saura's Breast Cancer and Melanoma Group at VHIO, this association provides integral support to breast cancer patients at the Vall d'Hebron University Hospital's (HUVH) Breast Cancer Unit, also directed by Cristina Saura, and organizes several fundraising initiatives throughout the year including several sports tournaments.

Thanks to these efforts, as well as donations received through its members and volunteers in 2021, Luisa presented Cristina Saura and VHIO's Judith Balmaña with a cheque for 17,200€ in 2022. This funding will support research toward improving outcomes and the quality of life of breast cancer patients at the at the Vall d'Hebron University Hospital's Breast Cancer Unit.

Research led by Judith Balmaña, Principal Investigator of our Hereditary Cancer Genetics Group, will focus on better calculating the risk of developing breast cancer using predictive models and anticipating and preventing disease in individual women. The investigators will use the CanRisk model that enables breast cancer risk prediction in unaffected women based on mutation screening information for rare (high risk and moderate risk) breast cancer genetic susceptibility variants, and common cancer genetic susceptibility variants using polygenic risk scores.

Judith and her team will study patients carrying alterations in the *ATM* and *CHEK2* genes and evaluate associated breast cancer risk by also considering individual family history, hormonal and reproductive risk factors, and mammographic density.

Marking this year's Breast Cancer Awareness month, the 5th edition of the Pink Run Mir fundraising 3K walk-runathon took place on 16 October in support of breast cancer research at VHIO. This annual event is organized by the Sin Teta Hay Paraiso association in collaboration with the Joventut Alètica Montacada and the City Council of Montcada i Reixac.

Funds raised will further fuel research into lobular carcinoma, a distinct type of breast cancer which represents around 10% of malignant breast tumors. This project, initiated in 2016 thanks to previous funds raised through Pink Run Mir, seeks to establish the value of prognostic parameter Ki67 as a biomarker in this patient population.

Using the EndoPredict multi-gene test, Cristina Saura and her team, with Meritxell Bellet leading this project, are also validating Ki-67 as a predictor of benefit from chemotherapy to help inform treatment decision making. This additional funding will enable the investigators to finalize the *El Lobulillar También Existe* project by achieving a better understanding of the prognosis of lobular breast cancer and guiding the selection of chemotherapy or longer-duration hormonal therapy.

Em dones força presents VHIO's Meritxell Bellet with 10,000€ to further support research aimed at improving outcomes for patients with triple negative breast cancer.

Em dones força is a not-for-profit association founded by a group of friends in Riudoms, Tarragona (Catalonia) to raise funds for breast cancer research through a variety of fundraising activities. Presented to Meritxell Bellet, a Clinical Investigator of VHIO's Breast Cancer Group and Medical Oncologist of Vall d'Hebron's Breast Cancer Unit led by Cristina Saura, a second consecutive donation of 10,000€ will further support her research project entitled: Recruiting ERβ in the fight against triple negative breast cancer (TNBC).

This study focuses on the co-expression of estrogen receptor beta (ERβ) and androgen receptor (AR) in tumor samples from patients with triple negative breast cancer and seeks to identify a group of patients who could benefit from hormonal therapy targeting ERβ, AR, or both.

Meritxell Bellet was Elvira Mas' oncologist. Elvira was a co-founder and President of Em dones força before she sadly passed away from breast cancer. The official presentation of this donation took place at VHIO's CELLEX Building in April this year, and paid tribute to Elvira and her legacy. Fifty people, including Elvira's family and friends, all of whom form part of Em dones força, attended this special event.

October 2022: the launch of the 5th Pañuelo Solidario campaign at Vall d'Hebron.

Pañuelo Solidario is a fundraising campaign organized by the Vall d'Hebron University Hospital (HUVH), in collaboration with the lifestyle store Natura that produces and distributes these charity scarves in its shops and online.

Established in 2017 by the campaign's ambassador Judit Mascó, this fundraiser centers on the treatment and wellbeing of women suffering with breast cancer and gynecological cancers.

The 5th annual campaign launched in October 2022 upon the eve of World Breast Cancer Day, and all proceeds will further support cancer research carried out by two predoctoral researchers. They are Alejandra Cano, Psycho-Oncologist of VHIO's Breast Cancer Group, and Carina Masferrer, PhD Student of the Gynecological Biomedical Research Group at the Vall d'Hebron Institute of Research (VHIR).

Alejandra Cano's research focuses on STEPS – therapeutic support for cancer survivors. This project provides more resources and tailored activities for patients after their diagnosis and post-treatment to alleviate anxiety and emotional stress, as well as tools to facilitate their reincorporation into daily life, both at the personal and professional levels.

Carina Masferrer's research focuses on developing new therapeutic strategies for the more effective treatment of endometrial cancer. She is currently evaluating targeted therapies for the treatment of metastatic ovarian cancer and has set up an experimental platform using several in vitro cancer models.

1. Amaia Goirigolzarri's solidarity scarf campaign to raise funds for sarcoma research. 2. With their family members, Ángel and Patricia Valero and Gloria Cerezo meet with César Serrano to discover more about his sarcModel project.

In 2022 different fundraising initiatives took place to support research carried out by our Sarcoma Translational Research Group directed by César Serrano. Representatives from the Basque cultural world and artists including Jon Maia, one of the Basque Country's leading bertsolaris (improvisers), joined together for a fundraising campaign through the sale of a solidarity scarves exclusively designed by Maitane Bilbao. This fundraiser was initiated by Amaia Goirigolzarri, a sarcoma patient receiving treatment at the Vall d'Hebron University Hospital (HUVH), a leading reference in the treatment of this type of cancer.

In addition, two books were published to raise funds for research against sarcoma. Led by family members of patients who sadly passed away from this disease, the first *El día que decidiste no morir* was compiled by Gloria Cerezo in memory of her sister Carolina Cerezo. Carolina's idea before she passed away in 2019 was to write a book about her cancer journey including her personal reflections. Her sister Gloria promised that she would honor this wish and completed this project on her behalf.

The second, *Ozelot*, recognizes the life and work of the artist Fernando Valero, known as 'Ozelot', who passed away in 2020. This book was compiled by Fernando's sister Patricia Valero and father Ángel Valero. Proceeds from the book go to the sarcModel project led by César Serrano to generate mouse and cellular models of different types of sarcomas to advance insights into these cancers toward identifying new therapeutic avenues.

VHIOVids
There's a light that never goes out.

The Festival VHIOVida music festival, that took place on 22 October in Cabrils (Maresme, Catalonia) is one of the initiatives of the #IrurtzunRules project that was initiated by friends and family of Sergi Irurtzun who was diagnosed with early-onset colorectal cancer (CRC), four years prior to this fundraising event. This project also involved the participation of the #IrurtzunRules cyclists in the TRANSPYR Coast to Coast 2022 mountain bike stage race.

We are deeply saddened to report that since Sergi Irurtzun visited VHIO in November 2022 he recently passed away from this disease. Sergi's passing illuminates the urgent need to address the rising incidence of CRC in adults under age 50, and advance crucial inisghts into the factors contributing to this alarming phenomenon.

It is thanks to Sergi's courage, fight and generosity, along with the support of his family, friends and all the voluteers involved in this fundraiser, that this initiative raised an incredible 28,169.73€, presented to Iosune Baraibar, a Clinical Investigator of VHIO's Gastrointestinal and Endocrine Tumors Group and Medical Oncologist at Vall d'Hebron, and Ariadna Garcia, a Clinical Nurse Specialist of the same group.

This donation will help our investigators to advance insights into the molecular signatures associated with early-onset CRC and identify new therapeutic targets for the treatment of these patients who typically have a more-advanced disease at diagnosis than patients with later onset colorectal cancer. As importanly, this research will also help to respond to the specific and particular needs of these young patients who require personalized and specialized care.

Organized by the Fundación Enric Masip a charity golf tournament took place at the Club de Golf Sant Cugat (Sant Cugat del Vallés, Catalonia) on 28 November with more than 70 professional as well as amateur golfers who took part to raise funds for research into endocrine and neuroendocrine tumors at VHIO, as well as raise awarness about these rare types of cancer.

Due to the rarity of these tumors, running clinical studies to develop and evaluate new therapies represents a challenge. Funds raised will support research led by Jaume Capdevila, a Senior Clinical Investigator of our Gastrointestinal and Endocrine Tumors Group, and Medical Oncologist at the Vall d'Hebron University Hospital's Medical Oncology Department, in order to advance insights into these diseases and identify more effective treatment strategies.

Left to right: Mafalda Oliveira, Ester Barrao and Cristina Saura.

Presented to Cristina Saura, Principal Investigator of VHIO's Breast Cancer and Melanoma Group and Head of the Breast Cancer Unit at the Vall d'Hebron University Hospital, and Mafalda Oliveira, a Clinical Investigator of Cristina's team and a Medical Oncologist at Vall d'Hebron, a donation of 1224.30€ will contribute to the fight against breast cancer.

Maribel González, a former patient at Vall d'Hebron who was treated and cared for by Cristina Saura's team, with Mafalda as her Medical Oncologist, sadly passed away from this disease in January 2021. In recognition of their dedication and care, and to support research into metastatic breast cancer, Maribel's daughter, Ester Barrao, set up a fundraising campaign. During two consecutive Sundays in December 2021, family and friends gathered for a Christmas solidarity photo shoot.

Funds raised will further enable Cristina and her team to pursue essential research aimed at advancing breast cancer treatment and care.

Cristina Saura presented with a donation of 1000 minutes to research by Jaime Chia, Managing Director of Galerías del Tresillo.

The Spanish sofa company Galerías del Tresillo's 30-year long corporate social responsibility *Sofás que Suman* program spurs and develops collaborations with several different entities in support of various causes for a better world.

Dedicated to breast cancer research, a newly launched campaign ran throughout the month of October 2022. This initiative culminated in a donation of 1000 minutes to research carried out by Cristina Saura's Breast Cancer Group at VHIO. Such initiatives help Cristina and her team to advance current projects as well as open new lines of research.

Public outreach and engagement

During one of the two roundtable sessions at the Vall d'Hebron Barcelona Hospital Campus' special event to mark World Cancer Day 2022. Left to right: Josep Tabernero, Lucas Moreno, Santiago Ramón y Cajal, and Juan García Vicente.

World Cancer Day 2022 (WCD), 04 February, marked the launch of the next 3-year campaign themed *Close the Care Gap* to address the major issue of inequities in cancer care around the world. For the third consecutive year the Vall d'Hebron Barcelona Hospital Campus (page 25) organized and hosted a dedicated WCD event that counted on the participation of several experts from Vall d'Hebron who discussed and debated the very latest advances in cancer research and precision medicine in oncology.

Participation from VHIO included our Director Josep Tabernero, Head of the Medical Oncology Department at the Vall d'Hebron University Hospital (HUVH), Enriqueta Felip, co-Director of Clinical Research at VHIO and Principal Investigator of our Thoracic Tumors & Head and Neck Group and Head of HUVH's Thoracic Cancer Unit, Francesc Bosch, Principal Investigator of VHIO's Experimental Hematology Group and Head of HUVH's Department of Hematology, Ana Vivancos, Principal Investigator of our Cancer Genomics Group, and Cristina Casal, Study Nurse Supervisor of our Clinical Research Oncology Nurses.

Inaugurated by HUVH's General Manager Albert Salazar this event also included the essential participation of cancer patients and covered a broad range of topics from personalized medicine in oncology, cutting-edge technologies and approaches in translational and clinical science, innovative clinical trials, cancer prevention, to important aspects regarding the wellbeing and care of patients.

This year's program also included two roundtable discussions. The first, moderated by Josep Tabernero,

centered on the incorporation of precision medicine in patient care. Joining Josep were invited speakers Lucas Moreno, Head of HUVH's Pediatric Oncology and Hematology and the Vall d'Hebron Research Institute's (VHIR) Childhood Cancer and Blood Disorders Group, Santiago Ramón y Cajal, Head of HUVH's Anatomical Pathology Service and VHIR's Translational Molecular Pathology Group, and Juan García Vicente who provided the essential patient perspective by sharing his personal experience of cancer care and treatment.

The second focused on treatment and innovative research. Moderated by Anna Santamaria, Coordinator of the Division of Oncology and Head of the Biomedical Research in Urology Group at VHIR, expert speakers included VHIO's Francesc Bosch, Ana Vivancos and Cristina Casal, as well as Ibane Abasolo, Director of CIBBIM-Nanomedicine at VHIR.

Antonio Roman, Director of Healthcare at HUVH, closed this 3rd consecutive annual WCD event organized by HUVH, the Vall d'Hebron Barcelona Hospital Campus.

Coinciding with the International Day of Women and Girls in Science, celebrated annually on 11 February, several of our researchers participated in three different initiatives:

CONÓCELAS, is organized by the Asociación Española de Investigación sobre el Cáncer - ASEICA (Spanish Association of Cancer Research), in collaboration with the Red de Asociaciones de Investigadores y Científicos Españoles en el Exterior - RAICEX (Network of Associations for Spanish Researchers and Scientists Abroad), and the Fundación Merck Salud (Merck Health Foundation).

The main objective of this event is to illuminate the important contributions made by female investigators in combating cancer. It connects over 200 in researchers - 'cancer detectives' - virtually with over 11,000 students throughout Spain for them to discover more about the work of today's female talents in cancer research.

ASEICA has also developed an interactive map plotting the whereabouts of each Spanish researcher in Spain and abroad also details the research background and scientific achievements as well as interesting facts about each of them beyond the realm of research. This year's edition, celebrated on 08 February, counted on the participation of VHIO faculty including María Abad, Sílvia Casacuberta, Alena Gros, Sandra Martínez, Sandra Peiró, Raquel Pérez-López, Elena Senís, and Laura Soucek.

#100tífiques

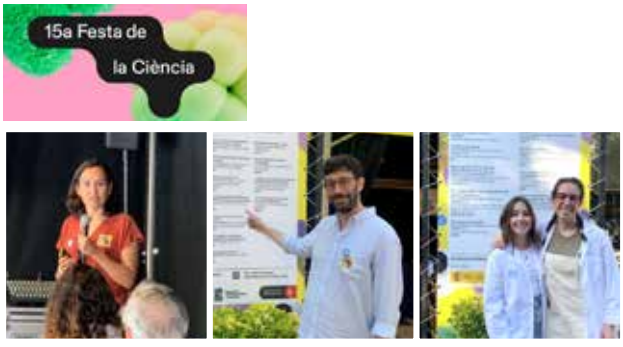
#100tífiques is a joint initiative of the Fundació Catalana per a la Recerca i la Innovació – FCRI (Catalan Foundation for Research and Innovation), and the Barcelona Institute of Science and Technology (BIST), in collaboration with the Departament d'Educació de la Generalitat de Catalunya (Department of Education, the Government of Catalonia).

The main goals of #100tífiques are to promote the relevance and role of women in science and technology and foster collaboration between scientists from academia and enterprise. It also seeks to forge a more direct and reciprocal relationship between science and society.

2022 counted on the participation of women in science (pre-doctoral students, postdocs, group leaders and directors of research from both the public and private sectors), including VHIO's Sarai Córdoba, Natalia Écija, Carmen Escudero, Alba Llop Guevara, Sara Gutiérrez-Enríquez, Olivia Prior and Maria Vieito, who gave virtual and/or in-person talks to students aged 11 and 12 across Catalonia.

Organized by the Scientific Foundation of the Asociación Española contra el Cáncer – AECC (Spanish Association against Cancer), the virtual event entitled *Investigadora, que nada te detenga* (Women in research, let nothing stop you), seeks to promote the work of female investigators who have received funding from AECC. Speakers are invited to discuss their current projects and talk about their respective career trajectories.

Taking place on the International Day of Women and Girls in Science, 11 February 2022, VHIO's Isabel Puig, Senior Investigator of VHIO's Stem Cells and Cancer Group, was joined by Amparo Cano, Full Professor of Biochemistry, the Autonomous University of Madrid (UAM), and Carmen Ortega, an AECC PhD Student at the Mathematical Oncology Laboratory (MoLAB), the University of Castilla-La Mancha, Spain. This interactive session was moderated by Sofía Hernández, AECC's science communicator.



Left to right: VHIO's Alena Gros, José A. Seoane, Joanna Doménech and Carmen Escudero.

Organized by the Ajuntament de Barcelona (Barcelona City Council), 2022 celebrated the 15th annual edition of the Festa de la Ciència (Celebration of Science). This public event was established as an educational forum to learn about, consider and update on latest scientific advances, the opportunities that lie ahead, as well as current challenges that are being tackled through research of excellence. This year's program included over 200 different activities for people of all ages.

Regarding VHIO's participation, Principal Investigator of VHIO's Tumor Immunology and Immunotherapy Group Alena Gros gave a mini talk on immune-based therapies that boost the immune system to target and kill cancer cells and how immunotherapy is increasingly becoming the fourth main pillar of cancer therapy alongside surgery, radiotherapy, and chemotherapy.

Principal Investigator of our Cancer Computational Biology Group José A. Seoane gave a mini talk on the promise of artificial intelligence (AI) in more effectively combating cancer through its potential application in the detection and diagnosis of disease as well as genetic testing and guiding treatment decision making.

Carmen Escudero, a PhD Student of our recently established Upper Gastrointestinal Cancer Translational Research Group led by Tian Tian and directed by Teresa Macarulla, and Joanna Doménech, a PhD Student of VHIO's Hereditary Cancer Genetics Group headed by Judith Balmaña, gave a talk on genetic mutations in cancer. Using pieces of LEGO® they creatively demonstrated how faulty genes lead to cancer.

From 22 - 23 October 2022, the Vall d'Hebron Barcelona Hospital Campus celebrated 48h Open House BCN by providing the public with a great opportunity to learn more about cutting-edge platforms, tools and techniques on-campus that are shaping the future of healthcare.

Participants were invited to tour different VHIO labs and meet some of our investigators, as well as visit many other spaces across campus including the Vall d'Hebron Research Institute (VHIR).

Forming part of Vall d'Hebron's strategic plan to promote its innovation, driven and developed in-house, this event was also established to provide researchers, clinical investigators, technicians, and healthcare professionals who spur advances in oncology and develop the very latest medical technologies, with increased visibility in society.

NIT EUROPEA DE LA RECERCA

The Nit Europea de la Recerca (European Night of Research) is celebrated annually in more than 25 countries throughout Europe. This event was established to enable members of the public to meet researchers, learn about their respective scientific disciplines, research lines and activities.

From 27 September – 02 October 2022, more than 100 activities took place in Barcelona including workshops, courses, and roundtable discussions. Coordinated by the Barcelona Institute for Global Health (ISGlobal), an initiative of the "la Caixa" Foundation, University of Barcelona, and the Catalan Association of Scientific Communication (ACCC), the program also included talks by VHIO's Paolo Nuciforo, Principal Investigator of our Molecular Oncology Group, and José A. Antonio, Principal Investigator of our Cancer Computational Biology Group, focused on the microbiome and artificial intelligence in cancer, respectively.

Barcelona Global

For the fourth consecutive year Barcelona MBA Day organized by Barcelona Global brought together 600 MBA international students, recently arrived in Barcelona from leading business schools in the world, to visit and learn about multinationals, renowned scale-ups, and research institutes.

Among these events, students came to our Vall d'Hebron Barcelona Hospital Campus on 20 October to discover more about research at Vall d'Hebron. During their visit they also toured VHIO to learn about our multidisciplinary translational research model, and technology transfer through a talk delivered by Héctor G. Palmer, Principal Investigator of our Stem Cells and Cancer Group, and co-founder and Chief Scientific Officer of the VHIO-University of Barcelona (UB)-ICREA Catalan Institution for Research and Advanced Studies spin off, ONIRIA Therapeutics, that officially launched this year (page 29).


International students, recently arrived in Barcelona, visit VHIO as part of the Barcelona MBA Day organized by Barcelona Global.

Raising awareness about breast cancer diagnosed during pregnancy: VHIO's Cristina Saura with patients attended at Vall d'Hebron, along with their families.

Led by VHIO's Cristina Saura, Principal Investigator of our Breast Cancer Research Group and Head of the Breast Cancer Unit at the Vall d'Hebron University Hospital (HUVH), Vall d'Hebron's multidisciplinary program dedicated to attending patients diagnosed with breast cancer during pregnancy was established in 2001 to care for and guide individual patients and their family members as well as discuss possible treatment pathways based on the specificities of each individual patient's disease and other considerations such as reproductive status and age.

Breast cancer diagnosed in women during pregnancy is rare; occurring about once in every 3,000 pregnancies, most often in women aged 32 to 38 years. To help raise awareness that highly specialized, multidisciplinary teams comprising surgeons, oncologists, and obstetricians, can balance breast cancer treatment based on the specificities of each individual patient and at the same time keep the baby safe and well, patients who were attended at Vall d'Hebron, including their family members, joined together with Cristina Saura, 20 October, Mount Tibidabo in Barcelona.

escolaciència

Our Escola i Ciència (Schools and Science) educational initiative was established in 2017 to invite under-twelves from local primary schools to meet our faculty, tour our laboratories and learn more about cancer biology and research.

The main objectives of these half day events are to teach young and inquisitive minds about the importance of research in combating cancer, how we conduct our investigations, and hopefully inspire some of our visitors to ultimately become the next generation of researchers.



Escola i Ciència - Schools and Science, 22 November 2022: we welcomed primary school pupils from the Escola Les Aigües to VHIO to meet our faculty, tour our laboratories and learn more about cancer biology and research.

Due to the COVID-19 pandemic this program had to be mostly suspended once again this year. As the restrictions began to ease, we were able start planning for new visits and in November 2022 we welcomed 53 primary school pupils from the Escola Les Aigües to learn about the origins and development of cancer through an especially tailored talk presented by David Gómez Peregrina, Predoctoral Fellow of VHIO's Sarcoma Translational Research Group.

They also participated in junior masterclasses and various hands-on activities led and supervised by VHIO faculty including José Jiménez, Alba Llop Guevara, Andrea Herencia, Heura Domènech and María López.

VHIO's social media channels & platforms

In addition to our comprehensive lay media program and the invited participation and presence of our researchers and clinical investigators across a broad range of communication channels, VHIO Communications directed by Bianca Pont continues to expand our outreach activities through news announcements, campaigns, images, and videos tailored to our social media platforms and respective target audiences.

To discover what we are excited about, our latest news, and other developments that are catching our attention elsewhere, we invite you to follow us, and join in on our 'conversation' today:

www.vhio.net

Scientific productivity: research articles

Articles published in 2022

In 2022, 412 scientific articles were published by VHIO researchers as corresponding/senior or co-authors.

Figure I

Number of articles published by VHIO researchers from 2007 - 2022

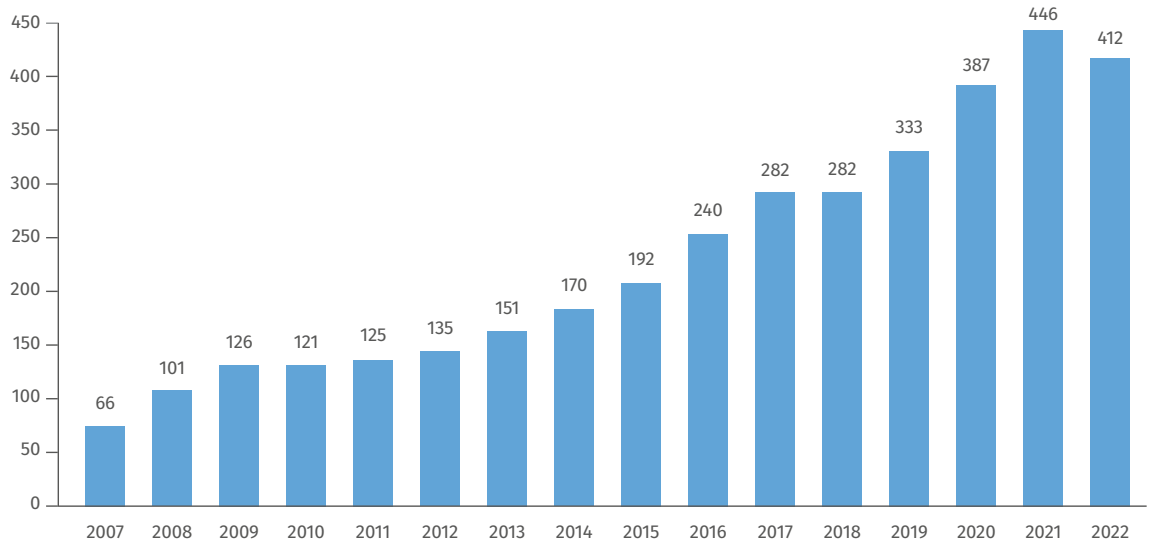
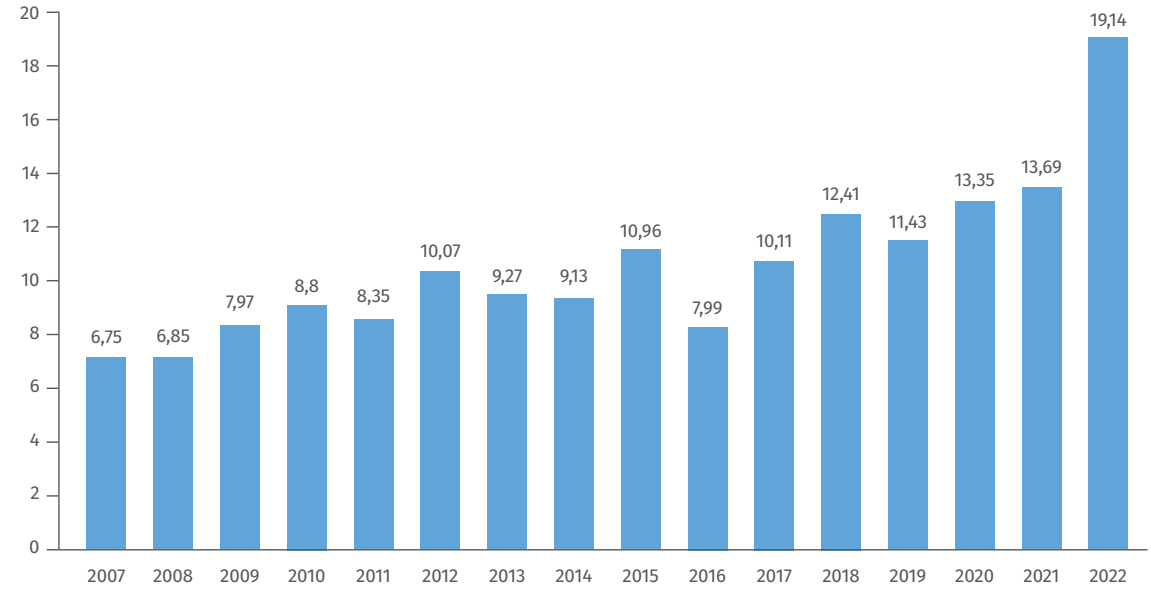


Figure II

Median Impact Factor of papers published by VHIO faculty from 2007 - 2022



For the complete list of VHIO scientific articles published in journals with allocated Impact Factor please see pages 156-181. To browse our selection of the most relevant articles (co) authored by VHIO researchers in 2022 please refer to pages 49-59 of this Scientific Report.

To view our Principal Investigators' selection of a maximum of 4 top papers per group in 2022 please see respective team pages (sub-section PI paper pick 2022). To access each group's full list of publications in 2022, as compiled by our Principal Investigators, visit the extended version of our Scientific Report online at: **http://memorias.vhio.net/2022**

INTRODUCING VHIO

Selection of some of the most relevant articles by VHIO researchers published in 2022

For the full listing of articles published by VHIO investigators in 2022 please refer to pages 156-181 of this report.

Antibody-drug conjugates: Smart chemotherapy delivery across tumor histologies. Tarantino P, Carmagnani Pestana R, Corti C, Modi S, Bardia A, Tolaney SM, Cortes J, Soria JC, Curigliano G. Antibody-drug conjugates: Smart chemotherapy delivery across tumor histologies. *CA Cancer J Clin*. 2022 Mar;72(2):165-182. IF: 286,130.

Adjuvant atezolizumab versus placebo for patients with renal cell carcinoma at increased risk of recurrence following resection (IMmotion010): a multicentre, randomised, double-blind, phase 3 trial. Pal SK, Uzzo R, Karam JA, Master VA, Donskov F, Suarez C, Albiges L, Rini B, Tomita Y, Kann AG, Procopio G, Massari F, Zibelman M, Antonyan I, Huseni M, Basu D, Ci B, Leung W, Khan O, Dubey S, Bex A. 2022 Oct 1;400(10358):1103-1116. IF: 202,731.

Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design. Fizazi K, Foulon S, Carles J, Roubaud G, McDermott R, Fléchon A, Tombal B, Supiot S, Berthold D, Ronchin P, Kacso G, Gravis G, Calabro F, Berdah JF, Hasbini A, Silva M, Thiery-Vuillemin A, Latorzeff I, Mourey L, Laguerre B, Abadie-Lacourtoisie S, Martin E, El Kouri C, Escande A, Rosello A, Magne N, Schlurmann F, Priou F, Chand-Fouche ME, Freixa SV, Jamaluddin M, Rieger I, Bossi A; PEACE-1 investigators. *Lancet*. 2022 Apr 30;399(10336):1695-1707. IF: 202,731.

Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. Dickinson MJ, Carlo-Stella C, Morschhauser F, Bachy E, Corradini P, Iacoboni G, Khan C, Wróbel T, Offner F, Trněný M, Wu SJ, Cartron G, Hertzberg M, Sureda A, Perez-Callejo D, Lundberg L, Relf J, Dixon M, Clark E, Humphrey K, Hutchings M. *N Engl J Med*. 2022 Dec 15;387(24):2220-2231. IF: 176,079.

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer. Modi S, Jacot W, Yamashita T, Sohn J, Vidal M, Tokunaga E, Tsurutani J, Ueno NT, Prat A, Chae YS, Lee KS, Niikura N, Park YH, Xu B, Wang X, Gil-Gil M, Li W, Pierga JY, Im SA, Moore HCF, Rugo HS, Yerushalmi R, Zagouri F, Gombos A, Kim SB, Liu Q, Luo T, Saura C, Schmid P, Sun T, Gambhire D, Yung L, Wang Y, Singh J, Vitazka P, Meinhardt G, Harbeck N, Cameron DA; DESTINY-Breast04 Trial Investigators. *N Engl J Med*. 2022 Jul 7;387(1):9-20. IF: 176,079.

Trastuzumab Deruxtecan for Breast Cancer. Reply. Cortés J, Im SA, Cathcart J. *N Engl J Med*. 2022 Jun 16;386(24):2347. IF: 176,079.

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. Forde PM, Spicer J, Lu S, Provencio M, Mitsudomi T, Awad MM, Felip E, Broderick SR, Brahmer JR, Swanson SJ, Kerr K, Wang C, Ciuleanu TE, Saylors GB, Tanaka F, Ito H, Chen KN, Liberman M, Vokes EE, Taube JM, Dorange C, Cai J, Fiore J, Jarkowski A, Balli D, Sausen M, Pandya D, Calvet CY, Girard N; CheckMate 816 Investigators. *N Engl J Med*. 2022 May 26;386(21):1973-1985. IF: 176,079.

Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma. Bishop MR, Dickinson M, Purtill D, Barba P, Santoro A, Hamad N, Kato K, Sureda A, Greil R, Thieblemont C, Morschhauser F, Janz M, Flinn I, Rabitsch W, Kwong YL, Kersten MJ, Minnema MC, Holte H, Chan EHL, Martinez-Lopez J, Müller AMS, Maziarz RT, McGuirk JP, Bachy E, Le Gouill S, Dreyling M, Harigae H, Bond D, Andreadis C, McSweeney P, Kharfan-Dabaja M, Newsome S, Degtyarev E, Awasthi R, Del Corral C, Andreola G, Masood A, Schuster SJ, Jäger U, Borchmann P, Westin JR. *N Engl J Med*. 2022 Feb 17;386(7):629-639. IF: 176,079.

Event-free Survival with Pembrolizumab in Early Triple-Negative Breast Cancer. Schmid P, Cortes J, Dent R, Pusztai L, McArthur H, Kümmel S, Bergh J, Denkert C, Park YH, Hui R, Harbeck N, Takahashi M, Untch M, Fasching PA, Cardoso F, Andersen J, Patt D, Danso M, Ferreira M, Mouret-Reynier MA, Im SA, Ahn JH, Gion M, Baron-Hay S, Boileau JF, Ding Y, Tryfonidis K, Aktan G, Karantza V, O'Shaughnessy J; KEYNOTE-522 Investigators. *N Engl J Med*. 2022 Feb 10;386(6):556-567. IF: 176,079.

Survival with Cemiplimab in Recurrent Cervical Cancer. Tewari KS, Monk BJ, Vergote I, Miller A, de Melo AC, Kim HS, Kim YM, Lisyanskaya A, Samouëlian V, Lorusso D, Damian F, Chang CL, Gotovkin EA, Takahashi S, Ramone D, Pikiel J, Mańkowiak-Matejczyk B, Guerra Alía EM, Colombo N, Makarova Y, Rischin D, Lheureux S, Hasegawa K, Fujiwara K, Li J, Jamil S, Jankovic V, Chen CI, Seebach F, Weinreich DM, Yancopoulos GD, Lowy I, Mathias M, Fury MG, Oaknin A; Investigators for GOG Protocol 3016 and ENGOT Protocol En-Cx9. *N Engl J Med*. 2022 Feb 10;386(6):544-555. IF: 176,079.

Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma. Tilly H, Morschhauser F, Sehn LH, Friedberg JW, Trněný M, Sharman JP, Herbaux C, Burke JM, Matasar M, Rai S, Izutsu K, Mehta-Shah N, Oberic L, Chauchet A, Jurczak W, Song Y, Greil R, Mykhalska L, Bergua-Burgués JM, Cheung MC, Pinto A, Shin HJ, Hapgood G, Munhoz E, Abrisqueta P, Gau JP, Hirata J, Jiang Y, Yan M, Lee C, Flowers CR, Salles G. *N Engl J Med*. 2022 Jan 27;386(4):351-363. IF: 176,079.

Trastuzumab Deruxtecan in HER2-Mutant Non-Small-Cell Lung Cancer. Li BT, Smit EF, Goto Y, Nakagawa K, Udagawa H, Mazières J, Nagasaka M, Bazhenova L, Saltos AN, Felip E, Pacheco JM, Pérol M, Paz-Ares L, Saxena K, Shiga R, Cheng Y, Acharyya S, Vitazka P, Shahidi J, Planchard D, Jänne PA; DESTINY-Lung01 Trial Investigators. *N Engl J Med*. 2022 Jan 20;386(3):241-251. IF: 176,079.

Circulating tumor DNA as a novel prognostic indicator. Vivancos A, Tabernero J. *Nat Med*. 2022 Nov;28(11):2255-2256. IF: 87,241.

RNF43 mutations predict response to anti-BRAF/EGFR combinatory therapies in BRAFV600E metastatic colorectal cancer. Elez E, Ros J, Fernández J, Villacampa G, Moreno-Cárdenas AB, Arenillas C, Bernatowicz K, Comas R, Li S, Kodack DP, Fasani R, Garcia A, Gonzalo-Ruiz J, Piris-Gimenez A, Nuciforo P, Kerr G, Intini R, Montagna A, Germani MM, Randon G, Vivancos A, Smits R, Graus D, Perez-Lopez R, Cremolini C, Lonardi S, Pietrantonio F, Dienstmann R, Tabernero J, Toledo RA. *Nat Med*. 2022 Oct;28(10):2162-2170. IF: 87,241.

A biomarker of response to therapy in metastatic BRAFV600E colorectal cancers. Toledo RA, Elez E. *Nat Med*. 2022 Oct;28(10):2015-2016. IF: 87,241.

Atezolizumab versus chemotherapy in advanced or metastatic NSCLC with high blood-based tumor mutational burden: primary analysis of BFAST cohort C randomized phase 3 trial. Peters S, Dziadziuszko R, Morabito A, Felip E, Gadgeel SM, Cheema P, Cobo M, Andric Z, Barrios CH, Yamaguchi M, Dansin E, Danchaivijitr P, Johnson M, Novello S, Mathisen MS, Shagan SM, Schleifman E, Wang J, Yan M, Mocci S, Voong D, Fabrizio DA, Shames DS, Riehl T, Gandara DR,

Mok T. *Nat Med*. 2022 Sep;28(9):1831-1839. IF: 87,241.

Pan-cancer efficacy of pralsetinib in patients with RET fusion-positive solid tumors from the phase 1/2 ARROW trial. Subbiah V, Cassier PA, Siena S, Garralda E, Paz-Ares L, Garrido P, Nadal E, Vuky J, Lopes G, Kalemkerian GP, Bowles DW, Seetharam M, Chang J, Zhang H, Green J, Zalutskaya A, Schuler M, Fan Y, Curigliano G. *Nat Med*. 2022 Aug;28(8):1640-1645. IF: 87,241.

Detection of early seeding of Richter transformation in chronic lymphocytic leukemia. Nadeu F, Royo R, Massoni-Badosa R, Playa-Albinyana H, Garcia-Torre B, Duran-Ferrer M, Dawson KJ, Kulis M, Diaz-Navarro A, Villamor N, Melero JL, Chapaprieta V, Dueso-Barroso A, Delgado J, Moia R, Ruiz-Gil S, Marchese D, Giró A, Verdaguer-Dot N, Romo M, Clot G, Rozman M, Frigola G, Rivas-Delgado A, Baumann T, Alcoceba M, González M, Climent F, Abrisqueta P, Castellví J, Bosch F, Aymerich M, Enjuanes A, Ruiz-Gaspà S, López-Guillermo A, Jares P, Beà S, Capella-Gutierrez S, Gelpí JL, López-Bigas N, Torrents D, Campbell PJ, Gut I, Rossi D, Gaidano G, Puente XS, Garcia-Roves PM, Colomer D, Heyn H, Maura F, Martín-Subero JI, Campo E. *Nat Med*. 2022 Aug;28(8):1662-1671. IF: 87,241.

Delivering precision oncology to patients with cancer. Mateo J, Steuten L, Aftimos P, André F, Davies M, Garralda E, Geissler J, Husereau D, Martinez-Lopez I, Normanno N, Reis-Filho JS, Stefani S, Thomas DM, Westphalen CB, Voest E. *Nat Med*. 2022 Apr;28(4):658-665. IF: 87,241.

Cerebrospinal fluid liquid biopsies for medulloblastoma. Seoane J, Escudero L. *Nat Rev Clin Oncol*. 2022 Feb;19(2):73-74. IF: 65,011.

Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB-IIIA non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial. O'Brien M, Paz-Ares L, Marreaud S, Dafni U, Oselin K, Havel L, Esteban E, Isla D, Martinez-Marti A, Faehling M, Tsuboi M, Lee JS, Nakagawa K, Yang J, Samkari A, Keller SM, Mauer M, Jha N, Stahel R, Besse B, Peters S; EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 Investigators. *Lancet Oncol*. 2022 Oct;23(10):1274-1286. IF: 54,433.

CNS prophylaxis for diffuse large B-cell lymphoma. Eyre TA, Savage KJ, Cheah CY, El-Galaly TC, Lewis KL, McKay P, Wilson MR, Evens AM, Bobillo S, Villa D, Maurer MJ, Cwynarski K, Ferreri AJM. *Lancet Oncol*. 2022 Sep;23(9):e416-e426. IF: 54,433.

Is upfront full molecular profiling needed in all patients with colorectal cancer in daily practice? Dienstmann R, Lonardi S. *Lancet Oncol*. 2022 Sep;23(9):1129-1131. IF: 54,433.

Outcomes of the SARS-CoV-2 omicron (B.1.1.529) variant outbreak among vaccinated and unvaccinated patients with cancer in Europe: results from the retrospective, multicentre, OnCovid registry study. Pinato DJ, Aguilar-Company J, Ferrante D, Hanbury G, Bower M, Salazar R, Mirallas O, Sureda A, Plaja A, Cucurull M, Mesia R, Townsend S, Jackson A, Dalla Pria A, Newsom-Davis T, Handford J, Sita-Lumsden A, Apthorp E, Vincenzi B, Bertuzzi A, Brunet J, Lambertini M, Maluquer C, Pedrazzoli P, Biello F, Sinclair A, Bawany S, Khalique S, Rossi S, Rogers L, Murphy C, Belessiotis K, Carmona-García MC, Sharkey R, García-Illescas D, Rizzo G, Perachino M, Saoudi-Gonzalez N, Doonga K, Fox L, Roldán E, Gaidano G, Ruiz-Camps I, Bruna R, Patriarca A, Martinez-Vila C, Cantini L, Zambelli A, Giusti R, Mazzoni F, Caliman E, Santoro A, Grosso F, Parisi A, Queirolo P, Aujayeb A, Rimassa L, Prat A, Tucci M, Libertini M, Grisanti S, Mukherjee U, Diamantis N, Fusco V, Generali D, Provenzano S, Gennari A, Tabernero J, Cortellini A; OnCovid study group. *Lancet Oncol*. 2022 Jul;23(7):865-875. IF: 54,433.

Immunotherapy in colorectal cancer: an unmet need deserving of change. Elez E, Baraibar I. *Lancet Oncol*. 2022 Jul;23(7):830-831. IF: 54,433.

Nivolumab plus cabozantinib versus sunitinib in first-line treatment for advanced renal cell carcinoma (CheckMate 9ER): long-term follow-up results from an open-label, randomised, phase 3 trial. Motzer RJ, Powles T, Burotto M, Escudier B, Bourlon MT, Shah AY, Suárez C, Hamzaj A, Porta C, Hocking CM, Kessler ER, Gurney H, Tomita Y, Bedke J, Zhang J, Simsek B, Scheffold C, Apolo AB, Choueiri TK. *Lancet Oncol*. 2022 Jul;23(7):888-898. IF: 54,433.

Pembrolizumab versus chemotherapy for microsatellite instability-high or mismatch repair-deficient metastatic colorectal cancer (KEYNOTE-177): final analysis of a randomised, open-label, phase 3 study. Diaz LA Jr, Shiu KK, Kim TW, Jensen BV, Jensen LH, Punt C, Smith D, Garcia-Carbonero R, Benavides M, Gibbs P, de la Fourchardiere C, Rivera F, Elez E, Le DT, Yoshino T, Zhong WY, Fogelman D, Marinello P, Andre T; KEYNOTE-177 Investigators. *Lancet Oncol*. 2022 May;23(5):659-670. IF: 54,433.

Rucaparib versus standard-of-care chemotherapy in patients with relapsed ovarian cancer and a deleterious BRCA1 or BRCA2 mutation (ARIEL4): an international, open-label, randomised, phase 3 trial. Kristeleit R, Lisyanskaya A, Fedenko A, Dvorkin M, de Melo AC, Shparyk Y, Rakhmatullina I, Bondarenko I, Colombo N, Svintsitskiy V, Biela L, Nechaeva M, Lorusso D, Scambia G, Cibula D, Póka R, Oaknin A, Safra T, Mackowiak-Matejczyk B, Ma L, Thomas D, Lin KK, McLachlan K, Goble S, Oza AM. *Lancet Oncol*. 2022 Apr;23(4):465-478. IF: 54,433.

Anetumab ravtansine versus vinorelbine in patients with relapsed, mesothelin-positive malignant pleural mesothelioma (ARCS-M): a randomised, open-label phase 2 trial. Kindler HL, Novello S, Bearz A, Ceresoli GL, Aerts JGJV, Spicer J, Taylor P, Nackaerts K, Greystoke A, Jennens R, Calabrò L, Burgers JA, Santoro A, Cedrés S, Serwatowski P, Ponce S, Van Meerbeeck JP, Nowak AK, Blumenschein G Jr, Siegel JM, Kasten L, Köchert K, Walter AO, Childs BH, Elbi C, Hassan R, Fennell DA. *Lancet Oncol*. 2022 Apr;23(4):540-552. IF: 54,433.

Niraparib in patients with metastatic castration-resistant prostate cancer and DNA repair gene defects (GALAHAD): a multicentre, open-label, phase 2 trial. Smith MR, Scher HI, Sandhu S, Efstathiou E, Lara PN Jr, Yu EY, George DJ, Chi KN, Saad F, Ståhl O, Olmos D, Danila DC, Mason GE, Espina BM, Zhao X, Urtishak KA, Francis P, Lopez-Gitlitz A, Fizazi K; GALAHAD investigators. *Lancet Oncol*. 2022 Mar;23(3):362-373.IF: 54,433.

Efficacy and safety of erdafitinib in patients with locally advanced or metastatic urothelial carcinoma: long-term follow-up of a phase 2 study. Siefker-Radtke AO, Necchi A, Park SH, García-Donas J, Huddart RA, Burgess EF, Fleming MT, Rezazadeh Kalebasty A, Mellado B, Varlamov S, Joshi M, Duran I, Tagawa ST, Zakharia Y, Akapame S, Santiago-Walker AE, Monga M, O'Hagan A, Loriot Y; BLC2001 Study Group. *Lancet Oncol*. 2022 Feb;23(2):248-258. IF: 54,433.

Patient-reported outcomes with first-line nivolumab plus cabozantinib versus sunitinib in patients with advanced renal cell carcinoma treated in CheckMate 9ER: an open-label, randomised, phase 3 trial. Cella D, Motzer RJ, Suarez C, Blum SI, Ejzykowicz F, Hamilton M, Wallace JF, Simsek B, Zhang J, Ivanescu C, Apolo AB, Choueiri TK. *Lancet Oncol*. 2022 Feb;23(2):292-303. IF: 54,433.

Overall survival in the OlympiA phase III trial of adjuvant olaparib in patients with germline pathogenic variants in BRCA1/2 and high-risk, early breast cancer. Geyer CE Jr, Garber JE, Gelber RD, Yothers G, Taboada M, Ross L, Rastogi P, Cui K, Arahmani A, Aktan G, Armstrong AC, Arnedos M, Balmaña J, Bergh J, Bliss J, Delaloge S, Domchek SM, Eisen A, Elsafy F, Fein LE, Fielding A, Ford JM, Friedman S, Gelmon KA, Gianni L, Gnant M, Hollingsworth SJ, Im SA, Jager A, Jóhannsson ÓÞ, Lakhani SR, Janni W, Linderholm B, Liu TW, Loman N, Korde L, Loibl S, Lucas PC, Marmé F, Martinez de Dueñas E, McConnell R, Phillips KA, Piccart M, Rossi G, Schmutzler R, Senkus E, Shao Z, Sharma P, Singer CF, Španić T, Stickeler E, Toi M, Traina TA, Viale G, Zoppoli G, Park YH, Yerushalmi R, Yang H, Pang D, Jung KH, Mailliez A, Fan Z, Tennevet I, Zhang J, Nagy T,

Sonke GS, Sun Q, Parton M, Colleoni MA, Schmidt M, Brufsky AM, Razaq W, Kaufman B, Cameron D, Campbell C, Tutt ANJ; OlympiA Clinical Trial Steering Committee and Investigators. *Ann Oncol*. 2022 Dec;33(12):1250-1268. IF: 51,769.

Safety and efficacy of pralsetinib in RET fusion-positive non-small-cell lung cancer including as first-line therapy: update from the ARROW trial. Griesinger F, Curigliano G, Thomas M, Subbiah V, Baik CS, Tan DSW, Lee DH, Misch D, Garralda E, Kim DW, van der Wekken AJ, Gainor JF, Paz-Ares L, Liu SV, Kalemkerian GP, Houvras Y, Bowles DW, Mansfield AS, Lin JJ, Smoljanovic V, Rahman A, Kong S, Zalutskaya A, Louie-Gao M, Boral AL, Mazières J. *Ann Oncol*. 2022 Nov;33(11):1168-1178.IF: 51,769.

Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Obermannová R, Alsina M, Cervantes A, Leong T, Lordick F, Nilsson M, van Grieken NCT, Vogel A, Smyth EC; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. *Ann Oncol*. 2022 Oct;33(10):992-1004. IF: 51,769.

Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Oaknin A, Bosse TJ, Creutzberg CL, Giornelli G, Harter P, Joly F, Lorusso D, Marth C, Makker V, Mirza MR, Ledermann JA, Colombo N; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. *Ann Oncol*. 2022 Sep;33(9):860-877. IF: 51,769.

ESMO recommendations on the use of circulating tumour DNA assays for patients with cancer: a report from the ESMO Precision Medicine Working Group. Pascual J, Attard G, Bidard FC, Curigliano G, De Mattos-Arruda L, Diehn M, Italiano A, Lindberg J, Merker JD, Montagut C, Normanno N, Pantel K, Pentheroudakis G, Popat S, Reis-Filho JS, Tie J, Seoane J, Tarazona N, Yoshino T, Turner NC. *Ann Oncol*. 2022 Aug;33(8):750-768. IF: 51,769.

3-Year CheckMate743 outcomes: ringing in immunotherapy for the treatment of malignant pleural mesothelioma. Cedres S, Felip E. *Ann Oncol*. 2022 May;33(5):457-459. IF: 51,769.

Effectiveness of PD-(L)1 inhibitors alone or in combination with platinum-doublet chemotherapy in first-line (1L) non-squamous non-small-cell lung cancer (Nsq-NSCLC) with PD-L1-high expression using real-world data. Pérol M, Felip E, Dafni U, Polito L, Pal N, Tsourti Z, Ton TGN, Merritt D, Morris S, Stahel R, Peters S. *Ann Oncol*. 2022 May;33(5):511-521. IF: 51,769.

ESMO expert consensus statements on the management of EGFR mutant non-small-cell lung cancer. Passaro A, Leighl N, Blackhall F, Popat S, Kerr K, Ahn MJ, Arcila ME, Arrieta O, Planchard D, de Marinis F, Dingemans AM, Dziadziuszko R, Faivre-Finn C, Feldman J, Felip E, Curigliano G, Herbst R, Jänne PA, John T, Mitsudomi T, Mok T, Normanno N, Paz-Ares L, Ramalingam S, Sequist L, Vansteenkiste J, Wistuba II, Wolf J, Wu YL, Yang SR, Yang JCH, Yatabe Y, Pentheroudakis G, Peters S. *Ann Oncol*. 2022 May;33(5):466-487. IF: 51,769.

Safety, pharmacokinetics, and antitumor activity of the anti-CEACAM5-DM4 antibody-drug conjugate tusamitamab ravtansine (SAR408701) in patients with advanced solid tumors: first-in-human dose-escalation study. Gazzah A, Bedard PL, Hierro C, Kang YK, Abdul Razak A, Ryu MH, Demers B, Fagniez N, Henry C, Hospitel M, Soria JC, Tabernero J. *Ann Oncol*. 2022 Apr;33(4):416-425. IF: 51,769.

VP3-2022: Pembrolizumab (pembro) versus placebo for early-stage non-small cell lung cancer (NSCLC) following complete resection and adjuvant chemotherapy (chemo) when indicated: Randomized, triple-blind, phase III EORTC-1416-LCG/ETOP 8-15 e PEARLS/KEYNOTE-091 study. Paz-Ares L, O'Brien MER, Mauer M, Dafni U, Oselin K, Havel L, Gonzalez EE, Isla D, Martinez A, Faehling M, Tsuboi M, Lee J-S, Nakagawa K, Yang J, Keller SM, Jha N, Marreaud SI, Stahel RA, Peters S, Besse B. *Ann Oncol*. 2022. 33(4): 451-453. IF: 51,769.

A Randomized, Phase III Trial to Evaluate Rucaparib Monotherapy as Maintenance Treatment in Patients With Newly Diagnosed Ovarian Cancer (ATHENA-MONO/GOG-3020/ENGOT-ov45). Monk BJ, Parkinson C, Lim MC, O'Malley DM, Oaknin A, Wilson MK, Coleman RL, Lorusso D, Bessette P, Ghamande S, Christopoulou A, Provencher D, Prendergast E, Demirkiran F, Mikheeva O, Yeku O, Chudecka-Glaz A, Schenker M, Littell RD, Safra T, Chou HH, Morgan MA, Drochýtek V, Barlin JN, Van Gorp T, Ueland F, Lindahl G, Anderson C, Collins DC, Moore K, Marme F, Westin SN, McNeish IA, Shih D, Lin KK, Goble S, Hume S, Fujiwara K, Kristeleit RS. *J Clin Oncol*. 2022 Dec 1;40(34):3952-3964. IF: 50,717.

Overall Survival Results From the POLO Trial: A Phase III Study of Active Maintenance Olaparib Versus Placebo for Germline BRCA-Mutated Metastatic Pancreatic Cancer. Kindler HL, Hammel P, Reni M, Van Cutsem E, Macarulla T, Hall MJ, Park JO, Hochhauser D, Arnold D, Oh DY, Reinacher-Schick A, Tortora G, Algül H, O'Reilly EM, Bordia S, McGuinness D, Cui K, Locker GY, Golan T. *J Clin Oncol*. 2022 Dec 1;40(34):3929-3939. IF: 50,717.

COAST: An Open-Label, Phase II, Multidrug Platform Study of Durvalumab Alone or in Combination With Oleclumab or Monalizumab in Patients With Unresectable, Stage III Non-Small-Cell Lung Cancer. Herbst RS, Majem M, Barlesi F, Carcereny E, Chu Q, Monnet I, Sanchez-Hernandez A, Dakhil S, Camidge DR, Winzer L, Soo-Hoo Y, Cooper ZA, Kumar R, Bothos J, Aggarwal C, Martinez-Marti A. *J Clin Oncol*. 2022 Oct 10;40(29):3383-3393. IF: 50,717.

Sacituzumab Govitecan in Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer. Rugo HS, Bardia A, Marmé F, Cortes J, Schmid P, Loirat D, Trédan O, Ciruelos E, Dalenc F, Pardo PG, Jhaveri KL, Delaney R, Fu O, Lin L, Verret W, Tolaney SM. *J Clin Oncol*. 2022 Oct 10;40(29):3365-3376. IF: 50,717.

Elacestrant (oral selective estrogen receptor degrader) Versus Standard Endocrine Therapy for Estrogen Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer: Results From the Randomized Phase III EMERALD Trial. Bidard FC, Kaklamani VG, Neven P, Streich G, Montero AJ, Forget F, Mouret-Reynier MA, Sohn JH, Taylor D, Harnden KK, Khong H, Kocsis J, Dalenc F, Dillon PM, Babu S, Waters S, Deleu I, García Sáenz JA, Bria E, Cazzaniga M, Lu J, Aftimos P, Cortés J, Liu S, Tonini G, Laurent D, Habboubi N, Conlan MG, Bardia A. *J Clin Oncol*. 2022 Oct 1;40(28):3246-3256. IF: 50,717.

Overall Survival and Biomarker Analysis of Neoadjuvant Nivolumab Plus Chemotherapy in Operable Stage IIIA Non-Small-Cell Lung Cancer (NADIM phase II trial). Provencio M, Serna-Blasco R, Nadal E, Insa A, García-Campelo MR, Casal Rubio J, Dómine M, Majem M, Rodríguez-Abreu D, Martínez-Martí A, De Castro Carpeño J, Cobo M, López Vivanco G, Del Barco E, Bernabé Caro R, Viñolas N, Barneto Aranda I, Viteri S, Pereira E, Royuela A, Calvo V, Martín-López J, García-García F, Casarrubios M, Franco F, Sánchez-Herrero E, Massuti B, Cruz-Bermúdez A, Romero A. *J Clin Oncol*. 2022 Sep 1;40(25):2924-2933. IF: 50,717.

Pembrolizumab Alone or With Chemotherapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma in KEYNOTE-048: Subgroup Analysis by Programmed Death Ligand-1 Combined Positive Score. Burtness B, Rischin D, Greil R, Soulières D, Tahara M, de Castro G Jr, Psyrri A, Brana I, Basté N, Neupane P, Bratland Å, Fuereder T, Hughes BGM, Mesia R, Ngamphaiboon N, Rordorf T, Wan Ishak WZ, Ge J, Swaby RF, Gumuscu B, Harrington K. *J Clin Oncol*. 2022 Jul 20;40(21):2321-2332. IF: 50,717.

Ibrutinib in Combination With Rituximab for Indolent Clinical Forms of Mantle Cell Lymphoma (IMCL-2015): A Multicenter, Open-Label, Single-Arm, Phase II Trial. Giné E, de la Cruz F, Jiménez Ubieto A, López Jimenez J, Martín García-Sancho A, Terol MJ, González Barca E, Casanova M, de la Fuente A, Marín-Niebla A, Muntañola A, González-López TJ, Aymerich M, Setoain X, Cortés-Romera M, Rotger A, Rodríguez S, Medina Herrera A, García Sanz R, Nadeu F, Beà S, Campo E, López-Guillermo A . *J Clin*

Oncol. 2022 Apr 10;40(11):1196-1205. IF: 50,717.

Single-Agent Mosunetuzumab Shows Durable Complete Responses in Patients With Relapsed or Refractory B-Cell Lymphomas: Phase I Dose-Escalation Study. Budde LE, Assouline S, Sehn LH, Schuster SJ, Yoon SS, Yoon DH, Matasar MJ, Bosch F, Kim WS, Nastoupil LJ, Flinn IW, Shadman M, Diefenbach C, O'Hear C, Huang H, Kwan A, Li CC, Piccione EC, Wei MC, Yin S, Bartlett NL. *J Clin Oncol*. 2022 Feb 10;40(5):481-491. IF: 50,717.

Adjuvant Palbociclib for Early Breast Cancer: The PALLAS Trial Results (ABCSG-42/AFT-05/BIG-14-03). Gnant M, Dueck AC, Frantal S, Martin M, Burstein HJ, Greil R, Fox P, Wolff AC, Chan A, Winer EP, Pfeiler G, Miller KD, Colleoni M, Suga JM, Rubovsky G, Bliss JM, Mayer IA, Singer CF, Nowecki Z, Hahn O, Thomson J, Wolmark N, Amillano K, Rugo HS, Steger GG, Hernando Fernández de Aránguiz B, Haddad TC, Perelló A, Bellet M, Fohler H, Metzger Filho O, Jallitsch-Halper A, Solomon K, Schurmans C, Theall KP, Lu DR, Tenner K, Fesl C, DeMichele A, Mayer EL; PALLAS groups and investigators. *J Clin Oncol*. 2022 Jan 20;40(3):282-293. IF: 50,717.

Molecular classification and biomarkers of clinical outcome in breast ductal carcinoma in situ: Analysis of TBCRC 038 and RAHBT cohorts. Strand SH, Rivero-Gutiérrez B, Houlahan KE, Seoane JA, King LM, Risom T, Simpson LA, Vennam S, Khan A, Cisneros L, Hardman T, Harmon B, Couch F, Gallagher K, Kilgore M, Wei S, DeMichele A, King T, McAuliffe PF, Nangia J, Lee J, Tseng J, Storniolo AM, Thompson AM, Gupta GP, Burns R, Veis DJ, DeSchryver K, Zhu C, Matusiak M, Wang J, Zhu SX, Tappenden J, Ding DY, Zhang D, Luo J, Jiang S, Varma S, Anderson L, Straub C, Srivastava S, Curtis C, Tibshirani R, Angelo RM, Hall A, Owzar K, Polyak K, Maley C, Marks JR, Colditz GA, Hwang ES, West RB. *Cancer Cell*. 2022 Dec 12;40(12):1521-1536.e7. IF: 38,585.

Fast track to personalized TCR T cell therapies. Levy PL, Gros A. *Cancer Cell*. 2022 May 9;40(5):447-449. IF: 38,585.

Trastuzumab Deruxtecan in HER2-Positive Metastatic Breast Cancer Patients with Brain Metastases: A DESTINY-Breast01 Subgroup Analysis. Jerusalem G, Park YH, Yamashita T, Hurvitz SA, Modi S, Andre F, Krop IE, Gonzàlez Farré X, You B, Saura C, Kim SB, Osborne CR, Murthy RK, Gianni L, Takano T, Liu Y, Cathcart J, Lee C, Perrin C. *Cancer Discov*. 2022 Dec 2;12(12):2754-2762. IF: 38,272.

UNCAN.eu, a European Initiative to UNderstand CANcer. Solary E, Blanc P, Boutros M, Girvalaki C, Locatelli F, Medema RH, Nagy P, Tabernero J. *Cancer Discov*. 2022 Nov 2;12(11):2504-2508. IF: 38,272.

Preclinical Characterization and Phase I Trial Results of a Bispecific Antibody Targeting PD-L1 and 4-1BB (GEN1046) in Patients with Advanced Refractory Solid Tumors. Muik A, Garralda E, Altintas I, Gieseke F, Geva R, Ben-Ami E, Maurice-Dror C, Calvo E, LoRusso PM, Alonso G, Rodriguez-Ruiz ME, Schoedel KB, Blum JM, Sänger B, Salcedo TW, Burm SM, Stanganello E, Verzijl D, Vascotto F, Sette A, Quinkhardt J, Plantinga TS, Toker A, van den Brink EN, Fereshteh M, Diken M, Satijn D, Kreiter S, Breij ECW, Bajaj G, Lagkadinou E, Sasser K, Türeci Ö, Forssmann U, Ahmadi T, Şahin U, Jure-Kunkel M, Melero I. *Cancer Discov*. 2022 May 2;12(5):1248-1265. IF: 38,272.

INK4 Tumor Suppressor Proteins Mediate Resistance to CDK4/6 Kinase Inhibitors. Li Q, Jiang B, Guo J, Shao H, Del Priore IS, Chang Q, Kudo R, Li Z, Razavi P, Liu B, Boghossian AS, Rees MG, Ronan MM, Roth JA, Donovan KA, Palafox M, Reis-Filho JS, de Stanchina E, Fischer ES, Rosen N, Serra V, Koff A, Chodera JD, Gray NS, Chandarlapaty S. *Cancer Discov*. 2022 Feb;12(2):356-371. IF: 38,272.

Futibatinib, an Irreversible FGFR1-4 Inhibitor, in Patients with Advanced Solid Tumors Harboring FGF/FGFR Aberrations: A Phase I Dose-Expansion Study. Meric-Bernstam F, Bahleda R, Hierro C, Sanson M, Bridgewater J, Arkenau HT, Tran B, Kelley RK, Park JO, Javle M, He Y, Benhadji KA, Goyal L. *Cancer Discov*. 2022 Feb;12(2):402-415. IF: 38,272.

Treatment With Etirinotecan Pegol for Patients With Metastatic Breast Cancer and Brain Metastases: Final Results From the Phase 3 ATTAIN Randomized Clinical Trial. Tripathy D, Tolaney SM, Seidman AD, Anders CK, Ibrahim N, Rugo HS, Twelves C, Diéras V, Müller V, Du Y, Currie SL, Hoch U, Tagliaferri M, Hannah AL, Cortés J; ATTAIN Investigators. *JAMA Oncol*. 2022 Jul 1;8(7):1047-1052. IF: 33,006.

Final Overall Survival and Molecular Analysis in IMmotion151, a Phase 3 Trial Comparing Atezolizumab Plus Bevacizumab vs Sunitinib in Patients With Previously Untreated Metastatic Renal Cell Carcinoma. Motzer RJ, Powles T, Atkins MB, Escudier B, McDermott DF, Alekseev BY, Lee JL, Suarez C, Stroyakovskiy D, De Giorgi U, Donskov F, Mellado B, Banchereau R, Hamidi H, Khan O, Craine V, Huseni M, Flinn N, Dubey S, Rini BI. *JAMA Oncol*. 2022 Feb 1;8(2):275-280. IF: 33,006.

Implications of Selection Bias Due to Delayed Study Entry in Clinical Genomic Studies. Brown S, Lavery JA, Shen R, Martin AS, Kehl KL, Sweeney SM, Lepisto EM, Rizvi H, McCarthy CG, Schultz N, Warner JL, Park BH, Bedard PL, Riely GJ, Schrag D, Panageas KS; AACR Project GENIE Consortium. *JAMA Oncol*. 2022 Feb 1;8(2):287-291. IF: 33,006.

Time-Dependent COVID-19 Mortality in Patients With Cancer: An Updated Analysis of the OnCovid Registry. OnCovid Study Group; Pinato DJ, Patel M, Scotti L, Colomba E, Dolly S, Loizidou A, Chester J, Mukherjee U, Zambelli A, Dalla Pria A, Aguilar-Company J, Bower M, Salazar R, Bertuzzi A, Brunet J, Lambertini M, Tagliamento M, Pous A, Sita-Lumsden A, Srikandarajah K, Colomba J, Pommeret F, Seguí E, Generali D, Grisanti S, Pedrazzoli P, Rizzo G, Libertini M, Moss C, Evans JS, Russell B, Harbeck N, Vincenzi B, Biello F, Bertulli R, Ottaviani D, Liñan R, Rossi S, Carmona-García MC, Tondini C, Fox L, Baggi A, Fotia V, Parisi A, Porzio G, Queirolo P, Cruz CA, Saoudi-Gonzalez N, Felip E, Roqué Lloveras A, Newsom-Davis T, Sharkey R, Roldán E, Reyes R, Zoratto F, Earnshaw I, Ferrante D, Marco-Hernández J, Ruiz-Camps I, Gaidano G, Patriarca A, Bruna R, Sureda A, Martinez-Vila C, Sanchez de Torre A, Berardi R, Giusti R, Mazzoni F, Guida A, Rimassa L, Chiudinelli L, Franchi M, Krengli M, Santoro A, Prat A, Tabernero J, Van Hemelrijck M, Diamantis N, Gennari A, Cortellini A. *JAMA Oncol*. 2022 Jan 1;8(1):114-122. IF: 33,006.

Melflufen or pomalidomide plus dexamethasone for patients with multiple myeloma refractory to lenalidomide (OCEAN): a randomised, head-to-head, open-label, phase 3 study. Schjesvold FH, Dimopoulos MA, Delimpasi S, Robak P, Coriu D, Legiec W, Pour L, Špička I, Masszi T, Doronin V, Minarik J, Salogub G, Alekseeva Y, Lazzaro A, Maisnar V, Mikala G, Rosiñol L, Liberati AM, Symeonidis A, Moody V, Thuresson M, Byrne C, Harmenberg J, Bakker NA, Hájek R, Mateos MV, Richardson PG, Sonneveld P; OCEAN (OP-103) Investigators. *Lancet Haematol*. 2022 Feb;9(2):e98-e110. IF: 30,153.

Breakthrough COVID-19 in vaccinated patients with hematologic malignancies: results from the EPICOVIDEHA survey. Pagano L, Salmanton-García J, Marchesi F, Blennow O, Gomes da Silva M, Glenthøj A, van Doesum J, Bilgin YM, López-García A, Itri F, Nunes Rodrigues R, Weinbergerová B, Farina F, Dragonetti G, Berg Venemyr C, van Praet J, Jaksic O, Valković T, Falces-Romero I, Martín-Pérez S, Jiménez M, Dávila-Valls J, Schönlein M, Ammatuna E, Meers S, Delia M, Stojanoski Z, Nordlander A, Lahmer T, Imre Pinczés L, Buquicchio C, Piukovics K, Ormazabal-Vélez I, et al. *Blood*. 2022 Dec 29;140(26):2773-2787. IF: 25,476.

Ibrutinib improves survival compared with chemotherapy in mantle cell lymphoma with central nervous system relapse. Rusconi C, Cheah CY, Eyre TA, Tucker D, Klener P, Giné E, Crucitti L, Muzi C, Iadecola S, Infante G, Bernard S, Auer RL, Pagani C, Duglosz-Danecka M, Mocikova H, van Meerten T, Cencini E, Marin-Niebla A, Williams ME, Angelillo P, Nicoli P, Arcari A, Morello L, Mannina D, Vitagliano O, Sartori R, Chiappella

A, Sciarra R, Stefani PM, Dreyling M, Seymour JF, Visco C. *Blood*. 2022 Oct 27;140(17):1907-1916. IF: 25,476.

Hematopoietic stem cell transplantation for adolescents and adults with inborn errors of immunity: an EBMT IEWP study. Albert MH, Sirait T, Eikema DJ, Bakunina K, Wehr C, Suarez F, Fox ML, Mahlaoui N, Gennery AR, Lankester AC, Beier R, Bernardo ME, Bigley V, Lindemans CA, Burns SO, Carpenter B, Dybko J, Güngör T, Hauck F, Lum SH, Balashov D, Meisel R, Moshous D, Schulz A, Speckmann C, Slatter MA, Strahm B, Uckan-Cetinkaya D, Meyts I, Vallée TC, Wynn R, Neven B, Morris EC, Aiuti A, Maschan A, Aljurf M, Gedde-Dahl T, Gurman G, Bordon V, Kriván G, Locatelli F, Porta F, Valcárcel D, Beguin Y, Faraci M, Kröger N, Kulagin A, Shaw PJ, Veelken JH, Diaz de Heredia C, Fagioli F, Felber M, Gruhn B, Holter W, Rössig C, Sedlacek P, Apperley J, Ayas M, Bodova I, Choi G, Cornelissen JJ, Sirvent A, Khan A, Kupesiz A, Lenhoff S, Ozdogu H, von der Weid N, Rovira M, Schots R, Vinh DC. *Blood*. 2022 Oct 6;140(14):1635-1649. IF: 25,476.

Comparative effectiveness of ZUMA-5 (axi-cel) vs SCHOLAR-5 external control in relapsed/refractory follicular lymphoma. Ghione P, Palomba ML, Patel AR, Bobillo S, Deighton K, Jacobson CA, Nahas M, Hatswell AJ, Jung AS, Kanters S, Snider JT, Neelapu SS, Ribeiro MT, Brookhart MA, Ghesquieres H, Radford J, Gribben JG. *Blood*. 2022 Aug 25;140(8):851-860. IF: 25,476.

Final Results of Neoadjuvant Atezolizumab in Cisplatin-ineligible Patients with Muscle-invasive Urothelial Cancer of the Bladder. Szabados B, Kockx M, Assaf ZJ, van Dam PJ, Rodriguez-Vida A, Duran I, Crabb SJ, Van Der Heijden MS, Pous AF, Gravis G, Herranz UA, Protheroe A, Ravaud A, Maillet D, Mendez MJ, Suarez C, Linch M, Prendergast A, Tyson C, Stanoeva D, Daelemans S, Rombouts M, Mariathasan S, Tea JS, Mousa K, Sharma S, Aleshin A, Banchereau R, Castellano D, Powles T. *Eur Urol*. 2022 Aug;82(2):212-222. IF: 24,267.

Predictive Genomic Biomarkers of Hormonal Therapy Versus Chemotherapy Benefit in Metastatic Castration-resistant Prostate Cancer. Graf RP, Fisher V, Mateo J, Gjoerup OV, Madison RW, Raskina K, Tukachinsky H, Creeden J, Cunningham R, Huang RSP, Mata DA, Ross JS, Oxnard GR, Venstrom JM, Zurita AJ. *Eur Urol*. 2022 Jan;81(1):37-47. IF: 24,267.

Molecular Genetic Determinants of Shorter Time on Active Surveillance in a Prospective Phase 2 Clinical Trial in Metastatic Renal Cell Carcinoma. Reig Torras O, Mishra A, Christie A, McKenzie T, Onabolu O, Singla N, Plimack ER, Suárez C, Ornstein MC, Alpaugh RK, Elias R, Bowman IA, McKay RM, Przybycin C, Kapur P, Brugarolas J, Rini B. *Eur Urol*. 2022 Jun;81(6):555-558. IF: 24,267.

ZFP281 drives a mesenchymal-like dormancy program in early disseminated breast cancer cells that prevents metastatic outgrowth in the lung. Nobre AR, Dalla E, Yang J, Huang X, Wullkopf L, Risson E, Razghandi P, Anton ML, Zheng W, Seoane JA, Curtis C, Kenigsberg E, Wang J, Aguirre-Ghiso JA. *Nat Cancer*. 2022 Oct;3(10):1165-1180. IF: 23,177.

Functional patient-derived organoid screenings identify MCLA-158 as a therapeutic EGFR × LGR5 bispecific antibody with efficacy in epithelial tumors. Herpers B, Eppink B, James MI, Cortina C, Cañellas-Socias A, Boj SF, Hernando-Momblona X, Glodzik D, Roovers RC, van de Wetering M, Bartelink-Clements C, Zondag-van der Zande V, Mateos JG, Yan K, Salinaro L, Basmeleh A, Fatrai S, Maussang D, Lammerts van Bueren JJ, Chicote I, Serna G, Cabellos L, Ramírez L, Nuciforo P, Salazar R, Santos C, Villanueva A, Stephan-Otto Attolini C, Sancho E, Palmer HG, Tabernero J, Stratton MR, de Kruif J, Logtenberg T, Clevers H, Price LS, Vries RGJ, Batlle E, Throsby M. *Nat Cancer*. 2022 Apr;3(4):418-436. IF: 23,177.

LCOR mediates interferon-independent tumor immunogenicity and responsiveness to immune-checkpoint blockade in triple-negative breast cancer. Pérez-Núñez I, Rozalén C, Palomeque JÁ, Sangrador I, Dalmau M, Comerma L, Hernández-Prat A, Casadevall D, Menendez S, Liu DD, Shen M, Berenguer J, Ruiz IR, Peña R, Montañés JC, Albà MM, Bonnin S, Ponomarenko J, Gomis RR, Cejalvo JM, Servitja S, Marzese DM, Morey L, Voorwerk L, Arribas J, Bermejo B, Kok M, Pusztai L, Kang Y, Albanell J, Celià-Terrassa T. *Nat Cancer*. 2022 Mar;3(3):355-370. IF: 23,177.

The Molecular Tumor Board Portal supports clinical decisions and automated reporting for precision oncology. Tamborero D, Dienstmann R, Rachid MH, Boekel J, Lopez-Fernandez A, Jonsson M, Razzak A, Braña I, De Petris L, Yachnin J, Baird RD, Loriot Y, Massard C, Martin-Romano P, Opdam F, Schlenk RF, Vernieri C, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium; Balmaña J, Apolone G, Caldas C, Bergh J, Ernberg I, Fröhling S, Garralda E, Karlsson C, Tabernero J, Voest E, Rodon J, Lehtiö J. *Nat Cancer*. 2022 Feb;3(2):251-261. IF: 23,177.

Efficacy of Brigatinib in Patients With Advanced ALK-Positive NSCLC Who Progressed on Alectinib or Ceritinib: ALK in Lung Cancer Trial of brigAtinib-2 (ALTA-2). Ou SI, Nishio M, Ahn MJ, Mok T, Barlesi F, Zhou C, Felip E, de Marinis F, Kim SW, Pérol M, Liu G, Migliorino MR, Kim DW, Novello S, Bearz A, Garrido P, Mazieres J, Morabito A, Lin HM, Yang H, Niu H, Zhang P, Kim ES. *J Thorac Oncol*. 2022 Dec;17(12):1404-1414. IF: 20,121.

A Definitive Prognostication System for Patients With Thoracic Malignancies Diagnosed With Coronavirus Disease 2019: An Update From the TERAVOLT Registry. Whisenant JG, Baena J, Cortellini A, Huang LC, Lo Russo G, Porcu L, Wong SK, Bestvina CM, Hellmann MD, Roca E, Rizvi H, Monnet I, Boudjemaa A, Rogado J, Pasello G, Leighl NB, Arrieta O, Aujayeb A, Batra U, Azzam AY, Unk M, Azab MA, Zhumagaliyeva AN, Gomez-Martin C, Blaquier JB, Geraedts E, Mountzios G, Serrano-Montero G, Reinmuth N, Coate L, Marmarelis M, Presley CJ, Hirsch FR, Garrido P, Khan H, Baggi A, Mascaux C, Halmos B, Ceresoli GL, Fidler MJ, Scotti V, Métivier AC, Falchero L, Felip E, Genova C, Mazieres J, Tapan U, Brahmer J, Bria E, Puri S, Popat S, Reckamp KL, Morgillo F, Nadal E, Mazzoni F, Agustoni F, Bar J, Grosso F, Avrillon V, Patel JD, Gomes F, Ibrahim E, Trama A, Bettini AC, Barlesi F, Dingemans AM, Wakelee H, Peters S, Horn L, Garassino MC, Torri V; TERAVOLT study group. *J Thorac Oncol*. 2022 May;17(5):661-674. IF: 20,121.

The Mettl3 epitranscriptomic writer amplifies p53 stress responses. Raj N, Wang M, Seoane JA, Zhao RL, Kaiser AM, Moonie NA, Demeter J, Boutelle AM, Kerr CH, Mulligan AS, Moffatt C, Zeng SX, Lu H, Barna M, Curtis C, Chang HY, Jackson PK, Attardi LD. *Mol Cell*. 2022 Jul 7;82(13):2370-2384.e10. IF: 19,328.

Giredestrant reverses progesterone hypersensitivity driven by estrogen receptor mutations in breast cancer. Liang J, Ingalla ER, Yao X, Wang BE, Tai L, Giltnane J, Liang Y, Daemen A, Moore HM, Aimi J, Chang CW, Gates MR, Eng-Wong J, Tam L, Bacarro N, Roose-Girma M, Bellet M, Hafner M, Metcalfe C. *Sci Transl Med*. 2022 Sep 21;14(663):eabo5959. IF: 19,319.

Acute kidney injury in patients receiving pembrolizumab combination therapy versus pembrolizumab monotherapy for advanced lung cancer. Gupta S, Strohbehn IA, Wang Q, Hanna PE, Seethapathy R, Prosek JM, Herrmann SM, Abudayyeh A, Malik AB, Loew S, Carlos CA, Chang WT, Beckerman P, Mithani Z, Shah CV, Renaghan AD, de Seigneux S, Campedel L, Kitchlu A, Shin DS, Coppock G, Lumlertgul N, Garcia P, Ortiz-Melo DI, Rashidi A, Sprangers B, Aggarwal V, Benesova K, Jhaveri KD, Cortazar FB, Weins A, Zuo Y, Mooradian MJ, Reynolds KL, Leaf DE, Sise ME; ICPi-AKI Consortium. *Kidney Int*. 2022 Oct;102(4):930-935. IF: 18,998.

The transcription factor DDIT3 is a potential driver of dyserythropoiesis in myelodysplastic syndromes. Berastegui N, Ainciburu M, Romero JP, Garcia-Olloqui P, Alfonso-Pierola A, Philippe C, Vilas-Zornoza A, San Martin-Uriz P, Ruiz-Hernández R, Abarrategi A, Ordoñez R, Alignani D, Sarvide S, Castro-Labrador L, Lamo-Espinosa JM, San-Julian M, Jimenez T, López-Cadenas F, Muntion S,

Sanchez-Guijo F, Molero A, Montoro MJ, Tazón B, Serrano G, Diaz-Mazkiaran A, Hernaez M, Huerga S, Bewicke-Copley F, Rio-Machin A, Maurano MT, Díez-Campelo M, Valcarcel D, Rouault-Pierre K, Lara-Astiaso D, Ezponda T, Prosper F. *Nat Commun*. 2022 Dec 9;13(1):7619. IF: 17,694.

Phosphoproteomic analysis of neoadjuvant breast cancer suggests that increased sensitivity to paclitaxel is driven by CDK4 and filamin A. Mouron S, Bueno MJ, Lluch A, Manso L, Calvo I, Cortes J, Garcia-Saenz JA, Gil-Gil M, Martinez-Janez N, Apala JV, Caleiras E, Ximénez-Embún P, Muñoz J, Gonzalez-Cortijo L, Murillo R, Sánchez-Bayona R, Cejalvo JM, Gómez-López G, Fustero-Torre C, Sabroso-Lasa S, Malats N, Martinez M, Moreno A, Megias D, Malumbres M, Colomer R, Quintela-Fandino M. *Nat Commun*. 2022 Dec 7;13(1):7529. IF: 17,694.

BRAF activation by metabolic stress promotes glycolysis sensitizing NRASQ61-mutated melanomas to targeted therapy. McGrail K, Granado-Martínez P, Esteve-Puig R, García-Ortega S, Ding Y, Sánchez-Redondo S, Ferrer B, Hernandez-Losa J, Canals F, Manzano A, Navarro-Sabaté A, Bartrons R, Yanes O, Pérez-Alea M, Muñoz-Couselo E, Garcia-Patos V, Recio JA. *Nat Commun*. 2022 Nov 19;13(1):7113. IF: 17,694.

pTINCR microprotein promotes epithelial differentiation and suppresses tumor growth through CDC42 SUMOylation and activation. Boix O, Martinez M, Vidal S, Giménez-Alejandre M, Palenzuela L, Lorenzo-Sanz L, Quevedo L, Moscoso O, Ruiz-Orera J, Ximénez-Embún P, Ciriaco N, Nuciforo P, Stephan-Otto Attolini C, Albà MM, Muñoz J, Tian TV, Varela I, Vivancos A, Ramón Y Cajal S, Muñoz P, Rivas C, Abad M. *Nat Commun*. 2022 Nov 11;13(1):6840. IF: 17,694.

Analysis of matched primary and recurrent BRCA1/2 mutation-associated tumors identifies recurrence-specific drivers. Shah JB, Pueschl D, Wubbenhorst B, Fan M, Pluta J, D'Andrea K, Hubert AP, Shilan JS, Zhou W, Kraya AA, Llop Guevara A, Ruan C, Serra V, Balmaña J, Feldman M, Morin PJ, Nayak A, Maxwell KN, Domchek SM, Nathanson KL. *Nat Commun*. 2022 Nov 7;13(1):6728. IF: 17,694.

A phase II trial of weekly nab-paclitaxel for progressive and symptomatic desmoid tumors. Martin-Broto J, Redondo A, Moura DS, Valverde C, Morales JM, Lopez-Pousa A, Martinez-Trufero J, Gutierrez A, Díaz-Beveridge R, Luna P, Martinez-Marin V, Marcilla D, Arribas I, Ledesma P, Lopez-Martin JA, Di Lernia D, Zamora J, Hindi N. A phase II trial of weekly nab-paclitaxel for progressive and symptomatic desmoid tumors. *Nat Commun*. 2022 Oct 21;13(1):6278. IF: 17,694.

High p16 expression and heterozygous RB1 loss are biomarkers for CDK4/6 inhibitor resistance in ER+ breast cancer. Palafox M, Monserrat L, Bellet M, Villacampa G, Gonzalez-Perez A, Oliveira M, Brasó-Maristany F, Ibrahimi N, Kannan S, Mina L, Herrera-Abreu MT, Òdena A, Sánchez-Guixé M, Capelán M, Azaro A, Bruna A, Rodríguez O, Guzmán M, Grueso J, Viaplana C, Hernández J, Su F, Lin K, Clarke RB, Caldas C, Arribas J, Michiels S, García-Sanz A, Turner NC, Prat A, Nuciforo P, Dienstmann R, Verma CS, Lopez-Bigas N, Scaltriti M, Arnedos M, Saura C, Serra V. *Nat Commun*. 2022 Sep 7;13(1):5258. IF: 17,694.

Stratification of hospitalized COVID-19 patients into clinical severity progression groups by immuno-phenotyping and machine learning. Mueller YM, Schrama TJ, Ruijten R, Schreurs MWJ, Grashof DGB, van de Werken HJG, Lasinio GJ, Álvarez-Sierra D, Kiernan CH, Castro Eiro MD, van Meurs M, Brouwers-Haspels I, Zhao M, Li L, de Wit H, Ouzounis CA, Wilmsen MEP, Alofs TM, Laport DA, van Wees T, Kraker G, Jaimes MC, Van Bockstael S, Hernández-González M, Rokx C, Rijnders BJA, Pujol-Borrell R, Katsikis PD. *Nat Commun*. 2022 Feb 17;13(1):915. IF: 17,694.

DSTYK inhibition increases the sensitivity of lung cancer cells to T cell-mediated cytotoxicity. Valencia K, Echepare M, Teijeira Á, Pasquier A, Bértolo C, Sainz C, Tamayo I, Picabea B, Bosco G, Thomas R, Agorreta J, López-Picazo JM, Frigola J, Amat R, Calvo A, Felip E, Melero I, Montuenga LM. *J Exp Med*. 2022 Dec 5;219(12):e20220726. IF: 17,579.

Engineering pH-Sensitive Stable Nanovesicles for Delivery of MicroRNA Therapeutics. Boloix A, Feiner-Gracia N, Köber M, Repetto J, Pascarella R, Soriano A, Masanas M, Segovia N, Vargas-Nadal G, Merlo-Mas J, Danino D, Abutbul-Ionita I, Foradada L, Roma J, Córdoba A, Sala S, de Toledo JS, Gallego S, Veciana J, Albertazzi L, Segura MF, Ventosa N. *Small*. 2022 Jan;18(3):e2101959. IF: 15,153.

Targeting HER2-AXL heterodimerization to overcome resistance to HER2 blockade in breast cancer. Adam-Artigues A, Arenas EJ, Martínez-Sabadell A, Brasó-Maristany F, Cervera R, Tormo E, Hernando C, Martínez MT, Carbonell-Asins J, Simón S, Poveda J, Moragón S, Zazo S, Martínez D, Rovira A, Burgués O, Rojo F, Albanell J, Bermejo B, Lluch A, Prat A, Arribas J, Eroles P, Cejalvo JM. *Sci Adv*. 2022 May 20;8(20):eabk2746. IF: 14,957.

Anti-tumoural activity of the G-quadruplex ligand pyridostatin against BRCA1/2-deficient tumours. Groelly FJ, Porru M, Zimmer J, Benainous H, De Visser Y, Kosova AA, Di Vito S, Serra V, Ryan A, Leonetti C, Bruna A, Biroccio A, Tarsounas M. *EMBO Mol Med*. 2022 Mar 7;14(3):e14501. IF: 14,260.

Identification of a Molecularly-Defined Subset of Breast and Ovarian Cancer Models that Respond to WEE1 or ATR Inhibition, Overcoming PARP Inhibitor Resistance. Serra V, Wang AT, Castroviejo-Bermejo M, Polanska UM, Palafox M, Herencia-Ropero A, Jones GN, Lai Z, Armenia J, Michopoulos F, Llop-Guevara A, Brough R, Gulati A, Pettitt SJ, Bulusu KC, Nikkilä J, Wilson Z, Hughes A, Wijnhoven PWG, Ahmed A, Bruna A, Gris-Oliver A, Guzman M, Rodríguez O, Grueso J, Arribas J, Cortés J, Saura C, Lau A, Critchlow S, Dougherty B, Caldas C, Mills GB, Barrett JC, Forment JV, Cadogan E, Lord CJ, Cruz C, Balmaña J, O'Connor MJ. *Clin Cancer Res*. 2022 Oct 14;28(20):4536-4550. IF: 13,801.

Association of Tumor Mutational Burden with Efficacy of Pembrolizumab±Chemotherapy as First-Line Therapy for Gastric Cancer in the Phase III KEYNOTE-062 Study. Lee KW, Van Cutsem E, Bang YJ, Fuchs CS, Kudaba I, Garrido M, Chung HC, Lee J, Castro HR, Chao J, Wainberg ZA, Cao ZA, Aurora-Garg D, Kobie J, Cristescu R, Bhagia P, Shah S, Tabernero J, Shitara K, Wyrwicz L. *Clin Cancer Res*. 2022 Aug 15;28(16):3489-3498. IF: 13,801.

Antitumor Activity of Lurbinectedin, a Selective Inhibitor of Oncogene Transcription, in Patients with Relapsed Ewing Sarcoma: Results of a Basket Phase II Study. Subbiah V, Braña I, Longhi A, Boni V, Delord JP, Awada A, Boudou-Rouquette P, Sarantopoulos J, Shapiro GI, Elias A, Ratan R, Fernandez C, Kahatt C, Cullell-Young M, Siguero M, Zeaiter A, Chawla SP. *Clin Cancer Res*. 2022 Jul 1;28(13):2762-2770. IF: 13,801.

A Phase I Study Investigating AZD8186, a Potent and Selective Inhibitor of PI3Kβ/δ, in Patients with Advanced Solid Tumors. Choudhury AD, Higano CS, de Bono JS, Cook N, Rathkopf DE, Wisinski KB, Martin-Liberal J, Linch M, Heath EI, Baird RD, García-Carbacho J, Quintela-Fandino M, Barry ST, de Bruin EC, Colebrook S, Hawkins G, Klinowska T, Maroj B, Moorthy G, Mortimer PG, Moschetta M, Nikolaou M, Sainsbury L, Shapiro GI, Siu LL, Hansen AR. *Clin Cancer Res*. 2022 Jun 1;28(11):2257-2269. IF: 13,801.

ESMO Scale for Clinical Actionability of Molecular Targets Driving Targeted Treatment in Patients with Cholangiocarcinoma. Verdaguer H, Saurí T, Acosta DA, Guardiola M, Sierra A, Hernando J, Nuciforo P, Miquel JM, Molero C, Peiró S, Serra-Camprubí Q, Villacampa G, Aguilar S, Vivancos A, Tabernero J, Dienstmann R, Macarulla T. *Clin Cancer Res*. 2022 Apr 14;28(8):1662-1671. IF: 13,801.

Tumor Genomic Testing for >4,000 Men with Metastatic Castration-resistant Prostate Cancer in the Phase III Trial

PROfound (Olaparib). Hussain M, Corcoran C, Sibilla C, Fizazi K, Saad F, Shore N, Sandhu S, Mateo J, Olmos D, Mehra N, Kolinsky MP, Roubaud G, Özgüroğlu M, Matsubara N, Gedye C, Choi YD, Padua C, Kohlmann A, Huisden R, Elvin JA, Kang J, Adelman CA, Allen A, Poehlein C, de Bono J. *Clin Cancer Res*. 2022 Apr 14;28(8):1518-1530. IF: 13,801.

Pan-cancer Analysis of Homologous Recombination Repair-associated Gene Alterations and Genome-wide Loss-of-Heterozygosity Score. Westphalen CB, Fine AD, André F, Ganesan S, Heinemann V, Rouleau E, Turnbull C, Garcia Palacios L, Lopez JA, Sokol ES, Mateo J. *Clin Cancer Res*. 2022 Apr 1;28(7):1412-1421. IF: 13,801.

IFNγ Signaling in Natural and Therapy-Induced Antitumor Responses. Martínez-Sabadell A, Arenas EJ, Arribas J. *Clin Cancer Res*. 2022 Apr 1;28(7):1243-1249. IF: 13,801.

Tepotinib Efficacy and Safety in Patients with MET Exon 14 Skipping NSCLC: Outcomes in Patient Subgroups from the VISION Study with Relevance for Clinical Practice. Le X, Sakai H, Felip E, Veillon R, Garassino MC, Raskin J, Cortot AB, Viteri S, Mazieres J, Smit EF, Thomas M, Iams WT, Cho BC, Kim HR, Yang JC, Chen YM, Patel JD, Bestvina CM, Park K, Griesinger F, Johnson M, Gottfried M, Britschgi C, Heymach J, Sikoglu E, Berghoff K, Schumacher KM, Bruns R, Otto G, Paik PK. *Clin Cancer Res*. 2022 Mar 15;28(6):1117-1126. IF: 13,801.

Co-Targeting of MDM2 and CDK4/6 with Siremadlin and Ribociclib for the Treatment of Patients with Well-Differentiated or Dedifferentiated Liposarcoma: Results from a Proof-of-Concept, Phase Ib Study. Abdul Razak AR, Bauer S, Suarez C, Lin CC, Quek R, Hütter-Krönke ML, Cubedo R, Ferretti S, Guerreiro N, Jullion A, Orlando EJ, Clementi G, Sand Dejmek J, Halilovic E, Fabre C, Blay JY, Italiano A. *Clin Cancer Res*. 2022 Mar 15;28(6):1087-1097. IF: 13,801.

Results from a First-in-Human Phase I Study of Siremadlin (HDM201) in Patients with Advanced Wild-Type TP53 Solid Tumors and Acute Leukemia. Stein EM, DeAngelo DJ, Chromik J, Chatterjee M, Bauer S, Lin CC, Suarez C, de Vos F, Steeghs N, Cassier PA, Tai D, Kiladjian JJ, Yamamoto N, Mous R, Esteve J, Minami H, Ferretti S, Guerreiro N, Meille C, Radhakrishnan R, Pereira B, Mariconti L, Halilovic E, Fabre C, Carpio C. *Clin Cancer Res*. 2022 Mar 1;28(5):870-881. IF: 13,801.

Functional Mapping of AKT Signaling and Biomarkers of Response from the FAIRLANE Trial of Neoadjuvant Ipatasertib plus Paclitaxel for Triple-Negative Breast Cancer. Shi Z, Wulfkuhle J, Nowicka M, Gallagher RI, Saura C, Nuciforo PG, Calvo I, Andersen J, Passos-Coelho JL, Gil-Gil MJ, Bermejo B, Pratt DA, Ciruelos EM, Villagrasa P, Wongchenko MJ, Petricoin EF, Oliveira M, Isakoff SJ. *Clin Cancer Res*. 2022 Mar 1;28(5):993-1003. IF: 13,801.

High FGFR1-4 mRNA Expression Levels Correlate with Response to Selective FGFR Inhibitors in Breast Cancer. Sánchez-Guixé M, Hierro C, Jiménez J, Viaplana C, Villacampa G, Monelli E, Brasó-Maristany F, Ogbah Z, Parés M, Guzmán M, Grueso J, Rodríguez O, Oliveira M, Azaro A, Garralda E, Tabernero J, Casanovas O, Scaltriti M, Prat A, Dienstmann R, Nuciforo P, Saura C, Graupera M, Vivancos A, Rodon J, Serra V. *Clin Cancer Res*. 2022 Jan 1;28(1):137-149. IF: 13,801.

A Randomized Phase II Study of Anti-CSF1 Monoclonal Antibody Lacnotuzumab (MCS110) Combined with Gemcitabine and Carboplatin in Advanced Triple-Negative Breast Cancer. Kuemmel S, Campone M, Loirat D, Lopez RL, Beck JT, De Laurentiis M, Im SA, Kim SB, Kwong A, Steger GG, Adelantado EZ, Duhoux FP, Greil R, Kuter I, Lu YS, Tibau A, Özgüroğlu M, Scholz CW, Singer CF, Vega E, Wimberger P, Zamagni C, Couillebault XM, Fan L, Guerreiro N, Mataraza J, Sand-Dejmek J, Chan A. *Clin Cancer Res*. 2022 Jan 1;28(1):106-115. IF: 13,801.

Response to "Analysis of the association between prospectively collected immune-related adverse events and survival in patients with solid tumor treated with immune-checkpoint blockers, taking into account immortal-time bias". Villacampa G, Hernando-Calvo A, Berché R, Saavedra O, Marmolejo D, Mirallas O, Braña I, Muñoz-Couselo E, Garralda E, Dienstmann R. *Cancer Treat Rev*. 2022 Dec;111:102465. IF: 13,608.

Multiple Bayesian network meta-analyses to establish therapeutic algorithms for metastatic triple negative breast cancer. Schettini F, Venturini S, Giuliano M, Lambertini M, Pinato DJ, Onesti CE, De Placido P, Harbeck N, Lüftner D, Denys H, Van Dam P, Arpino G, Zaman K, Mustacchi G, Gligorov J, Awada A, Campone M, Wildiers H, Gennari A, Tjan-Heijnen V, Bartsch R, Cortes J, Paris I, Martín M, De Placido S, Del Mastro L, Jerusalem G, Curigliano G, Prat A, Generali D. *Cancer Treat Rev*. 2022 Dec;111:102468. IF: 13,608.

The conundrum of breast cancer and microbiome - A comprehensive review of the current evidence. Papakonstantinou A, Nuciforo P, Borrell M, Zamora E, Pimentel I, Saura C, Oliveira M. *Cancer Treat Rev*. 2022 Dec;111:102470. IF: 13,608.

Molecular diagnosis and targeted treatment of advanced follicular cell-derived thyroid cancer in the precision medicine era. Capdevila J, Awada A, Führer-Sakel D, Leboulleux S, Pauwels P. *Cancer Treat Rev*. 2022 May;106:102380. IF: 13,608.

Prognostic value of ctDNA detection in patients with early breast cancer undergoing neoadjuvant therapy: A systematic review and meta-analysis. Papakonstantinou A, Gonzalez NS, Pimentel I, Suñol A, Zamora E, Ortiz C, Espinosa-Bravo M, Peg V, Vivancos A, Saura C, Villacampa G, Oliveira M. *Cancer Treat Rev*. 2022 Mar;104:102362. IF: 13,608.

Treatment-driven tumour heterogeneity and drug resistance: Lessons from solid tumours. Crucitta S, Cucchiara F, Mathijssen R, Mateo J, Jager A, Joosse A, Passaro A, Attili I, Petrini I, van Schaik R, Danesi R, Del Re M. *Cancer Treat Rev*. 2022 Mar;104:102340. IF: 13,608.

Addition of immune checkpoint inhibitors to chemotherapy versus chemotherapy alone in first-line metastatic triple-negative breast cancer: A systematic review and meta-analysis. Villacampa G, Tolosa P, Salvador F, Sánchez-Bayona R, Villanueva L, Dienstmann R, Ciruelos E, Pascual T. *Cancer Treat Rev*. 2022 Mar;104:102352. IF: 13,608.

Targeting brain metastases in breast cancer. Corti C, Antonarelli G, Criscitiello C, Lin NU, Carey LA, Cortés J, Poortmans P, Curigliano G. *Cancer Treat Rev*. 2022 Feb;103:102324. IF: 13,608.

A comprehensive overview of tumour deposits in colorectal cancer: Towards a next TNM classification. Delattre JF, Selcen Oguz Erdogan A, Cohen R, Shi Q, Emile JF, Taieb J, Tabernero J, André T, Meyerhardt JA, Nagtegaal ID, Svrcek M. *Cancer Treat Rev*. 2022 Feb;103:102325. IF: 13,608.

