VHIO

VALL D'HEBRON
Institute
of Oncology

SCIENTIFIC REPORT

2020

A year of challenges, opportunities and hope.

Institució CERCA
Centres de Recerca de Catalunya

Vall d'Hebron Institute of Oncology (VHIO)

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VALL D'HEBRON INSTITUTUE
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SCIENTIFIC REPORT 2020

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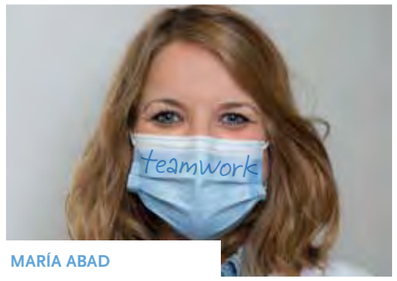
A year of challenges, opportunities and hope.

Championed by VHIO's Director, Josep Tabernero, our Principal Investigators as well as the Heads of our Transversal Clinical Trials Core Services, Units and Programs, spearhead efforts aimed at solving cancer sooner. They lead their respective groups and teams to turn obstacles in oncology into opportunities, and work tirelessly to resolve current and future challenges in combating this hugely complex disease.

Throughout 2020, the COVID-19 pandemic wreaked its havoc at societal level, affecting all aspects of humanity everywhere. It has undoubtedly had a tremendous effect on how the cancer research community has had to re-think interaction, adapt infrastructures and approaches to ensure that progress against cancer advances, no matter how disruptive this past year has been.

To mark this terribly challenging year, we invited each of our Group and Unit leaders to reflect on 2020, and submit a noun, adjective, concept, or priority area, which they felt was particularly relevant- though not exclusive- to this past year.



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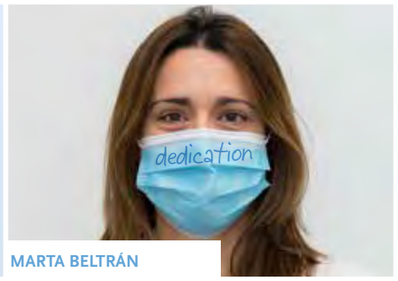

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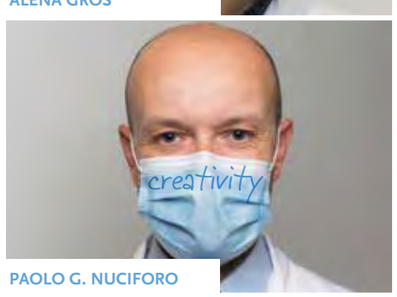

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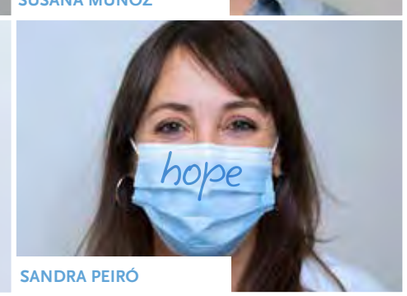

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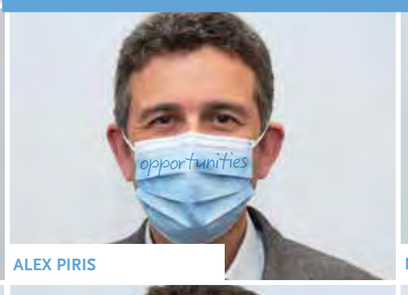

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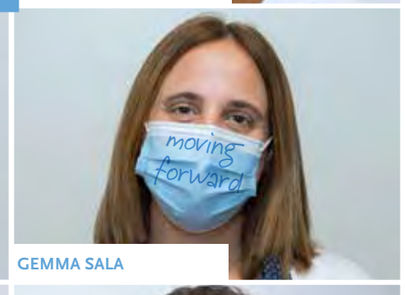

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FOREWORD

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

2020: An Extraordinary Year for Biomedicine, Cancer Science and Clinical Oncology

Considering the many challenges posed by the COVID-19 pandemic in 2020, I cannot forget the particularly dark times. How this terrible virus swept the world and ravaged human lives, with a devastating death toll. But, in the context of biomedicine, there were many bright moments that translated into opportunities and hope.

This pandemic has shone a light on the breathtaking ability of medical science to identify and combat a major new threat to public health globally. At lightning speed, researchers around the world worked tirelessly together to successfully develop COVID-19 vaccines.

They were able to do so quickly for several reasons: research experience in developing vaccines against related viruses; years of critical basic research in understanding and applying RNA biology; faster ways to manufacture vaccines; hefty funding that enabled the running of multiple trials in parallel; and regulatory bodies moving more quickly in response.

There are many lessons here that could be applied to other diseases including cancer in order to accelerate progress and accelerate improved clinical outcomes for countless patients worldwide.

Shaped by these reflections, the theme of this year's report -- *VHIO in 2020: a year of challenges, opportunities and hope* -- captures our experiences, endeavors, and collective spirit. We invited our Group and Unit leaders to reflect on 2020, and come up with a noun, adjective, concept, or priority area, which they each considered as particularly relevant -- though not exclusive -- to this momentous past year. Written on each of their respective masks (see fold-out pages 4-5), the design depicts the very familiar Zoom virtual meeting scenario, which is so symbolic of the COVID-19 era.

Due to the safety and logistical considerations brought about by COVID-19, and to reflect the reality of balancing those physically working in the lab and clinical settings with those working from home, we revisited our approach to this year's report's photo shoot. We translated this obstacle into opportunity.

With the exception of our larger groups, we sought to include as many group members as possible without masks. Each photo was taken individually, at a distance, in locations away from areas dedicated to the care of our cancer patients. We also welcomed faculty who were working at home during each photo session, inviting them to send their photos from home.

COVID-19: from crisis to opportunity

Using a combination of surveys and interviews of oncology clinical investigators globally, and analyses of data from IQVIA and Clinical Trials.gov, a study[1] explored how COVID-19 has affected the management of ongoing clinical trials.

The focus of this research was to provide an initial evaluation of COVID-19 on the landscape of clinical trials for cancer around the world. As noted

by the authors, while the data were limited by sample size, the findings indicated that patient enrolment in active clinical trials for cancer has been severely hampered by the pandemic during the survey assessment period (23 March–3 April).

Crucially, their data highlighted the importance of getting telemedicine running smoothly in advance to enable a seamless transition in patient care. I completely agree. The application of telemedicine has most certainly been expedited by COVID-19, possibly representing a tipping point, the advent of remote patient care in bringing crucial medical expertise to more patients.

Authors of a comprehensive survey[2] on what physicians have learned and the interrelationship between COVID-19 and cancer, argue that while COVID-19 has impacted many aspects of cancer research, treatment and patient care, it has also spurred creative solutions. I also believe that insights into this terrible virus, in addition to the speedy development of vaccines, have also been accelerated in part by what we have learned through years of research aimed at combating cancer.

Like many other medical oncology departments, the team at Vall d'Hebron had to overcome many challenges in 2020, including optimizing medical infrastructures overwhelmed by COVID-related illnesses and responding to the inevitable pressures on resources and staffing.

Spurred by our shared determination and dedication to providing the best treatment options and care for our patients, we swiftly adapted to new circumstances -- the essence of the scientific endeavor. We turned challenges into opportunities. Our cancer service underwent extensive changes to reduce COVID-19 exposure among patients and our healthcare teams. In addition to some deviations from existing protocols and administration of novel therapies, including immunosuppressive treatment regimens, we also adopted technology-based as well as remote interventions and patient care activities to reduce on-site monitoring visits and in-person visits, thereby minimizing risk of viral infection and disease spread.

Regarding the future impact of COVID-19 on cancer treatment and research, we should expect further challenges ahead, especially given the threat of new waves and strains. We must all continue to adapt and respond to the ongoing pressures, pursue our clinical research, and steadfastly improve the early detection and diagnosis of cancer.

A bright beacon of hope

With the roll-out of vaccines, preventative strategies on stream, and robust research focused on viral structural, genomic surveillance, and virus-host cell interactions, I am optimistic that the biomedical community and beyond will be able to more harness and control this epidemic.

Let us return to the crucial role of research. VHIO investigators also joined the historic, scientific effort in the COVID-19 era. Together with other partners in the Cancer Core Europe Consortium (page 175), we co-authored a paper sharing our experiences and new directions implemented to adapt to the pandemic, as well as highlighting issues implicated in adjusting conventional cancer care during the first wave of the pandemic. This timely Review[3] will help guide other experts and medical institutions in treating cancer during such difficult times.

We also co-led a multi-center observational study[4] to provide a clinical portrait of the epidemic in European cancer patients .This study addressed several important questions as to whether, within a broader population of cancer patients, outcome of COVID-19 is more strongly related to patients' demographic factors including age and comorbidities over oncologic features.

Between February and April 2020, almost 900 patients with confirmed COVID-19 and cancer were identified across the 19 surveyed European centers. (This was, at the time, the largest and most geographically diverse study to document COVID infection outcomes in cancer patients.)

The results argued against a detrimental influence of active anticancer therapy in determining outcome from virus infection. This data raises questions regarding the role of COVID-19-specific therapy in the management of infected patients with cancer. To support clinical risk stratification during the pandemic, and to avoid indiscriminate deferral of anti-cancer medicines aimed at improving outcomes for these patients, the combination of tumor type and demographic factors (including gender, age, and comorbidities) should be carefully considered in the clinic.

Championing transformative translational & clinical research against cancer

Despite the unprecedented difficulties we all faced in 2020, I can proudly report that we celebrated a record-breaking year in terms of scientific output. In collaboration with numerous groups across the globe, VHIO

researchers and clinical scientists published an extraordinary 387 scientific articles in leading journals as corresponding, senior, or co-authors. Many of these were published in the world's most prestigious scientific and medical journals.

I am pleased to report that 2020 celebrated a record-breaking year for us in terms of scientific output. In collaboration with numerous groups across the globe, VHIO researchers and clinical scientists published an impressive 387 scientific articles in leading journals as corresponding, senior, or co-authors. Many of these were published in the world's most prestigious scientific and medical journals.

In addition to my pick of 'core' studies co-authored by multiple VHIO groups, highlighted in my Foreword this year (pages 6, 17), as well as a position paper on enhancing global access to cancer medicines (page 15), here is just a small sample of our studies that also deservedly made headlines in 2020:

Advancing insights into predictive biomarkers of response & acquired resistance to targeted therapy against HER2-negative metastatic breast cancer

Research led by Violeta Serra, Principal Investigator of our Experimental Therapeutics Group (page 70), sought to identify response biomarkers and unmask mechanisms of resistance to capivasertib, an AKT inhibitor showing promising activity in combination with chemotherapy against triple-negative metastatic cancer harboring P13/AKT-pathway alterations, and estrogen receptor positive breast cancer.

This multi-center study assessed genetic and proteomic markers in 28 HER2-negative patient-derived xenografts (PDX), and in patient samples, and correlated capivasertib sensitivity as a single agent and in combination with chemotherapy, paclitaxel. In so doing, this study[5] provides additional preclinical insights into predictive biomarkers of response and acquired resistance to this therapy against HER2-negative metastatic breast cancer, toward the more precise selection of patients who would most likely benefit from this therapy..

Violeta Serra, Principal Investigator of VHIO's Experimental Therapeutics Group.

Cerebrospinal fluid as liquid biopsy for the precise characterization & policing of medulloblastoma

Building on previous research led by Joan Seoane, Principal Investigator of our Gene Expression & Cancer Group, and an ICREA Research Professor, findings from a proof-of-concept study[6], show that the analysis of cerebrospinal fluid (CSF) circulating tumor DNA (ctDNA), allows for the more precise characterization, molecular diagnosis (including subtyping and risk stratification), and real time tracking of medulloblastoma– the most prevalent malignant brain tumor in childhood.

Not only does circulating tumor DNA from cerebrospinal fluid reveal genomic alterations during disease evolution -even prior to surgery- to more precisely guide treatment decision making, this approach translates in less invasive sampling, better identification and characterization of disease relapse.

In short, cerebrospinal fluid as liquid biopsy, pioneered by Joan, enables an earlier and more accurate molecular diagnosis, closer monitoring of patients, and provides crucial data on minimal residual disease tumor evolution and disease at relapse. Larger cohort studies are now warranted to bring cerebrospinal fluid as liquid biopsy closer to the clinic and deliver on the promise of precision medicine for the treatment of this tumor type.

Joan Seoane, Principal Investigator of VHIO's Gene Expression & Cancer Group, and an ICREA Research Professor.

Practice-changing data in HER2+ breast cancer

First authored by Cristina Saura, Principal Investigator of our Breast Cancer & Melanoma Group (page 90), results reported from the multi-center phase III NALA study[7] provide a new, more effective treatment strategy for patients with metastatic HER2-positive breast cancer, which is generally more aggressive than other types of breast cancer.

This breakthrough study enrolled over 600 patients across the participating sites who had received two or more prior anti-HER2 based regiments in the metastatic setting. The investigators demonstrated that treatment combining neratinib plus capecitabine, significantly improved disease-free survival, compared with therapy with lapatinib plus capecitabine. More specifically, they reported that the risk of disease progression

can be reduced by 24% in this particular patient population.

On the basis of these results, in early 2020 the Food and Drug Administration (FDA) approved neratinib in combination with capecitabine for adult patients with advanced or metastatic HER2-positive breast cancer who have previously received two or more previous HER2-directed therapies in the metastatic setting. Notably, neratinib was granted FDA Fast Track designation.

Cristina Saura, Principal Investigator of our Breast Cancer & Melanoma Group.

KEYNOTE -177: the promise of pembrolizumab as monotherapy against MSI-H-dMMR Advanced Colorectal Cancer

As a leading cause of cancer death worldwide, colorectal cancer (CRC) is the third most-common cancer globally. The mismatch repair of microsatellite-instability- high (MSI-H) pathway, a major driver of this tumor type, can be found in around 15% of cases. This discovery has not only provided precious insights into the diversity of CRC, but also calls for a more personalized approach for the optimal treatment of these patients.

Building on the interim analysis of the phase III KEYNOTE-177 trial, showing that pembrolizumab as monotherapy without chemotherapy is both more effective and less toxic as first-line treatment for patients with MSI-H or mismatch repair–deficient (dMMR) CRC, subsequent data[8] from this phase III open-label trial, led by Thierry André, Sorbonne Université and Hôpital Saint Antoine, Paris (France) , not only represents important progress in biomarker-driven approaches to more effectively target this disease, but also highlights the promise of immunotherapy in this patient population.

Co-first authored by researchers including VHIO's Elena Élez, Medical Oncologist and Clinical Investigator of our Gastrointestinal & Endocrine Group (page 96) that I co-direct alongside Teresa Macarulla, the KEYNOTE-177 Investigators showed that pembrolizumab led to significantly longer progression-free survival than chemotherapy when received as first-line therapy for MSI-H-dMMR metastatic colorectal cancer, with fewer treatment-related adverse events.

KEYNOTE-177 demonstrates the value of MSI-H status in more precisely guiding the treatment of our patients and supports how a deeper understanding of the molecular makeup of these tumors are enabling researchers to advance personalized medicine as well develop more potent immune-based strategies against metastatic CRC.

As a KEYNOTE-177 Investigator, I was invited to comment on the relevance of this potentially practice-changing study in a recently published Research Highlight[9].

VHIO's Elena Élez, Medical Oncologist and Clinical Investigator of our Gastrointestinal & Endocrine Tumors Group (page 96), co-directed by Josep Tabernero and Teresa Macarulla.

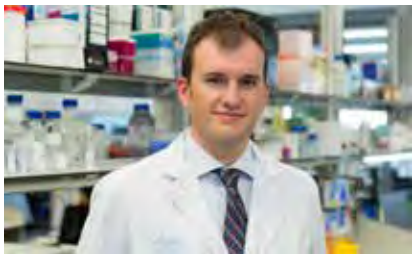
Gene-targeted olaparib delivers powerful blows against BRCA1/2 mutated prostate cancer

First authored by Joaquin Mateo, Principal Investigator of VHIO's Prostate Cancer Translational Research Group (page 78), results from the investigator-initiated TOPARP-B multi-center phase II trial[10] confirm the anti-tumor activity of single agent PARP inhibitor, olaparib, against metastatic castration-resistant prostate cancer (mCRPC).

Led by Corresponding Author Johann de Bono, Institute of Cancer Research – Royal Marsden NHS Foundation Trust, London (UK), the B-half of this academic study drew on the results reported from TOPARP-A, where the association between DNA repair defects and response to olaparib in 49 molecularly unselected patients was first described. Designed as an open-label single arm study, the second in this two part adaptive trial assessed the efficacy of treating mCRPC patients with DNA-damage repair (DDR) alterations, who had previously received chemotherapy and were no longer responding to standard treatments.

Investigating different doses of olaparib and correlating several genomic aberrations and anti-tumor activity, the researchers also confirmed the anti-tumor activity of this agent against advanced prostate cancer with defective DNA repair secondary to either germline or somatic gene inactivation. They found that overall, 47% of patients with these DNA repair defects responded to olaparib, putting the brakes on disease progression for an average of 5.5 months. The most common defects were BRCA mutations, although various others were also identified in other genes including PALB2 and ATM, among others.

Importantly, those men with BRCA1/2 mutated disease responded the best, with 80% responding and 40% free of cancer progression for over a year. The high and durable responses observed in this subpopulation of patients with mCRPC support the implementation of genomic stratification of metastatic castration-resistant prostate cancer in clinical practice based on tumor sequencing. Based on the findings, this gene-targeted approach could help guide treatment decisions as well as match more effective therapies to the molecular make up of individual patients' tumors.



Joaquin Mateo, Principal Investigator of VHIO's Prostate Cancer Translational Research Group.

Immune-based therapy promises a new therapeutic avenue for patients with advanced or recurrent endometrial cancer

Preliminary results[11] from the multi-center, non-randomized GARNET phase I study report promise of a novel anti PD-1 therapy, dostarlimab, for the more effective treatment of patients with recurrent or advanced mismatch repair-deficient endometrial cancer; representing 30% of patients suffering from this tumor type.

The study investigators, led by Ana Oaknin, Principal Investigator of VHIO's Gynecological Malignancies Group (page 100), seek to improve clinical outcomes for this patient population who have a poor prognosis, and for whom there is no effective standard of care once their disease progresses on treatment with chemotherapy. Specifically, the phase I GARNET trial enrolled 104 patients with recurrent or advanced mismatch repair-deficient endometrial cancer, and was designed to respond to an unmet clinical need. Namely, to improve outcomes for this sub-population of patients whose overall survival is approximately 12 months. Once these patients progress on prior first-line treatment with platinum-based chemotherapy, there are currently few other options available.

Initial data shows that the administration of dostarlimab as monotherapy achieves significant disease control with an objective response rate of 42%. Moving forward, the researchers will seek to complete the entire cohort of the study, with approximately 140 patients. Larger trials, including the currently enrolling randomized, placebo-controlled RUBY trial of dostarlimab in combination with carboplatin-paclitaxel in primary advanced or recurrent disease, should enable them to more deeply explore the efficacy and safety profile of this novel immunotherapy.

Ana Oaknin, Principal Investigator of our Gynecological Malignancies Group.

Novel MRI processing pipeline for the more precise evaluation of post-surgery residual tumor tissue in patients with glioblastoma

Research[12] directed by Raquel Perez-Lopez, Principal Investigator of VHIO's Radiomics Group (page 108), in collaboration with colleagues at the Bellvitge Biomedical Research Institute (IDIBELL), and Bellvitge University Hospital, Barcelona (Spain), sought to establish whether the enhancement of quantification in post-operative magnetic resonance imaging (MRI), as an indicator of residual tumor impact, can more effectively predict long and short survival in patients with glioblastoma.

Performed by MRI swiftly after surgical procedures, radiological visual assessment of remaining tumor tissue post-surgery is currently the standard of care in clinical practice. While the extent of resection is a well-known prognostic factor in glioblastomas, inter-reader reproducibility remains limited and hampers comparisons across centers and studies.

By potentiating the prognostic value of residual tumor enhancement, the researchers identified a method to facilitate the quantification of remaining tumor using a processing pipeline of multi-sequence MRI scans. They also analyzed and internally validated a multivariate prognostic model including quantified residual tumor, perfusion, radiomics and other clinical variables. Results showed that enhanced tumor thickness and radiomics have a high prognostic value and are simple to implement.

Importantly, their novel MRI processing pipeline described in this study is not only an easy and rapid approach to more accurately evaluate post-surgery residual tumor tissue, but could also be readily implemented in routine clinical practice.

Raquel Perez-Lopez, Principal Investigator of VHIO's Radiomics Group.

Ripretinib as breakthrough therapy for advanced gastrointestinal stromal tumors

The INVICTUS multi-center phase III study, directed by Jean-Yves Blay, Université Claude Bernard, Lyon (France), included 129 patients with advanced gastrointestinal stromal tumors (GIST) who had received prior treatment with 3 or more kinase inhibitors, including imatinib, with no other therapeutic options available.

Patients were randomized to receive either ripretinib, a novel therapy developed to treat GIST, or placebo. Results from this practice-changing study[13], co-authored by César Serrano, Principal Investigator of VHIO's Sarcoma Translational Research Group (page 80), demonstrated the efficacy of ripretinib in patients who had exhausted all other therapeutic options available.

Reporting several important outcomes, the investigators showed that ripretinib significantly reduced the risk of disease progression or death by up to 85%, as compared to placebo. This was translated into a higher overall survival, which reached 15.1 months compared to 6.6 months in the placebo group.

A lasting response was also achieved, and 51% of patients who received ripretinib remained progression-free at 6 months, compared to 3.2% in the placebo group.

Collectively, the results from the INVICTUS study led to the Food and Drug Administration's (FDA) approval (May 2020) of ripretinib for adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

Of note, FDA granted this application priority review, fast track, and breakthrough therapy designation. Ripretinib also received orphan drug designation.

César Serrano, Principal Investigator of VHIO's Sarcoma Translational Research Group.

Insights by VISION: tepotinib for the treatment of metastatic non-small cell lung cancer

The multi-cohort, open-label, phase II single-arm VISION study, directed by Paul K. Paik, Memorial Sloan Kettering Cancer Center (MSKCC), New York (USA), was designed to evaluate the efficacy and side effect profile of *MET* inhibitor tepotinib in patients with advanced non-small cell lung cancer (NSCLC), with a confirmed *MET* exon 14 skipping mutation.

The study primary endpoint was the objective response by independent review among patients who had undergone at least 9 months of follow-up. Response was also analyzed according to whether the presence of a *MET* exon 14 skipping mutation was detected on liquid biopsy or tissue biopsy.

The results[14], co-first authored by the study investigators including VHIO's Enriqueta Felip, Enriqueta Felip, Principal Investigator of our Thoracic Tumors & Head and Neck Cancer Group (page 110), showed that the selective *MET* inhibitor tepotinib has durable clinical activity in this patient population. This study validates *MET* exon 14 skipping mutation as a therapeutic target, and emphasizes importance of routine testing for these *MET* alterations by liquid or tissue biopsy.

On the basis of results reported in the VISION trial, in February 2021, the Food and Drug Administration (FDA) granted accelerated approval to tepotinib for adult patients with metastatic non-small cell lung cancer (NSCLC) harboring these mutations.

Enriqueta Felip, Principal Investigator of our Thoracic Tumors & Head and Neck Cancer Group.

VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch turned 10

VHIO continues to establish itself as a leading reference in advancing drug development and targeted therapies against cancer. Our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, founded in 2010, has rapidly become one of the few comprehensive facilities in Europe to translate discovery into improved outcomes for patients.

Turning 10 this year, UITM tightly connects healthcare professionals, VHIO researchers and clinical investigators, to identify 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), and focuses on the development of novel agents based on tumor molecular profile as well as the optimization of therapies using combinations of new drugs with existing ones. These efforts have already contributed to the development of several targeted agents including trastuzumab, pertuzumab, cetuximab, panitumumab, ramucirumab, trifluridine/tipiracil, gefitinib, osimertinib, ceritinib, crizotinib, loratinib and everolimus, among others.

As a direct result of the Unit's clinical studies since 2012, the FDA has approved 30 new therapies against several tumor types, which are becoming increasingly more targeted thanks to cancer discovery driven by precision medicine in oncology.

Throughout 2020 and during the COVID-19 pandemic peaks, we led 195 ongoing phase I plus Basket clinical trials. It is thanks to the dedication of Elena's team, and all our expert professionals across VHIO's Transversal Clinical Trials Core Services and Units, that despite the challenges posed by COVID-19, activity has been successfully maintained, and in some instances even surpassed, in order to respond to the needs of our patients.

I invite you to turn to page 29 for an especially extended section to mark the past decade's achievements as well as exciting developments in 2020.

Elena Garralda, Principal Investigator of our Early Clinical Drug Development Group, and Director of VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch.

The sharing of expertise & data exchange to guide clinical decision-making

We continue to extend our efforts to an increasing number of patients thanks to expanded collaborations with other centers, across borders. As an example, VHIO participates in AACR's Project GENIE: Genomics Evidence Neoplasia Information Exchange (page 29).

Catalyzing the sharing of integrated genomic and clinical datasets across multiple cancer centers, GENIE Incorporates 19 leading sites worldwide. Led by Rodrigo Dienstmann, Principal Investigator of our Oncology Data Science (ODysSey) Group (page 104), in collaboration with our Cancer Genomics Group, directed by Ana Vivancos (page 116), as well as Susana Aguilar, Project Manager of VHIO's Molecular Prescreening Program (page 140), our Institute is the only partner from Spain.

GENIE has just released its ninth data set, which contains more than 100,000 sequenced samples from over 100,000 patients. This achievement makes GENIE one of the largest fully public cancer genomic data sets released to date.

For GENIE 9.0, VHIO collaborated with data from close to 1,000 patients across several tumor types. This collective sharing and interpretation of anonymized clinical and genomic data will help inform treatment decisions in the clinic (see page 29 for more details).

Marking the launch of a web-based resource for the more precise selection of anti-cancer medicines, Cancer Core Europe's Molecular Tumor Board Portal, an Article[15] counting on the equal contribution of lead authors David Tamborero, Karolinska Institute (Sweden), and VHIO's Rodrigo Dienstmann, in collaboration with Cancer Core Europe - CCE (page 175) investigators, describes this innovative platform that provides data-rich personalized reports with comprehensive molecular data on each patient's tumor.

Not only does the portal automate data interpretation which helps to prevent errors associated with manual processing, it also facilitates systematic analysis based on clinical criteria developed by the experts. Opening secure access to the latest insights into tumor mutations of patients, it also allows for the discussion of individual cases with the clinical investigators across CCE's seven sites in a truly collaborative manner.

VHIO Rodrigo Dienstmann, Principal Investigator of our Oncology Data Science (ODysSey) Group.

Pioneering the tracking of cancer in liquid biopsies

At the preclinical and translational level, VHIO was the first academic test center to incorporate in-house BEAMING liquid biopsy RAS biomarker technology. As highlighted throughout this report, we continue to make significant progress in developing liquid biopsy technologies for more effective, less invasive monitoring of cancer in real time.

These efforts, focused on both ctDNA and tumor educated platelets (TEP), continue to advance thanks to our collaborative multidisciplinary teams in our Cancer Genomics and Molecular Oncology Groups

(pages 116-118) headed by Ana Vivancos and Paolo Nuciforo, respectively.

Celebrating another VHIO first, our Institute was the first center in Europe to incorporate Guardant Health's breakthrough liquid biopsy technology, officially announced in January 2021. This important development will enable more rapid detection of a greater number of mutations in patients' blood samples, and a deeper, more comprehensive follow up.

Ana Vivancos, Principal Investigator of our Cancer Genomics Group.

Paolo Nuciforo, Principal Investigator of VHIO's Molecular Oncology Group.

Our Molecular Prescreening Program: a jewel in VHIO's crown

Catalyzing precision medicine at VHIO, our prestigious Molecular Prescreening Program (page 140), initiated in 2010, uses emerging cancer biomarkers to optimize the selection of therapies for patients being considered for phase I clinical trials.

Representing a key driver of clinical-molecular correlative research at our Institute, this program is headed by VHIO's Rodrigo Dienstmann under the co-leadership of Ana Vivancos, Paolo Nuciforo, and Elena Garralda. The team regularly convenes to explore existing molecular tests, developed in-house, and novel biomarkers of interest for the potential inclusion in the program.

In addition, our cancer researchers and genomicists participate in weekly tumor board meetings with VHIO's medical oncologists to provide guidance on the interpretation of NGS results as well as discuss new markers for clinical testing in patients eligible for inclusion in our early phase clinical studies.

Reflective of our expertise in personalized prescreening, a 'core' paper[16] co-authored by multiple VHIO investigators across several of our groups, describes how our program has rapidly responded to the evolving landscape of molecular prescreening strategies for early clinical trials in oncology, through its dynamic model of biomarker-drug co-development.

Co-leaders of VHIO's Molecular Prescreening Program: Rodrigo Dienstmann - Oncology Data Science (ODysSey) Group, Ana Vivancos - Cancer Genomics Group, Paolo Nuciforo - Molecular Oncology Group, and Elena Garralda - Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, and Early Clinical Drug Development Group.

In order to accelerate progress in precision oncology, the researchers support clinical studies with adaptive designs to enroll patients on the basis of multi-omics enrichment criteria. They also underline the importance of larger portfolios of therapies that include immunotherapeutic and antibody-drug conjugates with recruitment guided by molecular tests, as well as international collaborations and data-sharing projects, such as VHIO's aforementioned participation in AACR's GENIE, and Cancer Core Europe.

I couldn't agree more!

Strengthening our research programs & growing teams

As our Institute goes from strength to strength, and further develop its research lines and projects based on defined strategic directions, we continue to expand our scientific faculty as well as scientific support units and teams.

In 2020, we welcomed José Fernández Navarro as Principal Investigator of our newly established Bioinformatics Support Unit (page 114). Joining our other Core Technologies (pages 112-121), José's Unit has been created to promote digital transformation, set optimal standards and best practices for the processing, analysis and visualization of omics datasets, and help to develop state-of-the-art pipelines and tools for the processing, analyses, and visualization of different omics datasets.

José Fernández Navarro, Principal Investigator of our newly established Bioinformatics Support Unit.

Headed by Gemma Sala, formerly Director of VHIO's Clinical Trials Office (page 130), VHIO's Quality & Processes Unit was established this year to further improve quality and unify

processes in clinical trials carried out at VHIO. This Unit is made up of quality, and transversal support teams including those dedicated to sample management and scheduling.

Gemma Sala, Director of VHIO's Quality & Pocesses Unit.

Accelerating progress through team science, VHIO's multidisciplinary teams, coordinated by our Scientific Coordination Area directed by Alejandro Piris (page 144), also work together as established Task Forces that have been created 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, oncologists, pathologists, other MD disciplines, clinical research nurses, data curators as well as study coordinators, and project managers, among others.

Now covering breast, colorectal, gastroesophageal, kidney, melanoma, neuroendocrine/ rectal, pancreatic, prostate, and gynecological cancers, as well as onco-imaging, our expanding number of dedicated Task Forces regularly convene to synergize efforts, boost collaborations among groups and between specialists, and continuously revise patients and samples' circuits and ethics toward advancing cancer science and precision medicine.

Alejandro Piris, Head of VHIO's Scientific Coordination Area.

Multi-center consortia & cross border collaborations of excellence

VHIO is dedicated to forming, fostering and developing strong, multi-center partnerships that combine the necessary expertise and resources to more rapidly advance cancer discovery.

In addition to our leadership of -- and participation in -- several existing international consortia and alliances (see pages 175-181), 2020 celebrated the launch of several new collaborative opportunities as follows:

DART

The EU-funded Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART), coordinated by VHIO (see page 179), is carried out in collaboration with other leading experts from within Cancer Core Europe Consortium (page 175). 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, CCE-DART will further enhance 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.

EURAMED ROCC-N-ROLL
European Medical Application and Radiation Protection Concept

The main objective of the EU-supported EURAMED rocc-n-roll (page 179) project 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 our Institute. Taking the lead on radiation application in oncological diseases, VHIO will work with other experts in other settings including neurovascular as well as cardiovascular diseases, and explore relevant clinical scenarios, as well as provide patients' perspectives.

VHIO researchers will analyze the needs of research in radiation application and corresponding radiation protection in oncology by identifying current gaps and future opportunities.

Interreg POCTEFA PROTEOblood

Coordinated by investigators at 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 leukemia

and lymphoma: acute myeloid leukemia (AML) and diffuse large b-cell lymphoma (CLBCL) in the POCTEFA region (Spain-France-Andorra).

Comprised of six other partners, including VHIO, the investigators will 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 that will then be validated through xenoinjerts.

The ERA-PerMed-supported RAD51predict Consortium (page 180), coordinated by VHIO, centers on patient stratification based on DNA repair functionality for precision cancer medicine. Consisting of five partners along with six other collaborators, this project seeks to further investigate the RAD51 in vitro diagnostic test to predict those patients who would be most likely to benefit from therapy with PARP inhibitors (PARPi).

Aimed at enabling the more precise and faster identification of patients with breastand this test has been developed to better guide the stratification of patients to clinical trials to evaluate the efficacy of PARPi across additional tumor types including prostate and endometrial cancers.

Global cancer incidence & mortality on the rise

As this report goes to press, GLOBOCAN published its estimates of cancer incidence and mortality worldwide[17]Global cancer statistics produced by the International Agency for Research on Cancer estimated 19.3 million new cancer cases and almost 10 million cancer deaths in 2020. This article also reports that the global cancer burden is expected to be 28.4 million cases in 2040, a 47% rise from 2020.

Added to these alarming statistics, global access to cancer medicines represents a critical international issue, particularly in resource-poor settings and emerging economies. Even some of the relatively inexpensive drugs included in the World Health Organization's Essential Medicines List are actually in chronically short supply in many countries and regions around the world. Collectively, we must steadfastly seek to resolve this stalled and appalling state of affairs.

The recently published position paper[18], *Enhanced global access to cancer medicines*, first authored by Javier Cortés, and co-authored by Joaquín Arribas (page 15) and myself, along with key opinion leaders in oncology, explores various preventers of access to cancer medicines, with particular focus on essential cancer medicines.

Joaquín Arribas, Prinicipal Investigator of our Growth Factors Group, and an ICREA Research Professor.

Javier Cortés, a translational investigator at VHIO.

The authors propose a road map of potential strategies to more effectively tackle major issues including limited access to timely diagnosis, to affordable, effective treatment, and to high-quality cancer care. Suggested directions include universal health coverage for essential cancer medicines, fairer methods for pricing cancer drugs, reducing development costs, optimizing regulation, improving reliability in the global supply chain, and improving schedules for cancer therapy.

Glaringly, there is much work to be done.

It is clear that while progress in advancing personalized cancer research, treatment and care should be applauded, we cannot accept complacency. As cancer researchers, clinical investigators and medical oncologists, we are privileged to help promote and guide more effective prevention strategies as well as national cancer planning. Working alongside all stakeholders in oncology, I believe that we can act together to alleviate the current and future global burden of cancer, which now weighs heavier than ever before.

An estimated 30-50% of all cancers can be prevented. Cancer control clearly begins with disease prevention through educational programs, well informed strategies, targeted interventions, as well as policies and planning tailored Nationally and regionally.

Aimed at strengthening cancer control and prevention, the European Society for Medical Oncology (ESMO) and World Health Organization's International Agency for Cancer Research on Cancer (IACR), co-launched the World Cancer Report's e-learning platform in 2020.

This resource, co-developed by ESMO and IACR, promotes and

enhances cancer prevention strategies, policies and actions globally, by incorporating especially created materials as well as learning opportunities and events for scientists, policy makers, students, early career researchers and citizens across borders.

Public engagement and outreach programs aimed at increasing our citizens' awareness about the importance of cancer research as well as disease prevention, also play a central role in more effective cancer control.

At VHIO, we support and organize activities to increase public interest in cancer research and promote the important advances reported by our scientists and clinical investigators (see pages 47-50).

These efforts are aimed at patients, youngsters and non-specialized adult 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.

We will continue to identify, lead and participate in all these precious initiatives and launch new ones based on identified opportunities.

The passing of a visionary in cancer research and clinical oncology: José Baselga, 1959-2021

José Baselga, MD, PhD: a global trailblazer in oncology, pioneer of translational cancer research, and VHIO's Founding Director.

The international scientific cancer community, along with all other stakeholders in oncology, continues to mourn the passing of a visionary scientific leader and trailblazer, José Baselga.

José, who passed away at the age of 61 on 21 March, 2021, was an icon in medical oncology, a pioneer of translational cancer research, who made essential contributions to improving outcomes for cancer patients worldwide. By integrating patient care within a multidisciplinary program connecting basic, clinical and translational science, where optimal patient care is conciliated with innovative translational research, he spearhead efforts to rapidly transform cancer discovery into clinical benefits for patients.

This unique research model emboldened him to create the Vall d'Hebron Institute of Oncology (VHIO), which he founded in 2006 as its first Director. 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, which I, as VHIO's Director, passionately pursue alongside our multidisciplinary teams.

While José's passing represents an unfillable void in cancer research, treatment and care, he leaves a tremendous legacy for the scientific community. This gift will continue to inspire present and future generations of cancer researchers and clinical investigators.

We'll miss him enormously. Please do carry on reading my personal tribute to José which leads off this year's report, pages 18-21.

The Last Word

While 2020 has been a year unlike any other, we will continue to transform the many challenges in cancer research and clinical oncology into opportunities for those who matter most; our cherished patients.

As VHIO's Director, I am honored and privileged to lead and work with our many research talents and dedicated healthcare professionals in oncology. Without our multidisciplinary and translational teams, cross-border collaborations and partnerships, and the passion and drive that unite us all in our ambition to solve cancer sooner, our Institute would cease to exist.

That same sustained devotion and belief is also shared in equal measure by our wonderful institutional supporters – the *Generalitat de Catalunya*, *Fundació Privada CELLEX*, *Fundación FERO*, *"la Caixa" Foundation*, and the *Fundación BBVA* (pages 23-27), as well as VHIO's many other funding entities, agencies, supporters, and individuals (pages 172-174). They all share the same intense desire as we do: to reduce the devastating burden that this disease has on society.

I ended last year's report Foreword by expressing my belief that we will overcome this global pandemic and progress to even bigger success in our efforts to combat cancer. Illustrated by the many research highlights and developments chaptered in the pages that follow, I am confident that we will continue to do so.

We can, and will, do even better.