SELNET clinical practice guidelines for soft tissue sarcoma and GIST. Blay JY, Hindi N, Bollard J, Aguiar S Jr, Angel M, Araya B, Badilla R, Bernabeu D, Campos F, Caro-Sánchez CHS, Carvajal B, Carvajal Montoya A, Casavilca-Zambrano S, Castro-Oliden V, Chacón M, Clara M, Collini P, Correa Genoroso R, Costa FD, Cuellar M, Dei Tos AP, Dominguez Malagon HR, Donati D, Dufresne A, Eriksson M, Farias-Loza M, Fernandez P, Frezza AM, Frisoni T, Garcia-Ortega DY, Gelderblom H, Gouin F, Gómez-Mateo MC, Gronchi A, Haro J, Huanca L, Jimenez N, Karanian M, Kasper B, Lopes David BB, Lopez-Pousa A, Lutter G, Martinez-Said H, Martinez-Tlahuel J, Mello CA, Morales Pérez JM, Moura David S, Nascimento AG, Ortiz-Cruz EJ, Palmerini E, Patel S, Pfluger Y, Provenzano S, Righi A, Rodriguez A, Salas R, Santos TTG, Scotlandi K, Soule T, Stacchiotti S, Valverde C, Waisberg F, Zamora Estrada E, Martin-Broto J. *Cancer Treat Rev*. 2022 Jan;102:102312. IF: 13,608.

Quality of Colonoscopy Is Associated With Adenoma Detection and Postcolonoscopy Colorectal Cancer

Prevention in Lynch Syndrome. Sánchez A, Roos VH, Navarro M, Pineda M, Caballol B, Moreno L, Carballal S, Rodríguez-Alonso L, Ramon Y Cajal T, Llort G, Piñol V, López-Fernández A, Salces I, Picó MD, Rivas L, Bujanda L, Garzon M, Pizarro A, Martinez de Castro E, López-Arias MJ, Poves C, Garau C, Rodriguez-Alcalde D, Herraiz M, Alvarez-Urrutia C, Dacal A, Carrillo-Palau M, Cid L, Ponce M, Barreiro-Alonso E, Saperas E, Aguirre E, Romero C, Bastiaansen B, Gonzalez-Acosta M, Morales-Romero B, Ocaña T, Rivero-Sánchez L, Jung G, Bessa X, Cubiella J, Jover R, Rodríguez-Moranta F, Balmaña J, Brunet J, Castells A, Dekker E, Capella G, Serra-Burriel M, Moreira L, Pellise M, Balaguer F. *Clin Gastroenterol Hepatol*. 2022 Mar;20(3):611-621.e9. IF: 13,576.

Retreatment With Immune Checkpoint Inhibitors After a Severe Immune-Related Hepatitis: Results From a Prospective Multicenter Study. Riveiro-Barciela M, Barreira-Díaz A, Callejo-Pérez A, Muñoz-Couselo E, Díaz-Mejía N, Díaz-González Á, Londoño MC, Salcedo MT, Buti M. *Clin Gastroenterol Hepatol*. 2023 Mar;21(3):732-740. IF: 13,576.

Imaging Response to Contemporary Immuno-oncology Combination Therapies in Patients With Metastatic Renal Cell Carcinoma. Navani V, Ernst M, Wells JC, Yuasa T, Takemura K, Donskov F, Basappa NS, Schmidt A, Pal SK, Meza L, Wood LA, Ernst DS, Szabados B, Powles T, McKay RR, Weickhardt A, Suarez C, Kapoor A, Lee JL, Choueiri TK, Heng DYC. *JAMA Netw Open*. 2022 Jun 1;5(6):e2216379. IF: 13,353.

Therapy-Induced Senescence Enhances the Efficacy of HER2-Targeted Antibody-Drug Conjugates in Breast Cancer. Duro-Sánchez S, Nadal-Serrano M, Lalinde-Gutiérrez M, Arenas EJ, Bernadó Morales C, Morancho B, Escorihuela M, Pérez-Ramos S, Escrivá-de-Romaní S, Gandullo-Sánchez L, Pandiella A, Esteve-Codina A, Rodilla V, Dijcks FA, Dokter WHA, Cortés J, Saura C, Arribas J. *Cancer Res*. 2022 Dec 16;82(24):4670-4679. IF: 13,312.

Activity and Resistance of a Brain-Permeable Paradox Breaker BRAF Inhibitor in Melanoma Brain Metastasis. Bonfill-Teixidor E, Iurlaro R, Handl C, Wichmann J, Arias A, Cuartas I, Emmenegger J, Romagnani A, Mangano L, Lorber T, Berrera M, Godfried Sie C, Köchl F, Eckmann J, Feddersen R, Kornacker M, Schnetzler G, Cicuendez M, Cordero E, Topczewski TE, Ferres-Pijoan A, González J, Martínez-Ricarte F, Muñoz-Couselo E, Tabernero J, Bischoff JR, Pettazzoni P, Seoane J. *Cancer Res*. 2022 Jul 18;82(14):2552-2564. IF: 13,312.

Preclinical In Vivo Validation of the RAD51 Test for Identification of Homologous Recombination-Deficient Tumors and Patient Stratification. Pellegrino B, Herencia-Ropero A, Llop-Guevara A, Pedretti F, Moles-Fernández A, Viaplana C, Villacampa G, Guzmán M, Rodríguez O, Grueso J, Jiménez J, Arenas EJ, Degasperi A, Dias JML, Forment JV, O'Connor MJ, Déas O, Cairo S, Zhou Y, Musolino A, Caldas C, Nik-Zainal S, Clarke RB, Nuciforo P, Díez O, Serres-Créixams X, Peg V, Espinosa-Bravo M, Macarulla T, Oaknin A, Mateo J, Arribas J, Dienstmann R, Bellet M, Oliveira M, Saura C, Gutiérrez-Enríquez S, Balmaña J, Serra V. *Cancer Res*. 2022 Apr 15;82(8):1646-1657. IF: 13,312.

Determinants of early triage for hospitalization in myeloproliferative neoplasm (MPN) patients with COVID-19. Barbui T, Carobbio A, Ghirardi A, Iurlo A, Sobas MA, Elli EM, Rumi E, De Stefano V, Lunghi F, Marchetti M, Daffini R, Gasior Kabat M, Cuevas B, Fox ML, Andrade-Campos MM, Palandri F, Guglielmelli P, Benevolo G, Harrison C, Foncillas MA, Bonifacio M, Alvarez-Larran A, Kiladjian JJ, Bolaños Calderón E, Patriarca A, Quiroz Cervantes K, Griesshammer M, Garcia-Gutierrez V, Marin Sanchez A, Magro Mazo E, Carli G, Hernandez-Boluda JC, Osorio S, Carreno-Tarragona G, Sagues Serrano M, Kusec R, Navas Elorza B, Angona A, Xicoy Cirici B, Lopez Abadia E, Koschmieder S, Cattaneo D, Bucelli C, Cichocka E, de Nałęcz AK, Cavalca F, Borsani O, Betti S, Bellini M, Curto-Garcia N, Rambaldi A, Vannucchi AM. *Am J Hematol*. 2022 Dec;97(12):E470-E473. IF: 13,265.

Outcome of infection with omicron SARS-CoV-2 variant in patients with hematological malignancies: An EPICOVIDEHA survey report. Blennow O, Salmanton-García J, Nowak P, Itri F, Van Doesum J, López-García A, Farina F, Jaksic O, Pinczés LI, Bilgin YM, Falces-Romero I, Jiménez M, Ormazabal-Vélez I, Weinbergerová B, Duléry R, Stojanoski Z, Lahmer T, Fernández N, Hernández-Rivas JÁ, Petzer V, De Jonge N, Glenthøj A, De Ramón C, Biernat MM, Fracchiolla N, Aujayeb A, Van Praet J, Schönlein M, Méndez GA, Cattaneo C, Guidetti A, Sciumè M, Ammatuna E, Cordoba R, García-Poutón N, Gräfe S, Cabirta A, Wolf D, Nordlander A, García-Sanz R, Delia M, Berg Venemyr C, Brones C, Di Blasi R, De Kort E, Meers S, Lamure S, Serrano L, Merelli M, Coppola N, Bergantim R, Besson C, Kohn M, Petiti J, Garcia-Vidal C, Dargenio M, Danion F, Machado M, Bailén-Almorox R, Hoenigl M, Dragonetti G, Chai LYA, Kho CS, Bonanni M, Liévin R, Marchesi F, Cornely OA, Pagano L. *Am J Hematol*. 2022 Aug;97(8):E312-E317. IF: 13,265.

Liquid biopsy in gliomas: A RANO review and proposals for clinical applications. Soffietti R, Bettegowda C, Mellinghoff IK, Warren KE, Ahluwalia MS, De Groot JF, Galanis E, Gilbert MR, Jaeckle KA, Le Rhun E, Rudà R, Seoane J, Thon N, Umemura Y, Weller M, van den Bent MJ, Vogelbaum MA, Chang SM, Wen PY. *Neuro Oncol*. 2022 Jun 1;24(6):855-871. IF: 13,029.

Second versus first wave of COVID-19 in patients with MPN. Barbui T, Iurlo A, Masciulli A, Carobbio A, Ghirardi A, Carioli G, Sobas MA, Elli EM, Rumi E, De Stefano V, Lunghi F, Marchetti M, Daffini R, Gasior Kabat M, Cuevas B, Fox ML, Andrade-Campos MM, Palandri F, Guglielmelli P, Benevolo G, Harrison C, Foncillas MA, Bonifacio M, Alvarez-Larran A, Kiladjian JJ, Bolaños Calderón E, Patriarca A, Quiroz Cervantes K, Griessammer M, Garcia-Gutierrez V, Marin Sanchez A, Magro Mazo E, Ruggeri M, Hernandez-Boluda JC, Osorio S, Carreno-Tarragona G, Sagues Serrano M, Kusec R, Navas Elorza B, Angona A, Xicoy Cirici B, Lopez Abadia E, Koschmieder S, Cattaneo D, Bucelli C, Cichocka E, Masternak Kulikowska de Nałęcz A, Cavalca F, Borsani O, Betti S, Benajiba L, Bellini M, Curto-Garcia N, Rambaldi A, Vannucchi AM. *Leukemia*. 2022 Mar;36(3):897-900. IF: 12,883.

Gasdermin B over-expression modulates HER2-targeted therapy resistance by inducing protective autophagy through Rab7 activation. Gámez-Chiachio M, Molina-Crespo Á, Ramos-Nebot C, Martinez-Val J, Martinez L, Gassner K, Llobet FJ, Soriano M, Hernandez A, Cordani M, Bernadó-Morales C, Diaz E, Rojo-Sebastian A, Triviño JC, Sanchez L, Rodríguez-Barrueco R, Arribas J, Llobet-Navás D, Sarrió D, Moreno-Bueno G. *J Exp Clin Cancer Res*. 2022 Sep 26;41(1):285. IF: 12,658.

A first-in-human phase 1/2 study of FGF401 and combination of FGF401 with spartalizumab in patients with hepatocellular carcinoma or biomarker-selected solid tumors. Chan SL, Schuler M, Kang YK, Yen CJ, Edeline J, Choo SP, Lin CC, Okusaka T, Weiss KH, Macarulla T, Cattan S, Blanc JF, Lee KH, Maur M, Pant S, Kudo M, Assenat E, Zhu AX, Yau T, Lim HY, Bruix J, Geier A, Guillén-Ponce C, Fasolo A, Finn RS, Fan J, Vogel A, Qin S, Riester M, Katsanou V, Chaudhari M, Kakizume T, Gu Y, Porta DG, Myers A, Delord JP. *J Exp Clin Cancer Res*. 2022 Jun 2;41(1):189. IF: 12,658.

Biomarkers of tumor-reactive CD4+ and CD8+ TILs associate with improved prognosis in endometrial cancer. Palomero J, Panisello C, Lozano-Rabella M, Tirtakasuma R, Díaz-Gómez J, Grases D, Pasamar H, Arregui L, Dorca Duch E, Guerra Fernández E, Vivancos A, de Andrea CE, Melero I, Ponce J, Vidal A, Piulats JM, Matias-Guiu X, Gros A. *J Immunother Cancer*. 2022 Dec;10(12):e005443. IF: 12,469.

Immune checkpoint inhibitor therapy and outcomes from SARS-CoV-2 infection in patients with cancer: a joint analysis of OnCovid and ESMO-CoCARE registries. Cortellini A, Dettorre GM, Dafni U, Aguilar-Company J, Castelo-Branco L, Lambertini M, Gennatas S, Angelis V, Sita-Lumsden A, Rogado J, Pedrazzoli P, Viñal D, Prat A, Rossi M, Berardi R, Alonso-Gordoa T, Grisanti S, Dimopoulou G, Queirolo P, Pradervand S, Bertuzzi A, Bower M, Arnold D, Salazar R, Tucci M, Harrington KJ, Mazzoni F, Mukherjee U, Tsourti Z, Michielin O, Pommeret F, Brunet J, Vincenzi B, Tonini G, Patriarca A, Biello F, Krengli M, Tabernero J, Pentheroudakis

G, Gennari A, Peters S, Romano E, Pinato DJ. *J Immunother Cancer*. 2022 Nov;10(11):e005732. IF: 12,469.

First-in-human phase I/II, open-label study of the anti-OX40 agonist INCAGN01949 in patients with advanced solid tumors. Davis EJ, Martin-Liberal J, Kristeleit R, Cho DC, Blagden SP, Berthold D, Cardin DB, Vieito M, Miller RE, Hari Dass P, Orcurto A, Spencer K, Janik JE, Clark J, Condamine T, Pulini J, Chen X, Mehnert JM. *J Immunother Cancer*. 2022 Oct;10(10):e004235. IF: 12,469.

Shorter versus longer corticosteroid duration and recurrent immune checkpoint inhibitor-associated AKI. Gupta S, Garcia-Carro C, Prosek JM, Glezerman I, Herrmann SM, Garcia P, Abudayyeh A, Lumlertgul N, Malik AB, Loew S, Beckerman P, Renaghan AD, Carlos CA, Rashidi A, Mithani Z, Deshpande P, Rangarajan S, Shah CV, Seigneux S, Campedel L, Kitchlu A, Shin DS, Coppock G, Ortiz-Melo DI, Sprangers B, Aggarwal V, Benesova K, Wanchoo R, Murakami N, Cortazar FB, Reynolds KL, Sise ME, Soler MJ, Leaf DE; ICPi-AKI Consortium Investigators. *J Immunother Cancer*. 2022 Sep;10(9):e005646. IF: 12,469.

Tumor microenvironment gene expression profiles associated to complete pathological response and disease progression in resectable NSCLC patients treated with neoadjuvant chemoimmunotherapy. Casarrubios M, Provencio M, Nadal E, Insa A, Del Rosario García-Campelo M, Lázaro-Quintela M, Dómine M, Majem M, Rodriguez-Abreu D, Martinez-Marti A, De Castro Carpeño J, Cobo M, López Vivanco G, Del Barco E, Bernabé R, Viñolas N, Barneto Aranda I, Massuti B, Sierra-Rodero B, Martinez-Toledo C, Fernández-Miranda I, Serna-Blanco R, Romero A, Calvo V, Cruz-Bermúdez A. *J Immunother Cancer*. 2022 Sep;10(9):e005320. IF: 12,469.

The CAR-HEMATOTOX risk-stratifies patients for severe infections and disease progression after CD19 CAR-T in R/R LBCL Rejeski K, Perez A, Iacoboni G, Penack O, Bücklein V, Jentzsch L, Mougiakakos D, Johnson G, Arciola B, Carpio C, Blumenberg V, Hoster E, Bullinger L, Locke FL, von Bergwelt-Baildon M, Mackensen A, Bethge W, Barba P, Jain MD, Subklewe M. *J Immunother Cancer*. 2022 May;10(5):e004475. IF: 12,469.

High levels of chromosomal aberrations negatively associate with benefit to checkpoint inhibition in NSCLC. Frigola J, Carbonell C, Irazno P, Pardo N, Callejo A, Cedres S, Martinez-Marti A, Navarro A, Soleda M, Jimenez J, Hernandez-Losa J, Vivancos A, Felip E, Amat R. *J Immunother Cancer*. 2022 Apr;10(4):e004197. IF: 12,469.

Phase I, multicenter, open-label study of intravenous VCN-01 oncolytic adenovirus with or without nab-paclitaxel plus gemcitabine in patients with advanced solid tumors. Garcia-Carbonero R, Bazan-Peregrino M, Gil-Martín M, Álvarez R, Macarulla T, Riesco-Martinez MC, Verdaguer H, Guillén-Ponce C, Farrera-Sal M, Moreno R, Mato-Berciano A, Maliandi MV, Torres-Manjon S, Costa M, Del Pozo N, Martínez de Villarreal J, Real FX, Vidal N, Capella G, Alemany R, Blasi E, Blasco C, Cascalló M, Salazar R. *J Immunother Cancer*. 2022 Mar;10(3):e003255. IF: 12,469.

Ascites and resistance to immune checkpoint inhibition in dMMR/MSI-H metastatic colorectal and gastric cancers. Fucà G, Cohen R, Lonardi S, Shitara K, Elez ME, Fakih M, Chao J, Klempner SJ, Emmett M, Jayachandran P, Bergamo F, García MD, Mazzoli G, Provenzano L, Colle R, Svrcek M, Ambrosini M, Randon G, Shah AT, Salati M, Fenocchio E, Salvatore L, Chida K, Kawazoe A, Conca V, Curigliano G, Corti F, Cremolini C, Overman M, Andre T, Pietrantonio F. *J Immunother Cancer*. 2022 Feb;10(2):e004001. IF: 12,469.

Safety and antitumor activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) or proficient/stable (MMRp/MSS) endometrial cancer: interim results from GARNET-a phase I, single-arm study. Oaknin A, Gilbert L, Tinker AV, Brown J, Mathews C, Press J, Sabatier R, O'Malley DM, Samouelian V, Boni V, Duska L, Ghamande S, Ghatage P, Kristeleit R, Leath C III, Guo W, Im E, Zildjian S, Han X, Duan T, Veneris J, Pothuri B. *J Immunother Cancer*. 2022 Jan;10(1):e003777. IF: 12,469.

Predictive Role of CD36 Expression in HER2-Positive Breast Cancer Patients Receiving Neoadjuvant Trastuzumab. Ligorio F, Di Cosimo S, Verderio P, Ciniselli CM, Pizzamiglio S, Castagnoli L, Dugo M, Galbardi B, Salgado R, Loi S, Michiels S, Triulzi T, Tagliabue E, El-Abed S, Izquierdo M, de Azambuja E, Nuciforo P, Huober J, Moscetti L, Janni W, Coccia-Portugal MA, Corsetto PA, Belfiore A, Lorenzini D, Daidone MG, Vingiani A, Gianni L, Pupa SM, Bianchini G, Pruneri G, Vernieri C. *J Natl Cancer Inst*. 2022 Dec 8;114(12):1720-1727. IF: 11,816.

COVID-19 Sequelae and the Host Proinflammatory Response: An Analysis From the OnCovid Registry. Cortellini A, Gennari A, Pommeret F, Patel G, Newsom-Davis T, Bertuzzi A, Viladot M, Aguilar-Company J, Mirallas O, Felip E, Lee AJX, Dalla Pria A, Sharkey R, Brunet J, Carmona-García M, Chester J, Mukherjee U, Scotti L, Dolly S, Sita-Lumsden A, Ferrante D, Van Hemelrijck M, Moss C, Russell B, Seguí E, Biello F, Krengli M, Marco-Hernández J, Gaidano G, Patriarca A, Bruna R, Roldán E, Fox L, Pous A, Griscelli F, Salazar R, Martinez-Vila C, Sureda A, Loizidou A, Maluquer C, Stoclin A, Iglesias M, Pedrazzoli P, Rizzo G, Santoro A, Rimassa L, Rossi S, Harbeck N, Sanchez de Torre A, Vincenzi B, Libertini M, Provenzano S, Generali D, Grisanti S, Berardi R, Tucci M, Mazzoni F, Lambertini M, Tagliamento M, Parisi A, Zoratto F, Queirolo P, Giusti R, Guida A, Zambelli A, Tondini C, Maconi A, Betti M, Colomba E, Diamantis N, Sinclair A, Bower M, Ruiz-Camps I, Pinato DJ; OnCovid study group. *J Natl Cancer Inst*. 2022 Jul 11;114(7):979-987. IF: 11,816.

Clinical Trial Endpoints in Metastatic Cancer: Using Individual Participant Data to Inform Future Trials Methodology. Goldberg RM, Adams R, Buyse M, Eng C, Grothey A, André T, Sobrero AF, Lichtman SM, Benson AB, Punt CJA, Maughan T, Burzykowski T, Sommeijer D, Saad ED, Shi Q, Coart E, Chibaudel B, Koopman M, Schmoll HJ, Yoshino T, Taieb J, Tebbutt NC, Zalcberg J, Tabernero J, Van Cutsem E, Matheson A, de Gramont A. *J Natl Cancer Inst*. 2022 Jun 13;114(6):819-828. IF: 11,816.

Tumor Cellularity and Infiltrating Lymphocytes as a Survival Surrogate in HER2-Positive Breast Cancer. Chic N, Luen SJ, Nuciforo P, Salgado R, Fumagalli D, Hilbers F, Wang Y, de Azambuja E, Láng I, Di Cosimo S, Saura C, Huober J, Prat A, Loi S. *J Natl Cancer Inst*. 2022 Mar 8;114(3):467-470. IF: 11,816.

Breast and Prostate Cancer Risks for Male BRCA1 and BRCA2 Pathogenic Variant Carriers Using Polygenic Risk Scores. Barnes DR, Silvestri V, Leslie G, McGuffog L, Dennis J, Yang X, Adlard J, Agnarsson BA, Ahmed M, Aittomäki K, Andrulis IL, Arason A, Arnold N, Auber B, Azzollini J, Balmaña J, Barkardottir RB, Barrowdale D, Barwell J, Belotti M, Benitez J, Berthet P, Boonen SE, Borg Å, Bozsik A, Brady AF, Brennan P, Brewer C, Brunet J, Bucalo A, Buys SS, Caldés T, Caligo MA, Campbell I, Cassingham H, Christensen LL, Cini G, Claes KBM; GEMO Study Collaborators; EMBRACE Collaborators; Cook J, Coppa A, Cortesi L, Damante G, Darder E, Davidson R, de la Hoya M, De Leeneer K, de Putter R, Del Valle J, Diez O, Ding YC, Domchek SM, Donaldson A, Eason J, Eeles R, Engel C, Evans DG, Feliubadaló L, Fostira F, Frone M, Frost D, Gallagher D, Gehrig A, Giraud S, Glendon G, Godwin AK, Goldgar DE, Greene MH, Gregory H, Gross E, Hahnen E, Hamann U, Hansen TVO, Hanson H, Hentschel J, Horvath J; KConFab Investigators; HEBON Investigators; Izatt L, Izquierdo A, James PA, Janavicius R, Jensen UB, Johannsson OT, John EM, Kramer G, Kroeldrup L, Kruse TA, Lautrup C, Lazaro C, Lesueur F, Lopez-Fernández A, Mai PL, Manoukian S, Matrai Z, Matricardi L, Maxwell KN, Mebirouk N, Meindl A, Montagna M, Monteiro AN, Morrison PJ, Muranen TA, Murray A, Nathanson KL, Neuhausen SL, Nevanlinna H, Nguyen-Dumont T, Niederacher D, Olah E, Olopade OI, Palli D, Parsons MT, Pedersen IS, Peissel B, Perez-Segura P, Peterlongo P, Petersen AH, Pinto P, Porteous ME, Pottinger C, Pujana MA, Radice P, Ramser J, Rantala J, Robson M, Rogers MT, Rønlund K, Rump A, Sánchez de Abajo AM, Shah PD, Sharif S, Side LE, Singer CF, Stadler Z, Steele L, Stoppa-Lyonnet D, Sutter C, Tan YY, Teixeira MR, Teulé A, Thull DL, Tischkowitz M, Toland AE, Tommasi S,

Toss A, Trainer AH, Tripathi V, Valentini V, van Asperen CJ, Venturelli M, Viel A, Vijai J, Walker L, Wang-Gohrke S, Wappenschmidt B, Whaite A, Zanna I, Offit K, Thomassen M, Couch FJ, Schmutzler RK, Simard J, Easton DF, Chenevix-Trench G, Antoniou AC, Ottini L; Consortium of Investigators of Modifiers of BRCA1 and BRCA2. *J Natl Cancer Inst*. 2022 Jan 11;114(1):109-122. IF: 11,816.

HER2DX genomic test in HER2-positive/hormone receptor-positive breast cancer treated with neoadjuvant trastuzumab and pertuzumab: A correlative analysis from the PerELISA trial. Guarneri V, Bras-Maristany F, Dieci MV, Griguolo G, Par L, Mar Ín-Aguilera M, Miglietta F, Bottosso M, Giorgi CA, Blasco P, Castillo O, Galv N P, Vivancos A, Villagrasa P, Parker JS, Perou CM, Conte P, Prat A. *EBioMedicine*. 2022 Nov;85:104320. IF: 11,205.

Treatment time and circadian genotype interact to influence radiotherapy side-effects. A prospective European validation study using the REQUITE cohort. Webb AJ, Harper E, Rattay T, Aguado-Barrera ME, Azria D, Bourgier C, Brengues M, Briers E, Bultijnck R, Chang-Claude J, Choudhury A, Cicchetti A, De Ruysscher D, De Santis MC, Dunning AM, Elliott RM, Fachal L, Gómez-Caamaño A, Gutiérrez-Enríquez S, Johnson K, Lobato-Busto R, Kerns SL, Post G, Rancati T, Reyes V, Rosenstein BS, Seibold P, Seoane A, Sosa-Fajardo P, Sperk E, Taboada-Valladares B, Valdagni R, Vega A, Veldeman L, Ward T, West CM, Symonds RP, Talbot CJ; REQUITE Consortium. *EBioMedicine*. 2022 Oct;84:104269. IF: 11,205.

Development and validation of the new HER2DX assay for predicting pathological response and survival outcome in early-stage HER2-positive breast cancer. Prat A, Guarneri V, Pascual T, Brasó-Maristany F, Sanfeliu E, Paré L, Schettini F, Martínez D, Jares P, Griguolo G, Dieci MV, Cortés J, Llombart-Cussac A, Conte B, Marín-Aguilera M, Chic N, Puig-Butillé JA, Martínez A, Galván P, Tsai YH, González-Farré B, Mira A, Vivancos A, Villagrasa P, Parker JS, Conte P, Perou CM. *EBioMedicine*. 2022 Jan;75:103801. IF: 11,205.

Interleukin-1 receptor associated kinase 1/4 and bromodomain and extra-terminal inhibitions converge on NF-κB blockade and display synergistic antitumoral activity in activated B-cell subset of diffuse large B-cell lymphoma with MYD88 L265P mutation. Dlouhy I, Armengol M, Recasens-Zorzo C, Ribeiro ML, Pérez-Galán P, Bosch F, López-Guillermo A, Roué G. *Haematologica*. 2022 Dec 1;107(12):2990. IF: 11,047.

Autologous stem-cell transplantation as consolidation of first-line chemotherapy in patients with peripheral T-cell lymphoma: a multicenter GELTAMO/FIL study. García-Sancho AM, Bellei M, López-Parra M, Gritti G, Cortés M, Novelli S, Panizo C, Petrucci L, Gutiérrez A, Dlouhy I, Bastos-Oreiro M, Sancho JM, Ramírez MJ, Moraleda JM, Carrillo E, Jiménez-Ubieto AI, Jarque I, Orsucci L, García-Torres E, Montalbán C, Dodero A, Arranz R, De Las Heras N, Pascual MJ, López-Jiménez J, Spina M, Re A, De Villambrosia SG, Bobillo S, Federico M, Caballero D. *Haematologica*. 2022 Nov 1;107(11):2675-2684. IF: 11,047.

Chromosome banding analysis and genomic microarrays are both useful but not equivalent methods for genomic complexity risk stratification in chronic lymphocytic leukemia patients. Ramos-Campoy S, Puiggros A, Beà S, Bougeon S, Larráyoz MJ, Costa D, Parker H, Rigolin GM, Ortega M, Blanco ML, Collado R, Salgado R, Baumann T, Gimeno E, Moreno C, Bosch F, Calvo X, Calasanz MJ, Cuneo A, Strefford JC, Nguyen-Khac F, Oscier D, Haferlach C, Schoumans J, Espinet B. *Haematologica*. 2022 Mar 1;107(3):593-603. IF: 11,047.

Mepolizumab Reduces Hypereosinophilic Syndrome Flares Irrespective of Blood Eosinophil Count and Interleukin-5. Rothenberg ME, Roufosse F, Faguer S, Gleich GJ, Steinfeld J, Yancey SW, Mavropoulou E, Kwon N; HES Mepolizumab Study Group. *J Allergy Clin Immunol Pract*. 2022 Sep;10(9):2367-2374.e3. IF: 11,022.

Multi-omic rejuvenation of naturally aged tissues by a single cycle of transient reprogramming. Chondronasiou D, Gill D, Mosteiro L, Urdinguio RG, Berenguer-Llergo A, Aguilera M, Durand S, Aprahamian F, Nirmalathasan N, Abad M, Martin-Herranz DE, Stephan-Otto Attolini C, Prats N, Kroemer G, Fraga MF, Reik W, Serrano M. *Aging Cell*. 2022 Mar;21(3):e13578. IF: 11,005.

Microfluidic-based dynamic BH3 profiling predicts anticancer treatment efficacy. Manzano-Muñoz A, Yeste J, Ortega MA, Martín F, López A, Rosell J, Castro S, Serrano C, Samitier J, Ramón-Azcón J, Montero J. *NPJ Precis Oncol*. 2022 Dec 1;6(1):90. IF: 10,092.

A randomised phase 2 study comparing different dose approaches of induction treatment of regorafenib in previously treated metastatic colorectal cancer patients (REARRANGE trial). Argilés G, Mulet N, Valladares-Ayerbes M, Viéitez JM, Grávalos C, García-Alfonso P, Santos C, Tobeña M, García-Paredes B, Benavides M, Cano MT, Loupakis F, Rodríguez-Garrote M, Rivera F, Goldberg RM, Cremolini C, Bennouna J, Ciardiello F, Tabernero JM, Aranda E; Spanish Cooperative Group for the Treatment of Digestive Tumors (TTD) and UNICANCER GI; The, REARRANGE investigators; Principal investigator; Argilés G, Tabernero J; Steering Committee; Investigators. *Eur J Cancer*. 2022 Dec;177:154-163. IF: 10,002.

Recent progress and current challenges of immunotherapy in advanced/metastatic esophagogastric adenocarcinoma. Moehler M, Högner A, Wagner AD, Obermannova R, Alsina M, Thuss-Patience P, van Laarhoven H, Smyth E. *Eur J Cancer*. 2022 Nov;176:13-29. IF: 10,002.

Next-generation sequencing analysis of cholangiocarcinoma identifies distinct IDH1-mutated clusters. Rimini M, Loi E, Fabregat-Franco C, Burgio V, Lonardi S, Niger M, Scartozzi M, Raposelli IG, Aprile G, Ratti F, Pedica F, Verdaguer H, Rizzato M, Nichetti F, Lai E, Cappetta A, Macarulla T, Fassan M, De Braud F, Pretta A, Simionato F, De Cobelli F, Aldrighetti L, Fornaro L, Cascinu S, Zavattari P, Casadei-Gardini A. *Eur J Cancer*. 2022 Nov;175:299-310. IF: 10,002.

EMPOWER CERVICAL-1: Effects of cemiplimab versus chemotherapy on patient-reported quality of life, functioning and symptoms among women with recurrent cervical cancer. Oaknin A, Monk BJ, Vergote I, Cristina de Melo A, Kim YM, Lisyanskaya AS, Samouëlian V, Kim HS, Gotovkin EA, Damian F, Chang CL, Takahashi S, Li J, Mathias M, Fury MG, Ivanescu C, Reaney M, LaFontaine PR, Lowy I, Harnett J, Chen CI, Tewari KS. *Eur J Cancer*. 2022 Oct;174:299-309. IF: 10,002.

Pre-operative ribociclib plus letrozole versus chemotherapy: Health-related quality of life outcomes from the SOLTI CORALLEEN trial. Villacampa G, Falato C, Paré L, Hernando C, Arumí M, Saura C, Gómez G, Muñoz M, Gil-Gil M, Izarzugaza Y, Ferrer N, Najera-Zuloaga J, Montaño A, Ciruelos E, González-Santiago S, Villagrasa P, Gavilá J, Prat A, Pascual T. *Eur J Cancer*. 2022 Oct;174:232-242. IF: 10,002.

Prognostic impact of performance status on the outcomes of immune checkpoint inhibition strategies in patients with dMMR/MSI-H metastatic colorectal cancer. Mazzoli G, Cohen R, Lonardi S, Corti F, Elez E, Fakih M, Jayachandran P, Colle R, Shah AT, Salati M, Fenocchio E, Salvatore L, Ambrosini M, Ros J, Intini R, Cremolini C, Overman MJ, André T, Pietrantonio F. *Eur J Cancer*. 2022 Sep;172:171-181. IF: 10,002.

Nazartinib for treatment-naive EGFR-mutant non-small cell lung cancer: Results of a phase 2, single-arm, open-label study. Tan DSW, Kim SW, Ponce Aix S, Sequist LV, Smit EF, Yang JCH, Hida T, Toyozawa R, Felip E, Wolf J, Grohé C, Leighl NB, Riely G, Cui X, Zou M, Ghebremariam S, O'Sullivan-Djentuh L, Belli R, Giovannini M, Kim DW. *Eur J Cancer*. 2022 Sep;172:276-286. IF: 10,002.

Overcoming acquired MET amplification after encorafenib-cetuximab in BRAF-V600E mutated colorectal cancer. Ros J,

Elez E. *Eur J Cancer*. 2022 Sep;172:326-328. IF: 10,002.

Lurbinectedin in patients with pretreated neuroendocrine tumours: Results from a phase II basket study. Longo-Muñoz F, Castellano D, Alexandre J, Chawla SP, Fernández C, Kahatt C, Alfaro V, Siguero M, Zeaiter A, Moreno V, Sanz-García E, Awada A, Santaballa A, Subbiah V. *Eur J Cancer*. 2022 Sep;172:340-348. IF: 10,002.

Radium-223 for patients with metastatic castration-resistant prostate cancer with asymptomatic bone metastases progressing on first-line abiraterone acetate or enzalutamide: A single-arm phase II trial. Carles J, Alonso-Gordoa T, Mellado B, Méndez-Vidal MJ, Vázquez S, González-Del-Alba A, Piulats JM, Borrega P, Gallardo E, Morales-Barrera R, Paredes P, Reig O, Garcías de España C, Collado R, Bonfill T, Suárez C, Sampayo-Cordero M, Malfettone A, Garde J. *Eur J Cancer*. 2022 Sep;173:317-326. IF: 10,002.

Gene mutational profile of BRCAness and clinical implication in predicting response to platinum-based chemotherapy in patients with intrahepatic cholangiocarcinoma. Rimini M, Macarulla T, Burgio V, Lonardi S, Niger M, Scartozzi M, Rapposelli IG, Aprile G, Ratti F, Pedica F, Verdaguer H, Nappo F, Nichetti F, Lai E, Valgiusti M, Cappetta A, Febregat C, Fassan M, De Braud F, Puzzoni M, Frassineti GL, Simionato F, De Cobelli F, Aldrighetti L, Fornaro L, Cascinu S, Casadei-Gardini A. *Eur J Cancer*. 2022 Aug;171:232-241. IF: 10,002.

Vaccination against SARS-CoV-2 protects from morbidity, mortality and sequelae from COVID19 in patients with cancer. Pinato DJ, Ferrante D, Aguilar-Company J, Bower M, Salazar R, Mirallas O, Sureda A, Bertuzzi A, Brunet J, Lambertini M, Maluquer C, Pedrazzoli P, Biello F, Lee AJX, Sng CCT, Liñan R, Rossi S, Carmona-García MC, Sharkey R, Eremiev S, Rizzo G, Bain HD, Yu T, Cruz CA, Perachino M, Saoudi-Gonzalez N, Fort-Culillas R, Doonga K, Fox L, Roldán E, Zoratto F, Gaidano G, Ruiz-Camps I, Bruna R, Patriarca A, Shawe-Taylor M, Fusco V, Martinez-Vila C, Berardi R, Filetti M, Mazzoni F, Santoro A, Delfanti S, Parisi A, Queirolo P, Aujayeb A, Rimassa L, Prat A, Tabernero J, Gennari A, Cortellini A; OnCovid study group. *Eur J Cancer*. 2022 Aug;171:64-74. IF: 10,002.

Statin and metformin use and outcomes in patients with castration-resistant prostate cancer treated with enzalutamide: A meta-analysis of AFFIRM, PREVAIL and PROSPER. Joshua AM, Armstrong A, Crumbaker M, Scher HI, de Bono J, Tombal B, Hussain M, Sternberg CN, Gillessen S, Carles J, Fizazi K, Lin P, Duggan W, Sugg J, Russell D, Beer TM. *Eur J Cancer*. 2022 Jul;170:285-295. IF: 10,002.

Persistence of long-term COVID-19 sequelae in patients with cancer: An analysis from the OnCovid registry. Cortellini A, Salazar R, Gennari A, Aguilar-Company J, Bower M, Bertuzzi A, Brunet J, Lambertini M, Maluquer C, Pedrazzoli P, Lee AJ, Carmona-García M, Newsom-Davis T, Van Hemelrijck M, Plaja A, Zambelli A, Tondini C, Generali D, Bertulli R, Diamantis N, Mukherjee U, Rizzo G, Yu T, Zoratto F, Bruna R, Sureda A, Martinez-Vila C, Cantini L, Mazzoni F, Grosso F, Parisi A, Saponara M, Prat A, Pinato DJ; On Covid study group. *Eur J Cancer*. 2022 Jul;170:10-16. IF: 10,002.

Effects of metformin and statins on outcomes in men with castration-resistant metastatic prostate cancer: Secondary analysis of COU-AA-301 and COU-AA-302. Wilson BE, Armstrong AJ, de Bono J, Sternberg CN, Ryan CJ, Scher HI, Smith MR, Rathkopf D, Logothetis CJ, Chi KN, Jones RJ, Saad F, De Porre P, Tran N, Hu P, Gillessen S, Carles J, Fizazi K, Joshua AM. *Eur J Cancer*. 2022 Jul;170:296-304. IF: 10,002.

ANtiangiogenic Second-line Lung cancer Meta-Analysis on individual patient data in non-small cell lung cancer: ANSELMA. Remon J, Lacas B, Herbst R, Reck M, Garon EB, Scagliotti GV, Ramlau R, Hanna N, Vansteenkiste J, Yoh K, Groen HJM, Heymach JV, Mandrekar SJ, Okamoto I, Neal JW, Heist RS, Planchard D, Pignon JP, Besse B; ANSELMA collaborative group. *Eur J Cancer*. 2022 May;166:112-125. IF: 10,002.

Definitions and treatment of oligometastatic oesophagogastric cancer according to multidisciplinary tumour boards in Europe. Kroese TE, van Hillegersberg R, Schoppmann S, Deseyne PRAJ, Nafteux P, Obermannova R, Nordsmark M, Pfeiffer P, Hawkins MA, Smyth E, Markar S, Hanna GB, Cheong E, Chaudry A, Elme A, Adenis A, Piessen G, Gani C, Bruns CJ, Moehler M, Liakakos T, Reynolds J, Morganti A, Rosati R, Castoro C, D'Ugo D, Roviello F, Bencivenga M, de Manzoni G, Jeene P, van Sandick JW, Muijs C, Slingerland M, Nieuwenhuijzen G, Wijnhoven B, Beerepoot LV, Kolodziejczyk P, Polkowski WP, Alsina M, Pera M, Kanonnikoff TF, Nilsson M, Guckenberger M, Monig S, Wagner D, Wyrwicz L, Berbee M, Gockel I, Lordick F, Griffiths EA, Verheij M, van Rossum PSN, van Laarhoven HWM; OMEC working group. *Eur J Cancer*. 2022 Mar;164:18-29. IF: 10,002.

Tumour mutational burden predicts resistance to EGFR/BRAF blockade in BRAF-mutated microsatellite stable metastatic colorectal cancer. Randon G, Intini R, Cremolini C, Elez E, Overman MJ, Lee J, Manca P, Bergamo F, Pagani F, Antista M, Angerilli V, Ros Montaña FJ, Lavacchi D, Boccaccino A, Fucà G, Brich S, Cattaneo L, Fassan M, Pietrantonio F, Lonardi S. *Eur J Cancer*. 2022 Jan;161:90-98. IF: 10,002.

The target antigen determines the mechanism of acquired resistance to T cell-based therapies. Martínez-Sabadell A, Morancho B, Rius Ruiz I, Román Alonso M, Ovejero Romero P, Escorihuela M, Chicote I, Palmer HG, Nonell L, Alemany-Chavarria M, Klein C, Bacac M, Arribas J, Arenas EJ. *Cell Rep*. 2022 Oct 18;41(3):111430. IF: 9,995.

Breakthrough infections in MPN-COVID vaccinated patients. Barbui T, Carobbio A, Ghirardi A, Iurlo A, De Stefano V, Sobas MA, Rumi E, Elli EM, Lunghi F, Gasior Kabat M, Cuevas B, Guglielmelli P, Bonifacio M, Marchetti M, Alvarez-Larran A, Fox L, Bellini M, Daffini R, Benevolo G, Carreno-Tarragona G, Patriarca A, Al-Ali HK, Andrade-Campos MMM, Palandri F, Harrison C, Foncillas MA, Osorio S, Koschmieder S, Magro Mazo E, Kiladjian JJ, Bolaños Calderón E, Heidel FH, Quiroz Cervantes K, Griesshammer M, Garcia-Gutierrez V, Sanchez AM, Hernandez-Boluda JC, Lopez Abadia E, Carli G, Sagues Serrano M, Kusec R, Xicoy Cirici B, Guenova M, Navas Elorza B, Angona A, Cichocka E, Kulikowska de Nałęcz A, Cattaneo D, Bucelli C, Betti S, Borsani O, Cavalca F, Carbonell S, Curto-Garcia N, Benajiba L, Rambaldi A, Vannucchi AM. *Blood Cancer J*. 2022 Nov 15;12(11):154. IF: 9,812.

A simple score to predict early severe infections in patients with newly diagnosed multiple myeloma. Encinas C, Hernandez-Rivas JÁ, Oriol A, Rosiñol L, Blanchard MJ, Bellón JM, García-Sanz R, de la Rubia J, de la Guía AL, Jímenez-Ubieto A, Jarque I, Iñigo B, Dourdil V, de Arriba F, Pérez-Ávila CC, Gonzalez Y, Hernández MT, Bargay J, Granell M, Rodríguez-Otero P, Silvent M, Cabrera C, Rios R, Alegre A, Gironella M, Gonzalez MS, Sureda A, Sampol A, Ocio EM, Krsnik I, García A, García-Mateo A, Soler JA, Martín J, Arguiñano JM, Mateos MV, Bladé J, San-Miguel JF, Lahuerta JJ, Martínez-López J; GEM/PETHEMA (Grupo Español de Mieloma/Programa para el Estudio de la Terapéutica en Hemopatías Malignas) cooperative study group. *Blood Cancer J*. 2022 Apr 19;12(4):68. IF: 9,812.

mobile version

scan to visit

VALL D'HEBRON INSTITUTE OF ONCOLOGY (VHIO)
SCIENTIFIC REPORT 2022

Programs

mobile version

scan to visit

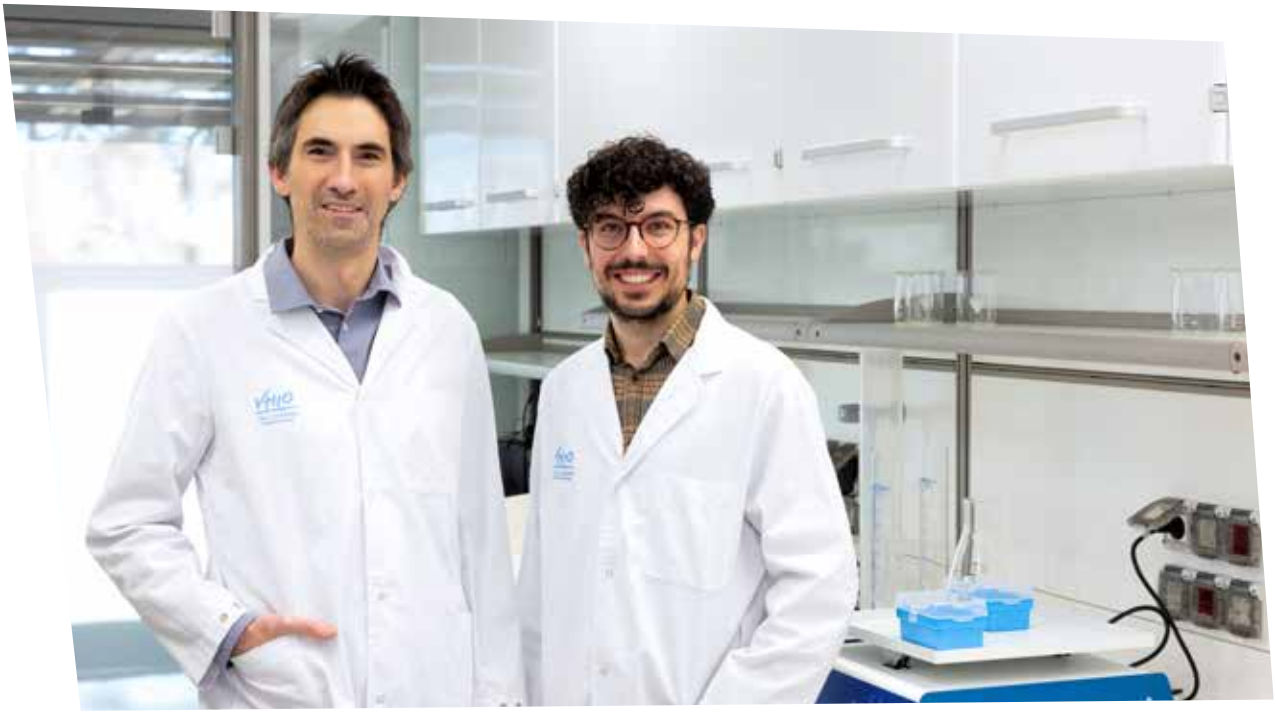
VALL D'HEBRON INSTITUTE OF ONCOLOGY (VHIO)
SCIENTIFIC REPORT 2022

Preclinical & Translational Research

PRECLINICAL & TRANSLATIONAL RESEARCH

Aging and Cancer Group

Principal Investigator Mate Maus **PhD Student** Marc Guasch



/ Strategic goals

- Aging of the microenvironment and cancer: we investigate processes that drive cellular senescence, fibrotic tissue remodeling and inflammation in aged tissues, and in the tumor microenvironment. We aim to better predict the course of aging and cancer with the aim of exposing novel, actionable insights for improved therapeutics and diagnostics in cancer.
- Immunosenescence and cancer: we explore cellular changes that accompany the aging of the immune system and seek to advance insights into the relevance and the therapeutic potential of immunosenescence in aging and cancer.
- Nutrient sensing in cellular senescence in aging and cancer: we investigate the processes that cause excessive nutrient uptake and storage in damaged cells and senescent cells toward improving diagnostics and therapeutics for aging and cancer.

/ Highlights

- Headed by Mate Maus, VHIO's Aging and Cancer Group launched in October 2022.

/ Summary

Led by Mate Maus, VHIO's Aging and Cancer Group was established in October 2022 and advances insights into the mechanisms of aging and its connections to cancer. His group focuses on novel paradigms that can quantify and modulate the processes of cellular senescence, immunosenescence, and organismal aging, and evaluates each in the context of oncology and longevity. His group is dedicated to accelerating discovery and developing new approaches to ultimately improve outcomes for cancer patients and increase the number of years spent in good health for all individuals.

With aging, our body accumulates senescent cells, our organs lose circulation and functionality in a process called fibrogenesis, all of which contribute to our decline in health. We have reported that iron accumulation can play an important role in several of these processes (Maus et al. *bioRxiv*. 2022). These findings have important implications for the pathobiology of aging and cancer. We are now investigating the function and the diagnostic and therapeutic potential of age-associated iron accumulation in longevity and cancer.

As we age our immune functions decline in a process known as immunosenescence. We have previously evidenced regulators of immunometabolism that are key in preserving immune function (Vaeth† and Maust† et al. *Immunity*. 2017*). We are currently developing approaches to measure and modulate the age of the immune system to better understand the implication as well as the possible diagnostic and therapeutic value of immunosenescence in aging and cancer.

Deregulated nutrient sensing is a shared characteristic of aged tissues, senescent cells, and cancer cells resulting in an excessive accumulation of biomaterials. We previously unveiled regulators of biomass accumulation (Maus et al. *Cell Metab*. 2017**) and are researching the underlying biology of excessive biomass accumulation in senescent cells with important implications in aging and cancer.

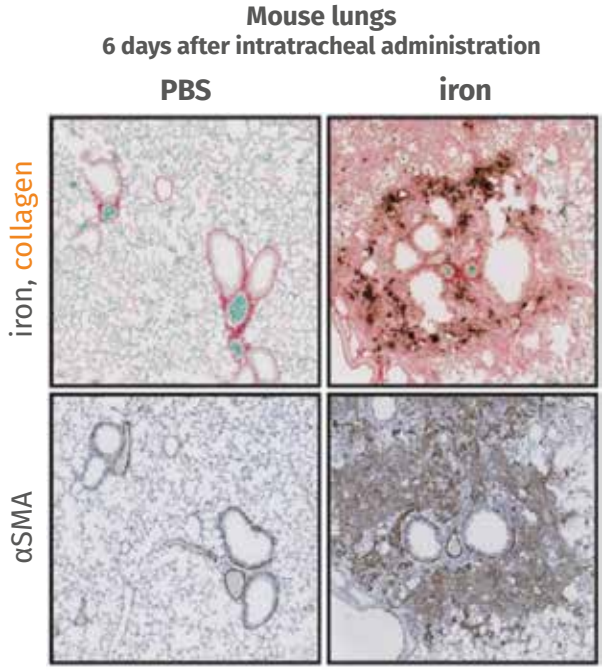


Figure: Iron accumulation drives fibrogenesis. Collagen levels, and collagen producing αSMA+ myofibroblasts in the lungs of mice 6 days after intratracheal delivery of PBS (left) or iron (right).

/ PI paper pick 2022

Maus M, López-Polo V, Lafarga M, Aguilera M, De Lama E, Meyer K, Manonelles A, Sola A, Lopez Martinez C, López-Alonso I, Hernandez-Gonzales F, Chaib S, Rovira M, Sanchez M, Faner R, Agusti A, Prats N, Albaiceta G, Cruzado JM, Serrano M. Iron accumulation drives fibrosis, senescence and the senescence associated secretory phenotype. *bioRxiv* 2022.07.29.501953.

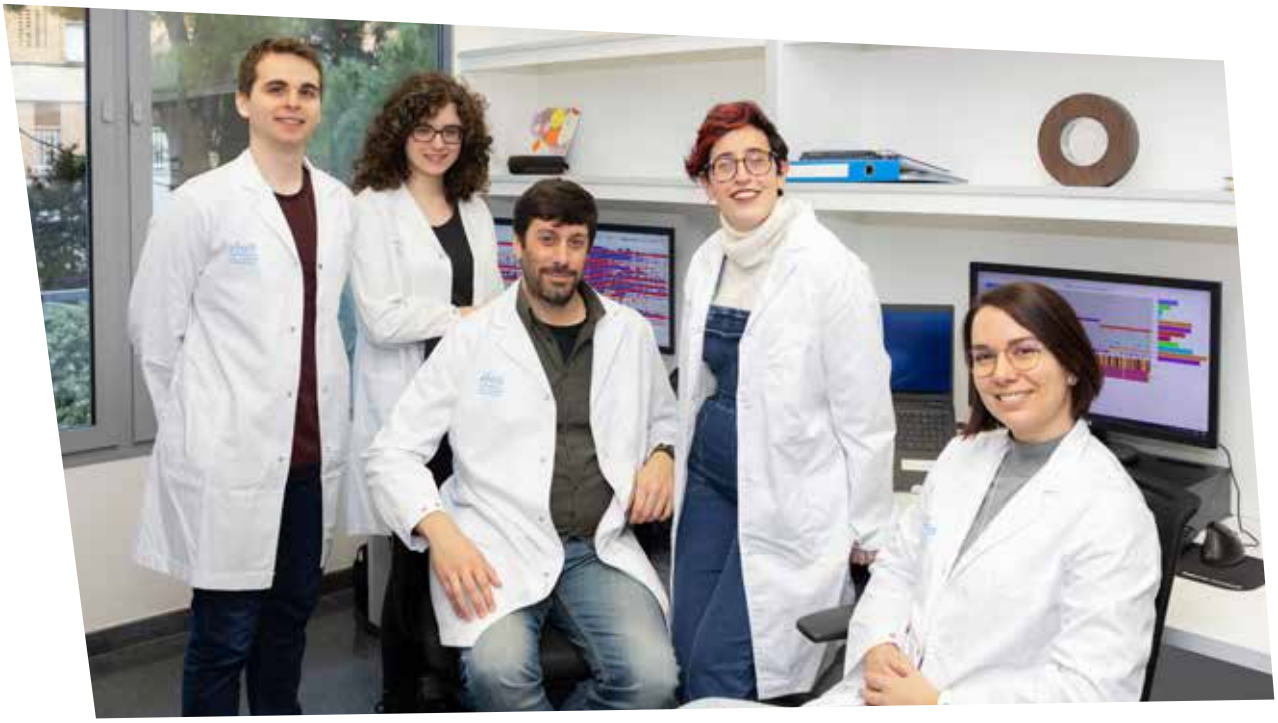
* Vaeth M†, Maus M†, Klein-Hessling S, Freinkman E, Yang J, Eckstein M, Cameron S, Turvey SE, Serfling E, Berberich-Siebelt F, Possemato R, Feske S. Store-Operated Ca2+ Entry Controls Clonal Expansion of T Cells through Metabolic Reprogramming. *Immunity*. 2017 Oct 17;47(4):664-679.e6.

** Maus M, Cuk M, Patel B, Lian J, Ouimet M, Kaufmann U, Yang J, Horvath R, Hornig-Do HT, Chrzanowska-Lightowlers ZM, Moore KJ, Cuervo AM, Feske S. Store-Operated Ca2+ Entry Controls Induction of Lipolysis and the Transcriptional Reprogramming to Lipid Metabolism. *Cell Metab*. 2017 Mar 7;25(3):698-712.

PRECLINICAL & TRANSLATIONAL RESEARCH

Cancer Computational Biology Group

Principal Investigator José A. Seoane **Postdoctoral Fellow** Silvana Maas **Graduate Students** María José Fariña, Arnau Llinàs, **Master's Degree Student** María Butjosa



/ Strategic goals

- Understand the role of chromatin regulatory elements in treatment response and metastasis.
- Discover new epigenetic biomarkers of drug response.
- Potentiate therapeutic options by combining epigenetic therapies with other agents.
- Discover potential environmental causes of early onset cancer.

/ Highlights

- José A. Seoane was awarded with a Fundación FERO-GHD Breast Cancer Grant (page 35).
- José Liñares read his PhD dissertation and graduated with distinction. He is currently a postdoc in Julio Saez-Rodriguez's lab, the Institute for Computational Biomedicine, Heidelberg, Germany.
- As part of a collaboration with the Human Tumor Atlas Network we developed a genomic classifier to identify risk of relapse in ductal carcinoma in situ.
- We participate in a study that identifies *METTL3* as an upstream regulator of *TP53*.

/ Summary

The Cancer Computational Biology Group, headed by José A. Seoane leverages epi(genetic) cancer datasets to unmask the molecular mechanisms implicated in cancer initiation, progression, drug resistance and metastasis toward improved outcomes for patients.

We aim to advance insights into the role of chromatin regulatory elements in treatment response and metastasis, develop novel epigenetic synthetic lethality-based therapeutic options, improve patient stratification guided by multi-omics analysis, and seek out novel epigenetic biomarkers of treatment response.

We have previously shown how the genetic modifiers of chromatin structure are associated with chemotherapy resistance in breast cancer (Seoane et al. 2019). Our group aims to establish how these epigenetic alterations affect drug resistance and how epigenetic therapies can be used to target tumor suppressor genes.

We are also exploring how the machine learning-based integration of multi-omic datasets can facilitate the discovery of new cancer subgroups and biomarkers, as well as help to better predict treatment outcomes and drug response.

Our group has participated/participates in multiple international consortia including The Cancer Genome Atlas, the Human Tumor Atlas Network, Cancer Target Discovery and Development (CTD 2) Network, and, most recently, AURORA (metastatic breast cancer multi-omic cohort).

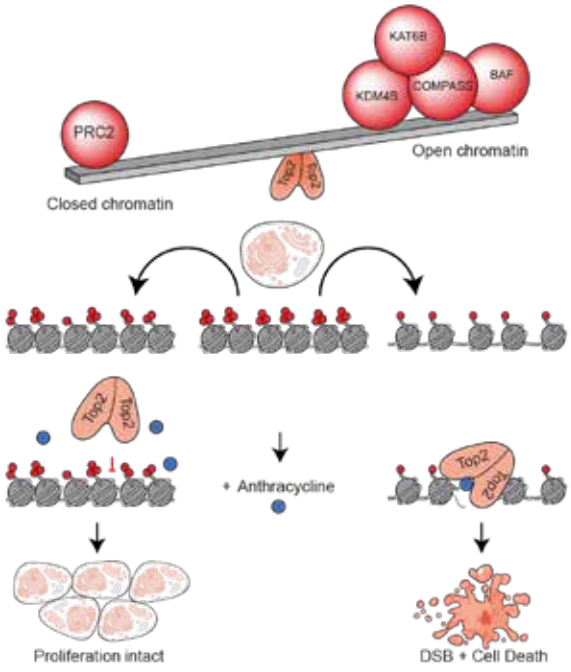


Figure: Epigenetic regulation of chromatin regulatory genes in response to anthracyclines. In the presence of anthracycline, when chromatin regulatory genes are highly expressed, the chromatin is compacted. The *TOP2A* protein cannot consequently access DNA and so the drug does not work as it should. However, if the chromatin machinery genes that open the chromatin are highly expressed, the DNA is accessible, *TOP2A* binds DNA properly, anthracycline poison *TOP2A* causing double strand break and apoptosis.

/ PI paper pick 2022

Strand SH, Rivero-Gutiérrez B, Houlahan KE, Seoane JA, King LM, Risom T, Simpson LA, Vennam S, Khan A, Cisneros L, Hardman T, Harmon B, Couch F, Gallagher K, Kilgore M, Wei S, DeMichele A, King T, McAuliffe PF, Nangia J, Lee J, Tseng J, Storniolo AM, Thompson AM, Gupta GP, Burns R, Veis DJ, DeSchryver K, Zhu C, Matusiak M, Wang J, Zhu SX, Tappenden J, Ding DY, Zhang D, Luo J, Jiang S, Varma S, Anderson L, Straub C, Srivastava S, Curtis C, Tibshirani R, Angelo RM, Hall A, Owzar K, Polyak K, Maley C, Marks JR, Colditz GA, Hwang ES, West RB. Molecular classification and biomarkers of clinical outcome in breast ductal carcinoma in situ: Analysis of TBCRC 038 and RAHBT cohorts. *Cancer Cell*. 2022 Dec 12;40(12):1521-1536.e7.

Nobre AR, Dalla E, Yang J, Huang X, Wullkopf L, Risson E, Razghandi P, Anton ML, Zheng W, Seoane JA, Curtis C, Kenigsberg E, Wang J, Aguirre-Ghiso JA. ZFP281 drives a mesenchymal-like dormancy program in early disseminated breast cancer cells that prevents metastatic outgrowth in the lung. *Nat Cancer*. 2022 Oct;3(10):1165-1180.

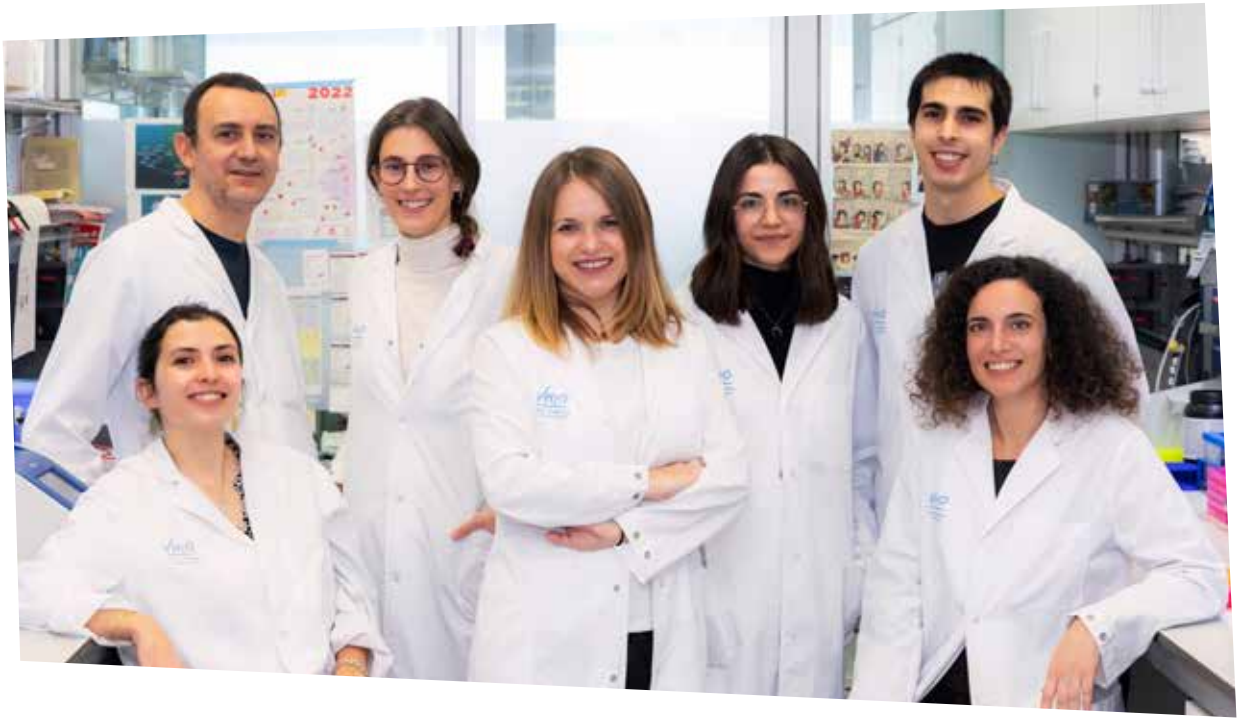
Raj N, Wang M, Seoane JA, Zhao RL, Kaiser AM, Moonie NA, Demeter J, Boutelle AM, Kerr CH, Mulligan AS, Moffatt C, Zeng SX, Lu H, Barna M, Curtis C, Chang HY, Jackson PK, Attardi LD. The Mettl3 epitranscriptomic writer amplifies p53 stress responses. *Mol Cell*. 2022 Jul 7;82(13):2370-2384.e10.

Liñares-Blanco J, Fernandez-Lozano C, Seoane JA, López-Campos G. Machine Learning Based Microbiome Signature to Predict Inflammatory Bowel Disease Subtypes. *Front Microbiol*. 2022 May 17;13:872671.

PRECLINICAL & TRANSLATIONAL RESEARCH

Cellular Plasticity & Cancer Group

Principal Investigator Maria Abad **Postdoctoral Fellows** Olga Boix, Emanuela Greco, Iñaki Merino **Research Assistant** Lluis Palenzuela **Graduate Students** Alba Escriche, Marion Martinez **Master's Students** Sandra Blázquez, Ander Sevillano



/ Strategic goals

- Advance insights into the interplay between therapy-induced senescence, cellular plasticity and cancer.
- Decipher the molecular mechanisms governing the acquisition of stem cell properties during tumorigenesis and after therapy.
- Discover and characterize novel microproteins involved in cancer cell plasticity.
- Develop novel anti-cancer therapies based on the inhibition of cancer cell plasticity.

/ Highlights

- We have published our work identifying and characterizing pTINCR, a novel tumour suppressor microprotein, in *Nature Communications*.
- We have reported the immunogenic role of therapy-induced senescence in *Cancer Discovery*.
- Our PhD students Olga Boix, Emanuela Greco, and Iñaki Merino defended their doctoral theses in 2022 obtaining Cum Laude distinction.

/ Summary

We focus on the interplay between stress responses, cellular plasticity and cancer. Cellular plasticity is now recognized as a critical feature of cancer cells, enabling them to transit between different cellular states and promote tumor growth, disease progression after therapy, and metastasis.

We have previously reported that inducing dedifferentiation with the so-called Yamanaka factors can lead to the development of a variety of tumors. We have also demonstrated that tissue damage –the main driver of cancer– triggers the onset of cellular senescence which then induces dedifferentiation and the acquisition of stem cell properties *in vivo*.

These findings have important therapeutic implications given that chemotherapy and radiotherapy – cornerstones for the treatment of most cancers – could have the side effect of inducing stemness in non- stem cancer cells and, in turn, possibly contribute to tumor recurrence and cancer cell spread.

Our main objective is to advance insights into the mechanisms and drivers implicated in this process, with the ultimate goal of developing novel therapies based on the inhibition of cancer cell plasticity.

Recent results have demonstrated that some genomic regions, previously considered as non-coding (including lncRNAs), contain small open reading frames encoding for evolutionary conserved, unannotated microproteins. The few that have been identified to date assume key functions in elemental cellular processes, leading to a new level of complexity with major implications – from basic research to the clinical setting.

Over the last few years, our efforts have focused on identifying and characterizing novel cancer microproteins which could be novel actors in carcinogenesis. We have discovered five new cancer microproteins and have obtained compelling evidence *in vitro* and *in vivo* that four of them act as novel tumor suppressors, inducing cell cycle arrest, differentiation or inhibition of mesenchymal traits in cancer cells. In addition, using a peptidomics approach, we have identified a set of microproteins secreted by pancreatic tumors, either soluble or secreted in exosomes. These novel microproteins could be crucial cellular messengers for pancreatic cancer metastasis. The identification of tumor-microproteins could be key to advancing insights into cancer physiopathology. Moreover, they could also serve as novel cancer biomarkers for the early detection of disease and patient stratification for tailored therapies, as well as therapeutic targets.

In 2022, we have continued to characterize our identified cancer microproteins and have published our work on pTINCR, a new ubiquitin-like microprotein that promotes epithelial differentiation and suppresses tumor growth (Boix et al. 2022). Please see below for our paper pick for 2022.

In addition, we have continued working on our collaborative project to study therapy-induced tumoral senescence and its potential as a therapeutic target and prognostic biomarker, funded by the Asociación Española Contra el Cáncer - AECC (Spanish Association Against Cancer). In collaboration with Manuel Serrano's group (IRB Barcelona) and Alena Gros' VHIO group (page 86); we published a paper in *Cancer Discovery* demonstrating the immunogenic role of therapy-induced senescence (Marin et al. Epub 2022 Oct 27).

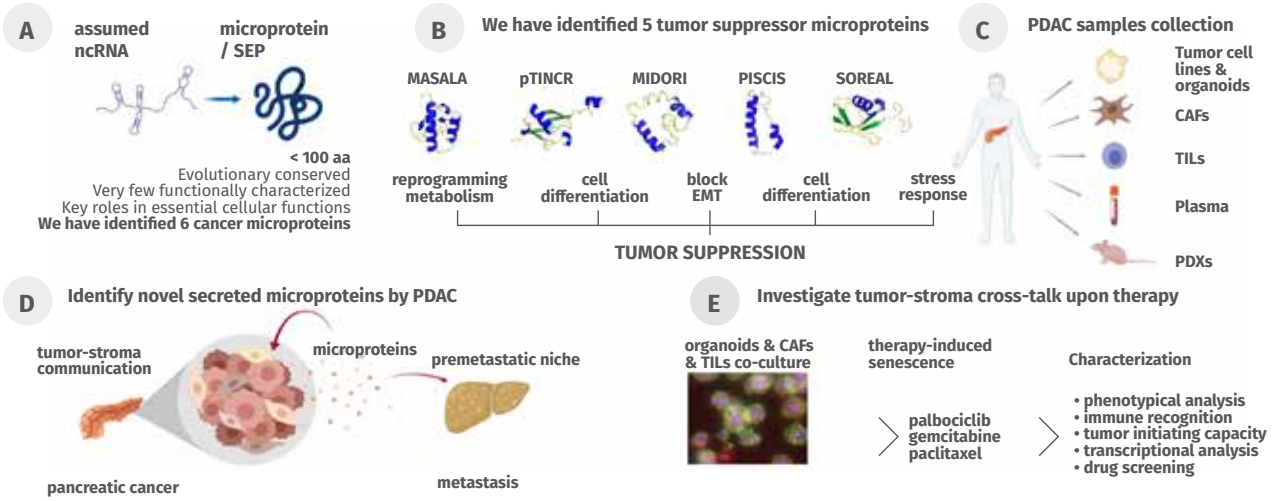


Figure: A) Recent findings have revealed that many genomic regions previously considered as non-coding in fact code for unannotated microproteins; some of them have been shown to be important for cancer. **B)** Our group has identified 5 novel microproteins with tumor suppressor activities. We have characterized them *in vitro* and *in vivo*. **C)** We have generated a comprehensive patient-match collection of pancreatic cancer samples, that is going to be instrumental for our research. **D)** We are investigating if cancer cells use unannotated secreted microproteins as intercellular messengers to promote tumor growth and metastasis. **E)** We are investigating the impact of therapy in the tumor-stroma cross-talk, by co-cultures of organoids-CAFs-TILs.

/ PI paper pick 2022

Boix O, Martinez M, Vidal S, Giménez-Alejandre M, Palenzuela L, Lorenzo-Sanz L, Quevedo L, Moscoso O, Ruiz-Orera J, Ximénez-Embún P, Ciriaco N, Nuciforo P, Stephan-Otto Attolini C, Albà MM, Muñoz J, Tian TV, Varela I, Vivancos A, Ramón Y Cajal S, Muñoz P, Rivas C, Abad M. pTINCR microprotein promotes epithelial differentiation and suppresses tumor growth through CDC42 SUMOylation and activation. *Nat Commun*. 2022 Nov 11;13(1):6840.

Marin I, Boix O, Garcia-Garijo A, Sirois I, Caballe A, Zarzuela E, Ruano I, Stephan-Otto Attolini C, Prats N, Lopez-Dominguez JA, Kovatcheva M, Garralda E, Munoz J, Caron E, Abad M, Gros A, Pietrocola F, Serrano M. Cellular senescence is immunogenic and promotes anti-tumor immunity. *Cancer Discov*. Epub 2022 Oct 27.

PRECLINICAL & TRANSLATIONAL RESEARCH

Experimental Therapeutics Group

Principal Investigator Violeta Serra **Postdoctoral Fellow** Alba Llop-Guevara **Graduate Students** Heura Domènech, Andrea Herencia, Laia Monserrat, Andreu Òdena, Flaminia Pedretti **Visiting Student** Giorgia Casali **Technicians** Marta Guzmán, Olga Rodríguez

/ Strategic goals

- Develop predictive biomarkers of targeted treatments in ER+ and triple negative breast cancers, including inhibitors directed against the DNA damage response (PARP, ATR) as well as signaling/cell cycle kinases (CDK4/6, PI3K/AKT or FGFR).
- Explore novel treatment combinations for ER+ and triple negative breast cancers.
- Contribute to personalized medicine by developing diagnostic tests to better guide treatment strategies based on targeted treatments (e.g. PARP inhibitors).
- Establishing patient tumor-derived breast cancer preclinical models to explore hypothesis-based combinatorial therapies.

/ Highlights

- Our group has contributed towards achieving a better understanding of the mechanisms underlying sensitivity to CDK4/6 inhibitors in breast cancer, as well as the clinical utility of diagnostic tools based on the identification of DNA repair deficiency.
- We have obtained funding from the Catalan Agency for Management of University and Research Grants (AGAUR), and the Spanish Ministry of Science and Innovation to study the mode of action of a novel ADC and to develop a pre-commercial prototype of the RAD51 test for implementation into the Vall d'Hebron University Hospital's (HUVH) diagnostic programs.
- We have established a panel of over one hundred ER+ and triple negative breast cancer PDXs, mainly from the metastatic setting. We particularly focus on models that recapitulate progression on CDK4/6 inhibitors, and *BRCA1/2*-associated tumors.

/ Summary

Our group conducts bench-to-bedside preclinical research in breast cancer to advance insights into biomarkers of response to targeted therapies. To do so, we generate preclinical models including patient-derived xenografts (PDXs) and patient-derived cultures (PDCs) from primary or metastatic breast cancer.

We have significantly contributed to the field of endocrine resistance and continue to more deeply explore mechanisms of sensitivity and resistance to CDK4/6 inhibitors, FGFR inhibitors, AKT inhibitors and AR modulators (SARMs) in breast tumors. Using clinically relevant PDXs, we have provided data to further support that the loss of G1-cell cycle checkpoint control, such as mutation/loss of *RB1* or *CCND1*- amplification, is associated with the lack of response to CDK4/6 blockade in estrogen receptor-positive breast cancer. Additionally, we have generated a collection of PDXs containing FGFR amplification to study biomarkers of sensitivity to FGFR inhibitors; both pan-FGFR1-4 and Multi-targeted Tyrosine Kinase Inhibitors (MTKIs).

Additionally, we are exploring the potential of a novel antibody-drug conjugate (ADC) as a therapeutic strategy for advanced breast cancers that have developed resistance to the current standard of care treatments.

Encouraged by the early success of DNA damage repair inhibitors in germline *BRCA1/2* mutated tumors, we initiated a project aimed at identifying response biomarkers of PARP inhibitors (PARPi) as well as other DNA damage repair inhibitors including those targeting WEE1 or ATR.

Our studies underpin the capacity of germline *BRCA1/2* mutant tumors to recover DNA repair functionality and develop resistance to PARPi. We have developed an assay, the RAD51 test, which accurately identifies germline *BRCA1/2* tumors that have restored DNA repair functionality and become resistant to these drugs. Importantly, this test also identifies tumors that are sensitive to PARPi through its alterations in DNA repair by homologous recombination beyond the germline *BRCA1/2* condition. We filed a patent (EU application in 2017 and PCT in 2018), and we are currently validating the use of this test in tumor samples from breast, ovarian, pancreatic, and prostate cancer patients.

Finally, we are also investigating the effects of PARPi on the tumor immune environment. DNA repair-deficient tumors accumulate cytosolic DNA, which can elicit an innate immune signal (the STING pathway) and upregulate interferon-related genes, leading to lymphocytic infiltration and PD-L1 expression. We are testing the hypothesis that treatment of DNA repair-deficient tumors with PARPi elicits a DNA damage response, resulting in upregulation of PD-L1 that might limit the antitumor immune-mediated cytotoxicity by lymphocytes, but sensitizes to anti-PD-L1 treatments.

Our group works closely together with Cristina Saura's Breast Cancer Group (page 90), and Judith Balmaña's Hereditary Cancer Genetics Group (page 102). Reflective of VHIO's purely multidisciplinary and translational approach, our research is also carried out in collaboration with other groups including VHIO's Molecular Oncology Group (page 118), Cancer Genomics Group (page 116), and Oncology Data Science – ODysSey Group (page 104), directed by Paolo Nuciforo, Ana Vivancos and Rodrigo Dienstmann, respectively.

In summary, our team has significantly advanced insights into the mode of action of novel targeted therapies, identified new response biomarkers, and developed a biomarker-based assay with potential clinical application. We have also demonstrated the efficacy of hypothesis-based drug combinations.

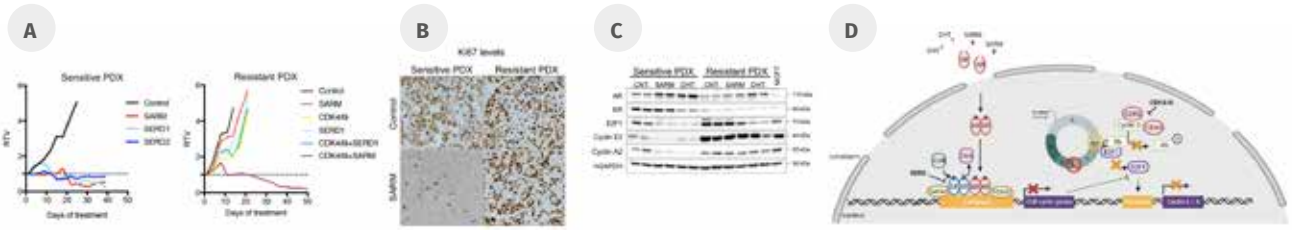


Figure: A) *In vivo* antitumor activity of an androgen receptor modulator (SARM) as monotherapy or in combination with a CDK4/6 inhibitor compared to current treatments in two ER+/AR+ PDX models. **B)** Representative images of the Ki-67 proliferation marker in a sensitive and a resistant PDX model upon treatment with a SARM. **C)** Modulation of cell cycle proteins upon treatment with a SARM or the AR-ligand DHT in a sensitive and a resistant model. **D)** Schematic representation of the potential mechanism of action. AR activation can displace ER co-activators or recruit co-repressors to inhibit ER activity at the chromatin, resulting in a downmodulation of cell cycle genes. CDK4/6 inhibition enhances SARM activity to further disrupt cell cycle progression and exert a potent antitumor activity.

/ PI paper pick 2022

Palafox M, Monserrat L, Bellet M, Villacampa G, Gonzalez-Perez A, Oliveira M, Brasó-Maristany F, Ibrahimi N, Kannan S, Mina L, Herrera-Abreu MT, Ödena A, Sánchez-Guixé M, Capelán M, Azaro A, Bruna A, Rodríguez O, Guzmán M, Grueso J, Viaplana C, Hernández J, Su F, Lin K, Clarke RB, Caldas C, Arribas J, Michiels S, García-Sanz A, Turner NC, Prat A, Nuciforo P, Dienstmann R, Verma CS, Lopez-Bigas N, Scaltriti M, Arnedos M, Saura C, Serra V. High p16 expression and heterozygous RB1 loss are biomarkers for CDK4/6 inhibitor resistance in ER+ breast cancer. *Nat Commun*. 2022 Sep 7;13(1):5258.

Serra V, Wang AT, Castroviejo-Bermejo M, Polanska UM, Palafox M, Herencia-Ropero A, Jones GN, Lai Z, Armenia J, Michopoulos F, Llop-Guevara A, Brough R, Gulati A, Pettitt SJ, Bulusu KC, Nikkilä J, Wilson Z, Hughes A, Wijnhoven PWG, Ahmed A, Bruna A, Gris-Oliver A, Guzman M, Rodríguez O, Grueso J, Arribas J, Cortés J, Saura C, Lau A, Critchlow S, Dougherty B, Caldas C, Mills GB, Barrett JC, Forment JV, Cadogan E, Lord CJ, Cruz C, Balmaña J, O'Connor MJ. Identification of a Molecularly-Defined Subset of Breast and Ovarian Cancer Models that Respond to WEE1 or ATR Inhibition, Overcoming PARP Inhibitor Resistance. *Clin Cancer Res*. 2022 Oct 14;28(20):4536-4550.

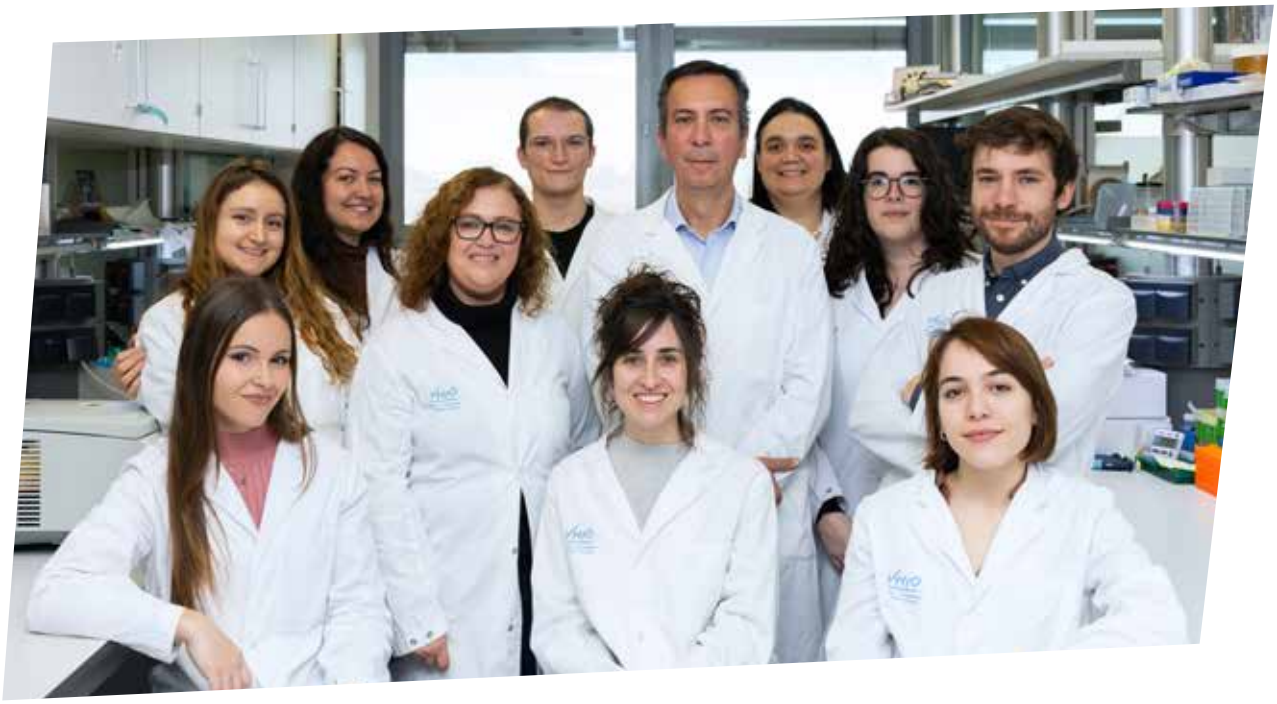
Pellegrino B, Herencia-Ropero A, Llop-Guevara A, Pedretti F, Moles-Fernández A, Viaplana C, Villacampa G, Guzmán M, Rodríguez O, Grueso J, Jiménez J, Arenas EJ, Degasperi A, Dias JML, Forment JV, O'Connor MJ, Déas O, Cairo S, Zhou Y, Musolino A, Caldas C, Nik-Zainal S, Clarke RB, Nuciforo P, Díez O, Serres-Créixams X, Peg V, Espinosa-Bravo M, Macarulla T, Oaknin A, Mateo J, Arribas J, Dienstmann R, Bellet M, Oliveira M, Saura C, Gutiérrez-Enríquez S, Balmaña J, Serra V. Preclinical In Vivo Validation of the RAD51 Test for Identification of Homologous Recombination-Deficient Tumors and Patient Stratification. *Cancer Res*. 2022 Apr 15;82(8):1646-1657.

Sánchez-Guixé M, Hierro C, Jiménez J, Viaplana C, Villacampa G, Monelli E, Brasó-Maristany F, Ogbah Z, Parés M, Guzmán M, Grueso J, Rodríguez O, Oliveira M, Azaro A, Garralda E, Tabernero J, Casanovas O, Scaltriti M, Prat A, Dienstmann R, Nuciforo P, Saura C, Graupera M, Vivancos A, Rodon J, Serra V. High *FGFR1-4* mRNA Expression Levels Correlate with Response to Selective FGFR Inhibitors in Breast Cancer. *Clin Cancer Res*. 2022 Jan 1;28(1):137-149.

PRECLINICAL & TRANSLATIONAL RESEARCH

Gene Expression & Cancer Group

Principal Investigator Joan Seoane **Staff Scientist** Ignasi Barba **Medical Fellow** Simona Casalino **Postdoctoral Fellows** Ester Bonfill-Teixidor, Laia Cuesta, Raffaella Iurlaro, Nicolás Pelaez, Gonçalo Rodrigues **Graduate Students** Laura Carrillo, Cayetano Galera, María López **Bioinformatician** Almudena Neva **Undergraduate Student** Carla Mercadal **Lab Manager** Alexandra Arias **Technicians** Isabel Cuartas, Iris Marcote



/ Strategic goals

- Identify new therapeutic targets against brain tumors and novel biomarkers to help predict response to therapy.
- The study of intratumor heterogeneity.
- Investigate the tumor microenvironment.
- Develop methods for non-invasive molecular diagnosis through the study of circulating biomarkers.
- Generate innovative patient-derived models.

/ Highlights

- Discovery of the mechanism of action (MoA) of the EGFRvIII TCB, now in clinical testing.
- Discovery of the MoA of the brain permeable BRAF inhibitor, now in clinical testing.
- Publication of MoA and phase I trial results of MSC-1/AZD0171.
- Running of a phase II trial testing MSC-1/AZD0171.
- Two Review articles (including clinical practice recommendations) on the clinical applications of liquid biopsies in brain cancer (Soffietti et al. 2022; Pascual et al. 2022).

/ Summary

We study primary brain tumors and brain metastasis; some of the most aggressive of all cancers. Both glioblastoma and brain metastasis are dismal diseases with limited therapeutic options. We strive to advance progress in this field toward improving outcomes for these patients.

Our group is designing tools to monitor and characterize brain tumors. We discovered that we could characterize brain tumors by analyzing immune cells and cell free circulating tumor DNA in cerebrospinal fluid. While no biomarker derived from liquid biopsy against these tumors has yet been integrated into clinical practice, mounting evidence reported in the literature, including our findings, point to its efficacy in the real-time evaluation of malignant disease and potential to better inform and guide the therapeutic management of patients.

Reflective of our work in the field, we were invited to participate in the writing of two Review articles (including clinical practice recommendations) on the clinical applications of liquid biopsies in brain cancer (Soffietti et al. 2022; Pascual et al. 2022) and write a News & Views article in *Nature Reviews Clinical Oncology* (Seoane and Escudero 2022).

We are committed to advancing research to develop novel therapeutic compounds to treat brain cancer. In 2022, we reported the preclinical development of two novel compounds that are now in clinical development:

1- Using patient-derived models, we demonstrated the efficacy and mechanism of action of a novel brain permeable BRAF inhibitor in the context of BRAF mutant melanomas that relapsed to standard of care (Bonfill-Teixidor et al. 2022). A clinical trial to test the compound is now recruiting patients in our Hospital (ISRCTN13713551).

2- Also using patient-derived models, we studied the mechanisms of action of a novel therapeutic bispecific antibody (EGFRvIII TCB) that binds both CD3 T cells and the somatic mutation EGFRvIII expressed in 20-30% of glioblastoma. The results were published (Iurlaro et al. 2022), and the graphical abstract (see Figure) featured on the front cover of the journal. This work was the basis of a clinical trial now running in VHIO (NCT05187624).

The role of the tumor microenvironment which, in the case of brain cancers, assumes a crucial role in cancer progression. Advancing insights into the tumor microenvironment promises powerful weaponry in combating cancer, regardless of heterogeneity. In this sense, we wrote an article about the advances and limitations of a new anti-cancer agent that targets TGF-β and PD-L1 (Gulley et al. 2022).

We have also reported that the cytokine LIF assumes an essential role in the tumor microenvironment and is consequently a promising therapeutic target. We have described the mechanism of action of our novel agent MSC-1 (now AZD0171) (Hallett et al. 2022). MSC-1 is a LIF neutralizing antibody developed by VHIO spin-off, Mosaic Biomedicals, founded by Joan Seoane in 2012. Mosaic Biomedicals was acquired by Medimmune/Astrazeneca in 2020. In 2022, we published the results of the phase I clinical trial (Borazanci et al. 2022, NCT03490669). A phase II clinical trial (NCT04999969) to test MSC-1 initiated patient recruitment in 2021.

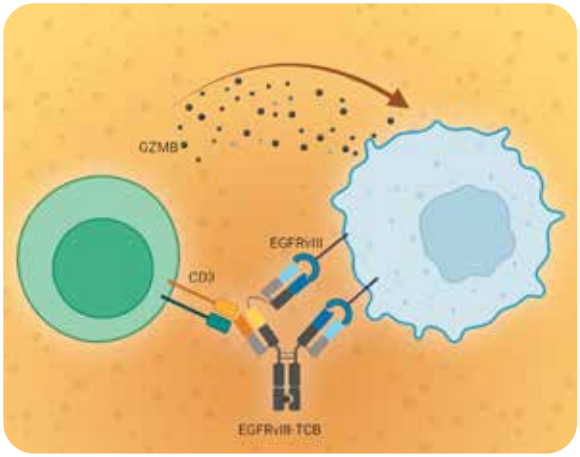


Figure: Mechanism of action of the therapeutic bispecific antibody, EGFRvIII TCB. The bispecific antibody binds T cells and tumor cells through the specific epitope found in EGFRvIII mutation and facilitates the T cell-induced killing of tumor cells. Journal cover image, Iurlaro et al. *Mol Cancer Ther*. 2022.

/ PI paper pick 2022

Hallett R, Bonfill-Teixidor E, Iurlaro R, Arias A, Raman S, Bayliss PE, Egorova O, Neva-Alejo A, McGray AR, Lau E, Bosch A, Beilschmidt M, Maetzel D, Fransson J, Huber-Ruano I, Anido J, Julien JP, Giblin PA, Seoane J. Therapeutic targeting of LIF overcomes macrophage mediated immunosuppression of the local tumor microenvironment. *Clin Cancer Res*. Epub 2022 Nov 28:CCR-21-1888.

Iurlaro R, Waldhauer I, Planas-Rigol E, Bonfill-Teixidor E, Arias A, Nicolini V, Freimoser-Grundschober A, Cuartas I, Martínez-Moreno A, Martínez-Ricarte F, Cordero E, Cicuendez M, Casalino S, Guardia-Reyes X, Fahrni L, Pöschinger T, Steinhart V, Richard M, Briner S, Mueller J, Osl F, Sam J, Colombetti S, Bacac M, Klein C, Pineda E, Reyes-Figueroa L, Di Somma A, González J, Nuciforo P, Carles J, Vieito M, Tabernero J, Umaña P, Seoane J. A Novel EGFRvIII T-Cell Bispecific Antibody for the Treatment of Glioblastoma. *Mol Cancer Ther*. 2022 Oct 7;21(10):1499-1509.

Bonfill-Teixidor E, Iurlaro R, Handl C, Wichmann J, Arias A, Cuartas I, Emmenegger J, Romagnani A, Mangano L, Lorber T, Berrera M, Godfried Sie C, Köchl F, Eckmann J, Feddersen R, Kornacker M, Schnetzler G, Cicuendez M, Cordero E, Topczewski TE, Ferres-Pijoan A, González J, Martínez-Ricarte F, Muñoz-Couselo E, Tabernero J, Bischoff JR, Pettazzoni P, Seoane J. Activity and Resistance of a Brain-Permeable Paradox Breaker BRAF Inhibitor in Melanoma Brain Metastasis. *Cancer Res*. 2022 Jul 18;82(14):2552-2564.

Borazanci E, Schram AM, Garralda E, Brana I, Vieito Villar M, Spreafico A, Oliva M, Lakhani NJ, Hoffman K, Hallett RM, Maetzel D, Hua F, Hilbert J, Giblin P, Anido J, Kelly A, Vickers PJ, Wasserman R, Seoane J, Siu LL, Hyman DM, Hoff DV, Tabernero J. Phase I, first-in-human study of MSC-1 (AZD0171), a humanized anti-leukemia inhibitory factor monoclonal antibody, for advanced solid tumors. *ESMO Open*. 2022 Aug;7(4):100530.

PRECLINICAL & TRANSLATIONAL RESEARCH

Growth Factors Group

Principal Investigator Joaquín Arribas **Postdoctoral Fellows** Enrique Javier Arenas, Vanesa Nogales **Graduate Students** Ariadna Grinyó, Marta Lalinde, Pablo Ovejero, Macarena Román Alonso **Technicians** Marta Escorihuela, Judit Gago, Sandra Perez **Visiting Scientists** Marta Bort, Constanza Cortes, Santiago Duro, Christopher George, Alex Martínez-Sabadell

/ Strategic goals

- Generation and characterization of CAR-Ts against tumor-specific antigens.
- Determine the role of cellular senescence in breast cancer progression and treatment.
- Characterization of new mechanisms of resistance to targeted therapies.

/ Highlights

- We have generated various fourth-generation CAR constructs and tested their efficacy and safety.
- We have tested a new ADC against p95HER2 to use in combinatorial therapy.
- We are exploring the differential role of cellular senescence in cancer depending on the stage of tumor progression.
- We have discovered that resistance to targeted therapies is antigen-dependent and are now characterizing the role of IFN-γ.

/ Summary

During 2022 our group has produced relevant results in all our research areas.

In immunotherapy, our studies showed that acquired resistance mechanisms are antigen-dependent since tumors can either trigger the antigen's epigenetic silencing or disrupt the IFNγ signaling (Martínez-Sabadell et al. 2022). The models generated for this study allowed us to publish a protocol to generate humanized patient-derived xenografts (PDX) models of acquired resistance to immunotherapies (Martínez-Sabadell et al. 2022). Moreover, we continued exploring the role of IFNγ signaling in therapy-induced antitumor responses. Based on this work, we were invited to write a Review article in *Clinical Cancer Research* (Martínez-Sabadell et al. 2022).

Regarding the development of immune redirection therapies, we have continued to focus on chimeric antigen receptor (CAR)-bearing cells and developed a fourth-generation CAR T-cell (CAR T) against p95HER2 that showed promising results (Román et al. 2022). We aim to refine its safety and efficacy to provide a therapeutical alternative for HER+ tumors that will be tested in a phase I clinical trial. Furthermore, we have started to develop and characterize p95HER2 CAR natural killer cells.

We have also continued to study the role of senescent cells in tumor progression, exploring the effect of antibody-drug conjugates (ADCs) on cells previously treated with senescence-inducing therapies used as standard-of-care. We discovered that therapy-induced senescence enhances the efficacy of HER2-targeted ADCs in breast cancer by potentiating the bystander effect (Duro-Sánchez et al. 2022).

Finally, our PDX platform and research endeavors have enabled us to continue collaborating with other VHIO groups and the CIBERONC network, leading to relevant reported discoveries such as:
1) LCOR mediates interferon-independent tumor immunogenicity and responsiveness to immune-checkpoint blockade in triple-negative breast cancer (Pérez-Nuñez et al. 2022); 2) Preclinical *In Vivo* Validation of the RAD51 Test for Identification of Homologous Recombination-Deficient Tumors and Patient Stratification (Pellegrino et al. 2022); 3) Identification of a Molecularly-Defined Subset of Breast and Ovarian Cancer Models that Respond to WEE1 or ATR Inhibition, Overcoming PARP Inhibitor Resistance (Serra et al. 2022); 4) High p16 expression and heterozygous *RB1* loss are biomarkers for CDK4/6 inhibitor resistance in ER+ breast cancer (Palafox et al. 2022); 5) Gasdermin B over-expression modulates HER2-targeted therapy resistance by inducing protective autophagy through Rab7 activation (Gámez-Chiachio et al. 2022): 6) Targeting HER2-AXL heterodimerization to overcome resistance to HER2 blockade in breast cancer (Adam-Artigues et al. 2022): 7) GDF15 Is an Eribulin Response Biomarker also Required for Survival of DTP Breast Cancer Cells (Bellio et al. 2022).

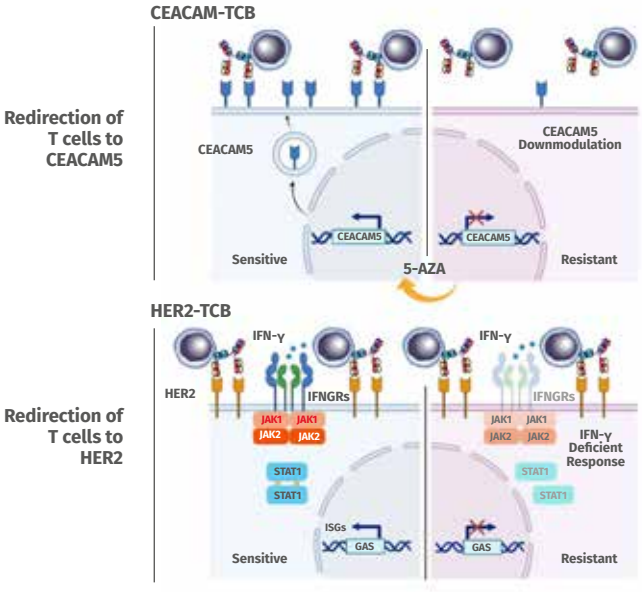


Figure: Targeting different antigens determines the acquired resistance mechanism to T-cell-based therapies. While targeting CEACAM5 induces its transcriptional silencing (top), the recognition of HER2 impairs the IFNγ signaling pathway (bottom). Image from (Martínez-Sabadell et al. *Cell* Rep. 2022).

/ PI paper pick 2022

Duro-Sánchez S, Nadal-Serrano M, Lalinde-Gutiérrez M, Arenas EJ, Bernadó Morales C, Morancho B, Escorihuela M, Pérez-Ramos S, Escrivá-de-Romaní S, Gandullo-Sánchez L, Pandiella A, Esteve-Codina A, Rodilla V, Dijcks FA, Dokter WHA, Cortés J, Saura C, Arribas J. Therapy-Induced Senescence Enhances the Efficacy of HER2-Targeted Antibody-Drug Conjugates in Breast Cancer. *Cancer Res*. 2022 Dec 16;82(24):4670-4679.

Martínez-Sabadell A, Morancho B, Rius Ruiz I, Román Alonso M, Ovejero Romero P, Escorihuela M, Chicote I, Palmer HG, Nonell L, Alemany-Chavarria M, Klein C, Bacac M, Arribas J, Arenas EJ. The target antigen determines the mechanism of acquired resistance to T cell-based therapies. *Cell Rep*. 2022 Oct 18;41(3):111430.

Martínez-Sabadell A, Arenas EJ, Arribas J. IFNγ Signaling in Natural and Therapy-Induced Antitumor Responses. *Clin Cancer Res*. 2022 Apr 1;28(7):1243-1249.

Adam-Artigues A, Arenas EJ, Martínez-Sabadell A, Brasó-Maristany F, Cervera R, Tormo E, Hernando C, Martínez MT, Carbonell-Asins J, Simón S, Poveda J, Moragón S, Zazo S, Martínez D, Rovira A, Burgués O, Rojo F, Albanell J, Bermejo B, Lluch A, Prat A, Arribas J, Eroles P, Cejalvo JM. Targeting HER2-AXL heterodimerization to overcome resistance to HER2 blockade in breast cancer. *Sci Adv*. 2022 May 20;8(20):eabk2746.

PRECLINICAL & TRANSLATIONAL RESEARCH

Models of Cancer Therapies Group

Principal Investigator Laura Soucek **Senior Investigator** Jonathan Whitfield **Research Associate** Mariano F. Zacarías-Fluck
Postdoctoral Fellow Jastrinjan Kaur **Technicians** Judit Grueso, Romina Mariel Rodriguez, Erika Serrano del Pozo
PhD Students Fabio Giuntini, Íñigo González-Larreategui

/ Strategic goals

- Preclinically validate novel therapeutic strategies against MYC in breast, brain, lung, neuroblastoma, melanoma, and colorectal cancer.
- Validate anti-MYC Omomyc-based cell penetrating mini-proteins for cancer therapy.
- Identify and validate biomarkers of response to MYC inhibition.
- Define the role of MYC in promoting cancer immune evasion and test the efficacy of MYC inhibitors and IO combination therapies in cancer treatment.
- Develop potent combinations of Omomyc with current therapeutics, including PARP inhibitors (PARPi) in the context of DNA Damage Response (DDR) deficient tumors.
- Investigate how the MYC network functions in Max-defective gastrointestinal stromal tumors (GISTs) and Small-Cell Lung Cancer (SCLC) to define actionable targets to tackle these unmet clinical needs.

/ Highlights

- In 2022 Laura Soucek was promoted as co-Director of VHIO's Preclinical and Translational Research Program.
- A successful Phase I clinical trial of Omomyc is completed in all-comers with solid tumor malignancies, sponsored by Peptomyc, a spin-off company from VHIO and ICREA.
- Senior Investigator Jonathan Whitfield is compiling a Special Collection for *Front. Cell Dev. Biol.* on *MYC as a disease target beyond cancer* along with Mariano Zacarías-Fluck and Trini Kaur from Laura's laboratory.
- Laura's group was awarded with the Chiara Giorgetti prize to study MYC inhibition in combination with PARPi against breast cancer.

/ Summary

Our group focuses on the pleiotropic and ubiquitous MYC oncoprotein, whose deregulation is implicated in almost all human cancers. The technical challenges of targeting nuclear transcription factors such as MYC –and the concern regarding potential side effects– had until recently precluded any preclinical validation of MYC inhibition as a possible therapeutic strategy.

Over the past few years, we have demonstrated in several mouse models that MYC inhibition has a dramatic therapeutic impact across several tumor types, with very mild and reversible side effects in normal tissue.

Encouraged by our results in mice, we are now interested in developing viable, non-toxic pharmacological options for MYC targeting in the clinic. To do so, we created a spin-off company, Peptomyc S.L., for the development of MYC-inhibiting peptides for cancer therapy. Our laboratory, in partnership with Peptomyc, is currently validating our novel approach against notoriously difficult-to-treat cancers that are resistant to standard treatments and in dire need of new therapeutic avenues (i.e., KRAS-driven Non-Small Cell Lung Cancer, glioblastoma, and metastatic triple negative breast cancer).

The first Omomyc-derived compound, OMO-103, successfully completed the phase I part of the Phase I/IIa clinical trial in October 2022. The trial was sponsored by Peptomyc and performed in 3 Spanish hospitals including the Vall d'Hebron University Hospital – HUVH (Vall d'Hebron Barcelona Hospital Campus). Results of the trial were presented at the 34th EORTC-NCI-AACR Symposium held in Barcelona, 26-28 October 2022. Notably, this is the first direct MYC inhibitor to have ever reached this stage of clinical development.

Our group has continued to contribute to cancer research in general and, more specifically, as a leader in the MYC field, by (co) authoring articles and reviews, exploring new aspects of MYC biology in different pathologies and summarizing efforts to develop a clinically viable MYC inhibitor.

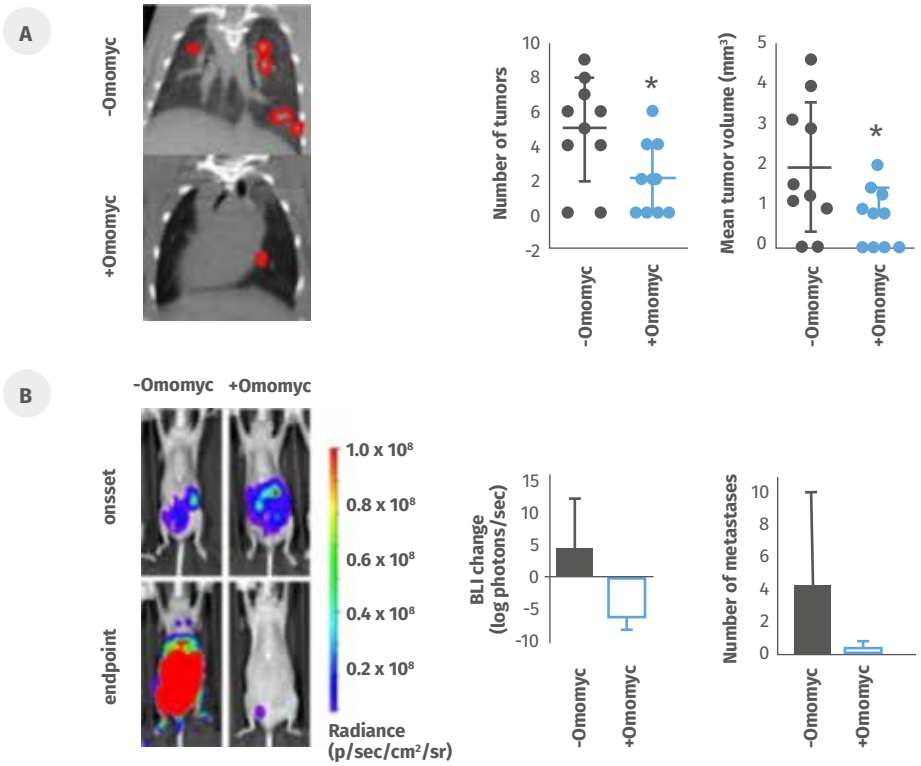


Figure: Adapted from Massó-Vallés et al. (2022) showing the reduction in both lung metastases and total tumour load by Omomyc in mouse models of metastatic TNBC.

/ PI paper pick 2022

Kaur, J, Soucek, L. Going for a "KDIP" in colorectal cancer treatment. *Clin Transl Disc*. 2022; 2:e108.

Massó-Vallés D, Beaulieu ME, Jauset T, Giuntini F, Zacarías-Fluck MF, Foradada L, Martínez-Martín S, Serrano E, Martín-Fernández G, Casacuberta-Serra S, Castillo Cano V, Kaur J, López-Estévez S, Morcillo MÁ, Alzrigat M, Mahmoud L, Luque-García A, Escorihuela M, Guzman M, Arribas J, Serra V, Larsson LG, Whitfield JR, Soucek L. MYC Inhibition Halts Metastatic Breast Cancer Progression by Blocking Growth, Invasion, and Seeding. *Cancer Res Commun*. 2022 Feb 21;2(2):110-130.

Prostate Cancer Translational Research Group

Principal Investigator Joaquin Mateo **Senior Investigator** Nicolas Herranz **Postdoctoral Fellows** Irene Casanova, Luisa Delgado **Clinical Research Fellow** Pablo Cresta **PhD Students** Sara Arce, Julian Brandariz **Technicians** Laura Agundez, Teresa Casals, Sarai Cordoba, Lara de Llobet, Andrei Salca **Clinical Data Curator** Anna Serradell **Bioinformatician** Daniel Aguilar **Master's Student** Arnau Solé

/ Strategic goals

- To investigate correlations between patient molecular profiling and clinical outcome that can guide more precise prostate cancer treatment strategies.
- Study how prostate cancers adapt to therapy, with a focus on targeting emerging vulnerabilities to delay disease recurrence.
- Investigate tumor heterogeneity in response to therapy in preclinical and patient-derived xenograft models (PDX), as well as by interrogating patient biopsies.
- Develop new liquid biopsy tools that can be used to monitor tumor evolution.
- Apply computational pipelines toward investigating genomic signatures in prostate cancer.
- Development of academic clinical trials to validate our laboratory results in the clinic, and leveraging patient biopsies for correlative studies.

/ Highlights

- We serve as the central sample repository for the IRONMAN Registry in Spain. This project is driven by academic team science and collects clinical data and biospecimens for correlative analysis from patients with advanced prostate cancer. VHIO acts as the national lead for this project that has now enrolled >400 men with advanced prostate cancer in Spain and >3000 worldwide.
- We received a Physician-Science Award from the U.S. Department of Defense (DoD), that will enable us to expand our research, integrating more advanced molecular profiling tools including spatial transcriptomics assays on clinical samples. We have also launched a study of patients' expectations around genomic testing thanks to an ESMO Fellowship Award.
- In collaboration with the Urology, Oncology and Radiology teams at the Vall d'Hebron University Hospital (HUVH), we have generated PDX models from prostate cancer biopsies.
- Recruitment for our first investigator-initiated clinical trial completed during 2022, a phase II study co-targeting AR and PARP in metastatic hormone-naïve prostate cancer, and we are now analyzing results and following up patients.
- We published a study correlating genomic signatures and patient outcomes and treatment exposure in metastatic prostate cancer samples.

/ Summary

Our research model follows a bench-to-bedside-and-back approach. We have set up a platform for acquiring longitudinal samples from advanced prostate cancer patients, both tumor tissue as well as liquid biopsies, that can be used to investigate the evolving features of disease, as well as generate patient-derived laboratory models of advanced prostate cancer that we can leverage to investigate new therapeutic strategies at the bench.

Moreover, the launch of investigator-initiated clinical trials is central to our research strategy, as a platform for correlative studies that can optimize the drug development pathway for prostate cancer patients. We are currently the central laboratory for two academic multi-center clinical trials, and also serve as the national repository for the IRONMAN registry; an important international effort to build a large bank of clinical data and biospecimens from metastatic prostate cancer (mPC) patients.

We aim to integrate insights in molecular biology, genomics, transcriptomics, computational sciences and clinical data toward developing precision medicine strategies for prostate cancer patients. To do so, our team comprises biomedical scientists with expertise in cancer biology, genomics and transcriptomics, bioinformatics and liquid biopsy, as well as medical oncologists and clinical data managers.

One of our main lines of research is to decipher how prostate cancers adapt to exposure to systemic therapies, particularly androgen-targeting agents, with a particular focus on the cell cycle and DNA damage response regulation and the emergence of quiescent and senescent phenotypes that can drive drug resistance. By studying in-vitro and in-vivo models, including patient-derived xenografts (PDX) from the patients participating in our clinical studies, we aim to target emergent phenotypes through drug combinations. These studies are currently funded by grants from the Spanish Ministry of Health, Fundación FERO (FERO Foundation), Asociación Española Contra el Cáncer - AECC (Spanish Association Against Cancer), and through collaborations with biopharmaceutical companies.

Our group also aims to pursue the molecular characterization of advanced prostate cancer, focusing on how tumors evolve in a heterogeneous manner as they acquire resistance to different treatments. We have therefore established a genomics and transcriptomics platform in the lab to perform DNA and RNA profiling from patient biopsies. We are developing novel liquid biopsy assays that will enable us to study the disease through longitudinal samples. By exploiting publicly available genomics datasets from patients at different stages of disease, our computational scientists investigate how the genomic profile of disease changes over time. These studies are currently funded by grants from the U.S. Department of Defense (DoD) Congressionally Directed Medical Research Programs (CDMRP), the Spanish Ministry of Health, CRIS Cancer Foundation, AECC, Fundación FERO, and the ”la Caixa” Foundation.

Lastly, given that well-annotated correlative clinical data is crucial to establish the potential relevance of molecular data, our team maintains databases collecting outcome data for all patients who donate samples for our studies to perform subsequent correlative analysis.

To more rapidly advance the field, we believe in team science. We therefore participate in several different collaborations that pool resources and combine cross-border expertise across several different research teams and groups.

In summary, our research integrates different modalities of data generated in the lab that can lead to the design of therapeutic interventions aimed at improving outcomes for prostate cancer patients.

/ PI paper pick 2022

Zurita AJ, Graf RP, Villacampa G, Raskina K, Sokol E, Jin D, Antonarakis ES, Li G, Huang RSP, Casanova-Salas I, Vivancos A, Carles J, Ross JS, Schrock AB, Oxnard GR, Mateo J. Genomic Biomarkers and Genome-Wide Loss-of-Heterozygosity Scores in Metastatic Prostate Cancer Following Progression on Androgen-Targeting Therapies. *JCO Precis Oncol*. 2022 Jul;6:e2200195.

Cresta Morgado P, Mateo J. Clinical implications of homologous recombination repair mutations in prostate cancer. *Prostate*. 2022 Aug;82 Suppl 1:S45-S59.

Westphalen CB, Fine AD, André F, Ganesan S, Heinemann V, Rouleau E, Turnbull C, Garcia Palacios L, Lopez JA, Sokol ES, Mateo J. Pan-cancer Analysis of Homologous Recombination Repair-associated Gene Alterations and Genome-wide Loss-of-Heterozygosity Score. *Clin Cancer Res*. 2022 Apr 1;28(7):1412-1421.

Mateo J, Steuten L, Aftimos P, André F, Davies M, Garralda E, Geissler J, Husereau D, Martinez-Lopez I, Normanno N, Reis-Filho JS, Stefani S, Thomas DM, Westphalen CB, Voest E. Delivering precision oncology to patients with cancer. *Nat Med*. 2022 Apr;28(4):658-665.

Sarcoma Translational Research Group

Principal Investigator César Serrano **Oncologist** Carlo M. Cicala **Predoctoral Fellows** Alfonso García Valverde, David Gómez Peregrina, Gemma Mur Bonet, Iván Olivares Rivas, Daniel Pilco Janeta **Senior Technician** Jordi Rosell Aluja **Graduate Student** David Camell Raventós

/ Strategic goals

- Identification of critical molecular mediators of oncogenic signaling in sarcomas.
- Characterization of response and resistance mechanisms to targeted therapies in sarcomas.
- Preclinical modelling and validation of therapeutic strategies to translate at the clinical level.
- Clinical drug development in sarcomas across phase I to phase III clinical trials.

/ Highlights

- Our group leads high-level studies toward the clinical implementation of liquid biopsy in GIST patients.
- We have been awarded by several funding bodies to study the evolutionary landscape of resistance in GIST.
- César Serrano has been part of the international research teams whose work has led to the approval of ripretinib and avapritinib for the treatment of GIST patients.
- Our group is fully committed to generating laboratory models from most sarcoma subtypes thanks to the support received from patients through the #SarcModel initiative.

/ Summary

Sarcoma encompasses >70 entities of mesenchymal origin, constituting 1-2% of all cancers. From a biological perspective, sarcomas can be classified into two broad categories: sarcomas driven by simple genetic alterations, such as translocations or specific activating mutations; and tumors with complex and unbalanced genomic aberrations. Both include diverse sarcoma subtypes often with profound differences in their molecular landscape, course of disease and therapeutic approach.

We focus on the study of sarcomas with oncogenic dependency on specific drivers of disease. Among these, gastrointestinal stromal tumor (GIST) is the most common malignant mesenchymal neoplasm and constitutes a paradigmatic model for studying oncogene addiction and identifying structural and functional mechanisms for drug response and resistance.

Ongoing efforts aim at achieving a deeper biological understanding of GIST and other sarcomas to advance drug development. The heterogeneity of mechanisms of resistance represents one of the major challenges in improving outcomes for these patients. We therefore seek to identify crucial molecules and signaling mechanisms in GIST biology that can serve as therapeutic vulnerabilities. The involvement of the ubiquitin pathway and by-pass signaling mechanisms have become a major focus over recent years.

We also perform high-throughput genomic and transcriptomic studies to decipher the evolving patterns of resistance in GIST throughout the course of disease, as well as investigate liquid biopsy in sarcoma to provide robust evidence that will help to more precisely guide treatment decisions by plasma sequencing. In addition, the GISTomics project, a European initiative driven by our group, aims to advance insights into the landscape of GIST evolution. In the same direction, our group is leading international initiatives to investigate the role of circulating tumor DNA (ctDNA) in GISTs and other sarcomas with the double aim of obtaining insights into the biological features of these tumors in heavily pretreated patients, and determine the main avenues for its clinical implementation.

Beyond GIST, our group has initiated new lines of research focused on other sarcoma subtypes, including muscle-derived sarcomas (leiomyosarcoma and rhabdomyosarcoma), angiosarcoma, and liposarcoma. Functional precision medicine is a major focus of research in these neoplasms.

Our aim is to have a true clinical impact by improving the daily treatment and care of our patients. We are proud to report that our Sarcoma Multidisciplinary Unit has been designated as an Expert Sarcoma Center of the European Reference Network ERN-EURACAN, and thus constitutes an optimal setting for translating cancer discovery into clinical benefits.

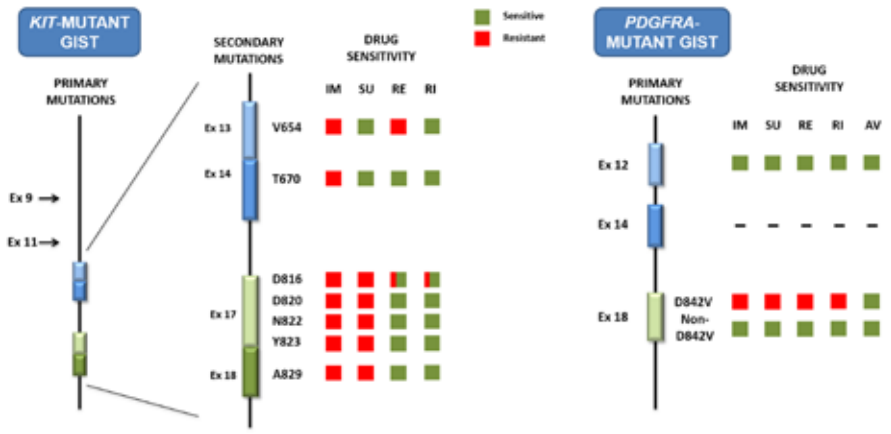


Figure: Over recent years, research undertaken by our group has reshaped the view of GIST progression, leading to a palpable impact in current drug development in this field. As shown in the figure, our research team first confirmed, through several studies, including laboratory, tumor tissue and ctDNA analyses, that secondary mutations in KIT are the main drivers of GIST progression, with other alternative mechanisms only seldomly involved; and second, we demonstrated that targeted agents approved for the treatment of metastatic GIST are active against molecular subsets of the KIT secondary mutational spectrum. Based on these results, several currently ongoing therapeutic initiatives are being tested worldwide: combination or rotation of therapies with complementary activity against secondary mutations; design of new-generation targeted agents aimed at covering most common secondary mutations; and implementing clinically ctDNA to guide therapeutic decisions. Adapted from Schaefer IM et al. 2022.

/ PI paper pick 2022

Schaefer IM, DeMatteo RP, Serrano C. The GIST of Advances in Treatment of Advanced Gastrointestinal Stromal Tumor. *Am Soc Clin Oncol Educ Book*. 2022 Apr;42:1-15.

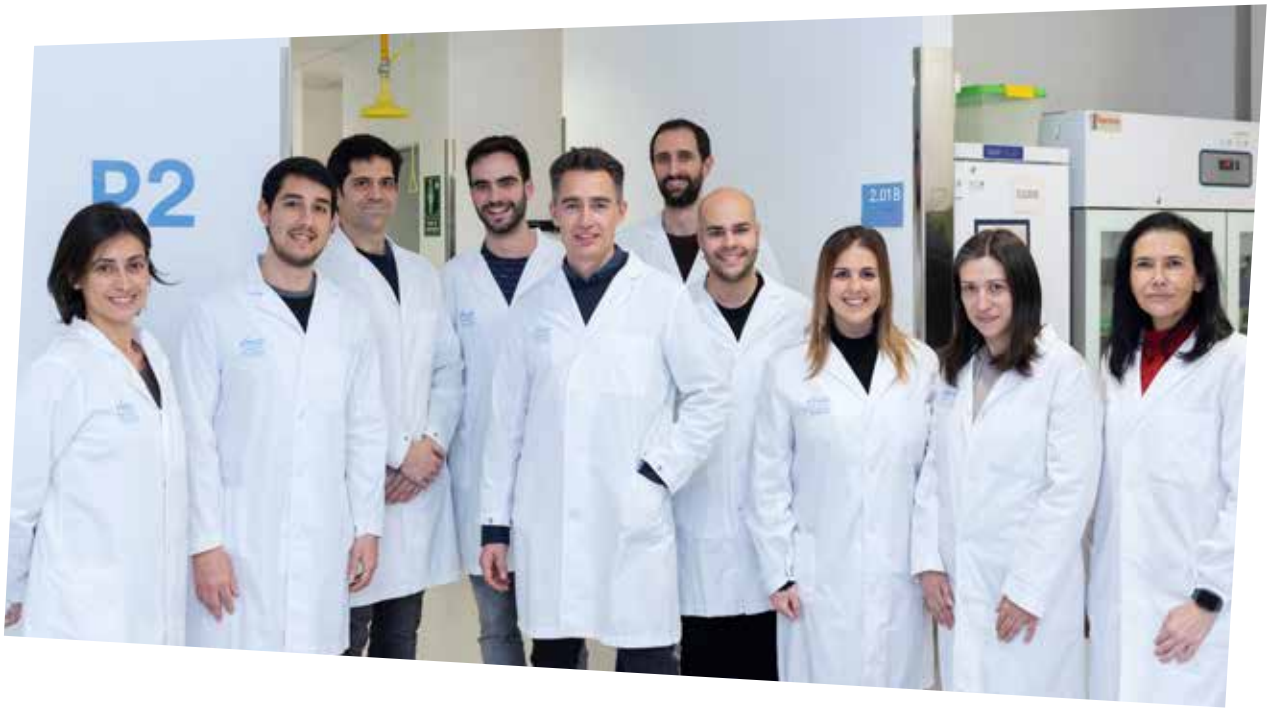
Ravegnini G, Fosso B, Ricci R, Gorini F, Turroni S, Serrano C, Pilco-Janeta DF, Zhang Q, Zanotti F, De Robertis M, Nannini M, Pantaleo MA, Hrelia P, Angelini S. Analysis of microbiome in gastrointestinal stromal tumors: Looking for different players in tumorigenesis and novel therapeutic options. *Cancer Sci*. 2022 Aug;113(8):2590-2599.

Manzano-Muñoz A, Yeste J, Ortega MA, Martín F, López A, Rosell J, Castro S, Serrano C, Samitier J, Ramón-Azcón J, Montero J. Microfluidic-based dynamic BH3 profiling predicts anticancer treatment efficacy. *NPJ Precis Oncol*. 2022 Dec 1;6(1):90.

PRECLINICAL & TRANSLATIONAL RESEARCH

Stem Cells & Cancer Group

Principal Investigator Héctor G. Palmer **Senior Investigator** Isabel Puig **Postdoctoral Fellows** David Aguilar, Oriol Arqués, Jordi Martínez-Quintanilla **PhD Students** Alex Mur, Lorena Ramirez, Candida Salvans Gorjón **Technicians** Anna Alcántara, Laia Cabellos, Debora Cabot, Irene Chicote, Raquel Flores, Jordi Vergés Sanjaime



/ Strategic goals

- Advance insights into tumor dormancy.
- Study the role of epigenetic factors governing dormancy in chemoresistance, minimal residual disease, relapse, dissemination, and metastasis.
- ONIRIA Therapeutics - modulating cell dormancy to combat cancer.
- Develop small drug modulators of cancer cell dormancy to block cancer progression.
- Molecularly matched targeted therapies.
- Unveil the mechanisms of response to drugs targeting EGFR, BRAF, MEK, ERK, LGR5, Wnt, PARP or Hippo pathways.
- Refinement of advanced cancer models.
- Expand our PDX collection and develop new orthotopic models as well as live imaging techniques.

/ Highlights

- Cancer cell dormancy: We have revealed key epigenetic factors ruling cancer cell dormancy, hypoxia, chemoresistance and tumor recurrence, as well as developed effective small drugs targeting some of these.
- Molecularly matched cancer therapies: Our group has described relevant determinants of response to BRAF and Notch inhibitors, demonstrated the efficacy of new rational drug combinations, and evaluated minimal residual disease of RET fused tumors.
- Advanced cancer models: In collaboration with several European-funded networks, we have generated and refined new cancer models of colorectal cancer.

/ Summary

VHIO's Stem Cells & Cancer Group studies the mechanisms that enable tumors to persist by evading effective treatments and progressing to advanced stages of disease.

We use multi-omics approaches to reveal unexpected alterations related to tumor and single cell phenotypes. Combining gene editing (CRISPR/Cas) with classical signaling biochemistry in cancer cell lines as well as genetically modified mice, patient-derived organoids (PDO) and xenografts (PDX), our group investigates the functional relevance of these newly identified alterations in patients' response to therapies.

We participate in a global multidisciplinary task force incorporating medical oncologists, surgeons, radiologists, and nurses. This strong collaboration aims to rapidly translate laboratory results to the clinic.

Main research lines include:

Tumor cell dormancy
The study of the intriguing biology of cancer cell dormancy as a driver of chemoresistance, formation of minimal residual disease, and disease relapse in patients.

We previously discovered a core epigenetic network that governs dormancy of tumor cells (Puig et al. 2018)*, and are now investigating the function of TET2, DPPA3 and other epigenetic and transcription factors governing dormancy in greater depth. Importantly, our group is rapidly progressing in developing drugs that modulate dormancy drivers including TET2, and defining novel biomarkers to detect chemo-resistant dormant tumor cells (DTC).

Response to target-directed drugs
We work in close collaboration with oncologists and pharmaceutical companies to identify molecular mechanisms responsible for the sensitivity or resistance to drugs blocking Wnt/beta-catenin, Notch, PI3K/AKT, EGFR/LGR5, BRAF/MEK/ERK or hippo oncogenic signals (Tenbaum et al. 2012; Puig et al. 2013; Capdevila et al. 2020)**.

Based on our discoveries, we are designing new prescreening tests for the genetic-guided enrolment of patients in clinical trials. Importantly, findings are helping to define new rational drug combinations to treat cancer patients with progressive disease that are the base of new academic clinical trials.

Preclinical cancer models
Our group is also expanding and characterizing its PDX collections (CRC, neuroendocrine and peritoneal pseudomyxoma), and optimizing their use in evaluating drug efficacy and metastasis by orthotopic injection and live imaging (TC, PET and Echography).

Lastly, we are developing ambitious projects through the EurOPDX, PERSIST-SEQ, CRCelerate, PMP Accelerate European Consortia for studying cancer resistance and new preclinical modelling.

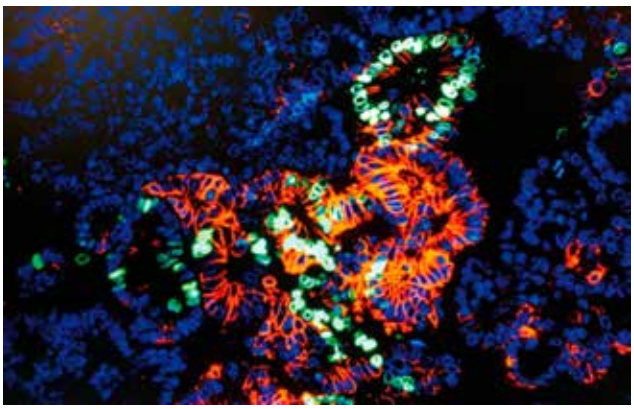


Figure: Slow Cycling Cancer Cells (SCCC) reside in hypoxic areas (CA9 marker). A set of epigenetic regulators sustain the survival of a reservoir of SCCC in low oxygen tumor niches.

/ PI paper pick 2022

Martínez-Sabadell A, Morancho B, Rius Ruiz I, Román Alonso M, Ovejero Romero P, Escorihuela M, Chicote I, Palmer HG, Nonell L, Alemany-Chavarria M, Klein C, Bacac M, Arribas J, Arenas EJ. The target antigen determines the mechanism of acquired resistance to T cell-based therapies. *Cell Rep*. 2022 Oct 18;41(3):111430.

Puig I, Palmer HG. A Label Retaining System to Capture Slow-Cycling Cancer Cells. *Methods Mol Biol*. 2022;2535:85-92.

Herpers B, Eppink B, James MI, Cortina C, Cañellas-Socias A, Boj SF, Hernando-Momblona X, Glodzik D, Roovers RC, van de Wetering M, Bartelink-Clements C, Zondag-van der Zande V, Mateos JG, Yan K, Salinaro L, Basmeleh A, Fatrai S, Maussang D, Lammerts van Bueren JJ, Chicote I, Serna G, Cabellos L, Ramírez L, Nuciforo P, Salazar R, Santos C, Villanueva A, Stephan-Otto Attolini C, Sancho E, Palmer HG, Tabernero J, Stratton MR, de Kruif J, Logtenberg T, Clevers H, Price LS, Vries RGJ, Batlle E, Throsby M. Functional patient-derived organoid screenings identify MCLA-158 as a therapeutic EGFR × LGR5 bispecific antibody with efficacy in epithelial tumors. *Nat Cancer*. 2022 Apr;3(4):418-436.

* Puig I, Tenbaum SP, Chicote I, Arqués O, Martínez-Quintanilla J, Cuesta-Borrás E, Ramírez L, Gonzalo P, Soto A, Aguilar S, Eguizabal C, Caratù G, Prat A, Argilés G, Landolfi S, Casanovas O, Serra V, Villanueva A, Arroyo AG, Terracciano L, Nuciforo P, Seoane J, Recio JA, Vivancos A, Dienstmann R, Tabernero J, Palmer HG. TET2 controls chemoresistant slow-cycling cancer cell survival and tumor recurrence. *J Clin Invest*. 2018 Aug 31;128(9):3887-3905.

** Tenbaum SP, Ordóñez-Morán P, Puig I, Chicote I, Arqués O, Landolfi S, Fernández Y, Herance JR, Gispert JD, Mendizabal L, Aguilar S, Ramón y Cajal S, Schwartz S Jr, Vivancos A, Espín E, Rojas S, Baselga J, Tabernero J, Muñoz A, Palmer HG. β-catenin confers resistance to PI3K and AKT inhibitors and subverts FOXO3a to promote metastasis in colon cancer. *Nat Med*. 2012 Jun;18(6):892-901.
Puig I, Chicote I, Tenbaum SP, Arqués O, Herance JR, Gispert JD, Jimenez J, Landolfi S, Caci K, Allende H, Mendizabal L, Moreno D, Charco R, Espín E, Prat A, Elez ME, Argilés G, Vivancos A, Tabernero J, Rojas S, Palmer HG. A personalized preclinical model to evaluate the metastatic potential of patient-derived colon cancer initiating cells. *Clin Cancer Res*. 2013 Dec 15;19(24):6787-801.
Capdevila J, Arqués O, Hernández Mora JR, Matito J, Caratù G, Mancuso FM, Landolfi S, Barriuso J, Jimenez-Fonseca P, Lopez Lopez C, Garcia-Carbonero R, Hernando J, Matos I, Paolo N, Hernández-Losa J, Esteller M, Martínez-Cardús A, Tabernero J, Vivancos A, Palmer HG. Epigenetic EGFR Gene Repression Confers Sensitivity to Therapeutic BRAFV600E Blockade in Colon Neuroendocrine Carcinomas. *Clin Cancer Res*. 2020 Feb 15;26(4):902-909.

PRECLINICAL & TRANSLATIONAL RESEARCH

Tumor Biomarkers Group

Principal Investigator Josep Villanueva **Postdoctoral Fellow** Chiara Bellio **Graduate Student** Mireia Pujals
Technicians Marta Emperador, José Ángel Robles, Ferran Soler

/ Strategic goals

- Characterize the role of RAGE in TNBC invasion and metastasis.
- The identification and characterization of mechanisms of response and acquired resistance to current therapies in breast cancer.
- The development and implementation of proteomic methodologies aimed at understanding cell communication in cancer biology.

/ Highlights

- We have identified the superoxide dismutase 2 (SOD2) protein as a candidate response biomarker for neoadjuvant therapy in breast cancer. Our results show that circulating levels of SOD2 increased when patients responded to treatment according to tumor shrinkage during neoadjuvant chemotherapy. Therefore, the measurement of SOD2 levels in plasma could improve the non-invasive monitoring of treatment in breast cancer patients.
- We have identified the growth differentiation factor 15 (GDF15) protein as an eribulin response biomarker, which is also required for the survival of drug tolerant persister (DTP) breast cancer cells. Our results show that the secretion of GDF15 is a response biomarker of eribulin treatment, as well as a specific biomarker of DTP cells in breast cancer. We have also shown that GDF15 plays a direct role in the survival of DTP cells. Thus, targeting GDF15 could help eradicate DTP cells and block the onset of stable acquired resistance.

/ Summary

Tumor cell communication with its microenvironment plays an important role in tumor initiation and progression. Cancer cells hijack the tumor microenvironment ecosystem via paracrine signaling to promote a pro-oncogenic microenvironment that is crucial for the development of primary and metastatic tumors. We aim to characterize the mechanisms adopted by these cells to communicate amongst themselves as well as with their microenvironment during tumorigenesis and exploit these data to advance biomarker and drug target discovery.

Our methodological focus centers on the quantitative proteomic profiling of sub-proteomes linked to cell communication including the secretome, exosomes and the cell surface proteome. Over the last few years our laboratory has gone from studying cancer proteomics using a data-driven approach to interrogating the tumor cell protein communication using a hypothesis-driven approach. Through these studies we have shown that an alternative extracellular function of the nuclear protein HMGA1 mediates tumor invasion and metastasis in triple-negative breast cancer (TNBC) by becoming a ligand for the Receptor for Advanced Glycation End-product (RAGE).

We are also involved in identifying response biomarkers and mechanisms of resistance for new therapies used in the clinic to treat TNBC patients. In a recent project aimed at identifying secretome-based biomarkers of eribulin, we have characterized the drug tolerant persister (DTP) cells generated by chemotherapeutic agents, and identified GDF15 as a specific biomarker for DTPs that also has a role in their survival. Our data also shows that DTP cells surviving a high dose of cytotoxic drugs will give rise to different stable resistance mechanisms.

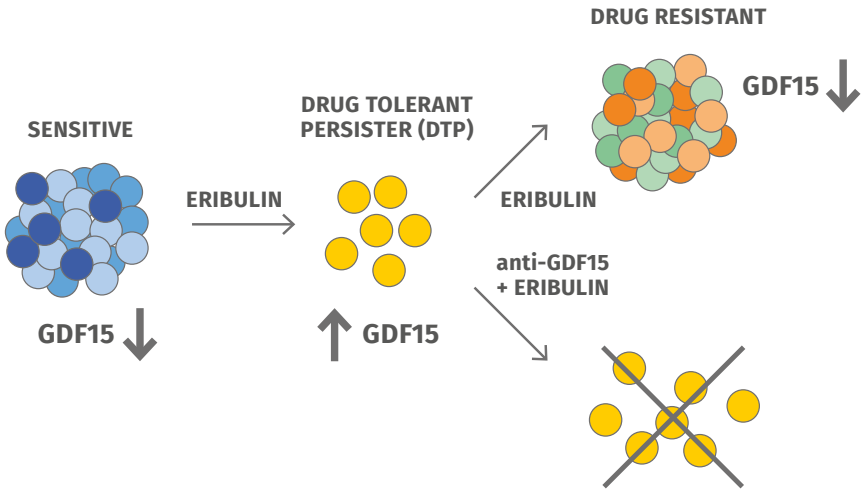


Figure: GDF15 is an eribulin response biomarker also required for survival of DTP breast cancer cells. The scheme illustrates how GDF15 expression is low or absent in cells sensitive to eribulin, strongly upregulated during response to the drug, and then downregulated when stable resistance is ultimately established. Our data also suggests that the combination of eribulin plus a GDF15 neutralizing antibody might be beneficial in the treatment of breast cancer.

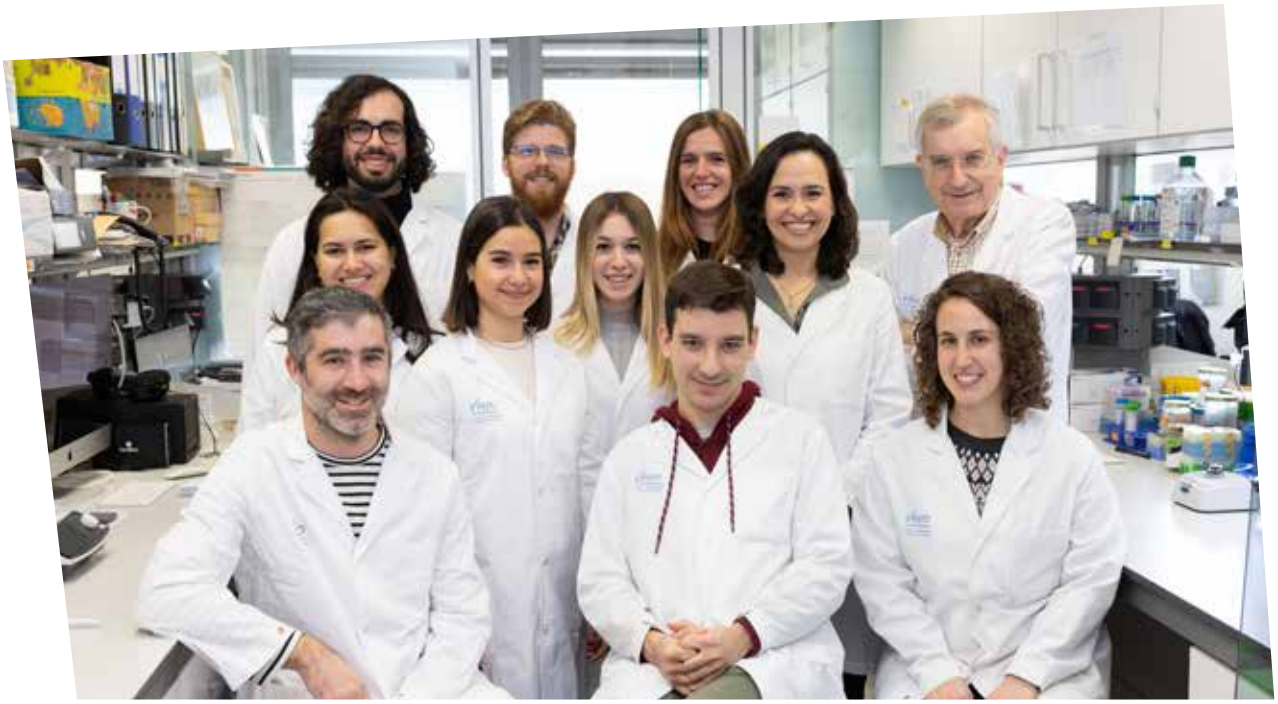
/ PI paper pick 2022

Juliachs M, Pujals M, Bellio C, Meo-Evoli N, Duran JM, Zamora E, Parés M, Suñol A, Méndez O, Sánchez-Pla A, Canals F, Saura C, Villanueva J. Circulating SOD2 Is a Candidate Response Biomarker for Neoadjuvant Therapy in Breast Cancer. *Cancers (Basel)*. 2022 Aug 10;14(16):3858.

Bellio C, Emperador M, Castellano P, Gris-Oliver A, Canals F, Sánchez-Pla A, Zamora E, Arribas J, Saura C, Serra V, Tabernero J, Littlefield BA, Villanueva J. GDF15 Is an Eribulin Response Biomarker also Required for Survival of DTP Breast Cancer Cells. *Cancers (Basel)*. 2022 May 23;14(10):2562.

Tumor Immunology & Immunotherapy Group

Principal Investigator Alena Gros **Postdoctoral Fellows** Pierre Levy, Maria Lozano, Jara Palomero, Endika Prieto **Graduate Students** Judit Diaz, Andrea Garcia, Anna Yuste **Technicians** Immaculada Creus, Albert Marín **Students** Alisha Atmopawiro, Carla Brujas **Lab Manager** Noelia Alcazar **Bioinformatician** Jonatan González



/ Strategic goals

- Develop minimally-invasive personalized T-cell therapies derived from peripheral blood.
- Track tumor-antigen specific T cells immune-dynamics in patients treated with immunotherapy to understand determinants of response and toxicity.
- Investigate novel strategies to rapidly identify shared neoantigens that can serve as targets for TCR gene-engineered therapies.
- Mine tumor cell intrinsic mechanisms of resistance to T-cell mediated cytotoxicity.

/ Highlights

- We finalized the clinical grade validations of TIL expansion for the treatment of patients at Vall d'Hebron in collaboration with the Blood and Tissue Bank (BST), a public agency of the Catalan Government's Department of Health. This work was supported by funding received from the BBVA Foundation and its Comprehensive Program of Cancer Immunotherapy & Immunology – CAIMI (page 128) at VHIO.
- Together with Elena Garralda, Principal Investigator of VHIO's Early Clinical Drug Development and Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138), we received authorization from the Agencia Española de Medicamentos y Productos Sanitarios (AEMPS - Spanish Regulatory Agency), and initiated patient recruitment for a phase I clinical study to test the safety and tolerability of neoantigen-selected TIL for patients with solid tumors refractory to standard therapies.

/ Summary

Immunotherapies exploit the immune system to attack cancer. Clinical studies have shown that immune checkpoint inhibitors and T-cell-based therapies can mediate tumor regression in patients with metastatic disease. Thus, in addition to surgery, radiation therapy and chemotherapy, immunotherapy has become the fourth pillar of anti-cancer therapy. Our group focuses on better understanding the naturally occurring T-cell response to cancer and establishing ways to exploit these antitumor responses to develop more effective, powerful, and personalized immunotherapies against cancer.

Accumulating evidence supports that neoantigens play an important role in the clinical efficacy of cancer immunotherapies. Thanks to the support received from the Fundación BBVA's Comprehensive Program of Cancer Immunotherapy & Immunology – CAIMI (page 128), as well as other funding agencies, and through our group's long-standing collaboration with Elena Garralda, Principal Investigator of VHIO's Early Clinical Drug Development Group (page 92), and Director of our Research Unit for Molecular Therapy of Cancer (UTIM) – CaixaResearch (page 138), we received authorization from the Agencia Española de Medicamentos y Productos Sanitarios (AEMPS - Spanish Regulatory Agency) in May 2021 to initiate a phase I clinical trial to test the safety and tolerability of neoantigen-selected TILs.

In this ongoing clinical trial we are using a highly personalized approach (see Figure) to screen for T-cell mediated recognition of mutated antigens using autologous antigen presenting cells that can process and present in all the potential human leukocyte antigen (HLA). In this pilot clinical study funded by the Instituto de Salud Carlos III – ISCIII (Carlos III Health Institute), we aim to treat up to 10 patients with epithelial cancers and melanoma refractory to standard therapies. By enriching for neoantigen-reactive lymphocytes, we hope to extend the efficacy of TIL therapy beyond melanoma.

Our group's work has demonstrated that tumor-reactive T cells can frequently be detected circulating in the blood of cancer patients, regardless of the specific tumor type. The ability to track and monitor tumor-reactive CD8+ and CD4+ T cells in blood has tremendous therapeutic potential, but it is more challenging due to their lower prevalence. Our group has contributed to defining a phenotypic signature that can guide the identification and enrichment of tumor- and neoantigen-reactive T cells from the blood of cancer patients and we aim to leverage this to develop minimally-invasive T-cell therapies to treat cancer patients. In addition, we now aim to conduct extensive profiling of the peripheral blood T-cell response at the single cell level in patients treated with immune checkpoint inhibitors to better understand the determinants of response.

In addition to the above-mentioned, our group is also interested in developing high-throughput technologies to better understand the landscape of tumor antigens that render tumors susceptible to immune attack, shared neoantigens as well as mechanisms of resistance to T-cell cytotoxicity.

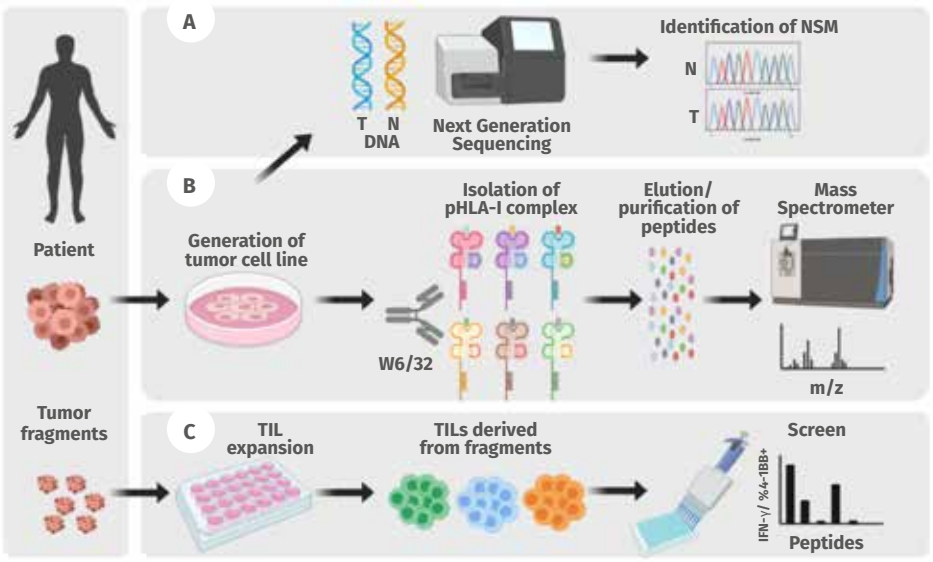


Figure: Personalized approach to identify tumor and neoantigen-specific TILs. **A)** We sequence normal and tumor DNA to identify all the non-synonymous mutations. **B)** In parallel we attempt to generate a tumor cell line. When generated, we isolate the peptide-MHCI complexes, and we identify the peptides presented by MHCI by the tumor cell line by Mass spectrometry. **C)** Finally, we screen the TILs expanded from the tumor for recognition of the candidate neoantigen peptides identified in A) or elluted from MHCI in B).

/ PI paper pick 2022

Marin I, Boix O, Garcia-Garijo A, Sirois I, Caballe A, Zarzuela E, Ruano I, Stephan-Otto Attolini C, Prats N, Lopez-Dominguez JA, Kovatcheva M, Garralda E, Munoz J, Caron E, Abad M, Gros A, Pietrocola F, Serrano M. Cellular senescence is immunogenic and promotes anti-tumor immunity. *Cancer Discov*. Epub 2022 Oct 27.

Palomero J, Panisello C, Lozano-Rabella M, Tirtakasuma R, Díaz-Gómez J, Grases D, Pasamar H, Arregui L, Dorca Duch E, Guerra Fernández E, Vivancos A, de Andrea CE, Melero I, Ponce J, Vidal A, Piulats JM, Matias-Guiu X, Gros A. Biomarkers of tumor-reactive CD4+ and CD8+ TILs associate with improved prognosis in endometrial cancer. *J Immunother Cancer*. 2022 Dec;10(12):e005443. doi: 10.1136/jitc-2022-005443. PMID: 36581331; PMCID: PMC9806064.

Levy PL, Gros A. Fast track to personalized TCR T cell therapies. *Cancer Cell*. 2022 May 9;40(5):447-449.

mobile version

scan to visit

VALL D'HEBRON INSTITUTE OF ONCOLOGY (VHIO)
SCIENTIFIC REPORT 2022

Clinical Research

Breast Cancer & Melanoma Group

Principal Investigator Cristina Saura **Medical Oncologists and Clinical Fellows** Miriam Arumi, Judith Balmaña, Meritxell Bellet, Maria Borrell, Mara Cruellas, Santiago Escrivá, Patricia Gómez, Eva Muñoz, Mafalda Oliveira, Carolina Ortiz, Isabel Pimentel, Lucia Sanz, Esther Zamora **Clinical Nurse** Anna Suñol **ESMO Translational Research Fellow** Andri Papakonstantinou

/ Strategic goals

Breast:

- Optimize therapies by introducing novel anti-cancer treatments and adding rational combinations to combat mechanisms of resistance.
- Incorporate proteomics, genomics, and ctDNA platforms in translational research to advance insights into tumor biology.
- Apply preclinical and predictive data to help guide innovative clinical trial design in early and advanced disease.

Melanoma:

- Our Melanoma Unit leads one of the largest networks in Spain and across Europe and is also one of the most active groups in early stage and metastatic disease clinical trials in melanoma and other skin tumors. We are committed to connecting clinical trials with the corresponding translational research lines led by VHIO scientists in collaboration with our clinical investigators.

/ Highlights

- Relevant contributions in drug approval. Thanks to the leadership of our investigators, we have contributed to the approval of therapies including trastuzumab deruxtecan for HER2-low breast cancer, and sacituzumab govitecan for HR-positive disease for patients with advanced breast cancer, pembrolizumab for stages IIB/IIC in the adjuvant melanoma setting, new combinations such as nivolumab plus relatlimab for the treatment of metastatic melanoma, tebentafust for metastatic uveal melanoma and pembrolizumab and cemiplimab for patients with advanced squamous cell carcinoma. We are currently involved in the development of some of the most promising therapies for breast and skin tumors with several IO combinations, targeted therapies, intratumoral treatments and new immunotherapies that will lead to new approvals in the near future.
- Precision medicine. Thanks to VHIO's Molecular Prescreening Program (page 146), driven by one of our Institutional Programs, the Advanced Molecular Diagnostics Program – DIAMAV supported by the Fundación FERO (page 126), we continue to identify potentially matched patients with molecular alterations as an enrichment strategy for clinical trials in breast cancer with *PI3KCA*, *ESR1* or *HER2* mutations, and *BRAF*, *NRAS*, *LAG3*, *TYRP1*, HLA-A*02:01 and other mutations for patients with melanoma and other cutaneous tumors.
- Our Institute's proteomics and ctDNA platforms have also helped us to advance insights into tumor biology. In skin tumors we are developing a personalized gene profiling platform to identify high risk tumors in the early setting and new mutational alterations in the metastatic in collaboration with VHIO's Molecular Prescreening Program and our Research Unit for Molecular Therapy of Cancer (UITM) - CaixaResearch (page 138). In breast cancer, promising results on the detection of ctDNA in breast milk have led us to embark on a prospective study for the early diagnosis of breast cancer using this technique in healthy women.

/ Summary

The main area of expertise of our Breast Cancer Group, led by Cristina Saura, is clinical research focused on drug development and associated translational research. In addition to maintaining high patient recruitment in our studies, we also play a leading role in many of the clinical trials that we run. This enables us to apply translational data to guide and accelerate drug development:

- HER2-positive disease: We are participating in the major trials testing novel therapies and the most promising agents in the field including trastuzumab deruxtecan, tucatinib and SYD985. We have opened recruitment for the first trial with cell therapy in this area and are translating the benefit observed from novel agents in the metastatic setting and early disease to potentially increase the number of patients cured at first diagnosis. In collaboration with VHIO's Growth Factors Group led by Joaquín Arribas (page 74), we explore cancer drug resistance to these new therapies through VHIO's in-house established PDX models.
- Luminal disease: In partnership with VHIO's Experimental Therapeutics Group headed by Violeta Serra (page 70), we have developed several PDX models to advance insights into mechanisms of resistance to several drugs, and how they may be reversed through treatment with PI3K, AKT, CDK4/6, and BET inhibitors, as well as novel oral SERDs and different PARP inhibitors.
- Triple negative disease: In addition to our participation in clinical trials testing combinations of immunotherapies and promising antibody drug conjugates, we have created an integrative multi-omics platform to identify predictive biomarkers of response to chemotherapy and immune checkpoint inhibitors in early TNBC and are collaborating in pioneering projects focused on cell-based therapies directed by Alena Gros, PI of VHIO's Tumor Immunology and Immunotherapy Group (page 86), to develop novel personalized T-cell therapies against cancer.
- ctDNA: In collaboration with VHIO's Cancer Genomics Group led by Ana Vivancos (page 116), we have analyzed concordance of genomic alterations in synchronous tumor biopsies and ctDNA from metastatic breast cancer patients. We are now participating in several projects to address the challenging scenario of early disease and the identification of ctDNA in unexplored biological samples including breast milk.
- Our skin cancer group focuses on melanoma and other malignant skin tumors, and is led by Eva Muñoz. She has actively participated in the development of -and active recruiting for- several phase I, II and III trials to study various emerging therapies for the treatment of these diseases including immunotherapies and targeted therapies. Her team leads its own research program incorporating clinical investigators, dermatologists, surgeons and VHIO investigators, in collaboration with other national and international institutions.
  Studies focus on new targeted therapies and resistance to immunotherapy by conducing purely translational research centered on cutaneous, mucosa, acral and uveal melanoma, and other skin tumors (squamous cutaneous cell carcinoma, basal cell carcinoma). Eva's group mainly investigates acquired resistance and disease progression to treatments and assesses new combinations for the treatment of melanoma and other skin cancers. The investigators also map therapeutic avenues, follow up standards, and seek to identify biomarkers for a more precise treatment selection matched to the specificities of our patients.

/ PI paper pick 2022

Modi S, Jacot W, Yamashita T, Sohn J, Vidal M, Tokunaga E, Tsurutani J, Ueno NT, Prat A, Chae YS, Lee KS, Niikura N, Park YH, Xu B, Wang X, Gil-Gil M, Li W, Pierga JY, Im SA, Moore HCF, Rugo HS, Yerushalmi R, Zagouri F, Gombos A, Kim SB, Liu Q, Luo T, Saura C, Schmid P, Sun T, Gambhire D, Yung L, Wang Y, Singh J, Vitazka P, Meinhardt G, Harbeck N, Cameron DA; DESTINY-Breast04 Trial Investigators. Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer. *N Engl J Med*. 2022 Jul 7;387(1):9-20.

Gnant M, Dueck AC, Frantal S, Martin M, Burstein HJ, Greil R, Fox P, Wolff AC, Chan A, Winer EP, Pfeiler G, Miller KD, Colleoni M, Suga JM, Rubovsky G, Bliss JM, Mayer IA, Singer CF, Nowecki Z, Hahn O, Thomson J, Wolmark N, Amillano K, Rugo HS, Steger GG, Hernando Fernández de Aránguiz B, Haddad TC, Perelló A, Bellet M, Fohler H, Metzger Filho O, Jallitsch-Halper A, Solomon K, Schurmans C, Theall KP, Lu DR, Tenner K, Fesl C, DeMichele A, Mayer EL; PALLAS groups and investigators. Adjuvant Palbociclib for Early Breast Cancer: The PALLAS Trial Results (ABCSG-42/AFT-05/BIG-14-03). *J Clin Oncol*. 2022 Jan 20;40(3):282-293.

Pellegrino B, Herencia-Ropero A, Llop-Guevara A, Pedretti F, Moles-Fernández A, Viaplana C, Villacampa G, Guzmán M, Rodríguez O, Grueso J, Jiménez J, Arenas EJ, Degasperi A, Dias JML, Forment JV, O'Connor MJ, Déas O, Cairo S, Zhou Y, Musolino A, Caldas C, Nik-Zainal S, Clarke RB, Nuciforo P, Díez O, Serres-Créixams X, Peg V, Espinosa-Bravo M, Macarulla T, Oaknin A, Mateo J, Arribas J, Dienstmann R, Bellet M, Oliveira M, Saura C, Gutiérrez-Enríquez S, Balmaña J, Serra V. Preclinical In Vivo Validation of the RAD51 Test for Identification of Homologous Recombination-Deficient Tumors and Patient Stratification. *Cancer Res*. 2022 Apr 15;82(8):1646-1657.

Weber JS, Schadendorf D, Del Vecchio M, Larkin J, Atkinson V, Schenker M, Pigozzo J, Gogas H, Dalle S, Meyer N, Ascierto PA, Sandhu S, Eigentler T, Gutzmer R, Hassel JC, Robert C, Carlino MS, Di Giacomo AM, Butler MO, Muñoz-Couselo E, Brown MP, Rutkowski P, Haydon A, Grob JJ, Schachter J, Queirolo P, de la Cruz-Merino L, van der Westhuizen A, Menzies AM, Re S, Bas T, de Pril V, Braverman J, Tenney DJ, Tang H, Long GV. Adjuvant Therapy of Nivolumab Combined With Ipilimumab Versus Nivolumab Alone in Patients With Resected Stage IIIB-D or Stage IV Melanoma (CheckMate 915). *J Clin Oncol*. Epub 2022 Sep 26.

Early Clinical Drug Development Group

Principal Investigator, Early Clinical Drug Development Group, Director, UITM – CaixaResearch Elena Garralda **Associate Investigators, Senior Consultants** Judith Balmaña, Joan Carles, Enriqueta Felip, Elena Garralda, Teresa Macarulla, Ana Oaknin, Belen Ortega, Cristina Saura, Josep Tabernero **CORE Phase I Investigators** Guzmán Alonso, Irene Braña, Vladimir Galvao, Julia Lostes, Honey K. Oberoi, Belen Ortega, Katerin Rojas, Omar Saavedra, Maria Vieito **Phase I Investigators** Daniel Acosta, Juan David Assaf, Iosune Baraibar, Pere Barba, Meritxell Bellet, Maria Borrell, Francesc Bosch, Alba Cabirta, Ana Callejo, Jaume Capdevila, Cecilia Carpio, Florian Castet, Susana Cedrés, Marc Diez, Elena Élez, Santiago Escrivá, Carles Fabregat, Lorena Fariñas, Ferran Ferragut, Maria Laura Fox, Alejandro Garcia, Carmen Garcia, David Garcia Illescas, Sara Garrido, Mercedes Gironella, Patricia Gómez, Macarena González, Jorge Hernando, Marta Hidalgo, Gloria Iacoboni, Patricia Iranzo, David Marmolejo, Lucia Martin, Alexandre Martinez, Joaquín Mateo, Antonieta Molero, Rafael Morales, Eva Muñoz, Alejandro Navarro, Mafalda Oliveira, Carolina Ortiz, Núria Pardo, Isabel Pimentel, Francisco Javier Ros, Francesc Salvà, Mario Sanchez, Lucia Sanz, Nadia Saoudi, Ángel Serna, César Serrano, Maria Sola, Cristina Suarez, Augusto Valdivia, Claudia Valverde **Data Manager** Roger Berché **Clinical Nurse Specialist** Marta Sanz

/ Strategic goals

- Early clinical development of the best-in-class targeted therapies, determining the optimal schedule and patient population that would most likely benefit most from these drugs by participating in novel clinical trials.
- Analyze patients' tumors for molecular aberrations that may predict the efficacy of targeted agents and enable a more precise selection of the most appropriate treatment matched to the specificities of individual patients with advanced cancer.
- Link clinical research at the UITM – CaixaResearch with various preclinical and translational research groups at VHIO, and foster powerful collaborations with different partners involved in drug development and translational research (phase I units, academic centers, consortia, and pharmaceutical companies).

/ Highlights

- We have successfully continued with our activities and programs to test the best-in-class drugs. We have carried out many clinical trials with new targeted agents, novel-novel combinations, immuno-oncology, ADCs, and epigenetic drugs. This year there has been a marked increase in patient recruitment in early drug development studies.
- Within the scope of our CaixaResearch Advanced Oncology Research Program (page 127) we have performed several clinical trials with patients selected based on molecular alterations: mutations in *AKT1, EGFR, IDH1, ALK, ROS1, BRAF, NRAS, KRAS, FGFR1* and *2, MET, HER2, HER3, RET; ATM; BRCA,* amplifications in *HER2, AKT 1, 2,* and *3, FGFR1, MET, NOTCH1-4,* rearrangements of *NTRK1-3 ROS1, ALK, BRAF, RSPO2/3, RET, NRG* and *FGFR1-3*.
- As part of our VHIO - BBVA Foundation Comprehensive Program of Cancer Immunotherapy & Immunology - CAIMI (page 128) we have continued our line of research to characterize hyperprogressive disease with immunotherapy. We are evaluating the biological mechanisms of hyperprogressive disease in collaboration with Paolo Nuciforo, PI of VHIO's Molecular Oncology Group (page 118), Rodrigo Toledo, one of VHIO's translational investigators, along with other international collaborators including Sergio Quezada, Professor of Cancer Immunology and Immunotherapy, University College London - UCL (UK).
- Within the scope of our CAIMI program and AZ Partners of Choice initiative we are validating a radiomic signature to predict response to immunotherapy and are correlating the results with the genomic evolution observed in patients. This research is carried out in collaboration with Raquel Perez Lopez, PI of our Radiomics Group (page 108).
- We have continued working on our program for advanced therapies in solid tumors, as well as implemented our own academic TILs program in collaboration with Alena Gros' Tumor Immunology & Immunotherapy Group (page 86). Moreover, our CAR-T cell project received funding from the Asociación Española Contra el Cáncer – AECC (Spanish Association Against Cancer) in 2019. We also continue to pursue our research into NK cells in collaboration with colleagues at the Clínica Universidad de Navarra (Spain), in addition to other cell-based therapies.
- Our group has launched a project to accelerate the digitalization of phase I units: SMART Experimental Cancer Medicine Trials eNABLED, in collaboration with Rodrigo Dienstmann, PI of VHIO's Oncology Data Science (ODysSey) Group (page 104). This initiative is supported by a Cancer Research UK (CRUK) Accelerator Award.
- Funded by EU's Horizon 2020 Framework Programme, we are coordinating the Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART), page 185. This pioneering project focuses on developing interconnected tools to reduce the current complexity of investigator-initiated trials and better guide clinical decision making by incorporating cutting-edge digital technologies and platforms.
- We are participating in two new EU Horizon 2020 projects, canSERV and PCM4EU (pages 193, 197), to strengthen expertise in personalized medicine and complex trials.

/ Summary

We focus on proof-of-concept and proof-of-mechanism clinical trials with targeted therapies, with particular emphasis on cell signaling, cancer stem cells, and immuno-oncology. These include first-in-human studies of targeted therapies, rational combinations of targeted therapies, biomarker-driven trials, and studies in molecularly selected populations.

Following a truly translational model, our group links clinical research at our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138) which is also led by Elena Garralda, with different areas of research carried out at VHIO. For selected projects we match molecular biology and optimal tumor models with pharmacology and innovative clinical research by involving VHIO scientists in our studies (biomarker development, profound understanding of mechanisms of action and resistance).

We participate in VHIO's Molecular Prescreening Program (page 146) to perform molecular analysis of patients' tumors. This enables us to select the optimal treatment for our patients with the experimental therapies available in our portfolio of clinical trials. Moreover, the close collaboration between the UITM – CaixaResearch and VHIO's Cancer Genomics Group directed by Ana Vivancos (page 116) has also been extended to different projects exploring novel immuno-oncology biomarkers for patient selection across our phase I clinical trials.

As an example, an international investigator-initiated project led to the development of the Vall d'Hebron immune gene expression signature (VIGex). This project was led by Alberto Hernando-Calvo, formerly a phase I investigator at our UITM-CaixaResearch, and awarded with different national and international grants that supported his fellowship at Princess Margaret Cancer Centre in Toronto (Canada), 2021-2022. Under the mentorship of Philipe Bedard and Lillian Siu in Toronto, Alberto set up a multicenter project to externally validate this signature in collaboration with Ana Vivancos and Elena Garralda.

This project has been awarded with multiple international grants and awards and presented as an oral presentation at international congresses including ESMO and ASCO meetings in 2022. The observations generated will lead to two manuscripts, currently in preparation. These initial findings will be prospectively validated in patients treated with immunotherapy across phase I clinical trials at VHIO.

Importantly, in relation to precision oncology, VHIO is a founding member of both the WIN - Worldwide Innovative Networking in personalized cancer medicine (page 193) and the Cancer Core Europe – CCE (page 185) consortia. These collaborations are non-governmental initiatives that connect international (WIN) and/or European (CCE) leading cancer centers to advance cancer diagnostics and therapeutics.

This year, our group and VHIO's UITM – CaixaResearch, have continued to lead the Basket of Baskets (BoB) trial (page 185). This academic study is endorsed by CCE and integrates molecular prescreening, the development of new diagnostic tests including circulating DNA, with the assessment of targeted therapies in populations of patients who, matched to specific molecular alterations, will be most likely to benefit from these treatments. During 2022 we have secured funding to explore amivantamab in selected patient populations with *MET* and *EGFR* alterations, and have also continued to search for funding to add new modules.

We also coordinate the EU-funded Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART) project, page 185. By harnessing and incorporating powerful cutting-edge technologies, methods and platforms, CCE-DART investigators will spur the design, development, and ringing in of a new generation of data rich, dynamic studies in oncology over the next years to come.

Our Early Drug Development Group and Phase I Unit UITM – CaixaResearch continue to establish VHIO as a leading reference in driving drug development and targeted therapies in oncology. Testament to this is the number of patients who entrust us with their care (651 patients enrolled in phase 0, I and basket studies in 2022), the portfolio of different trials available (239 phase I trials including 29 basket studies in 2022), and the novelty of our programs in precision medicine and immunotherapy drug development. This is also evidenced by our leading role in CCE's Clinical Trials Task Force.

Within the scope of the CaixaResearch Advanced Oncology Research Program (page 127) we have performed several clinical trials with patients selected based on molecular alterations: mutations in *AKT1, EGFR, IDH1, ALK, ROS1, BRAF, NRAS, KRAS, FGFR1* and *2, MET, HER2, HER3, RET; ATM; BRCA,* amplifications in *HER2, AKT 1, 2,* and *3, FGFR1, MET, NOTCH1-4,* rearrangements of *NTRK1-3 ROS1, ALK, BRAF, RSPO2/3, RET, NRG* and *FGFR1-3*.

VHIO's BBVA Comprehensive Program of Cancer Immunotherapy & Immunology – CAIMI (page 128) continues to expand. This year we have continued working with Alena Gros, PI of VHIO's Tumor Immunology & Immunotherapy Group (page 86), in our NEXTGEN-TIL trial, evaluating neoantigen selected TILS in epithelial tumors and melanoma. We have also initiated another cellular therapy trial based on allogenic NK cells in combination with HER2 therapy for HER2-positive breast cancer in collaboration with colleagues at the Cancer Center of the Universidad de Navarra (CIMA), and Cristina Saura, PI of VHIO's Breast Cancer Group (page 90). We have also been working extensively with Joaquin Arribas, PI of VHIO's Growth Factors Group (page 74) to bring a CAR T treatment against p95HER2 in HER2-positive breast cancer into the clinic.

We are involved in an additional two European projects that launched in 2022. PCM4EU – Personalised Cancer Medicine for all EU Citizens, a project funded under the Europe's Beating Cancer Plan by EU4Health, comprises partners from 15 countries across Europe (page 197) and centers on facilitating the implementation of molecular cancer diagnostics for precision oncology such as DRUP-like clinical trials.

canSERV is an EU-funded project under the Horizon Europe programme to provide cutting-edge, interdisciplinary and customized oncology services across the entire cancer continuum (page 193). Awarded through the HORIZON-INFRA-SERV call, this collaboration incorporates 19 European partners and aims to offer a comprehensive portfolio of oncology-related research services available to all scientists in EU member countries, associated countries and beyond.

We have also fostered important alliances with the pharmaceutical industry and collaborate closely with other clinical research organizations and academic centers of excellence, as well as companies dedicated to advancing personalized cancer medicine and care.

/ PI paper pick 2022

Mateo J, Steuten L, Aftimos P, André F, Davies M, Garralda E, Geissler J, Husereau D, Martinez-Lopez I, Normanno N, Reis-Filho JS, Stefani S, Thomas DM, Westphalen CB, Voest E. Delivering precision oncology to patients with cancer. *Nat Med*. 2022 Apr;28(4):658-665.

Subbiah V, Cassier PA, Siena S, Garralda E, Paz-Ares L, Garrido P, Nadal E, Vuky J, Lopes G, Kalemkerian GP, Bowles DW, Seetharam M, Chang J, Zhang H, Green J, Zalutskaya A, Schuler M, Fan Y, Curigliano G. Pan-cancer efficacy of pralsetinib in patients with RET fusion-positive solid tumors from the phase 1/2 ARROW trial. *Nat Med*. 2022 Aug;28(8):1640-1645.

Tamborero D, Dienstmann R, Rachid MH, Boekel J, Lopez-Fernandez A, Jonsson M, Razzak A, Braña I, De Petris L, Yachnin J, Baird RD, Loriot Y, Massard C, Martin-Romano P, Opdam F, Schlenk RF, Vernieri C, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium; Balmaña J, Apolone G, Caldas C, Bergh J, Ernberg I, Fröhling S, Garralda E, Karlsson C, Tabernero J, Voest E, Rodon J, Lehtiö J. The Molecular Tumor Board Portal supports clinical decisions and automated reporting for precision oncology. *Nat Cancer*. 2022 Feb;3(2):251-261.

Muik A, Garralda E, Altintas I, Gieseke F, Geva R, Ben-Ami E, Maurice-Dror C, Calvo E, LoRusso PM, Alonso G, Rodriguez-Ruiz ME, Schoedel KB, Blum JM, Sänger B, Salcedo TW, Burm SM, Stanganello E, Verzijl D, Vascotto F, Sette A, Quinkhardt J, Plantinga TS, Toker A, van den Brink EN, Fereshteh M, Diken M, Satijn D, Kreiter S, Breij ECW, Bajaj G, Lagkadinou E, Sasser K, Türeci Ö, Forssmann U, Ahmadi T, Şahin U, Jure-Kunkel M, Melero I. Preclinical Characterization and Phase I Trial Results of a Bispecific Antibody Targeting PD-L1 and 4-1BB (GEN1046) in Patients with Advanced Refractory Solid Tumors. *Cancer Discov*. 2022 May 2;12(5):1248-1265.

CLINICAL RESEARCH

Experimental Hematology Group

Principal Investigator Francesc Bosch **Translational Research Coordinator** Marta Crespo **Clinical Research Coordinator** Pau Abrisqueta **Lab Manager** Gemma Pujadas **Hematologists/Lead Investigators** Pere Barba, David Beneitez, David Valcárcel **Postdoctoral Scientists** Laura Palomo, Iñaki Salvador **PhD Students** Patricia Fernández, Cristina Hernandez, Daniel Medina, Carlota Pages, Soraya Peralta **Technicians** Laura Barberà, Ana María Garrido **Hematologists/Lab Specialists** Olga Benitez, Adoracion Blanco, Sabela Bobillo, Cecilia Carpio, Maria Laura Fox, Laura Gallur, Mercedes Gironella, Gloria Hidalgo, Gloria Iacoboni, Moraima Jiménez, Marta Julia, Ana Marin, Lucía Martín, Maria Martinez, Antonieta Molero, Julia Montoro, Mayda Navarrete, Margarita Ortega, Guillem Orti, Ana Ortuño, Carles Palacio, Ana Pérez, Elisa Roldán, Olga Salamero, Silvia Saumell, Ángel Serna, Barbara Tazon

/ Strategic goals

- We translate preclinical findings into clinical benefits by developing early phase clinical trials and defining new prognostic and predictive factors.
- Main research lines currently focus on:
  - Deciphering the mechanisms involved in pathogenesis and progression of hematological neoplasms.
  - The preclinical study of new therapeutic regimens in experimental models that mimic the tumoral microenvironment using primary cells, transgenic mice models, PDXs and 3D ex-vivo cultures.
  - Defining new biomarkers for a more rational and precise treatment of patients.
  - Understanding the longitudinal tumor-immune microenvironment crosstalk during the natural history of the disease for personalized and optimal development of immunotherapeutic strategies.

/ Highlights

- In 2022 we co-authored 85 scientific papers, and were main authors (first, last and/or corresponding) of 15 among these. 40% of these articles are published in journals in the first quartile, with a median Impact Factor of 14.
- This year we have initiated nine new projects as PIs/Coordinators, eight of which are supported through grants received from competitive calls, including the Ministerio de Ciencia e Innovación (Spanish Ministry of Science and Innovation) and the Instituto de Salud Carlos III - ISCIII (Institute of Health Carlos III).

/ Summary

VHIO's Experimental Hematology Group conducts preclinical, translational and clinical research on hematological neoplasms of both lymphoid and myeloid origin. Our research team comprises hematologists and biological scientists who work closely together to design, conduct and lead our research programs.

We aim to address unmet clinical needs identified by hematologists with the ultimate goal of translating our results to patients by developing early phase clinical trials and defining novel biomarkers to improve diagnosis, prognosis and treatment outcomes.

We seek to provide new therapeutic options for our patients by deciphering the mechanisms implicated in the pathogenesis and progression of hematological malignancies. Our investigators conduct preclinical studies of new therapeutic approaches for patients diagnosed with hematological malignancies. We identify novel biomarkers in hematology that will lead to a more rational and precise diagnosis, prognosis and treatment of patients.

The Hematology Clinical Trials Unit is currently participating in more than 152 recruiting clinical studies, including phase I and basket clinical trials (n=56) and first-in- human studies of targeted therapies, both in lymphoid and myeloid malignancies. Last year 175 patients were included in our clinical studies, with 73 patients enrolled in phase I and basket trials.

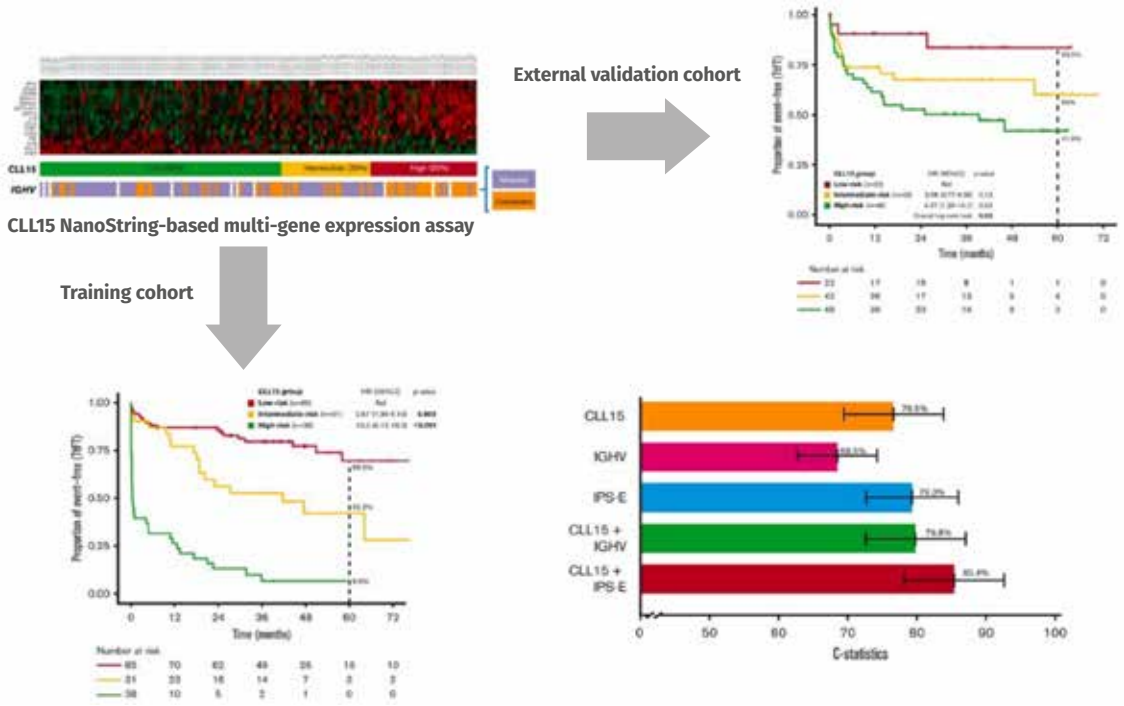


Figure: A gene expression assay based on chronic lymphocytic leukemia activation in the microenvironment to predict progression, Abrisqueta et al. *Blood Adv*. 2022.

/ PI paper pick 2022

Abrisqueta P, Medina D, Villacampa G, Lu J, Alcoceba M, Carabia J, Boix J, Tazón-Vega B, Iacoboni G, Bobillo S, Marín-Niebla A, González M, Zenz T, Crespo M, Bosch F. A gene expression assay based on chronic lymphocytic leukemia activation in the microenvironment to predict progression. *Blood Adv*. 2022 Nov 8;6(21):5763-5773.

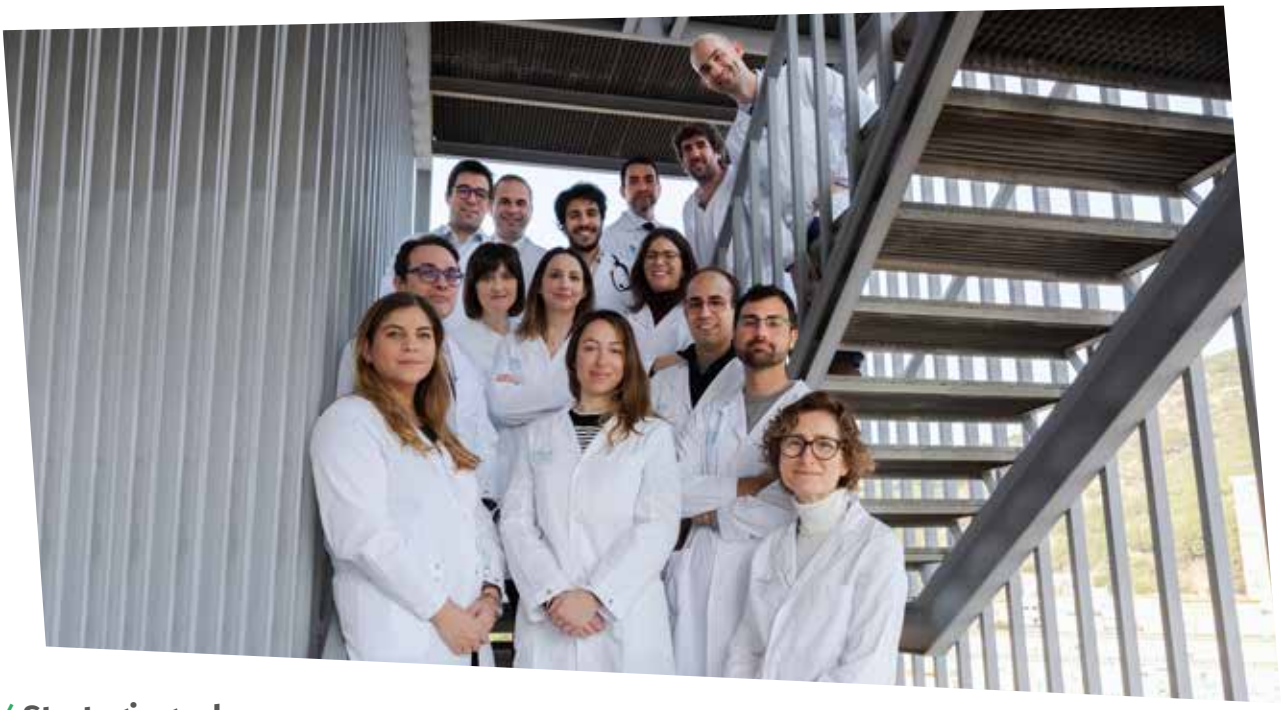
Jiménez M, Roldán E, Fernández-Naval C, Villacampa G, Martinez-Gallo M, Medina-Gil D, Peralta-Garzón S, Pujadas G, Hernández C, Pagès C, Gironella M, Fox L, Orti G, Barba P, Pumarola T, Cabirta A, Catalá E, Valentín M, Marín-Niebla A, Orfao A, González M, Campins M, Ruiz-Camps I, Valcárcel D, Bosch F, Hernández M, Crespo M, Esperalba J, Abrisqueta P. Cellular and humoral immunogenicity of the mRNA-1273 SARS-CoV-2 vaccine in patients with hematologic malignancies. *Blood Adv*. 2022 Feb 8;6(3):774-784.

Iacoboni G, Rejeski K, Villacampa G, van Doesum JA, Chiappella A, Bonifazi F, Lopez-Corral L, van Aalderen M, Kwon M, Martínez-Cibrian N, Bramanti S, Reguera-Ortega JL, Camacho-Arteaga L, Schmidt C, Marín-Niebla A, Kersten MJ, Martin Garcia-Sancho A, Zinzani PL, Corradini P, van Meerten T, Subklewe M, Barba P. Real-world evidence of brexucabtagene autoleucel for the treatment of relapsed or refractory mantle cell lymphoma. *Blood Adv*. 2022 Jun 28;6(12):3606-3610.

Dickinson MJ, Carlo-Stella C, Morschhauser F, Bachy E, Corradini P, Iacoboni G, Khan C, Wróbel T, Offner F, Trněný M, Wu SJ, Cartron G, Hertzberg M, Sureda A, Perez-Callejo D, Lundberg L, Relf J, Dixon M, Clark E, Humphrey K, Hutchings M. Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. *N Engl J Med*. 2022 Dec 15;387(24):2220-2231.

Gastrointestinal & Endocrine Tumors Group

Principal Investigator Teresa Macarulla **Senior Clinical Investigators and Medical Oncologists** Jaume Capdevila, Elena Élez **Medical Oncologists and Clinical Fellows** Daniel Alejandro Acosta, María Alsina, Iosune Baraibar, Jaume Capdevila, Florian Castet, Marc Diez, Carles Fabregat, Alejandro Garcia, Jorge Hernando, Marta Rodriguez Castells, Javier Ros, Francesc Salvà, Nadia Saoudi, Helena Verdaguer **Translational Investigator** Rodrigo A. Toledo **Senior Scientist Preclinical Team Leader** Tian Tian **Clinical Nurse Specialists** Ariadna García, Alexandre Sierra **Sample Managers** Gemma Pruna, Ines Suarez



/ Strategic goals

- Molecular characterization and biomarker discovery in GI malignancies, in particular colorectal, gastric, pancreatic, hepatobiliary cancers.
- Implementation of liquid biopsy approaches to monitor patterns of disease evolution in patients undergoing treatment.
- Clonal evolution studies, with particular focus on *BRAF* mutant tumors, to investigate the relationship between tumor heterogeneity, disease progression and treatment response.
- Development of disease-relevant preclinical models (in vitro organoid platforms, in vivo PDXs and transgenic models) to investigate mechanisms of primary and secondary resistance to therapy.
- Design of early clinical studies and investigator-initiated trials (IIT) to accelerate the development of innovative anti-tumor agents.
- Participation and coordination of late-stage clinical research studies to assess the clinical impact of new therapeutic strategies and identify novel prognostic and predictive biomarkers.
- Expansion of research lines in GI cancers including on the study of microbiota, cancer immunology and the tumor microenvironment.

/ Highlights

- Our research activities include more than 40 translational research projects in GI malignancies that are supported by long-standing and newly established national and international collaborations. These include the TuMICC study, which aims to understand the mechanisms of intrinsic resistance to therapy in CRC patients (funded by AECC); studies evaluating the mutant allele fraction (MAF) of *BRAF-V600E* in plasma for the monitoring of patients (supported by TTD, Mutual Médica, and Fundación CRIS contra el Cáncer); and the BioPrinted hydROgel MicrofluIdicS project, PROMISE, page 191, (funded by "la Caixa" Foundation), to develop experimental systems that recapitulate the metastatic microenvironment of patients.
- We coordinate one work package of the IMMUNE4ALL national consortium (page 196) that seeks to enhance the efficacy of immunotherapies in GI malignancies, including in colorectal cancer and cholangiocarcinoma. The study was submitted for approval to the Instituto de Salud Carlos III (ISCIII, Carlos III Health Institute) and launched in March 2023.
- We also coordinate several investigator-initiated-trials (IITs) testing innovative approaches or combination strategies in difficult-to-treat GI cancers. Illustrative of these efforts are the NoCanTher European consortium leading the development of magnetic nanoparticles in locally advanced pancreatic cancer (page 189); and the TALENT trial evaluating the potent VEGFR1-3 & FGFR1-4 inhibitor lenvatinib in advanced NETs.
- We are leading an ongoing multicenter academic phase Ib/II trial to evaluate the combination of anti-EGFR/BRAF (encorafenib, cetuximab) therapy with an inhibitor of the vascular endothelial growth factor (bevacizumab-bvzr) in patients with BRAF-mutant metastatic colorectal cancer.
- We further participate in an ongoing international consortium, OPTIMISTICC, (page 186) funded by the Cancer Research UK's Grand Challenge program aimed at understanding the relevance of the microbiome of colorectal cancer patients in modulating response to therapy. Additionally, we are active members of several national and international consortia and networks, including CIBER-ONC, Cancer Core Europe - CCE (page 185), the WIN consortium (page 193), and the ACRCelerate network (page 185) which is funded by the CRUK to improve patient stratification in clinical trials.
- We have also consolidated an academic-pharma partnership with AstraZeneca through the Partner of Choice program (page 198), that is supporting our efforts in studying the mechanisms of resistance to immunotherapy, as well as understanding the efficacy of PARP inhibitors in pancreatic cancer, among other ongoing projects.

/ Summary

The Gastrointestinal & Endocrine Tumors Group, led by Teresa Macarulla, is dedicated to developing molecular therapies against GI malignancies. Our group pioneers transformative research of excellence and leads the development of new anti-cancer agents in early phase clinical trials to generate novel biomarkers and targets that accelerate the delivery of precision oncology to our patients with colorectal, pancreatic, gastric, and neuroendocrine cancer, among others.

Our multidisciplinary team integrates medical oncologists and clinical investigators, a translational researcher with expertise in biomarker discovery, two research nurses dedicated to monitoring patients in research programs, laboratory technicians specialized in molecular biology and patient-derived xenografts (PDX), data curators, as well as other professionals involved in the study of precision medicine against GI malignancies. In addition, our investigators work closely with our recently established Upper Gastrointestinal Cancer Translational Research Group led by Tian Tian and directed by Teresa Macarulla. We also collaborate with other VHIO researchers and groups through our highly interactive and functional Task Forces in colorectal, cholangiocarcinoma, and pancreatic cancers.

In 2022, our group played a central role in several clinical trials evaluating the efficacy of immunotherapy and targeted agents in GI tumors. Among these, we contributed to reporting the overall survival results of the phase 3 POLO trial that supports the clinical benefit of olaparib maintenance therapy in pancreatic cancer patients harboring a germline *BRCA* mutation and led the clinical evaluation of a new antibody-drug conjugate (anti-CEACAM5-DM4) in patients with advanced solid tumors. Importantly, we opened many clinical studies across different phases that are evaluating the safety profile, efficacy and survival benefit of a wide range of therapeutic strategies in patients with GI tumors.

Thanks to our team's translational investigators, we have also made significant progress in validating and developing non-invasive liquid biopsy technologies and biomarkers to enable the more precise monitoring of cancer patients. Worth noting is the identification of mutations in the *RNF43* gene as the first predictive biomarker to optimize the clinical management of patients with *BRAF*-mutant metastatic colorectal cancer treated with anti-BRAF/EGFR combinatory therapies. Additionally, through leveraging our large resource of patient-derived models and preclinical resources, we have led numerous studies that uncover novel actionable biology in GI cancers and establish the rationale for pursuing clinical evaluation of new therapies.

Collectively, the cutting-edge research conducted by our clinical and translational investigators has positioned our multidisciplinary group as a reference in the field of GI malignancies, which is reflected by numerous invited talks at international conferences, and several opinion articles and editorials published in leading biomedical journals.

/ PI paper pick 2022

Tempero MA, Pelzer U, O'Reilly EM, Winter J, Oh DY, Li CP, Tortora G, Chang HM, Lopez CD, Bekaii-Saab T, Ko AH, Santoro A, Park JO, Noel MS, Frassineti GL, Shan YS, Dean A, Riess H, Van Cutsem E, Berlin J, Philip P, Moore M, Goldstein D, Tabernero J, Li M, Ferrara S, Le Bruchec Y, Zhang G, Lu B, Biankin AV, Reni M; APACT Investigators. Adjuvant *nab*-Paclitaxel + Gemcitabine in Resected Pancreatic Ductal Adenocarcinoma: Results From a Randomized, Open-Label, Phase III Trial. *J Clin Oncol*. Epub 2022 Dec 15:JCO2201134.

Elez E, Ros J, Fernández J, Villacampa G, Moreno-Cárdenas AB, Arenillas C, Bernatowicz K, Comas R, Li S, Kodack DP, Fasani R, Garcia A, Gonzalo-Ruiz J, Piris-Gimenez A, Nuciforo P, Kerr G, Intini R, Montagna A, Germani MM, Randon G, Vivancos A, Smits R, Graus D, Perez-Lopez R, Cremolini C, Lonardi S, Pietrantonio F, Dienstmann R, Tabernero J, Toledo RA. RNF43 mutations predict response to anti-BRAF/EGFR combinatory therapies in *BRAF-V600E* metastatic colorectal cancer. *Nat Med*. 2022 Oct;28(10):2162-2170.

Diaz LA Jr, Shiu KK, Kim TW, Jensen BV, Jensen LH, Punt C, Smith D, Garcia-Carbonero R, Benavides M, Gibbs P, de la Fourchardiere C, Rivera F, Elez E, Le DT, Yoshino T, Zhong WY, Fogelman D, Marinello P, Andre T; KEYNOTE-177 Investigators. Pembrolizumab versus chemotherapy for microsatellite instability-high or mismatch repair-deficient metastatic colorectal cancer (KEYNOTE-177): final analysis of a randomised, open-label, phase 3 study. *Lancet Oncol*. 2022 May;23(5):659-670.

Kindler HL, Hammel P, Reni M, Van Cutsem E, Macarulla T, Hall MJ, Park JO, Hochhauser D, Arnold D, Oh DY, Reinacher-Schick A, Tortora G, Algül H, O'Reilly EM, Bordia S, McGuinness D, Cui K, Locker GY, Golan T. Overall Survival Results From the POLO Trial: A Phase III Study of Active Maintenance Olaparib Versus Placebo for Germline *BRCA*-Mutated Metastatic Pancreatic Cancer. *J Clin Oncol*. 2022 Dec 1;40(34):3929-3939.

Genitourinary, CNS Tumors, Sarcoma & Cancer of Unknown Primary Site Group

Principal Investigator Joan Carles **Senior Clinical Investigators and Medical Oncologists** Rafael Morales, Cristina Suárez, Claudia Valverde, Maria Vieito **Medical Oncologists and Clinical Fellows** Ferran Ferragut, Macarena Gonzalez, David Marmolejo, Joaquin Mateo, César Serrano **Clinical Nurse Specialists** Alexandre Sierra, Anna Vazquez

/ Strategic goals

- Design and develop clinical trials covering all malignancies studied by our group. We seek to provide our patients with the most novel and optimal treatments including immune-based therapeutics, targeted therapies, and new treatments.
- Conduct clinical trials at different stages of disease with emphasis on a histology-tailored design and multidisciplinary approach.
- Continue developing our biopsy program for patients with mCRPC to target genomic alterations including PI3K pathways, DNA repair genes, and androgen receptor alterations.
- Further consolidate our Kidney Cancer Task Force at VHIO in collaboration with researchers at the Vall d'Hebron Research Institute (VHIR) and Biomedical Research Institute of Bellvitge (IDIBELL).
- Microbiota studies as a biomarker for immunotherapies to treat bladder and kidney cancers.
- Expand our translational research platform for glioblastoma in collaboration with VHIO's Gene Expression & Cancer Group (page 72).
- Develop our translational platform for GIST and expand research in collaboration with the Spanish Sarcoma Group (GEIS), and other European referral centers. We are also an active member of the European References Network (ERN) for rare tumors (EURACAN).
- Develop new tools and techniques including liquid biopsy for our patients to more precisely tailor treatments against mCRPC, GIST and kidney cancer.
- We have started several “quality of life and patient perspective” academic studies and collaborations with patient advocacy groups to incorporate the patient view in regular care and research in sarcoma.

/ Highlights

- In prostate cancer, we have consolidated our Task Force and Serum Bank, and have performed more than 750 blood extractions and saliva samples in 2022. These efforts enable us to participate in different translational studies including our lead of the IRONMAN project in Spain. At the end of 2022 more than 370 patients in Spain were included in this program, representing 13% of all patients included from around the world.
- We have expanded our serum bank to other tumor types within our scope and have included 188 samples in kidney cancer and 81 in sarcoma and GIST tumors.
- We have expanded our phase I program across all tumor types studied by our group.
- We continue to foster and develop new collaborations with different VHIO groups and external partners.

/ Summary

We are dedicated to advancing clinical and translational research against cancer, with extensive experience and expertise in treating various neoplasms. In collaboration with urologists, nuclear medicine physicians, and radiation therapists we design and develop clinical trials for genitourinary malignancies at different stages of disease.

In 2022 we continued to consolidate our expert Prostate Cancer Task Force. By closely connecting clinical and translational researchers at VHIO and the Vall d'Hebron Research Institute (VHIR), we have initiated various translational prostate cancer projects. In collaboration with other partners including the Biomedical Research Institute of Bellvitge (IDIBELL, Barcelona), we are also pursuing translational studies in kidney cancer.

Recent advances have led to the more effective treatment of GU malignancies. Immunotherapy is proving increasingly important against bladder and kidney cancers. We are studying new combinations including HIF-2 alpha inhibitors and other immunomodulators.

In bladder cancer, immunotherapy has shown activity in metastatic disease and is now being tested in the neoadjuvant setting and in non-muscle-invasive bladder cancer. Molecular alterations have been identified in bladder cancer such as FGFR mutations. The unmasking of molecular alterations enables us to develop new targeted drugs. Also under development are antibody-drug conjugates (ADCs) for patients with metastatic disease. Since these agents have shown activity in muscle invasive bladder cancer, we are now aiming to develop these drugs in non-muscle invasive bladder cancer. In collaboration with the Vall d'Hebron University Hospital's Urology Department, we are participating in phase I studies with drugs targeting FGFR as well as ADCs in patients who have relapsed to BCG, in order to avoid cystectomy as the standard treatment and preserve the bladder.

Another innovative treatment for prostate cancer is theragnosis by administering radioligands using beta emitters. This therapy requires close collaboration with nuclear medicine teams to coordinate administration and follow-up of patients.

Our group collaborates with various other research centers including the Cleveland Clinic (Ohio, USA), University of California, San Francisco (California, USA), and participates in studies in partnership with the Gustave Roussy Institute (Paris, France), Barts Health NHS Trust – Hospital (London, UK), and Kantonsspital St. Gallen (Switzerland). This year we have continued to expand our translational research program in prostate cancer working alongside VHIO's Prostate Cancer Translational Research Group (page 78), led by Joaquin Mateo, as well as other hospitals in Catalonia.

Our main focus is metastatic castration-resistant prostate cancer (mCRPC), and we are working on a project led by Joaquin Mateo entitled *Clinical Qualification of DNA Repair Defects as Biomarkers in Metastatic Prostate Cancer Using Integrated Genomics and Tissue-Based Functional Assays*. This research is supported by the U.S. Department of Defense (DoD) Congressionally Directed Medical Research Program. Additionally, we are participating in the IRONMAN project directed by the Memorial Sloan Kettering Cancer Center (MSKCC – New York, USA), as the Spanish national repository for the IRONMAN registry. This international program aims at building a comprehensive bank of clinical data and biospecimens from metastatic prostate cancer patients. Our involvement in this project is supported by the Movember Foundation and Fundación FERO (FERO Foundation).

We have started a new project with the SOLTI Group aimed at empowering patients with mCRPC through a web site to perform NGS genomic profiling of tumors and correlate results with blood sample tests (Guardant Health) that will be performed at the same time. We will also ask patients to complete a survey regarding their expectations before and after genomic profiling based on the results obtained and the new treatments that could be recommended by a panel of specialists. This study is supported by different Spanish prostate cancer societies (HOPE Prostate).

We collaborate with VHIO's Radiomics Group headed by Raquel Perez-Lopez (page 108), to analyze MRI alterations in patients who have started hormonal treatments for metastatic prostate cancer, and correlate these data with bone biopsies, performed in parallel. This project, *iPROMET: a study for clinical validation of whole- body diffusion-weighed MRI as a response biomarker of bone metastases in patients with prostate cancer*, counts on the combined expertise of a urologist, radiation oncologist, radiologist, and medical oncologist to establish a circuit for the systematic metastatic tissue acquisition from prostate cancer patients at Vall d'Hebron.