References

1. Upadhaya S, Xin Yu J, Oliva C, Hooton M, Hodge J, Hubbard-Lucey VM. Impact of COVID-19 on oncology clinical trials. *Nat. Rev. Drug Discov.* 19, 376-377 (2020).
2. Bakouny Z, Hawley JE, Choueiri TK, Peters S, Rini BI, Warner JL, Painter CA. COVID-19 and Cancer: Current Challenges and Perspectives. *Cancer Cell.* 2020 Nov 9;38(5):629-646.
3. van de Haar J, Hoes LR, Coles CE, Seamon K, Fröhling S, Jäger D, Valenza F, de Braud F, De Petris L, Bergh J, Ernberg I, Besse B, Barlesi F, Garralda E, Piris-Giménez A, Baumann M, Apolone G, Soria JC, Tabernero J, Caldas C, Voest EE. Caring for patients with cancer in the COVID-19 era. *Nat Med.* 2020 May;26(5):665-671.
4. Pinato DJ, Zambelli A, Aguilar-Company J, Bower M, Sng C, Salazar R, Bertuzzi A, Brunet J, Mesia R, Segui E, Biello F, Generali D, Grisanti S, Rizzo G, Libertini M, Maconi A, Harbeck N, Vincenzi B, Bertulli R, Ottaviani D, Carbo A, Bruna R, Benafif S, Marrari A, Wuerstlein R, Carmona-Garcia MC, Chopra N, Tondini C, Mirallas O, Tovazzi V, Betti M, Provenzano S, Fotia V, Cruz CA, Dalla Pria A, D'Avanzo F, Evans JS, Saoudi-Gonzalez N, Felip E, Galazi M, Garcia-Fructuoso I, Lee AJX, Newsom-Davis T, Patriarca A, Garcia-Illescas D, Reyes R, Dileo P, Sharkey R, Wong YNS, Ferrante D, Marco-Hernandez J, Sureda A, Maluquer C, Ruiz-Camps I, Gaidano G, Rimassa L, Chiudinelli L, Izuzquiza M, Cabirta A, Franchi M, Santoro A, Prat A, Tabernero J, Gennari A. Clinical portrait of the SARS-CoV-2 epidemic in European cancer patients. *Cancer Discov.* 2020 Jul 31;10(10):1465–74
5. Gris-Oliver A, Palafox M, Monserrat L, Brasó-Maristany F, Òdena A, Sánchez-Guixé M, Ibrahim YH, Villacampa G, Grueso J, Parés M, Guzmán M, Rodríguez O, Bruna A, Hirst CS, Barnicle A, de Bruin EC, Reddy A, Schiavon G, Arribas J, Mills GB, Caldas C, Dienstmann R, Prat A, Nuciforo P, Razavi P, Scaltriti M, Turner NC, Saura C, Davies BR, Oliveira M, Serra V. Genetic Alterations in the PI3K/AKT Pathway and Baseline AKT Activity Define AKT Inhibitor Sensitivity in Breast Cancer Patient-derived Xenografts. *Clin Cancer Res.* 2020 Jul 15;26(14):3720-3731.
6. Escudero L, Llort A, Arias A, Diaz-Navarro A, Martínez-Ricarte F, Rubio-Perez C, Mayor R, Caratù G, Martínez-Sáez E, Vázquez-Méndez É, Lesende-Rodríguez I, Hladun R, Gros L, Ramón Y Cajal S, Poca MA, Puente XS, Sahuquillo J, Gallego S, Seoane J. Circulating tumour DNA from the cerebrospinal fluid allows the characterisation and monitoring of medulloblastoma. *Nat Commun.* 2020 Oct 27;11(1):5376.
7. Saura C, Oliveira M, Feng YH, Dai MS, Chen SW, Hurvitz SA, Kim SB, Moy B, Delaloge S, Gradishar W, Masuda N, Palacova M, Trudeau ME, Mattson J, Yap YS, Hou MF, De Laurentiis M, Yeh YM, Chang HT, Yau T, Wildiers H, Haley B, Fagnani D, Lu YS, Crown J, Lin J, Takahashi M, Takano T, Yamaguchi M, Fujii T, Yao B, Bebchuk J, Keyvanjah K, Bryce R, Brufsky A; NALA Investigators. Neratinib Plus Capecitabine Versus Lapatinib Plus Capecitabine in HER2-Positive Metastatic Breast Cancer Previously Treated With ≥ 2 HER2-Directed Regimens: Phase III NALA Trial. *J Clin Oncol.* 2020 Sep 20;38(27):3138-3149.
8. André T, Shiu KK, Kim TW, Jensen BV, Jensen LH, Punt C, Smith D, Garcia-Carbonero R, Benavides M, Gibbs P, de la Fouchardiere C, Rivera F, Elez E, Bendell J, Le DT, Yoshino T, Van Cutsem E, Yang P, Farooqui MZH, Marinello P, Diaz LA Jr; KEYNOTE-177 Investigators. Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer. *N Engl J Med.* 2020 Dec 3;383(23):2207-2218.
9. Romero, D. New first-line therapy for dMMR/MSI-H CRC. *Nat Rev Clin Oncol.* 18, 63 (2021).
10. Mateo J, Porta N, Bianchini D, McGovern U, Elliott T, Jones R, Syndikus I, Ralph C, Jain S, Varughese M, Parikh O, Crabb S, Robinson A, McLaren D, Birtle A, Tanguay J, Miranda S, Figueiredo I, Seed G, Bertan C, Flohr P, Ebbs B, Rescigno P, Fowler G, Ferreira A, Riisnaes R, Pereira R, Curcean A, Chandler R, Clarke M, Gurel B, Crespo M, Nava Rodrigues D, Sandhu S, Espinasse A, Chatfield P, Tunariu N, Yuan W, Hall E, Carreira S, de Bono JS. Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial. *Lancet Oncol.* 2020 Jan;21(1):162-174.
11. Oaknin A, Tinker AV, Gilbert L, Samouëlian V, Mathews C, Brown J, Barretina-Ginesta MP, Moreno V, Gravina A, Abdeddaim C, Banerjee S, Guo W, Danaee H, Im E, Sabatier R. Clinical Activity and Safety of the Anti-Programmed Death 1 Monoclonal Antibody Dostarlimab for Patients With Recurrent or Advanced Mismatch Repair-Deficient Endometrial Cancer: A Nonrandomized Phase 1 Clinical Trial. *JAMA Oncol.* 2020 Oct 1;6(11):1–7.
12. Garcia-Ruiz A, Naval-Baudin P, Ligero M, Pons-Escoda A, Bruna J, Plans G, Calvo N, Cos M, Majós C, Perez-Lopez R. Precise enhancement quantification in post-operative MRI as an indicator of residual tumor impact is associated with survival in patients with glioblastoma. *Sci Rep.* 2021 Jan 12;11(1):695.
13. Blay JY, Serrano C, Heinrich MC, Zalcberg J, Bauer S, Gelderblom H, Schöffski P, Jones RL, Attia S, D'Amato G, Chi P, Reichardt P, Meade J, Shi K, Ruiz-Soto R, George S, von Mehren M. Ripretinib in patients with advanced gastrointestinal stromal tumours (INVICTUS): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2020 Jul;21(7):923-934.
14. Paik PK, Felip E, Veillon R, Sakai H, Cortot AB, Garassino MC, Mazieres J, Viteri S, Senellart H, Van Meerbeeck J, Raskin J, Reinmuth N, Conte P, Kowalski D, Cho BC, Patel JD, Horn L, Griesinger F, Han JY, Kim YC, Chang GC, Tsai CL, Yang JC, Chen YM, Smit EF, van der Wekken AJ, Kato T, Juraeva D, Stroh C, Bruns R, Straub J, Johne A, Scheele J, Heymach JV, Le X. Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. *N Engl J Med.* 2020 Sep 3;383(10):931-943.
15. Tamborero D, Dienstmann R, Rachid MH, Boekel J, Baird R, Braña I, De Petris L, Yachnin J, Massard C, Opdam FL, Schlenk R, Vernieri C, Garralda E, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium, Calvo F, Fröhling S, Eggermont A, Apolone G, Voest EE, Caldas C, Tabernero J, Ernberg I, Rodon J, Lehtiö J. Support systems to guide clinical decision-making in precision oncology: The Cancer Core Europe Molecular Tumor Board Portal. *Nat Med.* 2020 Jul;26(7):992-994.
16. Dienstmann R, Garralda E, Aguilar S, Sala G, Viaplana C, Ruiz-Pace F, González-Zorelle J, Grazia LoGiacco D, Ogbah Z, Ramos Masdeu L, Mancuso F, Fasani R, Jimenez J, Martinez P, Oaknin A, Saura C, Oliveira M, Balmaña J, Carles J, Macarulla T, Elez E, Alsina M, Braña I, Felip E, Tabernero J, Rodon J, Nuciforo P, Vivancos A. Evolving Landscape of Molecular Prescreening Strategies for Oncology Early Clinical Trials. *JCO Precis Oncol.* 2020 May 14;4:PO.19.00398.
17. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021 Feb 4. doi: 10.3322/caac.21660. Epub ahead of print.
18. Cortes J, Perez-García JM, Llombart-Cussac A, Curigliano G, El Saghir NS, Cardoso F, Barrios CH, Wagle S, Roman J, Harbeck N, Eniu A, Kaufman PA, Tabernero J, García-Estévez L, Schmid P, Arribas J. Enhancing global access to cancer medicines. *CA Cancer J Clin.* 2020 Mar;70(2):105-124.

JOSÉ "PEPE" BASELGA, MD, PHD: IN MEMORIAM (1959-2021)

A PERSONAL TRIBUTE* BY VHIO'S DIRECTOR, JOSEP TABERNERO

José Baselga, MD, PhD: a visionary leader in translational science and precision oncology, and VHIO's Founding Director.

José Baselga, a Barcelona-born and internationally acclaimed medical oncologist, very sadly passed away at the age of 61 on 21 March, 2021. Sending shock waves across our entire cancer community and beyond, he died from Creutzfeldt-Jakob disease (CJD), a rapidly progressing, neurodegenerative disease.

With his death, a guiding light in oncology and indeed society has been extinguished. We have lost a visionary, innovator, and eminent trailblazer in translational cancer research and precision medicine. José was an extraordinary person, impassioned by everything he did, whose incomparable devotion to his profession, patients, research and clinical colleagues, and mentorship were at his very core -- part of his fabric, his DNA. As was his love for his family and close friends whom he absolutely cherished.

I first met José Baselga when I was a student completing my finals in Medicine and he was a resident in Internal Medicine at the Vall d'Hebron University Hospital (HUVH), here in Barcelona. From that very first moment, I felt his passion for medical research and his desire to understand the biological and molecular makeup of disease (long before the fundamental insights into the human genome came to light). I believe that this inherent curiosity and belief in exploring unchartered ground set him apart from many other research talents of his epoque. A binding thread in the tapestry of his illustrious career.

Back in 1990: at MSKCC, where José completed his oncology training under the mentorship of John Mendelsohn and Larry Norton, for his laboratory investigations and clinical explorations, respectively.

He subsequently left for the United States to complete his residency in Internal Medicine, and later, in Medical Oncology at the prestigious Memorial Sloan Kettering Cancer Center (MSKCC) in New York, where he was appointed as an Associate Physician. In 1996, José returned to Barcelona to create a multidisciplinary Oncology Department at HUVH, integrating and connecting all professionals caring for cancer patients, and at the same time, implementing his new vision for cancer research.

He swiftly set up a combined preclinical, clinical and translational program in oncology with one clear objective: to accelerate cancer discovery and apply the insights generated at the bench and transform them into clinical benefits for patients at the bedside as quickly as possible.

José Baselga, VHIO's founder and first director, alongside our Director, Josep Tabernero: working in tandem to deliver on personalized medicine in oncology by championing a purely translational, multidisciplinary cancer research model.

I was very fortunate to join José's team back in 1997. Emboldened by the successes of his purely translational and multidisciplinary approach to research, he created the Vall d'Hebron Institute of Oncology (VHIO), as our Institute's founder and first director. Undoubtedly, his dual set up of the Oncology Department at HUVH and VHIO transformed patient care and stimulated cutting-edge cancer research. His leadership put Barcelona and Vall d'Hebron on the map of the best of the best centers in oncological research, and among the most prestigious centers across the globe.

2008: José with his clinical breast cancer research team in front of the HUVH-VHIO Breast Cancer Center.

His vision, coupled with his steadfast determination, succeeded in marrying excellence in clinical practice driven by multidisciplinary teams in oncology, with applied research. So much so, his inspirational model was rapidly adopted by many other hospitals in Spain and around the world.

Throughout his career, so many individuals, bodies, consortia of excellence, and scientific societies rightly sought -- and counted on -- his scientific expertise, leadership and mentorship. To mention just two examples, José served as President of the European Society for Medical Oncology – ESMO (2008-2009), and the American Association for Cancer Research – AACR (2015-2016). For both, he made fundamental changes by turning challenges into opportunities to help overturn obstacles hampering efforts in more effectively combating cancer, with the interest of patients at the heart of every action.

José was appointed to direct the Massachusetts General Hospital Cancer Center in 2010, and then joined MSKCC in 2013 as its Physician-in-Chief and Chief Medical Officer until 2018. Over the past two years, he served as AstraZeneca's Executive Vice President Oncology R&D, and member of its Senior Executive Committee.

In every leadership position that José occupied with equal vigor, zeal and driving spirit, his passion for the constant pursuit of knowledge, coupled with his ability to set up cohesive multidisciplinary teams of professionals, was breathtaking. His compassion and care for cancer patients was also incredible. He simply gave, unconditionally. With a second-to-none bedside manner and natural ability to communicate on a very human level, he gave patients the courage to fight their disease.

With a natural charisma and charm, José also knew how to get the right people, at the right time, together in the same room. Countless consortia of excellence, powerful partnerships, and groundbreaking results have been driven by his extraordinary ability to work together, across borders, in order to advance the oncology field at a rate of knots. He could not accept, or tolerate, time wasting. Sometimes, unlikely alliances at the time, were born to go on to achieve exceptional results.

José was also hugely dedicated to building great things, the careers of promising young talents in cancer research and oncology. This was apparent from very early on.

At the national level, he founded the FERO Foundation, one of VHIO's cherished patrons, to support translational research of excellence. He also nurtured and forged the essential collaborations with our other patrons and institutional supporters; Generalitat de Catalunya, Fundación Privada CELLEX, "la Caixa" Foundation, and the Fundación BBVA. Without which, VHIO would cease to exist -as well as its Units, leading Institutional Programs, as well as many facilities across Vall d'Hebron- would simply not exist**.

My relationship with José was always exceptional -- as my mentor, and as a much-loved friend. The same rigor and tenacity that he demanded from himself, he expected (respectfully) from others. He could be demanding at times, but this was simply a manifestation of his heartfelt determination to speed cancer research, treatment and patient care. His enthusiasm shone through – always, in everything he did. He believed that collectively we can practically eradicate cancer as long we join together with shared determination and collaborative spirit.

I consider myself hugely privileged to have witnessed first-hand just how José's remarkable vision in advancing precision medicine in oncology has spurred the development and approval of more potent, personalized therapies that have benefited numerous cancer patients . Many of those medicines might not have made it through the drug development and clinical trial processes without José's steady hand at the wheel. One of the most illustrative examples is perhaps trastuzumab (Herceptin), which has helped save countless lives of patients suffering from breast cancer.

His long-standing research interests centered on the development of targeted therapies against breast cancer and studying strategies to overcome mechanisms of resistance. Among others, José conducted the initial clinical trials with the monoclonal antibodies cetuximab and trastuzumab and led the clinical development of several new agents including pertuzumab, everolimus and PI3K inhibitors. His main focus in the laboratory and in the clinic surrounded novel anti-HER2 agents, and the identification of mechanisms of resistance to anti-HER2 agents and therapeutic approaches to target the PI3K pathway. He also directed several neo-adjuvant trials in breast cancer and was at the forefront of developing biomarker-based early and translational clinical trials.

In 2017: the European Society for Medical Oncology (ESMO) honored José Baselga with the ESMO Lifetime Achievement Award for his crucial role in breast cancer drug development, as well as his pivotal laboratory and clinical studies that subsequently the approval of trastuzumab, pertuzumab and everolimus, among many others. Photo courtesy of ESMO.

José's crucial role in breast cancer drug development in particular has been recognized through numerous prestigious awards and prizes. These accolades include the AACR Rosenthal Family Foundation Award, Fellow of the AACR Academy, the Gold Medal, Queen Sofia Spanish Institute, New York; Joseph B. Martin Award, Massachusetts General Hospital, Boston; Elected Member, National Academy of Medicine; XXVIII Catalonia International Prize; Dr. Trueta Medal; Rey Jaime I Prize; ESMO Award, and the ESMO Lifetime Achievement Award.

José, on behalf of cancer patients and all cancer professionals who had the honor to know and work with you, I thank you for the incredible legacy that you have left us. We also salute you for your enthusiasm and passion, each and every day. We strive to honor your legacy by applying the same dedication and fight in beating cancer.

You will never be forgotten.

* Excerpts from this personal tribute by Josep Tabernero, have sinced been used as invited content by leading journals including *Cancer Discovery* and *ESMO Open*.

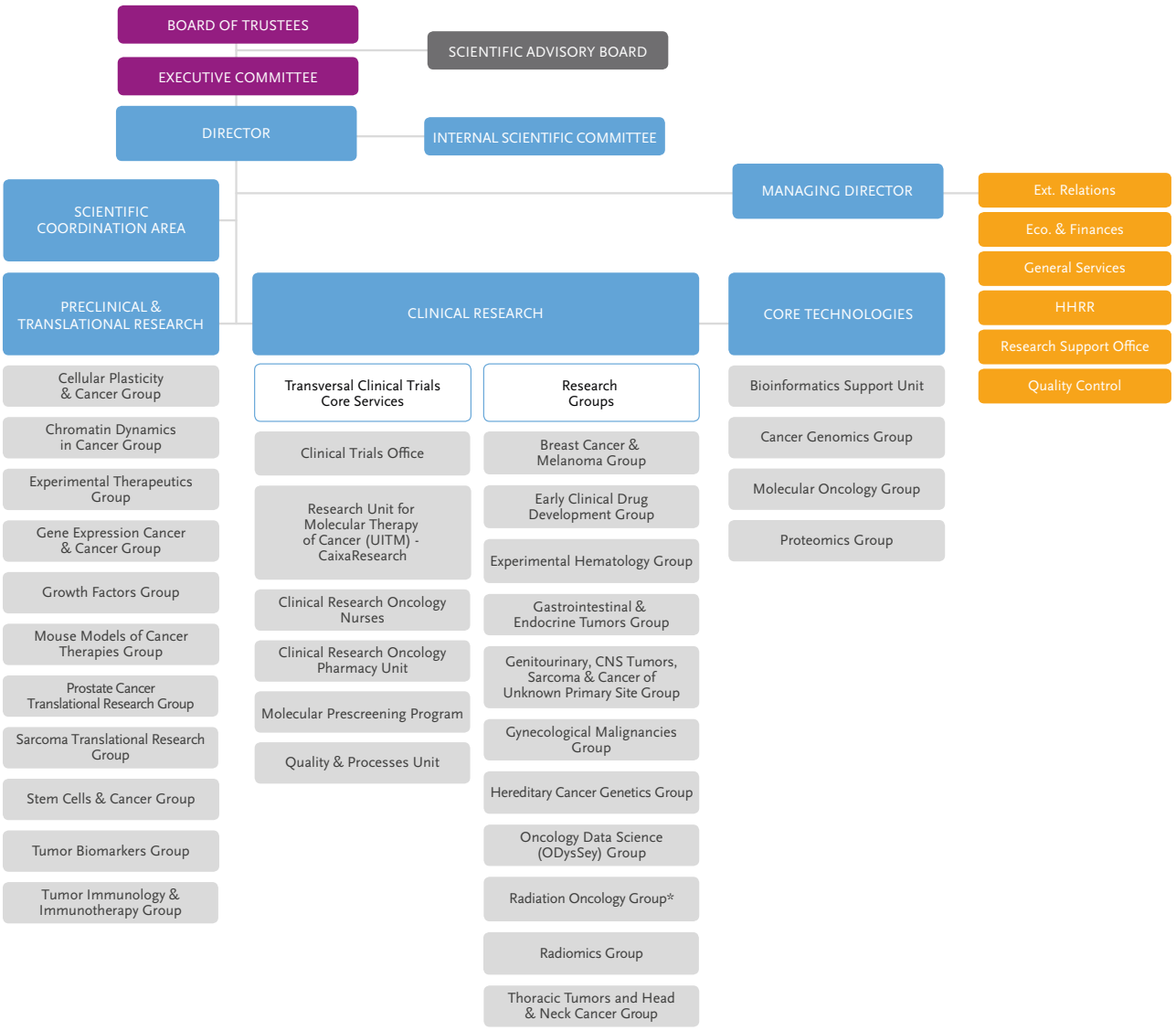
** For further information please refer to pages 23-27.

WHO WE ARE AND WHAT WE DO

VHIO's Organigram 2020

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

Our optimal organizational structure allows VHIO talents to continue to both anticipate and tackle the many unresolved questions in ultimately outsmarting the multifaceted, heterogeneous and complex disease that is cancer:



VHIO IN 2020: A YEAR OF CHALLENGES, OPPORTUNITIES AND HOPE

Our Director, Josep Tabernero: welcoming all stakeholders in oncology to discover more about who we are, what we do, and how we do it. In front of our CELLEX building – the home and heart of the Vall d'Hebron Institute of Oncology (VHIO).

Under the leadership of Josep Tabernero, the Vall d'Hebron Institute of Oncology (VHIO), created in 2006, has established itself as a comprehensive cancer center of proven excellence internationally.

It is thanks to the devotion of our Principal Investigators and their teams, coupled with VHIO's optimal organizational structure based on a purely multidisciplinary and translational model that VHIO talents continue to anticipate and tackle the many unresolved questions in combatting this multifaceted and heterogeneous disease.

That said, our Institute would cease to exist without the generous support it receives from its Institutional Supporters, public funding, private institutions, companies, and individuals, as well as International and National Competitive Grants (see pages 172-181).

Special mention here highlights the tremendous belief and backing that we continue to receive from our dedicated patrons: the *Generalitat de Catalunya, Fundació Privada CELLEX, FERO Fundación de Investigación Oncológica,*"la Caixa" Foundation, and the *Fundación BBVA.*

Just some of their respective, major contributions include the following:

Generalitat de Catalunya

Our public patron, the Government of Catalonia (*Generalitat de Catalunya*) – together with the Vall d'Hebron University Hospital (HUVH) – represented by its Departments of Health (*Departament de Salut*), and Industry and Knowledge (*Departament de Empresa I Coneixement*), 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 throughout our first decade and now, beyond, with the Catalan Minister of Health as the President of our Board of Trustees.

At 'home' 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 HUVH, the Vall d'Hebron Barcelona Hospital Campus, and the rest of the Catalan Public Health System.

The Catalan Department of Health has played an essential role in integrating VHIO's research activity into the Catalan Health System, through the

Catalan Institute of Health (ICS), 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 CERCA Institute of Research Centers of Catalonia (*Institució CERCA–Centres de Recerca de Catalunya*), 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*.

As an example in 2020, Joan Seoane, Principal Investigator of VHIO's Gene Expression & Cancer Group, received funding from the call, *Research projects and innovation for the prevention and treatment of COVID-19*, issued by its Department of Health, for his research focused on *MSC1, an anti-LIF therapeutic antibody, as a potential treatment for COVID-19*.

At the close of 2020, our Director, Josep Tabernero, was awarded as recipient of a Catalan Institute of Health (ICS) National Research Award in recognition of his illustrious career and outstanding contributions made to research against cancer. See page 38 for more information.

Fundació Privada CELLEX

It is thanks to one of our private patrons, the *Fundació Privada CELLEX* (CELLEX 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, now promotes the purely translational and multidisciplinary model for which VHIO is famed.

CELLEX Building: the home, heart and hub of translational research at VHIO.

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 VHIO chapter, our premises provided the necessary space and amenities 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 the valuable space through which to grow, the CELLEX Center has not only further enhanced collaborations and accelerated our dedicated efforts to combat cancer, it has also allowed us to expand our groups in order to pursue new emerging research areas as well as fortify our research structure.

As importantly, thanks to CELLEX, 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 enabled us to establish VHIO as a European reference in cancer modelling.

fundación fero
Investigando por un futuro sin cáncer

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

Concerning the former, the labs of 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, PI of our Chromatin Dynamics Group, and most recently, César Serrano, PI of our Sarcoma and Translational Research Group, have been able to grow their groups and advance their pioneering research lines thanks to FERO.

FERO has also contributed to the expansion of our facilities. As an example, the Foundation was a sponsor of our Breast Cancer Center *Endavant i de Cara*, along with a personal donation received from Maria Angels Sanahuja. Funding received from FERO also enables us to continue to develop the liquid biopsy of cancer and thus advance research into the more effective and less invasive tracking of disease. These investigations, spearhead by VHIO's Director, Josep Tabernero, are carried out within the scope of VHIO-FERO's Institutional Advanced Molecular Diagnostics Program (DIAMAV) – see page 122, which also fuels VHIO's Molecular Prescreening Program, page 140.

Regarding its Annual Awards for Translational Research, a total of thirteen of our research scientists 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-López, and Cristina Saura and Miriam Sansó – the second annual FERO-ghd award (2020).

More specifically, Raquel Perez-López, PI of VHIO's Radiomics Group, was awarded for the project entitled, *Unraveling the tumor immunotherapy with deep-learning based radiogenomics*. This funding will enable her team to apply deep-learning models to medical imaging to achieve a greater understanding of tumor immunophenotypes.

Cristina Saura, PI of our Breast Cancer Group, and Miriam Sansó, Post-Doctoral Fellow of VHIO's Cancer Genomics Group directed by Ana Vivancos, received the second joint FERO-ghd annual grant for pioneering research into Circulating tumor DNA (ctDNA) in breast milk for the early detection of pregnancy-associated breast cancer.

For additional information about VHIO-led projects funded by FERO Foundation see pages 182 **and** 186**.**

"la Caixa" Foundation

Thanks to the support received from the "la Caixa" Foundation, VHIO's Research Unit for Molecular Therapies of Cancer (UITM) – CaixaResearch, 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 tumor cell targeted agents including trastuzumab, pertuzumab, cetuximab, panitumumab, ramucirumab, trifluridine/tipiracil, gefitinib, osimertinib, ceritinib, crizotinib, loratinib and everolimus, among others. Current focus also centers on accelerating and advancing immunotherapies including atezolizumab, nivolumab and pembrolizumab.

The UITM, under the direction of Elena Garralda, PI of our Early Clinical Drug Development Group (see page 92), has subsequently established itself as a leading reference in developing novel therapies based on the molecular profile of each tumor and optimize treatment strategies using combinations of new agents with already existing ones. It also pioneers the design and development of novel, adaptive clinical studies including the so-called basket, multi-modular and umbrella trials. Elena's team is dedicated to studying the effectiveness of treatment approaches and anti-cancer studies

by allowing for the 'real time' and necessary adaptation in tune with the rapid pace of cancer discovery - especially in the academic setting.

By advancing clinical trial study design in the current era of precision medicine, VHIO continues to make important contributions to 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 these directions, was the launch of the EU-funded, multi-site project, Cancer Core Europe Building Data Rich Clinical Trials (CCE-DART), which is coordinated by Elena Garralda. See page 179.

In addition to various grants supporting several VHIO groups and projects (see pages 182 and 185 to view the VHIO groups who were awarded in 2020), the Foundation also fuels one of VHIO's three major institutional programs. Building on the successes of the two previous VHIO-"la Caixa" Institutional 3-year Programs, at the beginning of 2020, we launced a new 4-year VHIO-"la Caixa" program: CaixaResearch Advanced Oncology Research Program (2020-2023). Marking the UITM turning ten this year, this support will further spur our purely translational and multidisciplinary teams to develop more potent and precise anti-cancer medicines, fortify existing research lines as well as initiate new projects to lead frontier research in some of the most relevant and rising focus fields in precision oncology. For more information please refer to our Institutional Programs – page 122-124 of the report.

Also thanks to the "la Caixa" Foundation, our Clinical Research Oncology Pharmacy Unit's 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 Maria Queralt Gorgas' team to provide even higher quality pharmaceutical care and services, as well as continue to meet all regulatory requirements.

Finally, through our VHIO – CaixaResearch's Scientific Seminars Series, launched last year, 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. Naturally, due to the COVID-19 pandemic, these expert sessions were mostly hosted and conducted virtually. See pages 45-46 for additional information.

Fundación BBVA

Also driving programs to spur VHIO's avant-garde translational research in precision oncology, the *Fundación BBVA* (BBVA Foundation), financed our Tumor Biomarkers Research Program back in 2011. This five-year major framework agreement fueled collaborative science centering on the development of personalized therapies for cancer patients through biomarker research.

Building on the successes of this first program, our second BBVA-VHIO Institutional Program: the BBVA Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI), represents an important forward step in advancing agents that inhibit checkpoint regulation of the immune system, better understanding mechanisms of resistance and response to these therapies, and prioritizing the early development of those drugs showing most promise. It also supports various research lines across other VHIO groups.

Under the leadership of VHIO's Director, Josep Tabernero, these research efforts are headed by Alena Gros and Elena Garralda, PIs of our Tumor Immunology & Immunotherapy, and Early Clinical Drug Development Groups, pages 86 and 92, respectively, in collaboration with VHIO's in-house Molecular Prescreening Program of excellence, page 140 (please

also see: FERO Foundation's Advanced Molecular Diagnostics Program (DIAMAV) – page 122).

Main objectives of the BBVA-Foundation's CIAMI program include achieving a deeper understanding of naturally occurring T-cell response to cancer and establishing novel ways to exploit these anticancer responses to develop more effective, powerful and personalized immune-based strategies, approaches and therapies to combat this disease; across several tumor types.

Various pioneering translational projects linked to the early clinical development phases of immunotherapy are underway. Focus areas include the characterization of hyperprogressive disease with immunotherapy to advance insights into this phenomenon, as well as establishing a radiomic signature to predict response to immunotherapy; carried out in collaboration with Raquel Perez-Lopez, PI of our Radiomics Group (page 108).

Importantly, this year, Alena Gros and Elena Garralda's teams have worked together to finalize the clinical grade validations of tumor-infiltrating lymphocytes (TILs) expansion for the treatment of certain cancer patients at the Vall d'Hebron University Hospital HUVH).

Most recently, Alena's group filed an investigational new drug (IND) application to the AEMPS Spanish Regulatory Agency towards treating patients with metastatic epithelial or immunotherapy refractory tumors with neoantigen-reactive TILs. By enriching for neoantigen-reactive lymphocytes, the aim is to fortify the efficacy of TIL therapy in epithelial cancers.

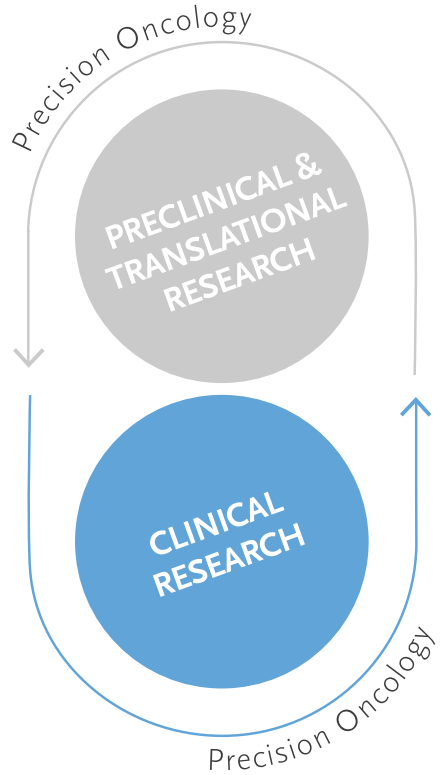
For a full listing of all VHIO's funding sources and entities see pages 172-181, **and, for new funding and corresponding projects awarded in 2020, please refer to pages 182-187.**

VHIO's TRANSLATION TOWARD PRECISION ONCOLOGY: A LITTLE MORE ON HOW WE DID IT IN 2020

Located within the Vall d'Hebron Barcelona Hospital Campus (see page 31), our researchers closely collaborate and interact with Vall d'Hebron University Hospital (HUVH) physician-scientists. Translational science and clinical research are therefore tightly connected which promotes superb interaction and teamwork which, in turn, accelerates the bench-bedside-bed cycle of knowledge.

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 and better practice for the care of patients.

VHIO's pioneering model and programs, coupled with its belief in combining strengths through cross-border collaborations, continue to spur advances in reversing cancer resistance, halting metastatic spread, and more effectively treating even the most 'undruggable' tumor types.



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

Areas of cancer research at VHIO: a snapshot

- Preclinical humanized models (PDXs – Avatars – and Organoids).
- Mechanisms of sensitivity, and primary and acquired resistance.
- Molecular and clinical Big Data to characterize subtypes of diseases.
- Early drug development.
- Clinical trials with innovative agents (phase I & II) and first-in-human studies.

The design, development & application of powerful platforms and empowering technologies

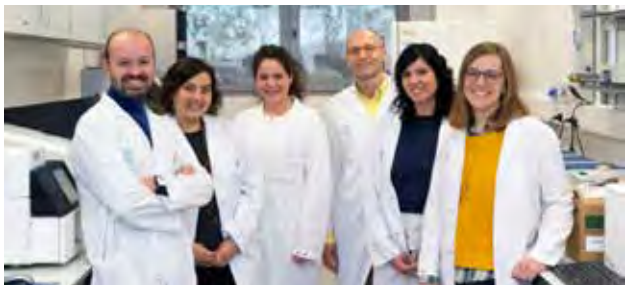
At the core of VHIO's research activities are our suite of cutting-edge core technology platforms which allow our expert teams to apply next-generation whole-genome sequencing for precision oncology as well as develop and improve existing applications to accelerate results.

By sequencing panels of genes or entire genomes in cancer patients, we are now better equipped than ever before to identify specific molecular risk factors and better predict the potential efficacy of specific agents matched to the specificities of individual patients.

VHIO's Cancer Genomics Group, headed by Ana Vivancos, serves as a Core Technology laboratory and provides cutting-edge applications in cancer genomics through state-of-the-art technologies and the development of novel, fully validated tests that are used in the clinical research setting (Molecular Prescreening Program – see below). Her lab is equipped with an n-Counter (Nanostring) platform, two digital PCR platforms (BEAMing Sysmex and ddPCR, BIO-RAD), and three NextGen Sequencers; MiSeq, NextSeq and HiSeq2500, Illumina.

VHIO's Molecular Prescreening Program (page 140), which is powered by one of our Institutional Programs, FERO Foundation's Institutional Advanced Molecular Diagnostics Program (DIAMAV) - page 122, catalyzes precision medicine at VHIO. Over the past decade, molecular prescreening at VHIO has provided access to advanced molecular diagnostics to more than 5,000 cancer patients, and is critical in

matching targeted therapeutic approaches with hundreds of clinical trial opportunities.



Nota de pie: VHIO's Molecular Prescreening team (left to right): Paolo Nuciforo, Ana Vivancos, Elena Garralda, Rodrigo Dienstmann, Susana Aguilar and Jenifer Gonzalez.
Disclaimer: this team picture was taken before the COVID-19 pandemic.

This program also counts on the expertise provided through our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, funded by the "la Caixa" Foundation (page 133), directed by Elena Garralda. Representing a key driver of clinical-molecular correlative research at our Institute, this program is headed by VHIO's Rodrigo Dienstmann under the co-leadership of Ana Vivancos, Paolo Nuciforo, and Elena Garralda. The team regularly convenes to explore existing molecular tests, developed in-house, and novel biomarkers of interest for the potential inclusion in the program. In addition, our cancer researchers and genomicists participate in weekly tumor board meetings with VHIO's medical oncologists to provide guidance on the interpretation of NGS results as well as discuss new markers for clinical testing in patients eligible for inclusion in our early phase clinical studies performed at UITM-CaixaResearch.

These expert teams collaborate together to perform molecular profiling in up to 1500 patients each year, establishing VHIO as one of the few centers in Europe to run such a comprehensive program.

We continue to extend our efforts to an increasing number of patients through collaborations with other centers, across borders. As an example, VHIO participates in AACR's Project Genomics Evidence Neoplasia Information Exchange (GENIE).

Launched by the American Association for Cancer Research (AACR) back in 2015, the *AACR Project Genomics Evidence Neoplasia Information Exchange (GENIE)* catalyzes the sharing of integrated genomic and clinical datasets across multiple cancer centers worldwide.

Incorporating 19 leading sites across the globe, VHIO is the only participant from Spain. This major international collaboration also counts on the expertise of its technical partners, SAGE and cBioPortal, that serve as secure data repository and visualization portals.

The first set of cancer genomic data aggregated through AACR's GENIE was available to the global oncology community in January 2017. The ninth data set, GENIE 9.0-public, was recently released (February 2021), with the registry now containing over 100,000 sequenced samples from over 100, 000 patients. This achievement makes GENIE one of the largest fully public cancer genomic data sets released to date.

Specifically, GENIE's registry now contains genomic information from almost 17,000 non-small cell lung carcinomas, and nearly 12,000 breast and over 11,000 colorectal cancers. Fulfilling an unmet need by providing the necessary statistical power to better guide clinical decision-making, particularly in the case of rare cancers and rare variants in common cancers, GENIE empowers novel clinical and translational research.

At the preclinical and translational level, VHIO was the first academic test center to incorporate in-house BEAMING liquid biopsy RAS biomarker technology (2015). As highlighted throughout the pages of this Scientific Report, we continue to make significant progress in validating and developing liquid biopsy technologies for the more effective, less invasive monitoring of cancer in real time. These efforts, focused on both ctDNA and tumor educated platelets (TEP), continue to advance thanks to our multidisciplinary teams in collaboration with two VHIO Core Facilities; our Cancer Genomics and Molecular Oncology Groups (pages 116-118) headed by Ana Vivancos and Paolo Nuciforo, respectively.

Our Institute was recently the first center in Europe to incorporate Guardant Health's liquid biopsy technology, officially announced in January 2021. This important development will enable the more rapid detection of a greater number of mutations in patients' blood samples, and a deeper, more comprehensive follow-up.

"la Caixa" Foundation

VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch turned 10 in 2020

VHIO's Research Unit for Molecular Therapy of Cancer (UITM) –CaixaResearch.

Thanks to the support we receive from one of our Institutional Supporters and Patrons, "la Caixa" Foundation (see page 25), VHIO continues to establish itself as a leading reference in progressing drug development and targeted therapies against cancer. Our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, founded back in 2010, has rapidly become one of the few comprehensive facilities in Europe to translate latest discovery into improved outcomes for patients, as rapidly as possible.

Led by our Director, Josep Tabernero, and headed by Elena Garralda, it has been able to do so not only through the bridging and tight connectivity between health care professionals, VHIO researchers and clinical investigators, but also 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's Early Clinical Drug Development Group (page 92), and focuses on the development of novel agents based on the molecular profile of each tumor as well as the optimization of therapies using combinations of new drugs with existing ones.

We 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 direct result of the clinical studies at our Unit, the FDA has approved 30 new therapies against several tumor types, which are becoming increasingly more targeted thanks to cancer discovery driven by precision medicine in oncology.

UITM-CaixaResearch facilities as well as VHIO-"la Caixa" Foundation's Institutional Program (page 123), enable VHIO to continuously expand its portfolio of early phase studies including complex trials such as basket studies, as well as spearhead next generation clinical trials in oncology. We are delighted to announce that 2020 celebrated the launch of our **Advanced Oncology Research Program – CaixaResearch** (2020-2023). Building on the successes of the two previous Institutional 3-year Programs, this new program will continue to spur our dedicated efforts aimed at solving cancer sooner. Please refer to page 123 for more information.

Throughout 2020 and during the COVID-19 pandemic peaks, this Unit led 195 ongoing phase I plus Basket clinical trials. It is thanks to the dedication of Elena's Group, and all our expert professionals across VHIO's Transversal Clinical Trials Core Services and Units (pages 130-143), that despite the challenges posed by COVID-19, activity was successfully maintained, and in some instances even surpassed, in order to respond to the needs of our patients.

Specifically, VHIO's clinical teams had to swiftly establish adaptive circuits and approaches to ensure the optimal running of clinical studies, while delivering –as always- optimal patient care. Newly introduced measures in response to the pandemic, whenever and wherever possible, included remote monitoring as well as dispensation of medication for certain patients receiving orally administered therapies, and telematics clinical consultations.

This year, 521 patients were enrolled in our phase I and basket studies. Our Clinical Trials Office (page 130), directed by Marta Beltran, and also located in the patient environment of the Vall d'Hebron University Hospital (HUVH), coordinates a large portfolio of Phase I, Baskets, Phase II & III clinical trials. In 2020 the number of patients included in these trials totaled at 1084 across 474 actively recruiting trials. In addition, 156 patients were enrolled in across a total of 34 post authorization and rollover studies.

Current research also centers on accelerating and advancing immunotherapies including atezolizumab, nivolumab and pembrolizumab. Concerning novel immunotherapeutics, we spearhead the early drug development of these agents and cell signaling. Specifically, we focus on second generation immunotherapies, including new cytokines, bispecifics, intratumoral agents, immunomodulatory agents and immune checkpoint inhibitors and combinations, as well as translational research in immuno-oncology in collaboration with several VHIO groups, including Alena Gros' Tumor Immunology & Immunotherapy Group (page 86).

Illustrative of our efforts aimed at pioneering novel clinical trial design in the current era of precision oncology, the **EU-funded Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART) project** launched in 2020. Incorporating experts from the seven European comprehensive cancer centers belonging to the Cancer Core Europe (CCE) Consortium, along with an additional four non-CCE partners, CCE-DART is coordinated by VHIO's Elena Garralda and carried out in collaboration with other leading experts from within Cancer Core Europe Consortium.

Building on the CCE-developed Basket of Baskets (BoB) investigator-initiated and adaptive trial which launched in 2018, which was also designed and co-developed by Elena's team at the UITM-CaixaResearch, CCE-DART will further enhance 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.

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.

For more information see page 33, and page 179.

Importantly, research conducted at VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch is also spurred through our two other Institutional Programs: FERO Foundation's Advanced Molecular Diagnostics Program (DIAMAV) – page 122, and BBVA's Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI) – page 124.

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.

Located within the Vall d'Hebron Barcelona Hospital Campus, which also incorporates a trio of research institutes of international reference; Vall d'Hebron Institute of Research (VHIR), CEMCAT – Multiple Sclerosis Center of Catalonia, and VHIO, the Vall d'Hebron University Hospital (HUVH), 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 Vall d'Hebron physician-scientists. Translational science and clinical research are therefore tightly connected, accelerating the bench-bedside-bed cycle of knowledge.

Championing translational and transformative clinical research against cancer

The *Fundació Privada CELLEX* (CELLEX Foundation), one of VHIO's Patrons and Institutional Supporters (see page 24), financed the construction of our state-of-the-art building – the CELLEX CENTER – that was completed back in 2015. Also supporting our infrastructures, CELLEX enables us to advance translational cancer science through our purely multidisciplinary research model and interconnected facilities and platforms.

In 2020, 387 scientific articles were published by VHIO researchers as corresponding/senior or co-authors.

To view each Principal Investigator's paper pick (maximum of four selected pages published in 2020), please refer to their corresponding group pages, as well as our Director's highlighted papers that made the headlines in 2020, please see Josep Tabernero's Foreword - pages 6-17.

For a selection of some of the most relevant articles by VHIO investigators published in 2020, see pages 53-61. To browse the full listing of articles published by our researchers in 2020, please turn to pages 148-171.

VHIO's trio of institutional programs: delivering on the promise of precision medicine and potentiating novel therapies and treatment strategies

VHIO can and will only deliver on its goal of accelerating the pace in advancing personalized and targeted therapies thanks to the generous support we receive from our Patrons and Institutional Supporters: the *Generalitat de Catalunya*, *Fundació Privada* CELLEX, *FERO Fundación de Investigación Oncológica*, *"la Caixa" Foundation*, and the *Fundación BBVA*. In addition to highlighting each of their myriad contributions - (pages 23-27) – our three Institutional Research Programs are as follows:

Advanced Molecular Diagnostics Program (DIAMAV). This program seeks to advance molecular profiling in patients in order 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. It aims to identify specific molecular risk factors better predict the potential efficacy of specific agents tailored to each particular tumor, further advance insights into the more effective and less invasive tracking of disease by liquid biopsy, and develop cancer diagnostics for the early detection of disease.

CaixaResearch Advanced Oncology Research Program. Building on the successes of the two previous VHIO-"la Caixa" Institutional 3-year Programs, this new CaixaResearch program (2020-2023) launched this year will further spur the development of more potent and precise anti-cancer medicines, fortify existing research lines as well as initiate new projects to lead frontier research in some of the most relevant and rising focus fields in precision oncology; those areas showing

particular promise in solving the multiple questions that stand in the way of more effectively combating cancer.

Fundación BBVA

Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI). Considering the achievements of the very first VHIO-BBVA Foundation Program on Tumor Biomarkers Research, the BBVA Foundation officially launched this second 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 those agents showing most promise.

To discover more about our three Institutional Programs, please refer to pages 122-124.

In addition to the support received through our Institutional Supporters, VHIO's research and activities are also funded by private institutions, companies, associations, societies, and individual donors.

We also continue to secure essential funding through several International and National Competitive Grants. Regarding the latter, we also gratefully thank the *Asociación Española Contra el Cáncer* (AECC) – Spanish Association against Cancer- for its longstanding support of several VHIO groups and researchers (pages 40-43).

For further details, please refer to pages 186-187:

Spinning-off and out: updates 2020

PEPTOMYC

2020 proved a particularly great year for VHIO's Laura Soucek, Principal Investigator of our Mouse Models of Cancer Therapies Group (page 76), an ICREA Research Professor, and co-Founder & CEO of VHIO spin-off, **Peptomyc S.L**. (www. peptomyc.com). This VHIO-born spin-off, established in 2014 and co-created by Marie-Eve Beaulieu, CSO of the company and formerly a Postdoc in Laura's group, focuses on the development of a new generation of cell penetrating peptides (CPPs) targeting the Myc oncoprotein for cancer treatment, and is based on Laura and her team's scientific research into Omomyc -the best direct Myc inhibitor known to date- over the last twenty years.

Officially announced at the end of 2020, a new equity financing round led by Aurora Science will help Peptomyc lead its drug candidate OMO103 into clinical phase I/II development as anti-cancer therapy against solid tumors. OMO103 has already demonstrated its safety and anti-tumor activity in multiple types of experimental models of cancer and it is now ready to be tested in clinical studies. The treatment of the first patient with this lead candidate is expected to start as soon as possible in 2021.

Peptomyc relies on a strong syndicate of life sciences investors: AurorA Science, Alta Life Sciences, HealthEquity, Business Angels, and the Spanish Centre for the Development of Industrial Technology (CDTI).

Peptomyc's team co-directed by Laura Soucek and Marie-Eve Beaulieu.