We have expanded our avatar program for kidney cancer tumors in collaboration with IDIBELL and implanted 42 tissue samples, 17 of which have grown. We were able to obtain data on treatment resistance in 8 cases. In organoids, we have sent 9 cases and 3 are growing. We also continue to participate in the REVOLUTION project, pREdiction of niVOLUmab acTION metastatic renal cancer patients: Treg function, tumoral access and NK interactions as predictive biomarkers of immunotherapy. This research is supported by TRANSCAN-2 ERA-NET, under the scope of the EU Framework Programme Horizon 2020.

In addition, we have established a collaboration with the Institute Gustave Roussy, thanks to a grant from the CRIS Cancer Foundation, for the CARE 1 clinical trial.

In collaboration with professionals in neurosurgery and radiation therapy, we lead and develop several multidisciplinary clinical studies and phase I trials in CNS tumors. Additionally, alongside VHIO's Gene Expression & Cancer Group led by Joan Seoane (page 72), we continue to develop our translational research platform for glioblastoma. We analyze cfDNA in blood and cephaloraquidic liquid to assess primary CNS tumors and metastases. We have also expanded the portfolio of available clinical trials for patients with brain tumors, including studies in the concomitant and perioperative setting. We partner with Joan Seoane's group in translational neuro-oncology projects, including a platform of patient-derived xenografts, including patients treated with immunotherapy, with the option to simultaneously test efficacy in patient-xenograft pairs and the possibility of analyzing patients' CSF to seek out potential resistance mechanisms.

We are founders and coordinators of the Adolescent Working Group in the Spanish Group of investigation in Neurooncology (GEINO), have participated in the first GEINO-SEOM guideline for adult medulloblastoma and have proposed the first classification of genomic alterations for primary brain tumors using the ESMO ESCAT guidelines.

We have also increased our participation in the EORTC, not only in the SPECTA-AYA project, but have also been chosen as the National Coordinator site for the EORTC 1634-BTG (PersoMed-I), the first clinical trial of targeted therapy in postpubertal patients with medulloblastoma.

We continue to work closely with the Spanish Sarcoma Group (GEIS) on clinical trials at different stages of disease with emphasis on a histology-tailored design, and are currently setting up a translational platform for sarcomas and basic research in partnership with IDIBELL and the Cancer Research Center of Salamanca – CIC (Spain). In GIST tumors, we are working with Jonathan Fletcher's lab at the Brigham and Women's Hospital (Boston, USA).

We are now recognized as a Reference Unit of the Spanish National Health System (*Centros, Servicios y Unidades de Referencia del Sistema Nacional de Salud* - CSUR) for the treatment of sarcoma patients. This accreditation enables us to participate in the European Reference Network (ERN) for sarcoma tumors and other rare diseases. We are part of the Executive Committee of European Consortia dedicated to osteosarcoma (FOSTER) and Ewing sarcoma (Euro-Ewing).

Since César Serrano set up his own research team, VHIO's Sarcoma Translational Research Group (page 80) in 2019, we have consolidated different clinical trials with new drugs in GIST by leading and participating in phase I-II-III studies. Our Serum Bank now incorporates the majority of tumor types that we study (CNS tumors, GIST; renal cell carcinoma and CRPC), and we will continue to collect samples from our patients. Dedicated to promoting education and exchange, in 2022 we welcomed three fellows from Spain for 3-month short stays.

/ PI paper pick 2022

Fizazi K, Foulon S, Carles J, Roubaud G, McDermott R, Fléchon A, Tombal B, Supiot S, Berthold D, Ronchin P, Kacso G, Gravis G, Calabro F, Berdah JF, Hasbini A, Silva M, Thiery-Vuillemin A, Latorzeff I, Mourey L, Laguerre B, Abadie-Lacourtoisie S, Martin E, El Kouri C, Escande A, Rosello A, Magne N, Schlurmann F, Priou F, Chand-Fouche ME, Freixa SV, Jamaluddin M, Rieger I, Bossi A; PEACE-1 investigators. Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2×2 factorial design. *Lancet*. 2022 Apr 30;399(10336):1695-1707.

Agarwal N, Azad A, Carles J, Chowdhury S, McGregor B, Merseburger AS, Oudard S, Saad F, Soares A, Benzaghou F, Kerloeguen Y, Kimura A, Mohamed N, Panneerselvam A, Wang F, Pal S. A phase III, randomized, open-label study (CONTACT-02) of cabozantinib plus atezolizumab versus second novel hormone therapy in patients with metastatic castration-resistant prostate cancer. *Future Oncol*. 2022 Mar;18(10):1185-1198.

Suarez C, Marmolejo D, Valdivia A, Morales-Barrera R, Gonzalez M, Mateo J, Semidey ME, Lorente D, Trilla E, Carles J. Update in collecting duct carcinoma: Current aspects of the clinical and molecular characterization of an orphan disease. *Front Oncol*. 2022 Oct 4;12:970199.

Carles J, Alonso-Gordoa T, Mellado B, Méndez-Vidal MJ, Vázquez S, González-Del-Alba A, Piulats JM, Borrega P, Gallardo E, Morales-Barrera R, Paredes P, Reig O, Garcías de España C, Collado R, Bonfill T, Suárez C, Sampayo-Cordero M, Malfettone A, Garde J. Radium-223 for patients with metastatic castration-resistant prostate cancer with asymptomatic bone metastases progressing on first-line abiraterone acetate or enzalutamide: A single-arm phase II trial. *Eur J Cancer*. 2022 Sep;173:317-326.

Gynecological Malignancies Group

Principal Investigator Ana Oaknin **Medical Oncologists** Lorena Fariñas, Carmen García Durán, David Garcia-Illescas, Francisco Grau

/ Strategic goals

- Determine the best treatment approaches against advanced gynecologic malignancies through optimally designed international clinical trials.
- Contribute to early clinical drug development in gynecologic cancers.
- Expand our translational research program to advance precision medicine.
- Specifically, we strive to:
  - Develop and advance novel immunotherapeutics for the treatment of endometrial cancer and cervical cancer.
  - Apply cellular therapy to metastatic cervical cancer through the adoptive cell transfer of tumor infiltrating lymphocytes (TILs).
  - Consolidate our position as a reference site for clinical research in gynecologic malignancies.
  - Continue to be a referral center for patients who seek to participate in our clinical studies.

/ Highlights

Our group continues to lead other clinical trials toward defining next generation treatment regimens:

- Ana Oaknin is the global lead of a phase III Investigator-Initiated Trial for first-line metastatic cervical cancer (the BEATcc trial) running in the USA, EU and Japan. She is also the European lead investigator of the EMPOWER trial, a phase III trial aimed at testing cemiplimab in recurrent cervical cancer. This study has generated practice-changing data and led to the approval of immunotherapy for the treatment of this disease.
- We led the GARNET study that included the largest series of patients with endometrial cancer treated with immunotherapy; the anti-PD-1 agent dostarlimab.
- She is also the Principal Investigator of the phase II ATOMICC clinical trial to test anti-PD-1 dostarlimab as maintenance therapy for patients with high-risk locally advanced cervical cancer after chemoradiation.

These efforts have positioned Ana Oaknin as a Key Opinion Leader in our field, which is also reflected by her participation at some of the largest, global oncology conferences and meetings.

/ Summary

Our clinical research focuses on gynecological malignancies and the development of novel therapies against these tumor types. We are also members of some of the most relevant societies and groups in gynecological oncology including the Gynecologic Cancer InterGroup (GCIG), with our Principal Investigator, Ana Oaknin, as the Spanish representative of its Cervix Cancer Committee serving as Chair, and the Spanish clinical lead of the Gynecologic Oncology Group (GOG). We also belong to the European Network of Gynecological Oncology Trial groups (ENGOT).

Contributing to the advancement of the treatment of gynecological malignancies, we have participated in the development of a number of therapies that are now the current standard of care for different malignancies. As an example, we led the GARNET study that included the largest series of patients with endometrial cancer (EC) treated with immunotherapy; the anti-PD-1 agent dostarlimab.

Dostarlimab was subsequently approved by both the European Commission (EC) and the U.S. Food and Drug Administration (FDA) in April 2021 for the treatment of patients with mismatch repair-deficient (dMMR)/ microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer who have progressed on or following prior treatment with a platinum containing regimen. Notably, this approval made dostarlimab the first anti-PD-1 therapy available for endometrial cancer in Europe.

We lead/participate in several important clinical trials that have generated new and compelling data and also seek to expand therapeutic strategies against metastatic cervical cancer, mainly driven by immunotherapy.

Illustrative of these contributions, Ana Oaknin co-led the Phase III EMPOWER study that assessed the efficacy of PD-1 inhibitor cemiplimab as monotherapy for the treatment of recurrent or metastatic cervical cancer that has progressed on or after first-line platinum-based chemotherapy. Results of this study (Tewari et al. *N Engl J Med*. 2022), led to the European Commission's approval in November 2022 of cemiplimab as the first second-line immunotherapy for this patient population, now also approved in Canada and Brazil.

Ana Oaknin serves as a Faculty Member of the European Society for Medical Oncology's (ESMO) Annual Congress Gynecological Tumors Track (2021-2025), and Subject Editor, Gynecological Malignancies, for ESMO's Guidelines Committee (2021-2024). In 2022 she first authored ESMO's Clinical Practice Guideline for diagnosis, treatment and follow-up of endometrial cancer (Oaknin et al. *Ann Oncol*. 2022).

In addition, she was a Member of the ESMO Congress 2022 Scientific Program Committee and Gynecological Tumors Track Chair for the ESMO Asia Congress 2022. Ana also serves as Co-Chair (2021-2024) for the ENGOT Gynecological Cancer Academy that aims to nurture and develop the next generation of leaders in gynaecological oncology. She was also Co-Chair of the virtual International Gynecologic Cancer Society's (IGCS) Annual Global Meeting 2021.

/ PI paper pick 2022

Kristeleit R, Lisyanskaya A, Fedenko A, Dvorkin M, de Melo AC, Shparyk Y, Rakhmatullina I, Bondarenko I, Colombo N, Svintsitskiy V, Biela L, Nechaeva M, Lorusso D, Scambia G, Cibula D, Póka R, Oaknin A, Safra T, Mackowiak-Matejczyk B, Ma L, Thomas D, Lin KK, McLachlan K, Goble S, Oza AM. Rucaparib versus standard-of-care chemotherapy in patients with relapsed ovarian cancer and a deleterious BRCA1 or BRCA2 mutation (ARIEL4): an international, open-label, randomised, phase 3 trial. *Lancet Oncol*. 2022 Apr;23(4):465-478.

Tewari KS, Monk BJ, Vergote I, Miller A, de Melo AC, Kim HS, Kim YM, Lisyanskaya A, Samouëlian V, Lorusso D, Damian F, Chang CL, Gotovkin EA, Takahashi S, Ramone D, Pikiel J, Mańkowiak-Matejczyk B, Guerra Alía EM, Colombo N, Makarova Y, Rischin D, Lheureux S, Hasegawa K, Fujiwara K, Li J, Jamil S, Jankovic V, Chen CI, Seebach F, Weinreich DM, Yancopoulos GD, Lowy I, Mathias M, Fury MG, Oaknin A; Investigators for GOG Protocol 3016 and ENGOT Protocol En-Cx9. Survival with Cemiplimab in Recurrent Cervical Cancer. *N Engl J Med*. 2022 Feb 10;386(6):544-555.

Oaknin A, Monk BJ, Vergote I, Cristina de Melo A, Kim YM, Lisyanskaya AS, Samouëlian V, Kim HS, Gotovkin EA, Damian F, Chang CL, Takahashi S, Li J, Mathias M, Fury MG, Ivanescu C, Reaney M, LaFontaine PR, Lowy I, Harnett J, Chen CI, Tewari KS. EMPOWER CERVICAL-1: Effects of cemiplimab versus chemotherapy on patient-reported quality of life, functioning and symptoms among women with recurrent cervical cancer. *Eur J Cancer*. 2022 Oct;174:299-309.

Oaknin A, Gilbert L, Tinker AV, Brown J, Mathews C, Press J, Sabatier R, O'Malley DM, Samouelian V, Boni V, Duska L, Ghamande S, Ghatage P, Kristeleit R, Leath C III, Guo W, Im E, Zildjian S, Han X, Duan T, Veneris J, Pothuri B. Safety and antitumor activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair deficient/ microsatellite instability-high (dMMR/ MSI-H) or proficient/stable (MMRp/ MSS) endometrial cancer: interim results from GARNET-a phase I, single-arm study. *J Immunother Cancer*. 2022 Jan;10(1):e003777.

CLINICAL RESEARCH

Hereditary Cancer Genetics Group

Principal Investigator Judith Balmaña **Senior Researcher** Sara Gutiérrez-Enríquez **Associate Investigator** Orland Díez **Postdoctoral Fellow** Renan Gomes **Medical Oncologist** Mara Cruellas **Genetic Counselors** Estela Carrasco, Adrià López-Fernández, Sara Torres **Postdoctoral Clinical Fellow** Mònica Pardo **Predoctoral Students** Ester Aguado, Joanna Domènech, Setareh Kompanian **Graduate Student** Laia Peralba **Clinical Nurse Specialist** Eduard Pérez Ballestero **Data Curators** Adriana Bareas, Maite Torres **Auxiliary Clinician** Carmen Aguilar

/ Strategic goals

- The characterization of new hereditary breast and ovarian cancer (HBOC) genes, psychological impact of multigene testing, and feasibility of Polygenic Risk Score (PRS) in HBOC.
- Targeting DNA damage response in breast cancer.
- Implementation of the RAD51 assay as a clinical biomarker for PARPi therapy, and a biomarker of homologous recombination repair deficiency (HRR-D) among non-*BRCA1/2* mutation carriers and those with variants of uncertain significance (VUS).
- Evaluate the preventive effect of denosumab on breast cancer prevention in *BRCA1* mutation carriers (BRCA-P trial).
- Optimize the genetic diagnosis of HBOC.
- Identify cellular and genomic biomarkers as predictors of late toxicity after radiotherapy.

/ Highlights

- We continue our longitudinal registry of mutation carriers in hereditary cancer, and we are investigating personality traits as predictors of the psychological impact of multigene testing, mainly focused on genetic uncertainty.
- We are investigating the feasibility of personalized breast cancer risk assessment and early detection through quantification of genetic and non-genetic risk factors.
- We are clinically validating the RAD51predict assay as a functional biomarker of homologous recombination repair deficiency and a predictor of PARPi resistance.
- In collaboration with the international ENIGMA consortium, we have compiled functional and splicing data suggesting that up to 10% of *BRCA1* exon 18 skipping in carriers of synonymous, intronic, and benign missense variants is well-tolerated.
- We are leading research into the value of RAD51 foci in the interpretation of variants of unknown clinical significance in *BRCA1*, *BRCA2* and *PALB2* genes as part of one of the ERAPerMed project's work packages. This project is coordinated by Violeta Serra, PI of VHIO's Experimental Therapeutics Group.
- In the RADprecise project, we have discovered a blood microRNA profile that has the potential to serve as a biomarker for predicting radiation-induced late toxicity in breast cancer patients prior to radiotherapy. This collaborative project funded by ERAPerMed aims to personalize radiotherapy by incorporating cellular response to irradiation in the treatment planning in order to minimize radiation toxicity.

/ Summary

Our group focuses on addressing the challenges associated with advances in the diagnosis of hereditary cancer susceptibility and applying these insights in clinical practice. In partnership with the hereditary cancer program at the Catalan Institute of Oncology (ICO), we are investigating the genetic complexity of hereditary cancer through the multidimensional analysis of a customized panel, low-risk alleles, and studying the psychological impact in our population.

Ongoing research centers on the role of personality traits in predicting the psychological impact of genetic results and the uptake of prevention strategies. We have received funding to assess genetic cancer risk estimation and cancer-risk adapted approaches including polygenic risk score (PRS) analysis. A longitudinal national-based registry of mutation carriers incorporates prospective data to explore health outcomes.

We are also involved in the clinical development of PARP inhibitors (PARPi) in early *gBRCA1/2* breast cancer, and novel combinations in the advanced disease setting. We have consolidated our collaboration with VHIO's Experimental Therapeutics Group led by Violeta Serra (page 70), which has resulted in a large collection of *BRCA1/2*-associated patient-derived xenografts (PDX) implanted in athymic mice. We are using these murine models to identify mechanisms of resistance to targeted therapies, identify novel biomarkers, and assess new combinatorial treatments at disease progression. Our group has identified a functional biomarker for PARPi sensitivity that has been tested preclinically. We are now validating this biomarker in samples from clinical trials and in standard clinical practice.

Led by our Senior Researcher and Laboratory Leader, Sara Gutiérrez-Enríquez, we pursue our interest in the genetic epidemiology of hereditary breast and ovarian cancer (HBOC). This research has shed important light on the characterization of new pathogenic variants in HBOC genes and has provided discriminatory tools to interpret variants of uncertain significance in *BRCA1/2* genes. We also aim to decipher the role of intronic, splicing, and missense variants in major HBOC genes and investigate the yield of whole genome sequencing (WGS) and long-read RNA-seq. In collaboration with VHIO's Radiation Oncology Group led by Jordi Giralt (page 106), Sara Gutiérrez-Enríquez is independently leading research on predictive genetic and cellular markers of susceptibility to radiotherapy-induced clinical toxicity.

I

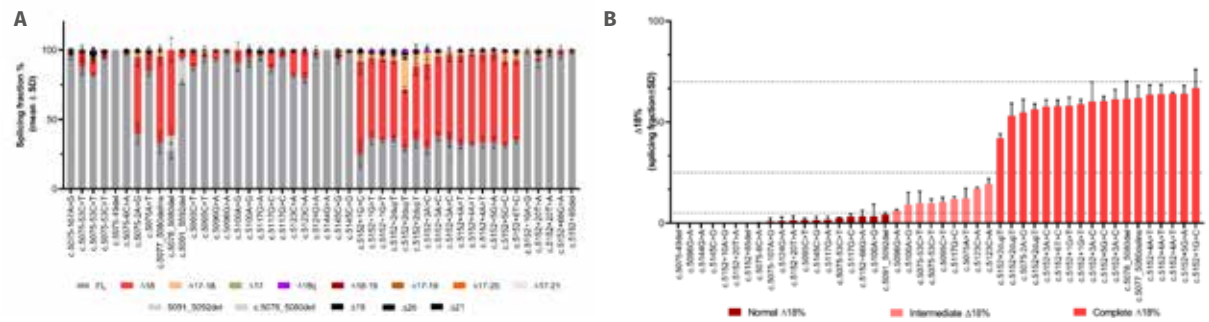


Figure I: Semi-quantitative mRNA splicing profiling by capillary electrophoresis of fluorescent amplicons. **A)** Results from patients' whole blood RNA; **B)** Patients' Δ18 levels in increasing order.

II

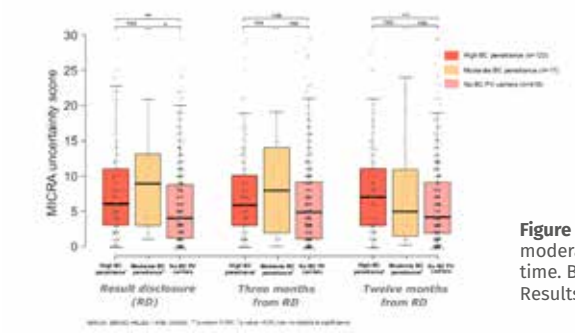


Figure II: Representation of the MICRA uncertainty subscale in high-penetrance, moderate-penetrance, and non-carriers of breast cancer pathogenic variants over time. BC, breast cancer; Nss, no statistical significance; PV, pathogenic variant; RD, Results disclosure.

/ PI paper pick 2022

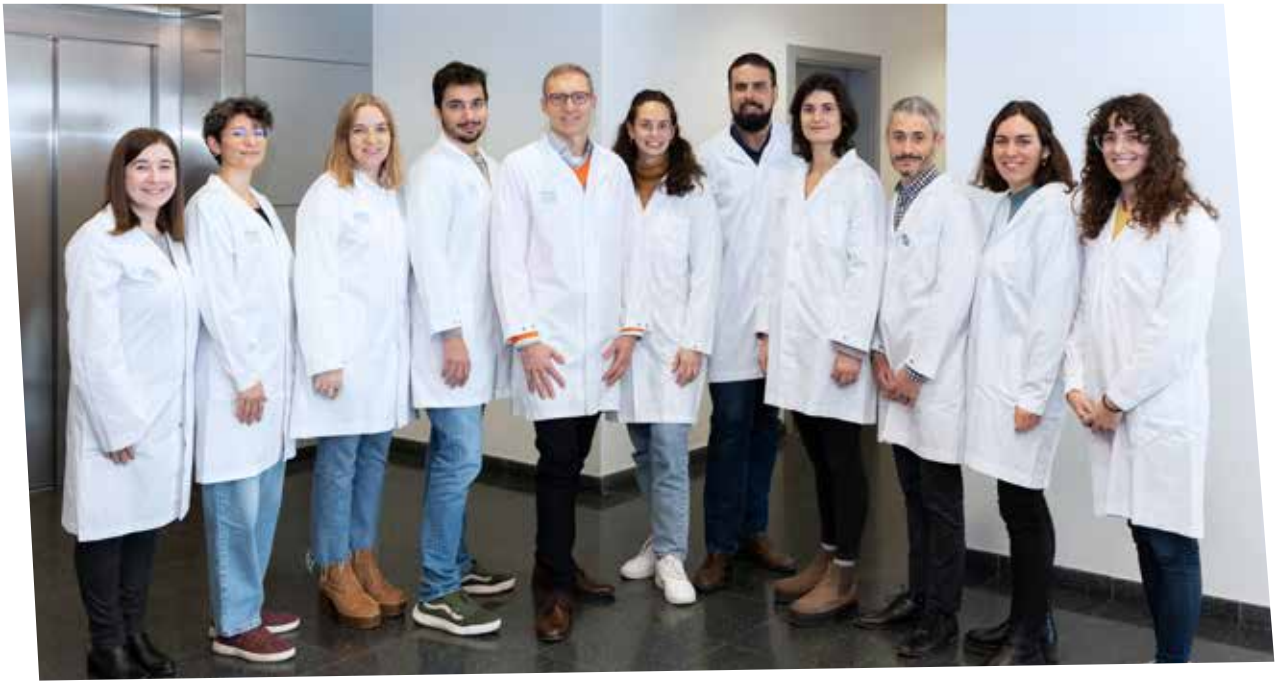
Carrasco E, López-Fernández A, Codina-Sola M, Valenzuela I, Cueto-González AM, Villacampa G, Navarro V, Torres-Esquius S, Palau D, Cruellas M, Torres M, Perez-Dueñas B, Abulí A, Diez O, Sábado-Álvarez C, García-Arumí E, Tizzano EF, Moreno L, Balmaña J. Clinical and psychological implications of secondary and incidental findings in cancer susceptibility genes after exome sequencing in patients with rare disorders. *J Med Genet*. 2022 Nov 29:jmg-2022-108929.

Aguado-Flor E, Fuentes-Raspall MJ, Gonzalo R, Alonso C, Ramón Y Cajal T, Fisas D, Seoane A, Sánchez-Pla Á, Giralt J, Díez O, Gutiérrez-Enríquez S. Cell Senescence-Related Pathways Are Enriched in Breast Cancer Patients With Late Toxicity After Radiotherapy and Low Radiation-Induced Lymphocyte Apoptosis. *Front Oncol*. 2022 May 24;12:825703.

Pellegrino B, Herencia-Ropero A, Llop-Guevara A, Pedretti F, Moles-Fernández A, Viaplana C, Villacampa G, Guzmán M, Rodríguez O, Grueso J, Jiménez J, Arenas EJ, Degasperi A, Dias JML, Forment JV, O'Connor MJ, Déas O, Cairo S, Zhou Y, Musolino A, Caldas C, Nik-Zainal S, Clarke RB, Nuciforo P, Díez O, Serres-Créixams X, Peg V, Espinosa-Bravo M, Macarulla T, Oaknin A, Mateo J, Arribas J, Dienstmann R, Bellet M, Oliveira M, Saura C, Gutiérrez-Enríquez S, Balmaña J, Serra V. Preclinical In Vivo Validation of the RAD51 Test for Identification of Homologous Recombination-Deficient Tumors and Patient Stratification. *Cancer Res*. 2022 Apr 15;82(8):1646-1657.

Oncology Data Science (ODysSey) Group

Principal Investigator Rodrigo Dienstmann **Biostatisticians** Eduardo García, Víctor Navarro, Guillermo Villacampa **Biomedical Engineer** Anna Pedrola **Data Analysts** Gloria Castillo, Raquel Comas, Laia Joval, Fiorella Ruiz, Anna Serradell, Cristina Viaplana **Medical Oncologist** Pablo Cresta



/ Strategic goals

Facilitate high-quality clinical-molecular correlative studies and investigator-initiated trials at VHIO:

- Development and maintenance of clinical-molecular databases, data management solutions, and decision-support systems as resources for clinicians, molecular pathologists, and translational investigators.
- Provide guidance to medical oncologists and cancer biologists during the design and interpretation of clinical trials and biomarker correlative studies, as well as the development and validation of omics-based tests that have a direct clinical application.

Promote evidence-based precision cancer care and clinical trial recruitment:

- Promote the clinical adoption of the Molecular Tumor Board Portal (MTBP, https://mtbp.org) and Cancer Genome Interpreter (CGI, https://www.cancergenomeinterpreter.org) as decision support systems for the correct interpretation of genomic data and selection of the most appropriate targeted treatment. These portals employ a variety of state-of-the-art tools to interpret the biological and clinical significance of tumor and germline alterations.
- Integrate the OncoTrialsTrack platform (https://oncotrialstrack.vhio.net) with other resources that empower healthcare providers in the difficult and time-consuming task of finding the most suitable clinical trial for cancer patients based on molecular data.

Collaborative research on Big Data, Real-World Data and Digital Oncology:

- Encourage interactions among computational oncology scientists and preclinical-clinical researchers to promote the identification of cancer subtypes and druggable drivers.
- Foster digital oncology with the development of technological solutions to monitor, process and integrate different data at the individual and population levels to help address the problems in the health systems and challenges faced by patients and clinicians.

/ Highlights

- We have provided support to VHIO investigators in the discovery and validation of new biomarkers. This has resulted in several impactful publications within our field as well as oral presentations at some of the most prestigious oncology conferences.
- As the number of investigator-initiated studies increase at VHIO, we have become an essential data management partner, providing professional assistance in electronic data capture and statistical leadership in multiple phase II-III trials.
- Our group is an active member of AACR's Genomics Evidence Neoplasia Information Exchange (GENIE) project, and other international data sharing initiatives such as EUCANCan (page 186), that catalyze precision oncology through the development of regulatory-grade registries aggregating and linking cancer genomics data with clinical outcomes from tens of thousands of cancer patients treated at the participating institutions.

/ Summary

VHIO's ODysSey Group promotes translational research in precision oncology by integrating cancer molecular profiling data with clinical outcomes of oncology patients treated at the Vall d'Hebron University Hospital (HUVH).

Our group designs and maintains comprehensive clinical-molecular databases and develops customized data management solutions for researchers who have an interest in correlative analyses for hypothesis-generation and biomarker validation. We also provide assistance to investigators in the identification of eligible patients for translational studies, calculation of sample size, clinical trial design, data capture with electronic case report forms, and statistical analyses.

We also participate in international real-world multi-omic data analyses projects, foster collaborative research in computational oncology, and are dedicated to connecting cancer researchers working on predictive and prognostic modelling, the identification of cancer drivers, molecular subtyping, primary-metastasis heterogeneity, microenvironment signatures and druggability in solid tumors.

Together with VHIO's Cancer Genomics Group (page 116), Molecular Oncology Group (page 118) and Early Clinical Drug Development Group (page 92), we co-lead VHIO's Molecular Prescreening Program (page 146). Additionally, we deploy informatics tools to explore and visualize multi-omics data for research purposes, and maintain web applications in the field of precision oncology care and clinical trial matching.

We provide support in the interpretation of next-generation sequencing tests and educate clinicians on emerging biomarkers. During Molecular Tumor Board meetings, we promote precision oncology by providing guidance regarding inclusion in early clinical trials with biomarker-guided targeted agents or immunotherapies, and genetic counseling alerts in the instance of pathogenic germline variants.

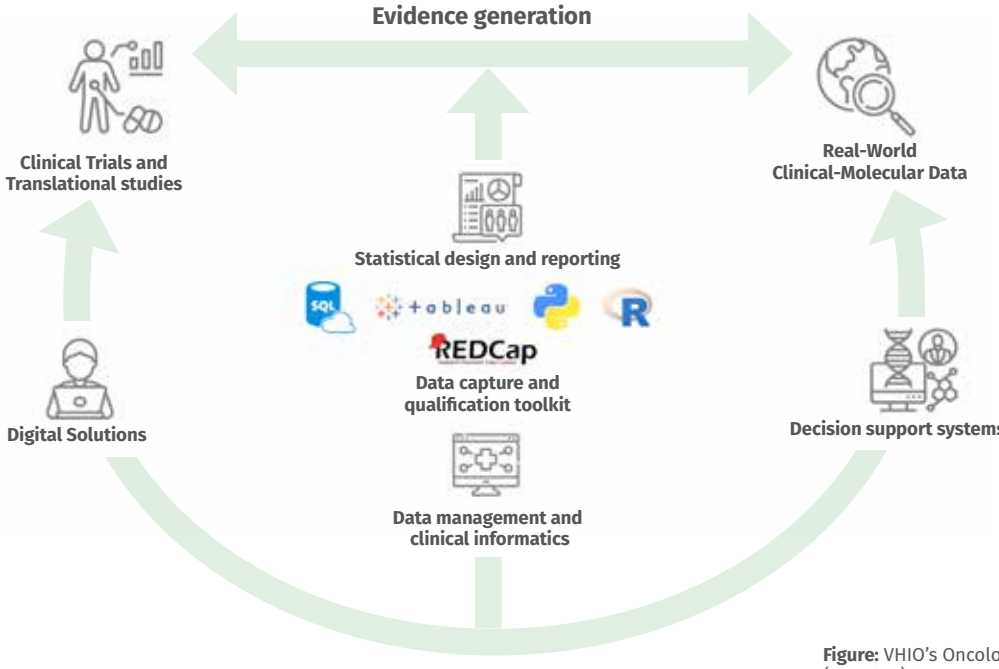


Figure: VHIO's Oncology Data Science (ODysSey) Group Workflow.

/ PI paper pick 2022

Tamborero D, Dienstmann R, Rachid MH, Boekel J, Lopez-Fernandez A, Jonsson M, Razzak A, Braña I, De Petris L, Yachnin J, Baird RD, Loriot Y, Massard C, Martin-Romano P, Opdam F, Schlenk RF, Vernieri C, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium; Balmaña J, Apolone G, Caldas C, Bergh J, Ernberg I, Fröhling S, Garralda E, Karlsson C, Tabernero J, Voest E, Rodon J, Lehtiö J. The Molecular Tumor Board Portal supports clinical decisions and automated reporting for precision oncology. *Nat Cancer.* 2022 Feb;3(2):251-261.

Verdaguer H, Saurí T, Acosta DA, Guardiola M, Sierra A, Hernando J, Nuciforo P, Miquel JM, Molero C, Peiró S, Serra-Camprubí Q, Villacampa G, Aguilar S, Vivancos A, Tabernero J, Dienstmann R, Macarulla T. ESMO Scale for Clinical Actionability of Molecular Targets Driving Targeted Treatment in Patients with Cholangiocarcinoma. *Clin Cancer Res.* 2022 Apr 14;28(8):1662-1671.

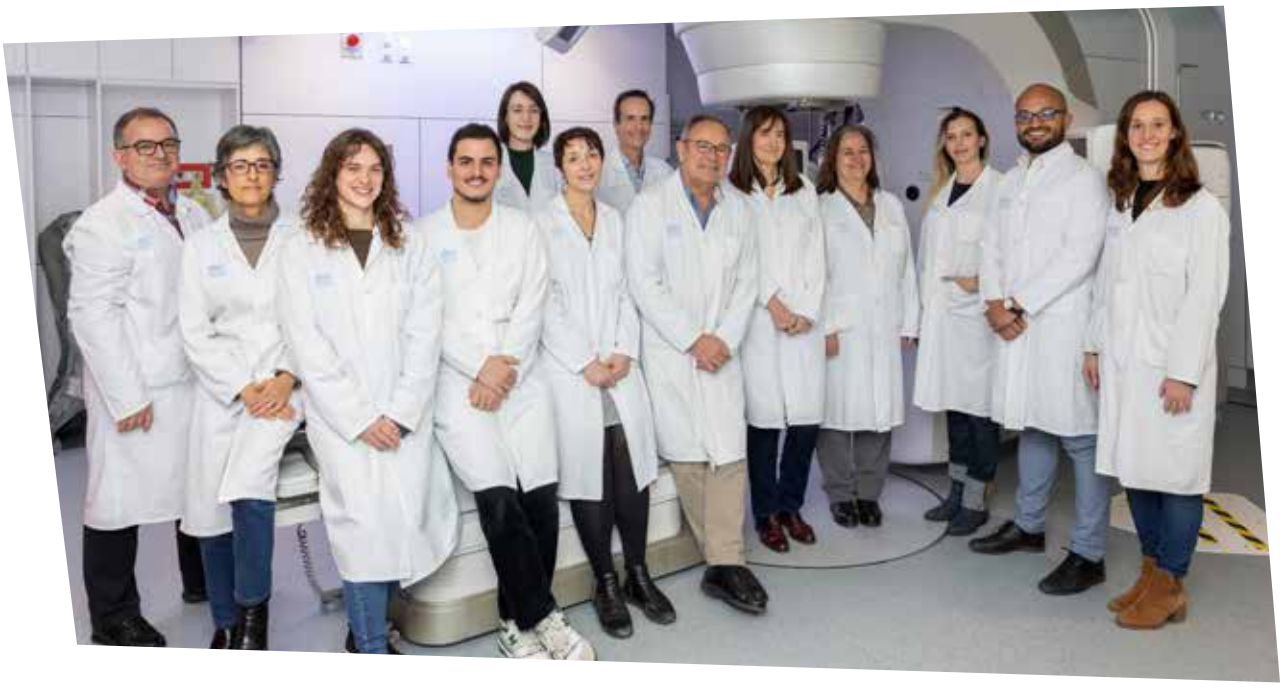
Villacampa G, Tolosa P, Salvador F, Sánchez-Bayona R, Villanueva L, Dienstmann R, Ciruelos E, Pascual T. Addition of immune checkpoint inhibitors to chemotherapy versus chemotherapy alone in first-line metastatic triple-negative breast cancer: A systematic review and meta-analysis. *Cancer Treat Rev.* 2022 Mar;104:102352.

Iacoboni G, Rejeski K, Villacampa G, van Doesum JA, Chiappella A, Bonifazi F, Lopez-Corral L, van Aalderen M, Kwon M, Martínez-Cibrian N, Bramanti S, Reguera-Ortega JL, Camacho-Arteaga L, Schmidt C, Marín-Niebla A, Kersten MJ, Martin Garcia-Sancho A, Zinzani PL, Corradini P, van Meerten T, Subklewe M, Barba P. Real-world evidence of brexucabtagene autoleucel for the treatment of relapsed or refractory mantle cell lymphoma. *Blood Adv.* 2022 Jun 28;6(12):3606-3610.

CLINICAL RESEARCH

Radiation Oncology Group

Principal Investigator Jordi Giralt **Radiation Oncologists** Manel Altabas, Sergio Benavente, André Geng, Alexandra Giraldo, Raquel Granado, Xavier Maldonado, Soraya Mico, Begoña Navalpotro, Monica Ramos, Victoria Reyes, Ramona Verges



/ Strategic goals

- Technology development: acquisition of new equipment to implement cutting edge clinical techniques such as rotational radiotherapy - with intensity modulated arc therapy (VMAT), adaptive radiotherapy, respiratory control radiotherapy (RT4D), and image-guided radiotherapy (IGRT).
- Translational research: application of insights into cancer biology as well as healthy tissue in order to personalize therapy matched to the characteristics and specificities of each patient, each individual tumor.
- Quality: continue to obtain ISO 9001/2008 recertification in the field of radiation oncology.
- Clinical research: accelerate and advance clinical research in radioimmunotherapy (RIT).

/ Highlights

- Over 90% of our patients treated with radical radiotherapy have been treated using highly complex techniques.
- Stereotactic radiotherapy for the treatment of refractory ventricular arrhythmias.
- We continue to participate in a project combining radiotherapy with nanoparticles against head and neck cancer.
- We have implemented the ‘breath hold’ technique and are treating some of our patients using this approach.
- Our continued participation as national representatives of radiotherapy in the International Society of Paediatric Oncology (SIOP).
- Safety: to obtain ISO 9001/2008 certification in the field of radiation oncology.
- International Society of Paediatric Oncology (SIOP) clinical studies for the treatment of medulloblastoma (PNET5), ependymoma (EP2), and Wilms (umbrella).

/ Summary

Our group is integrated within the Radiation Oncology Department of the Vall d'Hebron University Hospital (HUVH), and focuses on the multidisciplinary treatment of patients with malignant tumors. We also participate either as Principal Investigators or research collaborators in a number of pioneering clinical trials, translational research projects, as well as technology development programs.

The Department is equipped with 4 accelerators and 1 dual energy CT scan. The machines incorporate all the very latest technology and the implementation of these highly complex techniques requires additional expertise from our Service as well as specialized trainings for indications, administration procedures, quality control methods, as well as the incorporation of novel tools and approaches for the measurement of results.

Proton therapy is a type of external beam radiation therapy where a proton beam is used to irradiate a very well-defined volume. The main benefit of protons over photons is the reduction of irradiated tissue; a fact that is clinically manifested in the reduction of adverse effects. These effects can lead to significant neurocognitive deficits and the alterations in the growth of the child, and in adults, can lead to the loss of vital functions.

We are planning to install two proton therapy units and envisage that these will be operational for the treatment of patients in 2025.

Technology and techniques:

- Breathing control for the treatment of tumors that are located in moving body regions such as the lungs and liver. Therapy is synchronized with respiratory rhythm. This technique is especially indicated in stereotactic body radiotherapy (SBRT).
- Deep inspiration breath hold (DIBH) is a radiation therapy technique where patients take a deep breath during treatment. The patient is asked to take a deep breath and hold this breath while the radiation is delivered. Deep breathing ensures that the heart moves away from the chest and thus receives a lower dose.
- Real-time tumor-tracking radiotherapy (RTRT) is used in the hypofractionated treatment of prostate cancer. Markers are placed on the prostate and during therapy the system recognizes them. If the prostate moves (e.g. bladder or rectum), the technique can detect this and indicates the correction.
- Adaptive radiotherapy (ART) is used for the treatment of gynecological and bladder tumors, which move and can change position. A three-dimensional image is taken before therapy is administered and indicates where the organ requires therapy, with a treatment plan that best adapts to the position of the organ at that precise moment.
- Radiosurgery of small lesions is applied for the treatment of small brain tumors and/or metastases, and for some non-oncological conditions such as trigeminal neuralgia that no longer responds to standard therapy, and some Parkinsonism conditions. A very high dose is administered at a very small volume (5-10 mm in diameter), requiring extremely precise techniques.
- Stereotactic radiotherapy (SRT) for the treatment of refractory ventricular arrhythmias. To plan radiotherapy treatment, 4-dimensional CT is performed to control for and adjust the respiratory and cardiac movements, and the defibrillator keeps pacing at a heart rate of 100 beats per minute. Using the ADAS 3D tool, it is possible to combine previous MRI and cardiac CT images with the EAM as well as with the radiotherapy planning CT.

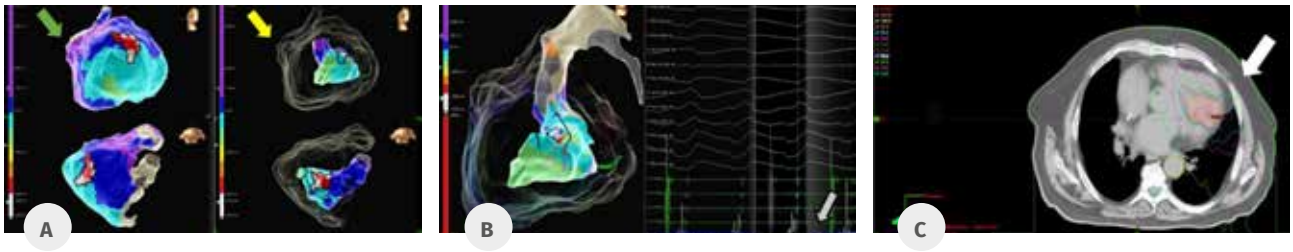


Figure: Electroanatomical activation mapping during ventricular tachycardia with Abbott EnSite Precision (Abbott, Minneapolis, MN). A: The left image (green arrow) shows epicardial mapping. The right image (yellow arrow) shows endocardial mapping. A significant part of the tachycardia cycle is not represented on any of the electroanatomical maps, suggesting an intramyocardial origin of the tachycardia. B: The left part of the image shows endocardial mapping. On the right, electrocardiogram showing ventricular tachycardia with right bundle brunch block morphology and a superior axis suggestive of an anterolateral left ventricle origin. Low-voltage mesodiastolic electrograms (gray arrow), suggestive of far-field signals, are found on catheter recordings during endocardial mapping, supporting an intramyocardial origin.C: Noninvasive cardiac radioablation treatment using a TrueBeam (Varian Medical Systems) radiotherapy plan showing the target volume (white arrow) and isodose lines.

/ PI paper pick 2022

Kishan AU, Steigler A, Denham JW, Zapatero A, Guerrero A, Joseph D, Maldonado X, Wong JK, Stish BJ, Dess RT, Pilar A, Reddy C, Wedde TB, Lilleby WA, Fiano R, Merrick GS, Stock RG, Demanes DJ, Moran BJ, Tran PT, Martin S, Martinez-Monge R, Krauss DJ, Abu-Isa EI, Pisansky TM, Choo CR, Song DY, Greco S, Deville C, McNutt T, DeWeese TL, Ross AE, Ciezki JP, Tilki D, Karnes RJ, Tosoian JJ, Nickols NG, Bhat P, Shabsovich D, Juarez JE, Jiang T, Ma TM, Xiang M, Philipson R, Chang A, Kupelian PA, Rettig MB, Feng FY, Berlin A, Tward JD, Davis BJ, Reiter RE, Steinberg ML, Elashoff D, Boutros PC, Horwitz EM, Tendulkar RD, Spratt DE, Romero T. Interplay Between Duration of Androgen Deprivation Therapy and External Beam Radiotherapy With or Without a Brachytherapy Boost for Optimal Treatment of High-risk Prostate Cancer: A Patient-Level Data Analysis of 3 Cohorts. *JAMA Oncol*. 2022 Mar 1;8(3):e216871.

Zapatero A, Guerrero A, Maldonado X, Álvarez A, San-Segundo CG, Rodríguez MÁC, Solé JM, Olivé AP, Casas F, Boladeras A, de Vidales CM, de la Torre MLV, Vara S, Sanz JL, Calvo FA. High-dose radiotherapy and risk-adapted androgen deprivation in localised prostate cancer (DART 01/05): 10-year results of a phase 3 randomised, controlled trial. *Lancet Oncol*. 2022 May;23(5):671-681.

Kishan AU, Sun Y, Hartman H, Pisansky TM, Bolla M, Neven A, Steigler A, Denham JW, Feng FY, Zapatero A, Armstrong JG, Nabid A, Carrier N, Souhami L, Dunne MT, Efstathiou JA, Sandler HM, Guerrero A, Joseph D, Maingon P, de Reijke TM, Maldonado X, Ma TM, Romero T, Wang X, Rettig MB, Reiter RE, Zaorsky NG, Steinberg ML, Nickols NG, Jia AY, Garcia JA, Spratt DE; MARCAP Consortium group. Androgen deprivation therapy use and duration with definitive radiotherapy for localised prostate cancer: an individual patient data meta-analysis. *Lancet Oncol*. 2022 Feb;23(2):304-316.

Biau J, Nutting C, Langendijk JA, Frédéric-Moreau T, Thariat J, Piram L, Bellini R, Saroul N, Pham Dang N, O'Sullivan B, Giralt J, Blanchard P, Bourhis J, Lapeyre M. Radiographic-anatomy, natural history and extension pathways of parotid and submandibular gland cancers. *Radiother Oncol*. 2022 May;170:48-54.

CLINICAL RESEARCH

Radiomics Group

Principal Investigator Raquel Perez-Lopez **Postdoctoral Fellows** Kinga Bernatowicz-Goma, Francesco Grussu, Caterina Tozzi **PhD Students** Alonso García, Athanasios Grigoriou, Marta Ligero, Olivia Prior, Anna Voronova **Students** Maria Balaguer, Ella Fokkinga, Bente Gielen, Nikolaos Staikoglou **Laboratory Technician** Carlos Macarro **Computer Scientists** Adrià Marcos, Camilo Monreal **Research Fellow** Luz María Atlagich

/ Strategic goals

- Develop and optimize pipelines for AI-models of data integration with particular interest in medical imaging and the integration process of explainable models.
- Provide expertise in engineering and bioinformatics for the development and clinical qualification of imaging biomarkers for precision medicine to improve outcomes for cancer patients.
- Use functional imaging for optimizing drug development in clinical trials.
- Integrate radiomics and genomics in translational studies to achieve a deeper understanding of tumor evolution and mechanisms of resistance to anti-cancer therapies.
- Develop and implement computational models for advanced image processing.

/ Highlights

- We participate in several EU-funded projects. Importantly, we now lead the imaging biomarker work for the Cancer Core Europe Consortium's DART project (page 185), aimed at optimizing clinical trial design. We also participate in the ODELIA Consortium (page 196), to establish decentralized platforms for AI-learning, collaborating in several tasks focused on deployment and clinical application.
- Our group has recently joined the TANGERINE Consortium (page 192), towards artificial-intelligence-based end-to-end prediction of cancer immunotherapy response.
- In 2022, Raquel Perez-Lopez was awarded with the best 2022 young physician scientist from the Institut Català de la Salut - ICS (Catalan Health Institute).
- The continued expansion of existing partnerships with other groups as well as new collaborative projects to increase the inclusion of imaging studies in translational research projects.

/ Summary

We are pleased to share that our Radiomics Group is expanding with the addition of new talents. Carlos Macarro joined our team in 2022, bringing with him extensive expertise in computer science, which has strengthened our data analysis capabilities. In addition, Caterina Tozzi has recently joined our group, having been granted a Juan de la Cierva Fellowship. She is exploring non-invasive imaging biomarkers to better characterize immunotherapy response in cancer patients with advanced disease. We are excited to see the innovative research that will result from her work. Finally, Maria Balaguer's MsC project has focused on developing an advanced tool that uses state-of-the-art neural networks to automatically segment liver tumors in medical imaging. This tool has the potential to revolutionize how we evaluate cancer patients' response to therapy by providing a more complete assessment of disease burden throughout treatment. We are delighted to welcome these new members of our team, and we look forward to the contributions they will make to our research.

Over the past year, we have fostered new collaborations with leading imaging research groups at Dresden (Wales, UK), the Champalimaud Foundation (Lisbon, Portugal), and the New York University School of Medicine (NY, USA). We have also forged new partnerships with other excellent research institutes including the German Cancer Research Center - Deutsches Krebsforschungszentrum, DKFZ (Heidelberg, Germany), and the Dresden University Hospital (Dresden, Germany).

We are thrilled to announce that two European projects, TANGERINE (page 192), and ODELIA (page 196), have recently received funding. These projects will provide a unique opportunity to establish valuable networks of collaborators with multidisciplinary and complementary expertise. This will accelerate the development and application of novel AI-tools in cancer research, ultimately leading to advancements in clinical practice. We are honored to be working alongside such esteemed partners, and we look forward to the groundbreaking discoveries that will come from these collaborations.

Continuing our collaboration with VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch led by Elena Garralda (page 138), and thanks to the support received through an AstraZeneca Partners of Choice Award, we are working on the PREDICT study to develop predictive biomarkers of response to immune checkpoint inhibitors by combining radiomics, genomics and the molecular characterization of the tumor microenvironment by multiplexed assays.

We also participate in the EU-funded Cancer Core Europe Consortium's DART project – Building Data Rich Clinical Trials (page 185), which is led by VHIO's Elena Garralda. Aimed at optimizing clinical trial design, we are providing support to achieve image protocol standardization and integration of novel imaging biomarkers.

We are also exploring new diffusion-weighted MRI protocols to evaluate biological-specific metrics regarding tissue cellularity and cell size in the liver. We envision that the metrics derived from this new assay will have important applications as non-invasive biomarkers in cancer. Francesco Grussu, a Post-Doctoral Fellow of our group, has been granted a *LaCaixa Retaining* post-doctoral fellowship this year to pursue this research.

Thanks to the support received from the Instituto de Salud Carlos III – ISCIII (Institute of Health Carlos III), and the Prostate Cancer Foundation's (PCF) Young Investigator Award, our group coordinates a multi-center prospective study of whole-body diffusion-weighted MRI as a response biomarker of bone metastasis in prostate cancer patients. This study was expanded to include breast cancer patients thanks to funding received from La Marató de TV3 (PreciMet study). We are pleased to announce that patient recruitment for our trial was completed by the final quarter of 2022. We are eagerly anticipating the announcement of results from this ambitious project.

We have established several interdisciplinary partnerships with various VHIO groups to work together on translational research projects. Our ethos of team science is key to optimizing imaging and accelerating translational research against cancer. Focused on applying imaging biomarkers and radiomics to cancer discovery, our efforts center on advancing precision imaging in personalized medicine to ultimately improve outcomes for cancer patients.

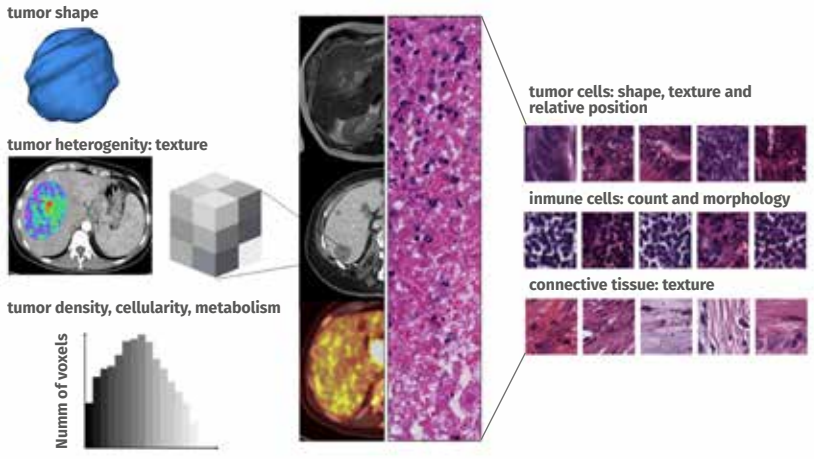


Figure: In radiology and pathology image data, neural networks can recognize a wide range of visual patterns which may be related to response to immunotherapy or targeted therapies in cancer patients. Integrating both imaging modalities provides a complementary view of the cancer phenotype.

/ PI paper pick 2022

Ramlee S, Hulse D, Bernatowicz K, Pérez-López R, Sala E, Aloj L. Radiomic Signatures Associated with CD8+ Tumour-Infiltrating Lymphocytes: A Systematic Review and Quality Assessment Study. *Cancers (Basel)*. 2022 Jul 27;14(15):3656.

Grussu F, Bernatowicz K, Casanova-Salas I, Castro N, Nuciforo P, Mateo J, Barba I, Perez-Lopez R. Diffusion MRI signal cumulants and hepatocyte microstructure at fixed diffusion time: Insights from simulations, 9.4T imaging, and histology. *Magn Reson Med*. 2022 Jul;88(1):365-379.

Elez E, Ros J, Fernández J, Villacampa G, Moreno-Cárdenas AB, Arenillas C, Bernatowicz K, Comas R, Li S, Kodack DP, Fasani R, Garcia A, Gonzalo-Ruiz J, Piris-Gimenez A, Nuciforo P, Kerr G, Intini R, Montagna A, Germani MM, Randon G, Vivancos A, Smits R, Graus D, Perez-Lopez R, Cremolini C, Lonardi S, Pietrantonio F, Dienstmann R, Tabernero J, Toledo RA. RNF43 mutations predict response to anti-BRAF/EGFR combinatory therapies in BRAFV600E metastatic colorectal cancer. *Nat Med*. 2022 Oct;28(10):2162-2170.

Pons-Escoda A, Garcia-Ruiz A, Naval-Baudin P, Grussu F, Fernandez JJS, Simo AC, Sarro NV, Fernandez-Coello A, Bruna J, Cos M, Perez-Lopez R, Majos C. Voxel-level analysis of normalized DSC-PWI time-intensity curves: a potential generalizable approach and its proof of concept in discriminating glioblastoma and metastasis. *Eur Radiol*. 2022 Jun;32(6):3705-3715.

Thoracic Tumors & Head and Neck Cancer Group

Principal Investigator Enriqueta Felip **Medical Oncologists and Clinical Fellows** Juan David Assaf, Irene Braña, Ana Callejo, Susana Cedres, Patricia Iranzo, Alexandre Martinez, Alejandro Navarro, Nuria Pardo, Augusto Valdivia **Associate Researcher** Ramon Amat **Post-Doctoral Fellows** Caterina Carbonell (wet-lab), Joan Frigola (bioinformatician) **Clinical Nurse Specialist** Mireia Soleda

/ Strategic goals

- Develop novel drug treatments and combinations through clinical trials.
- Determine the complexities of genetic profiling in cancer.
- Identify baseline biomarkers of response to immune checkpoint inhibitors (ICIs) and targeted therapies in thoracic malignancies (i.e. the value of tumor mutational burden, somatic copy number burden, and the tumor microenvironment).
- Establish the use of liquid biopsy to:
  - Monitor response to therapy in advanced non-small cell lung cancer (NSCLC).
  - Study relapse in early-stage NSCLC patients.
- The study of intratumor heterogeneity in matched primary and metastatic lesions (from cancer genome to tumor microenvironment).

/ Highlights

- We have further strengthened collaboration between our translational thoracic cancer genomics Unit and our clinical team. By integrating genomics, molecular biology and clinical data, we aim to advance insights into lung cancer physiology and response to therapy.
- Access to clinical trials using the most novel therapies
- Consolidation of our interdisciplinary group of oncologists, molecular biologists, a bioinformatician and a nurse.
- National and international collaborations of excellence.

/ Summary

VHIO's Thoracic Tumors & Head and Neck Cancer Group is dedicated to advancing cancer treatment and care for patients suffering from thoracic malignancies, including lung cancer, mesothelioma and thymic malignancies, and head and neck cancers. We focus on disease prevention, early detection and the more precise diagnosis and staging of disease toward improving clinical outcomes.

Our team strives to match currently available targeted therapies with specific molecular alterations identified in patients, unmask molecular mechanisms of acquired resistance, and optimize novel immunotherapy strategies.

For our patients with early stage thoracic malignancies we collaborate closely with a multidisciplinary team incorporating thoracic surgeons, radiation therapists, radiologists, pulmonologists, pathologists, and biologists. In so doing, we are potentiating several treatment approaches and modalities. Given that our patients can suffer from severe symptoms our efforts also focus on ameliorating clinical outcomes by working in close connectivity with professionals across other disciplines.

Precision medicine for the treatment of advanced lung cancer is no longer an ambition. It is a guiding principle. We establish molecular determinants of disease in individual tumors and circulating cell-free DNA (cfDNA) by liquid biopsy to more effectively tailor therapies to the specificities of each patient's individual disease.

For patients with head and neck tumors we work alongside expert surgeons, radiotherapists, radiologists, pathologists, and nutritionists, and also lead a clinical trial program to assess novel immunotherapeutics and targeted agents in this particular setting.

Immune-based strategies have a role in the treatment algorithm for the management of non-small cell lung cancer; a number of protocols are now ongoing at our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch led by Elena Garralda (page 138). Additionally, we contribute to VHIO's early clinical drug development efforts. We also manage other less common thoracic malignancies including head and neck cancer, small cell lung cancer, mesothelioma, thymoma and neuroendocrine tumors.

/ PI paper pick 2022

Solomon BJ, Bauer TM, Mok TSK, Liu G, Mazieres J, de Marinis F, Goto Y, Kim DW, Wu YL, Jassem J, López FL, Soo RA, Shaw AT, Polli A, Messina R, Iadeluca L, Toffalorio F, Felip E. Efficacy and safety of first-line lorlatinib versus crizotinib in patients with advanced, ALK-positive non-small-cell lung cancer: updated analysis of data from the phase 3, randomised, open-label CROWN study. *Lancet Respir Med*. 2022 Dec 16:S2213-2600(22)00437-4.

Frigola J, Carbonell C, Irazno P, Pardo N, Callejo A, Cedres S, Martinez-Marti A, Navarro A, Soleda M, Jimenez J, Hernandez-Losa J, Vivancos A, Felip E, Amat R. High levels of chromosomal aberrations negatively associate with benefit to checkpoint inhibition in NSCLC. *J Immunother Cancer*. 2022 Apr;10(4):e004197.

Forde PM, Spicer J, Lu S, Provencio M, Mitsudomi T, Awad MM, Felip E, Broderick SR, Brahmer JR, Swanson SJ, Kerr K, Wang C, Ciuleanu TE, Saylors GB, Tanaka F, Ito H, Chen KN, Liberman M, Vokes EE, Taube JM, Dorange C, Cai J, Fiore J, Jarkowski A, Balli D, Sausen M, Pandya D, Calvet CY, Girard N; CheckMate 816 Investigators. Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. *N Engl J Med*. 2022 May 26;386(21):1973-1985.

Li BT, Smit EF, Goto Y, Nakagawa K, Udagawa H, Mazières J, Nagasaka M, Bazhenova L, Saltos AN, Felip E, Pacheco JM, Pérol M, Paz-Ares L, Saxena K, Shiga R, Cheng Y, Acharyya S, Vitazka P, Shahidi J, Planchard D, Jänne PA; DESTINY-Lung01 Trial Investigators. Trastuzumab Deruxtecan in *HER2*-Mutant Non-Small-Cell Lung Cancer. *N Engl J Med*. 2022 Jan 20;386(3):241-251.

mobile version

scan to visit

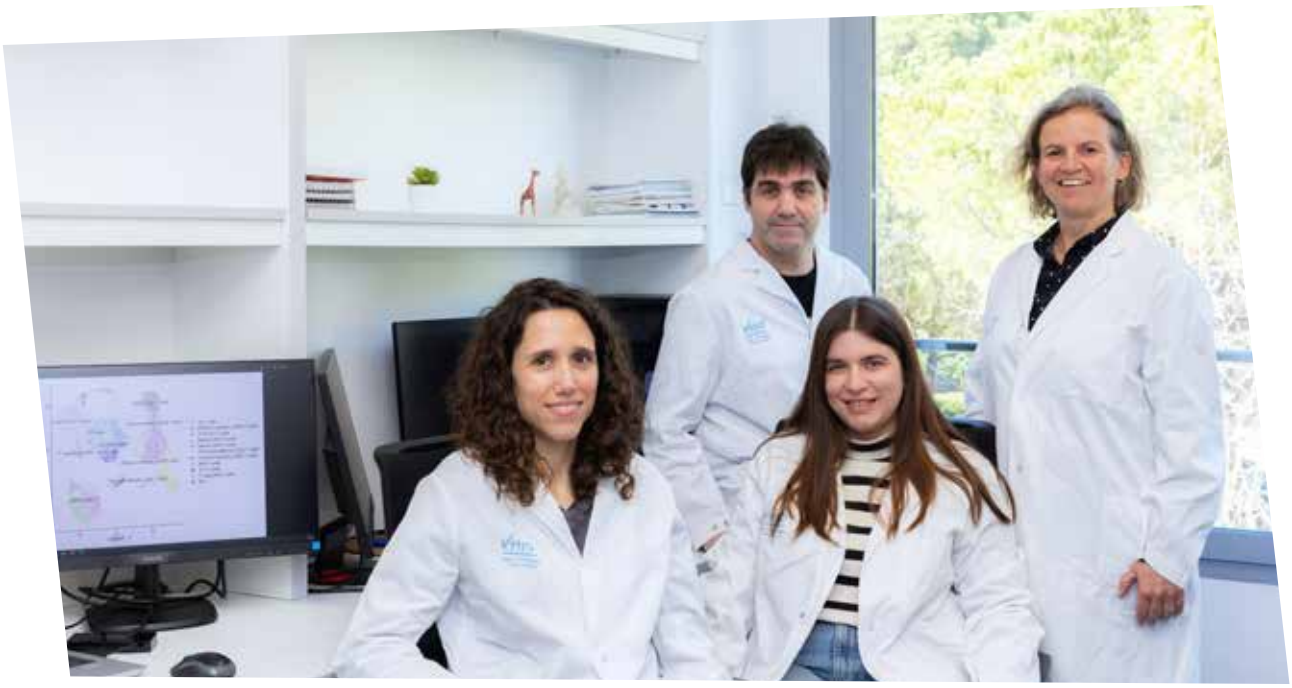
VALL D'HEBRON INSTITUTE OF ONCOLOGY (VHIO)
SCIENTIFIC REPORT 2022

Core Technologies

CORE TECHNOLOGIES

Bioinformatics Unit

Unit Head Lara Nonell **Bioinformaticians** Irene Agustí Barea, Mercè Alemany Chavarria, Alba Mas Malavila, Pau Marc Muñoz Torres



/ Strategic goals

- Set up an appropriate and scalable computational infrastructure for bioinformatics analyses.
- The implementation of state-of-the-art pipelines and tools for the analysis and visualization of different omics datasets, including publicly available datasets.
- Application of advanced bioinformatics techniques for the identification and validation of biomarkers for cancer diagnostics.
- Generation of computational models to integrate different types of omics data that foster personalized medicine using classical or cutting-edge machine learning techniques.
- Establish collaborative research with VHIO groups to promote the use of advanced computational methods for data analysis, visualization, and interpretation.
- Conform a group of skilled bioinformaticians who can support problem-solving in many omics data analysis scenarios.
- Coordinate an internal bioinformatics network aimed at sharing knowledge and optimizing resources. As an example, we organize a monthly Bioinformatics Journal Club to discuss a hot topic in the field.

/ Highlights

- The setting up of VHIO's computational cluster which operates with Slurm and Docker for task management. In addition, Nextflow facilitates the automation of bioinformatic pipelines.
- Recruitment of expert bioinformaticians to support VHIO's pioneering cancer research.
- Establishment of standard pipelines for the processing and analysis of omics datasets with special consideration in single cell and spatial transcriptomics data analysis.
- Collaboration with several groups for the analysis of omics data sets, ranging from raw sequencing data alignment to the development of functions for the appropriate visualization of assessment results. During 2022 we have collaborated in the data analysis of 28 translational projects of 12 research groups at VHIO.
- Our group provides guidance to several investigators for their computational procedures.
- We participate in various consortia, taskforces and institutional projects.
- This year, we have organized two courses for VHIO's personnel: *Exploring public cancer data through web resources* and *Functional analysis of omics data using public tools*. We are planning new editions of both in 2023.
- We have represented VHIO at the ECCB2022 (European Conference on Computational Biology) with two posters entitled *Macrophage subpopulations identification using single-cell RNA sequencing data* and *Implementing best practices for setting up a bioinformatics core facility*.

/ Summary

VHIO's Bioinformatics Unit (VHIOinformatics) provides research groups with cutting-edge computational resources for the analysis of cancer-related omics data. We support VHIO investigators through the implementation of state-of-the-art bioinformatic pipelines to process multi-omics datasets.

Collaborating with researchers across multiple projects, we participate in several phases of investigation from conception or experimental design through to bioinformatic data analysis and final publication, with particular focus on visualization and functional interpretation. In 2022 we collaborated with twelve VHIO research groups in the analysis of omics data. These are mainly RNA-seq and genomics (targeted or WES) data sets but we have also started with the analysis of single cell RNA-seq data, including immune profiling. The latter has been performed in collaboration with Joaquin Arribas (PI, VHIO's Growth Factors Group, page 74), and Alena Gros (PI, VHIO's Tumor Immunology and Immunotherapy Group, page 86). In addition, we have reassessed several public data sets to gather insights into cancer processes.

Our computational procedures are based on open-source software developed in a safe and reproducible environment. In 2022 we set up a cluster infrastructure for our Unit, to also to be used by other bioinformaticians in-house. Thanks to the Excelencia Severo Ochoa accreditation that VHIO received in 2021 (page 129) as a Severo Ochoa Center of Excellence (2022-2026), we envisage continued growth of this infrastructure in 2023.

This Unit is a member of the Spanish translational bioinformatics network, TransBioNet, which is coordinated by the Spanish National Bioinformatics Institute (INB) and works in conjunction with the European Life Science Infrastructure for Biological Information (ELIXIR). We also represent VHIO in various consortia and taskforces.

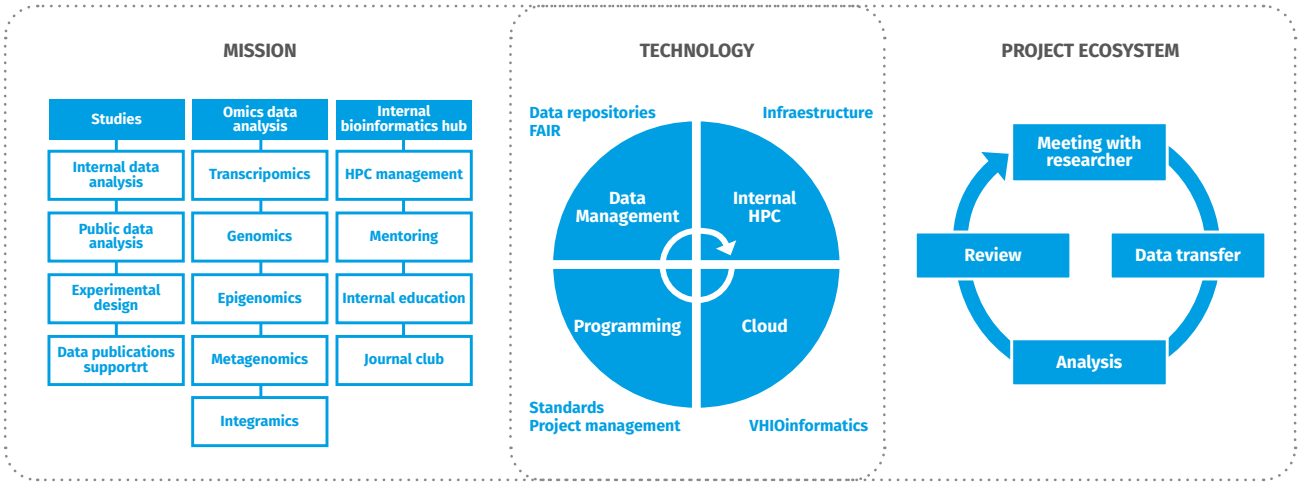


Figure: A summary of the VHIOinformatics Unit activity, with a project ecosystem, activities included in the Unit's mission and technology in use.

/ PI paper pick 2022

Martínez-Sabadell A, Morancho B, Rius Ruiz I, Román Alonso M, Ovejero Romero P, Escorihuela M, Chicote I, Palmer HG, Nonell L, Alemany-Chavarria M, Klein C, Bacac M, Arribas J, Arenas EJ. The target antigen determines the mechanism of acquired resistance to T cell-based therapies. *Cell Rep*. 2022 Oct 18;41(3):111430.

Cancer Genomics Group

Principal Investigator Ana Vivancos **Laboratory Manager** Judit Matito **Project Manager** Ester Castillo **Postdoctoral Fellow** Alberto González **Specialized Technicians** Vanessa Bach, Giuseppe Buono, Cecilia García, Deborah G. Lo Giacco, Agatha Martín **Predoctoral Fellow** Paula Romero **Bioinformaticians** Francisco Fuster, Marina Gómez, Maria Vila **Research Support Technician** Inmaculada Martos

/ Strategic goals

- Develop and implement improved strategies for routine patient prescreening with a large pan-cancer panel in a setting of excellence.
- Develop and implement cutting-edge tests for liquid biopsy analysis including the new VHIO360 panel (technology transfer from Guardant Health).
- Provide cutting-edge applications in cancer genomics through the use of novel technologies and protocol development.
- Prioritize translational projects and partnerships that further strengthen VHIO's renowned excellence in oncology.

/ Highlights

- VHIO is a founding partner of the Cancer Core Europe Consortium – CCE (page 185), alongside the Gustave Roussy Cancer Campus Grand Paris (Villejuif, France), Cambridge Cancer Centre (Cambridge, UK), Karolinska Institute (Stockholm, Sweden), Netherlands Cancer Institute – NKI (Amsterdam, The Netherlands), National Center for Tumor Diseases–DKFZ- NCT (Heidelberg, Germany), and the National Cancer Institute of Milan (INT). Our group serves as co-leader of CCE's Genomics Task Force and is responsible for the alignment of genomic testing across all member institutions.
- We have implemented and validated our VHIO360 test for liquid biopsy; technology transfer of the Guardant 360® DX test from Guardant Health (page 11).
- In liquid biopsy, we have developed our custom NGS test with Unique Molecular Identifiers (UMIs) combined with the Copy Number Alteration analysis using Shallow Whole Genome Sequencing (sWGS). This will be our first disease tracking test in the clinical setting.
- It is thanks to our institutional Advanced Molecular Diagnostics Program – DIAMAV (our molecular prescreening efforts, supported by the Fundación FERO – page 126), that VHIO is one of the few centers in Europe to run such a comprehensive program. Molecular profiling, performed in over 1100 patients each year as candidates for enrollment in our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138) early phase clinical trials, enables us to more precisely match an increasing number of individual patients to our studies.

/ Summary

VHIO's Cancer Genomics Group serves as a Core Technology laboratory. We are also dedicated to translational research as well as the development of novel genomic tests.

Our group provides cutting-edge applications in cancer genomics through state-of-the-art technologies and we develop new, fully validated tests that are used in the clinical research setting. Our lab is equipped with an n-Counter (Nanostring) platform, two digital PCR platforms (BEAMing Sysmex and ddPCR, BIO-RAD) and five NextGen Sequencers; MiSeq, NextSeq, HiSeq2500 and NovaSeq6000 from Illumina, and a MinION from Oxford Nanopore Technologies.

Our lab completed the technology transfer of the Food and Drug Administration (FDA)-approved Guardant360® CDx liquid biopsy test for comprehensive genomic profiling. With this test, VHIO360 (page 11), our Institute is the first cancer research center in Europe to have a laboratory equipped with this cutting-edge platform. Aimed at overcoming the limitations and challenges of tissue biopsies, this technology provides complete genomic results in all solid tumors from a simple blood draw in seven days.

Molecular Prescreening at VHIO (page 146) is co-led by our group's Principal Investigator, Ana Vivancos, alongside Paolo Nuciforo, Elena Garralda, and Rodrigo Dienstmann, Principal Investigators of our Molecular Oncology, Early Clinical Drug Development, and Oncology Data Science – OdysSey Groups, respectively (pages 118, 92, 104). Supported through our institutional Advanced Molecular Diagnostics Program (DIAMAV), powered by the Fundación FERO (page 126), we perform molecular profiling in over 1100 patients each year as potential candidates for enrollment in our phase I clinical trials led by VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138), directed by Elena Garralda. Patients' suitability for inclusion in any given clinical study is assessed based on their respective genomic profile and pathologic features.

We have developed and routinely implemented several tests for this program. Two are based on NGS: an Amplicon-seq approach to sequence 67 genes as well as a 450-gene capture panel (Illumina). We use nCounter (Nanostring) for our RNA- based gene fusion panel, with the capacity of detecting over 100 recurrent gene fusions (also enabling us to assess gene expression patterns in tumors). As a reflection of our dedication to excellence and quality in the services that we provide, we have attained ISO 15189 flexible accreditation for both our Amplicon-seq testing and large 450-gene capture panel.

Research activities focus on developing novel multiplexed tests that are optimized to FFPE-derived nucleic acids. Once developed, they are validated and used in both clinical and translational research. We are also involved in several translational research projects including the identification of mechanisms of resistance to targeted therapies, as well as predictive biomarkers for immunotherapies. Based on Nanostring and RNA-seq technologies for the detection of an immune signature, we use the VIGex tool. Our group is particularly interested in liquid biopsy and RNA-based analysis of tumors for microenvironment profiling.

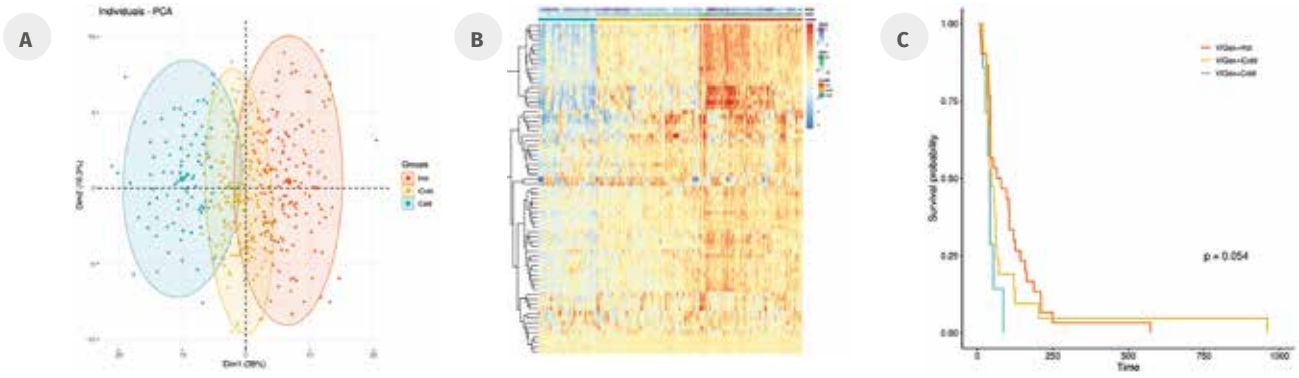


Figure: VIGex classification of 398 metastatic cancer samples according to nCounter (NanoString) gene expression (69 immuno-related genes). Gene expression values were normalized to the geometric mean expression of 19 housekeeping genes, then log2-transformed and centered around mean. **A)** PCA showing the 3 clusters identified with PAM (partioning around medoids) method (Hot, iCold, Cold). **B)** Heatmap showing relative gene expression and PCA values of the 69 immuno-related genes with Hot, iCold and Cold groups. **C)** Kaplan-Meier plot showing time to progressionofthe Hot, iCold and Cold groups of an independent cohort of 58 samples.

/ PI paper pick 2022

Élez E, Mulet-Margalef N, Sanso M, Ruiz-Pace F, Mancuso FM, Comas R, Ros J, Argilés G, Martini G, Sanz-Garcia E, Baraibar I, Salvà F, Nogueridо A, Cuadra-Urteaga JL, Fasani R, Garcia A, Jimenez J, Aguilar S, Landolfi S, Hernández-Losa J, Braña I, Nuciforo P, Dienstmann R, Tabernero J, Salazar R, Vivancos A. A Comprehensive Biomarker Analysis of Microsatellite Unstable/Mismatch Repair Deficient Colorectal Cancer Cohort Treated with Immunotherapy. *Int J Mol Sci*. 2022 Dec 21;24(1):118

Vivancos A, Tabernero J. Circulating tumor DNA as a novel prognostic indicator. *Nat Med*. 2022 Nov;28(11):2255-2256.

Boix O, Martinez M, Vidal S, Giménez-Alejandre M, Palenzuela L, Lorenzo-Sanz L, Quevedo L, Moscoso O, Ruiz-Orera J, Ximénez-Embún P, Ciriaco N, Nuciforo P, Stephan-Otto Attolini C, Albà MM, Muñoz J, Tian TV, Varela I, Vivancos A, Ramón Y Cajal S, Muñoz P, Rivas C, Abad M. pTINCR microprotein promotes epithelial differentiation and suppresses tumor growth through CDC42 SUMOylation and activation. *Nat Commun*. 2022 Nov 11;13(1):6840.

Garcia-Casado Z, Oaknin A, Mendiola M, Alkorta-Aranburu G, Antunez-Lopez JR, Moreno-Bueno G, Palacios J, Yubero A, Marquez R, Gallego A, Sanchez-Heras AB, Lopez-Guerrero JA, Perez-Segura C, Barretina-Ginesta P, Alarcon J, Gaba L, Marquez A, Matito J, Cueva J, Palacio I, Iglesias M, Arcusa A, Sanchez-Lorenzo L, Guerra-Alia E, Romero I, Vivancos A. Laboratory Cross-Comparison and Ring Test Trial for Tumor BRCA Testing in a Multicenter Epithelial Ovarian Cancer Series: The BORNEO GEICO 60-0 Study. *J Pers Med*. 2022 Nov 4;12(11):1842.

CORE TECHNOLOGIES

Molecular Oncology Group

Principal Investigator Paolo Nuciforo **Attending Physicians** Roberta Fasani, Siarhei Mauchanski, Sara Simonetti **Laboratory Supervisor** Jose Antonio Jiménez **Laboratory Assistant** Mª Ángeles Diaz **Postdoctoral Fellow** Francisca Gallego **PhD Students** Stefania Napoli, Garazi Serna **Technicians** Lidia Alonso, Antonella Cogoni, Luis Garcia, Margarita Gonzalez, Xavier Guardia, Paola Martinez, Gertrudis Sánchez, Lidia Sánchez, César Javier Sevillano

/ Strategic goals

As core facility:

- Application of molecular pathology strategies to support early clinical drug development programs.
- Better define target epidemiology to render treatment strategies more precise.
- Act as central and local academic laboratory in clinical trials.
- Serve as core facility for VHIO research programs.

As independent PI:

- Contribute significantly to the field of cancer microbiome by interrogating the cancer-associated microbiome in a search for diagnostic, prognostic and/or predictive biomarkers in colorectal cancer as well as expand our findings to other cancer types.
- Explore how tumor heterogeneity impacts on the response to anti-HER2 treatment in breast cancer by in situ single cell analysis methodology developed in the lab.
- Investigate the value of immune contexture analyses of tumor microenvironment as a biomarker of response to immunotherapy in different cancer types.
- Explore the utility of artificial intelligence in pathology, with a specific application to increase reproducibility in tumor cell content quantification and identification of image patterns from H&E stained slides that can be useful for patient stratification.

/ Highlights

- Molecular prescreening of >1000 patients for inclusion in early development clinical trials.
- Supporting more than 70% of all clinical studies open at our Institute.
- Performed more than 30K tests to support preclinical and translational research programs.
- Collecting and analyzing samples from >1000 patients enrolled in cancer microbiome translational research projects.

/ Summary

VHIO's Molecular Oncology Group applies state-of-the-art tissue-based technologies to basic, translational, and clinical research with a clear focus on developing and validating novel tumor biomarkers for precision medicine in oncology.

Together with VHIO's Cancer Genomics Group, page 116 (PI Ana Vivancos), Oncology Data Science - ODysSey Group, page 104 (PI Rodrigo Dienstmann), and our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, page 138 (directed by Elena Garralda), we participate in our in-house Molecular Prescreening Program (page 146). We molecularly profile over 1,100 patients each year as candidates for enrolment in early phase clinical trials at the UITM – CaixaResearch.

Our group also serves as one of VHIO's Core Technology Platforms and our laboratory is therefore key to VHIO's translational research lines and programs. We actively participate in all projects involving the use of human tissue collected from patients. These include biomarker analyses for patient stratification and inclusion in clinical trials, digital pathology, tissue banking, and the development of primary patient-derived xenograft (PDX) models. Our contributions are reflected by several high-impact factor collaborative papers published throughout 2022.

Additionally, we continue to work independently and in partnership to decipher the impact of the microbiome in colorectal cancer development and progression. In particular, we are investigating the tumor-associated microbiota at a spatial resolution by developing bacteria-specific probes within the OPTIMISTICC Grand Challenge project (page 186) funded by Cancer Research UK (CRUK).

We are also leading the FUSOMAP, a 3-year project funded by the Mutua Madrileña Foundation and Instituto de Salud Carlos III - ISCIII (Carlos III Health Institute), to develop microbiota-based diagnostic and prognostic models by mapping intratumoral Fusobacterium and associated gut microbiota in early-stage colorectal cancer. Lastly, we are studying the consequences of Sars-Cov-2 infection on the microbiome of cancer patients and how it impacts on clinical outcome (project funded by La Marató TV3).

As a Core Facility, we have provided support for 394 clinical studies conducted at Vall d'Hebron, representing approximately 70% of all currently open trials at our Institute. Our involvement in these trials includes the coordination of sample collection, storage and shipment, developing and running multiple assays for real-time patient inclusion, as well as pharmacodynamic monitoring and dose finding.

In 2022, we performed approximately 3000 molecular determinations on samples for patient inclusion in clinical trials, and over 30,000 tests to support basic and translation research. We have also served as the central laboratory of choice for several international studies, and successfully maintained the prestigious ISO15189 accreditation that endorses quality and competence.

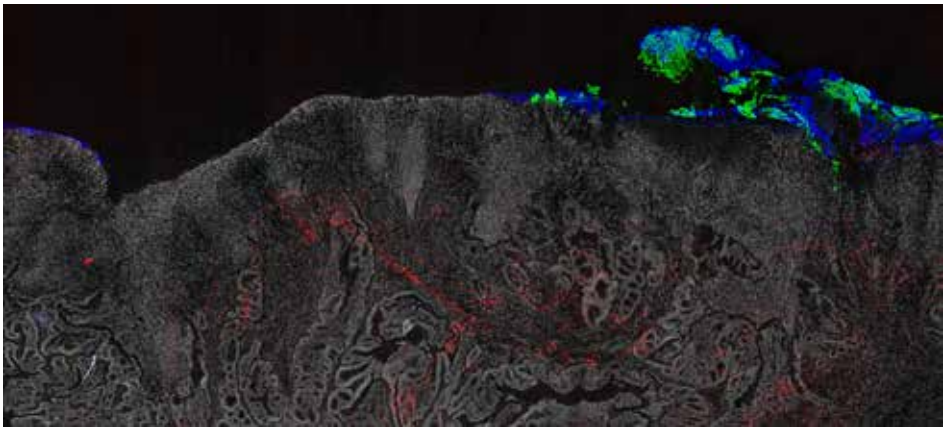


Figure: Fusobacterium (green), propionibacterium (blue) and t-cells (red) in a colorectal cancer tumor (grey). Bacterial stainings are obtained with RNA in situ hybridization (Rnascope, ACD) and t-cells with next generation immunohistoquemistry (NGI) methodologies. Images are virtually aligned and virtual colors are attributed for virtual multiplexed image generation.

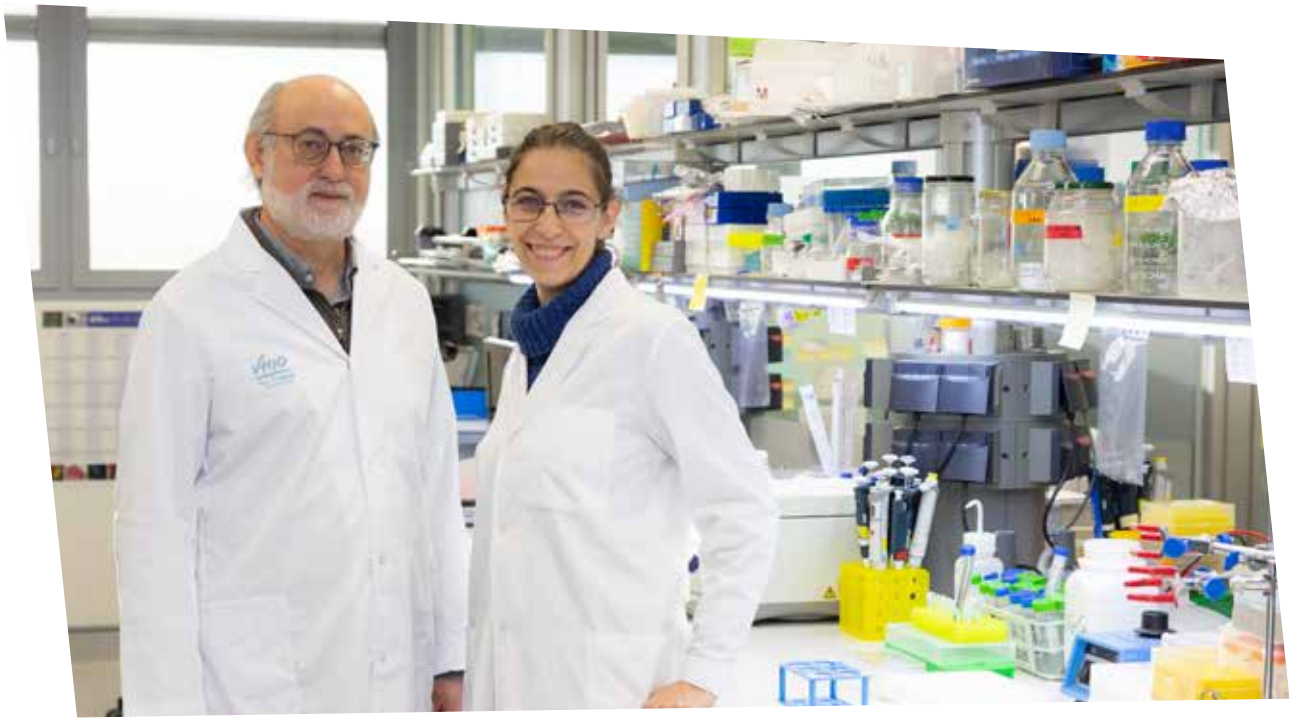
/ PI paper pick 2022

Nuciforo P, Townend J, Piccart MJ, Fielding S, Gkolfi P, El-Abed S, de Azambuja E, Werutsky G, Bliss J, Moebus V, Colleoni M, Aspitia AM, Gomez H, Gombos A, Coccia-Portugal MA, Tseng LM, Kunz G, Lerzo G, Sohn J, Semiglazov V, Saura C, Kroep J, Ferro A, Cameron D, Gelber R, Huober J, Di Cosimo S. Ten-year survival of neoadjuvant dual HER2 blockade in patients with HER2-positive breast cancer. *Eur J Cancer*. 2023 Mar;181:92-101. Epub 2022 Dec 27.

CORE TECHNOLOGIES

Proteomics Group

Principal Investigator Francesc Canals **Technician** Luna Martín



/ Strategic goals

- As a Core Facility, we provide services in proteomic techniques to other research groups.
- We perform proteomic screening for novel biomarkers to help develop cancer therapeutics.
- Development of mass spectrometry-based assays for the analysis of biomarkers in clinical samples.

/ Highlights

- The provision of proteomic services to VHIO groups, oncology professionals at the Vall d'Hebron University Hospital (HUVH), and members of the Vall d'Hebron Research Institute (VHIR).
- Application of proteomic and phosphoproteomic screening to the characterization of CRC PDX models.
- The setting up of mass spectrometry based analytical methods for the monitoring of specific drugs in plasma and tumor tissue to assess preliminary pharmacokinetics in preclinical mouse models.
- Characterization of specific protein interactomes.
- Proteome-wide thermal shift analysis to characterize protein-drug interactions.

/ Summary

Our group serves as a Core Technology Platform. We provide state-of-the-art proteomic methodologies to VHIO investigators and also incorporate new developments within the field to offer the very latest approaches and technologies.

We employ mass spectrometry-based proteomic strategies for the screening and validation of biomarkers for cancer diagnostics, precision therapy and the closer monitoring of disease.

One of our research lines focuses on the development of mass spectrometry-based assays for the analysis of biomarkers in clinical samples. We have developed immune-MS based assays with improved selectivity and accuracy in the analysis of low abundance biomarker proteins in plasma or CSF samples.

We have applied proteomic analysis methods to the proteomic and phosphoproteomic characterization of patient-derived xenograft (PDX) models of colorectal cancer (CRC). PDXs constitute an ideal platform for the molecular characterization of CRC at the proteomic level. Complementing genomic classification, we are exploring the suitability of this characterization as a tool for tumor subtype classification.

We have set up methodologies for the mass spectrometry analysis of drugs in biological samples to study their pharmacokinetics and bioavailability in mouse models. In addition, we have applied proteomic analysis to the characterization of protein-protein interactors, and protein-drug interactions.

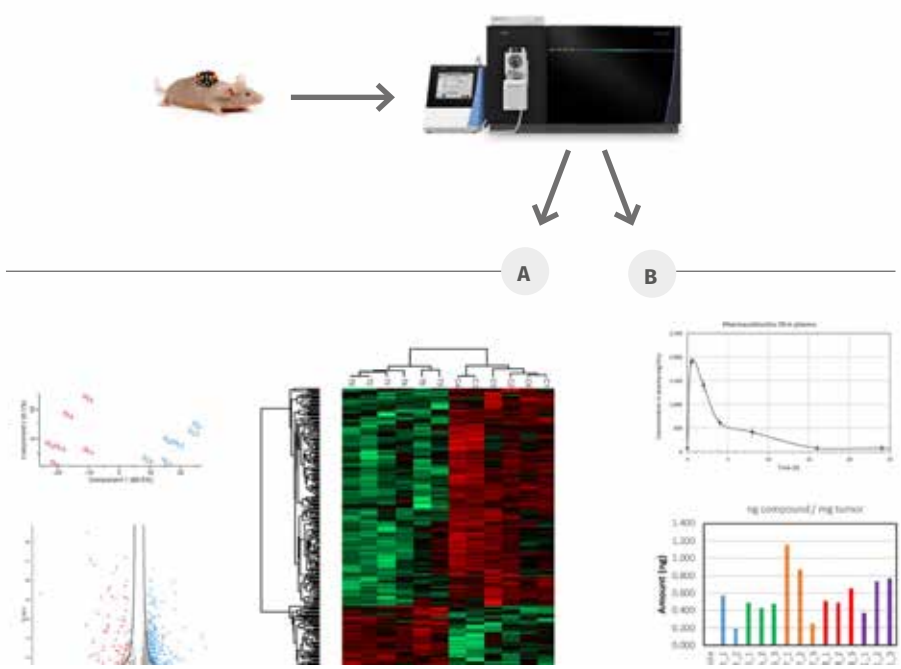


Figure: Proteomics in preclinical cancer research. Mass spectrometry-based proteomics constitutes a powerful tool for the study of different aspects of preclinical tumor models. **A)** Profiling of total proteome and phosphoproteome of PDX tumor models to explore pathways involved in therapeutic response. **B)** monitoring small drugs in plasma or tissue of model animals for pharmacokinetic characterization and tumor availability.

/ PI paper pick 2022

McGrail K, Granado-Martínez P, Esteve-Puig R, García-Ortega S, Ding Y, Sánchez-Redondo S, Ferrer B, Hernandez-Losa J, Canals F, Manzano A, Navarro-Sabaté A, Bartrons R, Yanes O, Pérez-Alea M, Muñoz-Couselo E, Garcia-Patos V, Recio JA. BRAF activation by metabolic stress promotes glycolysis sensitizing NRASQ61-mutated melanomas to targeted therapy. *Nat Commun*. 2022 Nov 19;13(1):7113.

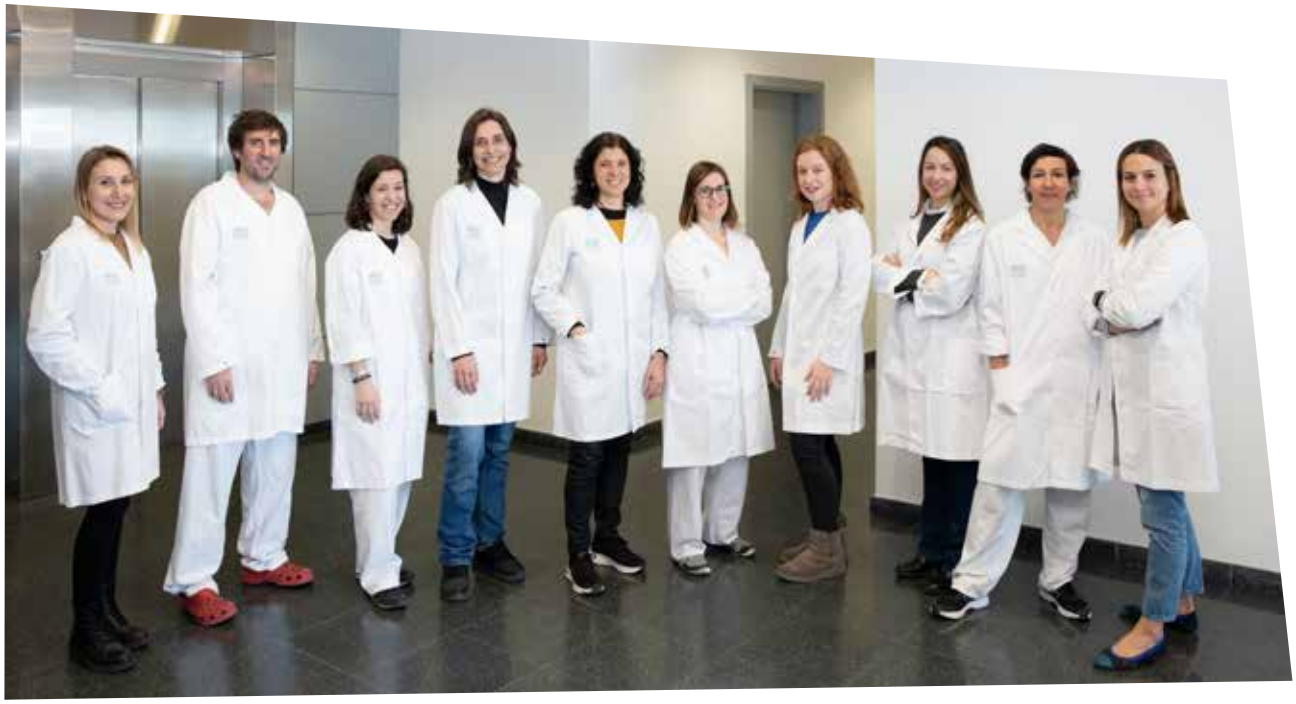
Juliachs M, Pujals M, Bellio C, Meo-Evoli N, Duran JM, Zamora E, Parés M, Suñol A, Méndez O, Sánchez-Pla A, Canals F, Saura C, Villanueva J. Circulating SOD2 Is a Candidate Response Biomarker for Neoadjuvant Therapy in Breast Cancer. *Cancers (Basel)*. 2022 Aug 10;14(16):3858.

Bellio C, Emperador M, Castellano P, Gris-Oliver A, Canals F, Sánchez-Pla A, Zamora E, Arribas J, Saura C, Serra V, Tabernero J, Littlefield BA, Villanueva J. GDF15 Is an Eribulin Response Biomarker also Required for Survival of DTP Breast Cancer Cells. *Cancers (Basel)*. 2022 May 23;14(10):2562.

Colomé N, Abian J, Aloria K, Arizmendi JM, Barceló-Batllori S, Braga-Lagache S, Burlet-Schiltz O, Carrascal M, Casal JI, Chicano-Gálvez E, Chiva C, Clemente LF, Elortza F, Estanyol JM, Fernandez-Irigoyen J, Fernández-Puente P, Fidalgo MJ, Froment C, Fuentes M, Fuentes-Almagro C, Gay M, Hainard A, Heller M, Hernández ML, Ibarrola N, Iloro I, Kieselbach T, Lario A, Locard-Paulet M, Marina-Ramírez A, Martín L, Morato-López E, Muñoz J, Navajas R, Odena MA, Odriozola L, de Oliveira E, Paradela A, Pasquarello C, de Los Rios V, Ruiz-Romero C, Sabidó E, Sánchez Del Pino M, Sancho J, Santamaría E, Schaeffer-Reiss C, Schneider J, de la Torre C, Valero ML, Vilaseca M, Wu S, Wu L, Ximénez de Embún P, Canals F, Corrales FJ; ProteoRed-ISCIII; EuPA. Multi-laboratory experiment PME11 for the standardization of phosphoproteome analysis. *J Proteomics*. 2022 Jan 16;251:104409.

VHIOTECA

Unit Head Susana Aguilar **Clinical Research Oncology Nurses** Ariadna García, Marta Sanz, Alex Sierra, Mireia Soleda, Anna Suñol, Anna Vázquez **Sample Managers** Inés Castro, Gemma Pruna **Research Support Technician** Laura Boleda, Lidia Fuertes.



/ Strategic goals

Consolidation of existing circuits:

- Provide support to researchers in the extraction, registration and storage of samples (mostly plasma) and database maintenance.
- Standardize protocols and establish Standard Operating Procedures (SOPs).
- Maintain optimal registration and archiving of the informed consent of the patients.
- Creation and consolidation of new circuits: establish new circuits for the collection of different plasma and tumor samples (e.g. feces, saliva, breast milk, etc.), sample and patients' data, and tailor them accordingly to meet the requirements and specificities of research projects.
- Research support: collaborate with different teams of clinical and preclinical researchers to help set up new projects and collaborations using existing or new samples.

/ Highlights

Active participation in the following international projects:

- EUCANCan (page 186): a federated network of aligned and interoperable infrastructures for the analysis, management and homogeneous sharing of genomic oncology data for Personalized Medicine.
- Molecular Tumor Board (MTB) of the Cancer Core Europe (CCE) Consortium's Baskets of Baskets (BoB, page 185).
- Genomics Evidence Neoplasia Information Exchange (GENIE) Project of the American Association for Cancer Research (AACR), page 24.

/ Summary

Our VHIOTECA Unit was created in 2021 to support researchers for the obtention, registration and preservation of biological samples other than tumoral tissue (plasma, feces, saliva, etc.) from cancer patients, and facilitate the use of these samples in research projects.