Mosaic Biomedicals

Pioneering research led by VHIO's Joan Seoane, also an ICREA Professor, previously established the role of leukemia inhibitor factor (LIF) in oncogenesis as a promoter of cancer progression by regulating the tumor microenvironment and inducing self-renewal in tumor-initiating cells, and led to the development of MSC-1, a therapeutic LIF neutralizing antibody. MSC-1's transition to the clinic and translation into benefits at the bedside thus represents an important addition to the current arsenal of powerful anti-cancer weaponry.

To do so, Joan went on to found VHIO-born spin-off, Mosaic Biomedicals, back in 2012, to design and develop the MSC-1 novel compound. At the end 2016, Mosaic merged with Northern Biologics Inc. (Toronto, Canada), towards accelerating the clinical development of this humanized antibody. This pairing reflected the same belief and backing received from other private investors including Versant, Caixa Captial Risc, as well as public funding received from the Spanish Ministry of Science and Innovation's *Retos de Colaboración* program, Spanish Ministry of Industry, Commerce and Tourism's ENISA, Spanish Centre for the Development of Industrial Technology (CDTI), two European Research Council's (ERC) Proof of Concept fundings, and private support received from its initial Business Angels. In 2020 Northern-Mosaic announced the global acquisition of clinical-stage MSC-1 by MedImmune.

Joan Seoane's Gene Expression & Cancer Group (page 72), helped to design the phase II clinical trial to test MSC-1, which will begin to recruit patients next year, 2021.

Joan Seoane, Principal Investigator of VHIO's Gene Expression & Cancer Group, and an ICREA Research Professor.

REVEAL GENOMICS

Created in 2020 to develop innovative diagnostic tests in oncology, the recently launched Reveal Genomics spin-off is led by Aleix Prat, Hospital Cliníc-IDIBAPS and the University of Barcelona (UB), together with Ana Vivancos, Principal Investigator of our Cancer Genomics Group (page 116), Charles M. Perou and Joel S. Parker, University of North Carolina-Chapel Hill (UNC-Chapel Hill, USA), and Patricia Villagrasa, the Cooperative Clinical Research Group SOLTI, who has most recently be appointed as Reveal Genomics' Chief Executive Officer.

The overarching goal is to develop diagnostic tools based on complex genomic data – initially for patients with advanced breast cancer- and combine genome-wide data to respond more precisely to clinical questions and the many challenges that currently hamper efforts aimed at solving cancer sooner.

Ana Vivancos, Principal Investigator of VHIO's Cancer Genomics Group and co-leader of the recently created spin-off, Reveal Genomics.

To discover more, please visit: www.reveal-genomics.com.

Advancing cancer science and clinical oncology in collaboration at 'home' and away

Accelerating progress through team science, VHIO's multidisciplinary teams, coordinated by our Scientific Manager and Head of VHIO's Scientific Area, Alejandro Piris (page 144), also work together as established Task Forces that have been created based on VHIO's strategic vision and core research priorities.

Each Task Force regularly convenes to synergize efforts, boost collaborations among groups and between specialists, and continuously revise respective circuits and ethics toward advancing cancer science and precision medicine. These comprehensive teams are comprised of preclinical and translational researchers, clinical investigators and medical oncologists, oncologists, pathologists, other MD disciplines, clinical research nurses, data curators and miners as well as study coordinators, and project managers, among others.

VHIO's task forcing in action.
Disclaimer: these team pictures were taken before the COVID-19 pandemic.

For more information please see page 126.

Multi-center consortia & cross border collaborations of excellence

VHIO is dedicated to forming, fostering and developing strong, multi-center partnerships that combine the necessary expertise and resources to more rapidly advance cancer discovery.

In addition to our leadership of -and participation in- several existing international consortia and alliances (see pages 175-179), 2020 celebrated the launch of several new collaborative opportunities as follows:

DART Cancer Core Europe

Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART)

The Cancer Core Europe Consortium – CCE (page 175), 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. It also spearheads next generation clinical trials by designing and development data rich, dynamic studies in oncology.

In the current era of precision medicine, the advent of novel, adaptive clinical studies including the so-called basket and umbrella clinical trials, among others, aim to address the current challenges in oncology including the globalization of clinical research, and the use and implementation of emerging health technologies.

While randomized controlled trials are considered the gold standard for studying the effectiveness of treatment approaches and anti-cancer therapies, they do not allow for the 'real time' and necessary adaptation in tune with the rapid pace of cancer discovery – especially in the academic setting.

To overcome this challenge, novel clinical trial designs promote the optimization of biomarker-drug co-development towards more precisely tailoring therapies to each disease setting, each individual patient. In short, these 'smarter' contenders seek to more effectively identify the optimal treatment for the right patient, at the right time, and promise to overcome the rigidity and limitations of traditional clinical trials.

The **EU-funded Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART)** project is coordinated by VHIO's Elena Garralda, Director of VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 133), and Principal Investigator of our Early Clinical Drug Development Group (page 92), and carried out in collaboration with other leading experts from within Cancer Core Europe Consortium. 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.

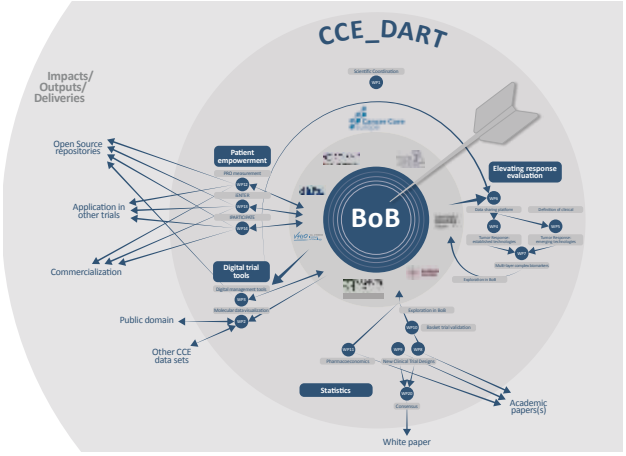
Building on the CCE-developed Basket of Baskets (BoB) investigator-initiated and adaptive trial which launched in 2018, CCE-DART will further enhance BoB's harmonized, molecular multi-tier profiling platform to more precisely match patients to novel anti-cancer medicines based on the genetic specificities of their individual tumors. In parallel, the researchers will continue to develop multiple treatments in genomically-selected populations.

By introducing new tools –or adapting existing ones- the project will also seek to elevate the management and decision-making of clinical studies to the digital age, and ultimately represent a groundbreaking example for driving a new generation of clinical trials in by leveraging novel technologies within existing clinical structures.

The wealth of expertise, cutting edge technologies, and clinical trial capabilities provided through CCE's member centers and sites, along with the additional four partners, the Digital Experimental Cancer Medicine Team, The Hyve, DataRiver, and Form Vision, will enable investigators to fortify and further develop the BoB trial's dynamic and highly adaptive design.

Common infrastructures and the wealth of experience gained through CCE sites' running of innovative academic studies, including the BoB study, will undoubtedly help the project partners to deliver on the four key objectives. Namely, to improve patient enrolment strategies and trial designs, accelerate the use of novel health technologies in the clinical setting, optimize clinical trial data management and analysis, and globalize the results of the project by promoting transparency of investigator-initiated studies.

Supported by EU's Horizon 2020 Framework Programme, CCE-DART will aim to elevate current networks and existing legal, technological and clinical infrastructures to further develop a new generation of methods and tools for more efficient, personalized, and effective clinical trials in oncology.



CCE-DART: Building Data Rich Clinical Trials.

This project has received funding from the European Union's Horizon 2020 framework programme research under grant agreement No: 965397.

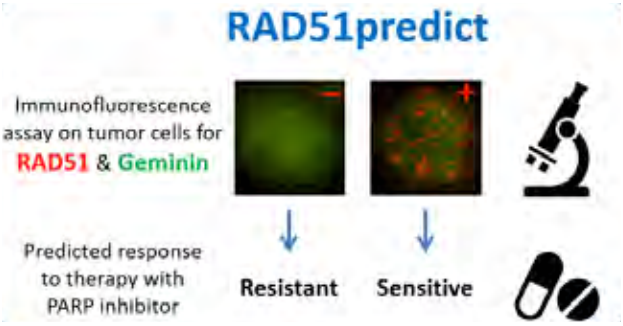
The ERA-PerMed supported RAD51predict Consortium: patient stratification based on DNA repair functionality for cancer precision medicine

The year 2020 celebrated the very first meeting of the **ERA-PerMed funded RAD51predict Consortium**, coordinated by VHIO's Violeta Serra, Principal Investigator of our Experimental Therapeutics Group (page 70). Held virtually due to the COVID-19 pandemic, the project's kick-off counted on the participation of 40 cancer researchers and clinical investigators across Europe and Canada.

ERA PerMed, is an ERA-Net Co-fund, comprising 32 partners from 23 countries and co-funded by the European Commission. This funding program aligns national research strategies, promotes excellence, reinforces the competitiveness of European players in personalized medicine, and enhances the European collaboration with non-EU countries. National funding organizations, including Spain's *Instituto de Salud Carlos III,* coordinate the *Joint Transnational Calls for collaborative innovative research projects in Personalised Medicine.*

The ERA-PerMed RAD51predict Consortium, centers on *RAD51predict: patient stratification based on DNA repair functionality for precision cancer medicine*, and consists of five partners: the University Clinic of Giessen and Marburg (Germany). Institut Gustave Roussy (IGR)-INSERM U981, Villejuif (France), German Breast Group Forschungs GmbH, Neu-Isenburg (Germany), Université Laval (CHUQ), Quebec (Canada), and VHIO, along with six other collaborators, including two companies.

Over the past few years, Violeta Serra's team has focused on various research projects based on the use of its RAD51 *in vitro* diagnostic test to predict those patients who would be most likely to benefit from therapy with PARP inhibitors (PARPi). Aimed at enabling the more precise and faster identification of patients with breast and ovarian cancer who could respond to these therapies, RAD51predict - headed by Alba Llop, Post-Doctoral Fellow of Violeta Serra's group- has been developed to better guide the stratification of patients to clinical trials to evaluate the efficacy of PARPi across additional tumor types including prostate and endometrial cancers.



The RAD51predict in vitro diagnostic test for the more precise selection of cancer patients who could benefit from treatment with PARP inhibitors.

In 2020, VHIO's **RAD51predict** test was also announced as one of the four projects selected in the first funding round of the CaixaResearch Consolidate. Reflective of the backing and belief in RAD51predict, initially called *PARPiPRED*, this test had already received finance and training in technology transfer through the CaixaResearch Validate program back in 2017.

Funding received through CaixaResearch Consolidate program will not only support this novel test through the next stages of the transfer-to-market process, but also facilitate access to mentors and innovation experts.

Interreg POCTEFA PROTEOblood

Coordinated by Gaël Roué and Pablo Menéndez, Group Leaders of the Barcelona-based Josep Carreras Leukemia Research Institute's Stem Cell Biology, Developmental Leukemia and Immunotherapy, and Lymphoma Translational Groups, respectively, the EU-funded **Interreg POCTEFA PROTEOblood Consortium**, co-funded by the European Regional Development Fund/European Social Fund, 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).

PROTEOblood, is a French-Spanish cooperative network for the analysis of proteinopathies and the development of individualized therapies in hematological cancers, co-funded by Interreg POCTEFA, and comprised of six other partners - CIC bioGUNE, IQS, CNRS, INSERM, Anaxomics Biotech, and VHIO. Using modelling collections from patient-derived studies to recreate the tumor microenvironment ex vivo, PROTEOblood's expert teams will 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 that will then be validated through xenoinjerts.

Key objectives of the PROTEOblood network include advancing personalized therapy for patients diagnosed with leukaemia or lymphoma, improving ex vivo experimental models for the prediction of response to treatment, developing advanced proteomic techniques for the study of protein related diseases, potentiating therapies against leukaemia and lymphoma, managing projects with large patient cohorts, and promoting the specialization and mobility of researchers and students.

VHIO's participation in this project is headed by David Valcárcel, a Hematologist and Lead Investigator of our Experimental Hematology Group, directed by Francesc Bosch (page 94). Considering this group's grounded expertise in SMD and allogenic transplants of stem cells, VHIO's main role is to identify patients with recently diagnosed LMA, acquire samples and provide clinical and analytical data for the development of various studies.

The project has been co-financed 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.

EURopeAn MEDical application and Radiation prOteCtion Concept: strategic research agenda aNd ROadmap interLinking to heaLth and digitisation aspects

The main objective of the 3-year **EURAMED rocc-n-roll** project 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 and therefore improve outcomes for patients throughout Europe.

Led by coordinating partner, the European Institute for Biomedical Imaging Research, Vienna (Austria), this pan-European consortium connects a total of 29 research centers of excellence, including VHIO.

VHIO's involvement, led by Jordi Giralt, Principal Investigator of our Radiation Oncology Group (page 106) centers on WP3: *The Health Perspective and Risk Benefit Approach*, to provide the health perspective of the application of ionizing radiation in medicine and radiation protection in selected disease areas, as well as analyze needs, opportunities, common interests and synergies.

Taking the lead on radiation application in oncological diseases, VHIO will work 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, Jordi Giralt and his team will analyze the needs of research in radiation application and corresponding radiation protection in oncology by identifying gaps and opportunities. They are tasked with compiling 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, and describe the current state-of-the-art in practice for patients and staff.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No: 899995.

Strengthening our research, growing teams & fortifying facilities

As our Institute goes from strength to strength, and further develop its research lines and projects based on defined strategic directions, we continue to expand our scientific faculty as well as scientific support units and teams.

In 2020, we welcomed José Fernández Navarro as Principal Investigator of our newly established Bioinformatics Support Unit (page 114).

Joining our other Core Technologies (pages 114-121), José's Unit has been created to promote digital transformation, set optimal standards and best-practices for the processing, analysis and visualization of omics datasets, and help to develop state-of-the-art pipelines and tools for the processing, analyses, and visualization of different omics datasets.

VHIO's Bioinformatics Support Unit will also provide support, expertise and resources to other VHIO teams and groups, establish collaborative research lines focused on advanced computational methods, machine learning, data analysis and visualization.

Watch this space!

José Fernández Navarro, Principal Investigator of our Core Technologies Program's Bioinformatics Support Unit.

Headed by Gemma Sala, formerly Director of VHIO's Clinical Trials Office, VHIO's Quality & Processes Unit was established this year, 2020, in order to further improve quality and unify processes in clinical trials carried out at VHIO.

This Unit is made up of quality, and transversal support teams including those dedicated to sample management and scheduling.

Gemma Sala, former Director of VHIO's Clinical Trials Office, now heads up our recently created Quality & Processes Unit.

For more information please see page 142.

Launched back in 1997, our Clinical Trials Office incorporates experts conducting clinical trials at the Vall d'Hebron University Hospital's (HUVH) Medical Oncology Department (Vall d'Hebron Barcelona Hospital Campus), which is headed by VHIO's Director, Josep Tabernero.

Directed by Marta Beltran since 2020, our Clinical Trials Office incorporates study coordinators, data managers, as well as administrative personnel, who coordinate phase I–IV clinical studies, and also participate in several translational research projects at VHIO.

Previously Head of gastrointestinal, lung, head & neck phase II-III clinical trials, Marta Beltran is now Director of our Clinical Trials Office.

For more information, please see page 130.

Prizes & Recognitions 2020

In addition to all our newly funded research lines and programs in 2020 (please see pages 182-187), also driven through the support received each year from our Institutional Programs (page 122-124), and public and private national, European, and International funding sources and entities (pages 172-181), VHIO's investigators and teams have also been recognized through prizes, accolades and recognitions. Just some of which include the following:

International

Recognized by their peers, applauded by the world, VHIO's Josep Tabernero and Enriqueta Felip once again featured among Clarivate's 6,167 Global Highly Cited Researchers in 2020.

Published at the end of 2020, Clarivate's Web of Science revealed its annual and global Highly Cited 2020 researchers list. Featuring among the world's elite scientists at academic research institutes and commercial organizations -across the 21 fields of the sciences and social sciences categories- are VHIO's Director, Josep Tabernero, and Enriqueta Felip, Principal Investigator of our Thoracic Tumors & Head and Neck Cancer Group (page 110).

Josep Tabernero, also Head of the Medical Oncology Department of the Vall d'Hebron University Hospital, Vall d'Hebron Barcelona Hospital Campus, was selected for the fifth consecutive year in recognition of his exceptional advancements in cancer research under the category of Clinical Medicine that lists a total of 492 named leaders in 2020.

Initially included in Clarivate's Cross-Field category in 2018, Enriqueta Felip, who is also Head of the Lung Cancer Unit at Vall d'Hebron, and currently serves as Vice President of the Spanish Society of Medical Oncology (SEOM), joined Josep under the same field for a second year running.

The 2020 listing for Clinical Medicine includes 10 others from across Spain. Josep Tabernero and Enriqueta Felip are in the company of an additional 6 leading researchers in biomedicine who are also leading figures and pioneers of research in oncology, 3 of whom are based in Barcelona.

They are: Joaquim Bellmunt, Hospital de Mar Medical Research Institute (IMIM, Barcelona), Jordi Bruix, University of Barcelona, Josep M. Llovet, University of Barcelona, Maria Victoria Mateos, University of Salamanca, Jesús F. San Miguel, University of Navarra, and Luis Paz-Ares, Complutense University of Madrid.

Statistics surrounding regional concentrations of top talent revealed that Spain ranks 10th in the Top 10 list of countries with the highest number of Highly Cited Researchers. Specifically, a total of 103 trailblazers from Spain were recognized in 2020, including 3 listed global experts from Vall d'Hebron who are recognized under the Cross-Field category in 2020: Javier Cortés, a Translational Investigator at VHIO, and Francisco Guarner and Xavier Montalban, Vall d'Hebron Research Institute (VHIR).

Josep Tabernero, VHIO's Director and a Clarivate Highly Cited Researcher, 2020.

Enriqueta Felip, Principal Investigator, VHIO's Thoracic Tumors & Head and Neck Cancer Group, and a Clarivate Highly Cited Researcher 2020.

In Vivo

Informa Pharma Intelligence

Laura Soucek recognized as a Life Science Leader by Pharma Intelligence

In 2020, In Vivo Informa Pharma Intelligence revealed its first listing of 'ones to watch' in the life sciences from around the world. Featuring among its 30 Rising Leaders across the biopharma, medtech and health technology sectors, is VHIO's Laura Soucek, Principal Investigator of our Mouse Models & Cancer Therapies Group (page 76), ICREA Professor, and co-Founder & CEO of VHIO spin-off, Peptomyc S.L. (page 32).

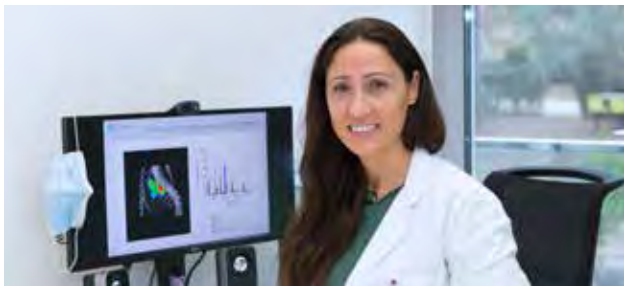
Specifically, this listing shines important light on entrepreneurs and innovators who represent the next wave of creativity in healthcare, and incorporates leading figures in academia, CEOs of small and mid-sized companies and rising employees in larger biopharma and medtech businesses.

Over the last 20 years Laura's determined research efforts have centered on combating resistance to therapy and putting the brakes on cancer cell spread through clinically inhibiting the Myc oncogene. Found deregulated in most, if not all tumor types, and as a key driver of cancer progression and maintenance, Myc is consequently a major contender as a cancer target

and yet, promise of its inhibition has not yet been successfully translated into benefits at the patient level.

As a leading figure in the Myc field, Laura co-founded Peptomyc back in 2014 to design and develop anti-Myc peptides for the treatment cancer. Building on the many successes to date, Laura Soucek and Marie-Eve Beaulieu, Chief Scientific Officer (CSO) of the company, most recently announced (2021) that Peptomyc has received approval from the Spanish Agency of Medicines and Medical Devices for conducting clinical trials in Spain (AEMPS), to initiate the first-in-human Phase I/II clinical trial with its first compound – a disruptive Myc inhibitor, Omomyc (OMO-103).

In short, this latest recognition celebrates these achievements as well as Laura's talent, creativity and strong leadership qualities.



Laura Soucek, Principal Investigator of our Mouse Models & Cancer Therapies Group, ICREA Professor, and co-Founder & CEO of VHIO spin-off, Peptomyc S.L.

César Serrano receives the Ramiro Carregal Award for New Talents in Oncological Research

Aimed at recognizing the dedicated contributions made by new talents in oncology, the Board of the Ramiro Carregal International Award for Scientific and Technical Oncological Research, broadened the scope of the Awards through by introducing the Ramior Carregal Award for New Talents in Oncological Research back in 2019.

Announced in 2020, César Serrano, Principal Investigator of VHIO's Sarcoma Translational Research Group (page 80), is the recipient of the 2nd edition of this prestigious award. His candidature was proposed by the *Grupo Español de Investigación en Sarcomas* (GEIS – Spainsh Group for Research in Sarcomas), for which César serves as Member of the Board of Directors in Medical Oncology.

This accolade salutes his research contributions in identifying molecular drivers of oncogenic signaling in sarcomas, characterizing mechanisms of response and resistance to targeted therapies, and the preclinical modeling and validation of novel therapeutic strategies for patients suffering from sarcoma.

César Serrano, Principal Investigator of VHIO's Sarcoma Translational Research Group.

VHIO's Ana Oaknin elected as co-Chair of the Gynecologic Cancer InterGroup's Cervix Cancer Committee

Recognized for her global expertise in developing and leading multi-center studies and innovative clinical trial design to more effectively and precisely treat gynecological cancers, VHIO's Ana Oaknin, was elected by the Executive Board of Directors of the Gynecological Cancer InterGroup (GCIG) as co-Chair of the Group's Cervix Cancer Committee for the next two-year term and thereafter, spearhead the same expert panel as Chair for a further two years.

The Gynecologic Cancer InterGroup seeks to enhance the global impact of clinical trials in gynecologic cancer by promoting international cooperation, supporting clinical research, performing studies in rare tumors, stimulating evidence-based medicine, and spurring educational activities. GCIG's mission is to promote and facilitate high quality clinical trials aimed at improving outcomes for women suffering from gynecological cancers.

Ana Oaknin, Principal Investigator of VHIO's Gynecological Malignancies Group, and Head of the Gynecological Cancer Program, Medical Oncology Department, the Vall d'Hebron University Hospital (HUVH – Vall d'Hebron Barcelona Hospital Campus).

National

Generalitat de Catalunya

VHIO's Director, Josep Tabernero, awarded the National Research Award 2019

The National Research Award, with a 30-year history, is one of the most prestigious awards bestowed by the

Catalonian Government and the Catalonian Foundation for Research and Innovation (FCRI). In 2020, our Director, Josep Tabernero, received the award as one of the most relevant clinical investigators, who has made exceptional contributions to global research in oncology, particularly in advancing anti-cancer medicines against gastrointestinal tumors, as well as pioneering the development of several novel targeted and immune-based therapies.

Also co-Director of VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 133), Josep is internationally renowned for developing and potentiating personalized treatments against colorectal cancer based on the molecular characteristics of each particular tumor, advancing cancer discovery for the more precise diagnosis and tracking of disease, and generating crucial insights into mechanisms of resistance and predictive biomarkers of response to therapy.

The National Research Award also honors his teams' development of state-of-the-art experimental technologies, tools and platforms including liquid biopsy, as well as significant contributions made to advancing preclinical and translational cancer modeling such as patient-derived xenografts (PDX), and defining molecular subtypes of disease, particularly in colorectal cancer.

Our Director, Josep Tabernero (to the right), receiving his Award. The National Research Awards Ceremony 2019, was postponed due to the COVID-19 pandemic, and was celebrated at the *Palau de la Generalitat de Catalunya*, in October 2020. The ceremony was presided by Meritxell Budó, Minister of the Presidency and Government Spokesman of Catalonia, and Ramon Tremosa (pictured left), Minister of Business and Knowledge, and President of the Catalan Foundation for Research and Innovation (FCRI).

fundación fero
Investigando por un futuro sin cáncer

VHIO's duo of annual FERO Awards

One of our Patrons and Institutional Supporters, FERO Foundation (pages 24 and 122) - whose late Honorary President is José Baselga, who passed away on 21 March 2021 (see *A Personal Tribute* by our Director, Josep Tabernero, page 18) - announced its 2020 annual Award back in May.

Unfortunately, due to the COVID-19 pandemic, the usual gathering of FERO's community in celebration of these prestigious Awards, as well as its annual fundraising gala dinner, presided by Sol Daurella, FERO's President, and Piru Cantarell, FERO's General Manager, could not take place.

Regarding FERO's Annual Awards for Translational Research, Raquel Perez-Lopez, PI of VHIO's Radiomics Group (page 108), was prized for her project entitled *Unraveling the tumor immunotherapy with deep-learning based radiogenomics*. This FERO funding, supported by the Ramón Areces Foundation, will enable her to apply deep-learning models to medical imaging to achieve a greater understanding of tumor immunophenotypes.

More specifically, Raquel will lead research to develop an algorithm to correlate images obtained by computed tomography on the characteristics of tumors with the immune profile and response to immune-base therapies of individual patients. Using artificial intelligence, this approach will help to better predict those patients who would most likely benefit from immunotherapy, and more swiftly gauge patients' response to these treatments.

The recipients of the second annual FERO-ghd Award for breast cancer research, were Cristina Saura, PI of our Breast Cancer Group (page 90), and Miriam Sansó, Post-Doctoral Fellow of VHIO's Cancer Genomics Group directed by Ana Vivancos (page 116), who were jointly awarded for their pioneering research into circulating tumor DNA (ctDNA) in breast milk for the early detection of pregnancy-associated breast cancer. This innovative project, investigating liquid biopsy in breast milk, seeks to ultimately improve the prognosis of this particular patient population.

From left to right: VHIO's Raquel Lopez-Perez, Cristina Saura, and Miriam Sansó.

For a full listing of the FERO Foundation's supported VHIO projects and research endeavors in 2020, please see: *New Funding and Projects in 2020*, pages 182-187.

"la Caixa" Foundation

VHIO's RAD51predict selected by CaixaResearch Consolidate

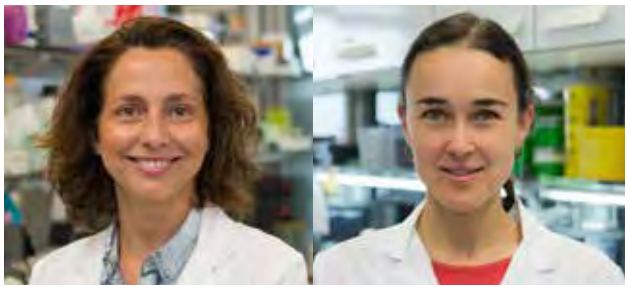
The "la Caixa" Foundation's CaixaResearch Consolidate program supports highly innovative solutions to achieve investment readiness and move closer to commercialization stages.

In 2020, VHIO's RAD51predict directed by Violeta Serra, Principal Investigator of our Experimental Therapeutics Group (page 70), and headed by Alba Llop, Post-Doctoral Fellow of Violeta's Group, was announced as one of the four projects selected in the

first funding round of the CaixaResearch Consolidate Reflective of the backing and belief in RAD51predict, initially called *PARPiPRED*, this test had already received finance and training in technology transfer through the CaixaResearch Validate program back in 2017.

Over the last few years, Violeta's team has focused on various research projects based on the use of RAD51 as a biomarker to help personalize cancer treatment, and expand the use of PARP inhibitors. The RAD51predict test enables the more precise and faster identification of those patients with breast and ovarian cancer who would be most likely to benefit from these therapies, as well as guide the stratification of patients to clinical trials in order to evaluate the efficacy of PARP inhibitors across additional tumor types.

Funding received through CaixaResearch Consolidate will not only support this innovative project through the next stages of the transfer-to-market process, but also facilitate access to mentors and innovation experts.



Violeta Serra (left), PI of the RAD51predict project, Alba Llop (right), project lead.

For a full listing of the "la Caixa" Foundation and CaixaResearch funded VHIO projects and research endeavors in 2020, please see: *New Funding and Projects in 2020*, page 182 and pages 185-186.

Of note, 2020 also celebrated the first virtual meeting of the ERA PerMed supported Consortium consisting of five partners, and six associates including two companies. Focused on validating the RAD51pedict test, and co-funded by the European Commission, this powerful partnership is coordinated by Violeta Serra. To discover more about this innovative research project entitled *RAD51predict: patient stratification based on DNA repair functionality for precision medicine*, please see pages 34-35.

Marking World Cancer Research Day 2020: VHIO researchers and projects granted by AECC

Launched back in 2016 by the *Asociación Española Contra el Cáncer* (Spanish Association against Cancer – AECC), and officially co-promoted in collaboration with leading organizations and Societies in oncology, **World Cancer Research Day (WCRD)** is held annually on 24 September to encourage the active involvement of citizens, institutions and leaders across various fields to support the advancement of research against cancer.

The global cancer burden rose to 19.3 million new cases and almost 10.0 million cancer deaths (9.9 million excluding nonmelanoma skin cancer) occurred in 2020. Overall, the burden of cancer incidence and mortality is rapidly increasing worldwide. This reflects both aging and growth of the population as well as changes in the prevalence and distribution of the main risk factors for cancer, several of which are associated with socioeconomic development.

Accelerating cancer science and translating insights into improved outcomes for patients as swiftly as possible, must therefore be a top priority for the entire oncology ecosystem as well as the public at large. It certainly is for the AECC as its continued funding of cancer research of excellence across Spain and beyond remains at the Association's very core.

In celebration of World Cancer Research Day, the AECC announced its 2020 awardees virtually on the big day itself, 24 September. Unfortunately due to the COVID-19 pandemic, its annual Award Ceremony in Madrid, presided each year by Her Majesty the Queen Letizia of Spain, AECC's Honorary President, did not take place.

To mark the occasion, the AECC organized a timely Dialogue Session focused on COVID-19 and the effects on cancer research as well as possible future implications for investigation. The discussion streamed live and counted on the presence of two renowned leaders in oncology, VHIO's Director and Head of the Medical Oncology Department at Vall d'Hebron, Josep Tabernero, and Mariano Barbacid, AXA-CNIO Professor of Molecular Oncology, the Spanish National Cancer Research Centre, Madrid.

Moderated by Spanish journalist, Purificación Beltrán, and joined by the other invited panelists, Isabel Orbe, Director General of AECC's Scientific Foundation, Marta Pujol, Director of Biomedical Research of AECC's Scientific Foundation, as well as Belén Pastor, an AECC-supported cancer researcher at the Valencian Institute of Oncology (IVO), conversations also centered on the importance of increased investment in cancer science and clinical research, incentives to nurture, grow and support the careers of researchers in Spain, and the strengthening of national cancer planning.

AECC's World Cancer Day 2020 streamed Dialogue Session (left to right): Isabel Orbe, Director General of AECC's Scientific Foundation, Purificación Beltrán (Moderator), Mariano Barbacid, AXA-CNIO Professor of Molecular Oncology - CNIO, Marta Pujol, Director of Biomedical Research of AECC's Scientific Foundation, Josep Tabernero, VHIO's Director, and Belén Pastor, cancer researcher at the Valencian Institute of Oncology (IVO).

VHIO AECC Award recipients announced on World Cancer Research Day 2020

Three of our Post-Doctoral Fellows, Isabel Puig, VHIO's Stem Cells & Cancer Group (PI: Héctor G. Palmer), Alba Llop, Experimental Therapeutics Group (PI: Violeta Serra), and Ester Bonfill, Gene Expression & Cancer Group (PI: Joan Seoane), were awarded across three of AECC's many funding programs and initiatives.

Isabel Puig received an ***Ideas Semilla*** (Seed Ideas) grant for her research on dormancy and autophagy: decoding the molecular mechanism that mediates cancer drug resistance. One of these mechanisms is the ability of some tumor cells to remain in a latent state and thus resist antitumor therapies.

Strategies to block autophagy as a possible mechanism enhancing dormant cancer cell survival have been proposed to eradicate these cells. However, despite the promise of autophagy modulators as pharmacotherapeutic agents, clinical results show that toxicity remains as a major limitation. It is therefore imperative to discover selective autophagy inhibitors that specifically target autophagic proteins that are defective only in a disease context to maximize therapeutics effects and minimize side effects.

Previous data published by Héctor's group revealed the central role of epigenetic factor DPPA3 in regulating cell dormancy and chemoresistance. It has been described that, in addition to its epigenetic nuclear function, DPPA3 also has a role in the cytoplasm, modulating the lysosome-dependent degradation step at the late stage of autophagy. Moreover, while DPPA3 is not expressed in normal adult tissues they found that it is abnormally overexpressed in slow-cycling/dormant cancer cells.

Based on the hypothesis that DPPA3 could improve the efficacy of hypoxia-induced autophagy in dormant tumor cells, thus enhancing its function as a protective cell survival mechanism against therapeutic stress and driver of resistance to therapy, this present project will aim to decode the molecular mechanisms underlying the crosstalk between dormancy, hypoxia, autophagy and drug resistance to provide a deeper understanding of dormant tumor cell biology. In so doing, the investigators hope to open up new research avenues to develop more effective therapies against disease recurrence.

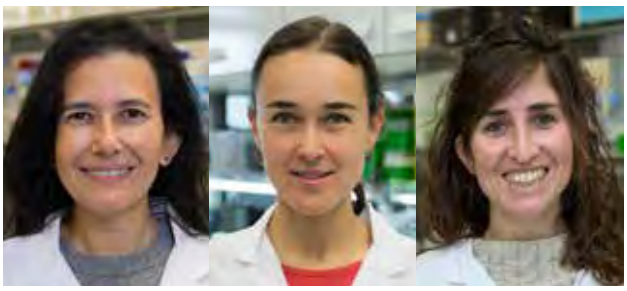
Alba Llop and Ester Bonfill were prized as an **AECC Investigator** and **AECC Postdoctoral Researcher**, respectively. This funding will enable Alba to pursue her research on Tumor DNA repair functionality and immunologic profile as predictive and prognostic biomarkers for cancer precision medicine, as well as spur Ester's investigations into the Impact of LIF and the tumor microenvironment on the immunomodulation of brain metastasis.

Directed by Violeta Serra Alba Llop's awarded project aims to establish the predictive and prognostic values of the RAD51 test (see pages 35 and 39), and immune-related biomarkers in four major tumor types: breast, ovarian, prostate and endometrial cancers). The overarching objectives are to more swiftly and precisely stratify patients for anti-cancer therapies, and propose more effective drug combinations, in order to combat disease relapse and improve the survival of patients.

Building on previous findings reported by Joan Seoane's Gene Expression & Cancer Group that identified the cytokine LIF as an immunomodulatory factor contributing to the brain immunosuppressive tumor microenvironment (TME) in glioblastoma, Ester Bonfill's research will use patient-derived models to study the role of TME in brain metastasis and its impact on TILs with a special focus on LIF. Achieving a deeper understanding of the molecular mechanisms involved in brain metastasis TME will help to identify novel therapeutic targets to more effectively tackle this disease.

Directed by Joan Seoane, Ester Bonfill will lead research into the brain tumor microenvironment in the context of brain metastasis, including the study of the impact of LIF on TILs, in order to identify robust therapeutic targets, including LIF. The investigators will study the immune profile of the brain TME in order to identify immunomodulatory factors that could be considered as potential targets. These novel therapeutic targets could lead to the development of therapeutic compounds to be used in combination.

The group's patient-derived functional models and the integration of their data with clinical findings will provide insights into the role of immunotherapy in the context of human tumors. This will accelerate the translation of results into the clinic, for the benefit of patients.



VHIO's AECC awardees announced in celebration of World Cancer Research Day, 24 September 2020. Left to right: Isabel Puig, VHIO's Stem Cells & Cancer Group (PI: Héctor G. Palmer), Alba Llop, Experimental Therapeutics Group (PI: Violeta Serra), and Ester Bonfill, Gene Expression & Cancer Group (PI: Joan Seoane).

César Serrano, Principal Investigator of VHIO's Sarcoma Translational Research Group, received support as an **AECC Senior Clinician** for his project on the *Molecular landscape of resistance to KIT/PDGFRA inhibition in gastrointestinal stromal tumors*.

This research will focus on patterns of resistance to targeted therapies in gastrointestinal stromal tumors (GISTs). Most GISTs have so-called addiction to the oncogenic power of two cell receptors, KIT and

PDGFRA, and its targeted inhibition with tyrosine kinase inhibitors (TKIs), such as first-line imatinib, significantly improves outcomes for patients.

Unfortunately, progression eventually occurs in 2 years through the expansion of several types of resistant mutations in KIT. Targeting KIT remains an important strategy after imatinib failure, but all available TKIs only achieve moderate activity, leading to a poor prognosis. Achieving a better understanding of the mechanisms of disease progression in order to design novel therapeutic approaches in GIST with no treatment options available, is consequently imperative.

The spectrum of resistance in this particular patient population remains unknown. Although acquired KIT mutations are relevant and well known, our preliminary work has enabled us to envisage two different, yet interrelated mechanisms progressively enriched throughout the course of disease: 1) by-pass of KIT as the critical driver; and 2) stepwise alterations involving big regions of the genes.

Led by César Serrano, research will aim to dissect the landscape of resistance in imatinib-resistant GIST patients to generate novel therapeutic strategies. To do so, his team will study all the DNA alterations present in GIST tumor tissue, its biologic function, and develop novel treatments in the laboratory that can be translated to GIST patients in the clinic.

AECC Senior Clinician: César Serrano, Principal Investigator of VHIO's Sarcoma Translational Research Group.

Throughout 2020, other VHIO investigators were also prized through other AECC funding initiatives:

The project entitled *Leveraging the AR-DDR interaction in de-novo metastatic prostate cancer towards precision combination therapies with PARP inhibitors*, directed by Joaquin Mateo, Principal Investigator of VHIO's Prostate Cancer Translational Research Group (page 78) was awarded through an **AECC Laboratory** grant.

Alterations in DNA damage repair (DDR) pathways are common in the advanced disease setting, and thus represent therapeutic targets. Joaquin Mateo's group, and others, have demonstrated that DDR alterations are predictive biomarkers for PARP inhibitors (PARPi) in metastatic castration-resistant prostate cancer (mCRPC); however, there is significant inter-patient variability in the duration of response.

Cross-regulation between AR signaling and DDR pathways has been demonstrated in preclinical models: PARP-1 modulates AR function and androgen deprivation has been shown to impair double-strand break repair. Clinical trials are ongoing to validate this approach towards improving outcomes for patients, and expanding target populations who might benefit from therapy with PARPi.

Prostate cancer is a particularly heterogeneous disease, both clinically and molecularly. Hence, understanding the molecular underpinnings of each case, and how these tumors change over the course of time is critical to delivering more personalized and precise care to patients. Most prostate cancers are treated with drugs that target androgens, the main male hormones; but these therapies collaterally affect other biological pathways tumors.

Based on the hypothesis that a deeper understanding into how these other pathways are affected will result in more effective combinations of treatments to delay cancer progression and improve patients' outcomes. Specifically, Joaquin's team will explore how the changes in tumors triggered by the exposure to a therapy could induce a liability for tumors, becoming responsive to a second drug. Using biopsy samples from over 120 patients who participated in two clinical trials, one conducted in the US, and the other in Spain, they will test two hormonal therapies with or without the addition of PARPi.

By evaluating how tumors adapt to treatment exposure from the perspective of other biology pathways becoming affected, how this determines response to the combination with PARPi, they will also assess serial blood samples from the same patients to establish whether the same effect in cancer traces present in the blood, to minimize the need for repeated tumor biopsies.

The investigators will capitalize existing resources, biopsies that were collected from patients participating in clinical trials, to provide new insights into how this tumor type becomes responsive or resistant to new drugs, and correlate findings with the outcomes of these patients in the clinical trial in order to translate our results into advances in patient care.

Joaquin Mateo, Principal Investigator of VHIO's Prostate Cancer Translational Research Group.

Héctor G. Palmer, Principal Investigator of VHIO's Stem Cells & Cancer Group, received funding through **AECC's Innova program** for his project on *First-in-class small drug activators of TET2 for the treatment of cancer.*

The global rise in the incidence of acute myeloid leukemia (AML) is expected to lead to a huge demand for novel and more effective therapies. Hypomethylating agents (HMAs) currently represent a non-intensive strategy for AML patients who cannot be treated with chemotherapy. HMAs randomly demethylate the genome overcoming differentiation blockage and promoting death of myeloid blasts. These drugs present unsatisfactory efficacy mostly due to their unspecific mechanisms of action and the lack of biomarkers for the selection of drug-sensitive patients.

In response, Héctor G. Palmer's group is developing a first-in-class agent to activate TET2 as a novel target in AML. Similar to HMAs, TET2 activation promotes differentiation and death of AML blasts, but in this case, by locus-specific instead of a global DNA demethylation. His team expects that TET2 activators will revolutionize AML treatment showing better efficacy than HMAs, for three main reasons: a precise selection of drug-sensitive patients based on mutations causing partial loss-of-TET2 function, monitoring target engagement (PD marker) by measuring the enzymatic product of TET2 activity, and improving drug combinations thanks to Héctor's group's detailed knowledge on drug mode of action.

Main objectives include the development of target-directed therapy in precision oncology for this patient population, and exploitation of the finding that TET2 is altered in other tumor types and diseases beyond oncology; a reality that could be exploited in their future development of anti-cancer therapies.

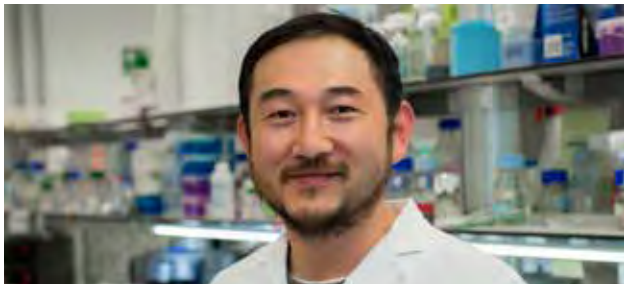
Héctor's group has already report the tumoral efficacy on leukemia cells in culture and animal models. With the present project they will aim to advance in optimizing the pharmacological properties of their lead TET2 activating drugs prior to evaluation in clinical trials.

Héctor G. Palmer, Principal Investigator of VHIO's Stem Cells & Cancer Group.

Post-Doctoral Fellow of VHIO's Chromatin Dynamics in Cancer Group (page 68), Tian Tian, has been awarded as an **AECC Investigator** for his research into the *Characterisation of fusion protein BRD-NUT in NUT midline carcinoma: from diagnosis to treatment.*

Directed by this group's Principal Investigator, Sandra Peiró, he will seek to advance insights into NUT midline carcinoma (NMC); a highly aggressive tumor type, occurring anywhere along the trunk or head. This type of cancer is frequently misdiagnosed, and lacks effective therapeutic strategies, with a mean survival of less than 7 months after diagnosis. Recent research shows that in NMC cells, there is a chromosomal translocation resulting in the fusion of BRD and NUT proteins. However, the role of fusion protein BRD-NUT in NMC oncogenesis and progression is not yet understood.

Tian Tian will seek out novel avenues for the more efficient diagnosis and effective treatment of NMC by implementing and standardizing NMC diagnosis in clinical practice, studying how BRD-NUT fusion proteins shape 3D genome configuration and its relation to cancer, and assessing the potential of two novel therapies.



AECC Investigator: Tian Tian, Post-Doctoral Fellow, VHIO's Chromatin Dynamics in Cancer Group (PI: Sandra Peiró).

We salute and applaud AECC's invaluable contribution to promoting cancer discovery and translational research of excellence, as well as the support it provides to countless researchers and groups across Spain and beyond.

For a full listing of the AECC's supported projects and research endeavors at VHIO in 2020, please see: *New Funding and Projects in 2020*, pages 186-187.

Instituto de Salud Carlos III

Elena Garralda to develop tumor-infiltrating lymphocyte (TIL) therapy against checkpoint inhibitor-resistant tumors

Based on research conducted by VHIO's Alena Gros, Principal Investigator of our Tumor Immunology & Immunotherapy Group (page 86), we established a working group in 2020 to develop our first VHIO TIL-based therapy trial. Awarded by the Carlos III Health Institute (ISCIII) in 2020, this study will commence in 2021, directed by Elena Garralda, Principal Investigator of our Early Clinical Drug Development Group (page 92), and Director of VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 133).

Entitled *Next generation TIL therapy targeting neoantigens for immune checkpoint blockade (ICB)-resistant tumors*, the goal of this pioneering project is to develop neo-antigen-specific TIL therapy for ICB-resistant solid cancers. To this end, the team will conduct a phase I clinical study to treat patients with advanced solid tumors refractory to standard therapy who progressed to at least one line of ICB with neo-antigen-reactive TIL.

By exploiting a personalized high-throughput screening strategy, the investigators will aim to advance insights into specific tumor or TIL traits associated with clinical outcomes, and potentiate the efficacy of neo-antigen-reactive TIL products in future clinical trials.

Elena Garralda, Principal Investigator of our Early Clinical Drug Development Group, and Director of VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch.

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

Raquel Perez-Lopez: prized winner of the CRIS Clinical Talent Program

In 2020, Raquel Perez-Lopez, Principal Investigator of our Radiomics Group (page 108), was announced as recipient of a **CRIS Cancer Foundation's Clinical Talent Program** award. Aimed at providing support and incentives for clinical research to develop their careers in Spain, this five-year funding program will enable Raquel to develop and advance her research lines carried out at VHIO and the Vall d'Hebron University Hospital (page 39).

This grant not only represents an important boost to her career as a Clinical Investigator, but will also enable Raquel and her team to advance insights in oncology and potentiate anti-cancer medicines through the application of precision imaging. Specifically, her group will seek out novel approaches to improve current imaging techniques used in both the diagnosis and tracking of disease, as well as combine imaging with genomic data in order to better identify those patients who would be most likely to respond to immune-based therapies, and those who will not.

Raquel Perez-Lopez, Principal Investigator, VHIO's Radiomics Group.

Paolo Nuciforo, Principal Investigator of VHIO's Molecular Oncology Group (page 118), was awarded this year through the ***Fundación Mutua Madrileña's* XVII edition of Awards** that support research in healthcare.

Building on his previous research establishing *Fusobacterium* as a relevant pathogenic intestinal bacterium of the microbiota which is associated with colorectal cancer (CRC), and showing that persistency of *Fusobacterium* nucleatum after neoadjuvant chemo-radiotherapy (nCRT), is associated with higher rates of relapse in patients with locally advanced rectal cancer, Paolo Nuciforo leads the FUSOMAP collaborative project, prized this year by the Mutua Madrileña Foundation.

Entitled *Mapping the geography of intratumoral Fusobacterium nucleatum and associated gut microbiota in early-stage CRC,* this Spanish multi-center project, represents an important step forward in facilitating the development of personalized microbiome-based CRC diagnosis and anti-cancer medicines against this disease. The project investigators directed by Paolo, will seize on this opportunity by researching the prevalence, patterns and composition of *F. nucleatum* and associated microbiota in patients from different metropolitan areas. At tissue level, they will study the topological distribution of microbiome contexture within the tumor.

This project counts on the expertise of colleagues across several Spanish research centers of excellence, and is also carried out in collaboration with other VHIO researchers including Elena Élez, Medical Oncologist and Clinical Investigator of our Gastrointestinal & Endocrine Tumors Group (PI: Teresa Macarulla, page 96), who will coordinate the enrolment of patients in this study at Vall d'Hebron, as well as Iosune Baraibar of this same group.

Paolo Nuciforo, Principal Investigator of our Molecular Oncology Group: awarded by the Fundación Mutua Mardrileña for the collaborative FUSOMAP project.

In addition to the examples highlighted here -featuring just some of the many newly funded research lines, initiatives and programs in 2020- we invite you to browse our comprehensive listing under *New funding and projects in 2020*, (please see pages 182-187), as well as view a complete listing of our Institutional Supporters (page 122-124), public and private national, European, and International funding sources and entities this year (pages 172-181).

To discover more about our dedicated patrons, the *Generalitat de Catalunya*, *Fundació Privada CELLEX, FERO Fundación de Investigación Oncológica*,*"la Caixa" Foundation*, and the *Fundación BBVA*, as well as our Institutional Research Programs please refer to pages 23-27, and 122-124, respectively.

VHIO-organized events: sharing the latest insights & developments in cancer science and clinical investigation

VHIO is dedicated to organizing events of the highest caliber 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.

VHIO - CaixaResearch Scientific Seminars Series

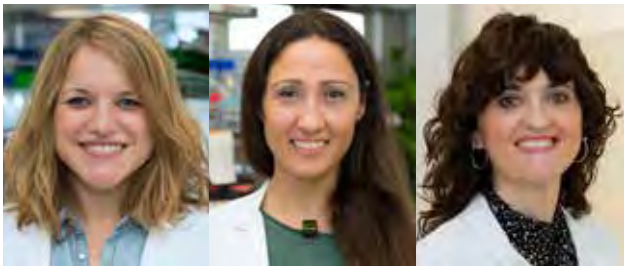
SCIENTIFIC SEMINARS SERIES

"la Caixa" Foundation

Launched in 2019, 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 take place in VHIO's state-of-the-art CELLEX Building Auditorium, although the majority in 2020, were hosted virtually due to the COVID-19 pandemic. Each seminar typically consists of a 30-45 minute talk followed by a Q&A round with the audience.

Chaired be each respective VHIO host, these expert talks are typically scheduled to take place on Fridays.



Scientific co-Chairs (left to right): María Abad, PI, Cellular Plasticity & Cancer Group, Laura Soucek, PI, Mouse Models of Cancer Therapies Group, and Elena Élez, Medical Oncologist and Clinical Investigator, Gastrointestinal & Endocrine Tumors Group.

In 2020, a total of 21 VHIO - CaixaResearch Scientific Seminars took place as follows:

Speaker: Romian Quidant, Plasmon Nano-Optics Group Leader and ICREA Professor, Institute of Photonic Sciences (ICFO)
Talk title: New opportunities in medicine enabled by light and nanotechnology
Date: 17 January (in person)
VHIO host: Josep Tabernero, VHIO's Director

Speaker: Marisol Soengas, Group Leader Melanoma, Spanish National Cancer Research Centre – CNIO, Madrid, Spain.
Talk title: Imaging and targeting premetastatic niches in melanoma
Date: 31 January (in person)
VHIO host: Maria Abad, PI, Cellular Plasticity & Cancer

Speaker: Shuji Ogino, Chief of Molecular Pathological Epidemiology (MPE) Program, Dept. of Pathology, Brigham & Women's Hospital (BWH). Professor of Pathology, BWH, Harvard Medical School. Professor of Epidemiology, Harvard T.H. Chan School of Public Health. Associate Member, Broad Institute of MIT and Harvard, Boston, USA.
Talk title: Integrative Analyses of Environment, Lifestyle, Microbiota, and Tumor Immunity for Precision Oncology
Date: 10 February (in person)
VHIO hosts: Josep Tabernero, VHIO's Director & Paolo Nuciforo, PI, Molecular Oncology

Speaker: Gerard I. Evan, Sir William Dunn Professor and Head of Biochemistry Department, University of Cambridge, UK.
Talk title: Switching the tumor immune microenvironment on and off with Myc
Date: 14 February (in person)
VHIO host: Laura Soucek, PI, Mouse Models of Cancer Therapies

Speaker: Gabriel Adrian Rabinovich, Vice-Director and Group Leader of Functional Glycomics and Head of Immunopathology, the Instituto de Biologia y Medicina Experimental (IBYME), Buenos Aires, Argentina.
Talk title: The emerging role of glycocheckpoints: the sweet side of cancer immunotherapy
Date: 06 March (in person)
VHIO host: Laura Soucek, PI, Mouse Models of Cancer Therapies

Speaker: Violeta Serra, PI, VHIO's Experimental Therapeutics Group
Talk title: Clinically relevant biomarkers of PARP1 inhibitor resistance and indicators of targeted combinatorial treatments
Date: 24 April (online)

Speaker: Raffaela Di Micco, Group Leader at San Raffaele Telethon Institute for Gene Therapy, Italy.
Talk title: Dissecting mechanisms of acute myeloid leukemia response to therapy and relapse
Date: 08 May (online)
VHIO host: Maria Abad, PI, Cellular Plasticity & Cancer

Speaker: Fran Balkwill, Professor of Cancer Biology, BartsCancer Institute, Queen Mary University of London (UK)
Talk title: Modelling and targeting the ovarian cancer microenvironment
Date: 22 May (online)
VHIO host: Laura Soucek, PI, Mouse Models of Cancer

Speaker: Oscar Fernández, Vice Director and Head of the Genomic Instability Group, Spanish National Cancer Research Center (CNIO), Madrid.
Talk title: Nucleolar Stress as a driver (and a vulnerability) in cancer
Date: 05 June (online)
VHIO host: Joan Seoane, Director of Translational Research at VHIO

Speaker: Maria Mittelbrunn, Associate Member, Head of Immunometabolism and Inflammation Lab, Centre for Molecular Biology «Severo Ochoa» (CBMSO), Madrid.
Talk title: Stressed T cells induce multimorbidity and premature senescence
Date: 19 June (online)
VHIO host: Maria Abad, PI, Cellular Plasticity & Cancer

Speaker: Alberto Bardelli, Director of Laboratory Molecular Oncology at the Candiolo Cancer Institute IRCCS and Associate Professor at the Department of Oncology, University of Turin, IRCCS, Italy.
Talk title: Inactivation of DNA repair and high dose Vitamin C boost cancer immunotherapy
Date: 03 July (online)
VHIO host: Joan Seoane, Director of Translational Research

Speaker: Roger Paredes, Chief of Section at the HIV Unit, Hospital Germans Trias i Pujol and Head of the Microbial Genomics Group at the IrsiCaixa AIDS Research Institute, Badalona, Catalonia, Spain.
Talk title: The human microbiome in HIV and cancer: what can we learn?
Date: 17 July (online)
VHIO host: Paolo Nuciforo, PI, Molecular Oncology

Speaker: Maurizio Scaltriti, Maurizio Scaltriti, Associate Laboratory Member, Human Oncology & Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York, USA
Talk title: Genomic dependencies and vulnerabilities in solid tumors
Date: 08 September (online)
VHIO host: Josep Tabernero, VHIO's Director

Speaker: Andrea Alimonti, Group Leader, Molecular Oncology and Mouse Models, Institute of Oncology Research, Bellinzona, Switzerland.
Talk title: Targeting MDSC for prostate cancer therapy
Date: 18 September (online)
VHIO host: Joaquin Mateo, PI, Prostate Cancer Translational Research

Speaker: Jose Antonio Seoane, Instructor, Curtis Lab, Cancer Computational and Systems Biology Group, Stanford Cancer Institute, California, USA.
Talk title: Role of chromatin regulatory genes in breast cancer
Date: 22 September (online)
VHIO host: Josep Tabernero, VHIO's Director

Speaker: Chris Lord, Deputy Head of Division, Team Leader of the CRUK Gene Function Laboratory and Professor of Cancer Genomics in the Breast Cancer Now Toby Robins Research Centre at The Institute of Cancer Research, London, UK.
Talk title: Exploiting synthetic lethality in the design of new therapeutic approaches for cancer
Date: 02 October (online)
VHIO hosts: Violeta Serra, PI, Experimental Therapeutics & Judith Balmaña, PI, Hereditary Cancer Genetics

Speaker: Marc Landanyi, Attending Pathologist and and Chief of the Molecular Diagnostics Service and Member in the Human Oncology & Pathogenesis Program at Memorial Sloan Kettering Cancer Center (MSKCC), New York, USA.
Talk title: Clinical Cancer Genomics: Lessons and Insights from 50,000 patients with advanced solid tumors
Date: 16 October (online)
VHIO host: César Serrano, PI, Sarcoma Translational

Speaker: Mariano Barbacid, Mariano Barbacid, Head of the Laboratory of Experimental Oncology, AXA-CNIO Professor of Molecular Oncology, CNIO, Madrid, Spain.
Talk title: Targeting KRAS mutant tumors: Light at the end of the tunnel
Date: 30 October (online)
VHIO host: Laura Soucek, PI, Mouse Models of Cancer Therapies

Speaker: Luís Enjuanes, CSIC Research Professor, Head of the Laboratory of Replication, Virus-Host Interactions and Protection in Coronavirus. National Biotechnology Center (CNB), Madrid. Spain.
Talk title: SARS-2 Human Coronavirus: pathology and protection
Date: 20 November 2020 (online)
VHIO host: Maria Abad, PI, Cellular Plasticity & Cancer

Speaker: Antonis Antoniou, Professor of Cancer Risk Prediction, Academic Course Director for the MPhil in Epidemiology, University of Cambridge, London, UK.
Talk title: Breast and ovarian cancer risk stratification: progress and challenges
Date: 27 November (online)
VHIO hosts: Judith Balmaña & Sara Gutiérrez-Enríquez, Judith Balmaña and Sara Gutiérrez, PI and Senior Scientist, respectively, Hereditary Cancer Genetics

Speaker: Amparo Cano, Full Professor, Department of Biochemistry, School of Medicine, Autonomous University of Madrid, Spain.
Talk title: LOXl2, Snail1 and E2A interplay in the regulation of breast cancer initiation and metastasis
Date: 11 December (online)
VHIO host: Josep Villanueva, PI, Tumor Biomarkers

Ad-hoc courses, workshops & 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, VHIO organized and hosted a total of 18 Courses, Workshops, Observerships and Perceptorships in 2020. Naturally, due to the COVID-19 pandemic, the majority of these were conducted virtually, online.

1.Sesión de Actualización en Terapias Dirigidas en Pacientes EGFR y ALK, 31 January. Coordinator: Enriqueta Felip, PI, VHIO's Thoracic Tumors & Head and Neck Cancer Group. 2. Preceptorship en Cáncer de Ovario, 06 March. Scientific Coordinator and Academic Tutor: Ana Oaknin, PI, VHIO's Gynecological Malignancies Group. 3. Preceptorship en Genética del Cáncer Hereditario, 17 July. Director: Judith Balmaña, PI, VHIO's Hereditary Cancer Genetics Group. 4. Masterclass en gestión sanitaria: las claves de un modelo de excelencia en MM y LLC, 17 September. Directors: Juan José Lahuerta, Head, Hematology Service, the 12 de Octubre University Hospital, Madrid, & Francesc Bosch, PI, VHIO's Experimental Hematology Group.

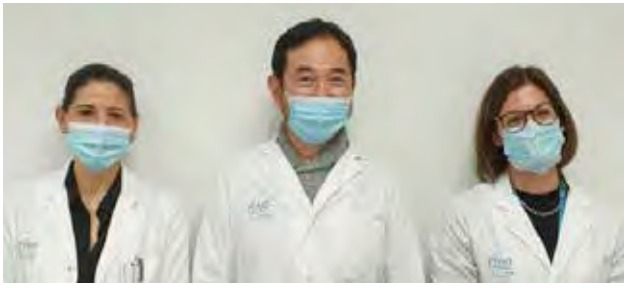
BENCH ST RMING SEMINARS

Established back in February 2016 by co-Founders Verónica Rodilla, a former Post-Doctoral Fellow of VHIO's Growth Factors Group (PI: Joaquín Arribas), and Jordi Martínez Quintanilla, Post-Doctoral Fellow of our Stem Cells & Cancer Group (PI: Héctor G. Palmer), our series of Benchstoming 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.

In 2019 Elena Senís, Post-Doctoral Fellow of VHIO's Cellular Plasticity & Cancer Group (PI: Maria Abad) and Benchstorming Co-Chair, announced that Chiara Bellio, Post-Doctoral Fellow of VHIO's Tumor Biomarkers Group (PI: Josep Villanueva), had taken over the reins from previous Co-Chair Toni Jauset, a former member of VHIO's Mouse Models of Cancer Therapies Group (PI: Laura Soucek).

At the end of 2020, Elena Senís stood down as Benchstorming co-Chair, and Sara Simonetti, Attending Physician of VHIO's Molecular Oncology Group (PI: Paolo Nuciforo), and Tian Tian, Post-Doctoral Fellow of our Chromatin Dynamics in Cancer Group (PI: Sandra Peiró), joined Chiara as Benchstorming co-Chairs. We take this opportunity to thank Elena for her hard work and dedication.



Our Benchstorming co-Chairs (left to right): Sara SImonetti, Tian Tian and Chiara Bellio.

In 2020, 11 Benchstorming Sessions took place, during which each invited VHIO investigator discussed and 'benchstormed' their respective research areas. Each session is graded by all attendees and one presenter is announced as winner of the best presentation. Emanuela Greco, Graduate Student of our Cellular Plasticity & Cancer Group (PI: María Abad), was 'crowned' for her presentation from season one: *MIDORI micropeptide: when epithelial-to-mesenchymal transition commits hara-kiri.*

Emanuela Greco, Graduate Student of our Cellular Plasticity & Cancer Group (PI: María Abad), was announced as the best 'Benchstormer' for her presentation during season one: *MIDORI micropeptide: when epithelial-to-mesenchymal transition commits hara-kiri.*

VHIO's public engagement & outreach

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, youngsters and non-specialized adult 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. We will continue to identify, lead and participate in all these precious initiatives and launch new ones based on identified opportunities.

In addition to VHIO's comprehensive lay media program and the invited participation and presence of our researchers and clinical investigators across a broad range of communication channels, as well as campaigns tailored to our social media platforms and respective target audiences, VHIO led and/or participated in over 20 public outreach events, programs and fundraising initiatives.

Due to the COVID-19 pandemic, many of our planned activities had to be cancelled. The majority those that could go ahead were either conducted virtually, or carried out in strict accordance with the stipulated social distancing rules and required safety measures.

Illustrative of these efforts, we take this opportunity to mention just a few of the many highlights in 2020:

6th edition of our annual breast cancer workshops, aimed at cancer patients, their friends and families, and the general public. These meetings are coordinated by Marta Capelan (featured in photos 2 and 4 below), Medical Oncologist and Clinical Investigator of VHIO's Breast Cancer Group (PI: Cristina Saura). Organized in collaboration with the Vall d'Hebron University Hospital's Breast Cancer Unit and other expert teams across the Vall d'Hebron Barcelona Hospital Campus, these workshops were supported by Pfizer this year.

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

Selected international media were invited by Barcelona Global to meet out research teams, and learn more about our various activities and programs. Hosted by VHIO, this event took place on 23 January, prior to the outbreak of the COVID-19 pandemic. This meeting was hosted by VHIO's Enriqueta Felip (PI: Thoracic Tumors & Head and Neck Cancer Group), on behalf of our Director, Josep Tabernero, who could not attend due to prior engagements.

To mark World Cancer Day, February 04, 2020, VHIO's Judith Balmaña (PI: Hereditary Cancer Genetics Group), Laura Soucek (PI: Mouse Models of Cancer Therapies Group), and Elena Garralda (PI: VHIO's Early Clinical Drug Development Group, and Director of our Research Unit for Molecular Cancer Therapy of Cancer – UITM, CaixaResearch), were invited among other leading experts in oncology across the Vall d'Hebron Barcelona Hospital Campus, to participate as panelists and speakers.

Including the participation of cancer patients, and aimed at the general public at large, this special session addressed key topics including the latest advancements and novel therapies in oncology driven through research, cancer prevention, and important aspects regarding the wellbeing and care of people suffering from this disease.

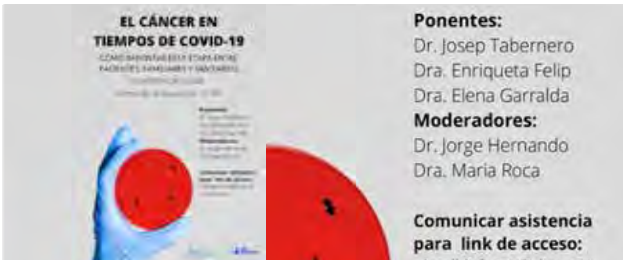
VHIO invesigators joined together with other reasearchers and healthcare professionals in oncology at Vall d'Hebron to mark World Cancer Day 2020.

Aimed at patients suffering from colorectal cancer, their friends and families, and organized within the scope of the COLOSSUS and MoTriColor consortia (see pages 175-177) an early evening session exploring the latest developments in the diagnosis and treatment of this tumor type, provided the perfect forum for interactive debate and a special Q&A session between experts in oncology and those effected and touched by this disease. This workshop was moderated by VHIO's Rodrigo Dienstmann (PI: Oncology Data Science –ODysSEy- Group).

Aimed at patients, their families and friends, VHIO co-organized a special workshop to update on the very latest developments in the diagnosis and treatment of colorectal cancer.

Specifically organized for cancer patients, their families and friends, a virtual conference was organized by VHIO to discuss and update on new measures, protocols, and infrastructures in place as a response to the COVID-19 pandemic. Expert speakers included Josep Tabernero (VHIO's Director), Enriqueta Felip (PI: Thoracic Tumors & Head and Neck Cancer Group), and Elena Garralda

(PI: VHIO's Early Clinical Drug Development Group, and Director of our Research Unit for Molecular Cancer Therapy of Cancer – UITM, CaixaResearch).



An HUVH-VHIO virtual conference aimed at patients, their families and caregivers in oncology, focused on how best to afront cancer in the COVID-19 era.

Launched back in 2016 by the *Asociación Española Contra el Cáncer* (Spanish Association against Cancer – AECC), and officially co-promoted in collaboration with leading organizations and Societies in oncology, World Cancer Research Day (WCRD) is held annually on 24 September to encourage the active involvement of citizens, institutions and leaders across various fields to support the advancement of research against cancer.

In celebration of WCRD 2020, the AECC organized a timely Dialogue Session focused on COVID-19 and the effects on cancer research as well as possible future implications for investigation. The discussion streamed live and counted on the presence of two renowned leaders in oncology, VHIO's Director and Head of the Medical Oncology Department at Vall d'Hebron, Josep Tabernero, and Mariano Barbacid, AXA-CNIO Professor of Molecular Oncology, the Spanish National Cancer Research Centre, Madrid.

Moderated by Spanish journalist, Purificación Beltrán, and joined by the other invited panelists, Isabel Orbe, Director General of AECC's Scientific Foundation, Marta Pujol, Director of Biomedical Research of AECC's Scientific Foundation, as well as Belén Pastor, an AECC-supported cancer researcher at the Valencian Institute of Oncology (IVO), conversations also centered on the importance of increased investment in cancer science and clinical research, incentives to nurture, grow and support the careers of researchers in Spain, and the strengthening of national cancer planning.

AECC's World Cancer Day 2020 streamed Dialogue Session (left to right): Isabel Orbe, Director General of AECC's Scientific Foundation, Purificación Beltrán (Moderator), Mariano Barbacid, AXA-CNIO Professor of Molecular Oncology, Spanish National Cancer Research Centre (CNIO), Marta Pujol, Director of Biomedical Research of AECC's Scientific Foundation, Josep Tabernero, VHIO's Director, and Belén Pastor, cancer researcher at the Valencian Institute of Oncology (IVO).

Pau Donés y Jarabe Contra el Cáncer. Regarding the amazing support that VHIO receives from individuals, we were all deeply saddened by the passing of Pau Donés, singer, songwriter, guitarist and leader of the renowned Spanish rock group *Jarabe de Palo*, who, having been diagnosed with colorectal cancer in 2015, succumbed to his disease in June 2020.

Receiving treatment at our Vall d'Hebron University Hospital (HUVH), and cared for by our medical teams and specialists, particularly Elena Élez, Medical Oncologist and Clinical Investigator of our Gastrointestinal & Endocrine Tumors Group, he was a treasured patient, friend, and an ardent believer in the importance of research against cancer.

To raise funds for research at VHIO, he not only organized four sell-out concerts (see photo collage below), but also spoke out to raise awareness on and around cancer. As Pau Donés prepared for his death, he contacted journalist Jordi Évole to discuss his final fundraising initiative against cancer. *Eso que tú me das* –the title of one of his very last songs recorded with and his band, *Jarabe de Palo*, was to be the title of the documentary and very final interview, which broadcasted in cinemas across Spain, following his passing.

Directed by Ramón Lara and Jordi Évole, and produced by *Producciones del Barrio y Atresmedia*, proceeds will help to support new VHIO research projects aimed at solving cancer sooner.

One of Pau Donés' fundraising concerts in 2018: Jarabe y Amigos Contra el Cáncer – in support of research at VHIO. Photo collage: Jarabe de Palo.

The Backstage 'Let's talk about sarcoma' documentary launched online in October 2020. This project was initiated two years ago by the family of patient treated at Vall d'Hebron who passed away from a sarcoma. More specifically, Carlota Coloma, Executive Producer and Founder of 15LFilms led the documentary in the memory of her mother in order to offer support to other patients and families going through a similar experience by explaining how cancer researchers and clinical investigators are determinedly working together to develop more effective and precise therapies against this tumor type.

Funded through a dedicated crowdfunding initiative, as well as support received from the Spanish Association against Cancer (AECC), Spanish Society of Medical Oncology (SEOM), Spanish Association of those Affected by Sarcomas (AEAS), Spanish Group of Investigation into Sarcomas (GEIS), and the Mari Paz Jiménez Casado Foundation, this documentary was filmed at the Vall d'Hebron University Hospital and captured the day to day of professionals leading research and treatment against sarcomas, including VHIO's César Serrano (PI: Sarcoma Translational Research Group) Ana Vivancos (PI: Cancer Genomics Group), Claudia Valverde, Medical Oncologist and Clinical Investigator of our Genitourinary, CNS Tumors, and Sarcoma Group (PI: Joan Carles), as well Manolo Pérez, a specialized surgeon in sarcoma at Vall d'Hebron.

The Movember movement against prostate cancer: much more than moustaches. November, celebrated globally throughout the month of November, was established back in 2003 by a few friends over a beer in a pub in Melbourne, Australia. Since then, this public awareness movement has gathered tremendous momentum worldwide. These collective efforts aim at reversing the burden of this disease which is the second most common cancer in men, with more than 1.3 million registered cases each year.

In celebration of Movember and to help raise funds for research against prostate cancer, a group of healthcare professionals and researchers from our Vall d'Hebron Barcelona Hospital Campus, set up its official VHIO-HUVH Movember Team page (pictured below), with Nicolas Herranz, an investigator of VHIO's Prostate Cancer Translational Research Group, directed by Joaquin Mateo , as the captain for their 2020 campaign.

HUVH-VHIO Movember movement: raising awareness on the importance of research against prostate cancer.

escolaciència

Prior to the COVID-19 pandemic, this dedicated VHIO educational program (established back in 2017) once again welcomed under-twelves from 3 local primary schools – Escolas Samaranch, Mireia, and Virolai, to meet our faculty, tour our laboratories and learn more about cancer biology and research.

The main objectives of this outreach program are to teach young and inquisitive minds about the importance of research in solving cancer sooner, how we at VHIO conduct our investigations, and to hopefully inspire some to ultimately become the next generation of cancer scientists.

During their half day visits our young visitors participated in junior masterclasses and hands-on activities to explain the origins and development of cancer, led and supervised by VHIO faculty. In view of the tremendous success and excellent feedback received from the students and teachers, we will continue to open our doors to all primary schools who wish to participate in this program, with dates already in the diary for 2021 – pandemic restrictions permitting.

VHIO's Schools and Science educational program.

The 2020 expansion of VHIO's social media channels & platforms

In addition to VHIO's comprehensive lay media program and the invited participation and presence of our researchers and clinical investigators across a broad range of communication channels, we continue to expand our outreach through news announcements, campaigns, images, and videos tailored to our social media platforms and respective target audiences.

Joining our established profiles and presence on LinkedIn and Twitter, we are pleased to announce that 2020 celebrated the launch of both VHIO's Facebook and Instagram accounts.

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 2020

In 2020, 387 scientific articles were published by VHIO researchers as corresponding/senior or co-authors.

Figure I

Number of articles published by VHIO researchers from 2007 - 2020

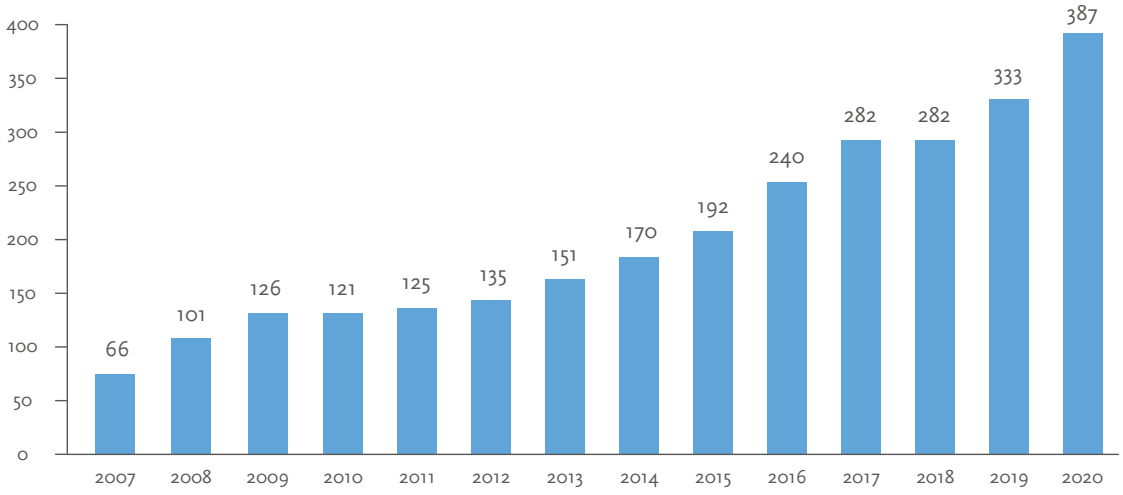
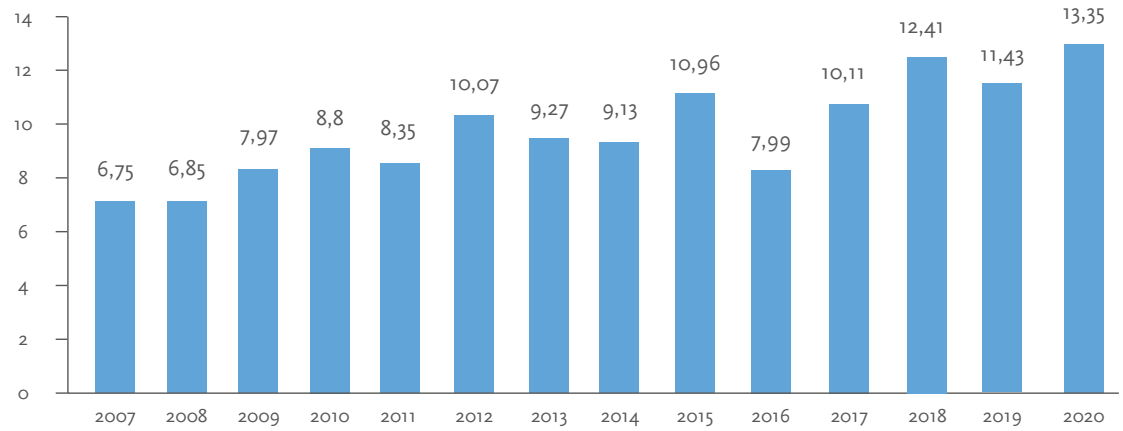


Figure II

Median Impact Factor of papers published by VHIO faculty from 2007 - 2020



For the complete list of VHIO scientific articles published in 2020 in journals with allocated Impact Factor please see pages 148-171. To browse our selection of most relevant articles by VHIO researchers published in 2020 please refer to pages 53-61 of this Scientific Report.

To view our Principal Investigators' selection of a maximum of 4 top papers per group please see respective team pages (sub-section *PI paper pick*). To access each group's full list of publications in 2020, as compiled by our Principal Investigators, visit the extended version of our Scientific Report online at: **http://memorias.vhio.net/2020**

SELECTION OF SOME OF THE MOST RELEVANT ARTICLES BY VHIO RESEARCHERS PUBLISHED IN 2020

Below is a selected list of articles published by VHIO researchers in 2020 with respective Impact Factors indicated. For the complete list of scientific articles published in 2020 in journals with allocated Impact Factor please see pages 148-171**.**

Enhancing global access to cancer medicines. Cortes, Javier; Perez-Garcia, Jose Manuel; Llombart-Cussac, Antonio; Curigliano, Giuseppe; El Saghir, Nagi S.; Cardoso, Fatima; Barrios, Carlos H.; Wagle, Shama; Roman, Javier; Harbeck, Nadia; Eniu, Alexandru; Kaufman, Peter A.; Tabernero, Josep; Garcia-Estevez, Laura; Schmid, Peter; Arribas, Joaquin. 2020. *CA Cancer J Clin.* 70(2): 105 - 124. IF: 292,278.

Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer. Hussain M; Mateo J; Fizazi K; Saad F; Shore N; Sandhu S; Chi KN; Sartor O; Agarwal N; Olmos D; Thiery-Vuillemin A; Twardowski P; Roubaud G; Özgüroglu M; Kang J; Burgents J; Gresty C; Corcoran C; Adelman CA; de Bono J; PROfound Trial Investigators. 2020. *N Engl J Med.* 383(24): 2345 - 2357. IF: 74,699.

Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer. André T; Shiu KK; Kim TW; Jensen BV; Jensen LH; Punt C; Smith D; Garcia-Carbonero R; Benavides M; Gibbs P; de la Fouchardiere C; Rivera F; Elez E; Bendell J; Le DT; Yoshino T; Van Cutsem E; Yang P; Farooqui MZH; Marinello P; Diaz LA Jr; KEYNOTE-177 Investigators. 2020. *N Engl J Med.* 383(23): 2207 - 2218. IF: 74,699.

First-Line Lorlatinib or Crizotinib in Advanced ALK-Positive Lung Cancer. Shaw AT; Bauer TM; de Marinis F; Felip E; Goto Y; Liu G; Mazieres J; Kim DW; Mok T; Polli A; Thurm H; Calella AM; Peltz G; Solomon BJ; CROWN Trial Investigators. 2020. *N Engl J Med.* 383(21): 2018 - 2029. IF: 74,699.

Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. Herbst RS; Giaccone G; de Marinis F; Reinmuth N; Vergnenegre A; Barrios CH; Morise M; Felip E; Andric Z; Geater S; Özgüroglu M; Zou W; Sandler A; Enquist I; Komatsubara K; Deng Y; Kuriki H; Wen X; McCleland M; Mocci S; Jassem J; Spigel DR. 2020. *N Engl J Med.* 383(14): 1328 - 1339. IF: 74,699.

Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. Paik PK; Felip E; Veillon R; Sakai H; Cortot AB; Garassino MC; Mazieres J; Viteri S; Senellart H; Van Meerbeeck J; Raskin J; Reinmuth N; Conte P; Kowalski D; Cho BC; Patel JD; Horn L; Griesinger F; Han JY; Kim YC; Chang GC; Tsai CL; Yang JC; Chen YM; Smit EF; van der Wekken AJ; Kato T; Juraeva D; Stroh C; Bruns R; Straub J; Johne A; Scheele J; Heymach JV; Le X. 2020. *N Engl J Med.* 383(10): 931 - 943. IF: 74,699.

Capmatinib in MET Exon 14-Mutated or MET-Amplified Non-Small-Cell Lung Cancer. Wolf, Juergen; Seto, Takashi; Han, Ji-Youn; Reguart, Noemi; Garon, Edward B.; Groen, Harry J. M.; Tan, Daniel S. W.; Hida, Toyoaki; de Jonge, Maja; Orlov, Sergey V.; Smit, Egbert F.; Souquet, Pierre-Jean; Vansteenkiste, Johan; Hochmair, Maximilian; Felip, Enriqueta; Nishio, Makoto; Thomas, Michael; Ohashi, Kadoaki; Toyozawa, Ryo; Overbeck, Tobias R.; de Marinis, Filippo; Kim, Tae-Min; Laack, Eckart; Robeva, Anna; Le Mouhaer, Sylvie; Waldron-Lynch, Maeve; Sankaran, Banu; Balbin, O. Alejandro; Cui, Xiaoming; Giovannini, Monica; Akimov, Mikhail; Heist, Rebecca S.; GEOMETRY Mono-1. 2020. *N Engl J Med.* 383(10): 944 - 957. IF: 74,699.

Efficacy of Selpercatinib in RET Fusion-Positive Non-Small-Cell Lung Cancer. Drilon, A.; Oxnard, G. R.; Tan, D. S. W.; Loong, H. H. F.; Johnson, M.; Gainor, J.; McCoach, C. E.; Gautschi, O.; Besse, B.; Cho, B. C.; Peled, N.; Weiss, J.; Kim, Y. -J.; Ohe, Y.; Nishio, M.; Park, K.; Patel, J.; Seto, T.; Sakamoto, T.; Rosen, E.; Shah, M. H.; Barlesi, F.; Cassier, P. A.; Bazhenova, L.; De Braud, F.; Garralda, E.; Velcheti, V.; Satouchi, M.; Ohashi, K.; Pennell, N. A.; Reckamp, K. L.; Dy, G. K.; Wolf, J.; Solomon, B.; Falchook, G.; Ebata, K.; Nguyen, M.; Nair, B.; Zhu, E. Y.; Yang, L.; Huang, X.; Olek, E.; Rothenberg, S. M.; Goto, K.; Subbiah, V. 2020. *N Engl J Med.* 383(9): 813 - 824. IF: 74,699.

Olaparib for Metastatic Castration-Resistant Prostate Cancer. de Bono J; Mateo J; Fizazi K; Saad F; Shore N; Sandhu S; Chi KN; Sartor O; Agarwal N; Olmos D; Thiery-Vuillemin A; Twardowski P; Mehra N; Goessl C; Kang J; Burgents J; Wu W; Kohlmann A; Adelman CA; Hussain M. 2020. *N Engl J Med.* 382(22): 2091 - 2102. IF: 74,699.

Pembrolizumab for Early Triple-Negative Breast Cancer. Schmid, Peter; Cortes, Javier; Pusztai, Lajos; McArthur, Heather; Kuemmel, Sherko; Bergh, Jonas; Denkert, Carsten; Park, Yeon Hee; Hui, Rina; Harbeck, Nadia; Takahashi, Masato; Foukakis, Theodoros; Fasching, Peter A.; Cardoso, Fatima; Untch, Michael; Jia, Liyi; Karantza, Vassiliki; Zhao, Jing; Aktan, Gursel; Dent, Rebecca; O'Shaughnessy, Joyce; Keynote-522 Investigators. 2020. *N Engl J Med.* 382(9): 810 - 821. IF: 74,699.

Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. Murthy RK; Loi S; Okines A; Paplomata E; Hamilton E; Hurvitz SA; Lin NU; Borges V; Abramson V; Anders C; Bedard PL; Oliveira M; Jakobsen E; Bachelot T; Shachar SS; Müller V; Braga S; Duhoux FP; Greil R; Cameron D; Carey LA; Curigliano G; Gelmon K; Hortobagyi G; Krop I; Loibl S; Pegram M; Slamon D; Palanca-Wessels MC; Walker L; Feng W; Winer EP. 2020. *N Engl J Med.* 382(7): 597 - 609. IF: 74,699.

Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer. Modi S; Saura C; Yamashita T; Park YH; Kim SB; Tamura K; Andre F; Iwata H; Ito Y; Tsurutani J; Sohn J; Denduluri N; Perrin C; Aogi K; Tokunaga E; Im SA; Lee KS; Hurvitz SA; Cortes J; Lee C; Chen S; Zhang L; Shahidi J; Yver A; Krop I; DESTINY-Breast01 Investigators. 2020. *N Engl J Med.* 382(7): 610 - 621. IF: 74,699.

Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial. Cortes J; Cescon DW; Rugo HS; Nowecki Z; Im SA; Yusof MM; Gallardo C; Lipatov O; Barrios CH; Holgado E; Iwata H; Masuda N; Otero MT; Gokmen E; Loi S; Guo Z; Zhao J; Aktan G; Karantza V; Schmid P; KEYNOTE-355 Investigators. 2020. *Lancet.* 396(10265): 1817 - 1828. IF: 60,392.

Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. Grosicki S; Simonova M; Spicka I; Pour L; Kriachok I; Gavriatopoulou M; Pylypenko H; Auner HW; Leleu X; Doronin V; Usenko G; Bahlis NJ; Hajek R; Benjamin R; Dolai TK; Sinha DK; Venner CP; Garg M; Gironella M; Jurczyszyn A; Robak P; Galli M; Wallington-Beddoe C; Radinoff A; Salogub G; Stevens DA; Basu S; Liberati AM; Quach H; Goranova-Marinova VS; Bila J; Katodritou E; Oliynyk H; Korenkova S; Kumar J; Jagannath S; Moreau P; Levy M; White D; Gatt ME; Facon T; Mateos MV; Cavo M; Reece D; Anderson LD Jr; Saint-Martin JR; Jeha

J; Joshi AA; Chai Y; Li L; Peddagali V; Arazy M; Shah J; Shacham S; Kauffman MG; Dimopoulos MA; Richardson PG; Delimpasi S. 2020. *Lancet.* 396(10262): 1563 - 1573. IF: 60,392.