The use of liquid biopsy testing in cancer patients for the identification of new biomarkers of response and resistance to therapy, coupled with its incorporation in clinical research projects requiring plasma, have led to a significant increase in the extraction of blood samples from cancer patients.

This activity requires a suitable structure, dynamization of circuits and the optimization of resources. For this reason, our main objectives are to consolidate existing circuits and processes so that they are consistent and reliable, and to ensure the optimal use of samples in the best possible conditions. We are also committed to supporting VHIO researchers in setting up new projects and collaborations that require the use of these types of samples.

Another area of growing interest of research in clinical oncology is the study of the microbiome during tumor development and progression, especially in colorectal cancer. These studies require the collection and genomic and molecular analysis of stool samples as well as the completion of questionnaires for subsequent epidemiological studies. To support our researchers, we aim to create a new sample and data collection circuit that facilitates the development and execution of projects. In 2022, in collaboration with Paolo Nuciforo, PI of VHIO's Molecular Oncology group, we have created a new sample and data collections circuit in which one of the research support technician from VHIOTECA is exclusively dedicated to carrying out all the tasks of the process. From this first year of the circuit, we have collected and process 205 samples from 120 patients.

Our team comprises clinical and translational research oncology nurses specialized in different tumor types, technical staff for sample processing and registration (sample managers), and technical support staff for sample logistics and management, database creation and maintenance.

VHIO's Molecular Prescreening Program

Since 2017 our Head of Unit, Susana Aguilar, has coordinated molecular prescreening at VHIO (page 146), and now collaborates closely with the program's Research Support Technician, Jenifer González. This program is co-led by Ana Vivancos, Elena Garralda, Paolo Nuciforo, and Rodrigo Dienstmann, PIs of our Cancer Genomics, Early Clinical Drug Development, Molecular Oncology, and Oncology Data Science (ODysSey) Groups, respectively.

mobile version

scan to visit

VALL D'HEBRON INSTITUTE OF ONCOLOGY (VHIO)
SCIENTIFIC REPORT 2022

Institutional Programs & Task Forces

Institutional Programs

FERO Foundation: driving advanced molecular diagnostics against cancer

Our Molecular Prescreening Program (page 146) is powered by one of our Institutional Supporters and Patrons, the Fundación FERO (page 19). FERO's Institutional Advanced Molecular Diagnostics Program (DIAMAV) catalyzes precision medicine at VHIO. Over the last decade, this program has provided access to advanced molecular diagnostics to more than 8,000 cancer patients, and is critical in matching targeted therapeutic approaches with hundreds of clinical trial opportunities.

This pioneering program, also counting on the support and expertise provided through our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138), is co-led by VHIO's Ana Vivancos, Paolo Nuciforo, Elena Garralda, and Rodrigo Dienstmann, Principal Investigators of our Cancer Genomics, Molecular Oncology, Early Clinical Drug Development, and Oncology Data Science (ODysSey) Groups, respectively, and coordinated by Susana Aguilar.

Our expert team focuses on the clinical implementation of advanced molecular diagnostics to optimize the selection of therapies for patients being considered for enrolment in clinical trials, as well as continued medical education on emerging cancer biomarkers for precision cancer therapy. By advancing molecular profiling in patients, personalized treatment strategies based on the genomic or pathologic profile of each individual patient can be more effectively matched to the molecular makeup of their respective disease.

Our researchers and clinical investigators identify specific molecular risk factors and better predict the potential efficacy of specific agents tailored to each particular tumor. These insights better guide our multidisciplinary teams to assess and establish patients' suitability for inclusion in early phase clinical trials conducted at VHIO's UTIM – CaixaResearch.

It is thanks to the backing received from FERO that our Molecular Prescreening Program continues to establish itself as a reference in prescreening and oncogenomics in Europe. Thanks to our cutting-edge technologies and platforms, we continue to extend the promise of precision medicine in oncology to an increasing number of individuals. In 2022, we performed tumor molecular profiling in over 1,100 cancer patients as candidates for enrolment in clinical trials.

In short, FERO's Institutional Program enables us to lead and run such a comprehensive program. In so doing, we continue to ensure that more of our patients can ultimately benefit from our powerful technology programs and approaches, further advance research into the more effective and less invasive tracking of cancer by liquid biopsy, and develop cancer diagnostics for the early detection of disease.

"la Caixa" Foundation

"la Caixa" Foundation: advancing research and rendering anti-cancer medicines more precise

Building on the successes of the two previous VHIO -"la Caixa" Institutional 3-year Programs, the CaixaResearch Advanced Oncology Research Program (2020-2023) is powered by one of VHIO's Patrons, "la Caixa" Foundation (page 20). It is thanks to this Institutional Program that we continues to spur our development of more potent and precise anti-cancer medicines. It also enables us to fortify existing research lines, initiate new projects, and lead frontier research in some of the most relevant and rising focus fields in precision oncology; those that show particular promise in solving the multiple questions that stand in the way of more effectively combating this disease.

Our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138), directed by Elena Garralda and also supported by the "la Caixa" Foundation, allows us to pursue our transformative research lines aimed at unpicking the complex role that the microbiome plays in cancer development, drive 'big data'-derived insights, develop and integrate cutting-edge platforms incorporating bioinformatics, biostatistics and machine learning applications in cancer prognosis and prediction, as well as harness the potential of Artificial Intelligence (AI) in the development of individually matched therapies.

Clinical trials performed at this Unit have led and/or contributed to the approval of more than 30 anti-cancer agents by either the U.S. Food and Drug Administration (FDA), or the European Medicines Agency (EMA), or both. It is thanks to the support received that we can continue to advance and apply novel anti-cancer approaches and armory including liquid biopsy, RNA expression analysis, immune-based therapies, bispecific antibodies, oncolytic virus, and intratumoral therapy. These efforts are driven thanks to the expertise of several VHIO groups and teams including our Early Clinical Drug Development, Cancer Genomics, Molecular Oncology, Oncology Data Science (ODysSey) Groups, led by Elena Garralda, Ana Vivancos, Paolo Nuciforo, and Rodrigo Dienstmann, respectively.

The matched dedication of our clinical and translational investigators across all VHIO programs and groups, as well as our Transversal Clinical Trials Core Services, enables us to expand our portfolio of early phase clinical studies including complex trials such as basket studies, and include an increasing number of patients, year-on-year. This year, we conducted 239 ongoing phase I clinical trials, 29 of which are Basket studies, as well as 3 phase 0 trials, with a total of 651 patients enrolled. In 2022 we opened 86 new studies. We have treated over 1,400 patients throughout the year, with a median of 400 patients per month.

We also lead the design and development of next generation clinical trials in oncology and participate in several ongoing European and international projects include the Cancer Core Europe (CCE)-developed Basket of Baskets (BoB) investigator initiated adaptive trial, and the EU-funded Cancer Core Europe Consortium – Building Data Rich Clinical Trials - CCE-DART (page 185). These projects facilitate the optimization of biomarker-drug codevelopment to more precisely match tailored therapies to each disease setting, each individual patient. These 'smarter' study designs seek to more effectively identify the optimal treatment for the right patient, at the right time. They also promise to overcome the rigidity and limitations associated with more traditional clinical trial designs

Fundación BBVA

BBVA Foundation: generating new insights into the mechanisms of resistance and response to immune-based therapies

Considering the successes of the very first VHIO-BBVA Foundation Program on Tumor Biomarkers Research that launched back in 2011, VHIO and the Fundación BBVA - one of our Institutional Supporters and Patrons (page 21), - renewed their agreement in in 2018. Building on the achievements of the first program, our 4-year Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI), centers on advancing research into the natural mechanisms governing how T lymphocytes react to cancer and how to use these anti-tumor responses to develop more personalized and potent immune-based therapies and treatment strategies.

Representing an important forward step in advancing agents that inhibit checkpoint regulation of the immune system, this VHIO Institutional Program aims at achieving a deeper understanding of mechanisms of resistance and response to these therapies, and prioritizes the early clinical drug development of those therapies and combinations that show most promise.

CAIMI counts on the expertise of Elena Garralda, Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, who heads up the program's clinical research, and Alena Gros, Principal Investigator of our Tumor Immunology & Immunotherapy Group (page 86), who leads its translational research. It also relies on our Molecular Prescreening Program, co-led by Ana Vivancos, Paolo Nuciforo, Elena Garralda, and Rodrigo Dienstmann, Principal Investigators of VHIO's Cancer Genomics, Molecular Oncology, Early Clinical Drug Development, and Oncology Data Science (ODysSey) Groups, respectively.

This program has spurred the development of various translational projects linked to the early clinical development phases of immunotherapy, including the development of cell-based therapies such as killer T cells for non-responders to current immunotherapies. Other areas of research include the characterization of hyperprogressive disease with immunotherapy to advance insights into this phenomenon, led by Elena Garralda, and the validation of a radiomic signature to predict response to immunotherapy. The investigators are correlating the results with the genomic evolution observed in patients. This work is carried out in collaboration with Raquel Perez-Lopez, Principal Investigator of our Radiomics Group (page 108).

Importantly, also thanks to the funding received through CAIMI, Elena Garralda's team and Alena Gros' group worked together to finalize the clinical grade validations of tumor-infiltrating lymphocytes (TILs) expansion for the treatment of different tumor types at the Vall d'Hebron University Hospital (HUVH). This work was carried out in collaboration with the Banc de Sang i Teixits - BST (Blood and Tissue Bank), a public agency of the Catalan Department of Health.

The NEXTGEN-TIL phase I trial at our Institute is now recruiting patients to assess the safety and tolerability of neoantigen-selected TIL therapy in advanced epithelial tumors and solid tumorsn in patients with metastatic or unresectable epithelial tumors and immune checkpoint blockade resistant solid tumors.

Excelencia Severo Ochoa: strengthening VHIO programs and teams in advancing cancer discovery and precision medicine in oncology

Announced at the end of 2021, our Institute is accredited and awarded as a Severo Ochoa Center of Excellence, 2022-2026. This prestigious distinction is granted within the subprogram of the Spanish Institutional Strengthening of the State Plan for Scientific and Technical Research & Innovation, and recognizes national research centers that demonstrate scientific leadership of excellence and impact at global level.

Conferring reputation and social and scientific recognition, this accreditation is awarded annually and is managed and supported by the Agencia Estatal de Investigación* - AEI (Spain's State Research Agency), a body affiliated with the Ministerio de Ciencia e Innovación (Spanish Ministry of Science and Innovation). Valid for four years, this accreditation is renewable thereafter through re-application for the same rigorous evaluation carried out independently by an international scientific committee of renowned researchers.

From the 2020 call, VHIO was the only newly accredited Severo Ochoa Center of Excellence in 2022, alongside the other six re-awarded research centers. Set within the Vall d'Hebron Barcelona Hospital Campus, VHIO is also the first research institute linked to the national healthcare system to have received this distinction.

This accolade reflects our Institute's important contributions to cancer science and precision medicine in oncology at a global level. It also confirms VHIO's scientific leadership and proven capacity to advance frontier research, generate high-impact results, as well as attract and retain research talent.

This VHIO Institutional Program further strengthens our various research programs and teams in driving important advances in cancer discovery and precision medicine in oncology.

---

*Supported by the State Agency for Research - *Agencia Estatal de Investigación* - AEI (CEX2020-001024-S / AEI / 10.13039 / 501100011033).

VHIO's Task Forces

/ Strategic goals

- By providing the multidisciplinary forum for interaction between researchers and other healthcare professionals in oncology, we foster research collaborations in-house and with external partners.
- Update on funding opportunities (competitive and non-competitive), for the development, coordination, compilation, writing, and logistical management of new research proposals.
- Create, maintain and standardize the necessary tools (CRF, informed consents, and databases), to optimize the development of ongoing research.
- Improve circuits in sampling, sampling procedures, and data collection to spur research development.
- Identify the needs of research groups and professionals in oncology who are participating in our task forces (including logistics, resources, mediation), and provide solutions to deliver on these requirements.
- Propose milestones and contingency plans.
- Improve the identification of patients' and clinical needs, and translate these into focused research opportunities.
- Central management of patients' data according to projects' pipelines and cohorts.
- Create specific Working Groups to manage and follow up research projects generated within the Task Forces.

/ Highlights

- We have consolidated our task forcing model by increasing the number of participants and projects.
- We have created a new Task Force focused on biliary tract cancers. During this year, the Task Force team has established circuits and is exploring new research ideas, with new projects envisaged to start in 2023.
- We are progressively incorporating VHIO's newly established Aging and Cancer Group (page 64) in our task forces. This work will continue in 2023 with the addition of new VHIO groups.

/ Summary

Accelerating progress through team science, VHIO's multidisciplinary teams, coordinated by VHIO's Scientific Management Area (page 152), also work together as dedicated Task Forces (TFs) that have been established based on VHIO's strategic vision and core research priorities.

These comprehensive teams are comprised of preclinical and translational researchers, clinical investigators and medical oncologists, pathologists, other MD disciplines, clinical research nurses, data curators, study coordinators and project managers, among others.

VHIO's TFs regularly convene to collaborate on a range of cancer types, including breast, colon, gastroesophageal, kidney, melanoma, neuroendocrine, rectal, pancreatic, prostate, and gynecological cancers, as well as onco-imaging, biliary tract cancers, and patients' involvement in research. Our TFs work together to synergize efforts, boost collaboration among groups and between specialists, and continuously revise patients' and samples' circuits and ethics to advance cancer science and precision medicine.

The structure of each team varies depending on its size, workflow, participants, and level of activity. An appointed Chair leads each task force, and an allocated project manager is responsible for setting agendas, writing meeting minutes, following up on action points and tasks, and establishing alignments, interactions, and synergies across VHIO's various task forces.

Illustrative of VHIO's commitment to team science in more effectively tackling the complexity of cancer, clinical researchers from other medical specialties across Vall d'Hebron and/or other local hospitals in Catalonia, as well as other investigators from the Vall d'Hebron Barcelona Hospital Campus and other research institutions, actively contribute to the activities of our task forces.

We are constantly working to identify any new areas that do not have a specific task team. In 2022, we created a new TF on biliary tract cancers to accelerate our research into these malignancies. We aim to create new transversal task force teams focused on other areas, such as cancer prevention and early detection, in alignment with ongoing policies and activities including the European Code Against Cancer and the Cancer Mission.

mobile version

scan to visit

VHIO's Transversal Clinical Trials Core Services

VHIO's TRANSVERSAL CLINICAL TRIALS CORE SERVICES

Clinical Trials Office

Director, Clinical Trials Office Marta Beltran **Heads, Start-Up Unit and Clinical Trials Liaison** Ana Matres, Silvia Perez **Head, Data Entries** Ignacio Carcela **Head, Hematology** Laura Segura **Lead Study Coordinators** Eulalia Aliende, Guillem Cunill, Queralt Ferrer, Montse Moreno, Gemma Mur, Olga Padrós, Cristina Perez, Julia Sedó **Lead Data Entries** Gloria García, Eva Lázaro, Joana Pinyol, Alberto Rojo **Study Coordinators** Aitana Almodóvar, Enric Alvarez, Gisela Andrés, Eva Banus, Marina Barbero, Jorge Bardina, Laura Blanco, Anna Cabrera, Júlia Caparrós, Laia Catalán, Paula Chiquillo, Natàlia Écija, Núria Farras, Carlos Fernández, Danis Fernández, Alba Galiana, Anna Giralt, Laia Gispert, Sara Gutiérrez, Sara Herbera, Montse Hernandez, Marta Horcas, Josu Iraola, Alejandro Lahire, Esther Llaudet, María López, , Raquel Madrenas, Alba Martínez, Elena Martinez, Sònia Martínez, Magda Masana, Alba Meire, Thais Miquel, Mireia Mira, Jordi Perera, Gemma Pujadas, Cristian Rosales, Marta Rotxes, Álvaro Rueda, Laura Sancho, Laura Saucedo, Samira Sehir, Jana Simón, Albert Texidor, Julia Toledo **Data Entries** Cristina Aguilar, David Alvarez, Iñigo Arauco, Nestor Babon, Samanta Bascuas, Carlota Bellot, Laia Benitez, Cristina Calderon, Helena Carbonero, Andrea Fores, Mariona Guillamet, Neus Iserte, Bàrbara Juanmiquel, Jordina Llavall Sanchez, Eva Marín, Sílvia Marín, Carla Martinez, Genís Mas, Raquel Masip, Miriam Meseguer, Carina Monclús, Paula Nuñez, Adriana Oños, Victor Ortega, Sergio Perez, Xavier Perez, Eva Puerma, Olga Reyes, Isabel Rico, Aina Mª Rigo Miralles, Jordi Romero, Rosa Romero, Blanca Ruiz de la Torre, Isabel Salado, Rebeca Sanchez, Lucia Sanchis, Judith Serrano, Inés Tejero, Marta Vidigal, Laia Vila Maria Padial **Clinical Trials Assistants** Cristian Campderros, Nuria Carballo, Sergi Folch, Marc Palomar

/ Strategic goals

- Contribute to the development of novel anti-cancer therapies.
- Consolidation as an international reference for clinical trials in oncology and hematology.
- Guide patients enrolled in clinical trials to comply with the protocol requirements and help them with daily life throughout the duration of their participation.
- Standardize clinical trial processes to ensure optimal quality and the compliance of Good Clinical Practice (GCP).

/ Highlights

- We continue to report important numbers of clinical trials performed and respective patient recruitment.
- The continued, optimal management of complex protocols which are increasingly demanding.
- Implementation of new tools and procedures to increase the quality and efficiency of research.

/ Summary

Established in 1997, our Clinical Trials Office is directed by Marta Beltran and incorporates experts conducting clinical trials at the Vall d'Hebron University Hospital's (HUVH) Medical Oncology Department, headed by VHIO's Director Josep Tabernero.

This Office comprises study coordinators, data managers and administrators who coordinate phase I–IV clinical studies and also participate in several translational research projects at VHIO. Our team is organized into 4 groups; start-up unit, oncology study coordinators, oncology data entries, hematology study coordinators and data entries, covering all tumor types and studies.

In oncology and hematology, in 2022 we managed a total of 3 phase 0 trials, 262 phase I trials, 33 basket studies, 186 phase II trials, 209 phase III clinical trials, and 1 medical device study, with active recruitment throughout the year, and patient enrollment in our oncology and hematology clinical trials totaled at 1,503. In addtion, we managed 2 phase III studies and 1 post-authorization trial in radiotherapy including a total of 10 patients.

230 new trials were initiated in 2022, including 14 post-authorization trials, and rollover studies. In addition, we continue to follow up patients who were recruited prior to 2022 and are still enrolled and receiving study treatment (1,180 patients in total, and 2,087 in follow-up).

Clinical Trials in Oncology

In 2022 we managed 3 phase 0, 210 phase I, 29 basket, 159 phase II, and 140 phase III clinical trials, and 1 medical device study with active recruitment throughout the year (Figure I), with patient enrollment totaling at 1,328 (Figure II). 181 new trials were initiated, including 12 post-authorization trials, and rollover studies. In addition, we continue to follow up patients who were recruited prior to 2022 and are still enrolled and receiving study treatment (1,170 patients in total, and 2,002 in follow-up).

Figure I: Annual distribution of oncology clinical trials (Phase 0, I + Basket, II, III, and a medical device) and post authorization trials with active recruitment.

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Phase 0							1	2	4	3
Phase I & basket trials	75	83	106	129	137	161	162	195	207	239
Phase I Specific Tumor Type (STT)	29	36	32	44	45	53	59	79	75	77
Phase I Non Specific Tumor Type (NSTT)	46	47	68	71	75	86	80	90	105	133
Basket			6	14	17	22	23	26	27	29
Phase II STT trials	96	99	94	117	107	131	141	148	153	159
Phase III trials	61	64	89	108	111	107	121	129	147	140
Medical device										1
Nº clinical trials	232	246	289	354	355	399	425	474	511	542
Post authorization & rollover trials		5	14	16	19	33	34	34	36	38

Figure II: Annual recruitment of patients enrolled in oncology clinical trials (Phase 0, I + Baskets, II, III, medical device), and post authorization trials.

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Included in Phase 0							1	1	15	4
Included in Phase I & basket trials	345	303	370	453	445	508	499	521	551	647
Phase I Specific Tumor Type (STT)	107	79	79	84	80	110	124	178	138	172
Phase I Non Specific Tumor Type (NSTT)	238	224	262	301	289	334	303	307	342	426
Basket			29	68	76	64	72	36	71	49
Included in Phase II STT trials	257	302	327	333	323	361	337	230	341	327
Included in Phase III trials	241	166	282	343	328	329	285	332	419	346
Medical device										4
Total number of patients included	843	771	979	1129	1096	1198	1122	1084	1326	1328
Included in post authorization & rollover trials		20	56	50	80	184	164	156	280	321

More than half of our patients included in our phase I clinical trials have been referred to us from other hospitals, which has consequently positioned our Unit as a leading reference in early clinical studies. Reflective of our recognized excellence, VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, directed by Elena Garralda (page 138), has been re-accredited by the Generalitat de Catalunya (Government of Catalonia).

As we continue to render personalized medicine more precise by matching therapies to the specificities of each individual patient, each individual tumor, the requirements and selection criteria for inclusion in certain studies are becoming more complex.

We are dedicated to expanding our portfolio of trials in to ultimately establish new treatment models with highly selective drugs. Our Unit continues to fine-tune patient selection criteria to identify those patients who are most likely to benefit from novel therapies, including emerging immune-based treatments, tailored to individual patients' molecular 'measurements'.

Clinical Trials in Hematology

In 2022 we managed 52 phase I, 4 baskets, 27 phase II and 69 phase III clinical studies with active recruitment throughout the year (Figure III), with patient enrollment totaling at 175 (Figure IV). 49 new trials were initiated, including 2 post-authorization trials, and rollover studies. In addition, we continue to follow up patients who were recruited prior to 2022 and are still enrolled and receiving study treatment (229 patients in total, and 150 in follow-up).

Figure III: Annual distribution of hematology clinical trials (Phase I + Basket, II and III) and post authorization trials with active recruitment

	2018	2019	2020	2021	2022
Phase I	25	31	39	51	56
Phase I Specific Disease	24	30	37	47	49
Phase I Non Specific Disease	1	1	2	2	3
Basket				2	4
Phase II trials	28	24	36	35	27
Phase II Specific Disease	28	23	35	34	24
Phase II Non Specific Disease		1	1	1	3
Phase III trials	50	51	45	60	69
Phase III Specific Disease	50	51	42	59	68
Phase III Non Specific Disease			3	1	1
Nº clinical trials	103	106	120	146	152
Post authorization & rollover trials	15	22	25	28	26

Figure IV: Annual recruitment of patients enrolled in hematology clinical trials (Phase I + Basket, II and III) and post authorization trials with active recruitment

	2018	2019	2020	2021	2022
Included in Phase I	38	55	59	84	73
Specific Disease (SD)	37	55	56	84	60
Non Specific Disease (NSD)	1		3		9
Basket					4
Included in Phase II trials	20	38	39	42	33
Specific Disease (SD)	20	38	39	42	32
Non Specific Disease (NSD)					1
Included in Phase III trials	52	56	55	56	69
Specific Disease (SD)	52	56	51	56	69
Non Specific Disease (NSD)			4		
Total of patients included	110	149	153	182	175
Included in post authorization & rollovers trials	1	6	38	51	32

The prestige of HUVH's Medical Oncology Department is recognized by pharmaceutical and biotechnology companies. It has also become a reference program and selected by the industry to carry out complex clinical trials. The number of participating centers in these studies is highly restricted.

Clinical sites are selected based on the highest quality standards and capacity for carrying out state-of-the-art research. We have participated in early phase trials of different drugs, ultimately enabling the pharmaceutical industry to market novel anti-cancer medicines. We are involved in studies promoted by the pharmaceutical industry as well as those developed by us in collaboration with other hospitals. In 2022, we also conducted more than 17 investigator-Initiated trials (IITs) in oncology.

VHIO's TRANSVERSAL CLINICAL TRIALS CORE SERVICES

Academic CRO (VHIO – aCRO)

Unit Head Susana Muñoz **Clinical Research Managers** Marta González, Darío López, Anna Palazón **Clinical Research Associates (CRAs)** Soraya Alonso de Caso, Pol Barbarroja, Carlos Márquez, Pablo Martínez, Judith Bautista **Medical Writer** Marta Carboneras **Clinical Trial Assistant (CTA)** Elena Guzmán

/ Area summary

VHIO's Academic Contract Research Organization (VHIO - aCRO), has extensive experience in conducting sponsored trials and investigator-initiated trials (IITs). We offer the complete range of start-to-end management services required to perform clinical trials and studies. Our multidisciplinary team enables us to operate as a full service CRO in clinical studies from phase I to IV.

We also provide guidance to investigators and sponsors on how to achieve the best experimental design and offer logistical advice to help them maximize their resources. With a team of 11 professionals, our Unit provides medical writing support, full regulatory activities, monitoring, project management, e-CRF creation, statistics, drug management, insurance management, and pharmacovigilance activities.

In 2022 we have incorporated a clinical trial assistant, and we aim to expand our Unit's structure with a CRA to be able to even more effectively manage current and future clinical trials, optimize CRO digital tools for working remotely, as well as continue to bring out the best in each team member to further strengthen our Facility.

We have also organized our Unit to start working under the new clinical trial regulation (Regulation EU 536/2014), that came into force in January 2022.

/ Strategic goals

- Provide clinical project management support to awarded R&D projects (European/Pharma funded), and academic oncology clinical trials led by our Medical Oncologists and Clinical Investigators at VHIO and the Vall d'Hebron University Hospital (HUVH), Vall d'Hebron Barcelona Hospital Campus.
- Serve as an Academic CRO for IITs.
- Academic CRO for pharmaceutical company sponsored trials that count on the participation of VHIO investigators in the development of these studies.

/ Highlights

- In 2022, we have successfully managed several major projects including TOPIC, IRONMAN, MONEO, DUREC, BRCA-P, CA209-7J3, MoTriColor, BoB, RAMPART, NIPU among others. Of particular note, two clinical trials in cell therapy with TILs and NKs initiated in 2021 are currently logistically managed by our Unit. Most of these studies are led by our Medical Oncologists and Clinical Investigators at HUVH's Medical Oncology Department, headed by VHIO's Director Josep Tabernero.
- During 2022, we successfully met the regulatory requirements for all of our trials (first submissions and amendments).
- Our CRA team monitored more than 160 patients in different hospitals across Spain.
- We managed clinical trial drug requirements in more than 30 national hospitals.
- We have also demonstrated sufficient benefits that support CRO activities for non-funded academic trials.

VHIO's TRANSVERSAL CLINICAL TRIALS CORE SERVICES

Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch

Director Elena Garralda **Executive Team** Marta Beltran, Cristina Casal, Elena Garralda, Gemma Sala **Clinical Head** Elena Garralda **Associated Investigators**, **Senior Consultants** Judith Balmaña, Joan Carles, Enriqueta Felip, Elena Garralda, Teresa Macarulla, Ana Oaknin, Cristina Saura, Josep Tabernero **CORE Phase I Investigators** Guzmán Alonso, Irene Braña, Vladimir Galvao, Julia Lostes, Honey K. Oberoi, Belén Ortega, Katerin Rojas, Omar Saavedra, María Vieito **Phase I Investigators** Daniel Acosta, Juan David Assaf, Iosune Baraibar, Pere Barba, Meritxell Bellet, Maria Borrell, Francesc Bosch, Alba Cabirta, Ana Callejo, Jaume Capdevila, Cecilia Carpio, Florian Castet, Susana Cedrés, Marc Diez, Elena Élez, Santiago Escrivá, Carles Fabregat, Lorena Fariñas, Ferran Ferragut, Maria Laura Fox, Alejandro Garcia, Carmen Garcia, David Garcia Illescas, Sara Garrido, Mercedes Gironella, Patricia Gómez, Macarena González, Jorge Hernando, Marta Hidalgo, Gloria Iacoboni, Patricia Iranzo, David Marmolejo, Lucia Martin, Alexandre Martinez, Joaquin Mateo, Antonieta Molero, Rafael Morales, Eva Muñoz, Alejandro Navarro, Mafalda Oliveira, Carolina Ortiz, Núria Pardo, Isabel Pimentel, Francisco Javier Ros, Francesc Salvà, Mario Sanchez, Lucia Sanz, Nadia Saoudi, Ángel Serna, César Serrano, Maria Sola, Cristina Suarez, Augusto Valdivia, Claudia Valverde **Clinical Trials Office Director** Marta Beltran **Start Up Unit Head** Ana Matres **Data Entries Head** Ignacio Carcela **Lead Study Coordinators** Eulàlia Aliende, Montserrat Moreno **Coordinators** Aitana Almodóvar, Eva Banús, Marina Barbero, Jorge Bardina, Anna Cabrera, Julia Caparros, Natalia Écija, Danis Fernández, Alba Galiana, Laia Gispert, Sara Herbera, Josu Iraola, María López, Elena Martínez, Sonia Martínez, Magda Massana, Mireia Mira, Gemma Pujadas, Marta Rotxes, Ana Laura Sancho, Laura Saucedo, Jana Simon, Albert Teixidor **Lead Data Entries** Gloria García, Alberto Rojo **Data Entries** Nestor Babon, Maria Barber, Cristina Calderón, Anna Cos, Nora Dieguez, Andrea Fores, Bárbara Juanmiquel, Sandra Justicia, Raquel Masip, Miriam Meseguer, Paula Núñez, Adriana Oñós, Víctor Ortega, Maria Padial, Sergio Pérez, Olga Reyes, Isabel Rico, Aina Maria Rigo, Jordi Romero, Blanca Ruiz de la Torre, Lucia Sanchis, Judith Serrano, Inés Tejero, Marta Vidigal **Clinical Trials Office Administrative Support** Nuria Carballo, Marc Palomar **Director of Oncology Nursing** Mª Ángeles Peñuelas **Study Nurse Supervisor** Cristina Casal **Nurse Coordinator** Sonia Valverde **Operational Research Nurses** Inés Depares, Andrea Martínez, Alba Silverio, Rubén Xavier Torres **Nurses** Raquel Alcaraz, Carla Barjola, Andrea Caballero, Anguiela Cachique, Elena de Cabo, Laura de la Hoz, Maria Luisa Fargas, Cristina Gómez, Eva Gómez, Margarida Marcos, Marta Mate, Carmen Moina, Mireia Moral, Isabel Muñoz, Carla Sánchez, Tania Sánchez, Adriana Terres, Judit Torres, Lydia Vélez, Marta Villalba **Nurses Assistants** Mª Ascensión Clop, Katherine Espinoza, Susana Manuela Flores, Mireia Hernández, Alba Pardes, Xénia Angeles Renedo **Inventory Manager** Melania Forniés **Sample Technician** Mª Teresa Romero **UITM – CaixaResearch Administrative Support (Schedulers)** Laura Abellán, Mª Teresa Mendoza, Noelia Moles **Head, Clinical Research Oncology Pharmacy Unit** Isabel Cidoncha **Pharmacists** Montserrat Carreres, Carla Esteban, Celia Fernández, Lorena García, Patricia García, Pablo González, Rocío Paucar, Pilar Rovira, Eugenia Serramontmany, Carlota Varon **Technicians** Montserrat Aguilar, Romina Bellini, Esther Carabantes, Bryan Cárdenas, Angelica Cely, Elisabeth Gabilan, Ariadna Jabalera, Roser Klimt, Susana Mulet, Isabel Pérez, Sergio Pizarro, Marta Pozo, Madiha Shaheen, Alan Thompson, Silvia Torralba, Noemi Visus **Pharmacy Assistant** Álex Valle **Data Entry** Carmen Torres **Secretary** Isabel Mª Alerany

/ Strategic goals

- Early clinical drug development and translational research led by our UITM – CaixaResearch clinical investigators and VHIO researchers: expansion of our broad portfolio of promising novel anticancer therapies, across a balanced spectrum of studies with particular focus on first-in-human studies, novel-novel combinations, best-in-class compounds, and a new class of drugs.
- Perform complex trials such as organ dysfunction trials, Octopus as well as Basket studies, and link clinical research at this Unit to VHIO's preclinical and translational projects. We also collaborate with various other partners involved in drug development and translational research.
- Genomic medicine trials in early drug development: perform molecular analysis of patients' tumors in order to select the best possible treatment with the experimental therapies available, co-develop medical informatics applied to genomic medicine, and integrate preclinical and clinical research by incorporating novel drugs, new insights, and study design together with customized molecular diagnostics.
- Immunotherapy: our Unit's Task Force in early drug development of immunotherapeutics and cell signaling focuses on second generation immunotherapies, including new cytokines, bispecifics, intratumoral agents, immunomodulatory, and immune checkpoint inhibitors and combinations, as well as translational research in immuno-oncology.

/ Highlights

- We have performed some of the most complex phase I trials, including those focused on molecularly-selected patient populations (trials in complex molecularly-selected patient populations Basket/Octopus trials), as well as studies in immuno-oncology.
- We have expanded our expertise in drugs targeting developmental pathways, cell signaling (ERK, MET, FGFR, RET, NOTCH, NTRK), ADCs, and immunotherapy including BITEs, bispecifics, T- cell engagers, TCRs and cellular therapy products.
- Developed by VHIO's Cancer Genomics Group (page 116) led by Ana Vivancos, we benefit from applications that enable us to generate faster results. These include an n-Counter (Nanostring) platform, two digital PCR platforms (BEAMing Sysmex and ddPCR, BIO-RAD), and five NextGen Sequencers; MiSeq, NextSeq, HiSeq2500 and NovaSeq6000 from Illumina, and a MinION from Oxford Nanopore Technologies. We also co-develop customized molecular tests for VHIO's Molecular Prescreening Program (page 146) namely, disease-oriented mutation panels for our NGS platforms.
- We have established alliances with several pharma companies as the preferred site for testing their novel and most relevant therapies, including GlaxoSmithKline OCTC, Roche ImCORE, and Astra Zeneca/MedImmune Partner of Choice Network (pages 198-199).
- Our investigators have successfully implemented the Basket of Baskets (BoB) trial which is a novel study in personalized medicine integrating cutting-edge molecular prescreening, the development of new diagnostic tests such as circulating DNA or Nanostring, with the testing of targeted therapies in populations of patients with identified molecular alterations and a high probability of benefiting from the selected treatments. This is an academic study, endorsed by the Cancer Core Europe (CCE) Consortium, and co-funded by pharmaceutical companies. We are engaged in ongoing and advanced negotiations with pharmaceutical companies to increase the number of modules.
- We have introduced Molecular Tumor Board meetings to discuss the most relevant genomic features of complicated cases and evaluate possible treatment options.
- We have launched an advanced cell-based therapy program and are participating in several pharma sponsored trials to evaluate the role of TIL therapy. We are also exploring an academic TIL product in collaboration with Alena Gros (PI: VHIO's Tumor Immunology & Immunotherapy Group, page 86).
- In collaboration with several other VHIO groups, we head our CaixaResearch Advanced Oncology Research Program (2020-2023), also supported by the "la Caixa" Foundation (page 127).

"la Caixa" Foundation

/ Summary

Inaugurated in June 2010, thanks to the support received from the "la Caixa" Foundation (page 127), VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch is dedicated to complex clinical trials with drugs in early development (phase I and early phase II trials), focusing on novel targets. Occupying a total surface area of 1000 m^2, our Unit is located within the General Area of the Vall d'Hebron University Hospital (HUVH), Vall d'Hebron Barcelona Hospital Campus.

This privileged environment with direct access to patients, coupled with VHIO's translational approach to research and superb scientific framework, has enabled our Unit to establish itself as one of the few comprehensive facilities in Europe to rapidly transform latest discovery into benefits for patients. Our UITM – CaixaResearch incorporates a multidisciplinary team comprised of medical oncologists, clinical trial coordinators and data managers, nurses and nurse technicians, pharmacists, as well as administrative personnel.

By promoting tight connectivity between oncology care and research we establish novel treatment models for patients with highly selective drugs, and advance insights into tumor types and how to treat them in an individualized way – getting the right therapy to the right patient, at the right time. As the statistics show, we continue to do so for an increasing number of patients.

During 2022, our Unit participated in 239 ongoing phase I clinical trials, 29 of which are Basket trials (a 15% increase compared with 2021). Thanks to our multidisciplinary team we have continued to expand our portfolio of phase I and basket studies (including 3 phase 0 trials) with 651 patients enrolled (a 17.5% increase compared with 2021). This year we opened 86 new trials. We have treated over 1,424 patients throughout the year, with a median of 400 patients per month.

To be able to sustain this growth and continue providing the best quality care to our patients we have increased our treatment room facilities in 2022. We have added 7 extra places to treat patients, so we currently have 17 treatment places, including two treatment beds for patients who are more fragile or studies that require an isolated area. We have also increased the space to process samples of patients and continued to increase the number of people working in the different teams.

Research carried out at our Unit by VHIO's Early Clinical Drug Development Group (page 92), directed by Elena Garralda, centers on the development of new drugs based on the molecular profile of each tumor as well as the optimization of treatment regimens using combinations of new agents with those that already exist.

Reflective of VHIO's purely translational model, our studies are also linked to several research lines led by other VHIO groups, thus connecting molecular biology and optimal tumor models with pharmacology and innovative clinical research. VHIO scientists collaborate in our trials to facilitate biomarker development, a deep understanding of the mechanism of action, as well as research into mechanisms of cancer drug resistance.

We also participate in VHIO's Molecular Prescreening Program (page 146) that performs molecular analyses of patients' tumors to select the best possible treatment with the experimental therapeutics available. Thanks to Ana Vivancos' Cancer Genomics Group (page 116) and their development of existing applications including an n-Counter (Nanostring) platform, two digital PCR platforms (BEAMing Sysmex and ddPCR, BIO-RAD), and five NextGen Sequencers; MiSeq, NextSeq, HiSeq2500 and NovaSeq6000 from Illumina, and a MinION from Oxford Nanopore Technologies, we are equipped to perform faster and more precise mutational analyses of tumor suppressor genes as well as translocations and gene amplifications.

Excellent patient treatment and care as well as pioneering research is also made possible thanks to the collaboration of many other oncology professionals including our oncology nurses directed by Mª Ángeles Peñuelas and our team of clinical study nurses led by Study Nurse Supervisor Cristina Casal, pathologists from the Vall d'Hebron University Hospital's Molecular Pathology Department, radiologists and interventional radiologists, our Clinical Trials Office directed by Marta Beltran, Database Managers, VHIO's Clinical Research Oncology Pharmacy Unit headed by Isabel Cidoncha, our Quality & Processes Unit directed by Gemma Sala, as well as many other healthcare specialists including dermatologists, cardiologists, and ophthalmologists.

VHIO's TRANSVERSAL CLINICAL TRIALS CORE SERVICES

Clinical Research Oncology Nurses

Director of Oncology Nursing Mª Ángeles Peñuelas **Study Nurse Supervisor** Cristina Casal **Nurse Director's Assistant** Juan Manuel Garcia **Coordinator** Sonia Valverde **Nurses** Raquel Alcaraz, Carla Barjola, Andrea Caballero, Anguiela Cachique, Anna Maria Carro, Mª Elena de Cabo, Laura de la Hoz, Mª Luisa Fargas, Cristina Gomez, Eva Gomez, Margarida Marcos, Marta Mate, Carmen Moína, Mireia Moral, Isabel Muñoz, Teresa Navarro, Carla Sanchez, Tania Sanchez, Adriana Terres, Judit Torres, Lydia Velez, Marta Villalba **Operational Research Nurses** Inés Depares, Andrea Martinez, Alba Silverio, Rubén X. Torres **Nursing Assistants** Xenia Ángeles, Katherine Espinoza, Susana Flores, Melania Fornies, Mireia Hernández, Mª Ascension Martin, Ana Belen Ortiz, Mª Teresa Romero

/ Summary

Clinical trials in oncology are essential for developing novel, more effective targeted therapies against cancer as well as improving survival, side effect profiles and the quality of life of our patients. Advances in oncology care and the delivery of more powerful anti-cancer medicines are driven by optimal processes in clinical trials.

Our expert clinical research oncology nurses assume a central role in clinical studies and work closely with multidisciplinary teams to develop and evaluate patient treatment. They also contribute to clinical trials by identifying trends in side effects of new generation drugs, collating samples and quality data for clinical trial validation, optimally managing patient symptoms and providing excellent nursing care.

Our team is directed by Cristina Casal and is specialized in molecular therapies. We represent an essential element of the multidisciplinary teams involved in the studies carried out and coordinated by VHIO's Research Unit for Molecular Therapy of Cancer (UITM) - CaixaResearch (page 138), and our Clinical Trials Office (page 134), led by Elena Garralda and Marta Beltrán, respectively.

Supporting these teams comprised of medical oncologists, molecular pathologists, oncology pharmacists, clinical researchers, and study coordinators, VHIO's oncology nurses are key to ensuring the delivery of optimal care for our patients who receive the full range of expertise, guidance, and the necessary follow-up throughout the course of their participation in clinical studies. As importantly is the psychological support that they provide, alongside the other superbly trained oncology care givers and specialists, including psychologists.

We also provide patients and their families with the information and professional guidance required to make fully informed decisions concerning their treatment options. In 2022, across the 542 actively recruiting trials in oncology, patient enrollment totaled at 1,328. Regarding clinical studies in hematology, across the 152 active trials, a total of 175 patients were enrolled. Our clinical teams also continue to follow up patients that were recruited prior to 2022 who are still enrolled and receiving treatment.

VHIO continues to expand its portfolio of clinical trials to establish novel treatments with highly selective drugs, as well as fine-tune patient selection criteria in order to identify those patients who are most likely to benefit from them. We can expect a steady increase in patient recruitment across our clinical studies in the future.

VHIO's TRANSVERSAL CLINICAL TRIALS CORE SERVICES

Clinical Research Oncology Pharmacy Unit

Head of the Clinical Research Oncology Pharmacy Unit Isabel Cidoncha **Pharmacists** Montserrat Carreres, Carla Esteban, Celia Fernández, Lorena García, Patricia García, Pablo González, Rocío Paucar, Pilar Rovira, Eugenia Serramontmany, Carlota Varon **Technicians** Montserrat Aguilar, Romina Bellini, Esther Carabantes, Bryan Cárdenas, Angelica Cely, Elisabeth Gabilan, Ariadna Jabalera, Roser Klimt, Susana Mulet, Isabel Pérez, Sergio Pizarro, Marta Pozo, Madiha Shaheen, Alan Thompson, Silvia Torralba, Noemi Visus **Pharmacy Assistant** Álex Valle **Data Entry** Carmen Torres **Secretary** Isabel Mª Alerany

/ Strategic goals

- Excellence in the services that we provide to clinical oncology research programs through optimal efficacy, efficiency and safety.
- Management, dispensing, preparation and administration of clinical study drugs according to protocol specifications. Ensure traceability of the entire circuit with the development and implementation of new software.
- Maximized control of storage temperature of samples and preparations.
- Optimal use of a computerized program, IPharma-FUNDANET®, for the management of clinical trial supplies.
- Provision of a pharmaceutical care program for patients in phase I, II and III studies treated with orally administered medicines to improve safety, compliance and the efficacy of these therapies.
- Successful sponsor audits as well as inspections carried out by regulatory authorities.

/ Highlights

- Replacing paper medical orders, we have implemented electronic prescription ordering for IV administration medication in our site prescription software.
- We have developed new traceability software that includes global pharmacotherapeutic processes; the prescription, validation, dispensing, preparation and administration of drugs in the oncology and hematology clinical trial setting.
- Our Unit provides clinical and technical support for the prescription, preparation, and administration of cytostatics in clinical trials, as well as e-records of usage and timings.
- Qualitative and quantitative quality control of all parenteral anticancer preparations to guarantee patient safety and protocol compliance.
- ISO9001:2015 certification renewed. Successful sponsor audits, regulatory inspections, and participation in the renewal of VHIO's Phase I Unit reaccreditation.

"la Caixa" Foundation

/ Summary

Our Unit is ISO 9001:2015 certified and is part of the Medical Oncology Department of the Vall d'Hebron University Hospital (HUVH), Vall d'Hebron Barcelona Hospital Campus. It is thanks to the funding received from the "la Caixa" Foundation, that our new Facility, the Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch- Clinical Research Onco-Hematology Unit opened in 2020. Equipped with all the very latest technologies, it enables us to provide even higher quality in pharmaceutical care and continue to respond to all regulatory requirements.

We focus on two main areas of clinical research in oncology:

Oncology Pharmaceutical Care Program

Our team of expert pharmacists are specialized in hospital and oncology pharmacy. The Unit's laboratory technicians prepare cytostatics and other parenteral therapies used in clinical trials, as well as closely monitor and follow-up our patients.

Pharmacological Research in Oncology Support Program

This program is directed by our team of pharmacists and laboratory technicians specialized in clinical trials. They are responsible for the management of study supplies including storage, dispensation, and traceability control.

In 2022 they managed drugs used in 710 active clinical trials in oncology & hematology, and 13,000 resupply deliveries/clinical trial supply deliveries. Our cutting-edge system for controlling storage temperature -performing electronic temperature recordings every 5 minutes daily- displays readings on computers equipped with audiovisual alarms as well as an around-the-clock SMS alert system for monitoring and reporting temperature deviations.

Regarding the design and validation of our Unit's drug preparation process traceability system, we ensure qualitative and quantitative quality control of our computerized system.

In 2022 our dispensing staff actively participated in 290 pre-study visits, 250 initial visits, 2,020 monitoring visits, 150 close-out visits, and also successfully passed 16 audits, and 1 ISO inspection.

Additionally, 51,351 clinical trial drugs have been dispensed and validated by our pharmacists, 14,125 of which were for oral administration, 1,754 for IM/ subcutaneous administration, and 35,443 for IV administration. A total of 226 Standardized Dispensing Procedures for clinical trials have been drawn up and we have performed 1,071 updates of these procedures due to subsequent amendments to protocols or pharmacy manuals. 103 storage temperature data reports have also been prepared by our dispensing team.

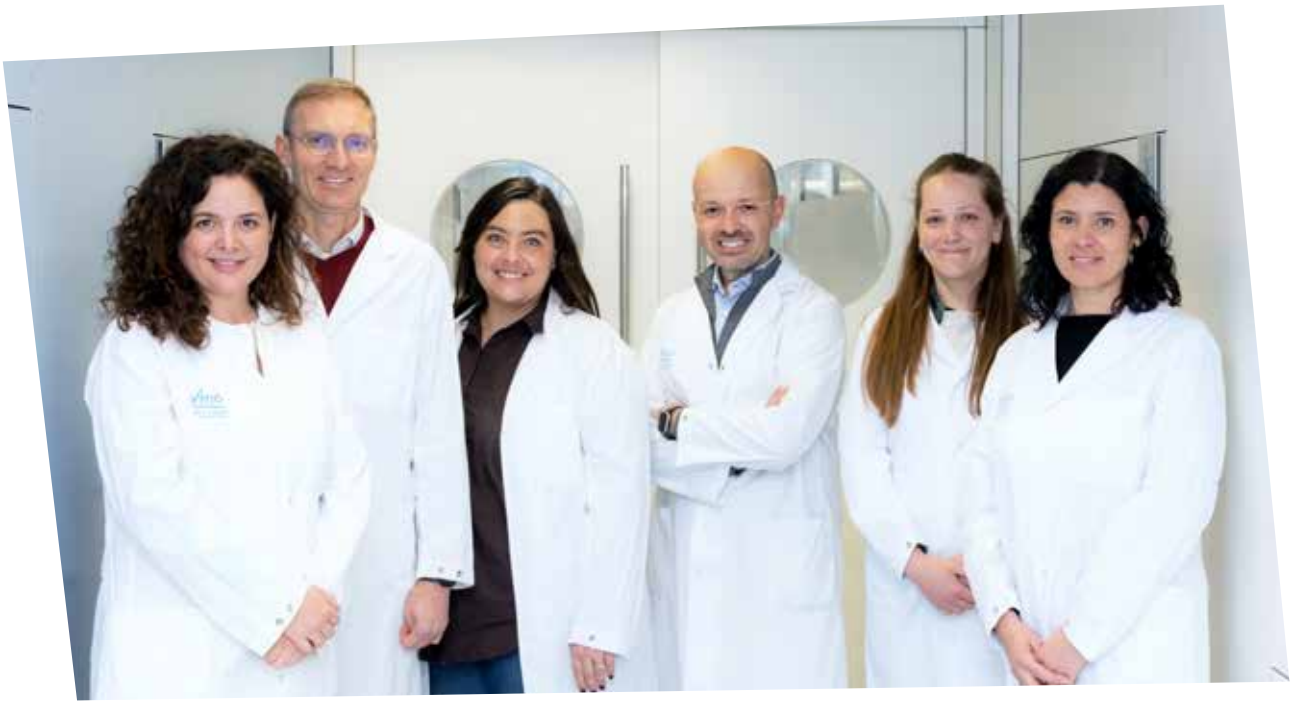
We also included 373 antineoplastic therapeutic schedules in our prescription software.

Our Pharmaceutical Care Program for patients enrolled in phase I clinical trials: we performed 1,601 visits, 600 screenings, 1,001 C1D1s, and 1,080 follow-ups, also compiling patient diaries and/or instructions for patients (in the absence of documentation provided by the respective sponsor).

VHIO's TRANSVERSAL CLINICAL TRIALS CORE SERVICES

Molecular Prescreening Program

Co-leadership Ana Vivancos, Principal Investigator, VHIO's Cancer Genomics Group, Elena Garralda, Director, VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, Principal Investigator, VHIO's Early Clinical Drug Development, Paolo Nuciforo, Principal Investigator, VHIO's Molecular Oncology Group, Rodrigo Dienstmann, Principal Investigator, VHIO's Oncology Data Science (ODysSey) Group **Program Coordination** Susana Aguilar **Research Support Technician** Jenifer González



/ Strategic goals

- Clinical implementation of advanced molecular diagnostics to optimize the selection of therapies for patients being considered for enrolment in clinical trials.
- Continued medical education with standardized reports of genomic alterations and weekly Molecular Tumor Boards.
- Constant revision and update of molecular diagnostic tests to cover emerging cancer biomarkers for precision cancer therapy.

/ Highlights

- VHIO is an active member of the American Association for Cancer Research's (AACR) Genomics Evidence Neoplasia Information Exchange (GENIE) project, a multi-phase, multi-year, international study that catalyzes precision oncology through the development of a regulatory-grade registry aggregating and linking clinical-grade cancer genomic data with clinical outcomes from tens of thousands of cancer patients treated at the participating institutions.

/ Summary

VHIO's Molecular Prescreening Program, driven by FERO's Institutional Advanced Molecular Diagnostics Program – DIAMAV (page 126), catalyzes precision medicine at VHIO. Over the last decade, this program has provided access to advanced molecular diagnostics to more than 9,000 cancer patients, and is critical in matching targeted therapeutic approaches with hundreds of clinical trial opportunities.

This program, also counting on the support and expertise provided through our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138), is co-led by VHIO's Ana Vivancos, Paolo Nuciforo, Elena Garralda (also Director of the UITM), and Rodrigo Dienstmann, Principal Investigators of our Cancer Genomics (page 116), Molecular Oncology (page 118), Early Clinical Drug Development (page 92), and Oncology Data Science – OdysSey (page 104) Groups, respectively. Activities are coordinated by Susana Aguilar, Head of the VHIOTECA Unit (page 122), in collaboration with Jenifer González, Research Support Technician (VHIO's Cancer Genomics Group).

The main objective of molecular prescreening at VHIO is to facilitate the clinical implementation of emerging cancer biomarkers that help to optimize the selection of therapies for patients being considered for enrollment in clinical trials. Our program guides clinicians in selecting both standard-of-care and investigational anti-cancer treatments and spurs clinical-molecular correlative research at VHIO. Diagnostic tests are developed and validated in-house for the cost-effective and streamlined identification of tumor molecular alterations of major interest in drug development.

Tumor profiling includes a variety of genomic techniques including next-generation sequencing panels (NGS) for the detection of mutations, copy number variations, gene fusions and RNA expression signatures, as well as histopathological techniques such as immunohistochemistry (IHC) and in situ hybridization (ISH) for protein and gene expression profiling.

In 2022, we have performed tumor molecular profiling of 1,137 cancer patients' tumors. These patients are candidates for enrollment in clinical trials. Remarkably, an NGS test was implemented to detect genomic alterations in liquid biopsy. This new test has been applied to more than 100 patients who may have acquired resistance to targeted therapies or that lacked metastatic tissue biopsies for testing. In total, 160 patients were treated with biomarker-matched innovative therapies as a result of these efforts.

Interpretation of next-generation sequencing tests and educating clinicians on emerging biomarkers is another of our priority areas. During Molecular Tumor Board and Genetic Tumor Board meetings, we facilitate data exchange among a broad range of experts for the review of patients' medical histories and cancer molecular profiles in order to more precisely guide treatment decisions and preventive measures.

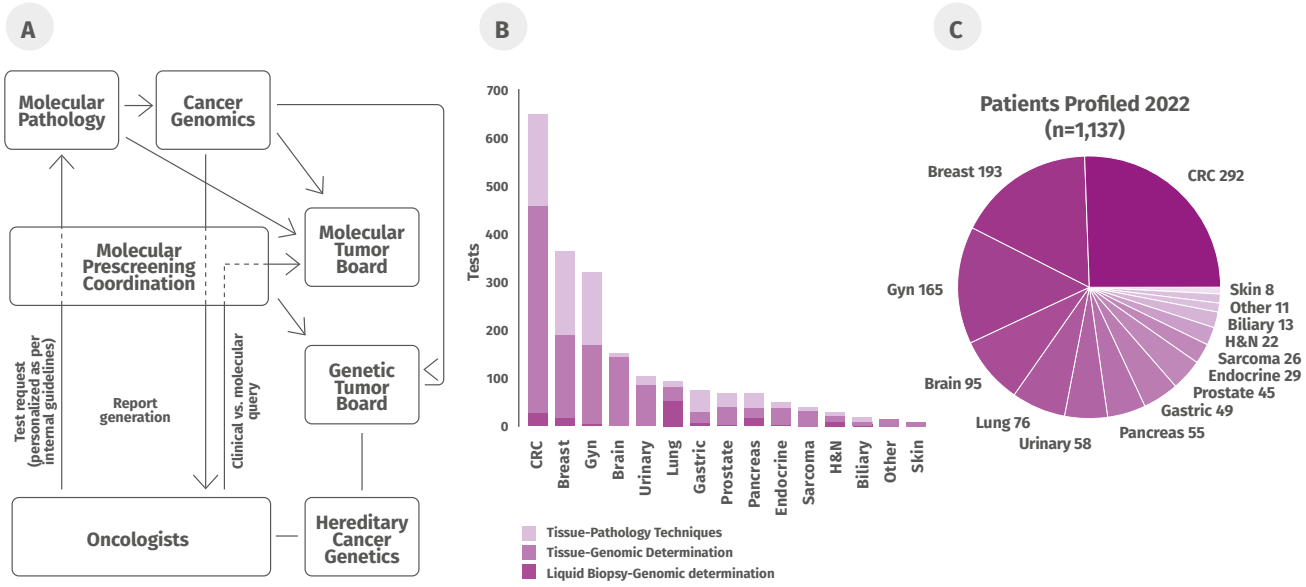


Figure: Molecular Prescreening Program at VHIO. **(A)** Interrelationship between Genomic and Molecular Pathology laboratories with clinical oncologists, and the functionality of the Prescreening Program. **(B)** Number of genomic and proteomic tests per tumor type. **(C)** Distribution of patients profiled in 2022.

/ Paper pick 2022

Verdaguer H, Saurí T, Acosta DA, Guardiola M, Sierra A, Hernando J, Nuciforo P, Miquel JM, Molero C, Peiró S, Serra-Camprubí Q, Villacampa G, Aguilar S, Vivancos A, Tabernero J, Dienstmann R, Macarulla T. ESMO Scale for Clinical Actionability of Molecular Targets Driving Targeted Treatment in Patients with Cholangiocarcinoma. *Clin Cancer Res*. 2022 Apr 14;28(8):1662-1671.

Pugh TJ, Bell JL, Bruce JP, Doherty GJ, Galvin M, Green MF, Hunter-Zinck H, Kumari P, Lenoue-Newton ML, Li MM, Lindsay J, Mazor T, Ovalle A, Sammut SJ, Schultz N, Yu TV, Sweeney SM, Bernard B; AACR Project GENIE Consortium, Genomics and Analysis Working Group. AACR Project GENIE: 100,000 Cases and Beyond. *Cancer Discov*. 2022 Sep 2;12(9):2044-2057.

VHIO's TRANSVERSAL CLINICAL TRIALS CORE SERVICES

Quality & Processes Unit

Director Gemma Sala **Quality Managers** Javier Fonts, Isabel González, Alba Martinez **Quality Technician** Miriam Artigas **Sample Managers** Alma Calahorro, Alba Novella, Gerard Perez, David Vendrell **Schedulers** Laura Abellan, Laura Castejon, Maria Teresa Mendoza, Noelia Moles, Marc Palomar

/ Strategic goals

- Cross-support and common clinical trial tasks including scheduling, sample management, and the direction of quality and processes.
- Collaborate with all teams participating in our clinical trials, detecting non-conformities and making improvements from the very outset.
- Promote prevention versus correction to ensure that the methodologies and improvements implemented.
- Successfully pass all audits and site inspections.
- Standardize processes and generate a good flow of communication between teams, as a key operating element.
- Carry out periodic and predefined quality controls relating to documentation, circuits and procedures.
- Conduct regular training sessions to review and further enhance quality.
- Renew and improve the implementation and development of the Government of Catalonia's Certification of VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 138).
- Develop and update Standard Operating Procedures (SOPs) to standardize circuits, and provide all necessary trainings.
- The organization of in-house courses: Good Clinical Practice (GCP), revision of electrocardiogram (ECG), cardiopulmonary resuscitation (CPR).

/ Highlights

- Clinical trials in oncology and hematology.
- Our Unit has collaborated in more than 600 active trials and we have successfully passed 16 external audits, 12 internal audits and 1 FDA inspection (Food and Drug Administration) in 2022.
- We have actively participated in the revision and improvement of circuits, detecting incidents, proposing corrective actions, and the homogenization and optimization of processes.
- We have also collaborated in the internal training of staff involved in clinical trials.

/ Summary

Headed by Gemma Sala, VHIO's Quality & Processes Unit was established in 2020 to further improve quality and unify processes in clinical trials carried out at VHIO.

Our Unit is made up of quality, and transversal support teams including sample managers and schedulers. We perform numerous tasks related to clinical trials and all of our activities are carried out by assuring excellent quality, ensuring that the processes governing them are both optimal and homogeneous.

Quality is of paramount importance in performing clinical trials. Guaranteeing that all the current regulations of these studies are complied with is therefore essential. These homogeneous efforts follow Good Clinical Practice (GCP) guidelines, with the safety of patients as the top priority throughout.

mobile version

scan to visit

VALL D'HEBRON INSTITUTE OF ONCOLOGY (VHIO)
SCIENTIFIC REPORT 2022

VHIO's Scientific Management Area

VHIO's SCIENTIFIC MANAGEMENT AREA

Scientific Management Area

Head of Area Alejandro Piris Giménez **Scientific Strategy Officer** Javier Carmona **Senior Grants Manager** Sandra Porta **Senior Scientific Managers** Neus Bayó, Javier Gonzalo, Josep Maria Miquel, Xenia Villalobos **Senior Finances & Projects Manager** Elena Chavarria **Senior Clinical Manager (Advanced Therapies)** Silvia Martin-Lluesma **Clinical Projects Manager** Arantxa Romero **Task Force Officers** Ana Carmona (Gastroesophageal Cancer and GI non-CRC), Mireia Sanchís (Colorectal Cancer) **Project Manager Technicians** Senior: Isabel Vallvé, Junior: Sara Belon Ubeda, Berta Colldeforns, Alba López, Marc López, Mireia Monràs **Master's Students** Ariadna Lechón, Raimon Vivancos

/ Strategic goals

- Identify and promote new research opportunities involving academic and industry partners.
- Lead/co-lead EU initiatives/projects – see our highlights below.
- Write, coordinate and manage scientific proposals.
- Launch and monitor institutional research programs.
- Promote intramural research through education, networking and communication programs.

/ Highlights

- In 2022, we maintained a good track record with a success rate of 30%, out of 208 grant (competitive) applications.
- Reflective of the research support that we provide to VHIO is our co-authorship of several publications (see Paper pick 2022).
- We have obtained funds from the prestigious AECC's Excellence Program to develop our Advanced Therapies Accelerator AECC Excellence Program (page 13), that will allow us to consolidate as one of the pioneering centers in Spain in the development of cancer cell therapies.
- We co-lead major EU consortia. Just some of these include the Coordination and Support Action (CSA – 4.UNCAN.eu) of the UNderstand CANcer (UNCAN.eu – page 198), the Cancer Core Europe (CCE) consortium's CCE-DART project – the first H2020 grant awarded to CCE, and CCE's Basket of Baskets (page 185). We are also collaborating with numerous project boards and are in involved in several other work packages.
- We have provided support to our Scientific Direction through the management of scientific data and all the necessary documentation and actions required to develop research proposals. Additionally, together with VHIO's Business Development Area we have secured funding for 8 collaborative private-public projects from the Ministerio de Asuntos Económicos y Transformación Digital – MINECO (Spanish Ministry of Economic Affairs and Digital Transformation), among many others.

/ Summary

VHIO's Scientific Management Area is a strategic Unit that supports our leadership and promotes the scientific activity of our research groups by facilitating the development and execution of scientific proposals and programs. In addition, we coordinate the activities of VHIO's Task Forces (page 130) to foster synergies between our multidisciplinary teams and spur joint research programs in oncology at the Vall d'Hebron University Hospital – HUVH (Vall d'Hebron Barcelona Hospital Campus).

Our responsibilities include financial and scientific management, strategic scientific support, and the implementation of institutional actions across transversal areas such as education, ethics and regulatory issues, scientific dissemination, and the coordination of research activities related to VHIO's participation in several consortia and partnerships globally. Additional activities include the assessment and preparation of grant application proposals, dissemination of national and international funding opportunities for our research groups, as well as the continued monitoring and coordination of awarded research projects, among others.

Our group further optimizes opportunities for the internationalization of researchers by devising personalized plans for VHIO's scientific groups, centralizes and conceptualizes research proposals from our Task Forces, and proactively matches selected research priorities with competitive calls. Importantly, we lead and co-lead EU initiatives including the Coordination and Support Action (CSA – 4.UNCAN.eu) of the UNderstand CANcer (UNCAN.eu) project linked to the EU's Horizon Europe Mission on Cancer, among others. We also spearhead highly innovative technological project proposals to increase VHIO's success rate in calls, such as the Innovative Health Initiative (IHI) within the Horizon Europe framework, and oversee VHIO's involvement in European projects as project coordinators or partners.

Lastly, our Area is continuously working to enhance its organizational structure and project management processes with the goal of expanding VHIO's capacity to conduct research of excellence in oncology.

/ Paper pick 2022

Elez E, Ros J, Fernández J, Villacampa G, Moreno-Cárdenas AB, Arenillas C, Bernatowicz K, Comas R, Li S, Kodack DP, Fasani R, Garcia A, Gonzalo-Ruiz J, Piris-Gimenez A, Nuciforo P, Kerr G, Intini R, Montagna A, Germani MM, Randon G, Vivancos A, Smits R, Graus D, Perez-Lopez R, Cremolini C, Lonardi S, Pietrantonio F, Dienstmann R, Tabernero J, Toledo RA. RNF43 mutations predict response to anti-BRAF/EGFR combinatory therapies in BRAFV600E metastatic colorectal cancer. *Nat Med*. 2022 Oct;28(10):2162-2170.

Tamborero D, Dienstmann R, Rachid MH, Boekel J, Lopez-Fernandez A, Jonsson M, Razzak A, Braña I, De Petris L, Yachnin J, Baird RD, Loriot Y, Massard C, Martin-Romano P, Opdam F, Schlenk RF, Vernieri C, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium; Balmaña J, Apolone G, Caldas C, Bergh J, Ernberg I, Fröhling S, Garralda E, Karlsson C, Tabernero J, Voest E, Rodon J, Lehtiö J. The Molecular Tumor Board Portal supports clinical decisions and automated reporting for precision oncology. *Nat Cancer*. 2022 Feb;3(2):251-261.

Verdaguer H, Saurí T, Acosta DA, Guardiola M, Sierra A, Hernando J, Nuciforo P, Miquel JM, Molero C, Peiró S, Serra-Camprubí Q, Villacampa G, Aguilar S, Vivancos A, Tabernero J, Dienstmann R, Macarulla T. ESMO Scale for Clinical Actionability of Molecular Targets Driving Targeted Treatment in Patients with Cholangiocarcinoma. *Clin Cancer Res*. 2022 Apr 14;28(8):1662-1671.

Monti M, Degenhardt T, Brain E, Wuerstlein R, Argusti A, Puntoni M, Rollandi GA, Corradengo D, Boni L, Ilhan H, Nanni O, Cortes J, Piris-Gimenez A, Piccardo A, Iacozzi M, Matteucci F, Di Iorio V, Alberini JL, Schröder C, Harbeck N, Gennari A. ERANET JTC 2011: Submission and Activation of an International Academic Translational Project in Advanced Breast Cancer. Experience From the ET-FES Study. *Front Med (Lausanne)*. 2022 Jan 13;8:817678.

VHIO's SCIENTIFIC MANAGEMENT AREA

VHIO Academy

Head of the VHIO Academy Imma Falero **Academic Officer** Natàlia Molner **Training Officer** Thomas Guegan
VHIO Academy Scientific Chairs Maria Abad, Elena Élez, César Serrano

/ Area summary

One of VHIO's main missions is to train and inspire the next generation of leading cancer researchers and medical doctors in oncology to drive research and innovation and tackle the societal challenges of tomorrow.

Established in September 2021, the VHIO Academy encompasses all educational programs at our Institute to attract young talent globally and provide state-of-the-art training and career development activities. These learning opportunities aim to equip and empower VHIO fellows to reach their full potential.

A broad portfolio of complementary courses ranging from scientific to vocational training is available to further promote professional growth and assist fellows to make informed decisions about their next career steps.

/ Strategic goals

- Develop cancer-focused educational programs and manage mentoring and training activities to help VHIO members further their education and careers, as well as foster a training environment of excellence.
- Launch and manage institutional academic programs aimed at attracting talented professionals in the field of oncology.
- Increase and consolidate collaborations with Comprehensive Cancer Centers (CCCs) and international cancer research consortia to further expand our educational activities, network of collaborators, as well as foster and promote the mobility of researchers and clinicians at international level.
- Establish new initiatives to strengthen and reinforce the sense of belonging to the VHIO community.
- Reinforce internal & external scientific communication and dissemination of cancer research findings.

/ Highlights

- Launch of the Institutional VHIO Academic Programs (Mobility, Bachelor, Master, PhD Calls) and implementation of an Open, Transparent, Merit-Based Recruitment Process for these progams.
- Implementation of a structured VHIO International PhD Program (+ 100 PhD students) within the frame of a Comprehensive Cancer Center and adhering to the principles of interdisciplinarity and internationality, early independence and scientific creativity, excellence in science and technology, collaboration, mentoring and peer mentoring.
- Launch of the VHIO Advanced Training Program (Scientific and Transferable skills training open to the VHIO Community).
- Creation of the Institutional Moodle VHIO e-Learning Platform.
- Coordination of the VHIO – CaixaResearch Scientific Seminars Series (pages 31-33).

Full listing of articles published by VHIO investigators in 2022

Articles published by VHIO investigators in 2022 with allocated Impact Factor (Web of Science):

Antibody-drug conjugates: Smart chemotherapy delivery across tumor histologies. Tarantino P, Carmagnani Pestana R, Corti C, Modi S, Bardia A, Tolaney SM, Cortes J, Soria JC, Curigliano G. Antibody-drug conjugates: Smart chemotherapy delivery across tumor histologies. *CA Cancer J Clin*. 2022 Mar;72(2):165-182. IF: 286,130.

Adjuvant atezolizumab versus placebo for patients with renal cell carcinoma at increased risk of recurrence following resection (IMmotion010): a multicentre, randomised, double-blind, phase 3 trial. Pal SK, Uzzo R, Karam JA, Master VA, Donskov F, Suarez C, Albiges L, Rini B, Tomita Y, Kann AG, Procopio G, Massari F, Zibelman M, Antonyan I, Huseni M, Basu D, Ci B, Leung W, Khan O, Dubey S, Bex A. *Lancet*. 2022 Oct 1;400(10358):1103-1116. IF: 202,731.

Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design. Fizazi K, Foulon S, Carles J, Roubaud G, McDermott R, Fléchon A, Tombal B, Supiot S, Berthold D, Ronchin P, Kacso G, Gravis G, Calabro F, Berdah JF, Hasbini A, Silva M, Thiery-Vuillemin A, Latorzeff I, Mourey L, Laguerre B, Abadie-Lacourtoisie S, Martin E, El Kouri C, Escande A, Rosello A, Magne N, Schlurmann F, Priou F, Chand-Fouche ME, Freixa SV, Jamaluddin M, Rieger I, Bossi A; PEACE-1 investigators. *Lancet*. 2022 Apr 30;399(10336):1695-1707. IF: 202,731.

Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. Dickinson MJ, Carlo-Stella C, Morschhauser F, Bachy E, Corradini P, Iacoboni G, Khan C, Wróbel T, Offner F, Trněný M, Wu SJ, Cartron G, Hertzberg M, Sureda A, Perez-Callejo D, Lundberg L, Relf J, Dixon M, Clark E, Humphrey K, Hutchings M. *N Engl J Med*. 2022 Dec 15;387(24):2220-2231. IF: 176,079.

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer. Modi S, Jacot W, Yamashita T, Sohn J, Vidal M, Tokunaga E, Tsurutani J, Ueno NT, Prat A, Chae YS, Lee KS, Niikura N, Park YH, Xu B, Wang X, Gil-Gil M, Li W, Pierga JY, Im SA, Moore HCF, Rugo HS, Yerushalmi R, Zagouri F, Gombos A, Kim SB, Liu Q, Luo T, Saura C, Schmid P, Sun T, Gambhire D, Yung L, Wang Y, Singh J, Vitazka P, Meinhardt G, Harbeck N, Cameron DA; DESTINY-Breast04 Trial Investigators. *N Engl J Med*. 2022 Jul 7;387(1):9-20. IF: 176,079.

Trastuzumab Deruxtecan for Breast Cancer. Reply. Cortés J, Im SA, Cathcart J. *N Engl J Med*. 2022 Jun 16;386(24):2347. IF: 176,079.

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. Forde PM, Spicer J, Lu S, Provencio M, Mitsudomi T, Awad MM, Felip E, Broderick SR, Brahmer JR, Swanson SJ, Kerr K, Wang C, Ciuleanu TE, Saylors GB, Tanaka F, Ito H, Chen KN, Liberman M, Vokes EE, Taube JM, Dorange C, Cai J, Fiore J, Jarkowski A, Balli D, Sausen M, Pandya D, Calvet CY, Girard N; CheckMate 816 Investigators. *N Engl J Med*. 2022 May 26;386(21):1973-1985. IF: 176,079.

Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma. Bishop MR, Dickinson M, Purtill D, Barba P, Santoro A, Hamad N, Kato K, Sureda A, Greil R, Thieblemont C, Morschhauser F, Janz M, Flinn I, Rabitsch W, Kwong YL, Kersten MJ, Minnema MC, Holte H, Chan EHL, Martinez-Lopez J, Müller AMS, Maziarz RT, McGuirk JP, Bachy E, Le Gouill S, Dreyling M, Harigae H, Bond D, Andreadis C, McSweeney P, Kharfan-Dabaja M, Newsome S, Degtyarev E, Awasthi R, Del Corral C, Andreola G, Masood A, Schuster SJ, Jäger U, Borchmann P, Westin JR. *N Engl J Med*. 2022 Feb 17;386(7):629-639. IF: 176,079.

Event-free Survival with Pembrolizumab in Early Triple-Negative Breast Cancer. Schmid P, Cortes J, Dent R, Pusztai L, McArthur H, Kümmel S, Bergh J, Denkert C, Park YH, Hui R, Harbeck N, Takahashi M, Untch M, Fasching PA, Cardoso F, Andersen J, Patt D, Danso M, Ferreira M, Mouret-Reynier MA, Im SA, Ahn JH, Gion M, Baron-Hay S, Boileau JF, Ding Y, Tryfonidis K, Aktan G, Karantza V, O'Shaughnessy J; KEYNOTE-522 Investigators. *N Engl J Med*. 2022 Feb 10;386(6):556-567. IF: 176,079.

Survival with Cemiplimab in Recurrent Cervical Cancer. Tewari KS, Monk BJ, Vergote I, Miller A, de Melo AC, Kim HS, Kim YM, Lisyanskaya A, Samouëlian V, Lorusso D, Damian F, Chang CL, Gotovkin EA, Takahashi S, Ramone D, Pikiel J, Maćkowiak-Matejczyk B, Guerra Alía EM, Colombo N, Makarova Y, Rischin D, Lheureux S, Hasegawa K, Fujiwara K, Li J, Jamil S, Jankovic V, Chen CI, Seebach F, Weinreich DM, Yancopoulos GD, Lowy I, Mathias M, Fury MG, Oaknin A; Investigators for GOG Protocol 3016 and ENGOT Protocol En-Cx9. *N Engl J Med*. 2022 Feb 10;386(6):544-555. IF: 176,079.

Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma. Tilly H, Morschhauser F, Sehn LH, Friedberg JW, Trněný M, Sharman JP, Herbaux C, Burke JM, Matasar M, Rai S, Izutsu K, Mehta-Shah N, Oberic L, Chauchet A, Jurczak W, Song Y, Greil R, Mykhalska L, Bergua-Burgués JM, Cheung MC, Pinto A, Shin HJ, Hapgood G, Munhoz E, Abrisqueta P, Gau JP, Hirata J, Jiang Y, Yan M, Lee C, Flowers CR, Salles G. *N Engl J Med*. 2022 Jan 27;386(4):351-363. IF: 176,079.

Trastuzumab Deruxtecan in HER2-Mutant Non-Small-Cell Lung Cancer. Li BT, Smit EF, Goto Y, Nakagawa K, Udagawa H, Mazières J, Nagasaka M, Bazhenova L, Saltos AN, Felip E, Pacheco JM, Pérol M, Paz-Ares L, Saxena K, Shiga R, Cheng Y, Acharyya S, Vitazka P, Shahidi J, Planchard D, Jänne PA; DESTINY-Lung01 Trial Investigators. *N Engl J Med*. 2022 Jan 20;386(3):241-251. IF: 176,079.

Circulating tumor DNA as a novel prognostic indicator. Vivancos A, Tabernero J. *Nat Med*. 2022 Nov;28(11):2255-2256. IF: 87,241.

RNF43 mutations predict response to anti-BRAF/EGFR combinatory therapies in BRAFV600E metastatic colorectal cancer. Elez E, Ros J, Fernández J, Villacampa G, Moreno-Cárdenas AB, Arenillas C, Bernatowicz K, Comas R, Li S, Kodack DP, Fasani R, Garcia A, Gonzalo-Ruiz J, Piris-Gimenez A, Nuciforo P, Kerr G, Intini R, Montagna A, Germani MM, Randon G, Vivancos A, Smits R, Graus D, Perez-Lopez R, Cremolini C, Lonardi S, Pietrantonio F, Dienstmann R, Tabernero J, Toledo RA. *Nat Med*. 2022 Oct;28(10):2162-2170. IF: 87,241.

A biomarker of response to therapy in metastatic BRAFV600E colorectal cancers. Toledo RA, Elez E. *Nat Med*. 2022 Oct;28(10):2015-2016. IF: 87,241.

Atezolizumab versus chemotherapy in advanced or metastatic NSCLC with high blood-based tumor mutational burden: primary analysis of BFAST cohort C randomized phase 3 trial. Peters S, Dziadziuszko R, Morabito A, Felip E, Gadgeel SM, Cheema P, Cobo M, Andric Z, Barrios CH, Yamaguchi M, Dansin E, Danchaivijitr P, Johnson M, Novello S, Mathisen MS, Shagan SM, Schleifman E, Wang J, Yan M, Mocci S, Voong D, Fabrizio DA, Shames DS, Riehl T, Gandara DR,

Mok T. *Nat Med*. 2022 Sep;28(9):1831-1839. IF: 87,241.

Pan-cancer efficacy of pralsetinib in patients with RET fusion-positive solid tumors from the phase 1/2 ARROW trial. Subbiah V, Cassier PA, Siena S, Garralda E, Paz-Ares L, Garrido P, Nadal E, Vuky J, Lopes G, Kalemkerian GP, Bowles DW, Seetharam M, Chang J, Zhang H, Green J, Zalutskaya A, Schuler M, Fan Y, Curigliano G. *Nat Med*. 2022 Aug;28(8):1640-1645. IF: 87,241.

Detection of early seeding of Richter transformation in chronic lymphocytic leukemia. Nadeu F, Royo R, Massoni-Badosa R, Playa-Albinyana H, Garcia-Torre B, Duran-Ferrer M, Dawson KJ, Kulis M, Diaz-Navarro A, Villamor N, Melero JL, Chapaprieta V, Dueso-Barroso A, Delgado J, Moia R, Ruiz-Gil S, Marchese D, Giró A, Verdaguer-Dot N, Romo M, Clot G, Rozman M, Frigola G, Rivas-Delgado A, Baumann T, Alcoceba M, González M, Climent F, Abrisqueta P, Castellví J, Bosch F, Aymerich M, Enjuanes A, Ruiz-Gaspà S, López-Guillermo A, Jares P, Beà S, Capella-Gutierrez S, Gelpí JL, López-Bigas N, Torrents D, Campbell PJ, Gut I, Rossi D, Gaidano G, Puente XS, Garcia-Roves PM, Colomer D, Heyn H, Maura F, Martín-Subero JI, Campo E. *Nat Med*. 2022 Aug;28(8):1662-1671. IF: 87,241.

Delivering precision oncology to patients with cancer. Mateo J, Steuten L, Aftimos P, André F, Davies M, Garralda E, Geissler J, Husereau D, Martinez-Lopez I, Normanno N, Reis-Filho JS, Stefani S, Thomas DM, Westphalen CB, Voest E. *Nat Med*. 2022 Apr;28(4):658-665. IF: 87,241.

Cerebrospinal fluid liquid biopsies for medulloblastoma. Seoane J, Escudero L. *Nat Rev Clin Oncol*. 2022 Feb;19(2):73-74. IF: 65,011.

Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB-IIIA non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial. O'Brien M, Paz-Ares L, Marreaud S, Dafni U, Oselin K, Havel L, Esteban E, Isla D, Martinez-Marti A, Faehling M, Tsuboi M, Lee JS, Nakagawa K, Yang J, Samkari A, Keller SM, Mauer M, Jha N, Stahel R, Besse B, Peters S; EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 Investigators. *Lancet Oncol*. 2022 Oct;23(10):1274-1286. IF: 54,433.

CNS prophylaxis for diffuse large B-cell lymphoma. Eyre TA, Savage KJ, Cheah CY, El-Galaly TC, Lewis KL, McKay P, Wilson MR, Evens AM, Bobillo S, Villa D, Maurer MJ, Cwynarski K, Ferreri AJM. *Lancet Oncol*. 2022 Sep;23(9):e416-e426. IF: 54,433.

Is upfront full molecular profiling needed in all patients with colorectal cancer in daily practice? Dienstmann R, Lonardi S. *Lancet Oncol*. 2022 Sep;23(9):1129-1131. IF: 54,433.

Outcomes of the SARS-CoV-2 omicron (B.1.1.529) variant outbreak among vaccinated and unvaccinated patients with cancer in Europe: results from the retrospective, multicentre, OnCovid registry study. Pinato DJ, Aguilar-Company J, Ferrante D, Hanbury G, Bower M, Salazar R, Mirallas O, Sureda A, Plaja A, Cucurull M, Mesia R, Townsend S, Jackson A, Dalla Pria A, Newsom-Davis T, Handford J, Sita-Lumsden A, Apthorp E, Vincenzi B, Bertuzzi A, Brunet J, Lambertini M, Maluquer C, Pedrazzoli P, Biello F, Sinclair A, Bawany S, Khalique S, Rossi S, Rogers L, Murphy C, Belessiotis K, Carmona-García MC, Sharkey R, García-Illescas D, Rizzo G, Perachino M, Saoudi-Gonzalez N, Doonga K, Fox L, Roldán E, Gaidano G, Ruiz-Camps I, Bruna R, Patriarca A, Martinez-Vila C, Cantini L, Zambelli A, Giusti R, Mazzoni F, Caliman E, Santoro A, Grosso F, Parisi A, Queirolo P, Aujayeb A, Rimassa L, Prat A, Tucci M, Libertini M, Grisanti S, Mukherjee U, Diamantis N, Fusco V, Generali D, Provenzano S, Gennari A, Tabernero J, Cortellini A; OnCovid study group. *Lancet Oncol*. 2022 Jul;23(7):865-875. IF: 54,433.

Immunotherapy in colorectal cancer: an unmet need deserving of change. Elez E, Baraibar I. *Lancet Oncol*. 2022 Jul;23(7):830-831. IF: 54,433.

Nivolumab plus cabozantinib versus sunitinib in first-line treatment for advanced renal cell carcinoma (CheckMate 9ER): long-term follow-up results from an open-label, randomised, phase 3 trial. Motzer RJ, Powles T, Burotto M, Escudier B, Bourlon MT, Shah AY, Suárez C, Hamzaj A, Porta C, Hocking CM, Kessler ER, Gurney H, Tomita Y, Bedke J, Zhang J, Simsek B, Scheffold C, Apolo AB, Choueiri TK. *Lancet Oncol*. 2022 Jul;23(7):888-898. IF: 54,433.

Pembrolizumab versus chemotherapy for microsatellite instability-high or mismatch repair-deficient metastatic colorectal cancer (KEYNOTE-177): final analysis of a randomised, open-label, phase 3 study. Diaz LA Jr, Shiu KK, Kim TW, Jensen BV, Jensen LH, Punt C, Smith D, Garcia-Carbonero R, Benavides M, Gibbs P, de la Fourchardiere C, Rivera F, Elez E, Le DT, Yoshino T, Zhong WY, Fogelman D, Marinello P, Andre T; KEYNOTE-177 Investigators. *Lancet Oncol*. 2022 May;23(5):659-670. IF: 54,433.

Rucaparib versus standard-of-care chemotherapy in patients with relapsed ovarian cancer and a deleterious BRCA1 or BRCA2 mutation (ARIEL4): an international, open-label, randomised, phase 3 trial. Kristeleit R, Lisyanskaya A, Fedenko A, Dvorkin M, de Melo AC, Shparyk Y, Rakhmatullina I, Bondarenko I, Colombo N, Svintsitskiy V, Biela L, Nechaeva M, Lorusso D, Scambia G, Cibula D, Póka R, Oaknin A, Safra T, Mackowiak-Matejczyk B, Ma L, Thomas D, Lin KK, McLachlan K, Goble S, Oza AM. *Lancet Oncol*. 2022 Apr;23(4):465-478. IF: 54,433.

Anetumab ravtansine versus vinorelbine in patients with relapsed, mesothelin-positive malignant pleural mesothelioma (ARCS-M): a randomised, open-label phase 2 trial. Kindler HL, Novello S, Bearz A, Ceresoli GL, Aerts JGJV, Spicer J, Taylor P, Nackaerts K, Greystoke A, Jennens R, Calabrò L, Burgers JA, Santoro A, Cedrés S, Serwatowski P, Ponce S, Van Meerbeeck JP, Nowak AK, Blumenschein G Jr, Siegel JM, Kasten L, Köchert K, Walter AO, Childs BH, Elbi C, Hassan R, Fennell DA. *Lancet Oncol*. 2022 Apr;23(4):540-552. IF: 54,433.

Niraparib in patients with metastatic castration-resistant prostate cancer and DNA repair gene defects (GALAHAD): a multicentre, open-label, phase 2 trial. Smith MR, Scher HI, Sandhu S, Efstathiou E, Lara PN Jr, Yu EY, George DJ, Chi KN, Saad F, Ståhl O, Olmos D, Danila DC, Mason GE, Espina BM, Zhao X, Urtishak KA, Francis P, Lopez-Gitlitz A, Fizazi K; GALAHAD investigators. *Lancet Oncol*. 2022 Mar;23(3):362-373.IF: 54,433.

Efficacy and safety of erdafitinib in patients with locally advanced or metastatic urothelial carcinoma: long-term follow-up of a phase 2 study. Siefker-Radtke AO, Necchi A, Park SH, García-Donas J, Huddart RA, Burgess EF, Fleming MT, Rezazadeh Kalebasty A, Mellado B, Varlamov S, Joshi M, Duran I, Tagawa ST, Zakharia Y, Akapame S, Santiago-Walker AE, Monga M, O'Hagan A, Loriot Y; BLC2001 Study Group. *Lancet Oncol*. 2022 Feb;23(2):248-258. IF: 54,433.

Patient-reported outcomes with first-line nivolumab plus cabozantinib versus sunitinib in patients with advanced renal cell carcinoma treated in CheckMate 9ER: an open-label, randomised, phase 3 trial. Cella D, Motzer RJ, Suarez C, Blum SI, Ejzykowicz F, Hamilton M, Wallace JF, Simsek B, Zhang J, Ivanescu C, Apolo AB, Choueiri TK. *Lancet Oncol*. 2022 Feb;23(2):292-303. IF: 54,433.

Overall survival in the OlympiA phase III trial of adjuvant olaparib in patients with germline pathogenic variants in BRCA1/2 and high-risk, early breast cancer. Geyer CE Jr, Garber JE, Gelber RD, Yothers G, Taboada M, Ross L, Rastogi P, Cui K, Arahmani A, Aktan G, Armstrong AC, Arnedos M, Balmaña J, Bergh J, Bliss J, Delaloge S, Domchek SM, Eisen A, Elsafy F, Fein LE, Fielding A, Ford JM, Friedman S, Gelmon KA, Gianni L, Gnant M, Hollingsworth SJ, Im SA, Jager A, Jóhannsson ÓÞ, Lakhani SR, Janni W, Linderholm B, Liu TW, Loman N, Korde L, Loibl S, Lucas PC, Marmé F, Martinez

de Dueñas E, McConnell R, Phillips KA, Piccart M, Rossi G, Schmutzler R, Senkus E, Shao Z, Sharma P, Singer CF, Španić T, Stickeler E, Toi M, Traina TA, Viale G, Zoppoli G, Park YH, Yerushalmi R, Yang H, Pang D, Jung KH, Mailliez A, Fan Z, Tennevet I, Zhang J, Nagy T, Sonke GS, Sun Q, Parton M, Colleoni MA, Schmidt M, Brufsky AM, Razaq W, Kaufman B, Cameron D, Campbell C, Tutt ANJ; OlympiA Clinical Trial Steering Committee and Investigators. *Ann Oncol.* 2022 Dec;33(12):1250-1268. IF: 51,769.

Safety and efficacy of pralsetinib in RET fusion-positive non-small-cell lung cancer including as first-line therapy: update from the ARROW trial. Griesinger F, Curigliano G, Thomas M, Subbiah V, Baik CS, Tan DSW, Lee DH, Misch D, Garralda E, Kim DW, van der Wekken AJ, Gainor JF, Paz-Ares L, Liu SV, Kalemkerian GP, Houvras Y, Bowles DW, Mansfield AS, Lin JJ, Smoljanovic V, Rahman A, Kong S, Zalutskaya A, Louie-Gao M, Boral AL, Mazières J. *Ann Oncol.* 2022 Nov;33(11):1168-1178.IF: 51,769.

Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Obermannová R, Alsina M, Cervantes A, Leong T, Lordick F, Nilsson M, van Grieken NCT, Vogel A, Smyth EC; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. *Ann Oncol.* 2022 Oct;33(10):992-1004. IF: 51,769.

Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Oaknin A, Bosse TJ, Creutzberg CL, Giornelli G, Harter P, Joly F, Lorusso D, Marth C, Makker V, Mirza MR, Ledermann JA, Colombo N; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. *Ann Oncol.* 2022 Sep;33(9):860-877. IF: 51,769.

ESMO recommendations on the use of circulating tumour DNA assays for patients with cancer: a report from the ESMO Precision Medicine Working Group. Pascual J, Attard G, Bidard FC, Curigliano G, De Mattos-Arruda L, Diehn M, Italiano A, Lindberg J, Merker JD, Montagut C, Normanno N, Pantel K, Pentheroudakis G, Popat S, Reis-Filho JS, Tie J, Seoane J, Tarazona N, Yoshino T, Turner NC. *Ann Oncol.* 2022 Aug;33(8):750-768. IF: 51,769.

3-Year CheckMate743 outcomes: ringing in immunotherapy for the treatment of malignant pleural mesothelioma. Cedres S, Felip E. *Ann Oncol.* 2022 May;33(5):457-459. IF: 51,769.

Effectiveness of PD-(L)1 inhibitors alone or in combination with platinum-doublet chemotherapy in first-line (1L) non-squamous non-small-cell lung cancer (Nsq-NSCLC) with PD-L1-high expression using real-world data. Pérol M, Felip E, Dafni U, Polito L, Pal N, Tsourti Z, Ton TGN, Merritt D, Morris S, Stahel R, Peters S. *Ann Oncol.* 2022 May;33(5):511-521. IF: 51,769.

ESMO expert consensus statements on the management of EGFR mutant non-small-cell lung cancer. Passaro A, Leighl N, Blackhall F, Popat S, Kerr K, Ahn MJ, Arcila ME, Arrieta O, Planchard D, de Marinis F, Dingemans AM, Dziadziuszko R, Faivre-Finn C, Feldman J, Felip E, Curigliano G, Herbst R, Jänne PA, John T, Mitsudomi T, Mok T, Normanno N, Paz-Ares L, Ramalingam S, Sequist L, Vansteenkiste J, Wistuba II, Wolf J, Wu YL, Yang SR, Yang JCH, Yatabe Y, Pentheroudakis G, Peters S. *Ann Oncol.* 2022 May;33(5):466-487. IF: 51,769.

Safety, pharmacokinetics, and antitumor activity of the anti-CEACAM5-DM4 antibody-drug conjugate tusamitamab ravtansine (SAR408701) in patients with advanced solid tumors: first-in-human dose-escalation study. Gazzah A, Bedard PL, Hierro C, Kang YK, Abdul Razak A, Ryu MH, Demers B, Fagniez N, Henry C, Hospitel M, Soria JC, Tabernero J. *Ann Oncol.* 2022 Apr;33(4):416-425. IF: 51,769.

VP3-2022: Pembrolizumab (pembro) versus placebo for early-stage non-small cell lung cancer (NSCLC) following complete resection and adjuvant chemotherapy (chemo) when indicated: Randomized, triple-blind, phase III EORTC-1416-LCG/ETOP 8-15 e PEARLS/KEYNOTE-091 study. Paz-Ares L, O'Brien MER, Mauer M, Dafni U, Oselin K, Havel L, Gonzalez EE, Isla D, Martinez A, Faehling M, Tsuboi M, Lee J-S, Nakagawa K, Yang J, Keller SM, Jha N, Marreaud SI, Stahel RA, Peters S, Besse B. *Ann Oncol.* 2022. 33(4): 451-453. IF: 51,769.

A Randomized, Phase III Trial to Evaluate Rucaparib Monotherapy as Maintenance Treatment in Patients With Newly Diagnosed Ovarian Cancer (ATHENA-MONO/GOG-3020/ENGOT-ov45). Monk BJ, Parkinson C, Lim MC, O'Malley DM, Oaknin A, Wilson MK, Coleman RL, Lorusso D, Bessette P, Ghamande S, Christopoulou A, Provencher D, Prendergast E, Demirkiran F, Mikheeva O, Yeku O, Chudecka-Glaz A, Schenker M, Littell RD, Safra T, Chou HH, Morgan MA, Drochýtek V, Barlin JN, Van Gorp T, Ueland F, Lindahl G, Anderson C, Collins DC, Moore K, Marme F, Westin SN, McNeish IA, Shih D, Lin KK, Goble S, Hume S, Fujiwara K, Kristeleit RS. *J Clin Oncol.* 2022 Dec 1;40(34):3952-3964. IF: 50,717.

Overall Survival Results From the POLO Trial: A Phase III Study of Active Maintenance Olaparib Versus Placebo for Germline BRCA-Mutated Metastatic Pancreatic Cancer. Kindler HL, Hammel P, Reni M, Van Cutsem E, Macarulla T, Hall MJ, Park JO, Hochhauser D, Arnold D, Oh DY, Reinacher-Schick A, Tortora G, Algül H, O'Reilly EM, Bordia S, McGuinness D, Cui K, Locker GY, Golan T. *J Clin Oncol.* 2022 Dec 1;40(34):3929-3939. IF: 50,717.

COAST: An Open-Label, Phase II, Multidrug Platform Study of Durvalumab Alone or in Combination With Oleclumab or Monalizumab in Patients With Unresectable, Stage III Non-Small-Cell Lung Cancer. Herbst RS, Majem M, Barlesi F, Carcereny E, Chu Q, Monnet I, Sanchez-Hernandez A, Dakhil S, Camidge DR, Winzer L, Soo-Hoo Y, Cooper ZA, Kumar R, Bothos J, Aggarwal C, Martinez-Marti A. *J Clin Oncol.* 2022 Oct 10;40(29):3383-3393. IF: 50,717.

Sacituzumab Govitecan in Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer. Rugo HS, Bardia A, Marmé F, Cortes J, Schmid P, Loirat D, Trédan O, Ciruelos E, Dalenc F, Pardo PG, Jhaveri KL, Delaney R, Fu O, Lin L, Verret W, Tolaney SM. *J Clin Oncol.* 2022 Oct 10;40(29):3365-3376. IF: 50,717.

Elacestrant (oral selective estrogen receptor degrader) Versus Standard Endocrine Therapy for Estrogen Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer: Results From the Randomized Phase III EMERALD Trial. Bidard FC, Kaklamani VG, Neven P, Streich G, Montero AJ, Forget F, Mouret-Reynier MA, Sohn JH, Taylor D, Harnden KK, Khong H, Kocsis J, Dalenc F, Dillon PM, Babu S, Waters S, Deleu I, García Sáenz JA, Bria E, Cazzaniga M, Lu J, Aftimos P, Cortés J, Liu S, Tonini G, Laurent D, Habboubi N, Conlan MG, Bardia A. *J Clin Oncol.* 2022 Oct 1;40(28):3246-3256. IF: 50,717.

Overall Survival and Biomarker Analysis of Neoadjuvant Nivolumab Plus Chemotherapy in Operable Stage IIIA Non-Small-Cell Lung Cancer (NADIM phase II trial). Provencio M, Serna-Blasco R, Nadal E, Insa A, García-Campelo MR, Casal Rubio J, Dómine M, Majem M, Rodríguez-Abreu D, Martínez-Martí A, De Castro Carpeño J, Cobo M, López Vivanco G, Del Barco E, Bernabé Caro R, Viñolas N, Barneto Aranda I, Viteri S, Pereira E, Royuela A, Calvo V, Martín-López J, García-García F, Casarrubios M, Franco F, Sánchez-Herrero E, Massuti B, Cruz-Bermúdez A, Romero A. *J Clin Oncol.* 2022 Sep 1;40(25):2924-2933. IF: 50,717.

Pembrolizumab Alone or With Chemotherapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma in KEYNOTE-048: Subgroup Analysis by Programmed Death Ligand-1 Combined Positive Score. Burtness B, Rischin D, Greil R, Soulières D, Tahara M, de Castro G Jr, Psyrri A, Brana I, Basté N, Neupane P, Bratland Å, Fuereder T, Hughes BGM, Mesia R, Ngamphaiboon N, Rordorf T, Wan Ishak WZ, Ge J, Swaby RF,

Gumuscu B, Harrington K. *J Clin Oncol.* 2022 Jul 20;40(21):2321-2332. IF: 50,717.

Ibrutinib in Combination With Rituximab for Indolent Clinical Forms of Mantle Cell Lymphoma (IMCL-2015): A Multicenter, Open-Label, Single-Arm, Phase II Trial. Giné E, de la Cruz F, Jiménez Ubieto A, López Jimenez J, Martín García-Sancho A, Terol MJ, González Barca E, Casanova M, de la Fuente A, Marín-Niebla A, Muntañola A, González-López TJ, Aymerich M, Setoain X, Cortés-Romera M, Rotger A, Rodríguez S, Medina Herrera A, García Sanz R, Nadeu F, Beà S, Campo E, López-Guillermo A . *J Clin Oncol.* 2022 Apr 10;40(11):1196-1205. IF: 50,717.

Single-Agent Mosunetuzumab Shows Durable Complete Responses in Patients With Relapsed or Refractory B-Cell Lymphomas: Phase I Dose-Escalation Study. Budde LE, Assouline S, Sehn LH, Schuster SJ, Yoon SS, Yoon DH, Matasar MJ, Bosch F, Kim WS, Nastoupil LJ, Flinn IW, Shadman M, Diefenbach C, O'Hear C, Huang H, Kwan A, Li CC, Piccione EC, Wei MC, Yin S, Bartlett NL. *J Clin Oncol.* 2022 Feb 10;40(5):481-491. IF: 50,717.