Support systems to guide clinical decision-making in precision oncology: The Cancer Core Europe Molecular Tumor Board Portal. Tamborero D; Dienstmann R; Rachid MH; Boekel J; Baird R; Braña I; De Petris L; Yachnin J; Massard C; Opdam FL; Schlenk R; Vernieri C; Garralda E; Masucci M; Villalobos X; Chavarria E; Cancer Core Europe consortium; Calvo F; Fröhling S; Eggermont A; Apolone G; Voest EE; Caldas C; Tabernero J; Ernberg I; Rodon J; Lehtiö J. 2020. *Nat Med.* 26(7): 992 - 994. IF: 36,130.

BL-8040, a CXCR4 antagonist, in combination with pembrolizumab and chemotherapy for pancreatic cancer: the COMBAT trial. Bockorny B; Semenisty V; Macarulla T; Borazanci E; Wolpin BM; Stemmer SM; Golan T; Geva R; Borad MJ; Pedersen KS; Park JO; Ramirez RA; Abad DG; Feliu J; Muñoz A; Ponz-Sarvise M; Peled A; Lustig TM; Bohana-Kashtan O; Shaw SM; Sorani E; Chaney M; Kadosh S; Vainstein Haras A; Von Hoff DD; Hidalgo M. 2020. *Nat Med.* 26(6): 878 - 885. IF: 36,130.

Caring for patients with cancer in the COVID-19 era. van de Haar J; Hoes LR; Coles CE; Seamon K; Fröhling S; Jäger D; Valenza F; de Braud F; De Petris L; Bergh J; Ernberg I; Besse B; Barlesi F; Garralda E; Piris-Giménez A; Baumann M; Apolone G; Soria JC; Tabernero J; Caldas C; Voest EE. 2020. *Nat Med.* 26(5): 665 - 671. IF: 36,130.

Durvalumab alone and durvalumab plus tremelimumab versus chemotherapy in previously untreated patients with unresectable, locally advanced or metastatic urothelial carcinoma (DANUBE): a randomised, open-label, multicentre, phase 3 trial. Powles T; van der Heijden MS; Castellano D; Galsky MD; Loriot Y; Petrylak DP; Ogawa O; Park SH; Lee JL; De Giorgi U; Bögemann M; Bamias A; Eigl BJ; Gurney H; Mukherjee SD; Fradet Y; Skoneczna I; Tsiatas M; Novikov A; Suárez C; Fay AP; Duran I; Necchi A; Wildsmith S; He P; Angra N; Gupta AK; Levin W; Bellmunt J; DANUBE study investigators. 2020. *Lancet Oncol.* 21(12): 1574 - 1588. IF: 33,752.

Neoadjuvant chemotherapy and nivolumab in resectable non-small-cell lung cancer (NADIM): an open-label, multicentre, single-arm, phase 2 trial. Provencio M; 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; Casarrubios M; Salas Antón C; Parra ER; Wistuba I; Calvo V; Laza-Briviesca R; Romero A; Massuti B; Cruz-Bermúdez A. 2020. *Lancet Oncol.* 21(11): 1413 - 1422. IF: 33,752.

Quality of life in patients with metastatic prostate cancer following treatment with cabazitaxel versus abiraterone or enzalutamide (CARD): an analysis of a randomised, multicentre, open-label, phase 4 study. Fizazi K; Kramer G; Eymard JC; Sternberg CN; de Bono J; Castellano D; Tombal B; Wülfing C; Liontos M; Carles J; Iacovelli R; Melichar B; Sverrisdóttir Á; Theodore C; Feyerabend S; Helissey C; Oudard S; Facchini G; Poole EM; Ozatilgan A; Geffriaud-Ricouard C; Bensfia S; de Wit R. 2020. *Lancet Oncol.* 21(11): 1513 - 1525. IF: 33,752.

A multivariable prognostic score to guide systemic therapy in early-stage HER2-positive breast cancer: a retrospective study with an external evaluation. Prat A; Guarneri V; Paré L; Griguolo G; Pascual T; Dieci MV; Chic N; González-Farré B; Frassoldati A; Sanfeliu E; Cejalvo JM; Muñoz M; Bisagni G; Brasó-Maristany F; Urso L; Vidal M; Brandes AA; Adamo B; Musolino A; Miglietta F; Conte B; Oliveira M; Saura C; Pernas S; Alarcón J; Llombart-Cussac A; Cortés J; Manso L; López R; Ciruelos E; Schettini F; Villagrasa P; Carey LA; Perou CM; Piacentini F; D'Amico R; Tagliafico E; Parker JS; Conte P. 2020. *Lancet Oncol.* 21(11): 1455 - 1464. IF: 33,752.

Trastuzumab emtansine plus atezolizumab versus trastuzumab emtansine plus placebo in previously treated, HER2-positive advanced breast cancer (KATE2): a phase 2, multicentre, randomised, double-blind trial. Emens LA; Esteva FJ; Beresford M; Saura C; De Laurentiis M; Kim SB; Im SA; Wang Y; Salgado R; Mani A; Shah J; Lambertini C; Liu H; de Haas SL; Patre M; Loi S. 2020. *Lancet Oncol.* 21(10): 1283 - 1295. IF: 33,752.

Dabrafenib plus trametinib in patients with BRAF(V600E)-mutated biliary tract cancer (ROAR): a phase 2, open-label, single-arm, multicentre basket trial. Subbiah, Vivek; Lassen, Ulrik; Elez, Elena; Italiano, Antoine; Curigliano, Giuseppe; Javle, Milind; de Braud, Filippo; Prager, Gerald W.; Greil, Richard; Stein, Alexander; Fasolo, Angelica; Schellens, Jan H. M.; Wen, Patrick Y.; Viele, Kert; Boran, Aislyn D.; Gasal, Eduard; Burgess, Paul; Ilankumaran, Palanichamy; Wainberg, Zev A. 2020. *Lancet Oncol.* 21(9): 1234 - 1243. IF: 33,752.

Ripretinib in patients with advanced gastrointestinal stromal tumours (INVICTUS): a double-blind, randomised, placebo-controlled, phase 3 trial. Blay JY; Serrano C; Heinrich MC; Zalcberg J; Bauer S; Gelderblom H; Schöffski P; Jones RL; Attia S; D'Amato G; Chi P; Reichardt P; Meade J; Shi K; Ruiz-Soto R; George S; von Mehren M. 2020. *Lancet Oncol.* 21(7): 923 - 934. IF: 33,752.

Avapritinib in advanced PDGFRA D842V-mutant gastrointestinal stromal tumour (NAVIGATOR): a multicentre, open-label, phase 1 trial. Heinrich MC; Jones RL; von Mehren M; Schöffski P; Serrano C; Kang YK; Cassier PA; Mir O; Eskens F; Tap WD; Rutkowski P; Chawla SP; Trent J; Tugnait M; Evans EK; Lauz T; Zhou T; Roche M; Wolf BB; Bauer S; George S. 2020. *Lancet Oncol.* 21(7): 935 - 946. IF: 33,752.

COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Garassino MC; Whisenant JG; Huang LC; Trama A; Torri V; Agustoni F; Baena J; Banna G; Berardi R; Bettini AC; Bria E; Brighenti M; Cadranel J; De Toma A; Chini C; Cortellini A; Felip E; Finocchiaro G; Garrido P; Genova C; Giusti R; Gregorc V; Grossi F; Grosso F; Intagliata S; La Verde N; Liu SV; Mazieres J; Mercadante E; Michielin O; Minuti G; Moro-Sibilot D; Pasello G; Passaro A; Scotti V; Solli P; Stroppa E; Tiseo M; Viscardi G; Voltolini L; Wu YL; Zai S; Pancaldi V; Dingemans AM; Van Meerbeeck J; Barlesi F; Wakelee H; Peters S; Horn L; TERAVOLT investigators. 2020. *Lancet Oncol.* 21(7): 914 - 922. IF: 33,752.

Ivosidenib in IDH1-mutant, chemotherapy-refractory cholangiocarcinoma (ClarIDHy): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study. Abou-Alfa GK; Macarulla T; Javle MM; Kelley RK; Lubner SJ; Adeva J; Cleary JM; Catenacci DV; Borad MJ; Bridgewater J; Harris WP; Murphy AG; Oh DY; Whisenant J; Lowery MA; Goyal L; Shroff RT; El-Khoueiry AB; Fan B; Wu B; Chamberlain CX; Jiang L; Gliser C; Pandya SS; Valle JW; Zhu AX. 2020. *Lancet Oncol.* 21(6): 796 - 807. IF: 33,752.

Rucaparib for patients with platinum-sensitive, recurrent ovarian carcinoma (ARIEL3): post-progression outcomes and updated safety results from a randomised, placebo-controlled, phase 3 trial. Ledermann JA; 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; O'Malley DM; Armstrong DK; Banerjee S; García-Donas J; Swisher EM; Cameron T; Maloney L; Goble S; Coleman RL. 2020. *Lancet Oncol.* 21(5): 710 - 722. IF: 33,752.

Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind,

randomised, placebo-controlled, phase 3 study. Swain SM; Miles D; Kim SB; Im YH; Im SA; Semiglazov V; Ciruelos E; Schneeweiss A; Loi S; Monturus E; Clark E; Knott A; Restuccia E; Benyunes MC; Cortés J; CLEOPATRA study group. 2020. *Lancet Oncol.* 21(4): 519 - 530. IF: 33,752.

Patient-reported outcomes following pembrolizumab or placebo plus pemetrexed and platinum in patients with previously untreated, metastatic, non-squamous non-small-cell lung cancer (KEYNOTE-189): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Garassino MC; Gadgeel S; Esteban E; Felip E; Speranza G; Domine M; Hochmair MJ; Powell S; Cheng SY; Bischoff HG; Peled N; Reck M; Hui R; Garon EB; Boyer M; Wei Z; Burke T; Pietanza MC; Rodríguez-Abreu D. 2020. *Lancet Oncol.* 21(3): 387 - 397. IF: 33,752.

Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial. Mateo J; Porta N; Bianchini D; McGovern U; Elliott T; Jones R; Syndikus I; Ralph C; Jain S; Varughese M; Parikh O; Crabb S; Robinson A; McLaren D; Birtle A; Tanguay J; Miranda S; Figueiredo I; Seed G; Bertan C; Flohr P; Ebbs B; Rescigno P; Fowler G; Ferreira A; Riisnaes R; Pereira R; Curcean A; Chandler R; Clarke M; Gurel B; Crespo M; Nava Rodrigues D; Sandhu S; Espinasse A; Chatfield P; Tunariu N; Yuan W; Hall E; Carreira S; de Bono JS. 2020. *Lancet Oncol.* 21(1): 162 - 174. IF: 33,752.

Ribociclib plus letrozole versus chemotherapy for postmenopausal women with hormone receptor-positive, HER2-negative, luminal B breast cancer (CORALLEEN): an open-label, multicentre, randomised, phase 2 trial. Prat A; Saura C; Pascual T; Hernando C; Muñoz M; Paré L; González Farré B; Fernández PL; Galván P; Chic N; González Farré X; Oliveira M; Gil-Gil M; Arumi M; Ferrer N; Montaño A; Izarzugaza Y; Llombart-Cussac A; Bratos R; González Santiago S; Martínez E; Hoyos S; Rojas B; Virizuela JA; Ortega V; López R; Céliz P; Ciruelos E; Villagrasa P; Gavilá J. 2020. *Lancet Oncol.* 21(1): 33 - 43. IF: 33,752.

First-in-Human Phase I Study of Iadademstat (ORY-1001): A First-in-Class Lysine-Specific Histone Demethylase 1A Inhibitor, in Relapsed or Refractory Acute Myeloid *Leukemia.* Salamero O; Montesinos P; Willekens C; Pérez-Simón JA; Pigneux A; Récher C; Popat R; Carpio C; Molinero C; Mascaró C; Vila J; Arévalo MI; Maes T; Buesa C; Bosch F; Somervaille TCP. 2020. *J Clin Oncol.* 38(36): 4260 - 4273. IF: 32,956.

Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2-, Node-Positive, High-Risk, Early Breast Cancer (monarchE). Johnston SRD; Harbeck N; Hegg R; Toi M; Martin M; Shao ZM; Zhang QY; Martinez Rodriguez JL; Campone M; Hamilton E; Sohn J; Guarneri V; Okada M; Boyle F; Neven P; Cortés J; Huober J; Wardley A; Tolaney SM; Cicin I; Smith IC; Frenzel M; Headley D; Wei R; San Antonio B; Hulstijn M; Cox J; O'Shaughnessy J; Rastogi P; monarchE Committee Members and Investigators. 2020. *J Clin Oncol.* 38(34): 3987 - 3998. IF: 32,956.

Brigatinib Versus Crizotinib in Advanced ALK Inhibitor-Naive ALK-Positive Non-Small Cell Lung Cancer: Second Interim Analysis of the Phase III ALTA-1L Trial. Camidge DR; Kim HR; Ahn MJ; Yang JCH; Han JY; Hochmair MJ; Lee KH; Delmonte A; García Campelo MR; Kim DW; Griesinger F; Felip E; Califano R; Spira A; Gettinger SN; Tiseo M; Lin HM; Gupta N; Hanley MJ; Ni Q; Zhang P; Popat S. 2020. *J Clin Oncol.* 38(31): 3592 - 3603. IF: 32,956.

Efficacy of Maintenance Olaparib for Patients With Newly Diagnosed Advanced Ovarian Cancer With a BRCA Mutation: Subgroup Analysis Findings From the SOLO1 Trial. DiSilvestro P; Colombo N; Scambia G; Kim BG; Oaknin A; Friedlander M; Lisyanskaya A; Floquet A; Leary A; Sonke GS; Gourley C; Banerjee S; Oza A; González-Martín A; Aghajanian CA; Bradley WH; Mathews CA; Liu J; Lowe ES; Bloomfield R; Moore KN. 2020. *J Clin Oncol.* 38(30): 3528 - 3537. IF: 32,956.

Patient-Centered Outcomes in ARIEL3, a Phase III, Randomized, Placebo-Controlled Trial of Rucaparib Maintenance Treatment in Patients With Recurrent Ovarian Carcinoma. 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; O'Malley DM; Armstrong DK; Banerjee S; García-Donas J; Swisher EM; Cella D; Meunier J; Goble S; Cameron T; Maloney L; Mörk AC; Bedel J; Ledermann JA; Coleman RL. 2020. *J Clin Oncol.* 38(30): 3494 - 3505. IF: 32,956.

Neratinib Plus Capecitabine Versus Lapatinib Plus Capecitabine in HER2-Positive Metastatic Breast Cancer Previously Treated With ≥ 2 HER2-Directed Regimens: Phase III NALA Trial. Saura C; Oliveira M; Feng YH; Dai MS; Chen SW; Hurvitz SA; Kim SB; Moy B; Delaloge S; Gradishar W; Masuda N; Palacova M; Trudeau ME; Mattson J; Yap YS; Hou MF; De Laurentiis M; Yeh YM; Chang HT; Yau T; Wildiers H; Haley B; Fagnani D; Lu YS; Crown J; Lin J; Takahashi M; Takano T; Yamaguchi M; Fujii T; Yao B; Bebchuk J; Keyvanjah K; Bryce R; Brufsky A; NALA Investigators. 2020. *J Clin Oncol.* 38(27): 3138 - 3149. IF: 32,956 .

Randomized Phase III Trial of Pegvorhyaluronidase Alfa With Nab-Paclitaxel Plus Gemcitabine for Patients With Hyaluronan-High Metastatic Pancreatic Adenocarcinoma. Van Cutsem E; Tempero MA; Sigal D; Oh DY; Fazio N; Macarulla T; Hitre E; Hammel P; Hendifar AE; Bates SE; Li CP; Hingorani SR; de la Fouchardiere C; Kasi A; Heinemann V; Maraveyas A; Bahary N; Layos L; Sahai V; Zheng L; Lacy J; Park JO; Portales F; Oberstein P; Wu W; Chondros D; Bullock AJ; HALO 109-301 Investigators. 2020. *J Clin Oncol.* 38(27): 3185 - 3194. IF: 32,956.

Lenvatinib Plus Pembrolizumab in Patients With Advanced Endometrial Cancer. Makker V; Taylor MH; Aghajanian C; Oaknin A; Mier J; Cohn AL; Romeo M; Bratos R; Brose MS; DiSimone C; Messing M; Stepan DE; Dutcus CE; Wu J; Schmidt EV; Orlowski R; Sachdev P; Shumaker R; Casado Herraez A. 2020. *J Clin Oncol.* 38(26): 2981 - 2992. IF: 32,956.

Pregnancy After Breast Cancer in Patients With Germline BRCA Mutations. Lambertini M; Ameye L; Hamy AS; Zingarello A; Poorvu PD; Carrasco E; Grinshpun A; Han S; Rousset-Jablonski C; Ferrari A; Paluch-Shimon S; Cortesi L; Senechal C; Miolo G; Pogoda K; Pérez-Fidalgo JA; De Marchis L; Ponzone R; Livraghi L; Estevez-Diz MDP; Villarreal-Garza C; Dieci MV; Clatot F; Berlière M; Graffeo R; Teixeira L; Córdoba O; Sonnenblick A; Luna Pais H; Ignatiadis M; Paesmans M; Partridge AH; Caron O; Saule C; Del Mastro L; Peccatori FA; Azim HA. 2020. *J Clin Oncol.* 38(26): 3012 - 3023. IF: 32,956.

PD-1 Blockade in Anaplastic Thyroid Carcinoma. Capdevila J; Wirth LJ; Ernst T; Ponce Aix S; Lin CC; Ramlau R; Butler MO; Delord JP; Gelderblom H; Ascierto PA; Fasolo A; Führer D; Hütter-Krönke ML; Forde PM; Wrona A; Santoro A; Sadow PM; Szpakowski S; Wu H; Bostel G; Faris J; Cameron S; Varga A; Taylor M. 2020. *J Clin Oncol.* 38(23): 2620 - 2627. IF: 32,956.

Intracranial Efficacy and Survival With Tucatinib Plus Trastuzumab and Capecitabine for Previously Treated HER2-Positive Breast Cancer With Brain Metastases in the HER2CLIMB Trial. Lin NU; Borges V; Anders C; Murthy RK; Paplomata E; Hamilton E; Hurvitz S; Loi S; Okines A; Abramson V; Bedard PL; Oliveira M; Mueller V; Zelnak A; DiGiovanna MP; Bachelot T; Chien AJ; O'Regan R; Wardley A; Conlin A; Cameron D; Carey L; Curigliano G; Gelmon K; Loibl S; Mayor J; McGoldrick

S; An X; Winer EP. 2020. *J Clin Oncol.* 38(23): 2610 - 2619. IF: 32,956.

Pembrolizumab or Placebo Plus Etoposide and Platinum as First-Line Therapy for Extensive-Stage Small-Cell Lung Cancer: Randomized, Double-Blind, Phase III KEYNOTE-604 Study. Rudin CM; Awad MM; Navarro A; Gottfried M; Peters S; Csoszi T; Cheema PK; Rodriguez-Abreu D; Wollner M; Yang JC; Mazieres J; Orlandi FJ; Luft A; Gümüs M; Kato T; Kalemkerian GP; Luo Y; Ebiana V; Pietanza MC; Kim HR; KEYNOTE-604 Investigators. 2020. *J Clin Oncol.* 38(21): 2369 - 2379. IF: 32 ,956.

HER2-Low Breast Cancer: Pathological and Clinical Landscape.Tarantino P; Hamilton E; Tolaney SM; Cortes J; Morganti S; Ferraro E; Marra A; Viale G; Trapani D; Cardoso F; Penault-Llorca F; Viale G; Andrè F; Curigliano G. 2020. *J Clin Oncol.* 38(17): 1951 - 1962. IF: 32,956.

Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non-Small-Cell Lung Cancer. Gadgeel S; Rodríguez-Abreu D; Speranza G; Esteban E; Felip E; Dómine M; Hui R; Hochmair MJ; Clingan P; Powell SF; Cheng SY; Bischoff HG; Peled N; Grossi F; Jennens RR; Reck M; Garon EB; Novello S; Rubio-Viqueira B; Boyer M; Kurata T; Gray JE; Yang J; Bas T; Pietanza MC; Garassino MC. 2020. *J Clin Oncol.* 38(14): 1505 - 1517. IF: 32,956.

Geographic and Ethnic Heterogeneity of Germline BRCA1 or BRCA2 Mutation Prevalence Among Patients With Metastatic Pancreatic Cancer Screened for Entry Into the POLO Trial. Golan, Talia; Kindler, Hedy L.; Park, Joon Oh; Reni, Michele; Macarulla, Teresa; Hammel, Pascal; Van Cutsem, Eric; Arnold, Dirk; Hochhauser, Daniel; McGuinness, David; Locker, Gershon Y.; Goranova, Teodora; Schatz, Philipp; Liu, Yu-Zhen; Hall, Michael J. 2020. *J Clin Oncol.* 38(13): 1442 - 1454. IF: 32,956.

Standard Anthracycline Based Versus Docetaxel-Capecitabine in Early High Clinical and/or Genomic Risk Breast Cancer in the EORTC 10041/BIG 3-04 MINDACT Phase III Trial. Delaloge S; Piccart M; Rutgers E; Litière S; van 't Veer LJ; van den Berkmortel F; Brain E; Dudek-Peric A; Gil-Gil M; Gomez P; Hilbers FS; Khalil Z; Knox S; Kuemmel S; Kunz G; Lesur A; Pierga JY; Ravdin P; Rubio IT; Saghatchian M; Smilde TJ; Thompson AM; Viale G; Zoppoli G; Vuylsteke P; Tryfonidis K; Poncet C; Bogaerts J; Cardoso F; MINDACT investigators and the TRANSBIG Consortium. 2020. *J Clin Oncol.* 38(11): 1186 - 1197. IF: 32,956.

Cancer Risks Associated With Germline PALB2 Pathogenic Variants: An International Study of 524 Families.Yang X; Leslie G; Doroszuk A; Schneider S; Allen J; Decker B; Dunning AM; Redman J; Scarth J; Plaskocinska I; Luccarini C; Shah M; Pooley K; Dorling L; Lee A; Adank MA; Adlard J; Aittomäki K; Andrulis IL; Ang P; Barwell J; Bernstein JL; Bobolis K; Borg Å; Blomqvist C; Claes KBM; Concannon P; Cuggia A; Culver JO; Damiola F; de Pauw A; Diez O; Dolinsky JS; Domchek SM; Engel C; Evans DG; Fostira F; Garber J; Golmard L; Goode EL; Gruber SB; Hahnen E; Hake C; Heikkinen T; Hurley JE; Janavicius R; Kleibl Z; Kleiblova P; Konstantopoulou I; Kvist A; Laduca H; Lee ASG; Lesueur F; Maher ER; Mannermaa A; Manoukian S; McFarland R; McKinnon W; Meindl A; Metcalfe K; Mohd Taib NA; Moilanen J; Nathanson KL; Neuhausen S; Ng PS; Nguyen-Dumont T; Nielsen SM; Obermair F; Offit K; Olopade OI; Ottini L; Penkert J; Pylkäs K; Radice P; Ramus SJ; Rudaitis V; Side L; Silva-Smith R; Silvestri V; Skytte AB; Slavin T; Soukupova J; Tondini C; Trainer AH; Unzeitig G; Usha L; van Overeem Hansen T; Whitworth J; Wood M; Yip CH; Yoon SY; Yussuf A; Zogopoulos G; Goldgar D; Hopper JL; Chenevix-Trench G; Pharoah P; George SHL; Balmaña J; et al.... 2020. *J Clin Oncol.* 38(7): 674 - 685. IF: 32,956.

Capivasertib Plus Paclitaxel Versus Placebo Plus Paclitaxel As First-Line Therapy for Metastatic Triple-Negative Breast Cancer: The PAKT Trial. Schmid, Peter; Abraham, Jacinta; Chan, Stephen; Wheatley, Duncan; Brunt, Adrian Murray; Nemsadze, Gia; Baird, Richard D.; Park, Yeon Hee; Hall, Peter S.; Perren, Timothy; Stein, Robert C.; Mangel, Laszlo; Ferrero, Jean-Marc; Phillips, Melissa; Conibear, John; Cortes, Javier; Foxley, Andrew; de Bruin, Elza C.; McEwen, Robert; Stetson, Daniel; Dougherty, Brian; Sarker, Shah-Jalal; Prendergast, Aaron; McLaughlin-Callan, Max; Burgess, Matthew; Lawrence, Cheryl; Cartwright, Hayley; Mousa, Kelly; Turner, Nicholas C. 2020. *J Clin Oncol.* 10;38(5):423-433. IF: 32,956.

Phase II Open-Label Study of Pembrolizumab in Treatment-Refractory, Microsatellite Instability-High/Mismatch Repair-Deficient Metastatic Colorectal Cancer: KEYNOTE-164. Le DT; Kim TW; Van Cutsem E; Geva R; Jäger D; Hara H; Burge M; O'Neil B; Kavan P; Yoshino T; Guimbaud R; Taniguchi H; Elez E; Al-Batran SE; Boland PM; Crocenzi T; Atreya CE; Cui Y; Dai T; Marinello P; Diaz LA; André T. 2020. *J Clin Oncol.* 38(1): 11 - 19. IF: 32,956.

RBMS1 Suppresses Colon Cancer Metastasis through Targeted Stabilization of Its mRNA Regulon. Yu J; Navickas A; Asgharian H; Culbertson B; Fish L; Garcia K; Olegario JP; Dermit M; Dodel M; Hanisch B; Luo Y; Weinberg EM; Dienstmann R; Warren RS; Mardakheh FK; Goodarzi H. 2020. *Cancer Discov.* 10(9): 1410 - 1423. IF: 29,497.

MYC Instructs and Maintains Pancreatic Adenocarcinoma Phenotype. Sodir NM; Kortlever RM; Barthet VJA; Campos T; Pellegrinet L; Kupczak S; Anastasiou P; Brown Swigart L; Soucek L; Arends MJ; Littlewood TD; Evan GI. 2020. *Cancer Discov.* 10(4): 588 - 607. IF: 29,497.

Efficacy and Determinants of Response to HER Kinase Inhibition in HER2-Mutant Metastatic Breast Cancer. Smyth LM; Piha-Paul SA; Won HH; Schram AM; Saura C; Loi S; Lu J; Shapiro GI; Juric D; Mayer IA; Arteaga CL; de la Fuente MI; Brufksy AM; Spanggaard I; Mau-Sorensen M; Arnedos M; Moreno V; Boni V; Sohn J; Schwartzberg LS; Gonzalez-Farre X; Cervantes A; Bidard FC; Gorelick AN; Lanman RB; Nagy RJ; Ulaner GA; Chandarlapaty S; Jhaveri K; Gavrila EI; Zimel C; Selcuklu SD; Melcer M; Samoila A; Cai Y; Scaltriti M; Mann G; Xu F; Eli LD; Dujka M; Lalani AS; Bryce R; Baselga J; Taylor BS; Solit DB; Meric-Bernstam F; Hyman DM. 2020. *Cancer Discov.* 10(2): 198 - 213. IF: 29,497.

Clinical portrait of the SARS-CoV-2 epidemic in European cancer patients. Pinato DJ; Zambelli A; Aguilar-Company J; Bower M; Sng C; Salazar R; Bertuzzi A; Brunet J; Mesia R; Segui E; Biello F; Generali D; Grisanti S; Rizzo G; Libertini M; Maconi A; Harbeck N; Vincenzi B; Bertulli R; Ottaviani D; Carbo A; Bruna R; Benafif S; Marrari A; Wuerstlein R; Carmona-Garcia MC; Chopra N; Tondini C; Mirallas O; Tovazzi V; Betti M; Provenzano S; Fotia V; Cruz CA; Dalla Pria A; D'Avanzo F; Evans JS; Saoudi-Gonzalez N; Felip E; Galazi M; Garcia-Fructuoso I; Lee AJX; Newsom-Davis T; Patriarca A; Garcia-Illescas D; Reyes R; Dileo P; Sharkey R; Wong YNS; Ferrante D; Marco-Hernandez J; Sureda A; Maluquer C; Ruiz-Camps I; Gaidano G; Rimassa L; Chiudinelli L; Izuzquiza M; Cabirta A; Franchi M; Santoro A; Prat A; Tabernero J; Gennari A. 2020. *Cancer Discov.* 10(10): 1465 - 1474. IF: 29,497.

Recognizing hypoxia in phaeochromocytomas and paragangliomas. Dahia PLM; Toledo RA. 2020. *Nat Rev Endocrinol.* 16(4): 191 - 192. IF: 28,800.

CTCF is dispensable for immune cell transdifferentiation but facilitates an acute inflammatory response. Stik G; Vidal E; Barrero M; Cuartero S; Vila-Casadesús M; Mendieta-Esteban J; Tian TV; Choi J; Berenguer C; Abad A; Borsari B; le Dily F; Cramer P; Marti-Renom MA;

Stadhouders R; Graf T. 2020. *Nat Genet.* 52(7): 655 - 661. IF: 27,603.

Genome-wide association study identifies 32 novel breast cancer susceptibility loci from overall and subtype-specific analyses. Zhang H; Ahearn TU; Lecarpentier J; Barnes D; Beesley J; Qi G; Jiang X; O'Mara TA; Zhao N; Bolla MK; Dunning AM; Dennis J; Wang Q; Ful ZA; Aittomäki K; Andrulis IL; Anton-Culver H; Arndt V; Aronson KJ; Arun BK; Auer PL; Azzollini J; Barrowdale D; Becher H; Beckmann MW; Behrens S; Benitez J; Bermisheva M; Bialkowska K; Blanco A; Blomqvist C; Bogdanova NV; Bojesen SE; Bonanni B; Bondavalli D; Borg A; Brauch H; Brenner H; Briceno I; Broeks A; Brucker SY; Brüning T; Burwinkel B; Buys SS; Byers H; Caldés T; Caligo MA; Calvello M; Campa D; Castelao JE; Chang-Claude J; Chanock SJ; Christiaens M; Christiansen H; Chung WK; Claes KBM; Clarke CL; Cornelissen S; Couch FJ; Cox A; Cross SS; Czene K; Daly MB; Devilee P; Diez O; et al....2020. *Nat Genet.* 52(6): 572 - 581. IF: 27,603.

A harmonized meta-knowledgebase of clinical interpretations of somatic genomic variants in cancer. Wagner AH; Walsh B; Mayfield G; Tamborero D; Sonkin D; Krysiak K; Deu-Pons J; Duren RP; Gao J; McMurry J; Patterson S; Del Vecchio Fitz C; Pitel BA; Sezerman OU; Ellrott K; Warner JL; Rieke DT; Aittokallio T; Cerami E; Ritter DI; Schriml LM; Freimuth RR; Haendel M; Raca G; Madhavan S; Baudis M; Beckmann JS; Dienstmann R; Chakravarty D; Li XS; Mockus S; Elemento O; Schultz N; Lopez-Bigas N; Lawler M; Goecks J; Griffith M; Griffith OL; Margolin AA; Variant Interpretation for Cancer Consortium. 2020. *Nat Genet.* 52(4): 448 - 457. IF: 27,603.

Fine-mapping of 150 breast cancer risk regions identifies 191 likely target genes. Fachal L; Aschard H; Beesley J; Barnes DR; Allen J; Kar S; Pooley KA; Dennis J; Michailidou K; Turman C; Soucy P; Lemaçon A; Lush M; Tyrer JP; Ghoussaini M; Moradi Marjaneh M; Jiang X; Agata S; Aittomäki K; Alonso MR; Andrulis IL; Anton-Culver H; Antonenkova NN; Arason A; Arndt V; Aronson KJ; Arun BK; Auber B; Auer PL; Azzollini J; Balmaña J; et al.... 2020. *Nat Genet.* 52(1): 56 - 73. IF: 27,603.

The Effective Targeting of KRAS G12C Elusiveness. Elez E; Tabernero J. 2020. *Cancer Cell.* 38(6): 785 - 787. IF: 26,602.

Metabolic Imaging Detects Resistance to PI3Ka Inhibition Mediated by Persistent FOXM1 Expression in ER(+) Breast Cancer. Ros S; Wright AJ; D'Santos P; Hu DE; Hesketh RL; Lubling Y; Georgopoulou D; Lerda G; Couturier DL; Razavi P; Pelossof R; Batra AS; Mannion E; Lewis DY; Martin A; Baird RD; Oliveira M; de Boo LW; Linn SC; Scaltriti M; Rueda OM; Bruna A; Caldas C; Brindle KM. 2020. *Cancer Cell.* 38(4): 516 - 516. IF: 26,602.

Safety and efficacy of nazartinib (EGF816) in adults with EGFR-mutant non-small-cell lung carcinoma: a multicentre, open-label, phase 1 study. Tan DS; Leighl NB; Riely GJ; Yang JC; Sequist LV; Wolf J; Seto T; Felip E; Aix SP; Jonnaert M; Pan C; Tan EY; Ko J; Moody SE; Kim DW. 2020. *Lancet Respir Med.* 8(6): 561 - 572. IF: 25,094.

Efficacy and Safety of Pembrolizumab or Pembrolizumab Plus Chemotherapy vs Chemotherapy Alone for Patients With First-line, Advanced Gastric Cancer: The KEYNOTE-062 Phase 3 Randomized Clinical Trial. Shitara K; Van Cutsem E; Bang YJ; Fuchs C; Wyrwicz L; Lee KW; Kudaba I; Garrido M; Chung HC; Lee J; Castro HR; Mansoor W; Braghiroli MI; Karaseva N; Caglevic C; Villanueva L; Goekkurt E; Satake H; Enzinger P; Alsina M; Benson A; Chao J; Ko AH; Wainberg ZA; Kher U; Shah S; Kang SP; Tabernero J. 2020. *JAMA Oncol.* 6(10): 1571 - 1580. IF: 24,799.

Characterization of the Cancer Spectrum in Men With Germline BRCA1 and BRCA2 Pathogenic Variants: Results From the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA). Silvestri V; Leslie G; Barnes DR; and the CIMBA Group; Agnarsson BA; Aittomäki K; Alducci E; Andrulis IL; Barkardottir RB; Barroso A; Barrowdale D; Benitez J; Bonanni B; Borg A; Buys SS; Caldés T; Caligo MA; Capalbo C; Campbell I; Chung WK; Claes KBM; Colonna SV; Cortesi L; Couch FJ; de la Hoya M; Diez O; et al.... 2020. *JAMA Oncol.* 6(8): 1218 - 1230. IF: 24,799.

Efficacy and Safety of Trastuzumab Emtansine Plus Capecitabine vs Trastuzumab Emtansine Alone in Patients With Previously Treated ERBB2 (HER2)-Positive Metastatic Breast Cancer: A Phase 1 and Randomized Phase 2 Trial. Cortés J; Diéras V; Lorenzen S; Montemurro F; Riera-Knorrenschild J; Thuss-Patience P; Allegrini G; De Laurentiis M; Lohrisch C; Oravcová E; Perez-Garcia JM; Ricci F; Sakaeva D; Serpanchy R; Šufliarský J; Vidal M; Irahara N; Wohlfarth C; Aout M; Gelmon K. 2020. *JAMA Oncol.* 6(8): 1203 - 1209. IF: 24,799.

Efficacy and Safety of Trifluridine/Tipiracil Treatment in Patients With Metastatic Gastric Cancer Who Had Undergone Gastrectomy Subgroup Analyses of a Randomized Clinical Trial. Ilson DH; Tabernero J; Prokharau A; Arkenau HT; Ghidini M; Fujitani K; Van Cutsem E; Thuss-Patience P; Beretta GD; Mansoor W; Zhavrid E; Alsina M; George B; Catenacci D; McGuigan S; Makris L; Doi T; Shitara K. 2020. *JAMA Oncol.* 6(1). IF: 24,799.

Clinical Activity and Safety of the Anti-Programmed Death 1 Monoclonal Antibody Dostarlimab for Patients With Recurrent or Advanced Mismatch Repair-Deficient Endometrial Cancer: A Nonrandomized Phase 1 Clinical Trial. Oaknin A; Tinker AV; Gilbert L; Samouëlian V; Mathews C; Brown J; Barretina-Ginesta MP; Moreno V; Gravina A; Abdeddaim C; Banerjee S; Guo W; Danaee H; Im E; Sabatier R. 2020. *JAMA Oncol.* 6(11): 1-7. IF: 24,799.

ESMO recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer. Miller RE; Leary A; Scott CL; Serra V; Lord CJ; Bowtell D; Chang DK; Garsed DW; Jonkers J; Ledermann JA; Nik-Zainal S; Ray-Coquard I; Shah SP; Matias-Guiu X; Swisher EM; Yates LR. 2020. *Ann Oncol.* 31(12): 1606 - 1622. IF: 18,274.

5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). Cardoso F; Paluch-Shimon S; Senkus E; Curigliano G; Aapro MS; André F; Barrios CH; Bergh J; Bhattacharyya GS; Biganzoli L; Boyle F; Cardoso MJ; Carey LA; Cortés J; El Saghir NS; Elzayat M; Eniu A; Fallowfield L; Francis PA; Gelmon K; Gligorov J; Haidinger R; Harbeck N; Hu X; Kaufman B; Kaur R; Kiely BE; Kim SB; Lin NU; Mertz SA; Neciosup S; Offersen BV; Ohno S; Pagani O; Prat A; Penault-Llorca F; Rugo HS; Sledge GW; Thomssen C; Vorobiof DA; Wiseman T; Xu B; Norton L; Costa A; Winer EP. 2020. *Ann Oncol.* 31(12): 1623 - 1649. IF: 18,274.

Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group. Mosele F; Remon J; Mateo J; Westphalen CB; Barlesi F; Lolkema MP; Normanno N; Scarpa A; Robson M; Meric-Bernstam F; Wagle N; Stenzinger A; Bonastre J; Bayle A; Michiels S; Bièche I; Rouleau E; Jezdic S; Douillard JY; Reis-Filho JS; Dienstmann R; André F. 2020. *Ann Oncol.* 31(11): 1491 - 1505. IF: 18,274.

Diagnosis and management of tropomyosin receptor kinase (TRK) fusion sarcomas: expert recommendations from the World Sarcoma Network. Demetri GD; Antonescu CR; Bjerkehagen B; Bovée JVMG; Boye K; Chacón M; Dei Tos AP; Desai J; Fletcher JA; Gelderblom H; George S; Gronchi A; Haas RL; Hindi N; Hohenberger P; Joensuu H; Jones RL; Judson I; Kang YK; Kawai A; Lazar AJ; Le Cesne A; Maestro R; Maki RG; Martín J; Patel S; Penault-Llorca F; Raut CP; Rutkowski P; Safwat A; Sbaraglia M; Schaefer IM; Shen L; Serrano C; Schöffski P; Stacchiotti S; Hall KS; Tap

WD; Thomas DM; Trent J; Valverde C; van der Graaf WTA; von Mehren M; Wagner A; Wardelmann E; Naito Y; Zalcberg J; Blay JY. 2020. *Ann Oncol.* 31(11): 1506 - 1517. IF: 18,274.

Fusobacterium nucleatum persistence and risk of recurrence after preoperative treatment in locally advanced rectal cancer. Serna G; Ruiz-Pace F; Hernando J; Alonso L; Fasani R; Landolfi S; Comas R; Jimenez J; Elez E; Bullman S; Meyerson M; Tabernero J; Capdevila J; Dienstmann R; Nuciforo P. 2020. *Ann Oncol.* 31(10): 1366 - 1375. IF: 18,274.

Phase I, first-in-human study of futibatinib, a highly selective, irreversible FGFR1-4 inhibitor in patients with advanced solid tumors. Bahleda R; Meric-Bernstam F; Goyal L; Tran B; He Y; Yamamiya I; Benhadji KA; Matos I; Arkenau HT. 2020. *Ann Oncol.* 31(10): 1405 - 1412. IF: 18,274.

Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. Curigliano G; Banerjee S; Cervantes A; Garassino M; Garrido P; Girard N; Haanen J; Jordan K; Lordick F; Machiels JP; Michielin O; Peters S; Tabernero J; Douillard JY; Pentheroudakis G; all Voting Panel members. 2020. *Ann Oncol.* 31(10): 1320 - 1335. IF: 18,274.

Clinical development of therapies targeting TGFß: current knowledge and future perspectives. Ciardiello D; Elez E; Tabernero J; Seoane J. 2020. *Ann Oncol.* 31(10): 1336 - 1349. IF: 18,274.

Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Argiles G; Tabernero J; Labianca R; Hochhauser D; Salazar R; Iveson T; Laurent-Puig P; Quirke P; Yoshino T; Taieb J; Martinelli E; Arnold D; ESMO Guidelines Committee. 2020. *Ann Oncol.* 31(10): 1291 - 1305. IF: 18,274.

Trifluridine/tipiracil plus bevacizumab in patients with untreated metastatic colorectal cancer ineligible for intensive therapy: the randomized 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; Kanehisa A; Egorov A; Aubel P; Amellal N; Moiseenko V. 2020. *Ann Oncol.* 31(9): 1160 - 1168. IF: 18,274.

JSCO-ESMO-ASCO-JSMO-TOS: international expert consensus recommendations for tumour-agnostic treatments in patients with solid tumours with microsatellite instability or NTRK fusions. Yoshino T; Pentheroudakis G; Mishima S; Overman MJ; Yeh KH; Baba E; Naito Y; Calvo F; Saxena A; Chen LT; Takeda M; Cervantes A; Taniguchi H; Yoshida K; Kodera Y; Kitagawa Y; Tabernero J; Burris H; Douillard JY. 2020. *Ann Oncol.* 31(7): 861 - 872. IF: 18,274.

Molecular correlates of response to capmatinib in advanced non-small-cell lung cancer: clinical and biomarker results from a phase I trial. Schuler M; Berardi R; Lim WT; de Jonge M; Bauer TM; Azaro A; Gottfried M; Han JY; Lee DH; Wollner M; Hong DS; Vogel A; Delmonte A; Akimov M; Ghebremariam S; Cui X; Nwana N; Giovannini M; Kim TM. 2020. *Ann Oncol.* 31(6): 789 - 797. IF: 18,274.

Phase I study of CC-90010, a reversible, oral BET inhibitor in patients with advanced solid tumors and relapsed/refractory non-Hodgkin's lymphoma. Moreno V; Sepulveda JM; Vieito M; Hernández-Guerrero T; Doger B; Saavedra O; Ferrero O; Sarmiento R; Arias M; De Alvaro J; Di Martino J; Zuraek M; Sanchez-Pérez T; Aronchik I; Filvaroff EH; Lamba M; Hanna B; Nikolova Z; Brana I. 2020. *Ann Oncol.* 31(6): 780 - 788. IF: 18,274.

Pembrolizumab plus chemotherapy as neoadjuvant treatment of high-risk, early-stage triple-negative breast cancer: results from the phase 1b open-label, multicohort KEYNOTE-173 study. Schmid P; Salgado R; Park YH; Muñoz-Couselo E; Kim SB; Sohn J; Im SA; Foukakis T; Kuemmel S; Dent R; Yin L; Wang A; Tryfonidis K; Karantza V; Cortés J; Loi S. 2020. *Ann Oncol.* 31(5): 569 - 581. IF: 18,274.

Antitumor activity of ipatasertib combined with chemotherapy: results from a phase Ib study in solid tumors. Isakoff SJ; Tabernero J; Molife LR; Soria JC; Cervantes A; Vogelzang NJ; Patel MR; Hussain M; Baron A; Argilés G; Conkling PR; Sampath D; Maslyar D; Patel P; Chan W; Gendreau S; Musib L; Xu N; Ma H; Lin K; Bendell J. 2020. *Ann Oncol.* 31(5): 626 - 633. IF: 18,274.

Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with intermediate and advanced/relapsed hepatocellular carcinoma: a TOS-ESMO initiative endorsed by CSCO, ISMPO, JSMO, KSMO, MOS and SSO. Chen, L.-T.; Martinelli, E.; Cheng, A.-L.; Pentheroudakis, G.; Qin, S.; Bhattacharyya, G.S.; Ikeda, M.; Lim, H.-Y.; Ho, G.F.; Choo, S.P.; Ren, Z.; Malhotra, H.; Ueno, M.; Ryoo, B.-Y.; Kiang, T.C.; Tai, D.; Vogel, A.; Cervantes, A.; Lu, S.-N.; Yen, C.-J.; Huang, Y.-H.; Chen, S.-C.; Hsu, C.; Shen, Y.-C.; Tabernero, J.; Yen, Y.; Hsu, C.-H.; Yoshino, T.; Douillard, J.-Y. 2020. *Ann Oncol.* 31(3): 334 - 351. IF: 18,274.

Genome-wide profiling of non-smoking-related lung cancer cells reveals common RB1 rearrangements associated with histopathologic transformation in EGFR-mutant tumors. Pros E; Saigi M; Alameda D; Gomez-Mariano G; Martinez-Delgado B; Alburquerque-Bejar JJ; Carretero J; Tonda R; Esteve-Codina A; Catala I; Palmero R; Jove M; Lazaro C; Patiño-Garcia A; Gil-Bazo I; Verdura S; Teulé A; Torres-Lanzas J; Sidransky D; Reguart N; Pio R; Juan-Vidal O; Nadal E; Felip E; Montuenga LM; Sanchez-Cespedes M. 2020. *Ann Oncol.* 31(2): 274 - 282. IF: 18,274.

Bevacizumab as adjuvant treatment of colon cancer: updated results from the S-AVANT phase III study by the GERCOR Group. André T; Vernerey D; Im SA; Bodoky G; Buzzoni R; Reingold S; Rivera F; McKendrick J; Scheithauer W; Ravit G; Fountzilas G; Yong WP; Isaacs R; Österlund P; Liang JT; Creemers GJ; Rakez M; Van Cutsem E; Cunningham D; Tabernero J; de Gramont A. 2020. *Ann Oncol.* 31(2): 246 - 256. IF: 18,274.

Cisplatin and 5-fluorouracil with or without epidermal growth factor receptor inhibition panitumumab for patients with non-resectable, advanced or metastatic oesophageal squamous cell cancer: a prospective, open-label, randomised phase III AIO/EORTC trial (POWER). Moehler M; Maderer A; Thuss-Patience PC; Brenner B; Meiler J; Ettrich TJ; Hofheinz RD; Al-Batran SE; Vogel A; Mueller L; Lutz MP; Lordick F; Alsina M; Borchert K; Greil R; Eisterer W; Schad A; Slotta-Huspenina J; Van Cutsem E; Lorenzen S. 2020. *Ann Oncol.* 31(2): 228 - 235. IF: 18,274.

Neutropenia and survival outcomes in metastatic colorectal cancer patients treated with trifluridine/tipiracil in the RECOURSE and J003 trials.Yoshino T; Cleary JM; Van Cutsem E; Mayer RJ; Ohtsu A; Shinozaki E; Falcone A; Yamazaki K; Nishina T; Garcia-Carbonero R; Komatsu Y; Baba H; Argilés G; Tsuji A; Sobrero A; Yamaguchi K; Peeters M; Muro K; Zaniboni A; Sugimoto N; Shimada Y; Tsuji Y; Hochster HS; Moriwaki T; Tran B; Esaki T; Hamada C; Tanase T; Benedetti F; Makris L; Yamashita F; Lenz HJ. 2020. *Ann Oncol.* 31(1): 88 - 95. IF: 18,274.

A phase I dose-escalation study of enzalutamide in combination with the AKT inhibitor AZD5363 (capivasertib) in patients with metastatic castration-resistant prostate cancer. Kolinsky, M.P.; Rescigno, P.; Bianchini, D.; Zafeiriou, Z.; Mehra, N.; Mateo, J.; Michalarea, V.; Riisnaes, R.; Crespo, M.; Figueiredo, I.; Miranda, S.; Nava Rodrigues, D.; Flohr, P.; Tunariu, N.; Banerji, U.; Ruddle, R.; Sharp, A.; Welti, J.; Lambros, M.; Carreira, S.; Raynaud, F.I.; Swales, K.E.;

Plymate, S.; Luo, J.; Tovey, H.; Porta, N.; Slade, R.; Leonard, L.; Hall, E.; de Bono, J.S. 2020. *Ann Oncol.* 31(5): 619 - 625. IF: 18,274.

Advanced Prostate Cancer with ATM Loss: PARP and ATR Inhibitors. Neeb A; Herranz N; Arce-Gallego S; Miranda S; Buroni L; Yuan W; Athie A; Casals T; Carmichael J; Rodrigues DN; Gurel B; Rescigno P; Rekowski J; Welti J; Riisnaes R; Gil V; Ning J; Wagner V; Casanova-Salas I; Cordoba S; Castro N; Fenor de la Maza MD; Seed G; Chandran K; Ferreira A; Figueiredo I; Bertan C; Bianchini D; Aversa C; Paschalis A; Gonzalez M; Morales-Barrera R; Suarez C; Carles J; Swain A; Sharp A; Gil J; Serra V; Lord C; Carreira S; Mateo J; de Bono JS. 2021. *Eur Urol.* 79(2): 200 - 211. Epub 2020 Nov 8. IF: 17,947.

Clinical outcome after progressing to frontline and second-line Anti-PD-1/PD-L1 in advanced urothelial cancer. Gómez de Liaño Lista A; van Dijk N; de Velasco Oria de Rueda G; Necchi A; Lavaud P; Morales-Barrera R; Alonso Gordoa T; Maroto P; Ravaud A; Durán I; Szabados B; Castellano D; Giannatempo P; Loriot Y; Carles J; Anguera Palacios G; Lefort F; Raggi D; Gross Goupil M; Powles T; Van der Heijden MS. 2020. *Eur Urol.* 77(2): 269 - 276. IF: 17,947.

Avadomide monotherapy in relapsed/refractory DLBCL: safety, efficacy, and a predictive gene classifier. Carpio C; Bouabdallah R; Ysebaert L; Sancho JM; Salles GA; Cordoba R; Pinto A; Gharibo M; Rasco D; Panizo C; Lopez-Martin JA; Santoro A; Salar A; Damian S; Martin Garcia-Sancho A; Verhoef G; Van Den Neste EW; Wang M; Couto S; Carrancio S; Weng A; Wang X; Schmitz F; Wei X; Hege KM; Trotter MWB; Risueno A; Buchholz T; Hagner PR; Gandhi AK; Pourdehnad M; Ribrag V. 2020. *Blood.* 135(13): 996 - 1007. IF: 17,543.

Venetoclax-obinutuzumab: harnessing complexity. Abrisqueta, Pau; Bosch, Francesc. 2020. *Blood.* 135(11): 789 - 790. IF: 17,543.

Arterial thrombosis in Philadelphia-negative myeloproliferative neoplasms predicts second cancer: a case-control study. De Stefano V; Ghirardi A; Masciulli A; Carobbio A; Palandri F; Vianelli N; Rossi E; Betti S; Di Veroli A; Iurlo A; Cattaneo D; Finazzi G; Bonifacio M; Scaffidi L; Patriarca A; Rumi E; Casetti IC; Stephenson CIM; Guglielmelli P; Elli EM; Palova M; Rapezzi D; Erez D; Gomez M; Wille K; Perez-Encinas M; Lunghi F; Angona A; Fox ML; Beggiato E; Benevolo G; Carli G; Cacciola R; McMullin MF; Tieghi A; Recasens V; Isfort S; Marchetti M; Griesshammer M; Alvarez-Larran A; Vannucchi AM; Rambaldi A; Barbui T. 2020. *Blood.* 135(5): 381 - 386. IF: 17,543.

Precision Therapy in RAS Mutant Colorectal Cancer. Dienstmann R; Connor K; Byrne AT. 2020. *Gastroenterology.* 158(4): 806 - 811. IF: 17,373.

Colorectal cancer residual disease at maximal response to EGFR blockade displays a druggable Paneth cell-like phenotype. Lupo B; Sassi F; Pinnelli M; Galimi F; Zanella ER; Vurchio V; Migliardi G; Gagliardi PA; Puliafito A; Manganaro D; Luraghi P; Kragh M; Pedersen MW; Horak ID; Boccaccio C; Medico E; Primo L; Nichol D; Spiteri I; Heide T; Vatsiou A; Graham TA; Élez E; Argiles G; Nuciforo P; Sottoriva A; Dienstmann R; Pasini D; Grassi E; Isella C; Bertotti A; Trusolino L. 2020. *Sci Transl Med.* 12(555). IF: 16,304.

The IDH-TAU-EGFR triad defines the neovascular landscape of diffuse gliomas. Gargini R; Segura-Collar B; Herránz B; García-Escudero V; Romero-Bravo A; Núñez FJ; García-Pérez D; Gutiérrez-Guamán J; Ayuso-Sacido A; Seoane J; Pérez-Núñez A; Sepúlveda-Sánchez JM; Hernández-Laín A; Castro MG; García-Escudero R; Ávila J; Sánchez-Gómez P. 2020. *Sci Transl Med.* 12(527). IF: 16,304.

The International Association for the Study of Lung Cancer Global Survey on Molecular Testing in Lung Cancer. Smeltzer MP; Wynes MW; Lantuejoul S; Soo R; Ramalingam SS; Varella-Garcia M; Meadows Taylor M; Richeimer K; Wood K; Howell KE; Dalurzo ML; Felip E; Hollenbeck G; Kerr K; Kim ES; Mathias C; Pacheco J; Postmus P; Powell C; Tsuboi M; Wistuba II; Wakelee HA; Belani CP; Scagliotti GV; Hirsch FR. 2020. *J Thorac Oncol.* 15(9): 1434 - 1448. IF: 13,357.

Bintrafusp Alfa, a Bifunctional Fusion Protein Targeting TGF-ß and PD-L1, in Second-Line Treatment of Patients With NSCLC: Results From an Expansion Cohort of a Phase 1 Trial. Paz-Ares L; Kim TM; Vicente D; Felip E; Lee DH; Lee KH; Lin CC; Flor MJ; Di Nicola M; Alvarez RM; Dussault I; Helwig C; Ojalvo LS; Gulley JL; Cho BC. 2020. *J Thorac Oncol.* 15(7): 1210 – 1222. IF: 13,357.

Final Overall Survival and Other Efficacy and Safety Results From ASCEND-3: Phase II Study of Ceritinib in ALKi-Naive Patients With ALK-Rearranged NSCLC. Nishio M; Felip E; Orlov S; Park K; Yu CJ; Tsai CM; Cobo M; McKeage M; Su WC; Mok T; Scagliotti GV; Spigel DR; Viraswami-Appanna K; Chen Z; Passos VQ; Shaw AT. 2020. *J Thorac Oncol.* 15(4): 609 - 617. IF: 13,357.

Ceritinib plus Nivolumab in Patients with Advanced ALK-Rearranged Non-Small Cell Lung Cancer: Results of an Open-Label, Multicenter, Phase 1B Study. Felip E; de Braud FG; Maur M; Loong HH; Shaw AT; Vansteenkiste JF; John T; Liu G; Lolkema MP; Selvaggi G; Giannone V; Cazorla P; Baum J; Balbin OA; Wang LV; Lau YY; Scott JW; Shao-Weng Tan D. 2020. *J Thorac Oncol.* 15(3): 392 - 403. IF: 13,357.

Evolution and Clinical Impact of EGFR Mutations in Circulating Free DNA in the BELIEF Trial. Molina-Vila MA; Stahel RA; Dafni U; Jordana-Ariza N; Balada-Bel A; Garzón-Ibáñez M; García-Peláez B; Mayo-de-Las-Casas C; Felip E; Fontecedro AC; Gautschi O; Peters S; Massutí B; Palmero R; Aix SP; Carcereny E; Früh M; Pless M; Popat S; Cuffe S; Bidoli P; Kammler R; Roschitzki-Voser H; Tsourti Z; Karachaliou N; Rosell R; results from the European Thoracic Oncology Platform (ETOP) BELIEF trial. 2020. *J Thorac Oncol.* 15(3): 416 - 425. IF: 13,357.

TGFß promotes widespread enhancer chromatin opening and operates on genomic regulatory domains. Guerrero-Martínez JA; Ceballos-Chávez M; Koehler F; Peiró S; Reyes JC. 2020. *Nat Commun.* 11(1): 6196 - 6196. IF: 12,121.

Circulating tumour DNA from the cerebrospinal fluid allows the characterisation and monitoring of medulloblastoma. Escudero, L.; Llort, A.; Arias, A.; Diaz-Navarro, A.; Martínez-Ricarte, F.; Rubio-Perez, C.; Mayor, R.; Caratù, G.; Martínez-Sáez, E.; Vázquez-Méndez, É.; Lesende-Rodríguez, I.; Hladun, R.; Gros, L.; Ramón y Cajal, S.; Poca, M.A.; Puente, X.S.; Sahuquillo, J.; Gallego, S.; Seoane, J. 2020. *Nat Commun.* 11(1): 5376 - 5376. IF: 12,121.

ITGB3-mediated uptake of small extracellular vesicles facilitates intercellular communication in breast cancer cells. Fuentes P; Sesé M; Guijarro PJ; Emperador M; Sánchez-Redondo S; Peinado H; Hümmer S; Ramón Y Cajal S. 2020. *Nat Commun.* 11(1): 4261 - 4261. IF: 12,121.

Multiple low dose therapy as an effective strategy to treat EGFR inhibitor-resistant NSCLC tumours. Fernandes Neto JM; Nadal E; Bosdriesz E; Ooft SN; Farre L; McLean C; Klarenbeek S; Jurgens A; Hagen H; Wang L; Felip E; Martinez-Marti A; Vidal A; Voest E; Wessels LFA; van Tellingen O; Villanueva A; Bernards R. 2020. *Nat Commun.* 11(1): 3157 - 3157. IF: 12,121.

Phenotypic changes of HER2-positive breast cancer during and after dual

HER2 blockade. Brasó-Maristany F; Griguolo G; Pascual T; Paré L; Nuciforo P; Llombart-Cussac A; Bermejo B; Oliveira M; Morales S; Martínez N; Vidal M; Adamo B; Martínez O; Pernas S; López R; Muñoz M; Chic N; Galván P; Garau I; Manso L; Alarcón J; Martínez E; Gregorio S; Gomis RR; Villagrasa P; Cortés J; Ciruelos E; Prat A. 2020. *Nat Commun.* 11(1): 385 - 385. IF: 12,121.

Genomics of lethal prostate cancer at diagnosis and castration resistance. Mateo J; Seed G; Bertan C; Rescigno P; Dolling D; Figueiredo I; Miranda S; Nava Rodrigues D; Gurel B; Clarke M; Atkin M; Chandler R; Messina C; Sumanasuriya S; Bianchini D; Barrero M; Petremolo A; Zafeiriou Z; Fontes MS; Perez-Lopez R; Tunariu N; Fulton BA; Jones R; McGovern UB; Ralph C; Varughese M; Parikh O; Jain S; Elliott T; Sandhu S; Porta N; Hall E; Yuan W; Carreira S; de Bono JS. 2020. *J Clin Invest.* 130(4): 1743 - 1751. IF: 11,864.

Ovarian and Breast Cancer Risks Associated With Pathogenic Variants in RAD51C and RAD51D. Yang X; Song H; Leslie G; Engel C; Hahnen E; Auber B; Horváth J; Kast K; Niederacher D; Turnbull C; Houlston R; Hanson H; Loveday C; Dolinsky JS; LaDuca H; Ramus SJ; Menon U; Rosenthal AN; Jacobs I; Gayther SA; Dicks E; Nevanlinna H; Aittomäki K; Pelttari LM; Ehrencrona H; Borg Å; Kvist A; Rivera B; Hansen TVO; Djursby M; Lee A; Dennis J; Bowtell DD; Traficante N; Diez O; Balmaña J; Gruber SB; Chenevix-Trench G; kConFab Investigators; Jensen A; Kjær SK; Høgdall E; Castéra L; Garber J; Janavicius R; Osorio A; Golmard L; Vega A; Couch FJ; Robson M; Gronwald J; Domchek SM; Culver JO; de la Hoya M; Easton DF; Foulkes WD; Tischkowitz M; Meindl A; Schmutzler RK; Pharoah PDP; Antoniou AC. 2020. *J Natl Cancer Inst.* 112(12): 1242 - 1250. IF: 11,577.

HER2-Enriched Subtype and ERBB2 Expression in HER2-Positive Breast Cancer Treated with Dual HER2 Blockade. Prat A; Pascual T; De Angelis C; Gutierrez C; Llombart-Cussac A; Wang T; Cortés J; Rexer B; Paré L; Forero A; Wolff AC; Morales S; Adamo B; Brasó-Maristany F; Vidal M; Veeraraghavan J; Krop I; Galván P; Pavlick AC; Bermejo B; Izquierdo M; Rodrik-Outmezguine V; Reis-Filho JS; Hilsenbeck SG; Oliveira M; Dieci MV; Griguolo G; Fasani R; Nuciforo P; Parker JS; Conte P; Schiff R; Guarneri V; Osborne CK; Rimawi MF. 2020. *J Natl Cancer Inst.* 112(1): 46 - 54. IF: 11,577.

Cdk9 and H2Bub1 signal to Clr6-CII/Rpd3S to suppress aberrant antisense transcription. Sansó M; Parua PK; Pinto D; Svensson JP; Pagé V; Bitton DA; MacKinnon S; Garcia P; Hidalgo E; Bähler J; Tanny JC; Fisher RP. 2020. *Nucleic Acids Res.* 48(13): 7154 - 7168. IF: 11,501.

Hierarchical chromatin organization detected by TADpole. Soler-Vila P; Cuscó P; Farabella I; Di Stefano M; Marti-Renom MA. 2020. *Nucleic Acids Res.* 48(7): 39 - 39. IF: 11,501.

Hyperprogression and Immunotherapy: Fact, Fiction, or Alternative Fact? Adashek, J.J.; Subbiah, I.M.; Matos, I.; Garralda, E.; Menta, A.K.; Ganeshan, D.M.; Subbiah, V. 2020. *Trends in Cancer.* 181 - 191. IF: 11,093.

Personalized cancer therapy prioritization based on driver alteration co-occurrence patterns. Mateo L; Duran-Frigola M; Gris-Oliver A; Palafox M; Scaltriti M; Razavi P; Chandarlapaty S; Arribas J; Bellet M; Serra V; Aloy P. 2020. *Genome Med.* 12(1): 78 - 78. IF: 10,675.

Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial. Male C; Lensing AWA; Palumbo JS; Kumar R; Nurmeev I; Hege K; Bonnet D; Connor P; Hooimeijer HL; Torres M; Chan AKC; Kenet G; Holzhauer S; Santamaría A; Amedro P; Chalmers E; Simioni P; Bhat RV; Yee DL; Lvova O; Beyer-Westendorf J; Biss TT; Martinelli I; Saracco P; Peters M; Kállay K; Gauger CA; Massicotte MP; Young G; Pap AF; Majumder M; Smith WT; Heubach JF; Berkowitz SD; Thelen K; Kubitza D; Crowther M; Prins MH; Monagle P; EINSTEIN-Jr Phase 3 Investigators. 2020. *Lancet Haematol.* 7(1): e18-e27. IF: 10,406.

Palbociclib and Trastuzumab in HER2-Positive Advanced Breast Cancer: Results from the Phase II SOLTI-1303 PATRICIA Trial. Ciruelos EM; Villagrasa P; Pascual T; Oliveira M; Pernas S; Paré L; Escrivá-de-Romaní S; Manso L; Adamo B; Martínez de Dueñas E; Cortés J; Vázquez S; Perelló A; Garau I; Melé M; Martínez Jañez N; Montaño A; Bermejo B; Morales S; Echarri MJ; Vega E; González-Farré B; Martínez D; Galván P; Canes J; Nuciforo P; Gonzàlez Farré X; Prat A. 2020. *Clin Cancer Res.* 26(22): 5820 - 5829. IF: 10,107.

Phase Ib Dose-escalation/Expansion Trial of Ribociclib in Combination With Everolimus and Exemestane in Postmenopausal Women with HR(+), HER2(-) Advanced Breast Cancer. Bardia A; Modi S; Oliveira M; Cortés J; Campone M; Ma BBY; Dirix LY; Weise A; Hewes B; Diaz-Padilla I; Han Y; Deshpande P; Samant T; Rodriguez Lorenc CK; He W; Su F; Chavez-MacGregor M. 2020. *Clin Cancer Res.* 26(24): 6417 - 6428. IF: 10,107.

Gastrointestinal Stromal Tumor: Challenges and Opportunities for a New Decade. Serrano C; George S. 2020. *Clin Cancer Res.* 26(19): 5078 - 5085. IF: 10,107.

A Phase Ib/II Study of the BRAF Inhibitor Encorafenib Plus the MEK Inhibitor Binimetinib in Patients with BRAF(V600E/K) -mutant Solid Tumors. Sullivan RJ; Weber JS; Patel SP; Dummer R; Carlino MS; Tan DS; Lebbe C; Siena S; Élez E; Wollenberg L; Pickard M; Sandor V; Ascierto PA. 2020. *Clin Cancer Res.* 26(19): 5102 - 5112. IF: 10,107.

First-in-Human Study of AT13148, a Dual ROCK-AKT Inhibitor in Patients with Solid Tumors. McLeod R; Kumar R; Papadatos-Pastos D; Mateo J; Brown J; Ingles Garces AH; Ruddle R; Decordova SA; Jueliger S; Ferraldeschi R; Maiques O; Sanz-Moreno V; Jones P; Traub S; Halbert G; Mellor S; Swales KE; Raynaud FI; Garrett MD; Banerji U. 2020. *Clin Cancer Res.* 26(18): 4777 - 4784. IF: 10,107.

EVOLVE: A Multicenter Open-Label Single-Arm Clinical and Translational Phase II Trial of Cediranib Plus Olaparib for Ovarian Cancer after PARP Inhibition Progression. Lheureux S; Oaknin A; Garg S; Bruce JP; Madariaga A; Dhani NC; Bowering V; White J; Accardi S; Tan Q; Braunstein M; Karakasis K; Cirlan I; Pedersen S; Li T; Fariñas-Madrid L; Lee YC; Liu ZA; Pugh TJ; Oza AM. 2020. *Clin Cancer Res.* 26(16): 4206 - 4215. IF: 10,107.

TCR Repertoire Changes during TIL Expansion: Clonal Selection or Drifting? Lozano-Rabella M; Gros A. 2020. *Clin Cancer Res.* 26(16): 4177 - 4179. IF: 10,107.

Capivasertib, an AKT Kinase Inhibitor, as Monotherapy or in Combination with Fulvestrant in Patients with AKT1 (E17K)-Mutant, ER-Positive Metastatic Breast Cancer. Smyth LM; Tamura K; Oliveira M; Ciruelos EM; Mayer IA; Sablin MP; Biganzoli L; Ambrose HJ; Ashton J; Barnicle A; Cashell DD; Corcoran C; de Bruin EC; Foxley A; Hauser J; Lindemann JPO; Maudsley R; McEwen R; Moschetta M; Pass M; Rowlands V; Schiavon G; Banerji U; Scaltriti M; Taylor BS; Chandarlapaty S; Baselga J; Hyman DM. 2020. *Clin Cancer Res.* 26(15): 3947 - 3957. IF: 10,107.

Patient-Derived Organoids from Multiple Colorectal Cancer Liver Metastases Reveal Moderate Intra-patient Pharmacotranscriptomic Heterogeneity. Bruun J; Kryeziu K; Eide PW; Moosavi SH; Eilertsen IA; Langerud J; Røsok BI; Totland MZ; Brunsell TH; Pellinen T;

Saarela J; Bergsland CH; Palmer HG; Brudvik KW; Guren T; Dienstmann R; Guren MG; Nesbakken A; Bjørnbeth BA; Sveen A; Lothe RA. 2020. *Clin Cancer Res.* 26(15): 4107 - 4119. IF: 10,107.

Genetic Alterations in the PI3K/AKT Pathway and Baseline AKT Activity Define AKT Inhibitor Sensitivity in Breast Cancer Patient-derived Xenografts. Gris-Oliver A; Palafox M; Monserrat L; Brasó-Maristany F; Òdena A; Sánchez-Guixé M; Ibrahim YH; Villacampa G; Grueso J; Parés M; Guzman M; Rodriguez O; Bruna A; Hirst CS; Barnicle A; de Bruin EC; Reddy A; Schiavon G; Arribas J; Mills GB; Caldas C; Dienstman R; Prat A; Nuciforo P; Razavi P; Scaltriti M; Turner NC; Saura C; Davies BR; Oliveira M; Serra V. 2020. *Clin Cancer Res.* 26(14): 3720 - 3731. IF: 10,107.

Phase I Study of TAK-659, an Investigational, Dual SYK/FLT3 Inhibitor, in Patients with B-Cell Lymphoma. Gordon LI; Kaplan JB; Popat R; Burris HA; Ferrari S; Madan S; Patel MR; Gritti G; El-Sharkawi D; Chau I; Radford JA; Perez de Oteyza J; Luigi Zinzani P; Iyer S; Townsend W; Karmali R; Miao H; Proscurshim I; Wang S; Wu Y; Stumpo K; Shou Y; Carpio C; Bosch F. 2020. *Clin Cancer Res.* 26(14): 3546 - 3556. IF: 10,107.

Multiparametric MR-PET Imaging Predicts Pharmacokinetics and Clinical Response to GDC-0084 in Patients with Recurrent High-Grade Glioma. Ellingson BM; Yao J; Raymond C; Nathanson DA; Chakhoyan A; Simpson J; Garner JS; Olivero AG; Mueller LU; Rodon J; Gerstner E; Cloughesy TF; Wen PY. 2020. *Clin Cancer Res.* 26(13): 3135 - 3144. IF: 10,107.

BRAF-Mutant Transcriptional Subtypes Predict Outcome of Combined BRAF, MEK, and EGFR Blockade with Dabrafenib, Trametinib, and Panitumumab in Patients with Colorectal Cancer. Middleton G; Yang Y; Campbell CD; André T; Atreya CE; Schellens JHM; Yoshino T; Bendell JC; Hollebecque A; McRee AJ; Siena S; Gordon MS; Tabernero J; Yaeger R; O'Dwyer PJ; De Vos F; Van Cutsem E; Millholland JM; Brase JC; Rangwala F; Gasal E; Corcoran RB. 2020. *Clin Cancer Res.* 26(11): 2466 - 2476. IF: 10,107.

Patient-Reported Outcomes from the Phase III Randomized IMmotion151 Trial: Atezolizumab + Bevacizumab versus Sunitinib in Treatment-Naïve Metastatic Renal Cell Carcinoma. Atkins MB; Rini BI; Motzer RJ; Powles T; McDermott DF; Suarez C; Bracarda S; Stadler WM; Donskov F; Gurney H; Oudard S; Uemura M; Lam ET; Grüllich C; Quach C; Carroll S; Ding B; Zhu Q; Piault-Louis E; Schiff C; Escudier B. 2020. *Clin Cancer Res.* 26(11): 2506 - 2514. IF: 10,107.

Design and Conduct of Early Clinical Studies of Immunotherapy: Recommendations from the Task Force on Methodology for the Development of Innovative Cancer Therapies 2019 (MDICT). Smoragiewicz M; Adjei AA; Calvo E; Tabernero J; Marabelle A; Massard C; Tang J; de Vries EGE; Douillard JY; Seymour L; task force on Methodology for the Development of Innovative Cancer Therapies. 2020. *Clin Cancer Res.* 26(11): 2461 - 2465. IF: 10,107.

Capturing Hyperprogressive Disease with Immune-Checkpoint Inhibitors Using RECIST 1.1 Criteria. Matos I; Martin-Liberal J; Garcia-Ruiz A; Hierro C; Ochoa de Olza M; Viaplana C; Azaro A; Vieito M; Brana I; Mur G; Ros J; Mateos J; Villacampa G; Berché R; Oliveira M; Alsina M; Élez E; Oaknin A; Muñoz-Couselo E; Carles J; Felip E; Rodon J; Tabernero J; Dienstmann R; Perez-Lopez R; Garralda E. 2020. *Clin Cancer Res.* 26(8): 1846 - 1855. IF: 10,107.

First-in-Human Phase I Study to Evaluate the Brain-Penetrant PI3K/mTOR Inhibitor GDC-0084 in Patients with Progressive or Recurrent High-Grade Glioma. Wen, Patrick Y.; Cloughesy, Timothy F.; Olivero, Alan G.; Morrissey, Kari M.; Wilson, Timothy R.; Lu, Xuyang; Mueller, Lars U.; Coimbra, Alexandre F.; Ellingson, Benjamin M.; Gerstner, Elizabeth; Lee, Eudocia Q.; Rodon, Jordi. 2020. *Clin Cancer Res.* 26(8): 1820 - 1828. IF: 10,107.

Epigenetic EGFR Gene Repression Confers Sensitivity to Therapeutic BRAFV600E Blockade in Colon Neuroendocrine Carcinomas. Capdevila J; Arqués O; Hernandez Mora JR; Matito J; Caratu 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. 2020. *Clin Cancer Res.* 26(4): 902 - 909. IF: 10,107.

Evaluation of the Predictive Role of Tumor Immune Infiltrate in Patients with HER2-Positive Breast Cancer Treated with Neoadjuvant Anti-HER2 Therapy without Chemotherapy. De Angelis C; Nagi C; Hoyt CC; Liu L; Roman K; Wang C; Zheng Y; Veeraraghavan J; Sethunath V; Nuciforo P; Wang T; Tsimelzon A; Mao S; Hilsenbeck SG; Trivedi MV; Cataldo ML; Pavlick A; Wolff AC; Weigelt B; Reis-Filho JS; Prat A; Gutierrez C; Osborne CK; Rimawi MF; Schiff R. 2020. *Clin Cancer Res.* 26(3): 738 - 745. IF: 10,107.

Impact of Prior Bevacizumab Treatment on VEGF-A and PlGF Levels and Outcome Following Second-Line Aflibercept Treatment: Biomarker Post Hoc Analysis of the VELOUR Trial. Van Cutsem E; Paccard C; Chiron M; Tabernero J. 2020. *Clin Cancer Res.* 26(3): 717 - 725. IF: 10,107.

Phase Ia Study of Anti-NaPi2b Antibody-Drug Conjugate Lifastuzumab Vedotin DNIB0600A in Patients with Non-Small Cell Lung Cancer and Platinum-Resistant Ovarian Cancer. Gerber DE; Infante JR; Gordon MS; Goldberg SB; Martín M; Felip E; Martinez Garcia M; Schiller JH; Spigel DR; Cordova J; Westcott V; Wang Y; Shames DS; Choi Y; Kahn R; Dere RC; Samineni D; Xu J; Lin K; Wood K; Royer-Joo S; Lemahieu V; Schuth E; Vaze A; Maslyar D; Humke EW; Burris HA. 2020. *Clin Cancer Res.* 26(2): 364 - 372. IF: 10,107.

Lucitanib for the Treatment of HR(+)/HER2(-) Metastatic Breast Cancer: Results from the Multicohort Phase II FINESSE Study. Hui R; Pearson A; Cortés J; Campbell C; Poirot C; Azim HA; Fumagalli D; Lambertini M; Daly F; Arahmani A; Pérez-Garcia J; Aftimos P; Bedard PL; Xuereb L; Scheepers ED; Vicente M; Goulioti T; Loibl S; Loi S; Pierrat MJ; Turner NC; Andre F; Curigliano G. 2020. *Clin Cancer Res.* 26(2): 354 - 363. IF: 10,107.

Randomized Phase 0/I Trial of the Mitochondrial Inhibitor ME-344 or Placebo Added to Bevacizumab in Early HER2-Negative Breast Cancer. Quintela-Fandino M; Morales S; Cortés-Salgado A; Manso L; Apala JV; Muñoz M; Gasol Cudos A; Salla Fortuny J; Gion M; Lopez-Alonso A; Cortés J; Guerra J; Malón D; Caleiras E; Mulero F; Mouron S. 2020. *Clin Cancer Res.* 26(1): 35 - 45. IF: 10,107.

Nivolumab and sunitinib combination in advanced soft tissue sarcomas: a multicenter, single-arm, phase Ib/II trial. Martin-Broto J; Hindi N; Grignani G; Martinez-Trufero J; Redondo A; Valverde C; Stacchiotti S; Lopez-Pousa A; D'Ambrosio L; Gutierrez A; Perez-Vega H; Encinas-Tobajas V; de Alava E; Collini P; Peña-Chilet M; Dopazo J; Carrasco-Garcia I; Lopez-Alvarez M; Moura DS; Lopez-Martin JA. 2020. *J Immunother Cancer.* Nov;8(2):e001561. IF: 9,913.

A first-in-human phase 1 dose escalation study of spartalizumab (PDR001), an anti-PD-1 antibody, in patients with advanced solid tumors. Naing A; Gainor JF; Gelderblom H; Forde PM; Butler MO; Lin CC; Sharma S; Ochoa de Olza M; Varga A; Taylor M; Schellens JHM; Wu H; Sun H; Silva AP; Faris J; Mataraza J; Cameron S; Bauer TM. 2020. *J Immunother Cancer.* Mar;8(1):e000530. IF: 9,913.


VHIO
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VHIO

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Due to safety and logistical considerations brought about by the COVID-19 pandemic, and to reflect the reality of balancing those physically working in the lab and clinical settings, with those working from home, we had to rethink our approach to this year's Scientific Report photo shoot and set up. We translated this obstacle into opportunity*.

To be able to include as many group members as possible, and photograph our researchers and investigators without masks, we took each picture individually, at a distance, and in locations away from areas dedicated to the care of our cancer patients. Designed to depict the very familiar "Zoom" virtual meeting scenario, we were able to also include faculty who were homeworking at the time of each photo session, by inviting them to send their pictures from home.

* Considering certain logistical and spatial issues, we have unfortunately had to repeat pictures of some of our larger groups and units from VHIO's Scientific Report 2019 - as indicated in the corresponding pages.

PRECLINICAL & TRANSLATIONAL RESEARCH

CELLULAR PLASTICITY & CANCER GROUP

Principal Investigator María Abad Post-Doctoral Fellow Elena Senís Research Assistants Marta Gimenez, Lluis Palenzuela Graduate Students Olga Boix, Emanuela Greco, Iñaki Merino, Alba Escriche, Marion Martinez Masters Student Alejandro Bernardo Visiting Student Camilla Bertrani

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

- Our PI, María Abad, was invited as Guest Editor for the first ever special issue on small-ORF encoded microproteins published in *Experimental Cell Research*.
- We published the first review on cancer microproteins.
- In collaboration with Teresa Macarulla, PI of VHIO's Gastrointestinal & Endocrine Tumors Group (page 96), pathologists and surgeons from the Vall d'Hebron University Hospital, we have generated a comprehensive collection of pancreatic cancer patients-derived samples, which comprises tumor organoids, cancer associated fibroblasts (CAFs), tumor infiltrating lymphocytes (TILs), patient-derived xenografts (PDX), and plasma.
- We have identified a set of microproteins secreted by pancreatic tumors that can be detected in plasma.

SUMMARY

Our group focuses on the interplay between stress responses, cellular plasticity and cancer. Cellular plasticity is recognized today as a critical feature of cancer cells that enable them to transit between different cellular states and promote tumor growth, disease progression after therapy, and metastasis.

We have 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 observations 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 metastasis.

Our main objective is to better understand the mechanisms and players implicated in this process, with the ultimate goal of developing novel therapies based on the inhibition of cancer cell plasticity.

Recent findings 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 past four years we 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.

The identification of tumor-microproteins could be crucial in 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 2020, we have expanded our microproteins studies. Using a peptidomics approach, the group has 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.

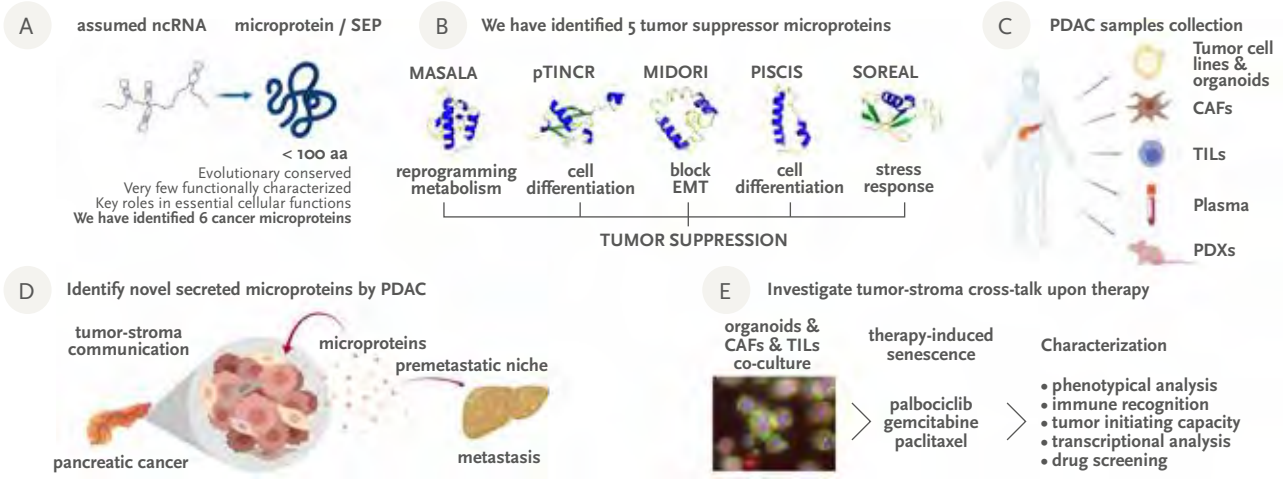


Figure: A) Recent findings have revealed that many genomic regions previously considered as non-coding in fact code for unannotated microproteins; some of them have been shown to be important for cancer. B) Our group has identified 5 novel microproteins with tumor suppressor activities. We have characterized 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 establishing co-cultures of organoids-CAFs-TILs to investigate the impact of therapy in the tumor-stroma cross-talk.

PI PAPER PICK

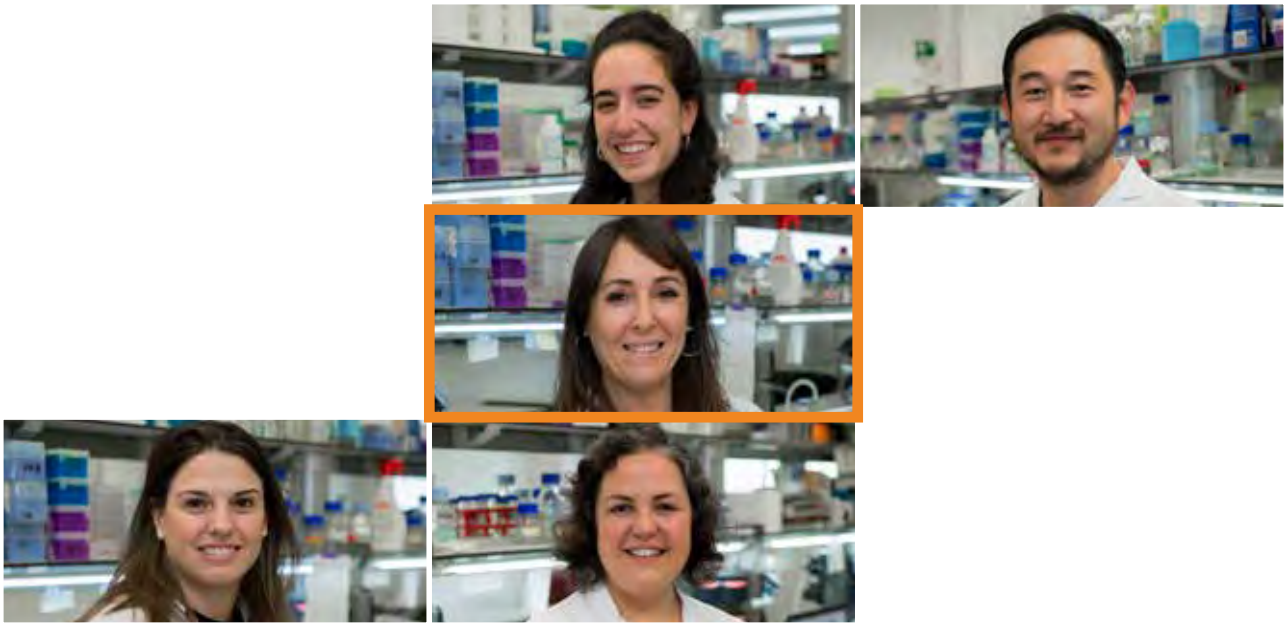
Salazar-Roa M, Trakala M, Alvarez-Fernandez M, Valdes-Mora F, Munoz J, Zapatero-Solana E, Grana O, Peters T, Abad M, Bueno M, Gomez de Cedron M, Fernandez-Piqueras J, De Martino A, Serrano M, Wang D, Clark S, Ortega S and Malumbres M. (2020). Transient exposure to miR-203 enhances the differentiation capacity of established pluripotent stem cells. *EMBO J*. 2020 Aug 17;39(16):e104324.

Abad M (2020). The hidden world of non-canonical ORFs. *Exp Cell Res*. 2020 Nov 15;396(2):112267.

Merino-Valverde I, Greco E, Abad M. The microproteome of cancer: From invisibility to relevance. *Exp Cell Res*. 2020 Jul 1;392(1):111997.