Adjuvant Palbociclib for Early Breast Cancer: The PALLAS Trial Results (ABCSG-42/AFT-05/BIG-14-03). Gnant M, Dueck AC, Frantal S, Martin M, Burstein HJ, Greil R, Fox P, Wolff AC, Chan A, Winer EP, Pfeiler G, Miller KD, Colleoni M, Suga JM, Rubovsky G, Bliss JM, Mayer IA, Singer CF, Nowecki Z, Hahn O, Thomson J, Wolmark N, Amillano K, Rugo HS, Steger GG, Hernando Fernández de Aránguiz B, Haddad TC, Perelló A, Bellet M, Fohler H, Metzger Filho O, Jallitsch-Halper A, Solomon K, Schurmans C, Theall KP, Lu DR, Tenner K, Fesl C, DeMichele A, Mayer EL; PALLAS groups and investigators. *J Clin Oncol.* 2022 Jan 20;40(3):282-293. IF: 50,717.

Molecular classification and biomarkers of clinical outcome in breast ductal carcinoma in situ: Analysis of TBCRC 038 and RAHBT cohorts. Strand SH, Rivero-Gutiérrez B, Houlahan KE, Seoane JA, King LM, Risom T, Simpson LA, Vennam S, Khan A, Cisneros L, Hardman T, Harmon B, Couch F, Gallagher K, Kilgore M, Wei S, DeMichele A, King T, McAuliffe PF, Nangia J, Lee J, Tseng J, Storniolo AM, Thompson AM, Gupta GP, Burns R, Veis DJ, DeSchryver K, Zhu C, Matusiak M, Wang J, Zhu SX, Tappenden J, Ding DY, Zhang D, Luo J, Jiang S, Varma S, Anderson L, Straub C, Srivastava S, Curtis C, Tibshirani R, Angelo RM, Hall A, Owzar K, Polyak K, Maley C, Marks JR, Colditz GA, Hwang ES, West RB. *Cancer Cell.* 2022 Dec 12;40(12):1521-1536.e7. IF: 38,585.

Fast track to personalized TCR T cell therapies. Levy PL, Gros A. *Cancer Cell.* 2022 May 9;40(5):447-449. IF: 38,585.

Trastuzumab Deruxtecan in HER2-Positive Metastatic Breast Cancer Patients with Brain Metastases: A DESTINY-Breast01 Subgroup Analysis. Jerusalem G, Park YH, Yamashita T, Hurvitz SA, Modi S, Andre F, Krop IE, Gonzàlez Farré X, You B, Saura C, Kim SB, Osborne CR, Murthy RK, Gianni L, Takano T, Liu Y, Cathcart J, Lee C, Perrin C. *Cancer Discov.* 2022 Dec 2;12(12):2754-2762. IF: 38,272.

UNCAN.eu, a European Initiative to UNderstand CANcer. Solary E, Blanc P, Boutros M, Girvalaki C, Locatelli F, Medema RH, Nagy P, Tabernero J. *Cancer Discov.* 2022 Nov 2;12(11):2504-2508. IF: 38,272.

Preclinical Characterization and Phase I Trial Results of a Bispecific Antibody Targeting PD-L1 and 4-1BB (GEN1046) in Patients with Advanced Refractory Solid Tumors. Muik A, Garralda E, Altintas I, Gieseke F, Geva R, Ben-Ami E, Maurice-Dror C, Calvo E, LoRusso PM, Alonso G, Rodriguez-Ruiz ME, Schoedel KB, Blum JM, Sänger B, Salcedo TW, Burm SM, Stanganello E, Verzijl D, Vascotto F, Sette A, Quinkhardt J, Plantinga TS, Toker A, van den Brink EN, Fereshteh M, Diken M, Satijn D, Kreiter S, Breij ECW, Bajaj G, Lagkadinou E, Sasser K, Türeci Ö, Forssmann U, Ahmadi T, Şahin U, Jure-Kunkel M, Melero I. *Cancer Discov.* 2022 May 2;12(5):1248-1265. IF: 38,272.

INK4 Tumor Suppressor Proteins Mediate Resistance to CDK4/6 Kinase Inhibitors. Li Q, Jiang B, Guo J, Shao H, Del Priore IS, Chang Q, Kudo R, Li Z, Razavi P, Liu B, Boghossian AS, Rees MG, Ronan MM, Roth JA, Donovan KA, Palafox M, Reis-Filho JS, de Stanchina E, Fischer ES, Rosen N, Serra V, Koff A, Chodera JD, Gray NS, Chandarlapaty S. *Cancer Discov.* 2022 Feb;12(2):356-371. IF: 38,272.

Futibatinib, an Irreversible FGFR1-4 Inhibitor, in Patients with Advanced Solid Tumors Harboring FGF/FGFR Aberrations: A Phase I Dose-Expansion Study. Meric-Bernstam F, Bahleda R, Hierro C, Sanson M, Bridgewater J, Arkenau HT, Tran B, Kelley RK, Park JO, Javle M, He Y, Benhadji KA, Goyal L. *Cancer Discov.* 2022 Feb;12(2):402-415. IF: 38,272.

Treatment With Etirinotecan Pegol for Patients With Metastatic Breast Cancer and Brain Metastases: Final Results From the Phase 3 ATTAIN Randomized Clinical Trial. Tripathy D, Tolaney SM, Seidman AD, Anders CK, Ibrahim N, Rugo HS, Twelves C, Diéras V, Müller V, Du Y, Currie SL, Hoch U, Tagliaferri M, Hannah AL, Cortés J; ATTAIN Investigators. *JAMA Oncol.* 2022 Jul 1;8(7):1047-1052. IF: 33,006.

Final Overall Survival and Molecular Analysis in IMmotion151, a Phase 3 Trial Comparing Atezolizumab Plus Bevacizumab vs Sunitinib in Patients With Previously Untreated Metastatic Renal Cell Carcinoma. Motzer RJ, Powles T, Atkins MB, Escudier B, McDermott DF, Alekseev BY, Lee JL, Suarez C, Stroyakovskiy D, De Giorgi U, Donskov F, Mellado B, Banchereau R, Hamidi H, Khan O, Craine V, Huseni M, Flinn N, Dubey S, Rini BI. *JAMA Oncol.* 2022 Feb 1;8(2):275-280. IF: 33,006.

Implications of Selection Bias Due to Delayed Study Entry in Clinical Genomic Studies. Brown S, Lavery JA, Shen R, Martin AS, Kehl KL, Sweeney SM, Lepisto EM, Rizvi H, McCarthy CG, Schultz N, Warner JL, Park BH, Bedard PL, Riely GJ, Schrag D, Panageas KS; AACR Project GENIE Consortium. *JAMA Oncol.* 2022 Feb 1;8(2):287-291. IF: 33,006.

Time-Dependent COVID-19 Mortality in Patients With Cancer: An Updated Analysis of the OnCovid Registry. OnCovid Study Group; Pinato DJ, Patel M, Scotti L, Colomba E, Dolly S, Loizidou A, Chester J, Mukherjee U, Zambelli A, Dalla Pria A, Aguilar-Company J, Bower M, Salazar R, Bertuzzi A, Brunet J, Lambertini M, Tagliamento M, Pous A, Sita-Lumsden A, Srikandarajah K, Colomba J, Pommeret F, Seguí E, Generali D, Grisanti S, Pedrazzoli P, Rizzo G, Libertini M, Moss C, Evans JS, Russell B, Harbeck N, Vincenzi B, Biello F, Bertulli R, Ottaviani D, Liñan R, Rossi S, Carmona-García MC, Tondini C, Fox L, Baggi A, Fotia V, Parisi A, Porzio G, Queirolo P, Cruz CA, Saoudi-Gonzalez N, Felip E, Roqué Lloveras A, Newsom-Davis T, Sharkey R, Roldán E, Reyes R, Zoratto F, Earnshaw I, Ferrante D, Marco-Hernández J, Ruiz-Camps I, Gaidano G, Patriarca A, Bruna R, Sureda A, Martinez-Vila C, Sanchez de Torre A, Berardi R, Giusti R, Mazzoni F, Guida A, Rimassa L, Chiudinelli L, Franchi M, Krengli M, Santoro A, Prat A, Tabernero J, Van Hemelrijck M, Diamantis N, Gennari A, Cortellini A. *JAMA Oncol.* 2022 Jan 1;8(1):114-122. IF: 33,006.

Melflufen or pomalidomide plus dexamethasone for patients with multiple myeloma refractory to lenalidomide (OCEAN): a randomised, head-to-head, open-label, phase 3 study. Schjesvold FH, Dimopoulos MA, Delimpasi S, Robak P, Coriu D, Legiec W, Pour L, Špička I, Masszi T, Doronin V, Minarik J, Salogub G, Alekseeva Y, Lazzaro A, Maisnar V, Mikala G, Rosiñol L, Liberati AM, Symeonidis A, Moody V, Thuresson M, Byrne C, Harmenberg J, Bakker NA, Hájek R, Mateos MV, Richardson PG, Sonneveld P; OCEAN (OP-103) Investigators. *Lancet Haematol.* 2022 Feb;9(2):e98-e110. IF: 30,153.

Breakthrough COVID-19 in vaccinated patients with hematologic malignancies: results from the EPICOVIDEHA survey. Pagano L, Salmanton-García J, Marchesi F, Blennow O, Gomes da Silva M, Glenthøj A, van Doesum J, Bilgin YM, López-García A, Itri F, Nunes Rodrigues R, Weinbergerová B, Farina F, Dragonetti G, Berg Venemyr C, van Praet J, Jaksic O, Valković T, Falces-Romero I, Martín-

Pérez S, Jiménez M, Dávila-Valls J, Schönlein M, Ammatuna E, Meers S, Delia M, Stojanoski Z, Nordlander A, Lahmer T, Imre Pinczés L, Buquicchio C, Piukovics K, Ormazabal-Vélez I, Fracchiolla N, Samarkos M, Méndez GA, Hernández-Rivas JÁ, Espigado I, Cernan M, Petzer V, Lamure S, di Blasi R, Marques de Almedia J, Dargenio M, Biernat MM, Sciumè M, de Ramón C, de Jonge N, Batinić J, Aujayeb A, Marchetti M, Fouquet G, Fernández N, Zambrotta G, Sacchi MV, Guidetti A, Demirkan F, Prezioso L, Ráčil Z, Nucci M, Mladenović M, Liévin R, Hanáková M, Gräfe S, Sili U, Machado M, Cattaneo C, Adžić-Vukičević T, Verga L, Labrador J, Rahimli L, Bonanni M, Passamonti F, Pagliuca A, Corradini P, Hoenigl M, Koehler P, Busca A, Cornely OA. Breakthrough COVID-19 in vaccinated patients with hematologic malignancies: results from the EPICOVIDEHA survey. *Blood*. 2022 Dec 29;140(26):2773-2787. IF: 25,476.

Ibrutinib improves survival compared with chemotherapy in mantle cell lymphoma with central nervous system relapse. Rusconi C, Cheah CY, Eyre TA, Tucker D, Klener P, Giné E, Crucitti L, Muzi C, Iadecola S, Infante G, Bernard S, Auer RL, Pagani C, Duglosz-Danecka M, Mocikova H, van Meerten T, Cencini E, Marin-Niebla A, Williams ME, Angelillo P, Nicoli P, Arcari A, Morello L, Mannina D, Vitagliano O, Sartori R, Chiappella A, Sciarra R, Stefani PM, Dreyling M, Seymour JF, Visco C. *Blood*. 2022 Oct 27;140(17):1907-1916. IF: 25,476.

Hematopoietic stem cell transplantation for adolescents and adults with inborn errors of immunity: an EBMT IEWP study. Albert MH, Sirait T, Eikema DJ, Bakunina K, Wehr C, Suarez F, Fox ML, Mahlaoui N, Gennery AR, Lankester AC, Beier R, Bernardo ME, Bigley V, Lindemans CA, Burns SO, Carpenter B, Dybko J, Güngör T, Hauck F, Lum SH, Balashov D, Meisel R, Moshous D, Schulz A, Speckmann C, Slatter MA, Strahm B, Uckan-Cetinkaya D, Meyts I, Vallée TC, Wynn R, Neven B, Morris EC, Aiuti A, Maschan A, Aljurf M, Gedde-Dahl T, Gurman G, Bordon V, Kriván G, Locatelli F, Porta F, Valcárcel D, Beguin Y, Faraci M, Kröger N, Kulagin A, Shaw PJ, Veelken JH, Diaz de Heredia C, Fagioli F, Felber M, Gruhn B, Holter W, Rössig C, Sedlacek P, Apperley J, Ayas M, Bodova I, Choi G, Cornelissen JJ, Sirvent A, Khan A, Kupesiz A, Lenhoff S, Ozdogu H, von der Weid N, Rovira M, Schots R, Vinh DC. *Blood*. 2022 Oct 6;140(14):1635-1649. IF: 25,476.

Comparative effectiveness of ZUMA-5 (axi-cel) vs SCHOLAR-5 external control in relapsed/refractory follicular lymphoma. Ghione P, Palomba ML, Patel AR, Bobillo S, Deighton K, Jacobson CA, Nahas M, Hatswell AJ, Jung AS, Kanters S, Snider JT, Neelapu SS, Ribeiro MT, Brookhart MA, Ghesquieres H, Radford J, Gribben JG. *Blood*. 2022 Aug 25;140(8):851-860. IF: 25,476.

Final Results of Neoadjuvant Atezolizumab in Cisplatin-ineligible Patients with Muscle-invasive Urothelial Cancer of the Bladder. Szabados B, Kockx M, Assaf ZJ, van Dam PJ, Rodriguez-Vida A, Duran I, Crabb SJ, Van Der Heijden MS, Pous AF, Gravis G, Herranz UA, Protheroe A, Ravaud A, Maillet D, Mendez MJ, Suarez C, Linch M, Prendergast A, Tyson C, Stanoeva D, Daelemans S, Rombouts M, Mariathasan S, Tea JS, Mousa K, Sharma S, Aleshin A, Banchereau R, Castellano D, Powles T. *Eur Urol*. 2022 Aug;82(2):212-222. IF: 24,267.

Predictive Genomic Biomarkers of Hormonal Therapy Versus Chemotherapy Benefit in Metastatic Castration-resistant Prostate Cancer. Graf RP, Fisher V, Mateo J, Gjoerup OV, Madison RW, Raskina K, Tukachinsky H, Creeden J, Cunningham R, Huang RSP, Mata DA, Ross JS, Oxnard GR, Venstrom JM, Zurita AJ. *Eur Urol*. 2022 Jan;81(1):37-47. IF: 24,267.

Molecular Genetic Determinants of Shorter Time on Active Surveillance in a Prospective Phase 2 Clinical Trial in Metastatic Renal Cell Carcinoma. Reig Torras O, Mishra A, Christie A, McKenzie T, Onabolu O, Singla N, Plimack ER, Suárez C, Ornstein MC, Alpaugh RK, Elias R, Bowman IA, McKay RM, Przybycin C, Kapur P, Brugarolas J, Rini B. *Eur Urol*. 2022 Jun;81(6):555-558. IF: 24,267.

ZFP281 drives a mesenchymal-like dormancy program in early disseminated breast cancer cells that prevents metastatic outgrowth in the lung. Nobre AR, Dalla E, Yang J, Huang X, Wullkopf L, Risson E, Razghandi P, Anton ML, Zheng W, Seoane JA, Curtis C, Kenigsberg E, Wang J, Aguirre-Ghiso JA. *Nat Cancer*. 2022 Oct;3(10):1165-1180. IF: 23,177.

Functional patient-derived organoid screenings identify MCLA-158 as a therapeutic EGFR × LGR5 bispecific antibody with efficacy in epithelial tumors. Herpers B, Eppink B, James MI, Cortina C, Cañellas-Socias A, Boj SF, Hernando-Momblona X, Glodzik D, Roovers RC, van de Wetering M, Bartelink-Clements C, Zondag-van der Zande V, Mateos JG, Yan K, Salinaro L, Basmeleh A, Fatrai S, Maussang D, Lammerts van Bueren JJ, Chicote I, Serna G, Cabellos L, Ramírez L, Nuciforo P, Salazar R, Santos C, Villanueva A, Stephan-Otto Attolini C, Sancho E, Palmer HG, Tabernero J, Stratton MR, de Kruif J, Logtenberg T, Clevers H, Price LS, Vries RGJ, Batlle E, Throsby M. *Nat Cancer*. 2022 Apr;3(4):418-436. IF: 23,177.

LCOR mediates interferon-independent tumor immunogenicity and responsiveness to immune-checkpoint blockade in triple-negative breast cancer. Pérez-Núñez I, Rozalén C, Palomeque JÁ, Sangrador I, Dalmau M, Comerma L, Hernández-Prat A, Casadevall D, Menendez S, Liu DD, Shen M, Berenguer J, Ruiz IR, Peña R, Montañés JC, Albà MM, Bonnin S, Ponomarenko J, Gomis RR, Cejalvo JM, Servitja S, Marzese DM, Morey L, Voorwerk L, Arribas J, Bermejo B, Kok M, Pusztai L, Kang Y, Albanell J, Celià-Terrassa T. *Nat Cancer*. 2022 Mar;3(3):355-370. IF: 23,177.

The Molecular Tumor Board Portal supports clinical decisions and automated reporting for precision oncology. Tamborero D, Dienstmann R, Rachid MH, Boekel J, Lopez-Fernandez A, Jonsson M, Razzak A, Braña I, De Petris L, Yachnin J, Baird RD, Loriot Y, Massard C, Martin-Romano P, Opdam F, Schlenk RF, Vernieri C, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium; Balmaña J, Apolone G, Caldas C, Bergh J, Ernberg I, Fröhling S, Garralda E, Karlsson C, Tabernero J, Voest E, Rodon J, Lehtiö J. *Nat Cancer*. 2022 Feb;3(2):251-261. IF: 23,177.

Efficacy of Brigatinib in Patients With Advanced ALK-Positive NSCLC Who Progressed on Alectinib or Ceritinib: ALK in Lung Cancer Trial of brigAtinib-2 (ALTA-2). Ou SI, Nishio M, Ahn MJ, Mok T, Barlesi F, Zhou C, Felip E, de Marinis F, Kim SW, Pérol M, Liu G, Migliorino MR, Kim DW, Novello S, Bearz A, Garrido P, Mazieres J, Morabito A, Lin HM, Yang H, Niu H, Zhang P, Kim ES. *J Thorac Oncol*. 2022 Dec;17(12):1404-1414. IF: 20,121.

A Definitive Prognostication System for Patients With Thoracic Malignancies Diagnosed With Coronavirus Disease 2019: An Update From the TERAVOLT Registry. Whisenant JG, Baena J, Cortellini A, Huang LC, Lo Russo G, Porcu L, Wong SK, Bestvina CM, Hellmann MD, Roca E, Rizvi H, Monnet I, Boudjemaa A, Rogado J, Pasello G, Leighl NB, Arrieta O, Aujayeb A, Batra U, Azzam AY, Unk M, Azab MA, Zhumagaliyeva AN, Gomez-Martin C, Blaquier JB, Geraedts E, Mountzios G, Serrano-Montero G, Reinmuth N, Coate L, Marmarelis M, Presley CJ, Hirsch FR, Garrido P, Khan H, Baggi A, Mascaux C, Halmos B, Ceresoli GL, Fidler MJ, Scotti V, Métivier AC, Falchero L, Felip E, Genova C, Mazieres J, Tapan U, Brahmer J, Bria E, Puri S, Popat S, Reckamp KL, Morgillo F, Nadal E, Mazzoni F, Agustoni F, Bar J, Grosso F, Avrillon V, Patel JD, Gomes F, Ibrahim E, Trama A, Bettini AC, Barlesi F, Dingemans AM, Wakelee H, Peters S, Horn L, Garassino MC, Torri V; TERAVOLT study group. *J Thorac Oncol*. 2022 May;17(5):661-674. IF: 20,121.

The Mettl3 epitranscriptomic writer amplifies p53 stress responses. Raj N, Wang M, Seoane JA, Zhao RL, Kaiser AM, Moonie NA, Demeter J, Boutelle AM, Kerr CH, Mulligan AS, Moffatt C, Zeng SX, Lu H, Barna M, Curtis C, Chang HY,

Jackson PK, Attardi LD. *Mol Cell.* 2022 Jul 7;82(13):2370-2384.e10. IF: 19,328.

Giredestrant reverses progesterone hypersensitivity driven by estrogen receptor mutations in breast cancer. Liang J, Ingalla ER, Yao X, Wang BE, Tai L, Giltnane J, Liang Y, Daemen A, Moore HM, Aimi J, Chang CW, Gates MR, Eng-Wong J, Tam L, Bacarro N, Roose-Girma M, Bellet M, Hafner M, Metcalfe C. *Sci Transl Med.* 2022 Sep 21;14(663):eabo5959. IF: 19,319.

Acute kidney injury in patients receiving pembrolizumab combination therapy versus pembrolizumab monotherapy for advanced lung cancer. Gupta S, Strohbehn IA, Wang Q, Hanna PE, Seethapathy R, Prosek JM, Herrmann SM, Abudayyeh A, Malik AB, Loew S, Carlos CA, Chang WT, Beckerman P, Mithani Z, Shah CV, Renaghan AD, de Seigneux S, Campedel L, Kitchlu A, Shin DS, Coppock G, Lumlertgul N, Garcia P, Ortiz-Melo DI, Rashidi A, Sprangers B, Aggarwal V, Benesova K, Jhaveri KD, Cortazar FB, Weins A, Zuo Y, Mooradian MJ, Reynolds KL, Leaf DE, Sise ME; ICPi-AKI Consortium. *Kidney Int.* 2022 Oct;102(4):930-935. IF: 18,998.

The transcription factor DDIT3 is a potential driver of dyserythropoiesis in myelodysplastic syndromes. Berastegui N, Ainciburu M, Romero JP, Garcia-Olloqui P, Alfonso-Pierola A, Philippe C, Vilas-Zornoza A, San Martin-Uriz P, Ruiz-Hernández R, Abarrategi A, Ordoñez R, Alignani D, Sarvide S, Castro-Labrador L, Lamo-Espinosa JM, San-Julian M, Jimenez T, López-Cadenas F, Muntion S, Sanchez-Guijo F, Molero A, Montoro MJ, Tazón B, Serrano G, Diaz-Mazkiaran A, Hernaez M, Huerga S, Bewicke-Copley F, Rio-Machin A, Maurano MT, Díez-Campelo M, Valcarcel D, Rouault-Pierre K, Lara-Astiaso D, Ezponda T, Prosper F. *Nat Commun.* 2022 Dec 9;13(1):7619. IF: 17,694.

Phosphoproteomic analysis of neoadjuvant breast cancer suggests that increased sensitivity to paclitaxel is driven by CDK4 and filamin A. Mouron S, Bueno MJ, Lluch A, Manso L, Calvo I, Cortes J, Garcia-Saenz JA, Gil-Gil M, Martinez-Janez N, Apala JV, Caleiras E, Ximénez-Embún P, Muñoz J, Gonzalez-Cortijo L, Murillo R, Sánchez-Bayona R, Cejalvo JM, Gómez-López G, Fustero-Torre C, Sabroso-Lasa S, Malats N, Martinez M, Moreno A, Megias D, Malumbres M, Colomer R, Quintela-Fandino M. *Nat Commun.* 2022 Dec 7;13(1):7529. IF: 17,694.

BRAF activation by metabolic stress promotes glycolysis sensitizing NRASQ61-mutated melanomas to targeted therapy. McGrail K, Granado-Martínez P, Esteve-Puig R, García-Ortega S, Ding Y, Sánchez-Redondo S, Ferrer B, Hernandez-Losa J, Canals F, Manzano A, Navarro-Sabaté A, Bartrons R, Yanes O, Pérez-Alea M, Muñoz-Couselo E, Garcia-Patos V, Recio JA. *Nat Commun.* 2022 Nov 19;13(1):7113. IF: 17,694.

pTINCR microprotein promotes epithelial differentiation and suppresses tumor growth through CDC42 SUMOylation and activation. Boix O, Martinez M, Vidal S, Giménez-Alejandre M, Palenzuela L, Lorenzo-Sanz L, Quevedo L, Moscoso O, Ruiz-Orera J, Ximénez-Embún P, Ciriaco N, Nuciforo P, Stephan-Otto Attolini C, Albà MM, Muñoz J, Tian TV, Varela I, Vivancos A, Ramón Y Cajal S, Muñoz P, Rivas C, Abad M. *Nat Commun.* 2022 Nov 11;13(1):6840. IF: 17,694.

Analysis of matched primary and recurrent BRCA1/2 mutation-associated tumors identifies recurrence-specific drivers. Shah JB, Pueschl D, Wubbenhorst B, Fan M, Pluta J, D'Andrea K, Hubert AP, Shilan JS, Zhou W, Kraya AA, Llop Guevara A, Ruan C, Serra V, Balmaña J, Feldman M, Morin PJ, Nayak A, Maxwell KN, Domchek SM, Nathanson KL. *Nat Commun.* 2022 Nov 7;13(1):6728. IF: 17,694.

A phase II trial of weekly nab-paclitaxel for progressive and symptomatic desmoid tumors. Martin-Broto J, Redondo A, Moura DS, Valverde C, Morales JM, Lopez-Pousa A, Martinez-Trufero J, Gutierrez A, Díaz-Beveridge R, Luna P, Martinez-Marin V, Marcilla D, Arribas I, Ledesma P, Lopez-Martin JA, Di Lernia D, Zamora J, Hindi N. A phase II trial of weekly nab-paclitaxel for progressive and symptomatic desmoid tumors. *Nat Commun.* 2022 Oct 21;13(1):6278. IF: 17,694.

High p16 expression and heterozygous RB1 loss are biomarkers for CDK4/6 inhibitor resistance in ER+ breast cancer. Palafox M, Monserrat L, Bellet M, Villacampa G, Gonzalez-Perez A, Oliveira M, Brasó-Maristany F, Ibrahimi N, Kannan S, Mina L, Herrera-Abreu MT, Òdena A, Sánchez-Guixé M, Capelán M, Azaro A, Bruna A, Rodríguez O, Guzmán M, Grueso J, Viaplana C, Hernández J, Su F, Lin K, Clarke RB, Caldas C, Arribas J, Michiels S, García-Sanz A, Turner NC, Prat A, Nuciforo P, Dienstmann R, Verma CS, Lopez-Bigas N, Scaltriti M, Arnedos M, Saura C, Serra V. *Nat Commun.* 2022 Sep 7;13(1):5258. IF: 17,694.

Stratification of hospitalized COVID-19 patients into clinical severity progression groups by immuno-phenotyping and machine learning. Mueller YM, Schrama TJ, Ruijten R, Schreurs MWJ, Grashof DGB, van de Werken HJG, Lasinio GJ, Álvarez-Sierra D, Kiernan CH, Castro Eiro MD, van Meurs M, Brouwers-Haspels I, Zhao M, Li L, de Wit H, Ouzounis CA, Wilmsen MEP, Alofs TM, Laport DA, van Wees T, Kraker G, Jaimes MC, Van Bockstael S, Hernández-González M, Rokx C, Rijnders BJA, Pujol-Borrell R, Katsikis PD. *Nat Commun.* 2022 Feb 17;13(1):915. IF: 17,694.

DSTYK inhibition increases the sensitivity of lung cancer cells to T cell-mediated cytotoxicity. Valencia K, Echepare M, Teijeira Á, Pasquier A, Bértolo C, Sainz C, Tamayo I, Picabea B, Bosco G, Thomas R, Agorreta J, López-Picazo JM, Frigola J, Amat R, Calvo A, Felip E, Melero I, Montuenga LM. *J Exp Med.* 2022 Dec 5;219(12):e20220726. IF: 17,579.

Engineering pH-Sensitive Stable Nanovesicles for Delivery of MicroRNA Therapeutics. Boloix A, Feiner-Gracia N, Köber M, Repetto J, Pascarella R, Soriano A, Masanas M, Segovia N, Vargas-Nadal G, Merlo-Mas J, Danino D, Abutbul-Ionita I, Foradada L, Roma J, Córdoba A, Sala S, de Toledo JS, Gallego S, Veciana J, Albertazzi L, Segura MF, Ventosa N. *Small.* 2022 Jan;18(3):e2101959. IF: 15,153.

Targeting HER2-AXL heterodimerization to overcome resistance to HER2 blockade in breast cancer. Adam-Artigues A, Arenas EJ, Martínez-Sabadell A, Brasó-Maristany F, Cervera R, Tormo E, Hernando C, Martínez MT, Carbonell-Asins J, Simón S, Poveda J, Moragón S, Zazo S, Martínez D, Rovira A, Burgués O, Rojo F, Albanell J, Bermejo B, Lluch A, Prat A, Arribas J, Eroles P, Cejalvo JM. *Sci Adv.* 2022 May 20;8(20):eabk2746. IF: 14,957.

Anti-tumoural activity of the G-quadruplex ligand pyridostatin against BRCA1/2-deficient tumours. Groelly FJ, Porru M, Zimmer J, Benainous H, De Visser Y, Kosova AA, Di Vito S, Serra V, Ryan A, Leonetti C, Bruna A, Biroccio A, Tarsounas M. *EMBO Mol Med.* 2022 Mar 7;14(3):e14501. IF: 14,260.

Identification of a Molecularly-Defined Subset of Breast and Ovarian Cancer Models that Respond to WEE1 or ATR Inhibition, Overcoming PARP Inhibitor Resistance. Serra V, Wang AT, Castroviejo-Bermejo M, Polanska UM, Palafox M, Herencia-Ropero A, Jones GN, Lai Z, Armenia J, Michopoulos F, Llop-Guevara A, Brough R, Gulati A, Pettitt SJ, Bulusu KC, Nikkilä J, Wilson Z, Hughes A, Wijnhoven PWG, Ahmed A, Bruna A, Gris-Oliver A, Guzman M, Rodríguez O, Grueso J, Arribas J, Cortés J, Saura C, Lau A, Critchlow S, Dougherty B, Caldas C, Mills GB, Barrett JC, Forment JV, Cadogan E, Lord CJ, Cruz C, Balmaña J, O'Connor MJ. *Clin Cancer Res.* 2022 Oct 14;28(20):4536-4550. IF: 13,801.

Association of Tumor Mutational Burden with Efficacy of Pembrolizumab±Chemotherapy as First-Line Therapy for Gastric Cancer in the Phase III KEYNOTE-062 Study. Lee KW, Van Cutsem E, Bang YJ, Fuchs CS, Kudaba I, Garrido M, Chung HC, Lee J, Castro HR, Chao J, Wainberg ZA, Cao ZA, Aurora-Garg D, Kobie J, Cristescu R, Bhagia P,

Shah S, Tabernero J, Shitara K, Wyrwicz L. *Clin Cancer Res.* 2022 Aug 15;28(16):3489-3498. IF: 13,801.

Antitumor Activity of Lurbinectedin, a Selective Inhibitor of Oncogene Transcription, in Patients with Relapsed Ewing Sarcoma: Results of a Basket Phase II Study. Subbiah V, Braña I, Longhi A, Boni V, Delord JP, Awada A, Boudou-Rouquette P, Sarantopoulos J, Shapiro GI, Elias A, Ratan R, Fernandez C, Kahatt C, Cullell-Young M, Siguero M, Zeaiter A, Chawla SP. *Clin Cancer Res.* 2022 Jul 1;28(13):2762-2770. IF: 13,801.

A Phase I Study Investigating AZD8186, a Potent and Selective Inhibitor of PI3Kβ/δ, in Patients with Advanced Solid Tumors. Choudhury AD, Higano CS, de Bono JS, Cook N, Rathkopf DE, Wisinski KB, Martin-Liberal J, Linch M, Heath EI, Baird RD, García-Carbacho J, Quintela-Fandino M, Barry ST, de Bruin EC, Colebrook S, Hawkins G, Klinowska T, Maroj B, Moorthy G, Mortimer PG, Moschetta M, Nikolaou M, Sainsbury L, Shapiro GI, Siu LL, Hansen AR. *Clin Cancer Res.* 2022 Jun 1;28(11):2257-2269. IF: 13,801.

ESMO Scale for Clinical Actionability of Molecular Targets Driving Targeted Treatment in Patients with Cholangiocarcinoma. Verdaguer H, Saurí T, Acosta DA, Guardiola M, Sierra A, Hernando J, Nuciforo P, Miquel JM, Molero C, Peiró S, Serra-Camprubí Q, Villacampa G, Aguilar S, Vivancos A, Tabernero J, Dienstmann R, Macarulla T. *Clin Cancer Res.* 2022 Apr 14;28(8):1662-1671. IF: 13,801.

Tumor Genomic Testing for >4,000 Men with Metastatic Castration-resistant Prostate Cancer in the Phase III Trial PROfound (Olaparib). Hussain M, Corcoran C, Sibilla C, Fizazi K, Saad F, Shore N, Sandhu S, Mateo J, Olmos D, Mehra N, Kolinsky MP, Roubaud G, Özgüroğlu M, Matsubara N, Gedye C, Choi YD, Padua C, Kohlmann A, Huisden R, Elvin JA, Kang J, Adelman CA, Allen A, Poehlein C, de Bono J. *Clin Cancer Res.* 2022 Apr 14;28(8):1518-1530. IF: 13,801.

Pan-cancer Analysis of Homologous Recombination Repair-associated Gene Alterations and Genome-wide Loss-of-Heterozygosity Score. Westphalen CB, Fine AD, André F, Ganesan S, Heinemann V, Rouleau E, Turnbull C, Garcia Palacios L, Lopez JA, Sokol ES, Mateo J. *Clin Cancer Res.* 2022 Apr 1;28(7):1412-1421. IF: 13,801.

IFNγ Signaling in Natural and Therapy-Induced Antitumor Responses. Martínez-Sabadell A, Arenas EJ, Arribas J. *Clin Cancer Res.* 2022 Apr 1;28(7):1243-1249. IF: 13,801.

Tepotinib Efficacy and Safety in Patients with MET Exon 14 Skipping NSCLC: Outcomes in Patient Subgroups from the VISION Study with Relevance for Clinical Practice. Le X, Sakai H, Felip E, Veillon R, Garassino MC, Raskin J, Cortot AB, Viteri S, Mazieres J, Smit EF, Thomas M, Iams WT, Cho BC, Kim HR, Yang JC, Chen YM, Patel JD, Bestvina CM, Park K, Griesinger F, Johnson M, Gottfried M, Britschgi C, Heymach J, Sikoglu E, Berghoff K, Schumacher KM, Bruns R, Otto G, Paik PK. *Clin Cancer Res.* 2022 Mar 15;28(6):1117-1126. IF: 13,801.

Co-Targeting of MDM2 and CDK4/6 with Siremadlin and Ribociclib for the Treatment of Patients with Well-Differentiated or Dedifferentiated Liposarcoma: Results from a Proof-of-Concept, Phase Ib Study. Abdul Razak AR, Bauer S, Suarez C, Lin CC, Quek R, Hütter-Krönke ML, Cubedo R, Ferretti S, Guerreiro N, Jullion A, Orlando EJ, Clementi G, Sand Dejmek J, Halilovic E, Fabre C, Blay JY, Italiano A. *Clin Cancer Res.* 2022 Mar 15;28(6):1087-1097. IF: 13,801.

Results from a First-in-Human Phase I Study of Siremadlin (HDM201) in Patients with Advanced Wild-Type TP53 Solid Tumors and Acute Leukemia. Stein EM, DeAngelo DJ, Chromik J, Chatterjee M, Bauer S, Lin CC, Suarez C, de Vos F, Steeghs N, Cassier PA, Tai D, Kiladjian JJ, Yamamoto N, Mous R, Esteve J, Minami H, Ferretti S, Guerreiro N, Meille C, Radhakrishnan R, Pereira B, Mariconti L, Halilovic E, Fabre C, Carpio C. *Clin Cancer Res.* 2022 Mar 1;28(5):870-881. IF: 13,801.

Functional Mapping of AKT Signaling and Biomarkers of Response from the FAIRLANE Trial of Neoadjuvant Ipatasertib plus Paclitaxel for Triple-Negative Breast Cancer. Shi Z, Wulfkuhle J, Nowicka M, Gallagher RI, Saura C, Nuciforo PG, Calvo I, Andersen J, Passos-Coelho JL, Gil-Gil MJ, Bermejo B, Pratt DA, Ciruelos EM, Villagrasa P, Wongchenko MJ, Petricoin EF, Oliveira M, Isakoff SJ. *Clin Cancer Res.* 2022 Mar 1;28(5):993-1003. IF: 13,801.

High FGFR1-4 mRNA Expression Levels Correlate with Response to Selective FGFR Inhibitors in Breast Cancer. Sánchez-Guixé M, Hierro C, Jiménez J, Viaplana C, Villacampa G, Monelli E, Brasó-Maristany F, Ogbah Z, Parés M, Guzmán M, Grueso J, Rodríguez O, Oliveira M, Azaro A, Garralda E, Tabernero J, Casanovas O, Scaltriti M, Prat A, Dienstmann R, Nuciforo P, Saura C, Graupera M, Vivancos A, Rodon J, Serra V. *Clin Cancer Res.* 2022 Jan 1;28(1):137-149. IF: 13,801.

A Randomized Phase II Study of Anti-CSF1 Monoclonal Antibody Lacnotuzumab (MCS110) Combined with Gemcitabine and Carboplatin in Advanced Triple-Negative Breast Cancer. Kuemmel S, Campone M, Loirat D, Lopez RL, Beck JT, De Laurentiis M, Im SA, Kim SB, Kwong A, Steger GG, Adelantado EZ, Duhoux FP, Greil R, Kuter I, Lu YS, Tibau A, Özgüroğlu M, Scholz CW, Singer CF, Vega E, Wimberger P, Zamagni C, Couillebault XM, Fan L, Guerreiro N, Mataraza J, Sand-Dejmek J, Chan A. *Clin Cancer Res.* 2022 Jan 1;28(1):106-115. IF: 13,801.

Response to "Analysis of the association between prospectively collected immune-related adverse events and survival in patients with solid tumor treated with immune-checkpoint blockers, taking into account immortal-time bias". Villacampa G, Hernando-Calvo A, Berché R, Saavedra O, Marmolejo D, Mirallas O, Braña I, Muñoz-Couselo E, Garralda E, Dienstmann R. *Cancer Treat Rev.* 2022 Dec;111:102465. IF: 13,608.

Multiple Bayesian network meta-analyses to establish therapeutic algorithms for metastatic triple negative breast cancer. Schettini F, Venturini S, Giuliano M, Lambertini M, Pinato DJ, Onesti CE, De Placido P, Harbeck N, Lüftner D, Denys H, Van Dam P, Arpino G, Zaman K, Mustacchi G, Gligorov J, Awada A, Campone M, Wildiers H, Gennari A, Tjan-Heijnen V, Bartsch R, Cortes J, Paris I, Martín M, De Placido S, Del Mastro L, Jerusalem G, Curigliano G, Prat A, Generali D. *Cancer Treat Rev.* 2022 Dec;111:102468. IF: 13,608.

The conundrum of breast cancer and microbiome - A comprehensive review of the current evidence. Papakonstantinou A, Nuciforo P, Borrell M, Zamora E, Pimentel I, Saura C, Oliveira M. *Cancer Treat Rev.* 2022 Dec;111:102470. IF: 13,608.

Molecular diagnosis and targeted treatment of advanced follicular cell-derived thyroid cancer in the precision medicine era. Capdevila J, Awada A, Führer-Sakel D, Leboulleux S, Pauwels P. *Cancer Treat Rev.* 2022 May;106:102380. IF: 13,608.

Prognostic value of ctDNA detection in patients with early breast cancer undergoing neoadjuvant therapy: A systematic review and meta-analysis. Papakonstantinou A, Gonzalez NS, Pimentel I, Suñol A, Zamora E, Ortiz C, Espinosa-Bravo M, Peg V, Vivancos A, Saura C, Villacampa G, Oliveira M. *Cancer Treat Rev.* 2022 Mar;104:102362. IF: 13,608.

Treatment-driven tumour heterogeneity and drug resistance: Lessons from solid tumours. Crucitta S, Cucchiara F, Mathijssen R, Mateo J, Jager A, Joosse A, Passaro A, Attili I, Petrini I, van Schaik R, Danesi R, Del Re M. *Cancer Treat Rev.* 2022 Mar;104:102340. IF: 13,608.

Addition of immune checkpoint inhibitors to chemotherapy versus chemotherapy alone in first-line metastatic triple-negative breast cancer:

A systematic review and meta-analysis. Villacampa G, Tolosa P, Salvador F, Sánchez-Bayona R, Villanueva L, Dienstmann R, Ciruelos E, Pascual T. *Cancer Treat Rev.* 2022 Mar;104:102352. IF: 13,608.

Targeting brain metastases in breast cancer. Corti C, Antonarelli G, Criscitiello C, Lin NU, Carey LA, Cortés J, Poortmans P, Curigliano G. *Cancer Treat Rev.* 2022 Feb;103:102324. IF: 13,608.

A comprehensive overview of tumour deposits in colorectal cancer: Towards a next TNM classification. Delattre JF, Selcen Oguz Erdogan A, Cohen R, Shi Q, Emile JF, Taieb J, Tabernero J, André T, Meyerhardt JA, Nagtegaal ID, Svrcek M. *Cancer Treat Rev.* 2022 Feb;103:102325. IF: 13,608.

SELNET clinical practice guidelines for soft tissue sarcoma and GIST. Blay JY, Hindi N, Bollard J, Aguiar S Jr, Angel M, Araya B, Badilla R, Bernabeu D, Campos F, Caro-Sánchez CHS, Carvajal B, Carvajal Montoya A, Casavilca-Zambrano S, Castro-Oliden V, Chacón M, Clara M, Collini P, Correa Genoroso R, Costa FD, Cuellar M, Dei Tos AP, Dominguez Malagon HR, Donati D, Dufresne A, Eriksson M, Farias-Loza M, Fernandez P, Frezza AM, Frisoni T, Garcia-Ortega DY, Gelderblom H, Gouin F, Gómez-Mateo MC, Gronchi A, Haro J, Huanca L, Jimenez N, Karanian M, Kasper B, Lopes David BB, Lopez-Pousa A, Lutter G, Martinez-Said H, Martinez-Tlahuel J, Mello CA, Morales Pérez JM, Moura David S, Nascimento AG, Ortiz-Cruz EJ, Palmerini E, Patel S, Pfluger Y, Provenzano S, Righi A, Rodriguez A, Salas R, Santos TTG, Scotlandi K, Soule T, Stacchiotti S, Valverde C, Waisberg F, Zamora Estrada E, Martin-Broto J. *Cancer Treat Rev.* 2022 Jan;102:102312. IF: 13,608.

Quality of Colonoscopy Is Associated With Adenoma Detection and Postcolonoscopy Colorectal Cancer Prevention in Lynch Syndrome. Sánchez A, Roos VH, Navarro M, Pineda M, Caballol B, Moreno L, Carballal S, Rodríguez-Alonso L, Ramon Y Cajal T, Llort G, Piñol V, López-Fernández A, Salces I, Picó MD, Rivas L, Bujanda L, Garzon M, Pizarro A, Martinez de Castro E, López-Arias MJ, Poves C, Garau C, Rodriguez-Alcalde D, Herraiz M, Alvarez-Urrutia C, Dacal A, Carrillo-Palau M, Cid L, Ponce M, Barreiro-Alonso E, Saperas E, Aguirre E, Romero C, Bastiaansen B, Gonzalez-Acosta M, Morales-Romero B, Ocaña T, Rivero-Sánchez L, Jung G, Bessa X, Cubiella J, Jover R, Rodríguez-Moranta F, Balmaña J, Brunet J, Castells A, Dekker E, Capella G, Serra-Burriel M, Moreira L, Pellise M, Balaguer F. *Clin Gastroenterol Hepatol.* 2022 Mar;20(3):611-621.e9. IF: 13,576.

Retreatment With Immune Checkpoint Inhibitors After a Severe Immune-Related Hepatitis: Results From a Prospective Multicenter Study. Riveiro-Barciela M, Barreira-Díaz A, Callejo-Pérez A, Muñoz-Couselo E, Díaz-Mejía N, Díaz-González Á, Londoño MC, Salcedo MT, Buti M. *Clin Gastroenterol Hepatol.* 2023 Mar;21(3):732-740. IF: 13,576.

Imaging Response to Contemporary Immuno-oncology Combination Therapies in Patients With Metastatic Renal Cell Carcinoma. Navani V, Ernst M, Wells JC, Yuasa T, Takemura K, Donskov F, Basappa NS, Schmidt A, Pal SK, Meza L, Wood LA, Ernst DS, Szabados B, Powles T, McKay RR, Weickhardt A, Suarez C, Kapoor A, Lee JL, Choueiri TK, Heng DYC. *JAMA Netw Open.* 2022 Jun 1;5(6):e2216379. IF: 13,353.

Therapy-Induced Senescence Enhances the Efficacy of HER2-Targeted Antibody-Drug Conjugates in Breast Cancer. Duro-Sánchez S, Nadal-Serrano M, Lalinde-Gutiérrez M, Arenas EJ, Bernadó Morales C, Morancho B, Escorihuela M, Pérez-Ramos S, Escrivá-de-Romaní S, Gandullo-Sánchez L, Pandiella A, Esteve-Codina A, Rodilla V, Dijcks FA, Dokter WHA, Cortés J, Saura C, Arribas J. *Cancer Res.* 2022 Dec 16;82(24):4670-4679. IF: 13,312.

Activity and Resistance of a Brain-Permeable Paradox Breaker BRAF Inhibitor in Melanoma Brain Metastasis. Bonfill-Teixidor E, Iurlaro R, Handl C, Wichmann J, Arias A, Cuartas I, Emmenegger J, Romagnani A, Mangano L, Lorber T, Berrera M, Godfried Sie C, Köchl F, Eckmann J, Feddersen R, Kornacker M, Schnetzler G, Cicuendez M, Cordero E, Topczewski TE, Ferres-Pijoan A, González J, Martínez-Ricarte F, Muñoz-Couselo E, Tabernero J, Bischoff JR, Pettazzoni P, Seoane J. *Cancer Res.* 2022 Jul 18;82(14):2552-2564. IF: 13,312.

Preclinical In Vivo Validation of the RAD51 Test for Identification of Homologous Recombination-Deficient Tumors and Patient Stratification. Pellegrino B, Herencia-Ropero A, Llop-Guevara A, Pedretti F, Moles-Fernández A, Viaplana C, Villacampa G, Guzmán M, Rodríguez O, Grueso J, Jiménez J, Arenas EJ, Degasperi A, Dias JML, Forment JV, O'Connor MJ, Déas O, Cairo S, Zhou Y, Musolino A, Caldas C, Nik-Zainal S, Clarke RB, Nuciforo P, Díez O, Serres-Créixams X, Peg V, Espinosa-Bravo M, Macarulla T, Oaknin A, Mateo J, Arribas J, Dienstmann R, Bellet M, Oliveira M, Saura C, Gutiérrez-Enríquez S, Balmaña J, Serra V. *Cancer Res.* 2022 Apr 15;82(8):1646-1657. IF: 13,312.

Determinants of early triage for hospitalization in myeloproliferative neoplasm (MPN) patients with COVID-19. Barbui T, Carobbio A, Ghirardi A, Iurlo A, Sobas MA, Elli EM, Rumi E, De Stefano V, Lunghi F, Marchetti M, Daffini R, Gasior Kabat M, Cuevas B, Fox ML, Andrade-Campos MM, Palandri F, Guglielmelli P, Benevolo G, Harrison C, Foncillas MA, Bonifacio M, Alvarez-Larran A, Kiladjian JJ, Bolaños Calderón E, Patriarca A, Quiroz Cervantes K, Griesshammer M, Garcia-Gutierrez V, Marin Sanchez A, Magro Mazo E, Carli G, Hernandez-Boluda JC, Osorio S, Carreno-Tarragona G, Sagues Serrano M, Kusec R, Navas Elorza B, Angona A, Xicoy Cirici B, Lopez Abadia E, Koschmieder S, Cattaneo D, Bucelli C, Cichocka E, de Nałęcz AK, Cavalca F, Borsani O, Betti S, Bellini M, Curto-Garcia N, Rambaldi A, Vannucchi AM. *Am J Hematol.* 2022 Dec;97(12):E470-E473. IF: 13,265.

Outcome of infection with omicron SARS-CoV-2 variant in patients with hematological malignancies: An EPICOVIDEHA survey report. Blennow O, Salmanton-García J, Nowak P, Itri F, Van Doesum J, López-García A, Farina F, Jaksic O, Pinczés LI, Bilgin YM, Falces-Romero I, Jiménez M, Ormazabal-Vélez I, Weinbergerová B, Duléry R, Stojanoski Z, Lahmer T, Fernández N, Hernández-Rivas JÁ, Petzer V, De Jonge N, Glenthøj A, De Ramón C, Biernat MM, Fracchiolla N, Aujayeb A, Van Praet J, Schönlein M, Méndez GA, Cattaneo C, Guidetti A, Sciumè M, Ammatuna E, Cordoba R, García-Poutón N, Gräfe S, Cabirta A, Wolf D, Nordlander A, García-Sanz R, Delia M, Berg Venemyr C, Brones C, Di Blasi R, De Kort E, Meers S, Lamure S, Serrano L, Merelli M, Coppola N, Bergantim R, Besson C, Kohn M, Petiti J, Garcia-Vidal C, Dargenio M, Danion F, Machado M, Bailén-Almorox R, Hoenigl M, Dragonetti G, Chai LYA, Kho CS, Bonanni M, Liévin R, Marchesi F, Cornely OA, Pagano L. *Am J Hematol.* 2022 Aug;97(8):E312-E317. IF: 13,265.

Liquid biopsy in gliomas: A RANO review and proposals for clinical applications. Soffietti R, Bettegowda C, Mellinghoff IK, Warren KE, Ahluwalia MS, De Groot JF, Galanis E, Gilbert MR, Jaeckle KA, Le Rhun E, Rudà R, Seoane J, Thon N, Umemura Y, Weller M, van den Bent MJ, Vogelbaum MA, Chang SM, Wen PY. *Neuro Oncol.* 2022 Jun 1;24(6):855-871. IF: 13,029.

Second versus first wave of COVID-19 in patients with MPN. Barbui T, Iurlo A, Masciulli A, Carobbio A, Ghirardi A, Carioli G, Sobas MA, Elli EM, Rumi E, De Stefano V, Lunghi F, Marchetti M, Daffini R, Gasior Kabat M, Cuevas B, Fox ML, Andrade-Campos MM, Palandri F, Guglielmelli P, Benevolo G, Harrison C, Foncillas MA, Bonifacio M, Alvarez-Larran A, Kiladjian JJ, Bolaños Calderón E, Patriarca A, Quiroz Cervantes K, Griessammer M, Garcia-Gutierrez V, Marin Sanchez A, Magro Mazo E, Ruggeri M, Hernandez-Boluda JC, Osorio S, Carreno-Tarragona G, Sagues Serrano M, Kusec R, Navas Elorza B, Angona A, Xicoy Cirici B, Lopez Abadia E, Koschmieder S, Cattaneo D, Bucelli C, Cichocka E, Masternak Kulikowska de Nałęcz A, Cavalca F, Borsani O, Betti S, Benajiba L, Bellini M, Curto-Garcia N, Rambaldi

A, Vannucchi AM. *Leukemia.* 2022 Mar;36(3):897-900. IF: 12,883.

Gasdermin B over-expression modulates HER2-targeted therapy resistance by inducing protective autophagy through Rab7 activation. Gámez-Chiachio M, Molina-Crespo Á, Ramos-Nebot C, Martinez-Val J, Martinez L, Gassner K, Llobet FJ, Soriano M, Hernandez A, Cordani M, Bernadó-Morales C, Diaz E, Rojo-Sebastian A, Triviño JC, Sanchez L, Rodríguez-Barrueco R, Arribas J, Llobet-Navás D, Sarrió D, Moreno-Bueno G. *J Exp Clin Cancer Res.* 2022 Sep 26;41(1):285. IF: 12,658.

A first-in-human phase 1/2 study of FGF401 and combination of FGF401 with spartalizumab in patients with hepatocellular carcinoma or biomarker-selected solid tumors. Chan SL, Schuler M, Kang YK, Yen CJ, Edeline J, Choo SP, Lin CC, Okusaka T, Weiss KH, Macarulla T, Cattan S, Blanc JF, Lee KH, Maur M, Pant S, Kudo M, Assenat E, Zhu AX, Yau T, Lim HY, Bruix J, Geier A, Guillén-Ponce C, Fasolo A, Finn RS, Fan J, Vogel A, Qin S, Riester M, Katsanou V, Chaudhari M, Kakizume T, Gu Y, Porta DG, Myers A, Delord JP. *J Exp Clin Cancer Res.* 2022 Jun 2;41(1):189. IF: 12,658.

Biomarkers of tumor-reactive CD4+ and CD8+ TILs associate with improved prognosis in endometrial cancer. Palomero J, Panisello C, Lozano-Rabella M, Tirtakasuma R, Díaz-Gómez J, Grases D, Pasamar H, Arregui L, Dorca Duch E, Guerra Fernández E, Vivancos A, de Andrea CE, Melero I, Ponce J, Vidal A, Piulats JM, Matias-Guiu X, Gros A. *J Immunother Cancer.* 2022 Dec;10(12):e005443. IF: 12,469.

Immune checkpoint inhibitor therapy and outcomes from SARS-CoV-2 infection in patients with cancer: a joint analysis of OnCovid and ESMO-CoCARE registries. Cortellini A, Dettorre GM, Dafni U, Aguilar-Company J, Castelo-Branco L, Lambertini M, Gennatas S, Angelis V, Sita-Lumsden A, Rogado J, Pedrazzoli P, Viñal D, Prat A, Rossi M, Berardi R, Alonso-Gordoa T, Grisanti S, Dimopoulou G, Queirolo P, Pradervand S, Bertuzzi A, Bower M, Arnold D, Salazar R, Tucci M, Harrington KJ, Mazzoni F, Mukherjee U, Tsourti Z, Michielin O, Pommeret F, Brunet J, Vincenzi B, Tonini G, Patriarca A, Biello F, Krengli M, Tabernero J, Pentheroudakis G, Gennari A, Peters S, Romano E, Pinato DJ. *J Immunother Cancer.* 2022 Nov;10(11):e005732. IF: 12,469.

First-in-human phase I/II, open-label study of the anti-OX40 agonist INCAGN01949 in patients with advanced solid tumors. Davis EJ, Martin-Liberal J, Kristeleit R, Cho DC, Blagden SP, Berthold D, Cardin DB, Vieito M, Miller RE, Hari Dass P, Orcurto A, Spencer K, Janik JE, Clark J, Condamine T, Pulini J, Chen X, Mehnert JM. *J Immunother Cancer.* 2022 Oct;10(10):e004235. IF: 12,469.

Shorter versus longer corticosteroid duration and recurrent immune checkpoint inhibitor-associated AKI. Gupta S, Garcia-Carro C, Prosek JM, Glezerman I, Herrmann SM, Garcia P, Abudayyeh A, Lumlertgul N, Malik AB, Loew S, Beckerman P, Renaghan AD, Carlos CA, Rashidi A, Mithani Z, Deshpande P, Rangarajan S, Shah CV, Seigneux S, Campedel L, Kitchlu A, Shin DS, Coppock G, Ortiz-Melo DI, Sprangers B, Aggarwal V, Benesova K, Wanchoo R, Murakami N, Cortazar FB, Reynolds KL, Sise ME, Soler MJ, Leaf DE; ICPi-AKI Consortium Investigators. *J Immunother Cancer.* 2022 Sep;10(9):e005646. IF: 12,469.

Tumor microenvironment gene expression profiles associated to complete pathological response and disease progression in resectable NSCLC patients treated with neoadjuvant chemoimmunotherapy. Casarrubios M, Provencio M, Nadal E, Insa A, Del Rosario García-Campelo M, Lázaro-Quintela M, Dómine M, Majem M, Rodriguez-Abreu D, Martinez-Marti A, De Castro Carpeño J, Cobo M, López Vivanco G, Del Barco E, Bernabé R, Viñolas N, Barneto Aranda I, Massuti B, Sierra-Rodero B, Martinez-Toledo C, Fernández-Miranda I, Serna-Blanco R, Romero A, Calvo V, Cruz-Bermúdez A. *J Immunother Cancer.* 2022 Sep;10(9):e005320. IF: 12,469.

The CAR-HEMATOTOX risk-stratifies patients for severe infections and disease progression after CD19 CAR-T in R/R LBCL. Rejeski K, Perez A, Iacoboni G, Penack O, Bücklein V, Jentzsch L, Mougiakakos D, Johnson G, Arciola B, Carpio C, Blumenberg V, Hoster E, Bullinger L, Locke FL, von Bergwelt-Baildon M, Mackensen A, Bethge W, Barba P, Jain MD, Subklewe M. *J Immunother Cancer.* 2022 May;10(5):e004475. IF: 12,469.

High levels of chromosomal aberrations negatively associate with benefit to checkpoint inhibition in NSCLC. Frigola J, Carbonell C, Irazno P, Pardo N, Callejo A, Cedres S, Martinez-Marti A, Navarro A, Soleda M, Jimenez J, Hernandez-Losa J, Vivancos A, Felip E, Amat R. *J Immunother Cancer.* 2022 Apr;10(4):e004197. IF: 12,469.

Phase I, multicenter, open-label study of intravenous VCN-01 oncolytic adenovirus with or without nab-paclitaxel plus gemcitabine in patients with advanced solid tumors. Garcia-Carbonero R, Bazan-Peregrino M, Gil-Martín M, Álvarez R, Macarulla T, Riesco-Martinez MC, Verdaguer H, Guillén-Ponce C, Farrera-Sal M, Moreno R, Mato-Berciano A, Maliandi MV, Torres-Manjon S, Costa M, Del Pozo N, Martínez de Villarreal J, Real FX, Vidal N, Capella G, Alemany R, Blasi E, Blasco C, Cascalló M, Salazar R. *J Immunother Cancer.* 2022 Mar;10(3):e003255. IF: 12,469.

Ascites and resistance to immune checkpoint inhibition in dMMR/MSI-H metastatic colorectal and gastric cancers. Fucà G, Cohen R, Lonardi S, Shitara K, Elez ME, Fakih M, Chao J, Klempner SJ, Emmett M, Jayachandran P, Bergamo F, García MD, Mazzoli G, Provenzano L, Colle R, Svrcek M, Ambrosini M, Randon G, Shah AT, Salati M, Fenocchio E, Salvatore L, Chida K, Kawazoe A, Conca V, Curigliano G, Corti F, Cremolini C, Overman M, Andre T, Pietrantonio F. *J Immunother Cancer.* 2022 Feb;10(2):e004001. IF: 12,469.

Safety and antitumor activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) or proficient/stable (MMRp/MSS) endometrial cancer: interim results from GARNET-a phase I, single-arm study. Oaknin A, Gilbert L, Tinker AV, Brown J, Mathews C, Press J, Sabatier R, O'Malley DM, Samouelian V, Boni V, Duska L, Ghamande S, Ghatage P, Kristeleit R, Leath C III, Guo W, Im E, Zildjian S, Han X, Duan T, Veneris J, Pothuri B. *J Immunother Cancer.* 2022 Jan;10(1):e003777. IF: 12,469.

Predictive Role of CD36 Expression in HER2-Positive Breast Cancer Patients Receiving Neoadjuvant Trastuzumab. Ligorio F, Di Cosimo S, Verderio P, Ciniselli CM, Pizzamiglio S, Castagnoli L, Dugo M, Galbardi B, Salgado R, Loi S, Michiels S, Triulzi T, Tagliabue E, El-Abed S, Izquierdo M, de Azambuja E, Nuciforo P, Huober J, Moscetti L, Janni W, Coccia-Portugal MA, Corsetto PA, Belfiore A, Lorenzini D, Daidone MG, Vingiani A, Gianni L, Pupa SM, Bianchini G, Pruneri G, Vernieri C. *J Natl Cancer Inst.* 2022 Dec 8;114(12):1720-1727. IF: 11,816.

COVID-19 Sequelae and the Host Proinflammatory Response: An Analysis From the OnCovid Registry. Cortellini A, Gennari A, Pommeret F, Patel G, Newsom-Davis T, Bertuzzi A, Viladot M, Aguilar-Company J, Mirallas O, Felip E, Lee AJX, Dalla Pria A, Sharkey R, Brunet J, Carmona-García M, Chester J, Mukherjee U, Scotti L, Dolly S, Sita-Lumsden A, Ferrante D, Van Hemelrijck M, Moss C, Russell B, Seguí E, Biello F, Krengli M, Marco-Hernández J, Gaidano G, Patriarca A, Bruna R, Roldán E, Fox L, Pous A, Griscelli F, Salazar R, Martinez-Vila C, Sureda A, Loizidou A, Maluquer C, Stoclin A, Iglesias M, Pedrazzoli P, Rizzo G, Santoro A, Rimassa L, Rossi S, Harbeck N, Sanchez de Torre A, Vincenzi B, Libertini M, Provenzano S, Generali D, Grisanti S, Berardi R, Tucci M, Mazzoni F, Lambertini M, Tagliamento M, Parisi A, Zoratto F, Queirolo P, Giusti R, Guida A, Zambelli A, Tondini C, Maconi A, Betti M, Colomba E, Diamantis N, Sinclair A, Bower M, Ruiz-Camps I, Pinato DJ;

OnCovid study group. *J Natl Cancer Inst.* 2022 Jul 11;114(7):979-987. IF: 11,816.

Clinical Trial Endpoints in Metastatic Cancer: Using Individual Participant Data to Inform Future Trials Methodology. Goldberg RM, Adams R, Buyse M, Eng C, Grothey A, André T, Sobrero AF, Lichtman SM, Benson AB, Punt CJA, Maughan T, Burzykowski T, Sommeijer D, Saad ED, Shi Q, Coart E, Chibaudel B, Koopman M, Schmoll HJ, Yoshino T, Taieb J, Tebbutt NC, Zalcberg J, Tabernero J, Van Cutsem E, Matheson A, de Gramont A. *J Natl Cancer Inst.* 2022 Jun 13;114(6):819-828. IF: 11,816.

Tumor Cellularity and Infiltrating Lymphocytes as a Survival Surrogate in HER2-Positive Breast Cancer. Chic N, Luen SJ, Nuciforo P, Salgado R, Fumagalli D, Hilbers F, Wang Y, de Azambuja E, Láng I, Di Cosimo S, Saura C, Huober J, Prat A, Loi S. *J Natl Cancer Inst.* 2022 Mar 8;114(3):467-470. IF: 11,816.

Breast and Prostate Cancer Risks for Male BRCA1 and BRCA2 Pathogenic Variant Carriers Using Polygenic Risk Scores. Barnes DR, Silvestri V, Leslie G, McGuffog L, Dennis J, Yang X, Adlard J, Agnarsson BA, Ahmed M, Aittomäki K, Andrulis IL, Arason A, Arnold N, Auber B, Azzollini J, Balmaña J, Barkardottir RB, Barrowdale D, Barwell J, Belotti M, Benitez J, Berthet P, Boonen SE, Borg Å, Bozsik A, Brady AF, Brennan P, Brewer C, Brunet J, Bucalo A, Buys SS, Caldés T, Caligo MA, Campbell I, Cassingham H, Christensen LL, Cini G, Claes KBM; GEMO Study Collaborators; EMBRACE Collaborators; Cook J, Coppa A, Cortesi L, Damante G, Darder E, Davidson R, de la Hoya M, De Leeneer K, de Putter R, Del Valle J, Diez O, Ding YC, Domchek SM, Donaldson A, Eason J, Eeles R, Engel C, Evans DG, Feliubadaló L, Fostira F, Frone M, Frost D, Gallagher D, Gehrig A, Giraud S, Glendon G, Godwin AK, Goldgar DE, Greene MH, Gregory H, Gross E, Hahnen E, Hamann U, Hansen TVO, Hanson H, Hentschel J, Horvath J; KConFab Investigators; HEBON Investigators; Izatt L, Izquierdo A, James PA, Janavicius R, Jensen UB, Johannsson OT, John EM, Kramer G, Kroeldrup L, Kruse TA, Lautrup C, Lazaro C, Lesueur F, Lopez-Fernández A, Mai PL, Manoukian S, Matrai Z, Matricardi L, Maxwell KN, Mebirouk N, Meindl A, Montagna M, Monteiro AN, Morrison PJ, Muranen TA, Murray A, Nathanson KL, Neuhausen SL, Nevanlinna H, Nguyen-Dumont T, Niederacher D, Olah E, Olopade OI, Palli D, Parsons MT, Pedersen IS, Peissel B, Perez-Segura P, Peterlongo P, Petersen AH, Pinto P, Porteous ME, Pottinger C, Pujana MA, Radice P, Ramser J, Rantala J, Robson M, Rogers MT, Rønlund K, Rump A, Sánchez de Abajo AM, Shah PD, Sharif S, Side LE, Singer CF, Stadler Z, Steele L, Stoppa-Lyonnet D, Sutter C, Tan YY, Teixeira MR, Teulé A, Thull DL, Tischkowitz M, Toland AE, Tommasi S, Toss A, Trainer AH, Tripathi V, Valentini V, van Asperen CJ, Venturelli M, Viel A, Vijai J, Walker L, Wang-Gohrke S, Wappenschmidt B, Whaite A, Zanna I, Offit K, Thomassen M, Couch FJ, Schmutzler RK, Simard J, Easton DF, Chenevix-Trench G, Antoniou AC, Ottini L; Consortium of Investigators of Modifiers of BRCA1 and BRCA2. *J Natl Cancer Inst.* 2022 Jan 11;114(1):109-122. IF: 11,816.

HER2DX genomic test in HER2-positive/hormone receptor-positive breast cancer treated with neoadjuvant trastuzumab and pertuzumab: A correlative analysis from the PerELISA trial. Guarneri V, Bras-Maristany F, Dieci MV, Griguolo G, Par L, Mar Ín-Aguilera M, Miglietta F, Bottosso M, Giorgi CA, Blasco P, Castillo O, Galv N P, Vivancos A, Villagrasa P, Parker JS, Perou CM, Conte P, Prat A. *EBioMedicine.* 2022 Nov;85:104320. IF: 11,205.

Treatment time and circadian genotype interact to influence radiotherapy side-effects. A prospective European validation study using the REQUITE cohort. Webb AJ, Harper E, Rattay T, Aguado-Barrera ME, Azria D, Bourgier C, Brengues M, Briers E, Bultijnck R, Chang-Claude J, Choudhury A, Cicchetti A, De Ruysscher D, De Santis MC, Dunning AM, Elliott RM, Fachal L, Gómez-Caamaño A, Gutiérrez-Enríquez S, Johnson K, Lobato-Busto R, Kerns SL, Post G, Rancati T, Reyes V, Rosenstein BS, Seibold P, Seoane A, Sosa-Fajardo P, Sperk E, Taboada-Valladares B, Valdagni R, Vega A, Veldeman L, Ward T, West CM, Symonds RP, Talbot CJ; REQUITE Consortium. *EBioMedicine.* 2022 Oct;84:104269. IF: 11,205.

Development and validation of the new HER2DX assay for predicting pathological response and survival outcome in early-stage HER2-positive breast cancer. Prat A, Guarneri V, Pascual T, Brasó-Maristany F, Sanfeliu E, Paré L, Schettini F, Martínez D, Jares P, Griguolo G, Dieci MV, Cortés J, Llombart-Cussac A, Conte B, Marín-Aguilera M, Chic N, Puig-Butillé JA, Martínez A, Galván P, Tsai YH, González-Farré B, Mira A, Vivancos A, Villagrasa P, Parker JS, Conte P, Perou CM. *EBioMedicine.* 2022 Jan;75:103801. IF: 11,205.

Interleukin-1 receptor associated kinase 1/4 and bromodomain and extra-terminal inhibitions converge on NF-κB blockade and display synergistic antitumoral activity in activated B-cell subset of diffuse large B-cell lymphoma with MYD88 L265P mutation. Dlouhy I, Armengol M, Recasens-Zorzo C, Ribeiro ML, Pérez-Galán P, Bosch F, López-Guillermo A, Roué G. *Haematologica.* 2022 Dec 1;107(12):2990. IF: 11,047.

Autologous stem-cell transplantation as consolidation of first-line chemotherapy in patients with peripheral T-cell lymphoma: a multicenter GELTAMO/FIL study. García-Sancho AM, Bellei M, López-Parra M, Gritti G, Cortés M, Novelli S, Panizo C, Petrucci L, Gutiérrez A, Dlouhy I, Bastos-Oreiro M, Sancho JM, Ramírez MJ, Moraleda JM, Carrillo E, Jiménez-Ubieto AI, Jarque I, Orsucci L, García-Torres E, Montalbán C, Dodero A, Arranz R, De Las Heras N, Pascual MJ, López-Jiménez J, Spina M, Re A, De Villambrosia SG, Bobillo S, Federico M, Caballero D. *Haematologica.* 2022 Nov 1;107(11):2675-2684. IF: 11,047.

Chromosome banding analysis and genomic microarrays are both useful but not equivalent methods for genomic complexity risk stratification in chronic lymphocytic leukemia patients. Ramos-Campoy S, Puiggros A, Beà S, Bougeon S, Larráyoz MJ, Costa D, Parker H, Rigolin GM, Ortega M, Blanco ML, Collado R, Salgado R, Baumann T, Gimeno E, Moreno C, Bosch F, Calvo X, Calasanz MJ, Cuneo A, Strefford JC, Nguyen-Khac F, Oscier D, Haferlach C, Schoumans J, Espinet B. *Haematologica.* 2022 Mar 1;107(3):593-603. IF: 11,047.

Mepolizumab Reduces Hypereosinophilic Syndrome Flares Irrespective of Blood Eosinophil Count and Interleukin-5. Rothenberg ME, Roufosse F, Faguer S, Gleich GJ, Steinfeld J, Yancey SW, Mavropoulou E, Kwon N; HES Mepolizumab Study Group. *J Allergy Clin Immunol Pract.* 2022 Sep;10(9):2367-2374.e3. IF: 11,022.

Multi-omic rejuvenation of naturally aged tissues by a single cycle of transient reprogramming. Chondronasiou D, Gill D, Mosteiro L, Urdinguio RG, Berenguer-Llergo A, Aguilera M, Durand S, Aprahamian F, Nirmalathasan N, Abad M, Martin-Herranz DE, Stephan-Otto Attolini C, Prats N, Kroemer G, Fraga MF, Reik W, Serrano M. *Aging Cell.* 2022 Mar;21(3):e13578. IF: 11,005.

Microfluidic-based dynamic BH3 profiling predicts anticancer treatment efficacy. Manzano-Muñoz A, Yeste J, Ortega MA, Martín F, López A, Rosell J, Castro S, Serrano C, Samitier J, Ramón-Azcón J, Montero J. *NPJ Precis Oncol.* 2022 Dec 1;6(1):90. IF: 10,092.

A randomised phase 2 study comparing different dose approaches of induction treatment of regorafenib in previously treated metastatic colorectal cancer patients (REARRANGE trial). Argilés G, Mulet N, Valladares-Ayerbes M, Viéitez JM, Grávalos C, García-Alfonso P, Santos C, Tobeña M, García-Paredes B, Benavides M, Cano MT, Loupakis F, Rodríguez-Garrote M, Rivera F, Goldberg RM, Cremolini C, Bennouna J, Ciardiello F, Tabernero JM, Aranda E; Spanish Cooperative Group for the Treatment of Digestive Tumors (TTD) and UNICANCER GI; The, REARRANGE investigators; Principal investigator; Argilés G, Tabernero J; Steering

Committee; Investigators. *Eur J Cancer.* 2022 Dec;177:154-163. IF: 10,002.

Recent progress and current challenges of immunotherapy in advanced/metastatic esophagogastric adenocarcinoma. Moehler M, Högner A, Wagner AD, Obermannova R, Alsina M, Thuss-Patience P, van Laarhoven H, Smyth E. *Eur J Cancer.* 2022 Nov;176:13-29. IF: 10,002.

Next-generation sequencing analysis of cholangiocarcinoma identifies distinct IDH1-mutated clusters. Rimini M, Loi E, Fabregat-Franco C, Burgio V, Lonardi S, Niger M, Scartozzi M, Raposelli IG, Aprile G, Ratti F, Pedica F, Verdaguer H, Rizzato M, Nichetti F, Lai E, Cappetta A, Macarulla T, Fassan M, De Braud F, Pretta A, Simionato F, De Cobelli F, Aldrighetti L, Fornaro L, Cascinu S, Zavattari P, Casadei-Gardini A. *Eur J Cancer.* 2022 Nov;175:299-310. IF: 10,002.

EMPOWER CERVICAL-1: Effects of cemiplimab versus chemotherapy on patient-reported quality of life, functioning and symptoms among women with recurrent cervical cancer. Oaknin A, Monk BJ, Vergote I, Cristina de Melo A, Kim YM, Lisyanskaya AS, Samouëlian V, Kim HS, Gotovkin EA, Damian F, Chang CL, Takahashi S, Li J, Mathias M, Fury MG, Ivanescu C, Reaney M, LaFontaine PR, Lowy I, Harnett J, Chen CI, Tewari KS. *Eur J Cancer.* 2022 Oct;174:299-309. IF: 10,002.

Pre-operative ribociclib plus letrozole versus chemotherapy: Health-related quality of life outcomes from the SOLTI CORALLEEN trial. Villacampa G, Falato C, Paré L, Hernando C, Arumí M, Saura C, Gómez G, Muñoz M, Gil-Gil M, Izarzugaza Y, Ferrer N, Najera-Zuloaga J, Montaño A, Ciruelos E, González-Santiago S, Villagrasa P, Gavilá J, Prat A, Pascual T. *Eur J Cancer.* 2022 Oct;174:232-242. IF: 10,002.

Prognostic impact of performance status on the outcomes of immune checkpoint inhibition strategies in patients with dMMR/MSI-H metastatic colorectal cancer. Mazzoli G, Cohen R, Lonardi S, Corti F, Elez E, Fakih M, Jayachandran P, Colle R, Shah AT, Salati M, Fenocchio E, Salvatore L, Ambrosini M, Ros J, Intini R, Cremolini C, Overman MJ, André T, Pietrantonio F. *Eur J Cancer.* 2022 Sep;172:171-181. IF: 10,002.

Nazartinib for treatment-naive EGFR-mutant non-small cell lung cancer: Results of a phase 2, single-arm, open-label study. Tan DSW, Kim SW, Ponce Aix S, Sequist LV, Smit EF, Yang JCH, Hida T, Toyozawa R, Felip E, Wolf J, Grohé C, Leighl NB, Riely G, Cui X, Zou M, Ghebremariam S, O'Sullivan-Djentuh L, Belli R, Giovannini M, Kim DW. *Eur J Cancer.* 2022 Sep;172:276-286. IF: 10,002.

Overcoming acquired MET amplification after encorafenib-cetuximab in BRAF-V600E mutated colorectal cancer. Ros J, Elez E. *Eur J Cancer.* 2022 Sep;172:326-328. IF: 10,002.

Lurbinectedin in patients with pretreated neuroendocrine tumours: Results from a phase II basket study. Longo-Muñoz F, Castellano D, Alexandre J, Chawla SP, Fernández C, Kahatt C, Alfaro V, Siguero M, Zeaiter A, Moreno V, Sanz-García E, Awada A, Santaballa A, Subbiah V. *Eur J Cancer.* 2022 Sep;172:340-348. IF: 10,002.

Radium-223 for patients with metastatic castration-resistant prostate cancer with asymptomatic bone metastases progressing on first-line abiraterone acetate or enzalutamide: A single-arm phase II trial. Carles J, Alonso-Gordoa T, Mellado B, Méndez-Vidal MJ, Vázquez S, González-Del-Alba A, Piulats JM, Borrega P, Gallardo E, Morales-Barrera R, Paredes P, Reig O, Garcías de España C, Collado R, Bonfill T, Suárez C, Sampayo-Cordero M, Malfettone A, Garde J. *Eur J Cancer.* 2022 Sep;173:317-326. IF: 10,002.

Gene mutational profile of BRCAness and clinical implication in predicting response to platinum-based chemotherapy in patients with intrahepatic cholangiocarcinoma. Rimini M, Macarulla T, Burgio V, Lonardi S, Niger M, Scartozzi M, Rapposelli IG, Aprile G, Ratti F, Pedica F, Verdaguer H, Nappo F, Nichetti F, Lai E, Valgiusti M, Cappetta A, Febregat C, Fassan M, De Braud F, Puzzoni M, Frassineti GL, Simionato F, De Cobelli F, Aldrighetti L, Fornaro L, Cascinu S, Casadei-Gardini A. *Eur J Cancer.* 2022 Aug;171:232-241. IF: 10,002.

Vaccination against SARS-CoV-2 protects from morbidity, mortality and sequelae from COVID19 in patients with cancer. Pinato DJ, Ferrante D, Aguilar-Company J, Bower M, Salazar R, Mirallas O, Sureda A, Bertuzzi A, Brunet J, Lambertini M, Maluquer C, Pedrazzoli P, Biello F, Lee AJX, Sng CCT, Liñan R, Rossi S, Carmona-García MC, Sharkey R, Eremiev S, Rizzo G, Bain HD, Yu T, Cruz CA, Perachino M, Saoudi-Gonzalez N, Fort-Culillas R, Doonga K, Fox L, Roldán E, Zoratto F, Gaidano G, Ruiz-Camps I, Bruna R, Patriarca A, Shawe-Taylor M, Fusco V, Martinez-Vila C, Berardi R, Filetti M, Mazzoni F, Santoro A, Delfanti S, Parisi A, Queirolo P, Aujayeb A, Rimassa L, Prat A, Tabernero J, Gennari A, Cortellini A; OnCovid study group. *Eur J Cancer.* 2022 Aug;171:64-74. IF: 10,002.

Statin and metformin use and outcomes in patients with castration-resistant prostate cancer treated with enzalutamide: A meta-analysis of AFFIRM, PREVAIL and PROSPER. Joshua AM, Armstrong A, Crumbaker M, Scher HI, de Bono J, Tombal B, Hussain M, Sternberg CN, Gillessen S, Carles J, Fizazi K, Lin P, Duggan W, Sugg J, Russell D, Beer TM. *Eur J Cancer.* 2022 Jul;170:285-295. IF: 10,002.

Persistence of long-term COVID-19 sequelae in patients with cancer: An analysis from the OnCovid registry. Cortellini A, Salazar R, Gennari A, Aguilar-Company J, Bower M, Bertuzzi A, Brunet J, Lambertini M, Maluquer C, Pedrazzoli P, Lee AJ, Carmona-García M, Newsom-Davis T, Van Hemelrijck M, Plaja A, Zambelli A, Tondini C, Generali D, Bertulli R, Diamantis N, Mukherjee U, Rizzo G, Yu T, Zoratto F, Bruna R, Sureda A, Martinez-Vila C, Cantini L, Mazzoni F, Grosso F, Parisi A, Saponara M, Prat A, Pinato DJ; On Covid study group. *Eur J Cancer.* 2022 Jul;170:10-16. IF: 10,002.

Effects of metformin and statins on outcomes in men with castration-resistant metastatic prostate cancer: Secondary analysis of COU-AA-301 and COU-AA-302. Wilson BE, Armstrong AJ, de Bono J, Sternberg CN, Ryan CJ, Scher HI, Smith MR, Rathkopf D, Logothetis CJ, Chi KN, Jones RJ, Saad F, De Porre P, Tran N, Hu P, Gillessen S, Carles J, Fizazi K, Joshua AM. *Eur J Cancer.* 2022 Jul;170:296-304. IF: 10,002.

ANtiangiogenic Second-line Lung cancer Meta-Analysis on individual patient data in non-small cell lung cancer: ANSELMA. Remon J, Lacas B, Herbst R, Reck M, Garon EB, Scagliotti GV, Ramlau R, Hanna N, Vansteenkiste J, Yoh K, Groen HJM, Heymach JV, Mandrekar SJ, Okamoto I, Neal JW, Heist RS, Planchard D, Pignon JP, Besse B; ANSELMA collaborative group. *Eur J Cancer.* 2022 May;166:112-125. IF: 10,002.

Definitions and treatment of oligometastatic oesophagogastric cancer according to multidisciplinary tumour boards in Europe. Kroese TE, van Hillegersberg R, Schoppmann S, Deseyne PRAJ, Nafteux P, Obermannova R, Nordsmark M, Pfeiffer P, Hawkins MA, Smyth E, Markar S, Hanna GB, Cheong E, Chaudry A, Elme A, Adenis A, Piessen G, Gani C, Bruns CJ, Moehler M, Liakakos T, Reynolds J, Morganti A, Rosati R, Castoro C, D'Ugo D, Roviello F, Bencivenga M, de Manzoni G, Jeene P, van Sandick JW, Muijs C, Slingerland M, Nieuwenhuijzen G, Wijnhoven B, Beerepoot LV, Kolodziejczyk P, Polkowski WP, Alsina M, Pera M, Kanonnikoff TF, Nilsson M, Guckenberger M, Monig S, Wagner D, Wyrwicz L, Berbee M, Gockel I, Lordick F, Griffiths EA, Verheij M, van Rossum PSN, van Laarhoven HWM; OMEC working group. *Eur J Cancer.* 2022 Mar;164:18-29. IF: 10,002.

Tumour mutational burden predicts resistance to EGFR/BRAF blockade in BRAF-mutated microsatellite stable metastatic colorectal cancer. Randon G, Intini R, Cremolini C, Elez E, Overman

MJ, Lee J, Manca P, Bergamo F, Pagani F, Antista M, Angerilli V, Ros Montaña FJ, Lavacchi D, Boccaccino A, Fucà G, Brich S, Cattaneo L, Fassan M, Pietrantonio F, Lonardi S. *Eur J Cancer.* 2022 Jan;161:90-98. IF: 10,002.

The target antigen determines the mechanism of acquired resistance to T cell-based therapies. Martínez-Sabadell A, Morancho B, Rius Ruiz I, Román Alonso M, Ovejero Romero P, Escorihuela M, Chicote I, Palmer HG, Nonell L, Alemany-Chavarria M, Klein C, Bacac M, Arribas J, Arenas EJ. *Cell Rep.* 2022 Oct 18;41(3):111430. IF: 9,995.

Breakthrough infections in MPN-COVID vaccinated patients. Barbui T, Carobbio A, Ghirardi A, Iurlo A, De Stefano V, Sobas MA, Rumi E, Elli EM, Lunghi F, Gasior Kabat M, Cuevas B, Guglielmelli P, Bonifacio M, Marchetti M, Alvarez-Larran A, Fox L, Bellini M, Daffini R, Benevolo G, Carreno-Tarragona G, Patriarca A, Al-Ali HK, Andrade-Campos MMM, Palandri F, Harrison C, Foncillas MA, Osorio S, Koschmieder S, Magro Mazo E, Kiladjian JJ, Bolaños Calderón E, Heidel FH, Quiroz Cervantes K, Griesshammer M, Garcia-Gutierrez V, Sanchez AM, Hernandez-Boluda JC, Lopez Abadia E, Carli G, Sagues Serrano M, Kusec R, Xicoy Cirici B, Guenova M, Navas Elorza B, Angona A, Cichocka E, Kulikowska de Nałęcz A, Cattaneo D, Bucelli C, Betti S, Borsani O, Cavalca F, Carbonell S, Curto-Garcia N, Benajiba L, Rambaldi A, Vannucchi AM. *Blood Cancer J.* 2022 Nov 15;12(11):154. IF: 9,812.

A simple score to predict early severe infections in patients with newly diagnosed multiple myeloma. Encinas C, Hernandez-Rivas JÁ, Oriol A, Rosiñol L, Blanchard MJ, Bellón JM, García-Sanz R, de la Rubia J, de la Guía AL, Jímenez-Ubieto A, Jarque I, Iñigo B, Dourdil V, de Arriba F, Pérez-Ávila CC, Gonzalez Y, Hernández MT, Bargay J, Granell M, Rodríguez-Otero P, Silvent M, Cabrera C, Rios R, Alegre A, Gironella M, Gonzalez MS, Sureda A, Sampol A, Ocio EM, Krsnik I, García A, García-Mateo A, Soler JA, Martín J, Arguiñano JM, Mateos MV, Bladé J, San-Miguel JF, Lahuerta JJ, Martínez-López J; GEM/PETHEMA (Grupo Español de Mieloma/Programa para el Estudio de la Terapéutica en Hemopatías Malignas) cooperative study group. *Blood Cancer J.* 2022 Apr 19;12(4):68. IF: 9,812.

Outcomes of patients with small and node-negative HER2-positive early breast cancer treated with adjuvant chemotherapy and anti-HER2 therapy-a sub-analysis of the ALTTO study. Nader-Marta G, Debien V, Eiger D, Tsourti Z, Caparica R, Kassapian M, Napoleone S, Hultsch S, Korde L, Wang Y, Chumsri S, Pritchard KI, Untch M, Bellet-Ezquerra M, Dornelles Rosa D, Moreno-Aspitia A, Piccart M, Dafni U, de Azambuja E. *Br J Cancer.* 2022 Nov;127(10):1799-1807. IF: 9,075.

Natural immunity to SARS-CoV-2 and breakthrough infections in vaccinated and unvaccinated patients with cancer. Cortellini A, Aguilar-Company J, Salazar R, Bower M, Sita-Lumsden A, Plaja A, Lee AJX, Bertuzzi A, Tondini C, Diamantis N, Martinez-Vila C, Prat A, Apthorp E, Gennari A, Pinato DJ. *Br J Cancer.* 2022 Nov;127(10):1787-1792. IF: 9,075.

First-line trifluridine/tipiracil + bevacizumab in patients with unresectable metastatic colorectal cancer: final survival analysis in the TASCO1 study. Van Cutsem E, Danielewicz I, Saunders MP, Pfeiffer P, Argilés G, Borg C, Glynne-Jones R, Punt CJA, Van de Wouw AJ, Fedyanin M, Stroyakovskiy D, Kroening H, Garcia-Alfonso P, Wasan H, Falcone A, Fougeray R, Egorov A, Amellal N, Moiseyenko V. *Br J Cancer.* 2022 Jun;126(11):1548-1554. IF: 9,075.

Effect of aflibercept plus FOLFIRI and potential efficacy biomarkers in patients with metastatic colorectal cancer: the POLAF trial. Élez E, Gómez-España MA, Grávalos C, García-Alfonso P, Ortiz-Morales MJ, Losa F, Díaz IA, Graña B, Toledano-Fonseca M, Valladares-Ayerbes M, Polo E, Salgado M, Martínez de Castro E, Safont MJ, Salud A, Ruiz-Casado A, Tabernero J, Riesco MDC, Rodriguez-Ariza A, Aranda E. *Br J Cancer.* 2022 Apr;126(6):874-880. IF: 9,075.

Basal expression of RAD51 foci predicts olaparib response in patient-derived ovarian cancer xenografts. Guffanti F, Alvisi MF, Anastasia A, Ricci F, Chiappa M, Llop-Guevara A, Serra V, Fruscio R, Degasperi A, Nik-Zainal S, Bani MR, Lupia M, Giavazzi R, Rulli E, Damia G. *Br J Cancer.* 2022 Jan;126(1):120-128. IF: 9,075.

Real-Life Use of Ceftolozane/Tazobactam for the Treatment of Bloodstream Infection Due to Pseudomonas aeruginosa in Neutropenic Hematologic Patients: a Matched Control Study (ZENITH Study). Bergas A, Albasanz-Puig A, Fernández-Cruz A, Machado M, Novo A, van Duin D, Garcia-Vidal C, Hakki M, Ruiz-Camps I, Del Pozo JL, Oltolini C, DeVoe C, Drgona L, Gasch O, Mikulska M, Martín-Dávila P, Peghin M, Vázquez L, Laporte-Amargós J, Durà-Miralles X, Pallarès N, González-Barca E, Álvarez-Uría A, Puerta-Alcalde P, Aguilar-Company J, Carmona-Torre F, Clerici TD, Doernberg SB, Petrikova L, Capilla S, Magnasco L, Fortún J, Castaldo N, Carratalà J, Gudiol C. *Microbiol Spectr.* 2022 Jun 29;10(3):e0229221. IF: 9,043.

Best Treatment Option for Patients With Refractory Aggressive B-Cell Lymphoma in the CAR-T Cell Era: Real-World Evidence From GELTAMO/GETH Spanish Groups. Bastos-Oreiro M, Gutierrez A, Reguera JL, Iacoboni G, López-Corral L, Terol MJ, Ortíz-Maldonado V, Sanz J, Guerra-Dominguez L, Bailen R, Mussetti A, Abrisqueta P, Hernani R, Luzardo H, Sancho JM, Delgado-Serrano J, Salar A, Grande C, Bento L, González de Villambrosía S, García-Belmonte D, Sureda A, Pérez-Martínez A, Barba P, Kwon M, Martín García-Sancho A. *Front Immunol.* 2022 Jul 12;13:855730. IF: 8,786.

AKT-mTORC1 reactivation is the dominant resistance driver for PI3Kβ/AKT inhibitors in PTEN-null breast cancer and can be overcome by combining with Mcl-1 inhibitors. Dunn S, Eberlein C, Yu J, Gris-Oliver A, Ong SH, Yelland U, Cureton N, Staniszewska A, McEwen R, Fox M, Pilling J, Hopcroft P, Coker EA, Jaaks P, Garnett MJ, Isherwood B, Serra V, Davies BR, Barry ST, Lynch JT, Yusa K. *Oncogene.* 2022 Nov;41(46):5046-5060. IF: 8,756.

Predictors of thrombosis and bleeding in 1613 myelofibrosis patients from the Spanish Registry of Myelofibrosis. Hernández-Boluda JC, Pastor-Galán I, Arellano-Rodrigo E, Raya JM, Pérez-Encinas M, Ayala R, Ferrer-Marín F, Velez P, Mora E, Fox ML, Hernández-Rivas JM, Xicoy B, Mata-Vázquez MI, García-Fortes M, Pérez-López R, Angona A, Cuevas B, Senín A, Ramírez MJ, Ramírez-Payer A, Gómez-Casares MT, Martínez-Valverde C, Magro E, Steegmann JL, Durán MA, García-Hernández C, Gasior M, de Villambrosia SG, Alvarez-Larrán A, Pereira A; Spanish MPN Group (GEMFIN). *Br J Haematol.* 2022 Nov;199(4):529-538. IF: 8,615.

Ocular involvement in patients with primary central-nervous-system lymphoma: Analysis of a multicentre study in Spain. Mercadal S, Alañá M, Barceló MI, Bruixola G, López-Pereira P, Bobillo S, Dlouhy I, Agud RC, Molina EG, Martínez P, Cacabelos P, Muntañola A, García-Catalán G, Sancho JM, Campos I, Lado T, Salar A, Caballero AC, Solé-Rodríguez M, Velasco R; Grupo Español de Linfomas y Trasplante Autólogo de Médula Ósea (GELTAMO) and Grupo de Estudio de Neuro-Oftalmología de la Sociedad Española de Neurología (GENOSEN) group. *Br J Haematol.* 2022 Jun;197(6):792-795.IF: 8,615.

Prognostic heterogeneity of adult B-cell precursor acute lymphoblastic leukaemia patients with t(1;19)(q23;p13)/TCF3-PBX1 treated with measurable residual disease-oriented protocols. Ribera J, Granada I, Morgades M, González T, Ciudad J, Such E, Calasanz MJ, Mercadal S, Coll R, González-Campos J, Tormo M, García-Cadenas I, Gil C, Cervera M, Barba P, Costa D, Ayala R, Bermúdez A, Orfao A, Ribera JM; Programa para el Tratamiento de Hemopatias Malignas (PETHEMA) Group (Spanish Society of Hematology, SEHH).

Br J Haematol. 2022 Feb;196(3):670-675. IF: 8,615.

Genetic and phenotypic characterisation of HIV-associated aggressive B-cell non-Hodgkin lymphomas, which do not occur specifically in this population: diagnostic and prognostic implications. Baptista MJ, Tapia G, Muñoz-Marmol AM, Muncunill J, Garcia O, Montoto S, Gribben JG, Calaminici M, Martinez A, Veloza L, Martínez-Trillos A, Aldamiz T, Menarguez J, Terol MJ, Ferrandez A, Alcoceba M, Briones J, González-Barca E, Climent F, Muntañola A, Moraleda JM, Provencio M, Abrisqueta P, Abella E, Colomo L, García-Ballesteros C, Garcia-Caro M, Sancho JM, Ribera JM, Mate JL, Navarro JT. *Histopathology.* 2022 Dec;81(6):826-840. IF: 7,778.

Consensus on prevention and treatment of cancer-associated thrombosis (CAT) in controversial clinical situations with low levels of evidence. Jiménez-Fonseca P, Gallardo E, Arranz Arija F, Blanco JM, Callejo A, Lavin DC, Costa Rivas M, Mosquera J, Rodrigo A, Sánchez Morillas R, Vares Gonzaléz M, Muñoz A, Carmona-Bayonas A. *Eur J Intern Med.* 2022 Jun;100:33-45. IF: 7,749.

Efficacy and safety of trifluridine/tipiracil in older and younger patients with metastatic gastric or gastroesophageal junction cancer: subgroup analysis of a randomized phase 3 study (TAGS). Shitara K, Doi T, Hosaka H, Thuss-Patience P, Santoro A, Longo F, Ozyilkan O, Cicin I, Park D, Zaanan A, Pericay C, Özgüroğlu M, Alsina M, Makris L, Benhadji KA, Ilson DH. *Gastric Cancer.* 2022 May;25(3):586-597. IF: 7,701.

Real-world effectiveness of caplacizumab vs the standard of care in immune thrombotic thrombocytopenic purpura. Izquierdo CP, Mingot-Castellano ME, Fuentes AEK, García-Arroba Peinado J, Cid J, Jimenez MM, Valcarcel D, Gómez-Seguí I, de la Rubia J, Martin P, Goterris R, Hernández L, Tallón I, Varea S, Fernández M, García-Muñoz N, Vara M, Zarzoso MF, García-Candel F, Paciello ML, García-García I, Zalba S, Campuzano V, Gala JM, Estévez JV, Jiménez GM, López Lorenzo JL, Arias EG, Freiría C, Solé M, Ávila Idrovo LF, Hernández Castellet JC, Cruz N, Lavilla E, Pérez-Montaña A, Atucha JA, Moreno Beltrán ME, Moreno Macías JR, Salinas R, Del Rio-Garma J. *Blood Adv.* 2022 Dec 27;6(24):6219-6227. IF: 7,637.

A gene expression assay based on chronic lymphocytic leukemia activation in the microenvironment to predict progression. Abrisqueta P, Medina D, Villacampa G, Lu J, Alcoceba M, Carabia J, Boix J, Tazón-Vega B, Iacoboni G, Bobillo S, Marín-Niebla A, González M, Zenz T, Crespo M, Bosch F. *Blood Adv.* 2022 Nov 8;6(21):5763-5773. IF: 7,637.

Pevonedistat plus azacitidine vs azacitidine alone in higher-risk MDS/chronic myelomonocytic leukemia or low-blast-percentage AML. Adès L, Girshova L, Doronin VA, Díez-Campelo M, Valcárcel D, Kambhampati S, Viniou NA, Woszczyk D, De Paz Arias R, Symeonidis A, Anagnostopoulos A, Munhoz EC, Platzbecker U, Santini V, Fram RJ, Yuan Y, Friedlander S, Faller DV, Sekeres MA. *Blood Adv.* 2022 Sep 13;6(17):5132-5145. IF: 7,637.

Safety and feasibility of stem cell boost as a salvage therapy for severe hematotoxicity after CD19 CAR T-cell therapy. Rejeski K, Burchert A, Iacoboni G, Sesques P, Fransecky L, Bücklein V, Trenker C, Hernani R, Naumann R, Schäfer J, Blumenberg V, Schmidt C, Sohlbach K, von Bergwelt-Baildon M, Bachy E, Barba P, Subklewe M. *Blood Adv.* 2022 Aug 23;6(16):4719-4725. IF: 7,637.

Real-world evidence of brexucabtagene autoleucel for the treatment of relapsed or refractory mantle cell lymphoma. Iacoboni G, Rejeski K, Villacampa G, van Doesum JA, Chiappella A, Bonifazi F, Lopez-Corral L, van Aalderen M, Kwon M, Martínez-Cibrian N, Bramanti S, Reguera-Ortega JL, Camacho-Arteaga L, Schmidt C, Marín-Niebla A, Kersten MJ, Martin Garcia-Sancho A, Zinzani PL, Corradini P, van Meerten T, Subklewe M, Barba P. *Blood Adv.* 2022 Jun 28;6(12):3606-3610. IF: 7,637.

COVID-19 and CAR T cells: a report on current challenges and future directions from the EPICOVIDEHA survey by EHA-IDWP. Busca A, Salmanton-García J, Corradini P, Marchesi F, Cabirta A, Di Blasi R, Dulery R, Lamure S, Farina F, Weinbergerová B, Batinić J, Nordlander A, López-García A, Drgoňa Ľ, Espigado-Tocino I, Falces-Romero I, García-Sanz R, García-Vidal C, Guidetti A, Khanna N, Kulasekararaj A, Maertens J, Hoenigl M, Klimko N, Koehler P, Pagliuca A, Passamonti F, Cornely OA, Pagano L. *Blood Adv.* 2022 Apr 12;6(7):2427-2433. IF: 7,637.

European LeukemiaNet 2017 risk stratification for acute myeloid leukemia: validation in a risk-adapted protocol. Bataller A, Garrido A, Guijarro F, Oñate G, Diaz-Beyá M, Arnan M, Tormo M, Vives S, de Llano MPQ, Coll R, Gallardo D, Vall-Llovera F, Escoda L, Garcia-Guiñon A, Salamero O, Sampol A, Merchan BM, Bargay J, Castaño-Díez S, Esteban D, Oliver-Caldés A, Rivero A, Mozas P, López-Guerra M, Pratcorona M, Zamora L, Costa D, Rozman M, Nomdedéu JF, Colomer D, Brunet S, Sierra J, Esteve J. *Blood Adv.* 2022 Feb 22;6(4):1193-1206. IF: 7,637.

Prognostic impact of DNMT3A mutation in acute myeloid leukemia with mutated NPM1. Oñate G, Bataller A, Garrido A, Hoyos M, Arnan M, Vives S, Coll R, Tormo M, Sampol A, Escoda L, Salamero O, Garcia A, Bargay J, Aljarilla A, Nomdedeu JF, Esteve J, Sierra J, Pratcorona M. *Blood Adv.* 2022 Feb 8;6(3):882-890. IF: 7,637.

Cellular and humoral immunogenicity of the mRNA-1273 SARS-CoV-2 vaccine in patients with hematologic malignancies. Jiménez M, Roldán E, Fernández-Naval C, Villacampa G, Martinez-Gallo M, Medina-Gil D, Peralta-Garzón S, Pujadas G, Hernández C, Pagès C, Gironella M, Fox L, Orti G, Barba P, Pumarola T, Cabirta A, Catalá E, Valentín M, Marín-Niebla A, Orfao A, González M, Campins M, Ruiz-Camps I, Valcárcel D, Bosch F, Hernández M, Crespo M, Esperalba J, Abrisqueta P. *Blood Adv.* 2022 Feb 8;6(3):774-784. IF: 7,637.

Association of CD2AP neuronal deposits with Braak neurofibrillary stage in Alzheimer's disease. Camacho J, Rábano A, Marazuela P, Bonaterra-Pastra A, Serna G, Moliné T, Ramón Y Cajal S, Martínez-Sáez E, Hernández-Guillamon M. *Brain Pathol.* 2022 Jan;32(1):e13016. IF: 7,611.

Safety analyses from the phase 3 ASCENT trial of sacituzumab govitecan in metastatic triple-negative breast cancer. Rugo HS, Tolaney SM, Loirat D, Punie K, Bardia A, Hurvitz SA, O'Shaughnessy J, Cortés J, Diéras V, Carey LA, Gianni L, Piccart MJ, Loibl S, Goldenberg DM, Hong Q, Olivo M, Itri LM, Kalinsky K. *NPJ Breast Cancer.* 2022 Aug 29;8(1):98. IF: 7,519.

Sacituzumab govitecan as second-line treatment for metastatic triple-negative breast cancer-phase 3 ASCENT study subanalysis. Carey LA, Loirat D, Punie K, Bardia A, Diéras V, Dalenc F, Diamond JR, Fontaine C, Wang G, Rugo HS, Hurvitz SA, Kalinsky K, O'Shaughnessy J, Loibl S, Gianni L, Piccart M, Zhu Y, Delaney R, Phan S, Cortés J. *NPJ Breast Cancer.* 2022 Jun 9;8(1):72. IF: 7,519.

Adaptive immune signature in HER2-positive breast cancer in NCCTG (Alliance) N9831 and NeoALTTO trials. Chumsri S, Li Z, Serie DJ, Norton N, Mashadi-Hossein A, Tenner K, Brauer HA, Warren S, Danaher P, Colon-Otero G, Partridge AH, Carey LA, Hilbers F, Van Dooren V, Holmes E, Di Cosimo S, Werner O, Huober JB, Dueck AC, Sotiriou C, Saura C, Moreno-Aspitia A, Knutson KL, Perez EA, Thompson EA. *NPJ Breast Cancer.* 2022 May 24;8(1):68. IF: 7,519.

Gene signatures in patients with early breast cancer and relapse despite pathologic complete response. Bruzas S, Gluz O, Harbeck N, Schmid P, Cortés J, Blohmer J, Seiberling C, Chiari O, Harrach H, Ataseven B, Shenoy S, Dyson MH, Traut E, Theuerkauf I, Gebauer D,

Kuemmel S, Reinisch M. *NPJ Breast Cancer.* 2022 Mar 29;8(1):42. IF: 7,519.

Immunotherapy for early triple negative breast cancer: research agenda for the next decade. Tarantino P, Corti C, Schmid P, Cortes J, Mittendorf EA, Rugo H, Tolaney SM, Bianchini G, Andrè F, Curigliano G. *NPJ Breast Cancer.* 2022 Feb 18;8(1):23. IF: 7,519.

Clonal heterogeneity and rates of specific chromosome gains are risk predictors in childhood high-hyperdiploid B-cell acute lymphoblastic leukemia. Ramos-Muntada M, Trincado JL, Blanco J, Bueno C, Rodríguez-Cortez VC, Bataller A, López-Millán B, Schwab C, Ortega M, Velasco P, Blanco ML, Nomdedeu J, Ramírez-Orellana M, Minguela A, Fuster JL, Cuatrecasas E, Camós M, Ballerini P, Escherich G, Boer J, DenBoer M, Hernández-Rivas JM, Calasanz MJ, Cazzaniga G, Harrison CJ, Menéndez P, Molina O. *Mol Oncol.* 2022 Aug;16(16):2899-2919. IF: 7,449.

Dual inhibition of TGF-β and PD-L1: a novel approach to cancer treatment. Gulley JL, Schlom J, Barcellos-Hoff MH, Wang XJ, Seoane J, Audhuy F, Lan Y, Dussault I, Moustakas A. *Mol Oncol.* 2022 Jun;16(11):2117-2134. IF: 7,449.

Safety, pharmacokinetic, pharmacodynamic and clinical activity of molibresib for the treatment of nuclear protein in testis carcinoma and other cancers: Results of a Phase I/II open-label, dose escalation study. Cousin S, Blay JY, Garcia IB, de Bono JS, Le Tourneau C, Moreno V, Trigo J, Hann CL, Azad AA, Im SA, Cassier PA, French CA, Italiano A, Keedy VL, Plummer R, Sablin MP, Hemming ML, Ferron-Brady G, Wyce A, Khaled A, Datta A, Foley SW, McCabe MT, Wu Y, Horner T, Kremer BE, Dhar A, O'Dwyer PJ, Shapiro GI, Piha-Paul SA. *Int J Cancer.* 2022 Mar 15;150(6):993-1006. IF: 7,316.

The trophectoderm acts as a niche for the inner cell mass through C/EBPα-regulated IL-6 signaling. Plana-Carmona M, Stik G, Bulteau R, Segura-Morales C, Alcázar N, Wyatt CDR, Klonizakis A, de Andrés-Aguayo L, Gasnier M, Tian TV, Torcal Garcia G, Vila-Casadesús M, Plachta N, Serrano M, Francesconi M, Graf T. *Stem Cell Reports.* 2022 Sep 13;17(9):1991-2004. IF:7,294.

Acute kidney injury as a risk factor for mortality in oncological patients receiving checkpoint inhibitors. García-Carro C, Bolufer M, Bury R, Castañeda Z, Muñoz E, Felip E, Lorente D, Carreras MJ, Gabaldon A, Agraz I, Serón D, Soler MJ. *Nephrol Dial Transplant.* 2022 Apr 25;37(5):887-894. IF: 7,186.

Voxel-level analysis of normalized DSC-PWI time-intensity curves: a potential generalizable approach and its proof of concept in discriminating glioblastoma and metastasis. Pons-Escoda A, Garcia-Ruiz A, Naval-Baudin P, Grussu F, Fernandez JJS, Simo AC, Sarro NV, Fernandez-Coello A, Bruna J, Cos M, Perez-Lopez R, Majos C. *Eur Radiol.* 2022 Jun;32(6):3705-3715. IF: 7,034.

Cabozantinib for previously treated radioiodine-refractory differentiated thyroid cancer: Updated results from the phase 3 COSMIC-311 trial. Brose MS, Robinson BG, Sherman SI, Jarzab B, Lin CC, Vaisman F, Hoff AO, Hitre E, Bowles DW, Sen S, Oliver JW, Banerjee K, Keam B, Capdevila J. *Cancer.* 2022 Dec 15;128(24):4203-4212. IF: 6,921.

Clinical activity of CC-90011, an oral, potent, and reversible LSD1 inhibitor, in advanced malignancies. Hollebecque A, Salvagni S, Plummer R, Niccoli P, Capdevila J, Curigliano G, Moreno V, de Braud F, de Villambrosia SG, Martin-Romano P, Baudin E, Arias M, de Alvaro J, Parra-Palau JL, Sánchez-Pérez T, Aronchik I, Filvaroff EH, Lamba M, Nikolova Z, de Bono JS. *Cancer.* 2022 Sep 1;128(17):3185-3195. IF: 6,921.

Real-world analysis of main clinical outcomes in patients with polycythemia vera treated with ruxolitinib or best available therapy after developing resistance/intolerance to hydroxyurea. Alvarez-Larrán A, Garrote M, Ferrer-Marín F, Pérez-Encinas M, Mata-Vazquez MI, Bellosillo B, Arellano-Rodrigo E, Gómez M, García R, García-Gutiérrez V, Gasior M, Cuevas B, Angona A, Gómez-Casares MT, Martínez CM, Magro E, Ayala R, Del Orbe-Barreto R, Pérez-López R, Fox ML, Raya JM, Guerrero L, García-Hernández C, Caballero G, Murillo I, Xicoy B, Ramírez MJ, Carreño-Tarragona G, Hernández-Boluda JC, Pereira A; MPN Spanish Group (Grupo Español de Enfermedades Mieloproliferativas Filadelfia Negativas). *Cancer.* 2022 Jul 1;128(13):2441-2448. IF: 6,921.

RESILIENT part 1: a phase 2 dose-exploration and dose-expansion study of second-line liposomal irinotecan in adults with small cell lung cancer. Paz-Ares L, Spigel DR, Chen Y, Jove M, Juan-Vidal O, Rich P, Hayes T, Calderón VG, Caro RB, Navarro A, Dowlati A, Zhang B, Moore Y, Yao X, Kokhreidze J, Ponce S, Bunn PA. *Cancer.* 2022 May 1;128(9):1801-1811. IF: 6,921.

The correlation between pre-treatment symptoms, acute and late toxicity and patient-reported health-related quality of life in non-small cell lung cancer patients: Results of the REQUITE study. van der Weijst L, Azria D, Berkovic P, Boisselier P, Briers E, Bultijnck R, Chang-Claude J, Choudhury A, Defraene G, Demontois S, Elliott RM, Ennis D, Faivre-Finn C, Franceschini M, Giandini T, Giraldo A, Gutiérrez-Enríquez S, Herskind C, Higginson DS, Kerns SL, Johnson K, Lambrecht M, Lang P, Ramos M, Rancati T, Rimner A, Rosenstein BS, De Ruysscher D, Salem A, Sangalli C, Seibold P, Sosa Fajardo P, Sperk E, Stobart H, Summersgill H, Surmont V, Symonds P, Taboada-Valladares B, Talbot CJ, Vega A, Veldeman L, Veldwijk MR, Ward T, Webb A, West CML, Lievens Y; REQUITE consortium. *Radiother Oncol.* 2022 Nov;176:127-137. IF: 6,901.

Quality of life and late toxicity after short-course radiotherapy followed by chemotherapy or chemoradiotherapy for locally advanced rectal cancer - The RAPIDO trial. Dijkstra EA, Hospers GAP, Kranenbarg EM, Fleer J, Roodvoets AGH, Bahadoer RR, Guren MG, Tjalma JJJ, Putter H, Crolla RMPH, Hendriks MP, Capdevila J, Radu C, van de Velde CJH, Nilsson PJ, Glimelius B, van Etten B, Marijnen CAM. *Radiother Oncol.* 2022 Jun;171:69-76. IF: 6,901.

Use of angiotensin converting enzyme inhibitors is associated with reduced risk of late bladder toxicity following radiotherapy for prostate cancer. Kerns SL, Amidon Morlang A, Lee SM, Peterson DR, Marples B, Zhang H, Bylund K, Rosenzweig D, Hall W, De Ruyck K, Rosenstein BS, Stock RG, Gómez-Caamaño A, Vega A, Sosa-Fajardo P, Taboada-Valladares B, Aguado-Barrera ME, Parker C, Veldeman L, Fonteyne V, Bultijnck R, Talbot CJ, Symonds RP, Johnson K, Rattay T, Webb A, Lambrecht M, de Ruysscher D, Vanneste B, Choudhury A, Elliott RM, Sperk E, Herskind C, Veldwijk MR, Rancati T, Avuzzi B, Valdagni R, Azria D, Farcy Jacquet MP, Chang-Claude J, Seibold P, West C, Janelsins M, Chen Y, Messing E, Morrow G; REQUITE Consortium. *Radiother Oncol.* 2022 Mar;168:75-82. IF: 6,901.

A first-in-human study of the anti-LAG-3 antibody favezelimab plus pembrolizumab in previously treated, advanced microsatellite stable colorectal cancer. Garralda E, Sukari A, Lakhani NJ, Patnaik A, Lou Y, Im SA, Golan T, Geva R, Wermke M, de Miguel M, Palcza J, Jha S, Chaney M, Abraham AK, Healy J, Falchook GS. *ESMO Open.* 2022 Dec;7(6):100639. IF: 6,883.

Antitumor activity of lurbinectedin in combination with oral capecitabine in patients with metastatic breast cancer. Awada AH, Boni V, Moreno V, Aftimos P, Kahatt C, Luepke-Estefan XE, Siguero M, Fernandez-Teruel C, Cullell-Young M, Tabernero J. *ESMO Open.* 2022 Dec;7(6):100651. IF: 6,883.

Pooled safety analysis from phase III studies of trifluridine/tipiracil in patients with metastatic gastric or gastroesophageal junction cancer and metastatic colorectal cancer. Van Cutsem E, Hochster H, Shitara K, Mayer R, Ohtsu A, Falcone A, Yoshino T, Doi T, Ilson DH, Arkenau HT, George B,

Benhadji KA, Makris L, Tabernero J. *ESMO Open.* 2022 Dec;7(6):100633. IF: 6,883.

Isatuximab plus atezolizumab in patients with advanced solid tumors: results from a phase I/II, open-label, multicenter study. Simonelli M, Garralda E, Eskens F, Gil-Martin M, Yen CJ, Obermannova R, Chao Y, Lonardi S, Melichar B, Moreno V, Yu ML, Bongiovanni A, Calvo E, Rottey S, Machiels JP, Gonzalez-Martin A, Paz-Ares L, Chang CL, Mason W, Lin CC, Reardon DA, Vieito M, Santoro A, Meng R, Abbadessa G, Menas F, Lee H, Liu Q, Combeau C, Ternes N, Ziti-Ljajic S, Massard C. *ESMO Open.* 2022 Oct;7(5):100562. IF: 6,883.

MODUL cohort 2: an adaptable, randomized, signal-seeking trial of fluoropyrimidine plus bevacizumab with or without atezolizumab maintenance therapy for BRAFwt metastatic colorectal cancer. Tabernero J, Grothey A, Arnold D, de Gramont A, Ducreux M, O'Dwyer P, Tahiri A, Gilberg F, Irahara N, Schmoll HJ, Van Cutsem E. *ESMO Open.* 2022 Oct;7(5):100559. IF: 6,883.

Lurbinectedin, a selective inhibitor of oncogenic transcription, in patients with pretreated germline BRCA1/2 metastatic breast cancer: results from a phase II basket study. Boni V, Pistilli B, Braña I, Shapiro GI, Trigo J, Moreno V, Castellano D, Fernández C, Kahatt C, Alfaro V, Siguero M, Zeaiter A, Longo F, Zaman K, Antón A, Paredes A, Huidobro G, Subbiah V. *ESMO Open.* 2022 Oct;7(5):100571. IF: 6,883.

Two phase I studies of BI 836880, a vascular endothelial growth factor/angiopoietin-2 inhibitor, administered once every 3 weeks or once weekly in patients with advanced solid tumors. Le Tourneau C, Becker H, Claus R, Elez E, Ricci F, Fritsch R, Silber Y, Hennequin A, Tabernero J, Jayadeva G, Luedtke D, He M, Isambert N. *ESMO Open.* 2022 Oct;7(5):100576. IF: 6,883.

Alternative academic approaches for testing homologous recombination deficiency in ovarian cancer in the MITO16A/MaNGO-OV2 trial. Capoluongo ED, Pellegrino B, Arenare L, Califano D, Scambia G, Beltrame L, Serra V, Scaglione GL, Spina A, Cecere SC, De Cecio R, Normanno N, Colombo N, Lorusso D, Russo D, Nardelli C, D'Incalci M, Llop-Guevara A, Pisano C, Baldassarre G, Mezzanzanica D, Artioli G, Setaro M, Tasca G, Roma C, Campanini N, Cinieri S, Sergi A, Musolino A, Perrone F, Chiodini P, Marchini S, Pignata S. *ESMO Open.* 2022 Oct;7(5):100585. IF: 6,883.

A phase II study of retifanlimab (INCMGA00012) in patients with squamous carcinoma of the anal canal who have progressed following platinum-based chemotherapy (POD1UM-202). Rao S, Anandappa G, Capdevila J, Dahan L, Evesque L, Kim S, Saunders MP, Gilbert DC, Jensen LH, Samalin E, Spindler KL, Tamberi S, Demols A, Guren MG, Arnold D, Fakih M, Kayyal T, Cornfeld M, Tian C, Catlett M, Smith M, Spano JP. *ESMO Open.* 2022 Aug;7(4):100529. IF: 6,883.

Phase I, first-in-human study of MSC-1 (AZD0171), a humanized anti-leukemia inhibitory factor monoclonal antibody, for advanced solid tumors. Borazanci E, Schram AM, Garralda E, Brana I, Vieito Villar M, Spreafico A, Oliva M, Lakhani NJ, Hoffman K, Hallett RM, Maetzel D, Hua F, Hilbert J, Giblin P, Anido J, Kelly A, Vickers PJ, Wasserman R, Seoane J, Siu LL, Hyman DM, Hoff DV, Tabernero J. *ESMO Open.* 2022 Aug;7(4):100530. IF: 6,883.

Advances in the systemic treatment of therapeutic approaches in biliary tract cancer. Mirallas O, López-Valbuena D, García-Illescas D, Fabregat-Franco C, Verdaguer H, Tabernero J, Macarulla T. *ESMO Open.* 2022 Jun;7(3):100503. IF: 6,883.

Quality of life with encorafenib plus cetuximab with or without binimetinib treatment in patients with BRAF V600E-mutant metastatic colorectal cancer: patient-reported outcomes from BEACON CRC. Kopetz S, Grothey A, Van Cutsem E, Yaeger R, Wasan H, Yoshino T, Desai J, Ciardiello F, Loupakis F, Hong YS, Steeghs N, Guren TK, Arkenau HT, Garcia-Alfonso P, Belani A, Zhang X, Tabernero J. *ESMO Open.* 2022 Jun;7(3):100477. IF: 6,883.

Results from the INMUNOSUN-SOGUG trial: a prospective phase II study of sunitinib as a second-line therapy in patients with metastatic renal cell carcinoma after immune checkpoint-based combination therapy. Grande E, Alonso-Gordoa T, Reig O, Esteban E, Castellano D, Garcia-Del-Muro X, Mendez MJ, García-Donas J, González Rodríguez M, Arranz-Arija JA, Lopez-Criado P, Molina-Cerrillo J, Mellado B, Alvarez-Fernandez C, De Velasco G, Cuéllar-Rivas MA, Rodríguez-Alonso RM, Rodríguez-Moreno JF, Suarez-Rodriguez C. *ESMO Open.* 2022 Apr;7(2):100463. IF: 6,883.

Safety and preliminary activity results of the GATTO study, a phase Ib study combining the anti-TA-MUC1 antibody gatipotuzumab with the anti-EGFR tomuzotuximab in patients with refractory solid tumors. Ochsenreither S, Fiedler WM, Conte GD, Macchini M, Matos I, Habel B, Ahrens-Fath I, Raspagliesi F, Lorusso D, Keilholz U, Rolling C, Kebenko M, Klinghammer KF, Saavedra O, Baumeister H, Zurlo A, Garralda E. *ESMO Open.* 2022 Apr;7(2):100447. IF: 6,883.

ESMO Congress 2021: highlights from the EORTC gastrointestinal tract cancer group's perspective. Koessler T, Alsina M, Arnold D, Ben-Aharon I, Collienne M, Lutz MP, Neuzillet C, Obermannova R, Peeters M, Sclafani F, Smyth E, Valle JW, Wagner AD, Wyrwicz L, Fontana E, Moehler M. *ESMO Open.* 2022 Apr;7(2):100392. IF: 6,883.

Phase II multicohort study of atezolizumab monotherapy in multiple advanced solid cancers. Tabernero J, Andre F, Blay JY, Bustillos A, Fear S, Ganta S, Jaeger D, Maio M, Mileshkin L, Melero I. *ESMO Open.* 2022 Apr;7(2):100419. IF: 6,883.

The impact of COVID-19 on oncology professionals-one year on: lessons learned from the ESMO Resilience Task Force survey series. Lim KHJ, Murali K, Thorne E, Punie K, Kamposioras K, Oing C, O'Connor M, Élez E, Amaral T, Garrido P, Lambertini M, Devnani B, Westphalen CB, Morgan G, Haanen JBAG, Hardy C, Banerjee S. *ESMO Open.* 2022 Feb;7(1):100374. IF: 6,883.

The impact of COVID-19 on cancer care and oncology clinical research: an experts' perspective. Sessa C, Cortes J, Conte P, Cardoso F, Choueiri T, Dummer R, Lorusso P, Ottmann O, Ryll B, Mok T, Tempero M, Comis S, Oliva C, Peters S, Tabernero J. *ESMO Open.* 2022 Feb;7(1):100339. IF: 6,883.

Systemic Therapy for HER2-Positive Metastatic Breast Cancer: Current and Future Trends. Vega Cano KS, Marmolejo Castañeda DH, Escrivá-de-Romaní S, Saura C. *Cancers (Basel).* 2022 Dec 22;15(1):51. IF: 6,575.

Simultaneous Onset of Haematological Malignancy and COVID: An Epicovideha Survey. Cattaneo C, Salmanton-García J, Marchesi F, El-Ashwah S, Itri F, Weinbergerová B, Gomes Da Silva M, Dargenio M, Dávila-Valls J, Martín-Pérez S, Farina F, Van Doesum J, Valković T, Besson C, Poulsen CB, López-García A, Žák P, Schönlein M, Piukovics K, Jaksic O, Cabirta A, Ali N, Sili U, Fracchiolla N, Dragonetti G, Adžić-Vukičević T, Marchetti M, Machado M, Glenthøj A, Finizio O, Demirkan F, Blennow O, Tisi MC, Omrani AS, Navrátil M, Ráčil Z, Novák J, Magliano G, Jiménez M, Garcia-Vidal C, Erben N, Del Principe MI, Buquicchio C, Bergantim R, Batinić J, Al-Khabori M, Verga L, Szotkowski T, Samarkos M, Ormazabal-Vélez I, Meers S, Maertens J, Pinczés LI, Hoenigl M, Drgoňa Ľ, Cuccaro A, Bilgin YM, Aujayeb A, Rahimli L, Gräfe S, Sciumè M, Mladenović M, Çolak GM, Sacchi MV, Nordlander A, Berg Venemyr C, Hanáková M, García-Poutón N, Emarah Z, Zambrotta GPM, Nunes Rodrigues R, Cordoba R, Méndez GA, Biernat MM, Cornely OA, Pagano L. *Cancers (Basel).* 2022 Nov 10;14(22):5530. IF: 6,575.

Combined Targeting of Pathogenetic Mechanisms in Pancreatic Neuroendocrine Tumors Elicits Synergistic Antitumor Effects. Gulde S, Foscarini A, April-Monn SL, Genio

E, Marangelo A, Satam S, Helbling D, Falconi M, Toledo RA, Schrader J, Perren A, Marinoni I, Pellegata NS. *Cancers (Basel).* 2022 Nov 8;14(22):5481. IF: 6,575.

Event-Free Survival in Patients with Early HER2-Positive Breast Cancer with a Pathological Complete Response after HER2-Targeted Therapy: A Pooled Analysis. Swain SM, Macharia H, Cortes J, Dang C, Gianni L, Hurvitz SA, Jackisch C, Schneeweiss A, Slamon D, Valagussa P, du Toit Y, Heinzmann D, Knott A, Song C, Cortazar P. *Cancers (Basel).* 2022 Oct 15;14(20):5051. IF: 6,575.

Pharmacogenomics for Prediction of Cardiovascular Toxicity: Landscape of Emerging Data in Breast Cancer Therapies. Altena R, Bajalica-Lagercrantz S, Papakonstantinou A. *Cancers (Basel).* 2022 Sep 25;14(19):4665. IF: 6,575.

Circulating SOD2 Is a Candidate Response Biomarker for Neoadjuvant Therapy in Breast Cancer. Juliachs M, Pujals M, Bellio C, Meo-Evoli N, Duran JM, Zamora E, Parés M, Suñol A, Méndez O, Sánchez-Pla A, Canals F, Saura C, Villanueva J. *Cancers (Basel).* 2022 Aug 10;14(16):3858. IF: 6,575.

Radiomic Signatures Associated with CD8+ Tumour-Infiltrating Lymphocytes: A Systematic Review and Quality Assessment Study. Ramlee S, Hulse D, Bernatowicz K, Pérez-López R, Sala E, Aloj L. *Cancers (Basel).* 2022 Jul 27;14(15):3656. IF: 6,575.

GDF15 Is an Eribulin Response Biomarker also Required for Survival of DTP Breast Cancer Cells. Bellio C, Emperador M, Castellano P, Gris-Oliver A, Canals F, Sánchez-Pla A, Zamora E, Arribas J, Saura C, Serra V, Tabernero J, Littlefield BA, Villanueva J. *Cancers (Basel).* 2022 May 23;14(10):2562. IF: 6,575.

Impact of Individual Comorbidities on Survival of Patients with Myelofibrosis. García-Fortes M, Hernández-Boluda JC, Álvarez-Larrán A, Raya JM, Angona A, Estrada N, Fox L, Cuevas B, García-Hernández MC, Gómez-Casares MT, Ferrer-Marín F, Saavedra S, Cervantes F, García-Delgado R, On Behalf Of The Grupo Español de Enfermedades Mieloproliferativas Filadelfia Negativas Gemfin. *Cancers (Basel).* 2022 May 9;14(9):2331. IF: 6,575.

Tumor Treating Fields Concomitant with Sorafenib in Advanced Hepatocellular Cancer: Results of the HEPANOVA Phase II Study. Gkika E, Grosu AL, Macarulla Mercade T, Cubillo Gracián A, Brunner TB, Schultheiß M, Pazgan-Simon M, Seufferlein T, Touchefeu Y. *Cancers (Basel).* 2022 Mar 18;14(6):1568. IF: 6,575.

Chemorefractory Gastric Cancer: The Evolving Terrain of Third-Line Therapy and Beyond. Alsina M, Tabernero J, Diez M. *Cancers (Basel).* 2022 Mar 10;14(6):1408. IF: 6,575.

Phase 2 Trial (POLA Study) of Lurbinectedin plus Olaparib in Patients with Advanced Solid Tumors: Results of Efficacy, Tolerability, and the Translational Study. Poveda A, Lopez-Reig R, Oaknin A, Redondo A, Rubio MJ, Guerra E, Fariñas-Madrid L, Gallego A, Rodriguez-Freixinos V, Fernandez-Serra A, Juan O, Romero I, Lopez-Guerrero JA. *Cancers (Basel).* 2022 Feb 12;14(4):915. IF: 6,57.

Constitutive Activation of p62/Sequestosome-1-Mediated Proteaphagy Regulates Proteolysis and Impairs Cell Death in Bortezomib-Resistant Mantle Cell Lymphoma. Quinet G, Xolalpa W, Reyes-Garau D, Profitós-Pelejà N, Azkargorta M, Ceccato L, Gonzalez-Santamarta M, Marsal M, Andilla J, Aillet F, Bosch F, Elortza F, Loza-Alvarez P, Sola B, Coux O, Matthiesen R, Roué G, Rodriguez MS. *Cancers (Basel).* 2022 Feb 12;14(4):923. IF: 6,575.

Regulation of B-Cell Receptor Signaling and Its Therapeutic Relevance in Aggressive B-Cell Lymphomas. Profitós-Pelejà N, Santos JC, Marín-Niebla A, Roué G, Ribeiro ML. *Cancers (Basel).* 2022 Feb 9;14(4):860. IF: 6,575.

Endocrine and Neuroendocrine Tumors Special Issue-Checkpoint Inhibitors for Adrenocortical Carcinoma and Metastatic Pheochromocytoma and Paraganglioma: Do They Work? Jimenez C, Armaiz-Pena G, Dahia PLM, Lu Y, Toledo RA, Varghese J, Habra MA. *Cancers (Basel).* 2022 Jan 18;14(3):467. IF: 6,575.

Copy number variants as modifiers of breast cancer risk for BRCA1/BRCA2 pathogenic variant carriers. Hakkaart C, Pearson JF, Marquart L, Dennis J, Wiggins GAR, Barnes DR, Robinson BA, Mace PD, Aittomäki K, Andrulis IL, Arun BK, Azzollini J, Balmaña J, Barkardottir RB, Belhadj S, Berger L, Blok MJ, Boonen SE, Borde J, Bradbury AR, Brunet J, Buys SS, Caligo MA, Campbell I, Chung WK, Claes KBM; GEMO Study Collaborators; EMBRACE Collaborators; Collonge-Rame MA, Cook J, Cosgrove C, Couch FJ, Daly MB, Dandiker S, Davidson R, de la Hoya M, de Putter R, Delnatte C, Dhawan M, Diez O, Ding YC, Domchek SM, Donaldson A, Eason J, Easton DF, Ehrencrona H, Engel C, Evans DG, Faust U, Feliubadaló L, Fostira F, Friedman E, Frone M, Frost D, Garber J, Gayther SA, Gehrig A, Gesta P, Godwin AK, Goldgar DE, Greene MH, Hahnen E, Hake CR, Hamann U, Hansen TVO, Hauke J, Hentschel J, Herold N, Honisch E, Hulick PJ, Imyanitov EN; SWE-BRCA Investigators; kConFab Investigators; HEBON Investigators; Isaacs C, Izatt L, Izquierdo A, Jakubowska A, James PA, Janavicius R, John EM, Joseph V, Karlan BY, Kemp Z, Kirk J, Konstantopoulou I, Koudijs M, Kwong A, Laitman Y, Lalloo F, Lasset C, Lautrup C, Lazaro C, Legrand C, Leslie G, Lesueur F, Mai PL, Manoukian S, Mari V, Martens JWM, McGuffog L, Mebirouk N, Meindl A, Miller A, Montagna M, Moserle L, Mouret-Fourme E, Musgrave H, Nambot S, Nathanson KL, Neuhausen SL, Nevanlinna H, Yie JNY, Nguyen-Dumont T, Nikitina-Zake L, Offit K, Olah E, Olopade OI, Osorio A, Ott CE, Park SK, Parsons MT, Pedersen IS, Peixoto A, Perez-Segura P, Peterlongo P, Pocza T, Radice P, Ramser J, Rantala J, Rodriguez GC, Rønlund K, Rosenberg EH, Rossing M, Schmutzler RK, Shah PD, Sharif S, Sharma P, Side LE, Simard J, Singer CF, Snape K, Steinemann D, Stoppa-Lyonnet D, Sutter C, Tan YY, Teixeira MR, Teo SH, Thomassen M, Thull DL, Tischkowitz M, Toland AE, Trainer AH, Tripathi V, Tung N, van Engelen K, van Rensburg EJ, Vega A, Viel A, Walker L, Weitzel JN, Wevers MR, Chenevix-Trench G, Spurdle AB, Antoniou AC, Walker LC. *Commun Biol.* 2022 Oct 6;5(1):1061. IF: 6,548.

Analysis of microbiome in gastrointestinal stromal tumors: Looking for different players in tumorigenesis and novel therapeutic options. Ravegnini G, Fosso B, Ricci R, Gorini F, Turroni S, Serrano C, Pilco-Janeta DF, Zhang Q, Zanotti F, De Robertis M, Nannini M, Pantaleo MA, Hrelia P, Angelini S. *Cancer Sci.* 2022 Aug;113(8):2590-2599. IF: 6,518.

A Randomized, Double-Blind Noninferiority Study to Evaluate the Efficacy of the Cabozantinib Tablet at 60 mg Per Day Compared with the Cabozantinib Capsule at 140 mg Per Day in Patients with Progressive, Metastatic Medullary Thyroid Cancer. Capdevila J, Klochikhin A, Leboulleux S, Isaev P, Badiu C, Robinson B, Hughes BGM, Keam B, Parnis F, Elisei R, Gajate P, Gan HK, Kapiteijn E, Locati L, Mangeshkar M, Faoro L, Krajewska J, Jarzab B. *Thyroid.* 2022 May;32(5):515-524. IF: 6,506.

Ongoing and evolving clinical trials enhancing future colorectal cancer treatment strategies. Ros J, Saoudi N, Salvà F, Baraibar I, Alonso G, Tabernero J, Elez E. *Expert Opin Investig Drugs.* 2022 Mar;31(3):235-247. IF: 6,498.

New transcriptome and clinical findings of platelet-activating factor in chronic spontaneous urticaria: Pathogenic and treatment relevance. Andrades E, Clarós M, Torres JV, Nonell L, González M, Curto-Barredo L, Rozas-Muñoz E, Gimeno R, Barranco C, Pujol RM, Izquierdo I, Giménez-Arnau AM. *Biofactors.* 2022 Nov;48(6):1284-1294. IF: 6,438.

mTOR Inhibition and T-DM1 in HER2-Positive Breast Cancer. Casadevall D, Hernández-Prat A, García-Alonso S, Arpí-Llucià O, Menéndez S, Qin M, Guardia C, Morancho B, Sánchez-Martín FJ, Zazo S, Gavilán E, Sabbaghi MA, Eroles P, Cejalvo

JM, Lluch A, Rojo F, Pandiella A, Rovira A, Albanell J. *Mol Cancer Res.* 2022 Jul 6;20(7):1108-1121. IF: 6,333.

Presence of Ceramidase Activity in Electronegative LDL. Puig N, Rives J, Estruch M, Aguilera-Simon A, Rotllan N, Camacho M, Colomé N, Canals F, Sánchez-Quesada JL, Benitez S. *Int J Mol Sci.* 2022 Dec 22;24(1):165.IF: 6,208.

A Comprehensive Biomarker Analysis of Microsatellite Unstable/Mismatch Repair Deficient Colorectal Cancer Cohort Treated with Immunotherapy. Élez E, Mulet-Margalef N, Sanso M, Ruiz-Pace F, Mancuso FM, Comas R, Ros J, Argilés G, Martini G, Sanz-Garcia E, Baraibar I, Salvà F, Noguerido A, Cuadra-Urteaga JL, Fasani R, Garcia A, Jimenez J, Aguilar S, Landolfi S, Hernández-Losa J, Braña I, Nuciforo P, Dienstmann R, Tabernero J, Salazar R, Vivancos A. *Int J Mol Sci.* 2022 Dec 21;24(1):118. IF: 6,208.

miRNA Expression May Have Implications for Immunotherapy in PDGFRA Mutant GISTs. Ravegnini G, Nannini M, Indio V, Serrano C, Gorini F, Astolfi A, Di Vito A, Morroni F, Pantaleo MA, Hrelia P, Angelini S. *Int J Mol Sci.* 2022 Oct 14;23(20):12248. IF: 6,208.

Patient-reported outcomes from the randomized phase 3 CROWN study of first-line lorlatinib versus crizotinib in advanced ALK-positive non-small cell lung cancer. Mazieres J, Iadeluca L, Shaw AT, Solomon BJ, Bauer TM, de Marinis F, Felip E, Goto Y, Kim DW, Mok T, Reisman A, Thurm H, Polli AM, Liu G. *Lung Cancer.* 2022 Dec;174:146-156. IF: 6,081.

Alectinib for the treatment of pretreated RET-rearranged advanced NSCLC: Results of the ETOP ALERT-lung trial. Felip E, Smit EF, Molina-Vila MA, Dafni U, Massuti B, Berghmans T, de Marinis F, Passiglia F, Dingemans AC, Cobo M, Viteri S, Britschgi C, Cuffe S, Provencio M, Merkelbach-Bruse S, Andriakopoulou C, Kammler R, Ruepp B, Roschitzki-Voser H, Peters S, Wolf J, Stahel R; ETOP 12-17 ALERT-lung Collaborators. *Lung Cancer.* 2022 Oct;172:94-99. IF: 6,081.

Phase Ib/II study of ceritinib in combination with ribociclib in patients with ALK-rearranged non-small cell lung cancer. Santoro A, Su WC, Navarro A, Simonelli M, Ch Yang J, Ardizzoni A, Barlesi F, Hyoung Kang J, DiDominick S, Abdelhady A, Chen X, Stammberger U, Felip E. *Lung Cancer.* 2022 Apr;166:170-177. IF: 6,081.

Phase II study of afatinib plus pembrolizumab in patients with squamous cell carcinoma of the lung following progression during or after first-line chemotherapy (LUX-Lung-IO). Levy B, Barlesi F, Paz-Ares L, Bennouna J, Erman M, Felip E, Isla D, Ryun Kim H, Kim SW, Madelaine J, Molinier O, Özgüroğlu M, Rodríguez Abreu D, Adeniji A, Lorence RM, Voccia I, Chisamore MJ, Riess JW. *Lung Cancer.* 2022 Apr;166:107-113. IF: 6,081.

Overview of health-related quality of life and toxicity of non-small cell lung cancer patients receiving curative-intent radiotherapy in a real-life setting (the REQUITE study). Van der Weijst L, Aguado-Barrera ME, Azria D, Berkovic P, Boisselier P, Briers E, Bultijnck R, Calvo-Crespo P, Chang-Claude J, Choudhury A, Defraene G, Demontois S, Dunning AM, Elliott RM, Ennis D, Faivre-Finn C, Franceschini M, Gutiérrez-Enríquez S, Herskind C, Higginson DS, Kerns SL, Johnson K, Mollà M, Lambrecht M, Ramos M, Rancati T, Rimner A, Rosenstein BS, De Ruysscher D, Salem A, Sangalli C, Seibold P, Sosa-Fajardo P, Sperk E, Stobart H, Summersgill H, Surmont V, Symonds P, Taboada-Lorenzo B, Talbot CJ, Valdagni R, Vega A, Veldeman L, Veldwijk MR, Ward T, Webb A, West CML; REQUITE Consortium; Lievens Y. *Lung Cancer.* 2022 Apr;166:228-241. IF: 6,081.

Randomized phase 3 study of the anti-disialoganglioside antibody dinutuximab and irinotecan vs irinotecan or topotecan for second-line treatment of small cell lung cancer. Edelman MJ, Dvorkin M, Laktionov K, Navarro A, Juan-Vidal O, Kozlov V, Golden G, Jordan O, Deng CQ, Bentsion D, Chouaid C, Dechev H, Dowlati A, Fernández Núñez N, Ivashchuk O, Kiladze I, Kortua T, Leighl N, Luft A, Makharadze T, Min Y, Quantin X; DISTINCT study investigators. *Lung Cancer.* 2022 Apr;166:135-142. IF: 6,081.

Genetic landscape of patients with ALK-rearranged non-small-cell lung cancer (NSCLC) and response to ceritinib in ASCEND-1 study. Tan DS, Thomas M, Kim DW, Szpakowski S, Urban P, Mehra R, Chow LQM, Sharma S, Solomon BJ, Felip E, Camidge DR, Vansteenkiste J, Petruzzelli L, Pantano S, Shaw AT. *Lung Cancer.* 2022 Jan;163:7-13. IF: 6,081.

Role of Common Cell Culture Media Supplements on Citrate-Stabilized Gold Nanoparticle Protein Corona Formation, Aggregation State, and the Consequent Impact on Cellular Uptake. Barbero F, Michelini S, Moriones OH, Patarroyo J, Rosell J, F Gusta M, Vitali M, Martín L, Canals F, Duschl A, Horejs-Hoeck J, Mondragón L, Bastús NG, Puntes V. *Bioconjug Chem.* 2022 Aug 17;33(8):1505-1514. IF: 6,069.

Machine Learning Based Microbiome Signature to Predict Inflammatory Bowel Disease Subtypes. Liñares-Blanco J, Fernandez-Lozano C, Seoane JA, López-Campos G. *Front Microbiol.* 2022 May 17;13:872671. IF: 6,064.

What is the status of immunotherapy in thyroid neoplasms? Garcia-Alvarez A, Hernando J, Carmona-Alonso A, Capdevila J. *Front Endocrinol (Lausanne).* 2022 Aug 5;13:929091. IF: 6,055.

A Novel EGFRvIII T-Cell Bispecific Antibody for the Treatment of Glioblastoma. Iurlaro R, Waldhauer I, Planas-Rigol E, Bonfill-Teixidor E, Arias A, Nicolini V, Freimoser-Grundschober A, Cuartas I, Martínez-Moreno A, Martínez-Ricarte F, Cordero E, Cicuendez M, Casalino S, Guardia-Reyes X, Fahrni L, Pöschinger T, Steinhart V, Richard M, Briner S, Mueller J, Osl F, Sam J, Colombetti S, Bacac M, Klein C, Pineda E, Reyes-Figueroa L, Di Somma A, González J, Nuciforo P, Carles J, Vieito M, Tabernero J, Umaña P, Seoane J. *Mol Cancer Ther.* 2022 Oct 7;21(10):1499-1509. IF: 6,009.

Development of a mouse model for spontaneous oral squamous cell carcinoma in Fanconi anemia. Errazquin R, Page A, Suñol A, Segrelles C, Carrasco E, Peral J, Garrido-Aranda A, Del Marro S, Ortiz J, Lorz C, Minguillon J, Surralles J, Belendez C, Alvarez M, Balmaña J, Bravo A, Ramirez A, Garcia-Escudero R. *Oral Oncol.* 2022 Nov;134:106184. IF: 5,972.

Pembrolizumab alone or with chemotherapy for recurrent or metastatic head and neck squamous cell carcinoma: Health-related quality-of-life results from KEYNOTE-048. Rischin D, Harrington KJ, Greil R, Soulières D, Tahara M, de Castro G Jr, Psyrri A, Braña I, Neupane P, Bratland Å, Fuereder T, Hughes BGM, Mesía R, Ngamphaiboon N, Rordorf T, Ishak WZW, Hong RL, Mendoza RG, Jia L, Chirovsky D, Norquist J, Jin F, Burtness B. *Oral Oncol.* 2022 May;128:105815. IF: 5,972.

Association of prior local therapy and outcomes with programmed-death ligand-1 inhibitors in advanced urothelial cancer. Makrakis D, Talukder R, Diamantopoulos LN, Carril-Ajuria L, Castellano D, De Kouchkovsky I, Koshkin VS, Park JJ, Alva A, Bilen MA, Stewart TF, McKay RR, Santos VS, Agarwal N, Jain J, Zakharia Y, Morales-Barrera R, Devitt ME, Grant M, Lythgoe MP, Pinato DJ, Nelson A, Hoimes CJ, Shreck E, Gartrell BA, Sankin A, Tripathi A, Zakopoulou R, Bamias A, Murgic J, Fröbe A, Rodriguez-Vida A, Drakaki A, Liu S, Kumar V, Di Lorenzo G, Joshi M, Isaacsson-Velho P, Buznego LA, Duran I, Moses M, Barata P, Sonpavde G, Yu EY, Wright JL, Grivas P, Khaki AR. *BJU Int.* 2022 Nov;130(5):592-603. IF: 5,969.

What Is the Status of Immunotherapy in Neuroendocrine Neoplasms? Garcia-Alvarez A, Cubero JH, Capdevila J. *Curr Oncol Rep.* 2022 Apr;24(4):451-461. IF: 5,945.

New Tyrosine Kinase Inhibitors for the Treatment of Gastrointestinal Stromal

Tumors. Serrano C, Bauer S. *Curr Oncol Rep.* 2022 Feb;24(2):151-159. IF: 5,945.

International initiative for a curated SDHB variant database improving the diagnosis of hereditary paraganglioma and pheochromocytoma. Ben Aim L, Maher ER, Cascon A, Barlier A, Giraud S, Ercolino T, Pigny P, Clifton-Bligh RJ, Mirebeau-Prunier D, Mohamed A, Favier J, Gimenez-Roqueplo AP, Schiavi F, Toledo RA, Dahia PL, Robledo M, Bayley JP, Burnichon N. *J Med Genet.* 2022 Aug;59(8):785-792. IF: 5,941.

Randomized Phase II Trial of Sapanisertib ± TAK-117 vs. Everolimus in Patients With Advanced Renal Cell Carcinoma After VEGF-Targeted Therapy. Choueiri TK, Porta C, Suárez C, Hainsworth J, Voog E, Duran I, Reeves J, Czaykowski P, Castellano D, Chen J, Sedarati F, Powles T. *Oncologist.* 2022 Dec 9;27(12):1048-1057. IF: 5,837.

Position Statement on the Diagnosis, Treatment, and Response Evaluation to Systemic Therapies of Advanced Neuroendocrine Tumors, With a Special Focus on Radioligand Therapy. Capdevila J, Grande E, García-Carbonero R, Simó M, Del Olmo-García MI, Jiménez-Fonseca P, Carmona-Bayonas A, Pubul V. *Oncologist.* 2022 Apr 5;27(4):e328-e339. IF: 5,837.

Current and emerging anti-angiogenic therapies in gastrointestinal and hepatobiliary cancers. Saoudi González N, Castet F, Élez E, Macarulla T, Tabernero J. *Front Oncol.* 2022 Oct 10;12:1021772. IF: 5,738.

Update in collecting duct carcinoma: Current aspects of the clinical and molecular characterization of an orphan disease. Suarez C, Marmolejo D, Valdivia A, Morales-Barrera R, Gonzalez M, Mateo J, Semidey ME, Lorente D, Trilla E, Carles J. *Front Oncol.* 2022 Oct 4;12:970199. IF: 5,738.

B-cell malignancies treated with targeted drugs and SARS-CoV-2 infection: A European Hematology Association Survey (EPICOVIDEHA). Infante MS, Salmanton-García J, Fernández-Cruz A, Marchesi F, Jaksic O, Weinbergerová B, Besson C, Duarte RF, Itri F, Valković T, Szotkovski T, Busca A, Guidetti A, Glenthøj A, Collins GP, Bonuomo V, Sili U, Seval GC, Machado M, Cordoba R, Blennow O, Abu-Zeinah G, Lamure S, Kulasekararaj A, Falces-Romero I, Cattaneo C, Van Doesum J, Piukovics K, Omrani AS, Magliano G, Ledoux MP, de Ramon C, Cabirta A, Verga L, López-García A, Da Silva MG, Stojanoski Z, Meers S, Lahmer T, Martín-Pérez S, Dávila-Vals J, Van Praet J, Samarkos M, Bilgin YM, Karlsson LK, Batinić J, Nordlander A, Schönlein M, Hoenigl M, Ráčil Z, Mladenović M, Hanakova M, Zambrotta GPM, De Jonge N, Adžić-Vukičević T, Nunes-Rodrigues R, Prezioso L, Navrátil M, Marchetti M, Cuccaro A, Calbacho M, Giordano A, Cornely OA, Hernández-Rivas JÁ, Pagano L. *Front Oncol.* 2022 Oct 3;12:992137. IF: 5,738.

Genetic and functional homologous repair deficiency as biomarkers for platinum sensitivity in TNBC: A case report. Gomez-Puerto D, Llop-Guevara A, Cruellas M, Torres-Esquius S, De La Torre J, Peg V, Balmaña J, Pimentel I. *Front Oncol.* 2022 Sep 14;12:963728. IF: 5,738.

Cell Senescence-Related Pathways Are Enriched in Breast Cancer Patients With Late Toxicity After Radiotherapy and Low Radiation-Induced Lymphocyte Apoptosis. Aguado-Flor E, Fuentes-Raspall MJ, Gonzalo R, Alonso C, Ramón Y Cajal T, Fisas D, Seoane A, Sánchez-Pla Á, Giralt J, Díez O, Gutiérrez-Enríquez S. *Front Oncol.* 2022 May 24;12:825703. IF: 5,738.

Hepatic Rupture as the Initial Presentation of an EGFR-Mutated Lung Adenocarcinoma: A Case Report. Mirallas O, Bosch-Schips M, Pardo N, Aubanell A, Salcedo-Allende MT, Callejo A, Iranzo P, Tabernero J, Felip E. *Front Oncol.* 2022 Mar 30;12:837630. IF: 5,738.

The Changing Landscape of Systemic Treatment for Cervical Cancer: Rationale for Inhibition of the TGF-β and PD-L1 Pathways. Birrer MJ, Fujiwara K, Oaknin A, Randall L, Ojalvo LS, Valencia C, Ray-Coquard I. *Front Oncol.* 2022 Feb 23;12:814169.IF: 5,738.

Defining a Standard Set of Health Outcomes for Patients With Squamous Cell Carcinoma of the Head and Neck in Spain. Arrazubi V, Cajaraville G, Cantero D, Giralt J, Mesia R, Monje F, Rueda A, Sistiaga A, Suarez J, Mut A, Comellas M, Lizán L. *Front Oncol.* 2022 Jan 24;11:747520. IF: 5,738.

Enzymatic lysine oxidation as a posttranslational modification. Serra-Bardenys G, Peiró S. *FEBS J.* 2022 Dec;289(24):8020-8031. IF: 5,622.

Biologics in rectal cancer. Jácome AA, Peixoto RD, Gil MV, Ominelli J, Prolla G, Dienstmann R, Eng C. *Expert Opin Biol Ther.* 2022 Oct;22(10):1245-1257. IF: 5,58.

Harmonizing PD-L1 testing in metastatic triple negative breast cancer. Giugliano F, Antonarelli G, Tarantino P, Cortes J, Rugo HS, Curigliano G. *Expert Opin Biol Ther.* 2022 Mar;22(3):345-348. IF: 5,589.

Clearance of ctDNA in triple-negative and HER2-positive breast cancer patients during neoadjuvant treatment is correlated with pathologic complete response. Ciriaco N, Zamora E, Escrivá-de-Romaní S, Miranda Gómez I, Jiménez Flores J, Saura C, Sloane H, Starus A, Fredebohm J, Georgieva L, Speight G, Jones F, Ramón Y Cajal S, Espinosa-Bravo M, Peg V. *Ther Adv Med Oncol.* 2022 Nov 29;14:17588359221139601. IF: 5,485.

Cabozantinib combination therapy for the treatment of solid tumors: a systematic review. Castellano D, Apolo AB, Porta C, Capdevila J, Viteri S, Rodriguez-Antona C, Martin L, Maroto P. *Ther Adv Med Oncol.* 2022 Jul 30;14:17588359221108691. IF: 5,485.

Cabozantinib for the treatment of solid tumors: a systematic review. Maroto P, Porta C, Capdevila J, Apolo AB, Viteri S, Rodriguez-Antona C, Martin L, Castellano D. *Ther Adv Med Oncol.* 2022 Jul 13;14:17588359221107112. IF: 5,485.

Transcriptomics in Tumor and Normal Lung Tissues Identify Patients With Early-Stage Non-Small-Cell Lung Cancer With High Risk of Postsurgery Recurrence Who May Benefit From Adjuvant Therapies. Lazar V, Girard N, Raymond E, Martini JF, Galbraith S, Raynaud J, Bresson C, Solomon B, Magidi S, Nechushtan H, Onn A, Berger R, Chen H, Al-Omari A, Ikeda S, Lassen U, Sekacheva M, Felip E, Tabernero J, Batist G, Spatz A, Pramesh CS, Girard P, Blay JY, Philip T, Berindan-Neagoe I, Porgador A, Rubin E, Kurzrock R, Schilsky RL. *JCO Precis Oncol.* 2022 Sep;6:e2200072. IF: 5,479.

Genomic Biomarkers and Genome-Wide Loss-of-Heterozygosity Scores in Metastatic Prostate Cancer Following Progression on Androgen-Targeting Therapies. Zurita AJ, Graf RP, Villacampa G, Raskina K, Sokol E, Jin D, Antonarakis ES, Li G, Huang RSP, Casanova-Salas I, Vivancos A, Carles J, Ross JS, Schrock AB, Oxnard GR, Mateo J. *JCO Precis Oncol.* 2022 Jul;6:e2200195. IF: 5,479.

An Approach to Solving the Complex Clinicogenomic Data Landscape in Precision Oncology: Learnings From the Design of WAYFIND-R, a Global Precision Oncology Registry. Le Tourneau C, Perret C, Hackshaw A, Blay JY, Nabholz C, Geissler J, Do T, von Meyenn M, Dienstmann R. *JCO Precis Oncol.* 2022 Jul;6:e2200019. IF: 5,479.

Landscape of *KRAS*^{G12C}, Associated Genomic Alterations, and Interrelation With Immuno-Oncology Biomarkers in *KRAS*-Mutated Cancers. Salem ME, El-Refai SM, Sha W, Puccini A, Grothey A, George TJ, Hwang JJ, O'Neil B, Barrett AS, Kadakia KC, Musselwhite LW, Raghavan D, Van Cutsem E, Tabernero J, Tie J. *JCO Precis Oncol.* 2022 Mar;6:e2100245. IF: 5,479.

Clinical and Molecular Characterization of POLE Mutations as Predictive Biomarkers of Response to Immune

Checkpoint Inhibitors in Advanced Cancers. Garmezy B, Gheeya J, Lin HY, Huang Y, Kim T, Jiang X, Thein KZ, Pilié PG, Zeineddine F, Wang W, Shaw KR, Rodon J, Shen JP, Yuan Y, Meric-Bernstam F, Chen K, Yap TA. *JCO Precis Oncol.* 2022 Feb;6:e2100267. IF: 5,479.

Relevance of infections on the outcomes of patients with myelodysplastic syndromes, chronic myelomonocytic leukemia, and acute myeloid leukemia treated with hypomethylating agents: a cohort study from the GESMD. Vilorio-Marqués L, Castañón Fernández C, Mora E, Gutiérrez L, Rey Bua B, Jiménez Lorenzo MJ, Díaz Beya M, Vara Pampliega M, Molero A, Sánchez-García J, Calabuig M, Cedena MT, Chen-Liang T, Díaz Santa JA, Padilla I, Hernández F, Díez R, Asensi P, Xicoy B, Sanz G, Valcárcel D, Diez-Campelo M, Bernal T. *Ther Adv Hematol.* 2022 Sep 29;13:20406207221127547. IF: 5,400.

Management of incidentally discovered appendiceal neuroendocrine tumors after an appendicectomy. Muñoz de Nova JL, Hernando J, Sampedro Núñez M, Vázquez Benítez GT, Triviño Ibáñez EM, Del Olmo García MI, Barriuso J, Capdevila J, Martín-Pérez E. *World J Gastroenterol.* 2022 Apr 7;28(13):1304-1314. IF: 5,374.

Polygenic risk modeling for prediction of epithelial ovarian cancer risk. Dareng EO, Tyrer JP, Barnes DR, Jones MR, Yang X, Aben KKH, Adank MA, Agata S, Andrulis IL, Anton-Culver H, Antonenkova NN, Aravantinos G, Arun BK, Augustinsson A, Balmaña J, Bandera EV, Barkardottir RB, Barrowdale D, Beckmann MW, Beeghly-Fadiel A, Benitez J, Bermisheva M, Bernardini MQ, Bjorge L, Black A, Bogdanova NV, Bonanni B, Borg A, Brenton JD, Budzilowska A, Butzow R, Buys SS, Cai H, Caligo MA, Campbell I, Cannioto R, Cassingham H, Chang-Claude J, Chanock SJ, Chen K, Chiew YE, Chung WK, Claes KBM, Colonna S; GEMO Study Collaborators; GC-HBOC Study Collaborators; EMBRACE Collaborators; Cook LS, Couch FJ, Daly MB, Dao F, Davies E, de la Hoya M, de Putter R, Dennis J, DePersia A, Devilee P, Diez O, Ding YC, Doherty JA, Domchek SM, Dörk T, du Bois A, Dürst M, Eccles DM, Eliassen HA, Engel C, Evans GD, Fasching PA, Flanagan JM, Fortner RT, Machackova E, Friedman E, Ganz PA, Garber J, Gensini F, Giles GG, Glendon G, Godwin AK, Goodman MT, Greene MH, Gronwald J; OPAL Study Group; AOCS Group; Hahnen E, Haiman CA, Håkansson N, Hamann U, Hansen TVO, Harris HR, Hartman M, Heitz F, Hildebrandt MAT, Høgdall E, Høgdall CK, Hopper JL, Huang RY, Huff C, Hulick PJ, Huntsman DG, Imyanitov EN; KConFab Investigators; HEBON Investigators; Isaacs C, Jakubowska A, James PA, Janavicius R, Jensen A, Johannsson OT, John EM, Jones ME, Kang D, Karlan BY, Karnezis A, Kelemen LE, Khusnutdinova E, Kiemeney LA, Kim BG, Kjaer SK, Komenaka I, Kupryjanczyk J, Kurian AW, Kwong A, Lambrechts D, Larson MC, Lazaro C, Le ND, Leslie G, Lester J, Lesueur F, Levine DA, Li L, Li J, Loud JT, Lu KH, Lubiński J, Mai PL, Manoukian S, Marks JR, Matsuno RK, Matsuo K, May T, McGuffog L, McLaughlin JR, McNeish IA, Mebirouk N, Menon U, Miller A, Milne RL, Minlikeeva A, Modugno F, Montagna M, Moysich KB, Munro E, Nathanson KL, Neuhausen SL, Nevanlinna H, Yie JNY, Nielsen HR, Nielsen FC, Nikitina-Zake L, Odunsi K, Offit K, Olah E, Olbrecht S, Olopade OI, Olson SH, Olsson H, Osorio A, Papi L, Park SK, Parsons MT, Pathak H, Pedersen IS, Peixoto A, Pejovic T, Perez-Segura P, Permuth JB, Peshkin B, Peterlongo P, Piskorz A, Prokofyeva D, Radice P, Rantala J, Riggan MJ, Risch HA, Rodriguez-Antona C, Ross E, Rossing MA, Runnebaum I, Sandler DP, Santamariña M, Soucy P, Schmutzler RK, Setiawan VW, Shan K, Sieh W, Simard J, Singer CF, Sokolenko AP, Song H, Southey MC, Steed H, Stoppa-Lyonnet D, Sutphen R, Swerdlow AJ, Tan YY, Teixeira MR, Teo SH, Terry KL, Terry MB; OCAC Consortium; CIMBA Consortium; Thomassen M, Thompson PJ, Thomsen LCV, Thull DL, Tischkowitz M, Titus L, Toland AE, Torres D, Trabert B, Travis R, Tung N, Tworoger SS, Valen E, van Altena AM, van der Hout AH, Van Nieuwenhuysen E, van Rensburg EJ, Vega A, Edwards DV, Vierkant RA, Wang F, Wappenschmidt B, Webb PM, Weinberg CR, Weitzel JN, Wentzensen N, White E, Whittemore AS, Winham SJ, Wolk A, Woo YL, Wu AH, Yan L, Yannoukakos D, Zavaglia KM, Zheng W, Ziogas A, Zorn KK, Kleibl Z, Easton D, Lawrenson K, DeFazio A, Sellers TA, Ramus SJ, Pearce CL, Monteiro AN, Cunningham J, Goode EL, Schildkraut JM, Berchuck A, Chenevix-Trench G, Gayther SA, Antoniou AC, Pharoah PDP. *Eur J Hum Genet.* 2022 Mar;30(3):349-362. IF: 5,351.

Clinical and molecular characteristics of ARIEL3 patients who derived exceptional benefit from rucaparib maintenance treatment for high-grade ovarian carcinoma. O'Malley DM, Oza AM, Lorusso D, Aghajanian C, Oaknin A, Dean A, Colombo N, Weberpals JI, Clamp AR, Scambia G, Leary A, Holloway RW, Gancedo MA, Fong PC, Goh JC, Swisher EM, Maloney L, Goble S, Lin KK, Kwan T, Ledermann JA, Coleman RL. *Gynecol Oncol.* 2022 Dec;167(3):404-413. IF: 5,304.

Olaparib maintenance monotherapy in platinum-sensitive relapsed ovarian cancer patients without a germline BRCA1/BRCA2 mutation: OPINION primary analysis. Poveda A, Lheureux S, Colombo N, Cibula D, Lindemann K, Weberpals J, Bjurberg M, Oaknin A, Sikorska M, González-Martín A, Madry R, Pérez MJR, Ledermann J, Davidson R, Blakeley C, Bennett J, Barnicle A, Škof E. *Gynecol Oncol.* 2022 Mar;164(3):498-504. IF: 5,304.

Leukocytapheresis variables and transit time for allogeneic cryopreserved hpc: better safe than sorry. Fernandez-Sojo J, Horton R, Cid J, Azqueta C, Garcia-Buendia A, Valdivia E, Martorell L, Rubio-Lopez N, Codinach M, Aran G, Marsal J, Mussetti A, Martino R, Diaz-de-Heredia C, Ferra C, Valcarcel D, Linares M, Ancochea A, García-Rey E, García-Muñoz N, Medina L, Carreras E, Villa J, Lozano M, Gibson D, Querol S. *Bone Marrow Transplant.* 2022 Oct;57(10):1531-1538. IF: 5,174.

Long-term outcomes in patients with relapsed/refractory acute myeloid leukemia and other high-risk myeloid malignancies after undergoing sequential conditioning regimen based on IDA-FLAG and high-dose melphalan. Guijarro F, Bataller A, Diaz-Beyá M, Garrido A, Coll-Ferrà C, Vives S, Salamero O, Valcárcel D, Tormo M, Arnan M, Sampol A, Castaño-Díez S, Martínez C, Suárez-Lledó M, Fernández-Avilés F, Hernández-Boluda JC, Ribera JM, Rovira M, Brunet S, Sierra J, Esteve J. *Bone Marrow Transplant.* 2022 Aug;57(8):1304-1312. IF: 5,174.

Post thawing viable CD34+ Cells dose is a better predictor of clinical outcome in lymphoma patients undergoing autologous stem cell transplantation. Fernandez-Sojo J, Cid J, Azqueta C, Valdivia E, Martorell L, Codinach M, Marsal J, Mussetti A, Esquirol A, Trabazo M, Benitez MI, Ferra C, Fox ML, Linares M, Alonso E, García-Rey E, García-Muñoz N, Medina L, Castillo-Flores N, Vall-Llovera F, Garcia A, Pinacho A, Talarn C, Arroba JG, Coll R, Santos M, Valero O, Carreras E, Lozano M, Querol S. *Bone Marrow Transplant.* 2022 Aug;57(8):1341-1343. IF: 5,174.

Streptozotocin, 1982-2022: Forty Years from the FDA's Approval to Treat Pancreatic Neuroendocrine Tumors. Capdevila J, Ducreux M, García Carbonero R, Grande E, Halfdanarson T, Pavel M, Tafuto S, Welin S, Valentí V, Salazar R. *Neuroendocrinology.* 2022;112(12):1155-1167. IF: 5,135.

External Validity of Somatostatin Analogs Trials in Advanced Neuroendocrine Neoplasms: The GETNE-TRASGU Study. Jimenez-Fonseca P, Carmona-Bayonas A, Lamarca A, Barriuso J, Castaño A, Benavent M, Alonso V, Riesco MDC, Alonso-Gordoa T, Custodio A, Sanchez Canovas M, Hernando J, López C, La Casta A, Fernandez Montes A, Marazuela M, Crespo G, Diaz JA, Feliciangeli E, Gallego J, Llanos M, Segura A, Vilardell F, Percovich JC, Grande E, Capdevila J, Valle J, Garcia-Carbonero R. *Neuroendocrinology.* 2022;112(1):88-100. IF: 5,135.

Incidence and characteristics of adverse drug reactions in a cohort of patients treated with PD-1/PD-L1 inhibitors in real-world practice. Sabaté Gallego M, Pérez Esquirol E, Garcia Doladé N, Vidal Guitart X, Carreras Soler MJ, Farriols Danés A, Felip E, Braña I, Carles Galceran J, Morales Barrera R, Muñoz-Couselo E,

Agustí Escasany A. *Front Med (Lausanne).* 2022 Aug 22;9:891179. IF: 5,058.

Case report: Cytokine hemoadsorption in a case of hemophagocytic lymphohistiocytosis secondary to extranodal NK/T-cell lymphoma. Ruiz-Rodríguez JC, Chiscano-Camón L, Ruiz-Sanmartin A, Palmada C, Bajaña I, Iacoboni G, Bonilla C, García-Roche A, Paola Plata-Menchaca E, Maldonado C, Pérez-Carrasco M, Martinez-Gallo M, Franco-Jarava C, Hernández-González M, Ferrer R. *Front Med (Lausanne).* 2022 Aug 15;9:925751. IF: 5,058.

ERANET JTC 2011: Submission and Activation of an International Academic Translational Project in Advanced Breast Cancer. Experience From the ET-FES Study. Monti M, Degenhardt T, Brain E, Wuerstlein R, Argusti A, Puntoni M, Rollandi GA, Corradengo D, Boni L, Ilhan H, Nanni O, Cortes J, Piris-Gimenez A, Piccardo A, Iacozzi M, Matteucci F, Di Iorio V, Alberini JL, Schröder C, Harbeck N, Gennari A. *Front Med (Lausanne).* 2022 Jan 13;8:817678. IF: 5,058.

Multidisciplinary approach to treatment with immune checkpoint inhibitors in patients with HIV, tuberculosis, or underlying autoimmune diseases. Aguilar-Company J, Lopez-Olivo MA, Ruiz-Camps I. *Front Med (Lausanne).* 2022 Jul 15;9:875910. IF:5,058

The Low Incidence of Viral Hepatitis Reactivation Among Subjects on Immunotherapy Reduces the Impact of Suboptimal Screening Rate. Aceituno L, Bañares J, Ruiz-Ortega L, Callejo-Pérez A, Muñoz-Couselo E, Ortiz-Velez C, Díaz-Mejía N, Barreira-Díaz A, Carreras MJ, Farriols A, Buti M, Riveiro-Barciela M. *Front Med (Lausanne).* 2022 Jul 15;9:916213.IF: 5,058.

Overview of Checkpoint Inhibitors Mechanism of Action: Role of Immune-Related Adverse Events and Their Treatment on Progression of Underlying Cancer. Iranzo P, Callejo A, Assaf JD, Molina G, Lopez DE, Garcia-Illescas D, Pardo N, Navarro A, Martinez-Marti A, Cedres S, Carbonell C, Frigola J, Amat R, Felip E. *Front Med (Lausanne).* 2022 May 30;9:875974. IF: 5,058.

Genomic analysis of early-stage lung cancer reveals a role for TP53 mutations in distant metastasis. Van Egeren D, Kohli K, Warner JL, Bedard PL, Riely G, Lepisto E, Schrag D, LeNoue-Newton M, Catalano P, Kehl KL, Michor F; AACR Project GENIE Consortium represented by Shawn Sweeney. *Sci Rep.* 2022 Nov 9;12(1):19055. IF: 4,996.

Molecular profile and its clinical impact of IDH1 mutated versus IDH1 wild type intrahepatic cholangiocarcinoma. Rimini M, Fabregat-Franco C, Burgio V, Lonardi S, Niger M, Scartozzi M, Rapposelli IG, Aprile G, Ratti F, Pedica F, Verdaguer H, Rizzato M, Nichetti F, Lai E, Cappetta A, Macarulla T, Fassan M, De Braud F, Pretta A, Simionato F, De Cobelli F, Aldrighetti L, Fornaro L, Cascinu S, Casadei-Gardini A. *Sci Rep.* 2022 Nov 5;12(1):18775. IF: 4,996.

Results of screening in early and advanced thoracic malignancies in the EORTC pan-European SPECTAlung platform. Morfouace M, Novello S, Stevovic A, Dooms C, Janžič U, Berghmans T, Dziadziuszko R, Gorlia T, Felip E, Paz-Ares L, Mazieres J, O'Brien M, Bironzo P, Vansteenkiste J, Lacroix L, Dingemans AC, Golfinopoulos V, Besse B. *Sci Rep.* 2022 May 18;12(1):8342. IF: 4,996.

Diffuse Large B-Cell Epstein-Barr Virus-Positive Primary CNS Lymphoma in Non-AIDS Patients: High Diagnostic Accuracy of DSC Perfusion Metrics. Pons-Escoda A, García-Ruíz A, Naval-Baudin P, Grussu F, Viveros M, Vidal N, Bruna J, Plans G, Cos M, Perez-Lopez R, Majós C. *AJNR Am J Neuroradiol.* 2022 Nov;43(11):1567-1574. IF: 4,966.

Association between Germline Single-Nucleotide Variants in ADME Genes and Major Molecular Response to Imatinib in Chronic Myeloid Leukemia Patients. Estrada N, Zamora L, Ferrer-Marín F, Palomo L, García O, Vélez P, De la Fuente I, Sagüés M, Cabezón M, Cortés M, Vallansot RO, Senín-Magán MA, Boqué C, Xicoy B. *J Clin Med.* 2022 Oct 21;11(20):6217. IF: 4,964.

Pharmacokinetics and pharmacodynamics of approved monoclonal antibody therapy for colorectal cancer. Saoudi Gonzalez N, López D, Gómez D, Ros J, Baraibar I, Salva F, Tabernero J, Élez E. *Expert Opin Drug Metab Toxicol.* 2022 Nov;18(11):755-767. IF: 4,936.

Spatial patterns of brain lesions assessed through covariance estimations of lesional voxels in multiple Sclerosis: The SPACE-MS technique. Tur C, Grussu F, De Angelis F, Prados F, Kanber B, Calvi A, Eshaghi A, Charalambous T, Cortese R, Chard DT, Chataway J, Thompson AJ, Ciccarelli O, Gandini Wheeler-Kingshott CAM. *Neuroimage Clin.* 2022;33:102904. IF: 4,891.

Neurotoxicity-associated sinus bradycardia after chimeric antigen receptor T-cell therapy. Catalá E, Iacoboni G, Vidal-Jordana Á, Oristrell G, Carpio C, Vilaseca A, Cabirta A, Bosch F, Tintoré M, Barba P. *Hematol Oncol.* 2022 Aug;40(3):482-487. IF: 4,850.

Safety of Tepotinib in Patients With MET Exon 14 Skipping NSCLC and Recommendations for Management. Veillon R, Sakai H, Le X, Felip E, Cortot AB, Smit EF, Park K, Griesinger F, Britschgi C, Wu YL, Melosky B, Baijal S, Jr GC, Sedova M, Berghoff K, Otto G, Paik PK. *Clin Lung Cancer.* 2022 Jun;23(4):320-332. IF: 4,840.

Efficacy and Safety of Brigatinib Compared With Crizotinib in Asian vs. Non-Asian Patients With Locally Advanced or Metastatic ALK-Inhibitor-Naive ALK+ Non-Small Cell Lung Cancer: Final Results From the Phase III ALTA-1L Study. Ahn MJ, Kim HR, Yang JCH, Han JY, Li JY, Hochmair MJ, Chang GC, Delmonte A, Lee KH, Campelo RG, Gridelli C, Spira AI, Califano R, Griesinger F, Ghosh S, Felip E, Kim DW, Liu Y, Zhang P, Popat S, Camidge DR. *Clin Lung Cancer.* 2022 Dec;23(8):720-730. IF: 4,840.

Encorafenib plus cetuximab for the treatment of BRAF-V600E-mutated metastatic colorectal cancer. Ros J, Saoudi N, Baraibar I, Salva F, Tabernero J, Elez E. *Therap Adv Gastroenterol.* 2022 Jul 4;15:17562848221110644. IF: 4,802.

A WIN Consortium phase I study exploring avelumab, palbociclib, and axitinib in advanced non-small cell lung cancer. Solomon B, Callejo A, Bar J, Berchem G, Bazhenova L, Saintigny P, Wunder F, Raynaud J, Girard N, Lee JJ, Sulaiman R, Prouse B, Bresson C, Ventura H, Magidi S, Rubin E, Young B, Onn A, Leyland-Jones B, Schilsky RL, Lazar V, Felip E, Kurzrock R. *Cancer Med.* 2022 Jul;11(14):2790-2800. IF: 4,711.

What if the future of HER2-positive breast cancer patients was written in miRNAs? An exploratory analysis from NeoALTTO study. Pizzamiglio S, Cosentino G, Ciniselli CM, De Cecco L, Cataldo A, Plantamura I, Triulzi T, El-Abed S, Wang Y, Bajji M, Nuciforo P, Huober J, Ellard SL, Rimm DL, Gombos A, Daidone MG, Verderio P, Tagliabue E, Di Cosimo S, Iorio MV. *Cancer Med.* 2022 Jan;11(2):332-339. IF: 4,711.

ADAGIO: a phase IIb international study of the Wee1 inhibitor adavosertib in women with recurrent or persistent uterine serous carcinoma. Liu J, Oza AM, Colombo N, Oaknin A. *Int J Gynecol Cancer.* 2022 Jan;32(1):89-92. IF: 4,661.

Patient-reported outcomes in individuals with advanced gastrointestinal stromal tumor treated with ripretinib in the fourth-line setting: analysis from the phase 3 INVICTUS trial. Schöffski P, George S, Heinrich MC, Zalcberg JR, Bauer S, Gelderblom H, Serrano C, Jones RL, Attia S, D'Amato G, Chi P, Reichardt P, Becker C, Shi K, Meade J, Ruiz-Soto R, Blay JY, von Mehren M. *BMC Cancer.* 2022 Dec 13;22(1):1302. IF: 4,638.

Pembrolizumab in combination with gemcitabine for patients with HER2-negative advanced breast cancer: GEICAM/2015-04 (PANGEA-Breast) study. de la Cruz-Merino L, Gion M, Cruz J,

Alonso-Romero JL, Quiroga V, Moreno F, Andrés R, Santisteban M, Ramos M, Holgado E, Cortés J, López-Miranda E, Cortés A, Henao F, Palazón-Carrión N, Rodriguez LM, Ceballos I, Soto A, Puertes A, Casas M, Benito S, Chiesa M, Bezares S, Caballero R, Jiménez-Cortegana C, Sánchez-Margalet V, Rojo F. *BMC Cancer.* 2022 Dec 3;22(1):1258. IF: 4,638.

The LEGACy study: a European and Latin American consortium to identify risk factors and molecular phenotypes in gastric cancer to improve prevention strategies and personalized clinical decision making globally. van Schooten TS, Derks S, Jiménez-Martí E, Carneiro F, Figueiredo C, Ruiz E, Alsina M, Molero C, Garrido M, Riquelme A, Caballero C, Lezcano E, O'Connor JM, Esteso F, Farrés J, Mas JM, Lordick F, Vogt J, Cardone A, Girvalaki C, Cervantes A, Fleitas T; members of LEGACy consortium. *BMC Cancer.* 2022 Jun 13;22(1):646. IF: 4,638.

A multicenter, dose-finding, phase 1b study of imatinib in combination with alpelisib as third-line treatment in patients with advanced gastrointestinal stromal tumor. Pantaleo MA, Heinrich MC, Italiano A, Valverde C, Schöffski P, Grignani G, Reyners AKL, Bauer S, Reichardt P, Stark D, Berhanu G, Brandt U, Stefanelli T, Gelderblom H. *BMC Cancer.* 2022 May 6;22(1):511. IF: 4,638.

An open label, randomized phase 2 trial assessing the impact of food on the tolerability of abemaciclib in patients with advanced breast cancer. Lim E, Boyle F, Okera M, Loi S, Goksu SS, van Hal G, Chapman SC, Gable JC, Chen Y, Price GL, Hossain AM, Gainford MC, Ezquerra MB. *Breast Cancer Res Treat.* 2022 Oct;195(3):275-287. IF: 4,624.

Incidence of adverse events with therapies targeting HER2-positive metastatic breast cancer: a literature review. Perez EA, Dang C, Lee C, Singh J, Wang K, Layton JB, Gilsenan A, Hackshaw MD, Cortes J. *Breast Cancer Res Treat.* 2022 Jul;194(1):1-11. IF: 4,624.

Ipatasertib plus paclitaxel for PIK3CA/AKT1/PTEN-altered hormone receptor-positive HER2-negative advanced breast cancer: primary results from cohort B of the IPATunity130 randomized phase 3 trial. Turner N, Dent RA, O'Shaughnessy J, Kim SB, Isakoff SJ, Barrios C, Saji S, Bondarenko I, Nowecki Z, Lian Q, Reilly SJ, Hinton H, Wongchenko MJ, Kovic B, Mani A, Oliveira M. *Breast Cancer Res Treat.* 2022 Feb;191(3):565-576. IF: 4,624.

Economic and Humanistic Burden of Triple-Negative Breast Cancer: A Systematic Literature Review. Huang M, Haiderali A, Fox GE, Frederickson A, Cortes J, Fasching PA, O'Shaughnessy J. *Pharmacoeconomics.* 2022 May;40(5):519-558. IF: 4,558.

Manufacturing-dependent change in biological activity of the TLR4 agonist GSK1795091 and implications for lipid A analog development. Steeghs N, Hansen AR, Hanna GJ, Garralda E, Park H, Strauss J, Adam M, Campbell G, Carver J, Easton R, Mays K, Skrdla P, Struemper H, Washburn ML, Matheny C, Piha-Paul SA. *Clin Transl Sci.* 2022 Nov;15(11):2625-2639. IF: 4,438.

Considerations on diagnosis and surveillance measures of PTEN hamartoma tumor syndrome: clinical and genetic study in a series of Spanish patients. Pena-Couso L, Ercibengoa M, Mercadillo F, Gómez-Sánchez D, Inglada-Pérez L, Santos M, Lanillos J, Gutiérrez-Abad D, Hernández A, Carbonell P, Letón R, Robledo M, Rodríguez-Antona C, Perea J, Urioste M; PHTS Working Group. *Orphanet J Rare Dis.* 2022 Feb 28;17(1):85. IF: 4,303.

Machine learning techniques to estimate the degree of binder activity of reclaimed asphalt pavement. Botella R, Lo Presti D, Vasconcelos K, Bernatowicz K, Martinez AH, Miro R, Specht L, Mercado EA, Pires GM, Pasquini E, Ogbo C, Preti F, Pasetto M, del Barco AJ, Roberto A, Oreskovic M, Kuna KK, Guduru G, Martin AE, Carter A, Giancontieri G, Abed A, Dave E, Tebaldi G. *Mater Struct.* 2022. 55. (4):112. IF: 4,285.

Safety and efficacy of ribociclib plus letrozole in patients with HR+, HER2- advanced breast cancer: Results from the Spanish sub-population of the phase 3b CompLEEment-1 trial. Salvador Bofill J, Moreno Anton F, Rodriguez Sanchez CA, Galve Calvo E, Hernando Melia C, Ciruelos Gil EM, Vidal M, Jiménez-Rodriguez B, De la Cruz Merino L, Martínez Jañez N, Villanueva Vazquez R, de Toro Salas R, Anton Torres A, Alvarez Lopez IM, Gavila Gregori J, Quiroga Garcia V, Vicente Rubio E, De la Haba-Rodriguez J, Gonzalez-Santiago S, Diaz Fernandez N, Barnadas Molins A, Cantos Sanchez de Ibargüen B, Delgado Mingorance JI, Bellet Ezquerra M, de Casa S, Gimeno A, Martin M. *Breast.* 2022 Dec;66:77-84. IF: 4,254.

A retrospective validation of CanAssist Breast in European early-stage breast cancer patient cohort. Gunda A, Basavaraj C, Serkad V CP, Adinarayan M, Kolli R, Siraganahalli Eshwaraiah M, Saura C, Ruiz F, Gomez P, Peg V, Jimenez J, Sprung S, Fiegl H, Brunner C, Egle D, Bhattacharyya GS, Bakre MM. *Breast.* 2022 Jun;63:1-8. IF: 4,254.

Transcriptional response to a Mediterranean diet intervention exerts a modulatory effect on neuroinflammation signaling pathway. Almanza-Aguilera E, Hernáez A, Corella D, Aguayo DM, Ros E, Portolés O, Valussi J, Estruch R, Coltell O, Subirana I, Salas-Salvadó J, Ruiz-Canela M, de la Torre R, Nonell L, Fitó M, Castañer O. *Nutr Neurosci.* 2022 Feb;25(2):256-265. IF: 4,062.

Binding of anisotropic curvature-inducing proteins onto membrane tubes. Noguchi H, Tozzi C, Arroyo M. *Soft Matter.* 2022 May 4;18(17):3384-3394. IF: 4,046.

Highlights from the 2022 ASCO gastrointestinal cancer symposium: An overview by the EORTC gastrointestinal tract cancer group. Sclafani F, Fontana E, Wyrwicz L, Wagner AD, Valle JW, Smyth E, Peeters M, Obermannova R, Neuzillet C, Lutz MP, Koessler T, Ben-Aharon I, Arnold D, Alsina M, Moehler M. *Clin Colorectal Cancer.* 2022 Sep;21(3):188-197. IF: 4,035.

Low-risk polycythemia vera treated with phlebotomies: clinical characteristics, hematologic control and complications in 453 patients from the Spanish Registry of Polycythemia Vera. Triguero A, Pedraza A, Pérez-Encinas M, Mata-Vázquez MI, Vélez P, Fox L, Gómez-Calafat M, García-Delgado R, Gasior M, Ferrer-Marín F, García-Gutiérrez V, Angona A, Gómez-Casares MT, Cuevas B, Martínez C, Pérez R, Raya JM, Guerrero L, Murillo I, Bellosillo B, Hernández-Boluda JC, Sanz C, Álvarez-Larrán A; On behalf of the MPN Spanish Group (GEMFIN). *Ann Hematol.* 2022 Oct;101(10):2231-2239. IF: 4,030.

Mortality in acquired thrombotic thrombocytopenic purpura in the pre-caplacizumab era. Del Río-Garma J, Bobillo S, de la Rubia J, Pascual C, García-Candel F, García-Gala JM, Gonzalez R, Abril L, Vidan J, Gomez MJ, Peña F, Arbona C, Martín-Sanchez J, Moreno G, Romón I, Viejo A, Oliva A, Linares M, Salinas R, Pérez S, Garcia-Erce JA, Pereira A; "Registro Español de la Púrpura Trombocitopénica Trombótica (REPTT)", and the "Grupo Español de Aféresis (GEA)". *Ann Hematol.* 2022 Jan;101(1):59-67. IF: 4,030.

Clinical implications of homologous recombination repair mutations in prostate cancer. Cresta Morgado P, Mateo J. *Prostate.* 2022 Aug;82 Suppl 1:S45-S59. IF: 4,012.

The impact of COVID-19 on the management of neuroendocrine tumors (NETS): An international NET CONNECT survey of NET patients and healthcare professionals treating net patients. Cives M, Hernando J, Lamarca A, Bouvier C, Caplin M, Pavel M. *J Neuroendocrinol.* 2022 Oct;34(10):e13196. IF: 3,870.

Development of a quality of life questionnaire for patients with pancreatic neuroendocrine tumours (the PANNET module). Ramage JK, Friend E, Randell J, King B, Fernandez Ortega

P, McNamara MG, Kaltsas G, Falconi M, Cwikla J, Capdevila J, Grozinsky-Glasberg S, Mandair D, Gamper E, Srirajaskanthan R, O Weickert M, Gray D; EORTC Quality of Life Group. *J Neuroendocrinol.* 2022 Apr;34(4):e13097. IF: 3,870.

Multi-laboratory experiment PME11 for the standardization of phosphoproteome analysis. Colomé N, Abian J, Aloria K, Arizmendi JM, Barceló-Batllori S, Braga-Lagache S, Burlet-Schiltz O, Carrascal M, Casal JI, Chicano-Gálvez E, Chiva C, Clemente LF, Elortza F, Estanyol JM, Fernandez-Irigoyen J, Fernández-Puente P, Fidalgo MJ, Froment C, Fuentes M, Fuentes-Almagro C, Gay M, Hainard A, Heller M, Hernández ML, Ibarrola N, Iloro I, Kieselbach T, Lario A, Locard-Paulet M, Marina-Ramírez A, Martín L, Morato-López E, Muñoz J, Navajas R, Odena MA, Odriozola L, de Oliveira E, Paradela A, Pasquarello C, de Los Rios V, Ruiz-Romero C, Sabidó E, Sánchez Del Pino M, Sancho J, Santamaría E, Schaeffer-Reiss C, Schneider J, de la Torre C, Valero ML, Vilaseca M, Wu S, Wu L, Ximénez de Embún P, Canals F, Corrales FJ; ProteoRed-ISCIII; EuPA. *J Proteomics.* 2022 Jan 16;251:104409. IF: 3,855.

Cytokine response as a biomarker for early diagnosis and outcome prediction of stem cell transplant recipients and acute leukemia patients with invasive aspergillosis. Puerta-Alcalde P, Ruiz-Camps I, Gudiol C, Salavert M, Barba P, Morandeira F, Jarque I, Cuervo G, Ayats J, Carratalà J, Garcia-Vidal C. *Med Mycol.* 2022 Jul 23;60(7):myac038. IF: 3,747.

Multi-echo quantitative susceptibility mapping: how to combine echoes for accuracy and precision at 3 Tesla. Biondetti E, Karsa A, Grussu F, Battiston M, Yiannakas MC, Thomas DL, Shmueli K. *Magn Reson Med.* 2022 Nov;88(5):2101-2116.IF: 3,737.

SENSE EPI reconstruction with 2D phase error correction and channel-wise noise removal. Powell E, Schneider T, Battiston M, Grussu F, Toosy A, Clayden JD, Wheeler-Kingshott CAMG. *Magn Reson Med.* 2022 Nov;88(5):2157-2166.IF: 3,737.

Comparison of multicenter MRI protocols for visualizing the spinal cord gray matter. Cohen-Adad J, Alonso-Ortiz E, Alley S, Lagana MM, Baglio F, Vannesjo SJ, Karbasforoushan H, Seif M, Seifert AC, Xu J, Kim JW, Labounek R, Vojtíšek L, Dostál M, Valošek J, Samson RS, Grussu F, Battiston M, Gandini Wheeler-Kingshott CAM, Yiannakas MC, Gilbert G, Schneider T, Johnson B, Prados F. *Magn Reson Med.* 2022 Aug;88(2):849-859. IF: 3,737.

Diffusion MRI signal cumulants and hepatocyte microstructure at fixed diffusion time: Insights from simulations, 9.4T imaging, and histology. Grussu F, Bernatowicz K, Casanova-Salas I, Castro N, Nuciforo P, Mateo J, Barba I, Perez-Lopez R. *Magn Reson Med.* 2022 Jul;88(1):365-379. IF: 3,737.

Tyrosine kinase inhibitor dose reduction during the management of accelerated phase chronic myeloid leukemia. Ortí G, García-Gutiérrez V, Bautista G, Ferrer-Marín F, Vallansot R, Xicoy B, Sánchez À, Simon I, Triguero A, Sierra M, Casado LF; Grupo Español de Leucemia Mieloide Crónica (GELMC). *Leuk Res.* 2022 Oct;121:106923. IF: 3,715.

5'-nucleotidase, cytosolic II genotype, and clinical outcome in patients with acute myeloid leukemia with intermediate-risk cytogenetics. Díaz-Santa J, Rodríguez-Romanos R, Coll R, Osca G, Pratcorona M, González-Bártulos M, Garrido A, Angona A, Talarn C, Tormo M, Arnan M, Vives S, Salamero O, Tuset E, Lloveras N, Díez I, Zamora L, Bargay J, Sampol A, Cruz D, Vila J, Sitges M, Garcia A, Vall-Llovera F, Esteve J, Sierra J, Gallardo D; "Grupo Cooperativo Para el Estudio y Tratamiento de las Leucemias Agudas y Mielodisplasias" (CETLAM group). *Eur J Haematol.* 2022 Dec;109(6):755-764. IF: 3,674.

Plain language summary of the design of the TALAPRO-2 study comparing talazoparib and enzalutamide versus enzalutamide and placebo in men with metastatic castration-resistant prostate cancer. Agarwal N, Azad A, Shore ND, Carles J, Fay AP, Dunshee C, Karsh LI, Paccagnella ML, Santo ND, Elmeliegy M, Lin X, Czibere A, Fizazi K. *Future Oncol.* 2022 Sep;18(27):2979-2986. IF: 3,674.

LIBRETTO-531: a phase III study of selpercatinib in multikinase inhibitor-naïve RET-mutant medullary thyroid cancer. Wirth LJ, Brose MS, Elisei R, Capdevila J, Hoff AO, Hu MI, Tahara M, Robinson B, Gao M, Xia M, Maeda P, Sherman E. *Future Oncol.* 2022 Sep;18(28):3143-3150. IF: 3,674.

HERIZON-GEA-01: Zanidatamab + chemo ± tislelizumab for 1L treatment of HER2-positive gastroesophageal adenocarcinoma. Tabernero J, Shen L, Elimova E, Ku G, Liu T, Shitara K, Lin X, Boyken L, Li H, Grim J, Ajani J. *Future Oncol.* 2022 Sep;18(29):3255-3266. IF: 3,674.

Phase I trial of the DLL3/CD3 bispecific T-cell engager BI 764532 in DLL3-positive small-cell lung cancer and neuroendocrine carcinomas. Wermke M, Felip E, Gambardella V, Kuboki Y, Morgensztern D, Hamed ZO, Liu M, Studeny M, Owonikoko TK. *Future Oncol.* 2022 Aug;18(24):2639-2649. IF: 3,674.

MATTERHORN: phase III study of durvalumab plus FLOT chemotherapy in resectable gastric/gastroesophageal junction cancer. Janjigian YY, Van Cutsem E, Muro K, Wainberg Z, Al-Batran SE, Hyung WJ, Molena D, Marcovitz M, Ruscica D, Robbins SH, Negro A, Tabernero J. *Future Oncol.* 2022 Jun;18(20):2465-2473. IF: 3,674.

A phase III, randomized, open-label study (CONTACT-02) of cabozantinib plus atezolizumab versus second novel hormone therapy in patients with metastatic castration-resistant prostate cancer. Agarwal N, Azad A, Carles J, Chowdhury S, McGregor B, Merseburger AS, Oudard S, Saad F, Soares A, Benzaghou F, Kerloeguen Y, Kimura A, Mohamed N, Panneerselvam A, Wang F, Pal S. *Future Oncol.* 2022 Mar;18(10):1185-1198. IF: 3,674.

Encorafenib plus binimetinib in patients with BRAFV600-mutant non-small cell lung cancer: phase II PHAROS study design. Riely GJ, Ahn MJ, Felip E, Ramalingam SS, Smit EF, Tsao AS, Alcasid A, Usari T, Wissel PS, Wilner KD, Johnson BE. *Future Oncol.* 2022 Mar;18(7):781-791. IF: 3,674.

Talazoparib plus enzalutamide in metastatic castration-resistant prostate cancer: TALAPRO-2 phase III study design. Agarwal N, Azad A, Shore ND, Carles J, Fay AP, Dunshee C, Karsh LI, Paccagnella ML, Santo ND, Elmeliegy M, Lin X, Czibere A, Fizazi K. *Future Oncol.* 2022 Feb;18(4):425-436. IF: 3,674.

MARIPOSA: phase 3 study of first-line amivantamab + lazertinib versus osimertinib in EGFR-mutant non-small-cell lung cancer. Cho BC, Felip E, Hayashi H, Thomas M, Lu S, Besse B, Sun T, Martinez M, Sethi SN, Shreeve SM, Spira AI. *Future Oncol.* 2022 Feb;18(6):639-647. IF: 3,674.

Temporal Trends in Grade 3/4 Adverse Events and Associated Costs of Nivolumab Plus Cabozantinib Versus Sunitinib for Previously Untreated Advanced Renal Cell Carcinoma. Geynisman DM, Burotto M, Porta C, Suarez C, Bourlon MT, Huo S, Del Tejo V, Du EX, Yang X, Betts KA, Choueiri TK, McGregor B. *Clin Drug Investig.* 2022 Jul;42(7):611-622. IF: 3,580.

Laboratory Cross-Comparison and Ring Test Trial for Tumor BRCA Testing in a Multicenter Epithelial Ovarian Cancer Series: The BORNEO GEICO 60-0 Study. Garcia-Casado Z, Oaknin A, Mendiola M, Alkorta-Aranburu G, Antunez-Lopez JR, Moreno-Bueno G, Palacios J, Yubero A, Marquez R, Gallego A, Sanchez-Heras AB, Lopez-Guerrero JA, Perez-Segura C, Barretina-Ginesta P, Alarcon J, Gaba L, Marquez A, Matito J, Cueva J, Palacio I, Iglesias M, Arcusa A, Sanchez-Lorenzo L, Guerra-Alia E, Romero I, Vivancos A. *J Pers Med.* 2022 Nov 4;12(11):1842. IF: 3,508.

Understanding the patient experience in hepatocellular carcinoma: a qualitative

patient interview study. Patel N, Maher J, Lie X, Gwaltney C, Barzi A, Karwal M, Macarulla T, Sun HC, Trojan J, Meyers O, Workman C, Morgan S, Negro A, Cohen G. *Qual Life Res.* 2022 Feb;31(2):473-485. IF: 3,440.

Confounding factors in the assessment of oral mucositis in head and neck cancer. Lorini L, Perri F, Vecchio S, Belgioia L, Vinches M, Brana I, Elad S, Bossi P. *Support Care Cancer.* 2022 Oct;30(10):8455-8463. IF: 3,359.

Randomized phase II trial of FOLFIRI-panitumumab compared with FOLFIRI alone in patients with RAS wild-type circulating tumor DNA metastatic colorectal cancer beyond progression to first-line FOLFOX-panitumumab: the BEYOND study (GEMCAD 17-01). Aparicio J, Virgili Manrique AC, Capdevila J, Muñoz Boza F, Galván P, Richart P, Oliveres H, Páez D, Hernando J, Serrano S, Vera R, Hernandez-Yagüe X, Gallego RÁ, Riesco-Martinez MC, García de Albeniz X, Maurel J. *Clin Transl Oncol.* 2022 Nov;24(11):2155-2165. IF: 3,340.

Expert consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology on the determination of biomarkers in pancreatic and biliary tract cancer. Vera R, Ibarrola-de-Andrés C, Adeva J, Pérez-Rojas J, García-Alfonso P, Rodríguez-Gil Y, Macarulla T, Serrano-Piñol T, Mondéjar R, Madrigal-Rubiales B. *Clin Transl Oncol.* 2022 Nov;24(11):2107-2119. IF: 3,340

Monitoring of RAS mutant clones in plasma of patients with RAS mutant metastatic colorectal cancer. Fernández Montes A, Élez E, Vivancos A, Martínez N, González P, Covela M, de la Cámara J, Cousillas A, Méndez JC, Graña B, Aranda E. *Clin Transl Oncol.* 2022 Jun;24(6):1209-1214. IF: 3,340.

SEOM-GECP-GETTHI Clinical Guidelines for the treatment of patients with thymic epithelial tumours (2021). Remon J, Bernabé R, Diz P, Felip E, González-Larriba JL, Lázaro M, Mielgo-Rubio X, Sánchez A, Sullivan I, Massutti B. *Clin Transl Oncol.* 2022 Apr;24(4):635-645. IF: 3,340.

SEOM-GEMCAD-TTD clinical guidelines for localized rectal cancer (2021). Capdevila J, Gómez MA, Guillot M, Páez D, Pericay C, Safont MJ, Tarazona N, Vera R, Vidal J, Sastre J. *Clin Transl Oncol.* 2022 Apr;24(4):646-657. IF: 3,340.

SEOM-GEMCAD-TTD Clinical Guideline for the diagnosis and treatment of esophageal cancer (2021). Fernández-Montes A, Alcaide J, Alsina M, Custodio AB, Franco LF, Gallego Plazas J, Gómez-Martín C, Richart P, Rivera F, Martin-Richard M. *Clin Transl Oncol.* 2022 Apr;24(4):658-669. IF: 3,340.

SEOM-SOGUG clinical guideline for localized muscle invasive and advanced bladder cancer (2021). Valderrama BP, González-Del-Alba A, Morales-Barrera R, Peláez Fernández I, Vázquez S, Caballero Díaz C, Domènech M, Fernández Calvo O, Gómez de Liaño Lista A, Arranz Arija JÁ. *Clin Transl Oncol.* 2022 Apr;24(4):613-624. IF: 3,340.

Exploratory analysis of clinical benefit of ipilimumab and nivolumab treatment in patients with metastatic melanoma from a single institution. Vila CM, Moreno FA, Estébanez MM, Ares GR, Villacampa G, Dashti P, Oberoi HS, Martin-Huertas R, Jares P, Alos L, Teixido C, Rull R, Sanchez M, Malvehy J, Carcelero E, Valduvieco I, Fernandez AA. *Clin Transl Oncol.* 2022 Feb;24(2):319-330. IF: 3,340.

Post-hematopoietic stem cell transplant squamous cell carcinoma in patients with Fanconi anemia: a dreadful enemy. Murillo-Sanjuán L, Balmaña J, de Pablo García-Cuenca A, Lorente Guerrero J, Uria Oficialdegui ML, Carrasco E, Diaz-de-Heredia C. *Clin Transl Oncol.* 2022 Feb;24(2):388-392. IF: 3,340.

Future care for long-term cancer survivors: towards a new model. Provencio M, Romero N, Tabernero J, Vera R, Baz DV, Arraiza A, Camps C, Felip E, Garrido P, Gaspar B, Llombart M, López A, Magallón I, Ibáñez VM, Olmos JM, Mur C, Navarro-Ruiz A, Pastor A, Peiró M, Polo J, Rodríguez-Lescure Á. *Clin Transl Oncol.* 2022 Feb;24(2):350-362. IF: 3,340.