Ramón Y Cajal S, Sancho P, Soucek L, Peinado H, Abad M, Valiente M, Efeyan A, Pardo J, Quesada V, Jimeno J, Duque PM, Antón A, Varela I, Schuhmacher AJ. A spotlight on cancer researchers in Spain: new paradigms and disruptive ideas. *Clin Transl Oncol*. 2020 Jun;22(6):798-801.

CHROMATIN DYNAMICS IN CANCER GROUP



Principal Investigator Sandra Peiró Post-Doctoral Fellows Gemma Serra, Tian Tian Graduate Students Marc Cosin, Carmen Escudero, Queralt Serra Student Macarena Palacios Technician Jessica Querol

STRATEGIC GOALS

The laboratory has two main goals:

1. Understand the 3D chromatin structure and dynamics in cancer from a basic research perspective;
2. Identify biomarkers and epigenetic mechanisms of drug response and resistance in ER+ breast cancer, cholangiocarcinomas, and NUT-midline carcinomas.

Specifically:

1.1. Which molecular events direct chromatin movements?

1.2. Are these events due to the specific binding of a subset of transcription factors?

1.3. To what extent are chromatin architecture changes reversible?

1.4. During the process of metastasis cells go through an intermediate state. Does this state possess a specific and genomic architecture that determines the metastatic fate? Could we block this?

1.5. What is the role of oxidized H3 in other tumor types? Could we inhibit this oxidation using a peptide-based therapy?

2.1. Identification of key epigenetic components using PDXs, Cas9–cholangiocarinoma cell lines, and organoids with epigenetic drugs currently used in clinical trials.

2.2. Can we combine different drugs (based on results from 2) to overcome resistance?

2.3. Which are the biomarkers that will enable us to stratify patients for more effective treatments?

HIGHLIGHTS

- We have discovered the molecular function of oxidize Histone H3 in TNBC.
- We have consolidated our collaboration with VHIO's Gastrointestinal & Endocrine Tumors Group (page 96) through a grant received from *La Marató TV3* Foundation.
- Gemma Serra obtained her PhD from the Pompeu Fabra University, Barcelona, with magna cum laude.

SUMMARY

Our laboratory seeks to better understand how epigenetics and chromatin structure and dynamics affect cell behavior, with specific focus on cancer. Through our comprehensive studies, we aim to dissect the role of epigenetic changes in cancer, identify mechanisms of response and resistance to anti-cancer medicines, and explore new therapeutic opportunities.

Over the last few years, we have elucidated epigenetic changes during EMT and cancer progression, and discovered a new histone H3 modification (oxidized H3) enriched in heterochromatin that is implicated in chromatin condensation and the transition to a metastatic cell fate (published in *Mol. Cell, FEBS J.*, and *Oncogene*). We have also discovered an important role for lamin B1 in the reorganization of 3D chromatin structure during EMT (published 2018, *Nat. Commun.*).

Dedicated to fully applying these insights to the epigenetic landscape and 3D structure during this malignant transformation, we have adopted chromosome conformation–based techniques together with ChIP-seq, ATAC-seq and RNA-seq. By combining these data with excellent computational and statistical tools in standard cancer models, such as cancer cell lines, and in a large and unique collection of patient- derived xenograft (PDX) models, we will continue to navigate this largely uncharted area which shows great promise in the early diagnosis of disease.

We are equally committed to describing the association of chromatin conformation modifications with the acquisition of malignant traits and evaluating the functional consequences of these developments in genes and pathways. Next steps will focus on deciphering how these alterations occur at the molecular level and more precisely identifying these putative culprits for future targeted therapy.

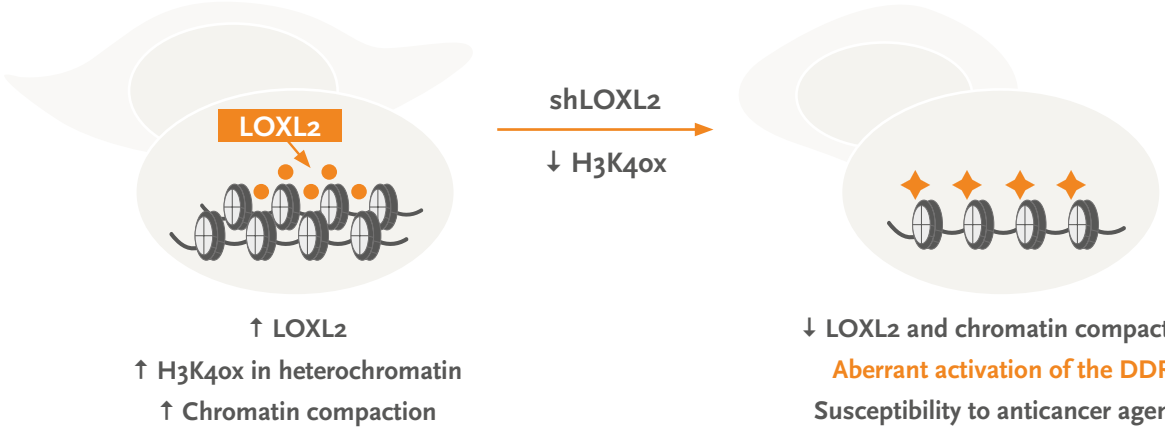


Figure: Triple negative breast cancer cells.

PI PAPER PICK

Alcalà-Vida R, Garcia-Forn M, Castany-Pladevall C, Creus-Muncunill , Ito Y, Blanco E, Golbano A, Crespí-Vázquez, Parry A, Slater G, Samarajiwa S, Peiró S, Di Croce L, Masashi N, Pérez-Navarro E. Neuron type-specific increase in Lamin B1 contributes to nuclear dysfunction in Hubtington's disease. *EMBO Mol Med*. 2021 Feb 5;13(2):e12105. Epub 2020 Dec 28.

Guerrero-Martinez J, Ceballos-Chávez M, Koehler F, Peiró S, Reyes JC. TGFβ Promotes Widespread Enhancer Chromatin Opening and Operates on Genomic Regulatory Domains. *Nat Commun*. 2020 Dec 3;11(1):6196.

EXPERIMENTAL THERAPEUTICS GROUP

Principal Investigator Violeta Serra Post-Doctoral Fellows Alba Llop-Guevara, Marta Palafox, Mónica Sánchez Graduate Students Laia Monserrat, Flaminia Pedretti, Andrea Herencia Visiting Students Andreu Odena, Cristina Molina Technicians Judit Grueso, Marta Guzmán, Olga Rodríguez

STRATEGIC GOALS

- Developing predictive biomarkers of targeted treatments in ER+ and triple negative breast cancers, including inhibitors directed against the DNA damage repair protein PARP as well as signaling/cell cycle kinases (CDK4/6, PI3K/AKT or FGFR).
- Exploring novel treatment combinations for ER+ and TN breast cancers.
- Contributing to personalized medicine by developing a diagnostic test to better guide treatment strategies based on PARP inhibitors.
- Establishing patient tumor-derived breast cancer preclinical models to explore hypothesis-based combinatorial therapies.

HIGHLIGHTS

- We have contributed towards achieving a better understanding of the mechanisms underlying sensitivity to AKT 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 *AGAUR* as well as *ISCIII* programs to develop a pre-commercial prototype of the RAD51 test and to implement it in the diagnostic programs at our Hospital.
- Our group has established a panel of over one hundred ER+ and TN breast cancer PDXs, mainly from the metastatic disease setting. We especially focus on models that recapitulate the progression to 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 breast cancer patient samples.

We have significantly contributed to the field of PI3K inhibitor resistance and continue to more deeply explore mechanisms of 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 lack of response to CDK4/6 blockade in estrogen receptor positive breast cancer. Additionally, we 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).

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 *BRCA* mutant tumors to recover HRR functionality and develop resistance to PARPi. We have developed an assay, the RAD51predict test, which accurately identifies germline *BRCA* tumors that have restored HRR functionality and become resistant to these drugs. Importantly, this test also identifies tumors that are sensitive to PARPi through HRR alterations beyond the germline *BRCA* 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, and prostate cancer patients.

Finally, we are also investigating the effects of PARPi on the tumor immune environment. HRR-deficient tumors have been shown to 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 HRR-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 through collaborations with other groups including VHIO's Molecular Oncology (page 118), and Oncology Data Science – OdysSey (page 104) Groups directed by Paolo Nuciforo and Rodrigo Dienstmann, respectively.

Our team has significantly advanced the understanding of 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.

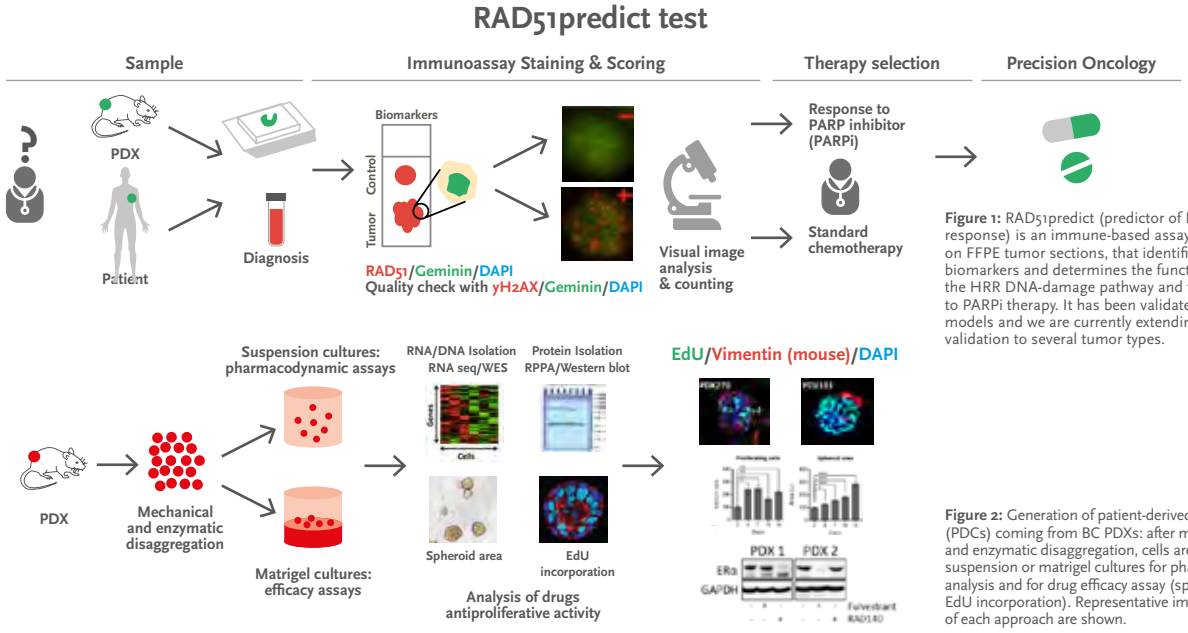


Figure 1: RAD51predict (predictor of PARPi response) is an immune-based assay, performed on FFPE tumor sections, that identifies nuclear biomarkers and determines the functionality of the HRR DNA-damage pathway and the response to PARPi therapy. It has been validated in PDX models and we are currently extending the clinical validation to several tumor types.

Figure 2: Generation of patient-derived culture cells (PDCs) coming from BC PDXs: after mechanical and enzymatic disaggregation, cells are seeded in suspension or matrigel cultures for pharmacodynamic analysis and for drug efficacy assay (spheroid area and EdU incorporation). Representative images and data of each approach are shown.

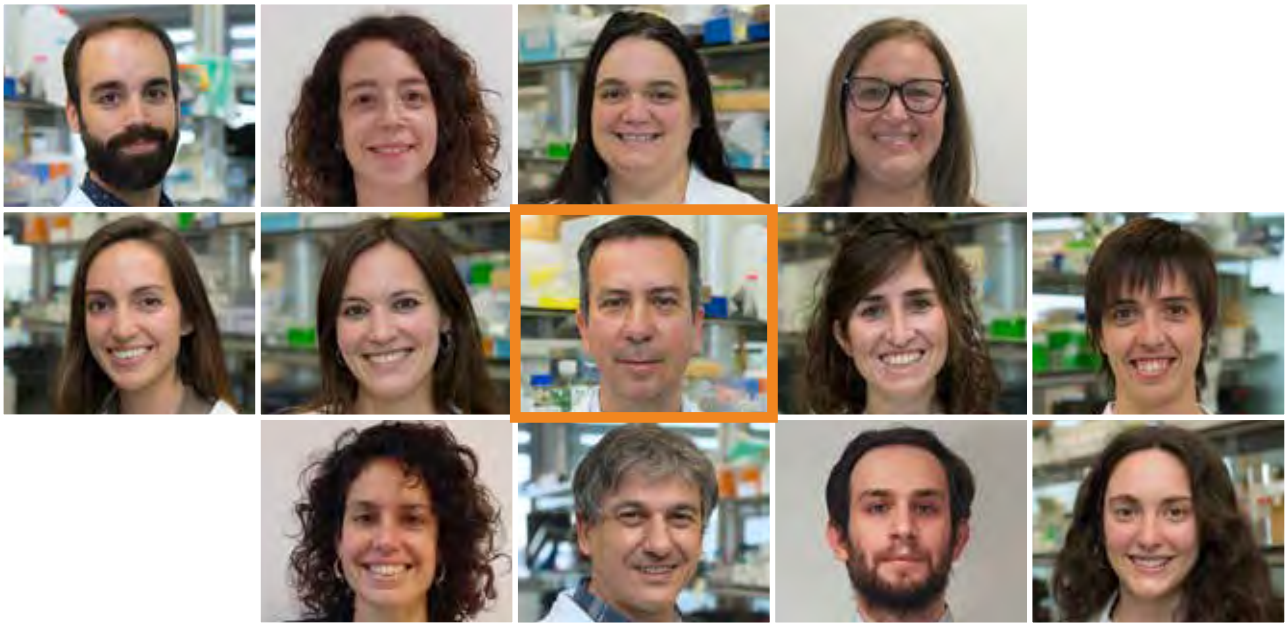
PI PAPER PICK

Gris-Oliver A, Palafox M, Monserrat L, Brasó-Maristany F, Òdena A, Sánchez-Guixé M, Ibrahim YH, Villacampa G, Grueso J, Parés M, Guzman M, Rodriguez O, Bruna A, Hirst CS, Barnicle A, de Bruin EC, Reddy A, Schiavon G, Arribas J, Mills GB, Caldas C, Dienstman R, Prat A, Nuciforo P, Razavi P, Scaltriti M, Turner NC, Saura C, Davies BR, Oliveira M, Serra V. Genetic alterations in the PI3K/AKT pathway and baseline AKT activity define AKT inhibitor sensitivity in breast cancer patient-derived xenografts. *Clin Cancer Res.* 2020 Jul 15;26(14):3720-3731.

Pellegrino B, Musolino A, Llop-Guevara A, Serra V, De Silva P, Hlavata Z, Sangiolo D, Willard-Gallo K, Solinas C. Homologous Recombination Repair Deficiency and the Immune Response in Breast Cancer: A Literature Review. *Transl Oncol.* 2020 Feb;13(2):410-422.

Miller RE, Leary A, Scott CL, Serra V, Lord CJ, Bowtell D, Chang DK, Garsed DW, Jonkers J, Ledermann JA, Nik-Zainal S, Ray-Coquard I, Shah SP, Matias-Guiu X, Swisher EM, Yates LR. ESMO recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer. *Ann Oncol.* 2020 Sep 28:S0923-7534(20)42164-7.

GENE EXPRESSION & CANCER GROUP



Principal Investigator Joan Seoane Staff Scientist Ignasi Barba Post-Doctoral Fellows Ester Bonfill, Laura Escudero, Raffaella Iurlaro, Monica Pascual, Ester Planas, Gonçalo Rodrigues, Carlota Rubio Research Fellow Davide Ciardiello Masters Student Samia Hajem Graduate Student Ester Arroba Technicians Alexandra Arias, Isabel Cuartas Maza, Alba Martinez

STRATEGIC GOALS

- Identify new therapeutic targets against brain tumors and novel biomarkers to more precisely predict response to therapy.
- Study intratumor heterogeneity.
- Investigate the tumor microenvironment.
- Develop methods for non-invasive molecular diagnosis through the study of circulating biomarkers.
- Generate patient-derived mouse models of brain cancers.

HIGHLIGHTS

- We have demonstrated the use of liquid biopsies based on the analysis of cell free circulating tumor DNA in cerebrospinal fluid for the diagnosis, prognosis and monitoring of patients with central nervous system lymphoma, Bovillo et al. *Hematologica* 2020, and medulloblastoma, Escudero et al. *Nature Comm*. 2020.
- MSC-1 (a novel compound designed and developed by the VHIO born spin-off, Mosaic Biomedicals, that Joan Seoane founded in 2012) was acquired by Medimmune/Astrazeneca.
- We designed the phase II clinical trial to test MSC-1. This study will begin recruiting patients next year, 2021.

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. Advancing progress in this field towards improving outcomes for these patients is therefore critical.

Evolving heterogeneity is among one of the major challenges that are currently hampering our efforts aimed at more effectively treating brain cancers. We focus on inter-tumor heterogeneity and evolution that includes genomic heterogeneity, cancer initiating cells and stroma/immune cell heterogeneity – including the study of TGF-β and LIF.

Tumors are composed of a mosaic of cell subclones that differ in their genomic alterations. We explore genomic diversity present in glioblastoma and analyze intratumor genomic heterogeneity as it evolves over time in response to therapy. Our group is designing tools to monitor evolving genomic heterogeneity and study the use of liquid biopsies for brain cancer through the study of circulating cell free tumor DNA in cerebrospinal fluid from patients.

Specifically, we are driving cerebrospinal fluid as liquid biopsy for the real time policing of brain cancer closer to the clinic. Reflective of our expertise in developing this novel approach in medulloblastoma and central nervous system lymphoma, we have authored several research articles (i.e. Escudero et al. *Nature Comm*. 2020; Bovillo et al. *Haematologica* 2020).

While no biomarker derived from liquid biopsy against these tumor types has yet been validated and integrated into clinical practice, there is an increasing body of evidence in the literature, including our findings, that points to its efficacy in the real time evaluation of malignant disease and potential to better inform and guide the therapeutic management of patients.

We are as committed to advancing research into the role of the tumor microenvironment which, in the case of brain cancers, assumes a crucial role in cancer progression. Increasing insights into the tumor microenvironment promises powerful weaponry in combating cancer, regardless of heterogeneity.

By eliminating the niche where tumors reside and thrive should enable us to develop more effective anti-cancer compounds. In this regard, we have reported that the cytokine LIF assumes an essential role in the tumor microenvironment and is consequently a promising therapeutic target.

We have now shown that the novel agent MSC-1, developed by VHIO, inhibits LIF and has a dual mechanism of action. In tumors expressing high levels of LIF, this protein promotes the proliferation of cancer stem cells. LIF blockade eliminates these tumor-initiating stem cells, putting the brakes on metastatic cell spread and disease recurrence.

Additionally, elevated LIF expression disables the anti- tumor alarm system and stops the immune system from thwarting cancer's plans. Blocking LIF consequently reactivates the alarm to call an anti-tumoral immune response.

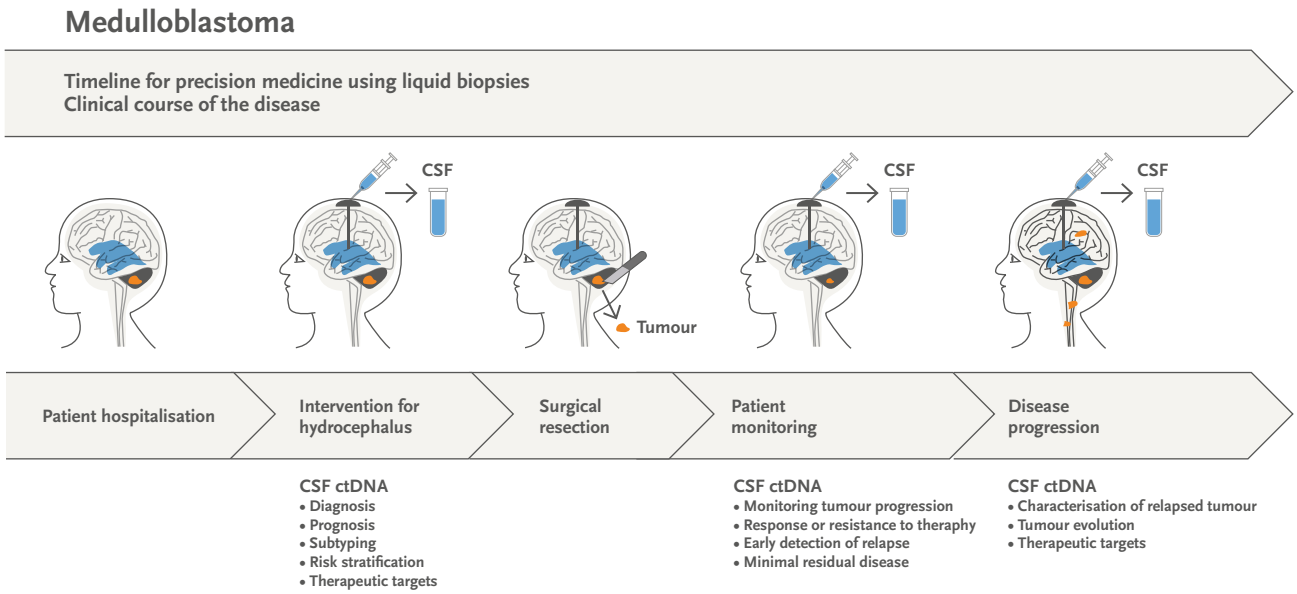


Figure: Liquid biopsies in the most common brain tumor in children.

PI PAPER PICK

Escudero L, Martínez-Ricarte F, Seoane J. Cerebrospinal fluid circulating tumour DNA as a liquid biopsy for central nervous system malignancies. *Curr Opin Neurol.* 2020; 33(6):736-741.

Escudero L, Llort A, Arias A, Diaz-Navarro A, Martínez-Ricarte F, Rubio-Perez C, Mayor R, Caratú G, Martínez-Sáez E, Vázquez-Méndez É, Lesende-Rodríguez I, Hladun R, Gros L, Ramón y Cajal S, Poca M, Puente X, Sahuquillo J, Gallego S, Seoane J. Circulating tumour DNA from the cerebrospinal fluid allows the characterisation and monitoring of medulloblastoma. *Nature Comm.* 2020; 11(1):5376.

Ciardiello D, Elez ME, Tabernero J, Seoane J. Clinical development of therapies targeting TGβ: current knowledge and future perspectives. *Ann Oncol.* 2020. 31 (10):1336 – 1349.

Bobillo S, Crespo M, Escudero L, Mayor R, Raheja P, Carpio C, Rubio-Perez C, Tazón-Vega B, Palacio C, Carabia J, Jiménez I, Nieto JC, Montoro J, Martínez-Ricarte F, Castellví J, Simó M, Puigdefàbregas L, Abrisqueta P, Bosch F, Seoane J. Cell free circulating tumor DNA in cerebrospinal fluid detects and monitors central nervous system involvement of B-cell lymphomas. *Haematologica.* 2020. Epub ahead of print.

PRECLINICAL & TRANSLATIONAL RESEARCH

GROWTH FACTORS GROUP

Principal Investigator Joaquín Arribas Post-Doctoral Fellows Enrique Javier Arenas, Cristina Bernadó, Irene Rius Graduate Students Santiago Duro, Alex Martínez-Sabadell, Beatriz Morancho, Macarena Román Alonso, Marta Lalinde Students Marta Bort, Llúcia Prohens Technicians Marta Escorihuela, Antonio Miguel Luque

STRATEGIC GOALS

- Generation and characterization of CARs against tumor specific antigens.
- Development of an ADC against p95HER2.
- Determine the role of cellular senescence in breast cancer progression and treatment.
- Identification of new mechanisms of resistance to targeted therapies.

HIGHLIGHTS

- We have continued to develop a novel T-cell based therapy against p95HER2 positive breast cancer, p95HER2-CARs.
- We have shown how to overcome resistance of breast cancers to T-DM1.
- We have also continued to determine how cellular senescence impacts on breast cancer progression and therapy.

SUMMARY

This year, 2020, has been a very unusual year for the scientific community due to the outbreak of COVID-19. Despite the restrictions imposed by the pandemic, I am proud to report that our group has managed to continue working on all our projects at an excellent pace.

We continued to pursue our research on mechanisms of resistance to targeted therapies and most importantly, how to overcome it by showing that breast cancers resistant to T-DM1, an antibody-drug conjugate ADC)-can be efficiently treated with the second generation ADC SYD985 (Nadal-Serrano et al.).

Our group has also contributed to determining the clinical value of plasma cell-free DNA and the efficacy of PI3K inhibition in gastrointestinal tumors and (Serrano et al; García-Valverde et al.). Finally, we have collaborated in a position paper on how to enhance global access to cancer medicines (Cortes el al.)

In addition, our ever-expanding platform of breast and pancreatic cancer patient-derived experimental models has enabled us to establish several fruitful collaborations with other groups at VHIO. We have collaborated in the characterization of the genetic abnormalities that determine sensitivity to Akt inhibitors (Gris-Oliver et al.), and in defining how epigenetic changes regulate the accessibility of chromatin in triple negative breast cancer (Cebrià-Costa el al.).

Regarding extramural collaborations, other groups have used our platform to identify precision therapies against co-occurrence of driver alterations (Mateo et al.) and novel therapies (Ferronato et al.).

In parallel, we have continued our research into novel immune therapies by generating novel CARs (chimeric antigen receptors). With the knowledge accumulated during the development and characterization of bispecific antibodies, we have been able to efficiently develop our CARS that are directed against the p95HER2 protein; only present in some mammary and gastric tumors, and completely absent in normal tissues. Importantly, this project has been funded by the Spanish Association against Cancer (AECC) for the next five years.

Mention must also be made regarding the continued backing and support received from the Breast Cancer Research Foundation (BCRF), for which we are extremely grateful.

Lastly, in 2020, our Principal Investigator, Joaquín Arribas, stepped down as Scientific Director of the *Centro de Investigación Biomédica en Red* (CIBER-ONC: Center for the Biomedical Research Network in Oncology), to join the Hospital del Mar Medical Research Institute (IMIM), as Director.

Joaquín will continue to serve as Principal Investigator at VHIO to both lead and participate in our aforementioned research lines and projects with other groups.

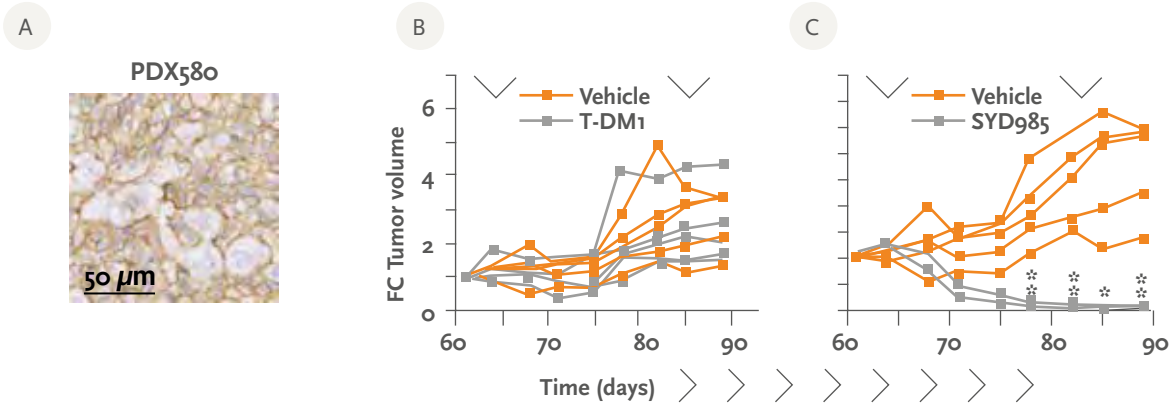


Figure: The second generation ADC SYD985 overcomes resistance to T-DM1. A: immunohistochemistry showing positivity to HER2 in PDX580. B: Growth of PDX580 in mice treated with vehicle or T-DM1. C: Growth of PDX580 in mice treated with vehicle or SYD985.

PI PAPER PICK

Nadal-Serrano M, Morancho B, Escrivá-de-Romaní S, Morales CB, Luque A, Escorihuela M, Espinosa Bravo M, Peg V, Dijcks FA, Dokter WHA, Cortés J, Saura C, Arribas J. The Second Generation Antibody-Drug Conjugate SYD985 Overcomes Resistances to T-DM1. *Cancers (Basel)*. 2020 Mar 13;12(3):670.

Cortes J, Perez-García JM, Llombart-Cussac A, Curigliano G, El Saghir NS, Cardoso F, Barrios CH, Wagle S, Roman J, Harbeck N, Eniu A, Kaufman PA, Tabernero J, García-Estévez L, Schmid P, Arribas J. Enhancing global access to cancer medicines. *CA Cancer J Clin.* 2020 Mar;70(2):105-124.

Serrano C, Vivancos A, López-Pousa A, Matito J, Mancuso FM, Valverde C, Quiroga S, Landolfi S, Castro S, Dopazo C, Sebio A, Virgili AC, Menso MM, Martín-Broto J, Sansó M, García-Valverde A, Rosell J, Fletcher JA, George S, Carles J, Arribas J. Clinical value of next generation sequencing of plasma cell-free DNA in gastrointestinal stromal tumors. *BMC Cancer.* 2020 Feb 5;20(1):99.

Ferronato MJ, Nadal Serrano M, Arenas Lahuerta EJ, Bernadó Morales C, Paolillo G, Martinez-Sabadell Aliguer A, Santalla H, Mascaró M, Vitale C, Fall Y, Arribas J, Facchinetti MM, Curino AC. Vitamin D analogues exhibit antineoplastic activity in breast cancer patient-derived xenograft cells. *J Steroid Biochem Mol Biol.* 2020 Aug 9:105735.

MOUSE MODELS OF CANCER THERAPIES GROUP

Principal Investigator Laura Soucek Staff Scientist Jonathan R. Whitfield Research Associate Mariano F. Zacarías-Fluck Post-Doctoral Fellows Jastrinjan Kaur, Sandra Martínez Martín Technicians Génesis Martín Fernandez, 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, colorectal cancer, and multiple myeloma.
- Validate anti-Myc Omomyc-based cell penetrating mini-proteins for cancer therapy.
- Define the role of Myc in promoting cancer immune evasion and test the efficacy of Myc-inhibitors and IO combination treatments in cancer treatment.
- 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

- As well as co-authoring key publications in *Cancer Discovery* and *Cancer Research*, Laura has also published several reviews in 2020. Of particular interest is a reflection on 2 decades of Omomyc research, published in *Cells*.
- This year Jonathan Whitfield and Laura Soucek finished compiling a book for Springer Nature on *The Myc gene: methods and protocols* with chapters from leading experts around the world. It will publish next year, 2021.
- Our lab received funding through 2 new main grants: *La Marató* and FIS (ISCIII).
- The latest graduate student in our group to have successfully defended her PhD thesis on *Targeting MYC in B-cell haematologic malignancies* is Sandra Martínez. Congratulations from all the lab!

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).

Our group has continued to contribute to cancer research in general and, more specifically, as a leader in the Myc field by (co) authoring a number of reviews. One explores new therapeutic options targeting Myc proteins in lung cancer. Two others focused on Omomyc – our Myc inhibitor – and described the two decades of work that has gone into developing this mini-protein therapeutic and demonstrating that Myc can be targeted clinically. The second one delved into the structural and biophysical properties of Myc, which are key to the development of specific and effective anti-Myc drugs.

An additional review, co-authored by leading Spanish researchers in oncology including Laura, discussed new paradigms and disruptive ideas currently under development in Spain.

This year has also celebrated several collaborative successes:

Our work with Gerard Evan's laboratory has led to the demonstration that Myc instructs and maintains the pancreatic adenocarcinoma phenotype. This important paper published in *Cancer Discovery*, advances insights into the role of Myc and its connection to Ras-induced tumors.

Finally, we contributed to a manuscript headed by Jordi Alcaraz and published in *Cancer Research*, showing that epigenetic SMAD3 repression in tumor-associated fibroblasts reduces fibrosis and sensitivity to the antifibrotic drug nintedanib in lung squamous cell carcinoma

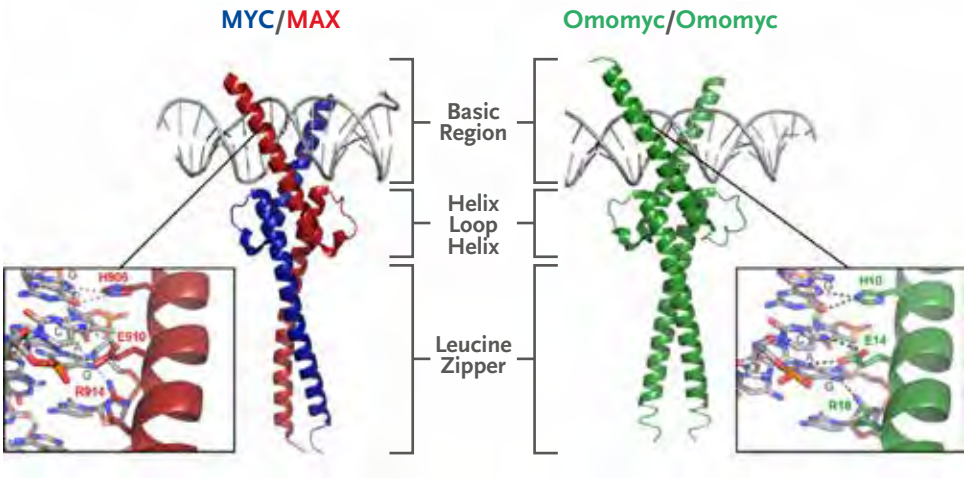


Figure: Adapted from Massó-Vallés and Soucek, 2020: Representation of the crystal structure of the MYC/MAX dimer (1NKP, left) and Omomyc/Omomyc dimer (5I50, right) bHLHZ bound to DNA.

PI PAPER PICK

Beaulieu ME, Castillo F, Soucek L. Structural and Biophysical Insights into the Function of the Intrinsically Disordered Myc Oncoprotein. *Cells*. 2020 Apr 22;9(4):1038.

Massó-Vallés D, Soucek L. Blocking Myc to Treat Cancer: Reflecting on Two Decades of Omomyc. *Cells*. 2020 Apr 4;9(4):883. doi: 10.3390/cells9040883.PMID: 32260326

Massó-Vallés D, Beaulieu ME, Soucek L. MYC, MYCL, and MYCN as therapeutic targets in lung cancer. Expert Opin *Ther Targets*. 2020 Feb;24(2):101-114.

Sodir NM, Kortlever RM, Barthet VJA, Campos T, Pellegrinet L, Kupczak S, Anastasiou P, Swigart LB, Soucek L, Arends MJ, Littlewood TD, Evan GI. MYC Instructs and Maintains Pancreatic Adenocarcinoma Phenotype. *Cancer Discov.* 2020 Apr;10(4):588-607.

PROSTATE CANCER TRANSLATIONAL RESEARCH GROUP

Principal Investigator Joaquin Mateo Senior Investigator Nicolas Herranz Post-Doctoral Fellows Alejandro Athie, Irene Casanova PhD Students Sara Arce, Julian Brandariz Technicians Teresa Casals, Sarai Cordoba, Natalia Castro Clinical Data Curator Magdalena Guardiola

STRATEGIC GOALS

- To establish a clinically relevant re-classification of metastatic prostate cancer integrating genotypic and phenotypic data with functional assays.
- Develop prostate cancer molecular stratification assays based on tumor tissue and circulating biomarkers.
- Optimize the combination of DNA repair-targeting drugs with androgen receptor inhibitors.
- Build a precision medicine core for prostate cancer patients treated at the Vall d'Hebron University Hospital (HUVH).

HIGHLIGHTS

- Launch of 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.
- We published our study looking into combinatory treatment approaches to optimize the management of men with metastatic prostate cancer and ATM mutations.
- We contributed to the approval of olaparib in 2020, the first-ever precision medicine drug for prostate cancer
- The launch of our first investigator-initiated clinical trial co-targeting AR and PARP in metastatic hormone-naïve prostate cancer, which is actively recruiting in 9 hospitals across Spain.

SUMMARY

Over the last decade, we have witnessed a revolution in the treatment of metastatic castration-resistant prostate cancer (mCRPC) which is an advanced and lethal form of prostate cancer. A deeper understanding of its underlying biology has led to the development of compounds targeting the androgen signaling pathway and the immune system, as well as taxanes and radiopharmaceuticals.

Despite these advances in more effectively managing mCRPC, it remains a lethal disease resulting in significant morbidity and mortality globally. Arguably, the most critical need in drug development against CRPC is treatment molecular stratification. In parallel efforts must continue to center on identification of robust predictive biomarkers of response and the development of targeted anti-cancer therapies. The advent of these novel treatments has driven tumor evolution towards a shift in the genomic landscape observed in patients with advanced disease.

We embrace a comprehensive and integrative approach to research. As such, our group encompasses molecular biology, tumor genomics, clinical trials and computational sciences in order to develop precision medicine strategies to treat advanced prostate cancer based on predictive biomarkers of response.

Defects in DNA damage repair genes (DDR) -particularly in double- strand breaks- are present in 20-25% of mCRPC cases, and allow us to study how we can deliver more precise cancer treatment and care. Some of these mutations have prognostic and predictive implications which are crucial in delivering on the promise of personalized medicine in oncology.

This year, we reported on final results for the registration trial of Olaparib, a PARPi,in prostate cancer, leading to its approval in Europe, Canada and the US, among other countries. Still, more work is needed for the optimal delivery of PARPi-based therapies for those patients with DDR gene mutations beyond *BRCA2*.

Along these lines, our group uses a range of tools (CRISPR gene editing, shRNA, siRNA and pharmacological inhibitors) to generate prostate cancer models and study how tumors adapt their DNA repair machinery; this year we published on optimal combinatory strategies for ATM-deficient cancers. Our interest in cell cycle modulation by DNA damage has also led us to study the senescence-like phenotype observed after exposure to targeted agents, which we hypothesize is a mechanism of drug resistance, and how to target it therapeutically.

Aiming at translating our findings into benefits for patients as rapidly as possible, we study the same genomic and transcriptomic signatures in biopsies from patients with metastatic prostate cancer. In parallel, we collect longitudinal liquid biopsies to study how a tumor evolves during response and progression to targeted agents.

Our research focuses on optimal patient stratification strategies for clinical care, with particular emphasis on combining DNA repair targeting agents with those that inhibit androgen signaling. Importantly, we have launched our first investigator-initiated clinical trials, translating our research studies in the lab to therapeutic interventions in patients.

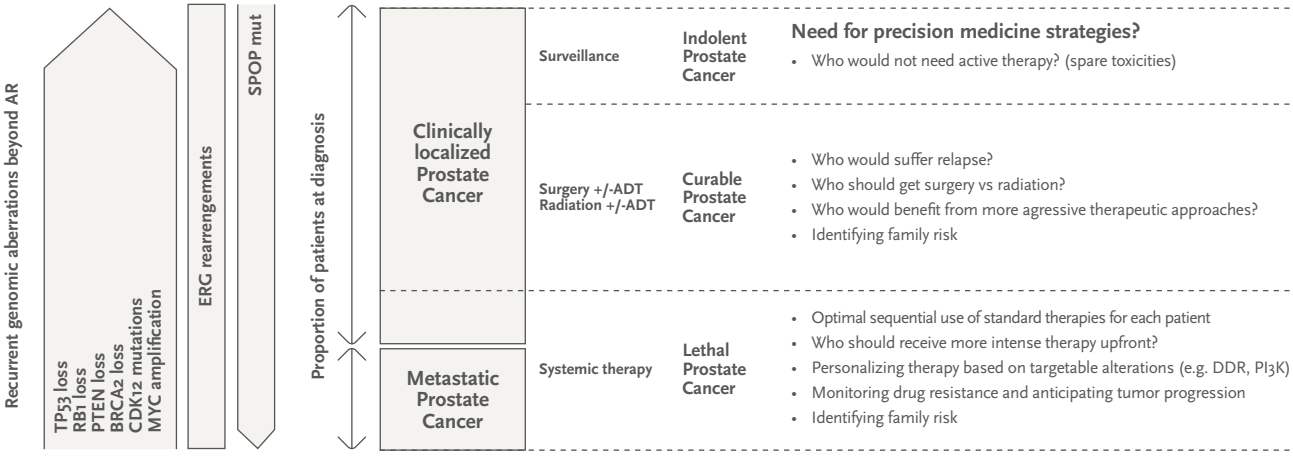


Figure: Lethal prostate cancer has a distinct molecular landscape to localised, curable, prostate cancer. A better understanding of the prognostic and predictive value of different genomic biomarkers across the different disease clinical states can help to advance many of the unmet clinical needs for prostate cancer patients, listed in the right column of the figure. Adapted from Mateo et al, *Nature Cancer* 2020.

PI PAPER PICK

Neeb A, Herranz N, Arce-Gallego S, Miranda S, Buroni L, Yuan W, Athie A, Casals T, Carmichael J, Rodrigues DN, Gurel B, Rescigno P, Rekowski J, Welti J, Riisnaes R, Gil V, Ning J, Wagner V, Casanova-Salas I, Cordoba S, Castro N, Fenor de la Maza MD, Seed G, Chandran K, Ferreira A, Figueiredo I, Bertan C, Bianchini D, Aversa C, Paschalis A, Gonzalez M, Morales-Barrera R, Suarez C, Carles J, Swain A, Sharp A, Gil J, Serra V, Lord C, Carreira S, Mateo J, de Bono JS. Advanced Prostate Cancer with ATM Loss: PARP and ATR Inhibitors. *Eur Urol.* 2021 Feb;79(2):200-211.

Mateo J, Seed G, Bertan C, Rescigno P, Dolling D, Figueiredo I, Miranda S, Nava Rodrigues D, Gurel B, Clarke M, Atkin M, Chandler R, Messina C, Sumanasuriya S, Bianchini D, Barrero M, Petermolo A, Zafeiriou Z, Fontes M, Perez-Lopez R, Tunariu N, Fulton B, Jones R, McGovern U, Ralph C, Varughese M, Parikh O, Jain S, Elliott T, Sandhu S, Porta N, Hall E, Yuan W, Carreira S, de Bono JS. Genomics of lethal prostate cancer at diagnosis and castration resistance. *J Clin Invest.* 2020 Apr 1;130(4):1743-1751.