Clinical nutrition as part of the treatment pathway of pancreatic cancer patients: an expert consensus. Carrato A, Cerezo L, Feliu J, Macarulla T, Martín-Pérez E, Vera R, Álvarez J, Botella-Carretero JI. *Clin Transl Oncol.* 2022 Jan;24(1):112-126. IF: 3,340.

Real-world data with the use of caplacizumab in the treatment of acquired thrombotic thrombocytopenic purpura: A single-center with homogeneous treatment experience. Jiménez M, Bobillo S, Pons V, Sánchez C, Pérez A, Molero A, Miranda N, Sánchez Á, Tabares E, Bosch F, Valcárcel D. *Transfusion.* 2022 Nov;62(11):2363-2369. IF: 3,337.

Prevalence of mutations in BRCA and homologous recombination repair genes and real-world standard of care of Asian patients with HER2-negative metastatic breast cancer starting first-line systemic cytotoxic chemotherapy: subgroup analysis of the global BREAKOUT study. Koh SJ, Ohsumi S, Takahashi M, Fukuma E, Jung KH, Ishida T, Dai MS, Chang CH, Dalvi T, Walker G, Bennett J, O'Shaughnessy J, Balmaña J. *Breast Cancer.* 2022 Jan;29(1):92-102. IF: 3,307.

A phase 1b study of crenigacestat (LY3039478) in combination with gemcitabine and cisplatin or gemcitabine and carboplatin in patients with advanced or metastatic solid tumors. Massard C, Cassier PA, Azaro A, Anderson B, Yuen E, Yu D, Oakley G 3rd, Benhadji KA, Pant S. *Cancer Chemother Pharmacol.* 2022 Oct;90(4):335-344. IF: 3,288.

First-in-human, open-label, phase 1/2 study of the monoclonal antibody programmed cell death protein-1 (PD-1) inhibitor cetrelimab (JNJ-63723283) in patients with advanced cancers. Felip E, Moreno V, Morgensztern D, Curigliano G, Rutkowski P, Trigo JM, Calvo A, Kowalski D, Cortinovis D, Plummer R, Maio M, Ascierto PA, Vladimirov VI, Cervantes A, Zudaire E, Hazra A, T'jollyn H, Bandyopadhyay N, Greger JG, Attiyeh E, Xie H, Calvo E. *Cancer Chemother Pharmacol.* 2022 Apr;89(4):499-514. IF: 3,288.

Recommendations for the diagnosis and treatment of patients with thrombotic thrombocytopenic purpura. Mingot Castellano ME, Pascual Izquierdo C, González A, Viejo Llorente A, Valcarcel Ferreiras D, Sebastián E, García Candel F, Sarmiento Palao H, Gómez Seguí I, de la Rubia J, Cid J, Martínez Nieto J, Hernández Mateo L, Goterris Viciedo R, Fidalgo T, Salinas R, Del Rio-Garma J; Grupo Español de Aféresis (GEA). *Med Clin (Barc).* 2022 Jun 24;158(12):630.e1-630.e14. English, Spanish. IF: 3,200.

Chimeric antigen receptor T-cell (CAR-T) therapy in patients with aggressive B-cell lymphomas. Current outlook after a decade of treatment. Catalá E, Iacoboni G, Barba P. *Med Clin (Barc).* 2022 Apr 8;158(7):327-332. English, Spanish. IF: 3,200.

Association of the Time to Immune Checkpoint Inhibitor (ICI) Initiation and Outcomes With Second Line ICI in Patients With Advanced Urothelial Carcinoma. Talukder R, Makrakis D, Lin GI, Diamantopoulos LN, Dawsey S, Gupta S, Carril-Ajuria L, Castellano D, de Kouchkovsky I, Jindal T, Koshkin VS, Park JJ, Alva A, Bilen MA, Stewart TF, McKay RR, Tripathi N, Agarwal N, Vather-Wu N, Zakharia Y, Morales-Barrera R, Devitt ME, Cortellini A, Fulgenzi CAM, Pinato DJ, Nelson A, Hoimes CJ, Gupta K, Gartrell BA, Sankin A, Tripathi A, Zakopoulou R, Bamias A, Murgic J, Fröbe A, Rodriguez-Vida A, Drakaki A, Liu S, Lu E, Kumar V, Lorenzo GD, Joshi M, Isaacsson-Velho P, Buznego LA, Duran I, Moses M, Barata P, Sonpavde G, Wright JL, Yu EY, Montgomery RB, Hsieh AC, Grivas P,

Khaki AR. *Clin Genitourin Cancer.* 2022 Dec;20(6):558-567. IF: 3,121.

Association Between Sites of Metastasis and Outcomes With Immune Checkpoint Inhibitors in Advanced Urothelial Carcinoma. Makrakis D, Talukder R, Lin GI, Diamantopoulos LN, Dawsey S, Gupta S, Carril-Ajuria L, Castellano D, de Kouchkovsky I, Koshkin VS, Park JJ, Alva A, Bilen MA, Stewart TF, McKay RR, Tripathi N, Agarwal N, Vather-Wu N, Zakharia Y, Morales-Barrera R, Devitt ME, Cortellini A, Fulgenzi CAM, Pinato DJ, Nelson A, Hoimes CJ, Gupta K, Gartrell BA, Sankin A, Tripathi A, Zakopoulou R, Bamias A, Murgic J, Fröbe A, Rodriguez-Vida A, Drakaki A, Liu S, Lu E, Kumar V, Lorenzo GD, Joshi M, Isaacsson-Velho P, Buznego LA, Duran I, Moses M, Jang A, Barata P, Sonpavde G, Yu EY, Montgomery RB, Grivas P, Khaki AR. *Clin Genitourin Cancer.* 2022 Oct;20(5):e440-e452. IF: 3,121.

Response and Outcomes to Immune Checkpoint Inhibitors in Advanced Urothelial Cancer Based on Prior Intravesical Bacillus Calmette-Guerin. Talukder R, Makrakis D, Diamantopoulos LN, Carril-Ajuria L, Castellano D, De Kouchkovsky I, Koshkin VS, Park JJ, Alva A, Bilen MA, Stewart TF, McKay RR, Santos VS, Agarwal N, Jain J, Zakharia Y, Morales-Barrera R, Devitt ME, Grant M, Lythgoe MP, Pinato DJ, Nelson A, Hoimes CJ, Shreck E, Gartrell BA, Sankin A, Tripathi A, Zakopoulou R, Bamias A, Murgic J, Fröbe A, Rodriguez-Vida A, Drakaki A, Liu S, Kumar V, Lorenzo GD, Joshi M, Velho PI, Buznego LA, Duran I, Moses M, Barata P, Sonpavde G, Yu EY, Wright JL, Grivas P, Khaki AR. *Clin Genitourin Cancer.* 2022 Apr;20(2):165-175. IF: 3,121.

Clinical Factors Associated With Long-Term Benefit in Patients With Metastatic Renal Cell Carcinoma Treated With Axitinib: Real-World AXILONG Study. Pinto Á, Reig O, Iglesias C, Gallardo E, García-Del Muro X, Alonso T, Anguera G, Suárez C, Muñoz-Langa J, Villalobos-León L, Rodríguez-Sánchez Á, Lainez N, Martínez-Ortega E, Campayo M, Velastegui A, Rodriguez-Vida A, Villa-Guzmán JC, Méndez-Vidal MJ, Rubio G, García I, Capdevila L, Lambea J, Vázquez S, Fernández O, Hernando-Polo S, Cerezo S, Santander C, García-Marrero R, Zambrana F, González-Del Alba A, Lazaro-Quintela M, Castellano D, Chirivella I, Anido U, Viana A, García A, Sotelo M, Arévalo MG, García-Donas J, Hernández C, Bolós MV, Llinares J, Climent MA. *Clin Genitourin Cancer.* 2022 Feb;20(1):25-34. IF: 3,121.

Survival With Cemiplimab in Recurrent Cervical Cancer. Tewari KS, Monk BJ, Vergote I, Miller A, de Melo AC, Kim H, Kim YM, Lisyanskaya A, Samouelian V, Lorusso D, Damian F, Chang C, Gotovkin EA, Takahashi S, Ramone D, Pikiel J, Mackowiak B, Alia EMG, Colombo N, Makarova Y, Rischin D, Lheureux S, Hasegawa K, Fujiwara K, Li J, Jamil S, Jankovic V, Chen CI, Seebach F, Weinreich DM, Yancopoulos GD+, Lowy I, Mathias M, Fury MG, Oaknin A, for the Investigators for GOG Protocol 3016 and ENGOT Protocol En-Cx9. *Obstet Gynecol Surv.* 2022. 77(6):p 348-350. IF: 3,015.

Validation of the Burkitt Lymphoma International Prognostic Index in patients treated with two prospective chemoimmunotherapy trials in Spain. Ribera JM, García O, Buendía-Ureña B, Terol MJ, Vicent A, Vall-Llovera F, Bergua J, García-Cadenas I, Esteve J, Ribera J, Acuña-Cruz E, Herrera P, Hernández-Rivas JM, Abrisqueta P, González-Campos J, Rodríguez C, Bastos-Oreiro M, Genescà E, Caminos N, Queipo de Llano MP, Cladera A, Sancho JM; Members of PETHEMA: Josep-Maria Riberaa, Olga Garcíaa, Ferran Vall-Lloverae, Juan Berguaf, Irene García-Cadenasg, Jordi Esteveh, Jordi Riberaa, Evelyn Acuña-Cruzi, Jesus-Maria Hernández-Rivas, José González-Camposm, Eulàlia Genescàa, Maria-Paz Queipo de Llanoq, Antònia Claderar Members of GELTAMO: Buenaventura Buendía-Ureñab, Maria-José Terolc, Ana Vicentd, Pilar Herreraj, Pau Abrisquetal, Carlos Rodríguezn, Mariana Bastos-Oreiroo, Nerea Caminosp, Juan-Manuel Sanchoa Groups. *Leuk Lymphoma.* 2022 Aug;63(8):1993-1996.IF: 2,996.

Variant t(11;22)(q13;q11.2) with IGL involvement in mantle cell lymphoma. Cabirta A, Hidalgo-Gómez G, Marín-Niebla A, Gallur L, Saumell S, Castellví J, Catalá E, Blanco A, López-Andreoni L, Montoro MJ, Navarrete M, Palacio-García C, Tazón-Vega B, Bobillo S, Bosch F, Ortega M. *Leuk Lymphoma.* 2022 Jul;63(7):1746-1749. IF: 2,996.

Prognostic impact of micromegakaryocytes in primary myelodysplastic syndromes. Saumell S, Fernández-Serrano M, Mesa A, López-Cadenas F, Arenillas L, Alfonso A, Montoro MJ, Molero A, Leoz P, Riego V, Gallur L, Salamero O, Navarrete M, Tazón-Vega B, Ortega M, Reig Ò, Roué G, Calvo X, Prosper F, Díez-Campelo M, Valcárcel D. *Leuk Lymphoma.* 2022 May;63(5):1227-1235. IF: 2,996.

A phase-II study of atezolizumab in combination with obinutuzumab or rituximab for relapsed or refractory mantle cell or marginal zone lymphoma or Waldenström's macroglobulinemia. Panayiotidis P, Tumyan G, Thieblemont C, Ptushkin VV, Marin-Niebla A, García-Sanz R, Le Gouill S, Stathis A, Bottos A, Hamidi H, Katz P, Perretti T, Willis JC, Buske C. *Leuk Lymphoma.* 2022 May;63(5):1058-1069. IF: 2,996.

Spanish Society of Hematology and Hemotherapy expert consensus opinion for SARS-CoV-2 vaccination in onco-hematological patients. Piñana JL, Vázquez L, Martino R, de la Cámara R, Sureda A, Rodríguez-Veiga R, Garrido A, Sierra J, Ribera JM, Torrent A, Mateos MV, de la Rubia J, Tormo M, Díez-Campelo M, García-Gutiérrez V, Álvarez-Larrán A, Sancho JM, MartínGarcía-Sancho A, Yañez L, Pérez Simón JA, Barba P, Abrisqueta P, Álvarez-Twose I, Bonanad S, Lecumberri R, Ruiz-Camps I, Navarro D, Hernández-Rivas JÁ, Cedillo Á, García-Sanz R, Bosch F. *Leuk Lymphoma.* 2022 Mar;63(3):538-550. IF: 2,996.

BCL2 translocation in high grade B cell lymphoma (NOS, DH/TH) is associated with reduced progression free survival. Gonzalez de Villambrosia S, Bastos M, Palanca JM, Cruz JG, Navarro JT, Tapia G, Alonso SA, Martin A, Blanco O, Abrisqueta P, Castellvi J, García-Noblejas A, Arranz R, Adrados M, López A, Montes-Moreno S; Grupo Español de linfomas y trasplante (GELTAMO). *Leuk Lymphoma.* 2022 Jan;63(1):101-108. IF: 2,996.

New Insights into Adjuvant Therapy for Localized Colon Cancer. González NS, Ros Montaña FJ, Illescas DG, Argota IB, Ballabrera FS, Élez Fernández ME. *Hematol Oncol Clin North Am.* 2022 Jun;36(3):507-520. IF: 2,861.

ABCL-412 Clinical Activity of CC-99282, a Novel, Oral, Small Molecule Cereblon E3 Ligase Modulator (CELMoD) Agent, in Patients With Relapsed/Refractory Non-Hodgkin Lymphoma (R/R NHL) -Results From CC-99282-NHL-001 (NCT03930953) a First-in-Human, Phase 1, Open-Label, Multicenter Study. Chavez JC, Michot JM, Carpio C, Ferrari S, Feldman TA, Morillo D, Kuruvilla J, Pinto A, Ribrag V, Bachy E, Buchholz TJ, Carrancio S, Chou WC, Guarinos C, Wu F, Li S, Patah P, Pourdehnad M, Nastoupil L. *Clin Lymphoma Myeloma Leuk.* 2022. 22 Suppl 2. S377-S378. IF: 2,822.

ABCL-388 L-MIND: Safety and Efficacy of Tafasitamab in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma on Treatment for at Least 2 Years. Duell J, Jurczak W, Liberati AM, Halka J, Carbó EP, Abrisqueta P, Maddocks KJ, Dreyling M, Rosenwald A, Bakuli A, Amin A, Gurbanov K, Salles G. *Clin Lymphoma Myeloma Leuk.* 2022. 22 Suppl 2. S375. IF: 2,822.

ABCL-073 Polatuzumab Vedotin Plus Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (Pola-R-CHP) Versus Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) Therapy in Patients With Previously Untreated Diffuse Large B-Cell Lymphoma (DLBCL): Results From the Phase III POLARIX Study. Flowers C, Tilly H, Morschhauser F, Sehn LH, Friedberg JW, Trnený M, Sharman JP, Herbaux C, Burke JM, Matasar M,Rai S,Izutsu K,Mehta N,Oberic L,Chauchet A,Jurczak W,Song Y,Greil R, Mykhalska L, Bergua JM, Cheung MC, Pinto A, Shin HJ, Hapgood G, Munhoz E, Abrisqueta P, Gau

JP, Hirata J, Jiang Y, Yan M, Lee C, Salles G. *Clin Lymphoma Myeloma Leuk.* 2022. 22 Suppl 2. S358-S359. IF: 2,822.

MPN-483 Thrombocytopenic Myelofibrosis (MF) Patients Previously Treated With a JAK Inhibitor in a Phase 3 Randomized Study of Momelotinib (MMB) versus Danazol (DAN) [MOMENTUM]. Gerds A, Verstovsek S, Vannucchi A, Al HK, Lavie D, Kuykendall A, Grosicki S, Iurlo A, Goh YT, Lazaroiu M, Egyed M, Fox ML, McLornan D, Perkins A, Yoon SS, Gupta V, Kiladjian JJ, Donahue R, Kawashima J, Mesa R. *Clin Lymphoma Myeloma Leuk.* 2022. 22 Suppl 2. S340. IF: 2,822.

MPN-478 MOMENTUM: Phase 3 Randomized Study of Momelotinib (MMB) versus Danazol (DAN) in Symptomatic and Anemic Myelofibrosis (MF) Patients Previously Treated With a JAK Inhibitor. Mesa R, Gerds A, Vannucchi A, Al HK, Lavie D, Kuykendall A, Grosicki S, Iurlo A, Goh YT, Lazaroiu M, Egyed M, Fox ML, McLornan D, Perkins A, Yoon SS, Gupta V, Kiladjian JJ, Donahue R, Kawashima J, Verstovsek S. *Clin Lymphoma Myeloma Leuk.* 2022. 22 Suppl 2. S339-S340. IF: 2,822.

Prognostic Value of Serum Paraprotein Response Kinetics in Patients With Newly Diagnosed Multiple Myeloma. Tamariz LE, Rodríguez P,J iménez A, Rosiñol L, Oriol A, Ríos R, Sureda A, Blanchard MJ, Hernández MT, Cabañas V, Jarque I, Bargay J, Gironella M, De Arriba F, Palomera L, Gonzalez Y, Martí JM, Krsnik I, Arguiñano JM, González ME, Casado LF, González AP, López L, Puig N, Cedena MT, Paiva B, Mateos MV, San J, Lahuerta JJ, Bladé J, Trocóniz IF. *Clin Lymphoma Myeloma Leuk.* 2022. 22. (9):e844-e852. IF: 2,822.

Real-World Evidence of Daratumumab Monotherapy in Relapsed/Refractory Multiple Myeloma Patients and Efficacy on Soft-Tissue Plasmacytomas. Moreno DF, Clapés V, Soler JA, González-Montes Y, Gironella M, Motlló C, Granell M, Abella E, García-Pintos M, García-Guiñón A, Cabezudo E, Bladé J, Rosiñol L. *Clin Lymphoma Myeloma Leuk.* 2022 Aug;22(8):635-642. IF: 2,822.

CNS prophylaxis in aggressive B-cell lymphoma. Wilson MR, Bobillo S, Cwynarski K. *Hematology Am Soc Hematol Educ Program.* 2022 Dec 9;2022(1):138-145. IF: 2,697.

Herpes simplex encephalitis in the context of immune checkpoint inhibitors: a complex interplay. Lallana S, Sánchez-Tejerina D, Auger C, Callejo A, Rio J, Cobo-Calvo Á. *Acta Neurol Belg.* 2022 Jun;122(3):823-825. IF: 2,471.

First international workshop of the ATM and cancer risk group (4-5 December 2019). Lesueur F, Easton DF, Renault AL, Tavtigian SV, Bernstein JL, Kote-Jarai Z, Eeles RA, Plaseska-Karanfia D, Feliubadaló L; Spanish ATM working group; Arun B, Herold N, Versmold B, Schmutzler RK; GC-HBOC; Nguyen-Dumont T, Southey MC, Dorling L, Dunning AM, Ghiorzo P, Dalmasso BS, Cavaciuti E, Le Gal D, Roberts NJ, Dominguez-Valentin M, Rookus M, Taylor AMR, Goldstein AM, Goldgar DE; CARRIERS and Ambry Groups; Stoppa-Lyonnet D, Andrieu N. *Fam Cancer.* 2022 Apr;21(2):211-227. IF: 2,446.

Severity of gastrointestinal bleeding is similar between patients receiving direct oral anticoagulants or vitamin K antagonists. Alcalá-González LG, Jiménez C, Cortina V, Jiménez A, Cerdá M, Johansson E, Olivera P, Santamaría A, Alonso-Cotoner C. *Rev Esp Enferm Dig.* 2022 Oct;114(10):599-604. IF: 2,389.

Optimising the management of patients with multiple myeloma in Spain: A measurement of the social return on investment. Merino M, Ivanova Y, Maravilla-Herrera P, Barragán B, Sierra J, Peñuelas-Saiz Á, Hidalgo-Vega Á. *Eur J Cancer Care (Engl).* 2022 Nov;31(6):e13706. IF: 2,328.

IBRORS-MCL study: a Spanish retrospective and observational study of relapsed/refractory mantle-cell lymphoma treated with ibrutinib in routine clinical practice. Sancho JM, Marín-Niebla A, Fernández S, Capote FJ, Cañigral C, Grande C, Donato E, Zeberio I, Puerta JM, Rivas A, Pérez-Ceballos E, Vale A, Martín García-Sancho A, Salar A, González-Barca E, Teruel A, Pastoriza C, Conde-Royo D, Sánchez-García J, Barrenetxea C, Arranz R, Hernández-Rivas JÁ, Ramírez MJ, Jiménez A, Rubio-Azpeitia E. *Int J Hematol.* 2022 Sep;116(3):381-392. IF: 2,319.

Risk-Adjusted Cancer Screening and Prevention (RiskAP): Complementing Screening for Early Disease Detection by a Learning Screening Based on Risk Factors. Schmutzler RK, Schmitz-Luhn B, Borisch B, Devilee P, Eccles D, Hall P, Balmaña J, Boccia S, Dabrock P, Emons G, Gaissmaier W, Gronwald J, Houwaart S, Huster S, Kast K, Katalinic A, Linn SC, Moorthie S, Pharoah P, Rhiem K, Spranger T, Stoppa-Lyonnet D, van Delden JJM, van den Bulcke M, Woopen C. *Breast Care (Basel).* 2022 Apr;17(2):208-223. IF: 2,268.

A Standardized Liquid Biopsy Preanalytical Protocol for Downstream Circulating-Free DNA Applications. Earl J, Calabuig-Fariñas S, Sarasquete ME, Muinelo Romay L, Lopez-Tarruella S, Bellosillo Paricio B, Rodríguez M, Valencia Leoz K, Dueñas Porto M, Tarazona N, Hernandez Losa J, Toledo RA. *J Vis Exp.* 2022 Sep 16;(187). IF: 1,424.

Avances en tumores del estroma gastrointestinal: ¿hacia dónde vamos? Fernández-Hernández JA, Cantín-Blázquez S, García-Somacarrera E, Varo-Pérez E, González-López JA, Asencio-Pascual JM, Mendiola M, Serrano C, García-Granero E, Artigas-Raventós V. *Cir Cir.* 2022;90(2):267-277. IF: 0,416.

Articles published by VHIO investigators in 2022 without allocated Impact Factor:

MYC Inhibition Halts Metastatic Breast Cancer Progression by Blocking Growth, Invasion, and Seeding. Massó-Vallés D, Beaulieu ME, Jauset T, Giuntini F, Zacarías-Fluck MF, Foradada L, Martínez-Martín S, Serrano E, Martín-Fernández G, Casacuberta-Serra S, Castillo Cano V, Kaur J, López-Estévez S, Morcillo MÁ, Alzrigat M, Mahmoud L, Luque-García A, Escorihuela M, Guzman M, Arribas J, Serra V, Larsson LG, Whitfield JR, Soucek L. *Cancer Res Commun.* 2022 Feb 21;2(2):110-130.

Protocol to generate a patient derived xenograft model of acquired resistance to immunotherapy in humanized mice. Martínez-Sabadell A, Ovejero Romero P, Arribas J, Arenas EJ. *STAR Protoc.* 2022 Oct 26;3(4):101712.

Impact of Cytomegalovirus Replication in Patients with Aggressive B Cell Lymphoma Treated with Chimeric Antigen Receptor T Cell Therapy. Márquez-Algaba E, Iacoboni G, Pernas B, Esperalba J, Los Arcos I, Navarro V, Monforte A, Beas F, Albasanz-Puig A, Carpio C, Barba P, Ruiz-Camps I. *Transplant Cell Ther.* 2022 Dec;28(12):851.e1-851.e8.

IRONMAN: A Novel International Registry of Men With Advanced Prostate Cancer. Mucci LA, Vinson J, Gold T, Gerke T, Filipenko J, Green RM, Anderson SG, Badal S, Bjartell A, Chi KN, Davis ID, Enting D, Fay AP, Lazarus J, Mateo J, McDermott R, Odedina FT, Olmos D, Omlin A, Popoola AA, Ragin C, Roberts R, Russnes KM, Waihenya C, Stopsack KH, Hyslop T, Villanti P, Kantoff PW, George DJ; IRONMAN Global Team. *JCO Glob Oncol.* 2022 Nov;8:e2200154.

Impact of the COVID-19 Pandemic on Cancer Staging: An Analysis of Patients With Breast Cancer From a Community Practice in Brazil. Resende CAA, Fernandes Cruz HM, Costa E Silva M, Paes RD, Dienstmann R, Barrios CHE, Goncalves AC, Cascelli FGA, Souto AKBA, Oliveira LC, Reinert T, Andrade DAP, Passos MP, Millen EC, Zerwes F, Moraes PL, Ferrari BL, Mano MS. *JCO Glob Oncol.* 2022 Nov;8:e2200289.

Trotabresib (CC-90010) in combination with adjuvant temozolomide or

concomitant temozolomide plus radiotherapy in patients with newly diagnosed glioblastoma. Vieito M, Simonelli M, de Vos F, Moreno V, Geurts M, Lorenzi E, Macchini M, van den Bent MJ, Del Conte G, de Jonge M, Martín-Soberón MC, Amoroso B, Sanchez-Perez T, Zuraek M, Hanna B, Aronchik I, Filvaroff E, Chang H, Mendez C, Arias Parro M, Wei X, Nikolova Z, Sepulveda JM. *Neurooncol Adv.* 2022 Oct 28;4(1):vdac146.

Addition of Immune Checkpoint Inhibitors to Chemotherapy vs Chemotherapy Alone as First-Line Treatment in Extensive-Stage Small-Cell Lung Carcinoma: A Systematic Review and Meta-Analysis. Arriola E, González-Cao M, Domine M, De Castro J, Cobo M, Bernabé R, Navarro A, Sullivan I, Trigo JM, Mosquera J, Crama L, Isla D. *Oncol Ther.* 2022 Jun;10(1):167-184.

Barriers in precision medicine implementation among Advanced Nonsquamous Cell Lung Cancer-patients: A Real-World Evidence Scenario. Duarte FA, Ferreira CG, Dienstmann R, Ferrari BL, Costa E Silva M, Nazareth A Junior P, Guilherme de O Salles P, Henrique C Diniz P. *J Mark Access Health Policy.* 2022 May 24;10(1):2077905.

Neurosurgery in a patient with severe hemophilia B: an experience using eftrenonacog alfa as perioperative management. Benitez Hidalgo O, Martinez Garcia MF, Bescos Cabestre A, Juarez Gimenez JC, Gironella Mesa M, Bosch Albareda F. *Clin Case Rep.* 2022 May 23;10(5):e05848.

Development and Optimization of a Machine-Learning Prediction Model for Acute Desquamation After Breast Radiation Therapy in the Multicenter REQUITE Cohort. Aldraimli M, Osman S, Grishchuck D, Ingram S, Lyon R, Mistry A, Oliveira J, Samuel R, Shelley LEA, Soria D, Dwek MV, Aguado-Barrera ME, Azria D, Chang-Claude J, Dunning A, Giraldo A, Green S, Gutiérrez-Enríquez S, Herskind C, van Hulle H, Lambrecht M, Lozza L, Rancati T, Reyes V, Rosenstein BS, de Ruysscher D, de Santis MC, Seibold P, Sperk E, Symonds RP, Stobart H, Taboada-Valadares B, Talbot CJ, Vakaet VJL, Vega A, Veldeman L, Veldwijk MR, Webb A, Weltens C, West CM, Chaussalet TJ, Rattay T; REQUITE consortium. *Adv Radiat Oncol.* 2022 Jan 3;7(3):100890.

Outcomes of Allogeneic Hematopoietic Cell Transplantation in T Cell Prolymphocytic Leukemia: A Contemporary Analysis from the Center for International Blood and Marrow Transplant Research. Murthy HS, Ahn KW, Estrada-Merly N, Alkhateeb HB, Bal S, Kharfan-Dabaja MA, Dholaria B, Foss F, Gowda L, Jagadeesh D, Sauter C, Abid MB, Aljurf M, Awan FT, Bacher U, Badawy SM, Battiwalla M, Bredeson C, Cerny J, Chhabra S, Deol A, Diaz MA, Farhadfar N, Freytes C, Gajewski J, Gandhi MJ, Ganguly S, Grunwald MR, Halter J, Hashmi S, Hildebrandt GC, Inamoto Y, Jimenez-Jimenez AM, Kalaycio M, Kamble R, Krem MM, Lazarus HM, Lazaryan A, Maakaron J, Munshi PN, Munker R, Nazha A, Nishihori T, Oluwole OO, Ortí G, Pan DC, Patel SS, Pawarode A, Rizzieri D, Saba NS, Savani B, Seo S, Ustun C, van der Poel M, Verdonck LF, Wagner JL, Wirk B, Oran B, Nakamura R, Scott B, Saber W. *Transplant Cell Ther.* 2022 Apr;28(4):187.e1-187.e10.

Novel Therapies in Gynecologic Cancer. Bejar FG, Oaknin A, Williamson C, Mayadev J, Peters PN, Secord AA, Wield AM, Coffman LG. *Am Soc Clin Oncol Educ Book.* 2022 Apr;42:1-17.

The GIST of Advances in Treatment of Advanced Gastrointestinal Stromal Tumor. Schaefer IM, DeMatteo RP, Serrano C. *Am Soc Clin Oncol Educ Book.* 2022 Apr;42:1-15.

The Evolving Treatment Landscape in BRAF-V600E-Mutated Metastatic Colorectal Cancer. Tabernero J, Ros J, Élez E. *Am Soc Clin Oncol Educ Book.* 2022 Apr;42:1-10.

Metastatic Colorectal Cancer Outcomes by Age Among ARCAD First- and Second-Line Clinical Trials. McCleary NJ, Harmsen WS, Haakenstad E, Cleary JM, Meyerhardt JA, Zalcberg J, Adams R, Grothey A, Sobrero AF, Van Cutsem E, Goldberg RM, Peeters M, Tabernero J, Seymour M, Saltz LB, Giantonio BJ, Arnold D, Rothenberg ML, Koopman M, Schmoll HJ, Pitot HC, Hoff PM, Tebbutt N, Masi G, Souglakos J, Bokemeyer C, Heinemann V, Yoshino T, Chibaudel B, deGramont A, Shi Q, Lichtman SM. *JNCI Cancer Spectr.* 2022 Mar 2;6(2):pkac014.

Cervical dissecting extravasation of oxaliplatin: A case report. Hernando J, Riera-Arnau J, Roca M, Garcia A, Capdevila J. *Mol Clin Oncol.* 2022 Mar;16(3):60.

A Label Retaining System to Capture Slow-Cycling Cancer Cells. Puig I, Palmer HG. *Methods Mol Biol.* 2022;2535:85-92.

Expert consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology on the determination of biomarkers in pancreatic and biliary tract cancer. Vera R, Ibarrola C, Adeva J, Pérez J, García P, Rodríguez Y, Macarulla T, Serrano T, Mondéjar R, Madrigal B. *Rev Esp Patol.* 2022.

Funding & Consortia

Funding

VHIO can and will only deliver on its goal of accelerating the pace in advancing personalized and targeted therapies against cancer thanks to the public funding it receives as well as the generous support from institutional supporters, private institutions, companies, associations, societies, and individual donors. As a direct reflection of VHIO's research of excellence, VHIO also continues to secure essential funding through several International and National Competitive Grants. Regarding the latter, we would like to also recognize the Asociación Española Contra el Cáncer (AECC) for its longstanding support of several VHIO groups and researchers.

Only with such continued support will the clock continue to tick in our favor - against cancer. We would therefore like to express our immense gratitude to the following supporters, funding entities and agencies:

Institutional Supporters

Generalitat de Catalunya

Fundació Privada CELLEX

fundación fero
Investigando por un futuro sin cáncer

"la Caixa" Foundation

Fundación BBVA

EXCELENCIA SEVERO OCHOA
2022 - 2026

Public Funding

International

erc
European Research Council
Established by the European Commission

European Commission
Horizon 2020
European Union funding for Research & Innovation

FONDO EUROPEO DE DESARROLLO REGIONAL
Una manera de hacer Europa
FONDO SOCIAL EUROPEO
El FSE invierte en tu futuro
Unión Europea

imi innovative medicines initiative

Interreg POCTEFA

National

AGAUR Agència de Gestió d'Ajuts Universitaris i de Recerca

Generalitat de Catalunya
Departament de Salut

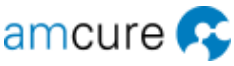
ICREA

CERCA Centres de Recerca de Catalunya

ciberonc isciii

ISC Instituto de Salud Carlos III

Private Funding




GRIFOLS

TTD
GRUPO DE TRATAMIENTO DE LOS TUMORES DIGESTIVOS

GEICO
Grupo Español de Investigación en Cáncer de Ovario


GETNE
Grupo Español de Tumores Neuroendocrinos y Endocrinos

gsk
GlaxoSmithKline
Oncology

Incyte

IPSEN
Innovation for patient care

Irurtzun
cycling

janssen
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

KALEIDO
IDEAS & LOGISTICS

KURA
ONCOLOGY

labcorp

Lilly

Mª Ángeles
Sanahuja

MedImmune

the
MENARINI
group

MERCK

Merus

migranodearena
FUNDACIÓN

Takeda
MILLENNIUM
THE TAKEDA ONCOLOGY COMPANY

MOVEMBER

MSD

Nocturna
MALGRAT DE MAR

NOVARTIS
ONCOLOGY

OMNIPREX
Scientific Medical Education

Palo
Biofarma
Innovation through medicinal chemistry

Pau
Donés

PETHEMA

Pierre Fabre

Pfizer

Pharma
Mar
Grupo Zeltia

POLYPHOR

PRODUCCIONES
DEL BARRIO

Prostate Cancer
Foundation
Curing Together.

Puma
Biotechnology

rejuversen

Roche

SANOFI

save the mama

SEOM
Sociedad Española
de Oncología Médica

SERVIER

Sin teta hay paraíso

SOGUG

SOLTI
INNOVATIVE BREAST CANCER RESEARCH

sosciathlon

SWISS BRIDGE

TAIHO
TAIHO PHARMA

The
Breast
Cancer
Research
Foundation

the
PARADIFFERENCE
foundation

Urrutia

VARIAS
IMPRESORES

O GALLEGA
SOCIEDAD CARTE
Opiniones Empresa

WN

ZENITH
EPIGENETICS

Consortia

The ACRCelerate: Colorectal Cancer Stratified Medicine Network is a European-wide consortium of researchers at the forefront of CRC research. The overall aim of this project is to generate robust and reproducible preclinical data to de-risk future clinical trials based on patient stratification. The ACRCelerate partners work together to develop preclinical models that recapitulate the molecular subtypes of CRC and characterize their signaling pathways using DNA and RNA sequencing to subtype the models, as well as identify and test new therapeutics integrating data in a bioinformatic analysis pipeline.

This partnership between Cancer Research UK (CRUK), Fundación Científica de la Asociación Española Contra el Cáncer (FC AECC), and the Fondazione AIRC per la Ricerca sul Cancro (AIRC), capitalizes on shared priorities across their respective research communities and is driven by a shared ambition to advance progress in translational research by building outstanding global networks. By bringing together renowned teams in the UK, Italy, and Spain, including VHIO, ACRCelerate harnesses the collective expertise of leading investigators to develop new resources and accelerate progress in collaboration.

Cancer Core Europe (CCE) is a unique partnership aimed at addressing the cancer care - cancer research continuum challenge. Launched in 2014, this working consortium represents a critical mass of activity for the successful integration of all cancer care information, clinical research and outcome research, led by its founding partners and European comprehensive cancer centers of excellence: the Gustave Roussy Cancer Campus Grand Paris (Villejuif, France), Cambridge Cancer Centre (Cambridge, UK), Karolinska Institute (Stockholm, Sweden), Netherlands Cancer Institute – NKI (Amsterdam, The Netherlands), National Center for Tumor Diseases – DKFZ-NCT (Heidelberg, Germany), VHIO, as well as The National Cancer Institute of Milan (Italy).

CEE promotes the pooling and exchange of expertise, research findings, common platforms and processes, and empowers researchers and clinicians to rapidly exploit this trove of biological insights and clinical data for the benefit of patients.

www.cancercoreeurope.eu

CCE's Basket of Baskets (BoB) trial is a modular, open-label, phase II, multicenter study to evaluate targeted agents in molecularly selected populations with advanced solid tumors. This study is carried out under the Cancer Core Europe (CCE) umbrella, with VHIO as trial sponsor.

This modular basket clinical trial consists of two parts: part A (iPROFILER), which includes the common procedures for tumor molecular profiling and treatment recommendation, and part B (iBASKET), which corresponds to the therapeutic portion. The purpose of part A is to assess participants' tumor tissue in order to identify whether their respective tumors have certain mutations in cancer-related genes. This analysis provides information about potential targeted therapies that specifically attack those gene mutations. The purpose of part B is to offer participants a personalized anti-cancer treatment based on the detected gene mutations in tumors.

www.basketofbaskets.eu

The EU-funded CCE's Building Data Rich Clinical Trials (CCE-DART), coordinated by VHIO, is carried out in collaboration with other leading experts from within the Cancer Core Europe Consortium (CCE). By harnessing and incorporating powerful cutting-edge technologies, methods and platforms, CCE-DART investigators will design and develop a new generation of data-rich, dynamic studies in oncology.

Building on the CCE-developed Basket of Baskets (BoB) investigator-initiated and adaptive trial which launched in 2018, CCE-DART further enhances BoB's harmonized, molecular multi-tier profiling platform to more precisely match patients to novel anti-cancer medicines based on the genetic specificities of their individual tumors. In parallel, the researchers will continue to develop multiple treatments in genomically-selected populations.

www.cce-dart.com

This project has received funding from the European Union's Horizon 2020 framework programme research under grant agreement No: 965397.

Launched in 2019, the OPTIMISTICC Cancer Grand Challenge – Opportunity to Investigate the Microbiome's Impact on Science and Treatment In Colorectal Cancer, is a 5-year consortium funded by Cancer Research UK's Grand Challenge, led by researchers at the Dana-Farber Cancer Institute-Harvard Medical School, and Harvard T.H. Chan School of Public Health (USA).

Aimed at better understanding the difference between a healthy microbiome and a microbiome associated with the development of colorectal cancer, the co-investigators from the US, Canada, UK, the Netherlands, and Spain, are seeking to identify ways to manipulate this collection of microorganisms to better prevent and treat cancer. It is thanks to the Grand Challenge funding that the project partners, including VHIO, are able to pool the necessary expertise in order to establish how the microbiome influences a cancer's response to treatment, develop new treatments that alter the microbiome, and decipher how an individual's external environment may affect their microbiome.

www.optimisticc.org

COLOSSUS – Advancing a Precision Medicine Paradigm in metastatic Colorectal Cancer: Systems based patient stratification solutions, is a multi-center European Commission Horizon 2020-supported project powered by 13 leading clinical investigators and researchers spanning 7 European countries, with expertise in cancer immunology, systems biology, computational modelling, bioinformatics, omics analysis, clinical oncology/pathology, preclinical research, medical imaging, clinical trials, health economics and patient management.

This 5-year undertaking aims at better classifying and treating metastatic colorectal cancer (mCRC). Focused on microsatellite stable RAS mutant (MSS RAS mt) disease – a genetically identified type of CRC with very few therapeutic options available once patients develop resistance to existing chemotherapies, the COLOSSUS team seeks to expand and refine the classification of this particular subset of colorectal cancer.

www.colossusproject.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 754923.

EUCanCAN – the European-Canadian Cancer Network, led by the Barcelona Supercomputing Center (Spain), comprises a total of 18 partners from 5 different countries to pursue the homogeneous analysis, management and exchange of genomic-driven oncology data to advance precision medicine in cancer.

Jointly funded by the European Union's Horizon 2020 research and innovation programme and the Canadian Institutes of Health, this project strives to provide a functional platform for federated genome analysis systems towards efficiently analyzing, managing, sharing and reusing mass genomic data at the global level. The participating reference nodes seek to process, store and share between 30-35 thousand patient samples across various tumor types.

This consortium also promises to drive discovery into robust and clinically-relevant patterns of genomic variation in cancer, including predictive biomarkers.

www.eucancan.com

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825835.

The main objective of the EU-supported EURAMED *ROCC-N-ROLL*: EURopeAn MEDical application and Radiation prOteCtion Concept: strategic research agenda aNd ROadmap interLinking to heaLth and digitization aspects, is to generate a European consensus on research needs and priorities in medical radiation applications and corresponding radiation protection to optimize the use of ionizing radiation in medicine.

Led by coordinating partner, the European Institute for Biomedical Imaging Research, Vienna (Austria), this pan-European consortium connects a total of 29 research centers, including VHIO. Taking the lead on radiation application in oncological diseases, VHIO is working with other experts in other settings including neurovascular as well as cardiovascular diseases, and explore relevant clinical scenarios, as well as provide patients' perspectives.

Specifically, VHIO researchers are analyzing the needs of research in radiation application and corresponding radiation protection in oncology by identifying gaps and opportunities. Compile an overview of clinical situations that require the application of ionizing radiation in diagnosis and treatment, provide an outlook on envisaged future applications and trends in the oncology field.

https://roccnroll.euramed.eu/

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 899995.

The EurOPDX Consortium – Translating Knowledge in Oncology, launched in 2013 to create a network of clinically relevant models of human cancer, and in particular patient-derived xenograft (PDX) models.

Connecting 18 cancer centers across 13 countries that are developing PDX cancer models, this initiative promotes the sharing and exchange of findings on promising therapeutics as well as leads multicenter preclinical studies. EurOPDX strives to reduce the duplication of efforts in oncology drug development and ultimately improve the quality of life and overall survival of cancer patients.

Supported by the European Union's Horizon 2020 research and innovation programme and launched in 2018, EDIReX – EurOPDX Distributed Infrastructure for Research on patient-derived cancer Xenografts, is led by the EurOPDX Consortium counting on the research excellence of 19 entities -including VHIO- spanning 13 European countries.

The main aims of this project are to facilitate data exchange among academic and industrial preclinical and translational cancer professionals and, to spur and consolidate scientific collaborations in PDX research across Europe.

www.europdx.eu

The EDIReX project has received funding from the European Union's Horizon 2020 research and innovation programme, grant agreement No. 731105.

Immune-Image is a 22 stakeholder-strong consortium incorporating public and private partners across 9 countries, including VHIO and the Vall d'Hebron Institute of Research (VHIR) from Spain.

Powered by the Innovative Medicines Initiative Joint Undertaking (IMI 2 JU), this initiative is led by Roche and coordinated by the Amsterdam University Medical Center (VUmC), the Netherlands. Set to run for an initial duration of five years, this project is entitled *Specific imaging of immune cell dynamics using novel tracer strategies*, and seeks to develop a novel non-invasive imaging strategy for assessing immune cell activation and dynamics in oncology and inflammatory disease.

Main deliverables include developing clinically validated radio-and optical immunotracers for the monitoring and measurement of immune cell presence, activation status and trafficking, and designing and implementing a ready-to-use sustainable molecular imaging platform, incorporating standardized protocols, best practices, quantitative image analyses, immune-based tracking design and development.

www.immune-image.eu

IMPaCT – Infraestructura de Medicina de Precision asociada a la Ciencia y Tecnología, is a collaborative structure for the implementation of genomic medicine in the Spanish National Health System, coordinated by CIBER (Spanish Biomedical Research Networking Centers).

VHIO participates in Work Package 4, focused on cancer, and leads the unknown primary tumors part. WP4 aims to establish genomic methods to analyze tumors, create a portfolio of diagnostic services, standardize laboratory protocols and sample processing methods in order to establish variant interpretation guidelines and establish a clinical reporting model.

A network of high-capacity genomic analysis from existing centers will be established. This infrastructure will focus on rare diseases, cancers of unknown origin, and pharmacogenetics. This is a national program aimed at establishing standardized procedures to guarantee equitable access to genomic analysis. The Centre for Genomic Regulation (CRG), Barcelona, will be responsible for the centralization of samples.

www.impact-genomica.com

This project is funded by the Subdirección General de Evaluación y Fomento de la investigación dentro del Fondo Europeo de Desarrollo. Convocatoria Infraestructura de Medicina de Precisión Asociada a la Ciencia y Tecnología - IMPaCT. Ref: IMP/00009.

INGENIO

INGENIO - INtegrative GENomic, digital Imaging and clinical information towards precision Oncology optimization, is a 4-year interdisciplinary program aimed at boosting precision oncology through the implementation of predictive biomarkers, digital imaging and pathology, as well as artificial intelligence (clinical and genomic).

Main goals include the development of a CIBER (Spanish Biomedical Research Networking Centers) platform that integrates data on biomarker determination and clinical outcomes in lung cancer, advancing digital imaging (pathology and radiomics) and validation for precision oncology, validating new technologies and strategies for clinical and biomarker implementation, and evaluating emerging biomarkers in other solid tumors. Program partners, including VHIO, will also seek to test clinical intervention in agnostic targets, and establish a strategy for the creation and implementation of a Molecular Tumor Board (MTB).

INGENIO comprises groups with predominant experience in clinical and translational research in biomarker assessment, personalized patient care, digital imaging, artificial intelligence and data science, from research centers of excellence across Spain belonging to the CIBER network.

This project is funded by a grant received from the Carlos III Institute of Health (ISCIII) for personalized precision medicine research projects, as part of the Strategic Action in Health (AES) 2017-2020.

Coordinated by the Josep Carreras Leukemia Research Institute, Barcelona (Spain), the EU-funded Interreg POCTEFA PROTEOblood Consortium is co-funded by the European Regional Development Fund/European Social Fund, and aims to optimize, share and exploit latest technologies for the study of protein homeostasis in two prevalent subtypes of leukaemia and lymphoma: acute myeloid leukemia (AML) and diffuse large b-cell lymphoma (CLBCL) in the POCTEFA region (Spain-France-Andorra).

Comprising six other partners - CIC bioGUNE, IQS, CNRS, INSERM, Anaxomics Biotech, and VHIO, the investigators use modelling collections from patient-derived studies to recreate the tumor microenvironment ex vivo, and apply innovative proteomic approaches associated with system biology analysis and small molecule design, to facilitate the complete characterization of proteopathies and development of more effective therapies to be validated through xenoinjerts.

http://proteoblood.eu/

The project has been co-funded by:

The European Regional Development Fund (ERDF) through the Interreg V-A Spain-France-Andorra Programme (POCTEFA 2014-2020) – Ref: EFA360/19.

European Regional Development Fund/European Social Fund.

Funded by the European Union's Horizon 2020 research and innovation programme, the CELAC and European Consortium for a Personalized Medicine Approach to Gastric Cancer (LEGACy) is a 4-year project led by the INCLIVA Health Research Institute (Spain), in partnership with 11 other members across 9 different countries including VHIO.

Focused on advancing personalized medicine against gastric cancer, this project aims to improve diagnosis and treatment by using data obtained through extensive research in four EU countries and four countries within the Community of Latin American and Caribbean (CELAC) States.

Seeking to improve patient outcomes by applying personalized medicine at the three levels of prevention, this consortium implements a personalized medicine strategy at the first level of prevention, improves early gastric cancer detection at the second level of prevention, and improves treatment through the identification of high-risk populations.

www.legacy-h2020.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825832.

MESI-STRAT combines the expertise of 15 partners from 7 European countries to establish the interplay of breast cancer metabolism and oncogenic signaling (Metabolic Signaling) by systems medicine approaches.

Aimed at developing new models for knowledge-based STRATification of patients into subgroups with different endocrine therapy resistance mechanisms, this pan-European 57-month project, supported by the European Union's Horizon 2020 research and innovation programme, represents an important forward step towards improving outcomes for these patients.

The team pioneers breast cancer metabolism as a novel approach for the stratification of patients, tracking of resistance and better guiding clinical decision-making throughout the course of endocrine therapy. Through the development of new computational models in combination with network analyses, pharmacogenomics and integrated multi-omics data, MESI-STRAT aims at better deciphering the metabolic and signaling networks that drive resistance to endocrine-based therapies.

www.mesi-strat.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 754688.

Funded through a grant received from the European Union's Horizon 2020 research and innovation programme, the NoCanTher–Nanomedicine upscaling for early clinical phases of multimodal cancer therapy is a multi-center–Consortium is led by IMDEA Nanoscience and represents an important step forward in utilizing nanoparticles than can better target and more precisely combat cancer cells.

This project builds on the preclinical successes reported by the former FP7-funded MultiFun Consortium that evidenced the efficacy of a multi-modal therapeutic approach based on functionalized magnetic nanoparticles and magnetic hyperthermia for the intra-tumoral treatment of breast and pancreatic tumors.

Connecting 11 leading European research centers, including industry partners, NoCanTher assesses this nano-based approach, provides preliminary data on its efficacy in humans, and aims to translate these preclinical findings into early clinical development for the treatment of pancreatic cancer.

www.nocanther-project.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 685795.

The EU-funded ONCNGS project aims to tackle a common, unmet need in oncology; namely to profile multiple tumor types at the molecular level in the broadest possible way and establish an economically sustainable and de-centralized model that facilitates secure and transparent access to sensitive data.

ONCNGS challenges the market to research and develop novel, affordable solutions to provide the best NGS tests for all solid tumor and lymphoma patients. The challenge consists of providing efficient molecular DNA/RNA profiling of tumor-derived material in liquid biopsies by means of a pan-cancer tumor marker analysis kit including NGS analysis integrated with an ICT decision support system, and an analytical test for interpretation and reporting.

www.oncngs.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 874467.

ONCODISTINCT is a research network that brings together leading academic investigators with a shared vision for innovative clinical research.

Established by several cancer institutes in and outside of Europe, this network comprises a multidisciplinary group of investigators with expertise in early drug development and clinical research.

Together, they aim to address the current challenges in oncology and improve patient outcomes by designing and conducting innovative clinical studies, and accelerating the development of anti-cancer medicines in solid tumors, particularly in settings with unmet medical needs.

ONCODISTINCT currently connects 28 cancer centers and university hospitals, and fosters collaborations between oncologists, organ specialists, radiotherapists and scientists across the ONCODISTINCT sites, as well as pharmaceutical companies. Established seven years ago, the network is dynamically evolving as it continues to incorporate new clinical centers as well as think tank institutes as members.

www.oncodistinct.net

PERSIST-SEQ is a public-private partnership funded by the Innovative Medicines Initiative (IMI), with representation from academic institutions, small- and medium-sized enterprises, public organizations and pharmaceutical companies.

The PERSIST-SEQ five-year international collaboration, led by the Oncode Institute (Utrecht, The Netherlands) and AstraZeneca, comprises 14 partners including VHIO and aims to provide the cancer research community with a new gold standard workflow for single-cell sequencing by developing and validating best practices as well as generating and analyzing high-quality FAIR data.

Empowering the scientific community to unravel therapeutic resistance and develop smarter therapeutic strategies to better treat cancer and prevent drug resistance, PERSIST-SEQ will employ an open access model to build and sustain its benchmarking procedures and centralized European data infrastructure. This model reduces duplication of efforts, thereby promoting collaboration across disciplines and ensuring efficient adoption of state-of-the-art single cell technologies.

www.persist-seq.org

PERSIST-SEQ is funded by the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No. 101007937. This Joint Undertaking receives support from the European Union's Horizon 2020 research an innovation programme and EFPIA.

The PhD PI3K biology in health & disease network incorporates 10 academic, clinical and industrial partners with renowned expertise in research focused on PI3K signaling. Leading a unique training network, this collaboration connects complementary expertise and brings additional value, novel tools and leadership of excellence in order to train talented early-stage researchers and suitably equip them for leading roles in cancer science and drug discovery in European industry and academia.

This research training program not only represents unparalleled educational opportunity for these young scientists, but also aims to increase the international competitiveness of European research in PI3K discovery and drug development.

www.pi3k-phdproject.eu

PROMISE

PROMISE - BioPrinted hydrogel MicrofluidicS to mimic patient-specific tumor mEtastatic microenvironment, is coordinated by the Bioengineering Institute of Catalonia (IBEC), in partnership with INL - International Iberian Nanotechnology and VHIO, and funded by the "La Caixa" Foundation. The project partners aim to develop and apply 3D bioprinting toward improving outcomes for cancer patients.

3D bioprinting facilitates the generation of three-dimensional cell models that imitate human physiology to test new therapeutic strategies in the laboratory. These models can accurately mimic patients' specific tumors and the main features of the tumor microenvironment.

This project, which combines 3D bioprinting and advanced liquid biopsy techniques in an organ-on-a-chip device, seeks to provide physicians with new tools to understand and monitor disease evolution in patients with metastatic colorectal cancer aimed at improving survival rates.

VHIO participates in the clinical validation of this microfluidic platform based on hydrogels that mimic the tumor microenvironment on cells derived from patients with metastatic colorectal cancer, to be validated in specific patient cohorts.

"la Caixa" Foundation

RAD51predict – Patient stratification based on DNA repair functionality for cancer precision medicine, is an ERAPerMed funded project led by VHIO. It aims to establish the prevalence of functional HRR deficiency (HRD) and its predictive value for personalized treatment with platinum salts and PARPi in breast cancer, ovarian cancer, prostate cancer, and endometrial cancer using the RAD51 immuno-assay and genomic assays.

This project seeks to perform an economic evaluation of selecting patients for PARPi treatment based on the RAD51 assay, genomic assays, or the current selection criteria to provide functional validation of germline/somatic genetic variants of unknown significance (VUS) using patients' data, cell lines and assessment of HRR markers in the tumor; integrate functional HRD data into existing public genomic databases; transfer the RAD51 assay as a predictive test in the clinic, and develop multiplexed protocols, automatization of image analysis, and real-time monitoring in circulating tumor cells.

This project is supported by the ERAPERMED2019-215 award, granted by *Fundación Científica de la Asociación Española Contra el Cáncer* (AECC FC) and by the *Instituto de Salud Carlos III* (ISCIII) through the *Acción Estrategica en Salud* (AES) 2019, both within the ERA PerMed framework.

Incorporating a network of 27 research entities spanning 10 countries, SPECTAcolor - Screening Platform for Efficient Clinical Trials Access in Colorectal cancer, is an initiative within the framework of the research program of the EORTC, supported by Alliance Boots.

Launched in 2013, this is the first prospective fully annotated tumor samples Biobank and Biomarker analysis platform for the genetic profiling of patients suffering from advanced colorectal cancer.

www.eortc.org/blog/category/spectacolor

Through the ERA-NET Sustained collaboration of national and regional programmes in cancer research activities, the Spanish Association Against Cancer (AECC) and Institute of Health Carlos III (ISCIII) awarded VHIO with two TRANSCAN-3 projects funded by the EU's Horizon Europe framework program in 2021, officially granted in 2022.

Supported by the Joint Transnational Call for Proposals *Next Generation cancer immunotherapy: targeting the tumour microenvironment*, the first proposal entitled *Evaluating the therapeutic potential of immunosuppressive paracrine cytokines in the tumour microenvironment of metastatic lesions* (IParaCyts), is coordinated by Joan Seoane, co-Director of VHIO's Preclinical and Translational Research Program . This project aims to advance and apply insights into druggable paracrine cytokines that interfere with immunotherapy in liver metastasis, addressing these matters in an integrative fashion based on the specific expertise of our partnership.

The second project entitled *Artificial Intelligence-based end-to-end prediction of cancer immunotherapy* (TANGERINE), is coordinated by Raquel Perez-Lopez, Principal Investigator of VHIO's Radiomics Group.

Both projects are supported by TRANSCAN-2 JTC 2021 and granted by the Fundación Científica de la Asociación Española Contra el Cáncer (FCAECC) and the Instituto de Salud Carlos III (ISCIII) through the Acción Estratégica en Salud (AES) 2021, within the TRANSCAN-2 framework.

TRANSCAN-2 has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 643638.

TRANSCAN-2 has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 643638.

UpSMART Accelerator seeks to improve experimental cancer development across the UK, Italy, and Spain, by providing early-phase clinical teams with digital healthcare products (DHP) for the real-time access to a wealth of patient data, and thus enable faster decision making.

The UpSMART Consortium consists of 23 participating institutes across Experimental Cancer Medicine Centres (ECMCs) in the UK, and Early Drug Development Units (EDDUs) in Spain and Italy. The program will test existing digital tools at these 23 phase I Units.

UpSMART will develop and provide all clinical sites with free to use access to new digital healthcare technology tools and improved approaches in trials that enable patients' access to tomorrow's medicines today. This project promotes the wider scale sharing and implementation of digital healthcare products as well as training in digital healthcare product approaches.

upsmart.digitalecmt.com

The program was awarded a Cancer Research UK (CRUK) Accelerator Award.

Announced in 2018, one of the U.S. Department of Defense's (DoD) Innovative Minds in Prostate Cancer (IMPaCT) Awards, funds a four-year collaborative partnership to advance precision medicine against metastatic prostate cancer (mPC). This coalition counts on the multidisciplinary expertise of investigators at VHIO, the Spanish National Cancer Research Center – CNIO (Madrid, Spain), and the University of Washington (USA).

Aimed at more precisely gauging response in patients to standard therapies, the team is developing new, more effective and tailored treatment strategies, as well as designing a clinical trial to assess the performance of a DNA damaging platinum chemotherapy, carboplatin, that is already used to treat other tumor types including ovarian and breast cancer.

http://cdmrp.army.mil/pcrp

WIN - Worldwide Innovative Networking in personalized cancer medicine, initiated by the Institut Gustave Roussy (France) and The University of Texas, MD Anderson Cancer Center (USA) is a non-profit, non-governmental organization incorporating 32 leading organizations representing all stakeholders in personalized cancer medicine covering 18 countries and 5 continents, united by their vision to deliver on the promise of effective, personalized cancer medicine to patients worldwide.

Under the tagline WINning together, WIN was formed on the premise that members can accomplish more together than each organization can achieve working alone. Aimed at improving cancer patients' survival and quality of life, WIN members also collaboratively design and carry out global studies designed to achieve breakthroughs for cancer patients across the globe.

www.winconsortium.org

Newly launched consortia in 2022

canSERV is an EU-funded project under the Horizon Europe programme to provide cutting-edge, interdisciplinary and customized oncology services across the entire cancer continuum. Incorporating 19 European partners including VHIO, it aims to offer a comprehensive portfolio of oncology-related research services available to all scientists in EU member countries, associated countries and beyond.

This network combines expertise in the oncology development pipeline and seeks to foster a pan-European collaboration to promote innovative research projects and deliver precision medicine solutions for the benefit of cancer patients. Awarded through the HORIZON-INFRA-SERV call, canSERV will offer state-of-the-art services to the cancer research community in order to provide the necessary resources to develop new projects in personalized medicine.

By connecting, coordinating, and aligning existing oncology and complimentary research infrastructures and providing services in a synergistic way transnationally, this project will capitalize on the critical mass of experts and services offered by the 13 research infrastructures that it brings together.

Various VHIO groups are participating in this translational and multidisciplinary initiative including Joaquin Arribas' Growth Factors Group, Violeta Serra's Experimental Therapeutics Group, and out Stem Cells and Cancer Group led by Héctor G. Palmer, with Elena Garralda, Head of VHIO's Early Clinical Drug Development Group and Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, as Principal Investigator of the project at VHIO.

www.canserv.eu

Funded by the European Union

This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No. 101058620.

CGI-Clinics aims at advancing personalized medicine in oncology by optimizing genomic data interpretation (after sequencing and before advising on compatible targeted therapies). Interpretation is a bottleneck for the full deployment and broad accessibility of Next Generation Sequencing (NGS) in the management of cancer. This project will address 3 main issues in genomic data interpretation, namely, it is not systematic, it deals with a majority of variants of unknown significance and fails to empower patients.

Cancer genomic data requires experts reviewing scattered databases and resources, in a time-consuming process that may lead to suboptimal clinical decisions. By integrating relevant public and private hospital databases, this project seeks to offer a one-stop shop solution that systematises tumour genome interpretation, to support medical doctors in choosing the most effective treatment for each patient, as well as facilitate virtual molecular tumor boards co-facilitated by reference hospitals.

This project will be developed through three phases: a setup (assess needs), validation (pilot with the 9 clinical partners) and replication (30 hospitals across EU) and will enable the democratization of genomic data interpretation (independent of their size, resources and profiling technology), provide health economics validation, and universalize the interpretation of tumor genomes for personalized cancer medicine.

CGI-Clinics was awarded under the European Commission's HORIZON-RIA call. Led by the Institute for Research in Biomedicine (IRB, Barcelona) and VHIO, it brings together 17 project partners from four countries, including organizations representing patients, clinicians and researchers. VHIO's role in the project counts on the leading participation of Ana Vivancos, Principal Investigator of our Cancer Genomics Group.

www.cgiclinics.eu

Funded by the European Union

This project has received funding from the European Union's Horizon program HORIZON-HLTH-2021-CARE-05-02 under grant agreement No. 101057509.

EOSC4Cancer will make diverse types of cancer data accessible: genomics, imaging, medical, clinical, environmental, and socio-economic. It will use and enhance federated and interoperable systems for securely identifying, sharing, processing and reusing FAIR data across borders and offer them via community-driven analysis environments.

EOSC4 Cancer's well curated data sets will be essential input for reproducible and robust analytics and computational methods – including machine learning and artificial intelligence. EOSC4Cancer's five use cases will cover the patient journey from cancer prevention over diagnosis to treatment, laying the foundation of data trajectories and workflows for future European Cancer Mission projects.

The EOSC4Cancer consortium, jointly coordinated by the Barcelona Supercomputing Center (BSC, Barcelona) and ELIXIR (Cambridge, UK), comprises 29 partners, including VHIO, from 13 countries. Participating organizations include cancer research centers, research infrastructures, leading research groups, hospitals, supercomputing centers, as well as affiliated entities.

To make the developments sustainable, EOSC4Cancer will leverage the partners' research infrastructures partners and the EOSC ecosystem. It will also serve the European Cancer Mission, by engaging with large international coalitions (e.g., ICGC-Argo, GA4GH, 1+MG/B1MG, Cancer Core Europe, European Cancer Information System, European Network of Cancer Registries, Innovative Partnership for Action Against Cancer Joint Action) and patients/survivors associations.

www.eosc4cancer.eu

Funded by the European Union

This project has received funding from the European Union's Horizon program HORIZON-INFRA-2021-EOSC-01 under grant agreement No. 101058427.

The MIRACLE project has been awarded under the ERA PerMed Joint Transnational Call 2021: *Multidisciplinary research projects on personalized medicine – development of clinical support tools for personalised medicine implementation*. This consortium comprises 5 partners and is jointly led by Paola Ulivi, Scientific Institute for Research, Hospitalization and Healthcare (IRCCS, Italy), and VHIO's Enriqueta Felip.

MIRACLE - *A machine learning approach to identify patients with resected non-small-cell lung cancer with high risk of relapse*, aims to develop and validate a machine learning algorithm acting as a clinical decision support tool for disease free survival prediction based on joint analysis of biological, clinical, and radiologic features.

Funded by the European Union's Horizon Europe Research and Innovation Programme EUonQoL is a 4-year project that aims to develop, pilot and validate the EUonQoL-Kit, a patient-driven, unified system for the assessment of quality of life (QoL) based on evaluations and preferences of cancer patients and survivors.

Led by the Instituto Nazionale Tumori (Milan, Italy), the project partners including VHIOI, will develop the EUonQoL-Kit from a patient perspective, and will be administered digitally, available in the EU27 and Associated countries languages, and applicable in future, periodic surveys to contribute to the EU's Cancer Mission.

At the core of the EUonQoL there is the adoption of a multistakeholder, co-design methodology, engaging patient representatives, healthcare professionals, administrators, policymakers, and citizens in all project related activities.

To be validated in a pilot survey using digital data collection within month 24 of the project, a total of 4,000 cancer patients and survivors will be enrolled through a network of EU cancer centers. An analysis of factors potentially impacting on cancer patients and survivors QoL, will also be performed. Implementation and exploitation strategies, as well as the linkage with other Cancer Mission projects and actions will be explored to develop future periodic surveys.

EUonQoL is composed by research institutions, cancer centres, as well as scientific, professional, and patient representative organizations, all with extensive experience and robust scientific background in the development of self-report QoL measures. This partnership fuels the ambition of EUonQoL to translate QoL information into future changes in cancer care policy and clinical practice.

www.euonqol.eu

This project has received funding from the European Union's Horizon Europe Research and Innovation Programme HORIZON-MISS-2021-CANCER-02-02 under Grant Agreement No. 101096362.

I3LUNG is a five-year European project funded under the framework of the H2020 call: *Ensuring access to innovative, sustainable and high-quality health care*. The consortium gathers 16 partners, including VHIO, with different expertise located worldwide, with the common goal of providing optimal care and perosonalized treatment for patients affected by metastatic lung cancer.

Thanks to the collection of biological, molecular, radiological, and clinical data from more than 2000 metastatic non-small cell lung cancer (mNSCLC) patients, I3LUNG will integrate all the collected information and thanks to the power of AI, generate a machine learning algorithm that will be able to predict the individual response to immunotherapy regimens. This tool will help to stratify mNSCLC patients and match tailored treatment to each case, moving lung cancer care away from a one-size-fits-all approach to more of a personalized treatment plan.

This individualized patient selection strategy will also help to reduce the European economic burden and improve patient outcomes by better matching available treatments to patients.

www.i3lung.eu

Funded by the European Union

This project has received funding from the European Union's Horizon program HORIZON-HLTH-2021-CARE-05 under grant agreement No. 101057695.

Immune4ALL

Immune4ALL is a 3-year project comprising 29 research groups and 215 researchers from 8 Spanish autonomous communities, encompassing three different areas of the CIBER – *Centro de Investigación Biomédica en Red* network (cancer, hepatic diseases, and rare diseases) and the National Biobank and Biomodel Platform.

Aimed at exploring the feasibility of predictive and pharmacodynamics biomarkers of immunotherapy in solid tumors, this nationwide program is coordinated by Enrique de Álava, Virgen del Rocío University Hospital (University of Seville), and is structured around several pilot studies that include developing and validating these markers for immunotherapy and the generation of a computational framework for data processing analysis, filtering visualization, and clinical decision support aligned with IMPaCT.

Focused on solid tumor types that cause high mortality, specifically in women, such as carcinoma of the breast, ovary, and cervix, or in both sexes, including hepatocellular carcinoma, bile duct carcinoma, GI-tract neuroendocrine tumors, and colorectal carcinoma, this project also has two general objectives devoted to social and economic perspectives (creating shared decision-making spaces with patients and generating cost-effective evidence) and training activities with patients and professionals in the field of precision medicine.

Immune4ALL's strategy is to integrate leading groups with outstanding experience in clinical, translational, and technological research in the development and validation of immuno-oncology biomarkers (including Digital Pathology/Artificial Intelligence, liquid biopsy, and experimental models) and the development of personalized immunotherapies working in recognized institutes across Spain, under the umbrella of CIBER.

This project has been granted under the scope of the *Proyectos de investigación de medicina personalizada program* of the Instituto de Salud Carlos III (Institute of Health Carlos III – ISCIII).

ODELIA

Aimed at revolutionizing Artificial Intelligence (AI) in healthcare using Swarm Learning (SL), the 5-year EU-funded ODELIA research project: Open Consortium for Decentralized Medical Artificial Intelligence, will establish the first pan-European SL network that allows for privacy conserving training of medical AI algorithms with the true democratic participation of all 12 partners from across Europe including VHIO (academic institutions and industry partners).

Through this network, AI algorithms will be developed and validated for the detection of breast cancer in magnetic resonance imaging (MRI) screening examinations as a demonstration case. Training clinically useful AI models usually requires sharing of patient related data which often faces several obstacles. This problem has been tackled by federated learning (FL). However, in FL AI models are combined by a central coordinator requiring participants to relinquish control over the AI model, concentrating control and commercial exploitation in a single actor. This limitation has been addressed by swarm learning, in which AI models are trained decentrally and models are combined without the requirement for a central coordinator. SL in medical AI has never previously been applied in a real-world large-scale setting, which is the main objective of ODELIA.

This pan-European academic and clinical consortium will develop, implement and evaluate SL-based workflows to train AI models in medical imaging, in particular- and as an exemplary demonstration case - in the context of breast cancer screening. A blockchain will be created to enable institutions across Europe to jointly train AI models without having to share their data or rely on a central coordinator.

www.eibir.org/projects/odelia/

Funded by the European Union

The ODELIA project receives funding from the European Union's Horizon Europe and innovation programme HORIZON-HLTH-2021-CARE-05 under grant agreement No. 101057091.

OncoExoPeptides

Recent findings have shown that some RNA molecules previously annotated as non-protein coding actually contain small open reading frames that code for evolutionary conserved, unannotated, micropeptides. The few micropeptides characterized to date play key functions in fundamental processes such as DNA repair, muscle physiology and regeneration. However, the relevance of micropeptides in cancer and metastasis has not yet been defined.

Their small molecular size makes them ideal candidates to be shed into tumor-derived exosomes. Exosomes are small vesicles containing peptides, proteins and genetic materials such as small RNAs that are secreted by many cancer types. Recent data demonstrate that exosomes secreted from pancreatic cancer cells can be used as surrogate markers of metastasis and prepare pre-metastatic niches in the liver.

The OncoExoPeptides project's hypothesis is that exosome-secreted micropeptides are novel biomarkers secreted by pancreatic cancer cells and play an active role in tumor-microenvironment communication and metastasis. To date, we have discovered 6 novel micropeptides dysregulated in cancer that have tumor suppressor activities. Here, we propose an innovative research program to: (1) identify exosome-secreted micropeptides involved in tumor communication; (2) detect exosome-secreted micropeptides in patient-derived plasma; (3) characterize their function in pancreatic cancer; and (4) establish novel prognostic signatures and stratification tools.

To do so, this collaboration gathers a multidisciplinary team including the expertise of VHIO's Maria Abad in micropeptides, Hector Peinado, Spanish National Cancer Research Center (CNIO, Madrid, Spain) in exosomes, and Bruno Costa-Silva, Champalimaud Foundation (Lisbon, Portugal) in liver pre-metastatic niches, pancreatic cancer clinicians and experts in proteomics and biocomputing. This project will advance insights into the unexplored field of the exosome-secreted micropeptides and may facilitate the development of new therapeutic strategies in oncology.

"la Caixa" Foundation

PCM4EU

PCM4EU – Personalised Cancer Medicine for all EU Citizens, is a project under the Europe's Beating Cancer Plan by EU4Health and comprises partners from 15 countries across Europe, including VHIO. Centered on facilitating the implementation of molecular cancer diagnostics for precision oncology such as DRUP-like clinical trials, PCM4EU is coordinated by Hans Gelderblom at the Leiden University Medical Centre (LUMC), the Netherlands.

PCM4EU is divided into six workpackages (WPs): WP2 focuses on mapping and facilitating the use of molecular cancer diagnostics, and WP3 involves precision oncology and promoting and initiating more national DRUP-like clinical trials in European countries. WP4 is dedicated to implementing precision oncology and standards for use in diagnostics and molecular tumour boards (MTBs) in European countries. WP5 promotes equitable and cross-border access, and WP6 focuses on the training of the next generation of oncologists. PCM4EU also includes a patient engagement strategy to ensure access to molecular-based clinical trials and will also build a data aggregation platform. VHIO participates in WP2, WP3 and WP5.

Funded by the European Union

The PCM4EU project receives funding from the European Union's Horizon Europe and innovation programme HORIZON-HLTH-2021-CARE-05 under grant agreement No. 101057091.

Preventable

Coordinated by the Instituto de Investigação e Inovação em Saúde da Universidade do Porto (Porto, Portugal), the 3-year PREVENTABLE consortium is funded by the European Commission under the topic HORIZON-HLTH-2022-CARE-08-04 - Better financing models for health systems, and comprises 10 partners, including VHIO, in 8 countries.

The main aim of this project is to merge specialized clinical knowledge on rare tumor risk syndromes (RTRS) pathways of care, real-life clinical data from RTRS patients and experiences from professionals and patients, with health economic models and social sciences approaches to estimate the cost-benefit of risk-reduction interventions in RTRS and delineate guidelines for its communication among and within clinical teams and RTRS patients.

PREVENTABLE project results will be delivered to a diversity of stakeholders, including policy-makers, in order to promote the implementation of cost-effective RTRS patient-centered care in Europe.

Funded by the European Union

The PREVENTABLE project receives funding from the European Union's Horizon Europe and innovation programme HORIZON-HLTH-2022-CARE-08 under grant agreement No. 101095483.

The European Commission has launched the Cancer Mission as one of five missions to boost research and innovation through funding under the Horizon Europe programme. The aim of the Cancer Mission is to improve the life expectancy and quality of life of more than 3 million patients by 2030, through prevention measures, early detection and more effective treatments.

Implementation plans of two convergent European initiatives, the Horizon Europe Mission Cancer and the Europe's Beating Cancer Plan, spur for a European Initiative to UNderstand CANcer - UNCAN.eu. More precisely, the UNCAN.eu initiative is one of the 13 specific objectives of the Mission on Cancer and one of the ten flagships of the Europe's Cancer Beating plan. The Coordination and Support Action (CSA), named 4.UNCAN.eu, is planned to generate a blueprint for UNCAN.eu.

The blueprint for UNCAN.eu will propose to set up a European Federated Cancer Research data hub and to generate a series of use cases, addressing major challenges in cancer research. These ambitious and innovative, but realistic and focused, use cases will be cross-border and trans-disciplinary research programs built in a problem-solving manner. Results of these use cases will feed the Cancer Research data hub with findable, accessible, interoperable, and re-usable (FAIR) cancer research data.

4.UNCAN.eu is coordinated by Eric Solary, Gustave Roussy Cancer Campus, Grand Paris (France), and with the participation of VHIO and the CIBERONC network as Spanish representatives. VHIO's Director Josep Tabernero is leading one of the six work packages to develop a methodology to identify translational cancer research lines to be prioritized and funded by the European Commission until 2027.

https://uncan.eu/

The UNCAN.eu initiative receives funding from the European Union's Horizon Europe and innovation programme HORIZON-MISS-2021-UNCAN-01-01 under grant agreement No. 101069496.

Other collaborations

The AstraZeneca/MedImmune – VHIO Alliance drives advancements at the preclinical, clinical and translational research levels across AstraZeneca's oncology portfolio. Combining VHIO's strengths in promoting cancer discovery through the integration of translational science and clinical research with AstraZeneca's promising early-stage oncology pipeline, the alliance focuses on areas including DNA damage repair, drug resistance, new drug combinations and molecular profiles for patient selection.

In 2020, AstraZeneca/Medimmune announced its Partner of Choice Network, comprising nine of the world's most renowned research centers and institutes in oncology to accelerate research against some of the most difficult-to-treat cancers. Selected partners of choice are the Cambridge Cancer Center (UK), Institut Gustave Roussy (France), Johns Hopkins University (USA), Memorial Sloan Kettering Cancer Center (USA), Oregon Health and Science University/Knight Cancer Institute (USA), Peter MacCallum Cancer Center (Australia) Princess Margaret Cancer Center (Canada), University of Navarra (Spain), and VHIO.

This network serves a forum for data sharing and cancer discovery in real-time. Scientific insights and findings generated through clinical studies are exchanged among partner institutions for the development and implementation as best practices in oncology. AstraZeneca will support selected clinical and non-clinical research proposals from the partners' investigators to expedite novel scientific research and innovative clinical trial design aimed at developing new strategies in precision medicine against cancer.

www.astrazeneca.com

Launched by Roche in 2016, the imCORE - immunotherapy Centres of Research Excellence Network is a 27 partner-strong collaboration that aims to advance discovery in cancer immunotherapy. It connects internationally renowned scientific and clinical experts in immune-based therapeutic strategies in oncology who work together to assess and advance the most promising novel treatment approaches.

Working in collaboration with scientists from Roche and Genentech, researchers and physician-scientists in cancer immunotherapy from across the globe aim to drive the application and extension of immune-based strategies to more tumor types, as well as advance insights into the cellular and molecular mechanisms modulating immune response to cancer.

This network was designed to significantly advance anti-cancer immunotherapeutics and accelerate discovery towards benefiting patients who may stand to gain from novel immune agents as mono therapy or in combination.

www.roche.com

The SCITRON Consorcio público-privado de Investigación Científica y Translacional en Oncología (Consortium for Scientific Translational Research in Oncology) is a scientific program which was established in collaboration with Novartis in 2017.

As a new model of R&D collaboration, this initiative connects experts from Novartis and VHIO in applied and translational research to increase the impact of basic research in clinical practice. The specific areas of interest include the development of a technology platform that analyses tumor clonal evolution and resistance mechanisms to targeted immunotherapy.

www.novartis.com

The OCTC - Oncology Clinical and Translational Consortium, a collaborative scientific research network comprised of 6 renowned comprehensive cancer centers, was launched by GSK in 2013.

While GSK gains OCTC's expertise in preclinical, translational and clinical development of novel anticancer therapeutics, the participating centers have access to studies with GSK's early-stage oncology pipeline and opportunities to accelerate and advance the next generation of novel oncology therapeutics.

www.gsk.com

Accreditation

In 2022 VHIO underwent evaluation for accreditation of the Institució CERCA–Centres de Recerca de Catalunya (CERCA Institute of Research Centres of Catalunya) for the period 2017–2021.

In recognition of VHIO's progress, performance in knowledge transfer activities and management of excellence, VHIO was awarded the maximum qualification of an A grading. This achievement recognizes the excellence and quality of work carried out by all individuals, teams, and groups at our Institute.

www.cerca.cat/en/

In 2021 VHIO received the Severo Ochoa Center of Excellence Award, granted within the subprogram of the Spanish Institutional Strengthening of the State Plan for Scientific and Technical Research & Innovation, that recognizes national research centers that demonstrate scientific leadership of excellence and impact at global level.

Conferring reputation and social and scientific recognition, this accreditation, awarded annually, is valid for four years and renewable thereafter through re-application for the same rigorous evaluation carried out independently by an international scientific committee comprised of prestigious researchers with high impact.

From the 2020 call, managed by the Agencia Estatal de Investigación (State Research Agency), VHIO is the only newly accredited Center of Excellence Severo Ochoa Center (2022 - 2026), alongside the other six re-awarded research centers. Set within the Vall d'Hebron Barcelona Hospital Campus, VHIO is also the first research center linked to the national healthcare system to have received this distinction.

The Award is funded by the Agencia Estatal de Investigación (State Agency for Research) (CEX2020-001024-S / AEI / 10.13039 / 501100011033).

The European Commission's Human Resources for Research (HRS4R) strategy enables research institutions of excellence to actively implement and uphold the requisites of The European Charter for Researchers and Code of Conduct for the Recruitment of Researchers for their HR policies and practices.

VHIO's comprehensive analysis and action plan was officially approved by HRS4R assessors in 2018 and our Institute was consequently granted permission to use the HR Excellence in Research Award logo as demonstration of its stimulating and favorable work environment.

www.vhio.net/about-vhio/hrs4r/

Also reflective of our dedication to excellence and the quality of our services and procedures, VHIO's Cancer Genomics and Molecular Oncology Groups are both ISO-accredited for their testing methods and technologies

VHIO continues to meet the high standards in quality and procedures in the audit of our clinical trials Units, carried out by the Generalitat de Catalunya (Government of Catalonia). Our Research Management is also endorsed by ISO 9001 Certification.

New Funding and Projects in 2022

Institutional Supporters

Departament de Salut: Budgetary support
Departament d'Empresa i Coneixement: Budgetary support

VHIO's CELLEX Building & Infrastructures

Advanced Molecular Diagnostics Program (DIAMAV), and other VHIO investigators, groups and projects

CaixaResearch Advanced Oncology Research Program
Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch
UNderstanding cancer through sIngle cell seQUEncing: the UNIQUE platform

Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI)

Center of Excellence Severo Ochoa

Excellence Program AECC 2022- Advanced Therapies Accelerator Program

International Support

HORIZON-HLTH-2021-CARE-05-02 – International Consortium
Integrative science, Intelligent data platform for Individualized LUNG cancer care with Immunotherapy - I3LUNG
Ref: 101057695
PI VHIO: Enriqueta Felip
Thoracic Tumors Group

HORIZON-HLTH-2021-CARE-05-02 – International Consortium
Data-driven cancer genome interpretation for personalised cancer treatment - CGI-Clinics
Ref: 101057509
PI VHIO: Ana Vivancos
Cancer Genomics Group

HORIZON-INFRA-2021-EOSC-01-06 – International Consortium
A European-wide foundation to accelerate Data-driven Cancer Research - EOSC4Cancer
Ref: 101058427
PI VHIO: Xenia Villalobos & Alejandro Piris
Scientific Coordination Area

HORIZON-INFRA-2021-SERV-01-01 - International Consortium
Providing cutting edge cancer research services across Europe - CanServ
Ref: 101058620
PI VHIO: Elena Garralda
Early Clinical Drug Development Group

HORIZON-MISS-2021-UNCAN-01-01 – International Consortium
A Coordination and Support Action to prepare UNCAN.eu platform - 4.UNCAN.eu
Ref: 101069496
PI VHIO: Alejandro Piris
Scientific Coordination Area

HORIZON-HLTH-2021-CARE-05-02 – International Consortium
Open Consortium for Decentralized Medical Artificial Intelligence- ODELIA
Ref: 101057091
PI VHIO: Raquel Pérez-López
Radiomics Group

HORIZON-HLTH-2022-CARE-08-04 – International Consortium
Cancer Prevention vs Cancer Treatment: the rare tumour risk syndromes battle – PREVENTABLE
Ref: 101095483
PI VHIO: Judith Balmaña
Hereditary Cancer Genetics Group

EU4H-2021-PJ-15 – International Consortium
Personalised Cancer Medicine for all EU citizens – PCM4EU
Ref: 101079984
PI VHIO: Elena Garralda
Early Clinical Drug Development Group

Unraveling the Functional Complexity of Cancer Genomes through Chromosome Engineering – MACHETE
Ref: 101041659
PI: Francisco Barriga
Genome Engineering Group

ESMO Research Fellowship
PARP inhibitors associated tumour immune microenvironment changes in pancreatic ductal adenocarcinoma
Granted to Anthony Turpin
Mentor: Teresa Macarulla
Gastrointestinal & Endocrine Tumors Group

Breast Cancer Research Foundation Grant
Immune Senolysis Against Breast Cancer
Ref: BCRF-22-008
PI: Joaquín Arribas
Growth Factors Group

Paradifference Foundation Grant call
Detection and monitorization of genetic markers for metastasis in PPGL patients using a non-invasive liquid biopsy assay
PI: Rodrigo Toledo Almeida
Gastrointestinal & Endocrine Tumors Group

National Funding

ICREA Position Granted to Marcos Malumbres
Cancer Cell Cycle Group

Premi Trajectòria Investigadora als Hospitals de l'ICS
Granted to Enriqueta Felip
Thoracic Tumors Group

Premi a la Investigadora Jove de l'ICS
Granted to Raquel Pérez-López
Radiomics Group

Ajuts per a la incorporació de personal investigador postdoctoral al sistema català de ciència i tecnologia dins del programa Beatriu de Pinós
Immune Signatures for Immune Drug prediction in Oncology (ISIDOra)
Ref: 2021 BP 00149
Granted to Artur Mezheyeuski
Project Director: Paolo Nuciforo
Molecular Oncology Group
Radiomics Group
Co-funded by the H2020 Programme - Marie Skłodowska-Curie Actions COFUND (BP3, Ref: 801370)

Ajuts per a la contractació de personal investigador Predoctoral en Formació– (FI)
Ref: 2022 FI B 00664
Granted to Andreu Ódena
Project Director: Violeta Serra
Experimental Therapeutics Group
Grant funded by the European Commission European Social Fund: Investing in your future

Ajuts per a la contractació de personal investigador novell – FI Predoctoral
Ref: 2022 FI B 00092
Granted to Daniel Medina
Project Director: Francesc Bosch
Experimental Hematology Group
Grant funded by the European Commission European Social Fund: Investing in your future

Proyectos de Generación de Conocimiento
Co-evolutionary dynamics landscape of neoplastic cells and T-cells interactions during cancer immunotherapy. (IMMUNOMICS-2)
Ref: PID2021-126297OA-I00
PI: Rodrigo Toledo Almeida
Gastrointestinal & Endocrine Tumors Group
Grant funded by the European Commission European Development Fund: A way of making Europe

Proyectos en Colaboración Público-Privada
Innovative treatment with ABTL0812 for metastatic pancreatic cancer: shortening timelines for its approval and arrival to patients (INNOPANC)
Ref: CPP2021-009064
PI: Teresa Macarulla
Gastrointestinal & Endocrine Tumors Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos en Colaboración Público-Privada
Development of DNA-based diagnostic tests to personalize the treatment of Advanced breast cancer
Ref: CPP2021-009037
PI: Ana Vivancos
Cancer Genomics Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos en Colaboración Público-Privada
Novel HER3 bispecific antibody drug conjugates for the treatment of aggressive tumours (TRADBI)
Ref: CPP2021-008924
PI: Josep Villanueva
Tumor Biomarkers Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos en Colaboración Público-Privada
Clinical development of IDP-121, a new drug for Myc-dependent hematologic malignancies (IDP121CLNC)
Ref: CPP2021-008561
PI: Francesc Bosch
Experimental Hematology Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos en Colaboración Público-Privada
Phase I clinical trial of a new antitumor therapy based on nanoparticles: development, characterization and toxicity studies
Ref: CPP2021-008871
PI: Irene Braña
Early Clinical Drug Development Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos en Colaboración Público-Privada
Targeted treatment of triple-negative breast cancer with the new oral serotonin 1B receptor antagonist (LB208)
Ref: CPP2021-008715
PI: Irene Braña
Early Clinical Drug Development Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos en Colaboración Público-Privada
Transfer to the Clinic of a new directed therapy for the treatment of Erwing's Sarcoma
Ref: CPP2021-008515
PI: César Serrano
Sarcoma Translational Research Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Convocatoria de Preparación y Gestión de Proyectos Europeos
VHIOSfera Europa: towards a succesful model of tailored scientific management of International Cooperative Programs and Calls
Ref: GPE2022-001029
PI: Alejandro Piris
Scientific Coordination Area

Ayudas para Contratos Ramon y Cajal
Ref: RYC2021-031213-I
Granted to Endika Prieto
Tumor Immunology & Immunotherapy Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Ayudas Contratos Juan de la Cierva Formación
Ref: FJC2021-047969-I
Granted to Caterina Tozzi
Project Director: Raquel Pérez-López
Radiomics Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Ayudas contratos Predoctorales para la formación de doctores (FPI)
Ref: PRE2021-096899
Granted to Maria Lopez
Project Director: Joan Seoane
Gene Expression & Cancer Group
Grant funded by the European Commission European Social Fund: Investing in your future

Ayudas contratos Predoctorales para la formación de doctores (FPI)
Ref: PRE2021-097020
Granted to Iván Olivares
Project Director: César Serrano
Sarcoma Translational Research Group
Grant funded by the European Commission European Social Fund: Investing in your future

Ayudas contratos Predoctorales para la formación de doctores (FPI)
Ref: PRE2021-099661
Granted to Marta Lalinde
Project Director: Joaquín Arribas
Growth Factors Group
Grant funded by the European Commission European Social Fund: Investing in your future

Ayudas contratos Predoctorales para la formación de doctores (FPI)
Ref: PRE2021-099087
Granted to Heura Domenech
Project Director: Violeta Serra
Experimental Therapeutics Group
Grant funded by the European Commission European Social Fund: Investing in your future

Ayudas contratos Predoctorales para la formación de doctores (FPI)
Ref: PRE2021-096930
Granted to Arnau Llinás
Project Director: Jose Antonio Seoane
Cancer Computational Biology Group
Grant funded by the European Commission European Social Fund: Investing in your future

Ayudas contratos Predoctorales para la formación de doctores (FPI)
Ref: PRE2021-101048
Granted to Maria José Fariñas
Project Director: Jose Antonio Seoane
Cancer Computational Biology Group
Grant funded by the European Commission European Social Fund: Investing in your future

VHIO projects managed through the *Instituto de Investigación Sanitaria Acreditado Institut de Recerca* (Accredited Research Institute - Vall d'Hebron)

Proyectos de Investigación Clínica Independiente
Design and implementation of a pase I, open-label, doce-escalation clinical trial using p95HER2 CAR HER2 BiTE T son patients with p95Her2 positive advanced solid tumors
Ref: ICI22/00088
PI: Irene Braña
Early Clinical Drug Development Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos de Investigación en Salud
Study of the tumor microenvironment and immune response in chemotherapy-induced high tumor mutational burden glioblastoma
Ref: PI22/00130
PI: Joan Seoane
Gene Expression & Cancer Group
Grant funded by the European Commission European Development Fund: A way of making Europe

Proyectos de Investigación en Salud
Phase I-Ib clinical trial of safety and immunobiology of prophylactic infusion of γδ lymphocytes and NK cells from HLA identical donor after T-cell depleted Allo-HCT
Ref: PI22/00710
PI: Guillermo Orti
Experimental Hematology Group
Grant funded by the European Commission European Development Fund: A way of making Europe

Proyectos de Investigación en Salud
Drivers of chromosome instability in karyotypically simple sarcomas: gastrointestinal stromal tumor as a paradigm
Ref: PI22/00720
PI: César Serrano
Sarcoma Translational Research Group
Grant funded by the European Commission European Development Fund: A way of making Europe

Proyectos de Investigación en Salud
Whole genome sequencing as a first-tier test to improve hereditary breast/ovarian genetic diagnosis
Ref: PI22/01200
PI: Sara Gutierrez-Enríquez
Hereditary Cancer Genetics Group
Grant funded by the European Commission European Development Fund: A way of making Europe

Proyectos de Investigación en Salud
Identification of determinants of response to CAR T-cell therapy and bispecific T cell engagers in patients with diffuse large B-cell lymphoma (DLBCL)
Ref: PI22/01204
PI: Pau Abrisqueta
Experimental Hematology Group
Grant funded by the European Commission European Development Fund: A way of making Europe

Proyectos de Investigación en Salud
Dissecting the role of copy number alterations as molecular biomarker in advanced NSCLC
Ref: PI22/01585
PI: Ramon Amat
Thoracic Tumors Group
Grant funded by the European Commission European Development Fund: A way of making Europe

Proyectos de I+D+i vinculados a la Medicina Personalizada y Terapias Avanzadas
(ALMA) Inteligencia Artificial para diagnóstico, tratamiento y pronóstico de enfermedades hematológicas
Ref: PMPTA22/00023
PI: Julia Montoro
Experimental Hematology Group
Grant funded by the European Commission European Development Fund: A way of making Europe

Proyectos de Colaboración Internacional
Evaluating the therapeutic potential of immunosuppressive paracrine cytokines in the tumor microenvironment of metastatic lesions (iParaCyts)
Ref: AC22/00037
PI: Joan Seoane
Gene Expression & Cancer Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos de Colaboración Internacional
Artificial-intelligence-based end-to-end prediction of cancer immunotherapy response (TANGERINE)
Ref: AC22/00041
PI: Raquel Pérez-López
Radiomics Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Proyectos de Investigación de Medicina Personalizada de Precisión
Explorando la viabilidad de biomarcadores predictivos y farmacodinámicos de inmunoterapia en tumores sólidos (Immune4ALL)
Ref: PMP22/00054
Gastrointesinal & Endocrine Tumors
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Miguel Servet Tipo II
Ref: CPII22/00002
Granted to Rodrigo Toledo de Almeida
Gastrointestinal & Endocrine Tumors Group
Grant funded by the European Commission European Social Fund: Investing in your future

Ayuda Juan Rodés
Ref: JR22/00071
Granted to Helena Ariño
Mentor: Josep Tabernero
Gastrointestinal & Endocrine Tumors Group
Grant funded by the European Commission European Social Fund: Investing in your future

Acciones Individuales MSCA – Sello de Excelencia ISCIII-Health
Studying the relevance of drug persistent cells as the seed of recurrence upon treatment with RET inhibitors (SeedRET)
Ref: IHMC22/00018
Granted to Belen Elguero
Mentor: Héctor G Palmer
Stem Cells & Cancer Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Acciones Individuales MSCA – Sello de Excelencia ISCIII-Health
High-throughput personalized screening of tumor expanded proteomes for immunogenic antigens (UPSCALE)
Ref: IHMC22/00046
Granted to Pierre Levy
Mentor: Alena Gros
Tumor Immunology & Immunotherapy Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Ayudas para la Intensificación de la Actividad Investigadora
Ref: INT22/00019
Granted to Cristina Saura
Breast Cancer Group

Ayudas para Contratos Predoctorales de Formación en Investigación en Salud
Ref: FI22/00307
Granted to Humaira Abdul
Project Director: Raquel Pérez-López
Radiomics Group
Grant funded by the European Union NextGenerationEU/Plan de Recuperación, Transformación y Resilencia (PRTR)

Contratos de personal técnico bioinformático de apoyo a la investigación en los IIS
Ref: FI22/00007
Granted to Pau Marc Muñoz
Mentor: Lara Nonell
Bioinformatics Unit
Grant funded by the European Commission European Social Fund: Investing in your future

Private Funding

Beca Junior Leader 2022
New-generation oncological MRI (New-OncoMRI): development, validation and application
Granted to Francesco Grussu
Mentor: Raquel Pérez-López
Radiomics Group

Ayudas Predoctorales InPhinit Retaining
Study of the molecular mechanisms underlying the tumor microenvironment in bone metastasis in order to identify novel therapeutic targets
Granted to Cayetano Galera
Project Director: Joan Seoane
Gene Expression & Cancer Group

XXII Beca FERO en Investigación Oncológica Traslacional
Deciphering epigenetic features hidden in the plasma of colangiocarcinoma patients
PI: Tian Tian
Gastrointestinal & Endocrine Tumors Group

IV Proyecto FERO-ghd en Cáncer de Mama
Epigenetic differences associated with hormone treatment resistant breast cancer heterogeneity
PI: Jose Antonio Seoane
Cancer Computational Biology Group

Estudios Clínicos AECC- NATIONAL CONSORTIUM
Centralization of pathological diagnosis and implementation of precision medicine strategies in sarcoma
PI VHIO: César Serrano
Sarcoma Translational Research Group

TRANSCAN
Evaluating the therapeutic potential of immunosuppressive paracrine cytokines in the tumor microenvironment of metastatic lesions (iParaCyts)
PI: Joan Seoane
Gene Expression & Cancer Group

TRANSCAN
Artificial-intelligence-based end-to-end prediction of cancer immunotherapy response (TANGERINE)
PI: Raquel Pérez-López
Radiomics Group

Programa Joves i Ciència. Premio Pedrera Talents
Granted to David García-Illescas
Project Director: Ana Oaknin
Gynecological Malignancies Group

Programa Joves i Ciència. Premio Pedrera Talents
Granted to Patricia Fernández Guzmán
Project Director: Marta Crespo
Experimental Hematology Group

Becas SEOM/FECMA para Proyectos de Investigación en Cáncer de Mama
Redefiniendo el pronóstico del carcinoma lobulillar invasivo (CLI) de mama en estadío precoz.
PI: Meritxell Bellet
Breast Cancer Group

Becas SEOM/BMS para proyectos de investigación Traslacional en inmuno.oncología
Validación del valor predictivo de la firma de expresión génica vigex-RCC en pacientes con cáncer renal metastásico tratados con combinaciones basadas en inmunoterapia en primera linea
PI: Cristina Suárez
Genitourinary, Central Nervous System (CNS) Tumors, Sarcoma and Cancer of Uknown Primary Site Group

Becas SEOM/Fundación CRIS contra el Cancer de Retorno de investigadores jóvenes
Prospective validation of the VIGEx gene-expression signature
Granted to Alberto Hernando
Co-Mentors: Elena Garralda & Ana Vivancos
Early Clinical Drug Development Group
Cancer Genomics Group

Premio SEOM Tesis doctoral para investigadores jóvenes
Granted to Iosune Baraibar
Gastrointestinal & Endocrine Tumors Group

Premio SEOM/MERCK "Somos futur0"
Granted to Nadia Saoudi
Gastrointestinal & Endocrine Tumors Group

Bolsa de viaje SEOM para rotaciones externas de dos meses para residentes de 5º año
Granted to Oriol Mirallas

Premios a la Investigación en Cancer de Mama Metastásico
Combining MYC and PARP inhibitors as a novel therapeutic strategy against triple-negative breast cancer.
PI: Laura Soucek
Models of Cancer Therapies Group

Premios a la Investigación en Cancer de Mama Metastásico
Clinical and molecular characterization of oligometastatic breast cancer: Revealing and improving the potential benefit of a local treatment on primary or metastatic sites. A multicentric study.
PI: Meritxell Bellet
Breast Cancer Group

Becas Jose MªBuesa del Grupo GEIS de Ayuda a la Investigación en Sarcomas
Inhibición dirigida de la ubiquitina ligasa E3 Atrogin-1/FBXO32 en sarcomas de origen muscular.
PI: César Serrano
Sarcoma Translational Research Group

VI Beca Trienal de la Fundación Mari Paz Jimenez Casado (FMPJC) de ayuda a la Investigación en Sarcomas en colaboración con el GEIS
Targeted kinase inhibition and immune response in gastrointestional stromal tumor (GIST): It takes two to tango
PI: César Serrano
Sarcoma Translational Research Group


VHIO
VALL D'HEBRON
Institute
of Oncology

Patrons:

Generalitat de Catalunya

Fundació Privada CELLEX

fundación fero
Investigando por un futuro sin cáncer

"la Caixa" Foundation

Fundación BBVA

www.vhio.net

mobile version
scan to visit

› Extended version online: memorias.vhio.net/2022
› PDF version: memorias.vhio.net/2022/SR-VHIO-2022.pdf