Hussain M, Mateo J, Fizazi K, Saad F, Shore N, Sandhu S, Chi KN, Sartor O, Agarwal N, Olmos D, Thiery-Vuillemin A, Twardowski P, Roubaud G, Özgüroğlu M, Kang J, Burgents J, Gresty C, Corcoran C, Adelman CA, de Bono J; PROfound Trial Investigators. Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer. *N Engl J Med.* 2020 Dec 10;383(24):2345-2357.

de Bono J, Mateo J, Fizazi K, Saad F, Shore N, Sandhu S, Chi KN, Sartor O, Agarwal N, Olmos D, Thiery-Vuillemin A, Twardowski P, Mehra N, Goessl C, Kang J, Burgents J, Wu W, Kohlmann A, Adelman CA, Hussain M. Olaparib for Metastatic Castration-Resistant Prostate Cancer. *N Engl J Med.* 2020 May 28;382(22):2091-2102.

SARCOMA TRANSLATIONAL RESEARCH GROUP

Principal Investigator César Serrano Graduate Students Alfonso García Valverde, Daniel Pilco Janeta, David Gómez Peregrina, Iván Olivares Rivas, Gemma Mur Bonet Senior Technician Jordi Rosell Aluja

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 has led high-level studies towards the clinical implementation of liquid biopsy in GIST patients.
- We have been awarded by the Spanish Association Against Cancer (AECC- Senior Clinician Program) to study the evolutionary landscape of resistance in GIST.
- César Serrano has been part of the international teams that have led to the approval of ripretinib and avapritinib in GIST patients.
- Our group has launched the #SarcModel project aiming to generate laboratory models from most sarcoma subtypes.

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: genomically simple sarcomas driven by simple genetic alterations, such as translocations or specific activating mutations; and tumors with complex and unbalanced genomic aberrations. Each of these categories include diverse sarcomas subtypes often with profound differences in their molecular makeup, course of disease and therapeutic approach.

Our group focuses 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 drug resistance.

Ongoing efforts aim at a deeper biological understanding of GIST and other sarcomas in order to advance drug development. One of the major hurdles with a direct impact on patients' outcomes, concerns the heterogeneity of mechanisms of resistance.

Our overarching goal is therefore to identify crucial molecules and signaling mechanisms in GIST biology that can serve as therapeutic vulnerabilities.

We also continue to validate a core set of molecules that are co-regulated by KIT downstream pathways and identified through extensive whole transcriptome studies across several clinically representative human GIST models.

Our group is particularly interested in those with pro-survival function to better understand cellular adaptation to driver inhibition, which may eventually be novel therapeutic targets.

We are as interested in performing high- throughput genomic and transcriptomic studies in order to decipher the evolving patterns of resistance in GIST throughout the course of disease, as well as researching liquid biopsy in sarcoma to provide robust evidence that will help to more precisely guide treatment decisions through plasma sequencing.

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.

Our aim is to have a true clinical impact by improving the daily treatment and care of our sarcoma patients. We are proud to report that our Sarcoma Multidisciplinary Unit has been designated as an Expert National Sarcoma Center by the Spanish Ministry of Health, and thus constitutes an optimal setting for translating cancer discovery into clinical benefits.

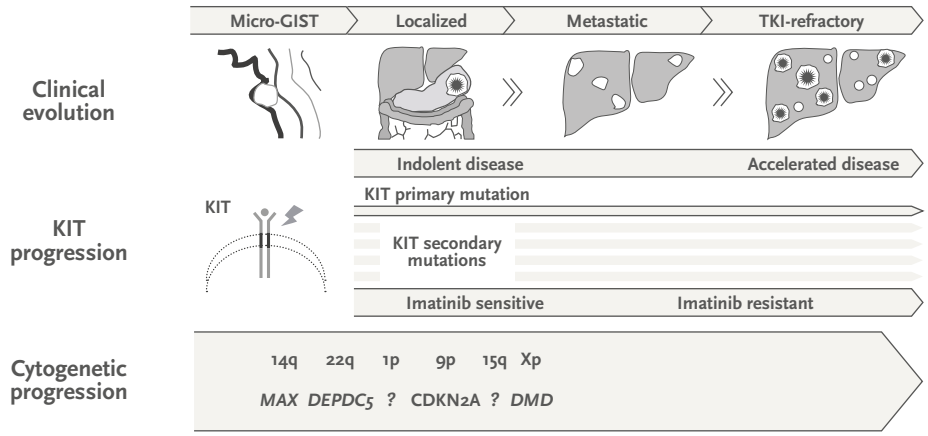


Figure: Gastrointestinal stromal tumor (GIST) is the most common malignant mesenchymal tumor and a successful and paradigmatic model to dissect mechanisms of response and resistance to molecularly targeted agents. Ongoing research from our group is advancing this knowledge in two directions: first, we are interrogating mutation-based mechanisms affecting the sensitivity to approved KIT inhibitors.

Second, we are investigating the cytogenetic progression that fuels GIST growth. These findings have a direct impact on the future of drug development in GIST and other diseases (Figure from Serrano & George, *Clin Cancer Res* 2020; 26: 923-934.).

PI PAPER PICK

Serrano C, Vivancos A, López-Pousa A, Matito J, Mancuso FM, Valverde C, Quiroga S, Landolfi S, Castro S, Dopazo C, Sebio A, Virgili AC, Menso MM, Martín-Broto J, Sansó M, García-Valverde A, Rosell J, Fletcher JA, George S, Carles J, Arribas J. Clinical value of next generation sequencing of plasma cell-free DNA in gastrointestinal stromal tumors. *BMC Cancer*. 2020 Feb 5;20(1):99.

Blay JY, Serrano C, Heinrich MC, Zalcberg J, Bauer S, Gelderblom H, Schöffski P, Jones RL, Attia S, D'Amato G, Chi P, Reichardt P, Meade J, Shi K, Ruiz-Soto R, George S, von Mehren M. Ripretinib in patients with advanced gastrointestinal stromal tumours (INVICTUS): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2020 Jul;21(7):923-934.

Serrano C, George S. Gastrointestinal Stromal Tumor: Challenges and Opportunities for a New Decade. *Clin Cancer Res*. 2020 Oct 1;26(19):5078-5085.

Heinrich MC, Jones RL, von Mehren M, Schöffski P, Serrano C, Kang YK, Cassier PA, Mir O, Eskens F, Tap WD, Rutkowski P, Chawla SP, Trent J, Tugnait M, Evans EK, Lauz T, Zhou T, Roche M, Wolf BB, Bauer S, George S. Avapritinib in advanced PDGFRA D842V-mutant gastrointestinal stromal tumour (NAVIGATOR): a multicentre, open-label, phase 1 trial. *Lancet Oncol*. 2020 Jul;21(7):935-946.

PRECLINICAL & TRANSLATIONAL RESEARCH

STEM CELLS & CANCER GROUP

Principal Investigator Héctor G. Palmer Post-Doctoral Fellows Oriol Arqués, Estefania Cuesta, Jordi Martínez- Quintanilla, Isabel Puig Phd Student Candida Salvans Gorjón Graduate Student Alex Mur Technicians Laia Cabellos Irene Chicote, Jordi Vergés San Jaime

STRATEGIC GOALS

- Achieve a deeper understanding Tumor Dormancy.
- Studying the role of epigenetic factors ruling dormancy in chemoresistance, minimal residual disease, relapse, dissemination and metastasis.
- ONIRIA - modulating cell dormancy to combat cancer.
- The development of small drugs modulators of cancer cell dormancy to block cancer progression.
- Matching targeted therapies.
- Unveil the mechanisms of response to drugs targeting EGFR, BRAF, MEK, ERK, LGR5, Wnt or PARP.
- Refining advanced cancer models.
- Expand our collection of PDXs and develop new orthotopic models and 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.
- Matched 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.
- We have generated and refined new cancer models of colorectal cancer in collaboration with several European-funded networks.

SUMMARY

Héctor G. Palmer's Stem Cells & Cancer Group studies the mechanisms that enable tumors to evade effective treatments and progress to advanced stages.

His team uses 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 and xenografts (PDX) they study the functional relevance of these newly identified alterations in patients' response to therapies.

Héctor's group is also part of a global multidisciplinary task force incorporating medical oncologists, surgeons, radiologists, and nurses. This strong collaboration means that laboratory results can be rapidly translated to the clinic.

Main research lines include:

Tumor cell dormancy

The study of the intriguing biology of cancer cell dormancy that is responsible for chemoresistance, formation of minimal residual disease, and disease relapse in patients.

His team discovered a core epigenetic network governing dormancy of tumor cells (J Clin Invest. 2018), and is now investigating the function of TET2, DPPA3 and other epigenetic and transcription factors governing dormancy in greater depth. Importantly, they are 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

This group works 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 or BRAF/MEK/ERK oncogenic signals (*Nat Med*. 2012; *Clin Can Res*. 2014; *Clin Can Res*. 2019).

Based on their discoveries, they are designing new prescreening tests for the genetic-guided enrolment of patients in clinical trials. Crucially, findings are helping to define new rational drug combinations to treat cancer patients with progressive disease.

Advanced pre-clinical models of cancer

The group is also expanding and characterizing its PDX collections (CRC, neuroendocrine and peritoneal pseudomyxoma), and improving their potential to evaluate drug efficacy and metastasis by orthotopic injection and live imaging (TC, PET and Echography).

Lastly, the investigators are developing ambitious projects through the EuroPDX Consortium (page 176), a collaboration that VHIO co-founded which incorporates all the main reference groups working with PDX in Europe.

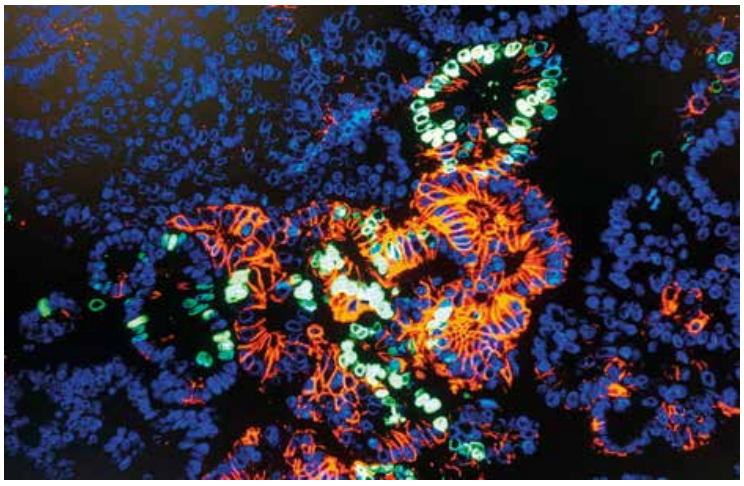


Figure: Chemoresistant dormant tumor cells (green nuclei) hide within hypoxic niches (red) in growing carcinomas.

PI PAPER PICK

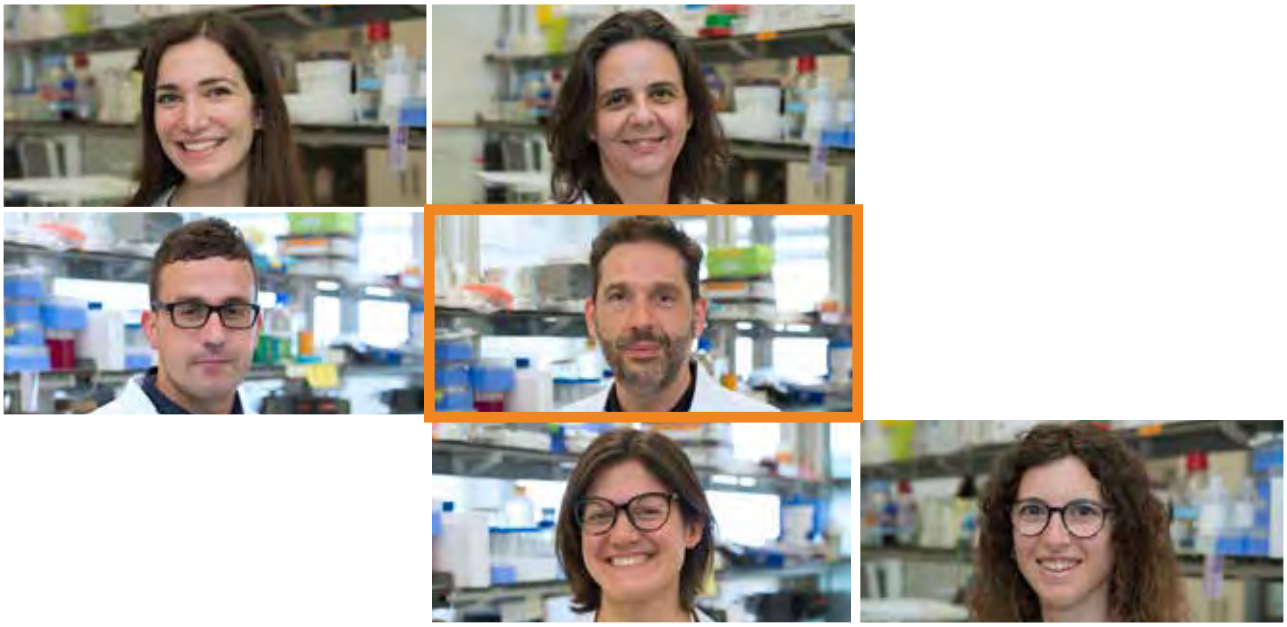
Chicote I, Cámara JA, Palmer HG. Advanced Colorectal Cancer Orthotopic Patient-Derived Xenograft Models for Cancer and Stem Cell Research. *Methods Mol Biol*. 2020; 2171:321-329.

Lehal R, Zaric J, Vigolo M, Urech C, Frismantas V, Zangger N, Cao L, Berger A, Chicote I, Loubéry S, Choi SH, Koch U, Blacklow SC, Palmer HG, Bornhauser B, González-Gaitán M, Arsenijevic Y, Zoete V, Aster JC, Bourquin JP, Radtke F. Pharmacological disruption of the Notch transcription factor complex. *Proc Natl Acad Sci U S A*. 2020 Jul 14;117(28):16292-16301.

Bruun J, Kryeziu K, Eide PW, Moosavi SH, Eilertsen IA, Langerud J, Røsok B, Totland MZ, Brunsell TH, Pellinen T, Saarela J, Bergsland CH, Palmer HG, Brudvik KW, Guren T, Dienstmann R, Guren MG, Nesbakken A, Bjørnbeth BA, Sveen A, Lothe RA. Patient-Derived Organoids from Multiple Colorectal Cancer Liver Metastases Reveal Moderate Intra-patient Pharmacotranscriptomic Heterogeneity. *Clin Cancer Res*. 2020 Aug 1;26(15):4107-4119.

Capdevila J, Arqués O, Hernandez Mora JR, Matito J, Caratu 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. Epub 2019 Oct 31.

TUMOR BIOMARKERS GROUP



Principal Investigator Josep Villanueva Post-Doctoral Fellows Chiara Bellio, Olga Méndez Graduate Student Mireia Pujals Technicians Marta Emperador, Mireia Pares, José Ángel Robles, Candida Salvans, Gabriel Tamayo

STRATEGIC GOALS

- Exploit the role of non-classical secretion linked to tumor invasion and metastasis to identify biomarkers and therapeutic targets against breast cancer.
- Characterize the role of extracellular HMGA1-RAGE pathway in breast cancer invasion and metastasis.
- The characterization of mechanisms adopted by tumor cells to communicate with their microenvironment during treatment to establish secreted response/resistance biomarkers to cancer drug therapies.

HIGHLIGHTS

- We have continued with the characterization of the extracellular HMGA1-RAGE pathway in Triple-Negative Breast Cancer (TNBC). While HMGA1 is still a clear focus of our investigations, we have also expanded our research to study RAGE. We have been performing research to delineate the role of RAGE in tumor invasion and metastasis in TNBC.
- Major research efforts center on the development of response and resistance biomarkers to cancer drugs used in the clinic to treat TNBC patients. Furthermore, we have been working towards the identification of mechanisms of acquired resistance for current anti-cancer medicines.

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.

Our main aim is to characterize the mechanisms adopted by these cells to communicate amongst themselves as well as with their microenvironment during tumorigenesis. We aim to exploit these data to advance biomarker and drug target discovery.

Our team's working hypothesis is that cellular signaling pathways undergo alterations during the tumorigenesis process and that these changes are translated into differential protein secretion, which can also potentially be used to identify secreted markers. Furthermore, some of the differentially regulated proteins could be direct extracellular messengers of intracellular signaling pathways contributing to fundamental stages implicated in cancer initiation and progression, therefore representing potential therapeutic targets.

The methodological focus of our group centers on profiling the secreted sub-proteome ('secretome') of cells by quantitative mass spectrometry. Most secreted proteins contain a signal peptide that directs their sorting to the extracellular space through the endoplasmic reticulum (ER)–Golgi secretory pathway. One of the most striking observations when secretome profiles are carefully produced and analyzed is that they contain hundreds of theoretical intracellular proteins.

Recent reports showing intracellular proteins with alternative extracellular functions suggest that new protein functions associated with alternative subcellular localizations could implicated in tumorigenesis.

In line with this notion, our recent efforts within the context of therapeutics and tumor invasion have led us to hypothesize that the characterization of non-classical protein secretion could lead to the development of novel anti-cancer therapies.

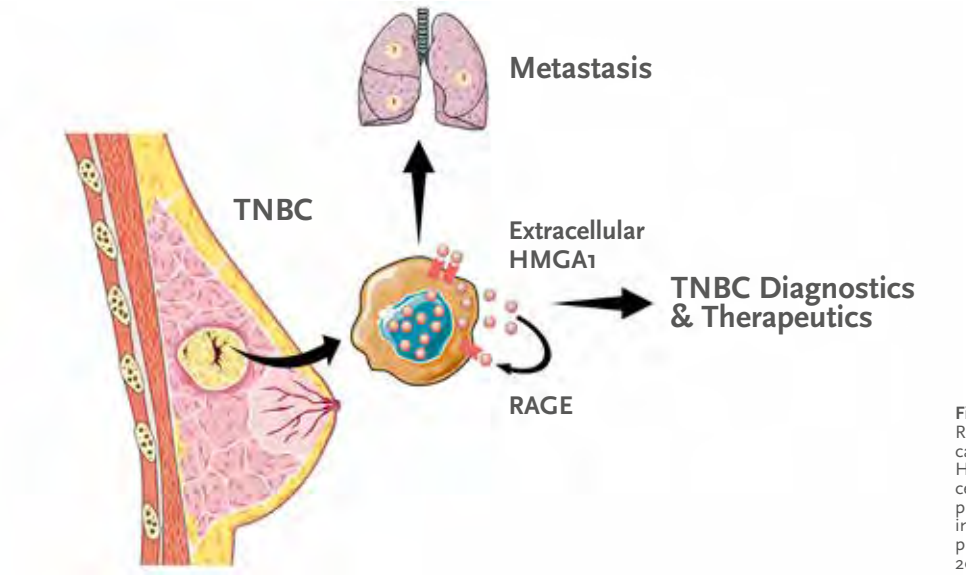


Figure: Role of extracellular the HMGA1-RAGE pathway in triple-negative breast cancer (TNBC). The establishment of an HMGA1-RAGE autocrine loop in TNBC cells increases their migratory and invasive phenotype, and correlates with an increased incidence of distant metastasis in TNBC patients. Méndez et al. *Int J Mol Sci.* 2019. 20(23), 5950.

PI PAPER PICK

Granado-Martínez P, Garcia-Ortega S, González-Sánchez E, McGrail K, Selgas R, Grueso J, Gil R, Naldaiz-Gastesi N, Rhodes AC, Hernandez-Losa J, Ferrer B, Canals F, Villanueva J, Méndez O, Espinosa-Gil S, Lizcano JM, Muñoz-Couselo E, García-Patos V, Recio JA. STK11 (LKB1) missense somatic mutant isoforms promote tumor growth, motility and inflammation. *Commun Biol.* 2020 Jul 9;3(1):366.

Bellio C, Villanueva J. Hitting the brakes on autophagy for overcoming acquired resistance in triple negative breast cancer. *Ann Transl Med.* 2020 Jul;8(14):848.

TUMOR IMMUNOLOGY & IMMUNOTHERAPY GROUP

Principal Investigator Alena Gros Post-Doctoral Fellows Ricky Fong, Jara Palomero Graduate Students Judit Díaz, Andrea García, Maria Lozano, Anna Yuste Technicians Immaculada Creus, Albert Marín Student Carla Panisello Lab Manager Noelia Alcazar

STRATEGIC GOALS

- Characterize the personalized anti-tumor T-cell response in cancer patients.
- Mine the personalized repertoire of tumor-reactive lymphocytes for potential biomarkers of response to cancer immunotherapy.
- Investigate novel strategies to more swiftly identify tumor-reactive lymphocytes as well as the target antigens driving this response.
- Study the tumor cell intrinsic mechanisms of resistance to T cell mediated cytotoxicity
- Develop personalized T-cell-based cancer immunotherapies for patients with solid tumors.

HIGHLIGHTS

- We have finalized the clinical grade validations of TIL expansion for the treatment of patients at VHIO in collaboration with the Blood and Tissue Bank (BST), a Public Health Department of the Government of Catalonia. and thanks to the funding received from the BBVA Foundation and its Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI – page 124) at VHIO.
- Elena Garralda, Principal Investigator of VHIO's Early Clinical Drug Development (page 92) and Director of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 133), has designed the clinical protocol to treat patients with solid and immunotherapy refractory tumors with TILs enriched for neoantigen recognition. We have recently submitted the investigational new drug (IND) application and clinical protocol to the *Agencia Española de Medicamentos y Productos Sanitarios* (AEMPS – Spanish Regulatory Agency), in February 2021. Our aim is to treat patients by mid-2021.
- Our group is now collaborating with Holger Heyn, Team Leader at the National Center for Genomic Analysis (CNAG-CRG), Barcelona, to study the T cells infiltrating endometrial cancers with unprecedented detail, at the single cell level. These studies will guide the identification of T cells with superior traits for adoptive cell transfer.

SUMMARY

The immune system can recognize, hone in on and eliminate cancer. Through multiple mechanisms however, tumors can evade the immune response.

Immunotherapies against cancer exploit the immune system to more effectively attack disease. Clinical studies have shown that immune checkpoint inhibitors and T-cell-based therapies can mediate tumor regression in cancer patients with metastatic disease. Thus, in addition to surgery, radiation therapy and chemotherapy, immunotherapy is increasingly representing the fourth pillar of anti-cancer therapy across various tumor types.

Despite encouraging antitumor responses, currently only a fraction of patients treated with immune-based therapies respond, and some unfortunately report autoimmune- related adverse events. There is therefore a critical need to develop and personalize these promising treatments.

To do so, and thanks to the support received from the BBVA Foundation's Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI) at VHIO (see page 124), we study mechanisms of response, toxicity and resistance to cancer immunotherapeutics in patients at the Vall d'Hebron University Hospital (HUVH). We aim to identify biomarkers of response in liquid biopsies.

One correlative biomarker described to-date is mutation burden. Tumor-specific somatic mutations are optimal targets for cancer immunotherapy and render tumors immunogenic; some of these can bind to the patients' human leukocyte antigen (HLA) molecules and elicit T-cell responses.

We adopt a highly personalized approach to screen for T-cell mediated recognition of mutated antigens as well as shared antigens using autologous antigen presenting cells that can process and present in all the potential HLA restriction elements.

Following this strategy, we aim to establish whether the presence of lymphocytes recognizing these antigens is associated with response. In parallel, we plan to advance personalized T-cell therapies to treat metastatic colorectal cancer, which is largely resistant to current anti-cancer strategies. We have recently filed an investigational new drug (IND) application to the *Agencia Española de Medicamentos y Productos Sanitarios* (AEMPS - Spanish Regulatory Agency), in February 2021 that will enable us to treat patients with metastatic epithelial or immunotherapy refractory cancers with neoantigen-reactive TILs using this personalized approach. By enriching for neoantigen-reactive lymphocytes, we hope to enhance the efficacy of TIL therapy in epithelial cancers.

In summary, 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.

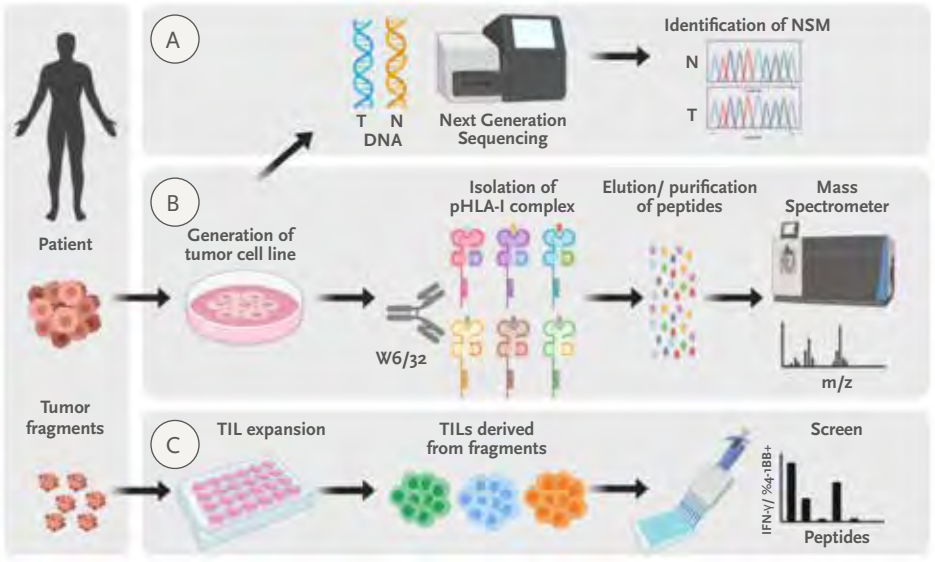


Figure: Personalized approach to identify tumor and neoantigen- specific TILs. a) We sequence normal and tumor DNA to identify all the non-synonymous mutations. b) In parallel we attempt to generate a tumor cell line. When generated, we isolate the peptide-MHCI complexes and we identify the peptides 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

Lozano-Rabella M, Gros A. TCR Repertoire Changes during TIL Expansion: Clonal Selection or Drifting? *Clin Cancer Res.* 2020 Aug 15;26(16):4177-4179.


3
Consulta

CLINICAL RESEARCH

90 Breast Cancer & Melanoma Group

92 Early Clinical Drug Development Group

94 Experimental Hematology Group

96 Gastrointestinal & Endocrine Tumors Group

98 Genitourinary, CNS Tumors, Sarcoma & Cancer of Unknown Primary Site Group

100 Gynecological Malignancies Group

102 Hereditary Cancer Genetics Group

104 Oncology Data Science (ODysSey) Group

106 Radiation Oncology Group

108 Radiomics Group

110 Thoracic Tumors & Head and Neck Cancer Group

Due to safety and logistical considerations brought about by the COVID-19 pandemic, and to reflect the reality of balancing those physically working in the lab and clinical settings, with those working from home, we had to rethink our approach to this year's Scientific Report photo shoot and set up. We translated this obstacle into opportunity*.

To be able to include as many group members as possible, and photograph our researchers and investigators without masks, we took each picture individually, at a distance, and in locations away from areas dedicated to the care of our cancer patients. Designed to depict the very familiar "Zoom" virtual meeting scenario, we were able to also include faculty who were homeworking at the time of each photo session, by inviting them to send their pictures from home.

* Considering certain logistical and spatial issues, we have unfortunately had to repeat pictures of some of our larger groups and units from VHIO's Scientific Report 2019 - as indicated in the corresponding pages.

BREAST CANCER & MELANOMA GROUP

Principal Investigator Cristina Saura Medical Oncologists and Clinical Fellows Miriam Arumi, Judith Balmaña, Meritxell Bellet, Marta Capelan, Mara Cruellas, Santiago Escrivá, Laia Garrigos, Patricia Gómez, Eva Muñoz, Mafalda Oliveira, Carolina Ortiz, Isabel Pimentel, Esther Zamora Clinical Nurse Anna Suñol

STRATEGIC GOALS

Breast:

- Optimize therapies by introducing novel anti-cancer treatments and adding rational combinations to combat mechanisms of resistance.
- Incorporate proteomics, genomics, and cfDNA 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 spearheads one of the largest networks in Spain and across Europe, and is also one of the most active in metastatic and adjuvant clinical trials in melanoma and other skin tumors. Each trial is tightly connected with the corresponding translational research lines led by VHIO scientists.

HIGHLIGHTS

- Relevant contributions in drug approval. Thanks to the leadership position of our investigators, we have contributed to the approval of drugs including trastuzmab deruxtecan, tucatinb, sacituzumab govitecan or margetuximab for patients with advanced breast cancer, nivolumab in the melanoma adjuvant setting 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 cancer or several IO combinations, targeted therapies and anti-PD1 for SCC and BSC treatment that will led to new approvals in the near future.
- Precision medicine. Thanks to VHIO's Molecular Prescreening Program (page 140), driven by one of our Institutional Programs, Advanced Molecular Diagnostics Program (DIAMAV), which is supported by the FERO Foundation (page 122), we continue to identify potential 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* and other mutations for patients with melanoma and other cutaneous tumors. Our Institute's proteomics and cfDNA platforms have also helped us to advance insights into tumor biology.

SUMMARY

The main area of expertise of the Breast Cancer Group led by Cristina Saura is clinical research focused on drug development and associated translational research.

In addition to high patient recruitment in our studies maintained even the challenging scenario of the Covid-19 pandemic, we also play a leading role in many of the clinical trials that we run. This enables us to have a direct impact in applying 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 DS8201, tucatinib, neratinib, margetuximab and SYD985. In collaboration with VHIO's Growth Factors Group (page 74), led by Joaquín Arribas, we explore cancer drug resistance to these agents through VHIO's in-house established PDX models.
  Alongside Paolo Nuciforo's Molecular Oncology Group (page 118), we are aiming to validate more precise methods to quantify HER2 expression.
- Luminal disease: In partnership with VHIO's Experimental Therapeutics Group, headed by Violeta Serra (page 70), we have developed several PDX models to advance our understanding of 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 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.
- cfDNA: 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 various projects to address the challenging scenario of early disease and the identification of cfDNA in unexplored biological samples including breast milk.

Our Melanoma and other skin tumors Group is led by Eva Muñoz. She has actively participated in the development of -and active recruiting in- several phase I, II and III trials mainly focused on melanoma and other skin cancers to study various emerging therapies for the treatment of these diseases. This group leads its own research program incorporating clinical investigators, dermatologists and cancer researchers at VHIO.

The team's 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. Eva's group mainly focuses on squamous and basocellular carcinoma resistance acquisition and disease progression. Her team also maps therapeutic avenues, follows up standards, and identifies biomarkers for a more precise treatment selection matched to the specificities of our patients.

PI PAPER PICK

Saura C, Oliveira M, Feng YH, Dai MS, Chen SW, Hurvitz SA, Kim SB, Moy B, Delaloge S, Gradishar W, Masuda N, Palacova M, Trudeau ME, Mattson J, Yap YS, Hou MF, De Laurentiis M, Yeh YM, Chang HT, Yau T, Wildiers H, Haley B, Fagnani D, Lu YS, Crown J, Lin J, Takahashi M, Takano T, Yamaguchi M, Fujii T, Yao B, Bebchuk J, Keyvanjah K, Bryce R, Brufsky A; NALA Investigators. Neratinib Plus Capecitabine Versus Lapatinib Plus Capecitabine in HER2-Positive Metastatic Breast Cancer Previously Treated With ≥ 2 HER2-Directed Regimens: Phase III NALA Trial. *J Clin Oncol*. 2020 Sep 20;38(27):3138-3149.

Schmid P, Salgado R, Park YH, Muñoz-Couselo E, Kim SB, Sohn J, Im SA, Foukakis T, Kuemmel S, Dent R, Yin L, Wang A, Tryfonidis K, Karantza V, Cortés J, Loi S. Pembrolizumab plus chemotherapy as neoadjuvant treatment of high-risk, early-stage triple-negative breast cancer: results from the phase 1b open-label, multicohort KEYNOTE-173 study. *Ann Oncol*. 2020 May;31(5):569-581.

Lin NU, Borges V, Anders C, Murthy RK, Paplomata E, Hamilton E, Hurvitz S, Loi S, Okines A, Abramson V, Bedard PL, Oliveira M, Mueller V, Zelnak A, DiGiovanna MP, Bachelot T, Chien AJ, O'Regan R, Wardley A, Conlin A, Cameron D, Carey L, Curigliano G, Gelmon K, Loibl S, Mayor J, McGoldrick S, An X, Winer EP. Intracranial Efficacy and Survival With Tucatinib Plus Trastuzumab and Capecitabine for Previously Treated HER2-Positive Breast Cancer With Brain Metastases in the HER2CLIMB Trial. *J Clin Oncol*. 2020 Aug 10;38(23):2610-2619.

Prat A, Saura C, Pascual T, Hernando C, Muñoz M, Paré L, González Farré B, Fernández PL, Galván P, Chic N, González Farré X, Oliveira M, Gil-Gil M, Arumi M, Ferrer N, Montaño A, Izarzugaza Y, Llombart-Cussac A, Bratos R, González Santiago S, Martínez E, Hoyos S, Rojas B, Virizuela JA, Ortega V, López R, Céliz P, Ciruelos E, Villagrasa P, Gavilá J. Ribociclib plus letrozole versus chemotherapy for postmenopausal women with hormone receptor-positive, HER2-negative, luminal B breast cancer (CORALLEEN): an open-label, multicentre, randomised, phase 2 trial. *Lancet Oncol*. 2020 Jan;21(1):33-43.

EARLY CLINICAL DRUG DEVELOPMENT GROUP

Director of Clinical Research at VHIO Josep Tabernero Principal Investigator, Early Clinical Drug Development Group, Director, UITM - CaixaResearch Elena Garralda Associated Investigators - Senior Consultants Judith Balmaña, Joan Carles, Enriqueta Felip, Elena Garralda, Teresa Macarulla, Ana Oaknin, Cristina Saura, Josep Tabernero Phase I Investigators Daniel Acosta, Guzman Alonso, Juan David Assaf, Analia Azaro, Iosune Baraibar, Irene Braña, Meritxell Bellet, Ana Callejo, Jaume Capdevila, Marta Capelan, Susana Cedres, Marc Diez, Elena Élez, Santiago Escrivà, Lorena Fariñas, Vladimir Galvao, Carmen Garcia, Patricia Gómez, Macarena González, Francisco Grau, Alberto Hernando, Jorge Hernando, Patricia Iranzo, Alexandre Martínez, Joaquin Mateo, Ignacio Matos, Rafael Morales, Eva Muñoz, Alejandro Navarro, Honey Oberoi, Mafalda Oliveira, Nuria Pardo, Francisco Javier Ros, Omar Saavedra, Carolina Ortiz, Isabel Pimentel, Cesc Salvá, César Serrano, Cristina Suárez, Claudia Valverde, Helena Verdaguer, Maria Vieito, Esther Zamora Data Manager Roger Berche Clinical Nurse Specialist Natassia Ann Wornham

HIGHLIGHTS

- Despite the COVID- 19 Pandemic, 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, ADC and epigenetic drugs.
- Within the scope of the CaixaResearch Advanced Oncology Research Program (page 123), we have performed several clinical trials with patients selected 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 124), we have continued our line of research to characterize hyperprogressive disease with immunotherapy. We have secured further funding to evaluate 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 (Sergio Quezada, University College London (UCL), UK).
- We have continued our collaboration with VHIO's Rodrigo Toledo, to monitor the cfDNA of patients receiving immunotherapy and characterize the clonal evolution of these patients.
- Also within the context of our VHIO-BBVA Foundation's CAIMI program, in collaboration with Raquel Perez-Lopez, PI of our Radiomics Group (page 108), we have established a radiomic signature to predict response to immunotherapy. We have secured further funding to see how this correlates with the genomic evolution seen in patients.
- 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, PI of VHIO's Tumor Immunology & Immunotherapy Group (page 86), our CAR-T cell project funded through a grant received from the Spanish Association against Cancer (AECC) in 2019, and NK cells research in collaboration with colleagues at the Clínica Universitaria de Navarra, in addition to other cell-based therapies.
- We have secured competitive funding to perform the first academic TIL trial performed at VHIO, with NEXTGEN- TIL in collaboration with Alena Gros.
- We have initiated a project to increase 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), through a CRUK Accelerator Award.
- Supported by EU's Horizon 2020 Framework Programme, we are coordinating the Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART) Project (page 179). This pioneering project will develop 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.

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 (page 133), with the 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, pharmaceutical companies).

SUMMARY

We focus on proof-of-concept and proof-of-mechanism 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.

We link clinical research at the Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 133), with different areas of investigation carried out at VHIO, following a truly translational model. For selected projects, we match molecular biology and optimal tumor models with pharmacology and innovative clinical research by involving VHIO scientists in our trials (biomarker development, profound understanding of mechanisms of action and resistance).

We participate in VHIO's Molecular Prescreening Program (page 140) 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.

Importantly, in relation to precision oncology, VHIO is a founding member of both the WIN (Worldwide Innovative Networking in personalized cancer medicine) – page 179, and the Cancer Core Europe (CCE) – page 175, consortia. Both are non-governmental organizations that connect international (WIN) and/or European (CCE) cancer centers, including VHIO, 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. This academic study, endorsed by Cancer Core Europe, integrates molecular prescreening, the development of new diagnostic tests such as 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 this year we have continued to search for funding to add new modules.

We have been working in the EU-funded Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART) project. 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 in the next years to come.

Our Early Drug Development Group and Phase I Unit - UITM – CaixaResearch - continues 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 (521 patients enrolled in phase I and basket studies in 2020), the portfolio of different trials available (195 phase I trials including 22 basket studies in 2020), and the novelty of our programs in precision medicine and immunotherapy drug development. This is also evidenced by our leading role in Cancer Core Europe's Clinical Trials Task Force.

Our CaixaResearch Advanced Oncology Research Program (page 123), continues to expand. This year we have collaborated with Alena Gros to complete the preclinical work to generate the first VHIO TIL therapy, NEXTGEN- TIL, and have secured funding to start the trial next year, in 2021.

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

Tamborero D, Dienstmann R, Rachid MH, Boekel J, Baird R, Braña I, De Petris L, Yachnin J, Massard C, Opdam FL, Schlenk R, Vernieri C, Garralda E, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium, Calvo F, Fröhling S, Eggermont A, Apolone G, Voest EE, Caldas C, Tabernero J, Ernberg I, Rodon J, Lehtiö J. Support systems to guide clinical decision-making in precision oncology: The Cancer Core Europe Molecular Tumor Board Portal. *Nat Med.* 2020 Jul;26(7):992-994.

Matos I, Martin-Liberal J, García-Ruiz A, Hierro C, Ochoa de Olza M, Viaplana C, Azaro A, Vieito M, Braña I, Mur G, Ros J, Mateos J, Villacampa G, Berché R, Oliveira M, Alsina M, Elez E, Oaknin A, Muñoz-Couselo E, Carles J, Felip E, Rodón J, Tabernero J, Dienstmann R, Perez-Lopez R, Garralda E. Capturing Hyperprogressive Disease with Immune-Checkpoint Inhibitors Using RECIST 1.1 Criteria. *Clin Cancer Res.* 2020 Apr 15;26(8):1846-1855.

Drilon A, Oxnard GR, Tan DSW, Loong HHF, Johnson M, Gainor J, McCoach CE, Gautschi O, Besse B, Cho BC, Peled N, Weiss J, Kim YJ, Ohe Y, Nishio M, Park K, Patel J, Seto T, Sakamoto T, Rosen E, Shah MH, Barlesi F, Cassier PA, Bazhenova L, De Braud F, Garralda E, Velcheti V, Satouchi M, Ohashi K, Pennell NA, Reckamp KL, Dy GK, Wolf J, Solomon B, Falchook G, Ebata K, Nguyen M, Nair B, Zhu EY, Yang L, Huang X, Olek E, Rothenberg SM, Goto K, Subbiah V. Efficacy of Selpercatinib in RET Fusion-Positive Non-Small-Cell Lung Cancer. *N Engl J Med.* 2020 Aug 27;383(9):813-824.

van de Haar J, Hoes LR, Coles CE, Seamon K, Fröhling S, Jäger D, Valenza F, de Braud F, De Petris L, Bergh J, Ernberg I, Besse B, Barlesi F, Garralda E, Piris-Giménez A, Baumann M, Apolone G, Soria JC, Tabernero J, Caldas C, Voest EE. Caring for patients with cancer in the COVID-19 era. *Nat Med.* 2020 May;26(5):665-671.

EXPERIMENTAL HEMATOLOGY GROUP

* For logistical issues brought about by the current COVID-19 pandemic, we are repeating pictures of some of our larger groups, services and units from our 2019 Scientific Report.

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 Hematologists/Lab Specialists Adoracion Blanco, Sabela Bobillo, Olga Benitez, Maria Cerda, Cecilia Carpio, Sally Franco, Maria Laura Fox, Laura Gallur, Mercedes Gironella, Gloria Hidalgo, Gloria Iacoboni, Macarena Izuzquiza, Marta Julia, Ana Marin, Maria Martinez, Alba Mesa, Antonieta Molero, Julia Montoro, Mayda Navarrete, Margarita Ortega, Guillem Orti, Ana Ortuño, Carles Palacio, Gloria Passarelli, Gustavo Robayo, Elisa Roldan, Olga Salamero, Silvia Saumell, Milagros Suito, Barbara Tazon, Marta Villalba Post-Doctoral Scientists Laura Palomo, Panagiota Spantidea Phd Students Cristina Hernandez, Daniel Medina, Carlota Pages Technician Sergio Manresa

STRATEGIC GOALS

- We translate preclinical findings into clinical benefit 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 and patient-derived xenograft (PDX) models.
- Defining new biomarkers for a more rational and precise treatment of patients.

HIGHLIGHTS

- In 2020 we have participated in the publication of 56 scientific papers, and as main authors (first, last and/or corresponding) of 15 of these. 67% of these articles are published in journals in the first quartile, with an accumulative Impact Factor of 135.
- This year we have initiated five new projects, four of which are supported through grants received from competitive calls, including *La Fundació La Marató de TV3* and the Institute of Health Carlos III (ISCIII).

SUMMARY

VHIO's Experimental Hematology Group conducts translational, pre-clinical and clinical research on hematological neoplasms of both lymphoid and myeloid origin. Our research team is composed of hematologists and biological scientists who work closely together to design, conduct and lead our programs.

Our projects are always based on the unmet medical 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 outcomes.

We aim to provide new therapeutic options for our patients by deciphering the mechanisms involved in the pathogenesis and progression of hematological malignancies. We also conduct pre-clinical studies of new therapeutic proposals for patients diagnosed with hematological malignancies. Our group fosters the definition of new biomarkers in hematology that will lead to a more rational and precise diagnosis, prognosis and treatment of our patients.

Finally, our Hematology Clinical Trials Unit is currently participating in more than 120 clinical studies, including phase I clinical trials (n=39) and first-in-human studies of targeted therapies, both in lymphoid and myeloid malignancies. Last year 153 patients were included in our clinical studies, with 56 patients enrolled in phase I studies.

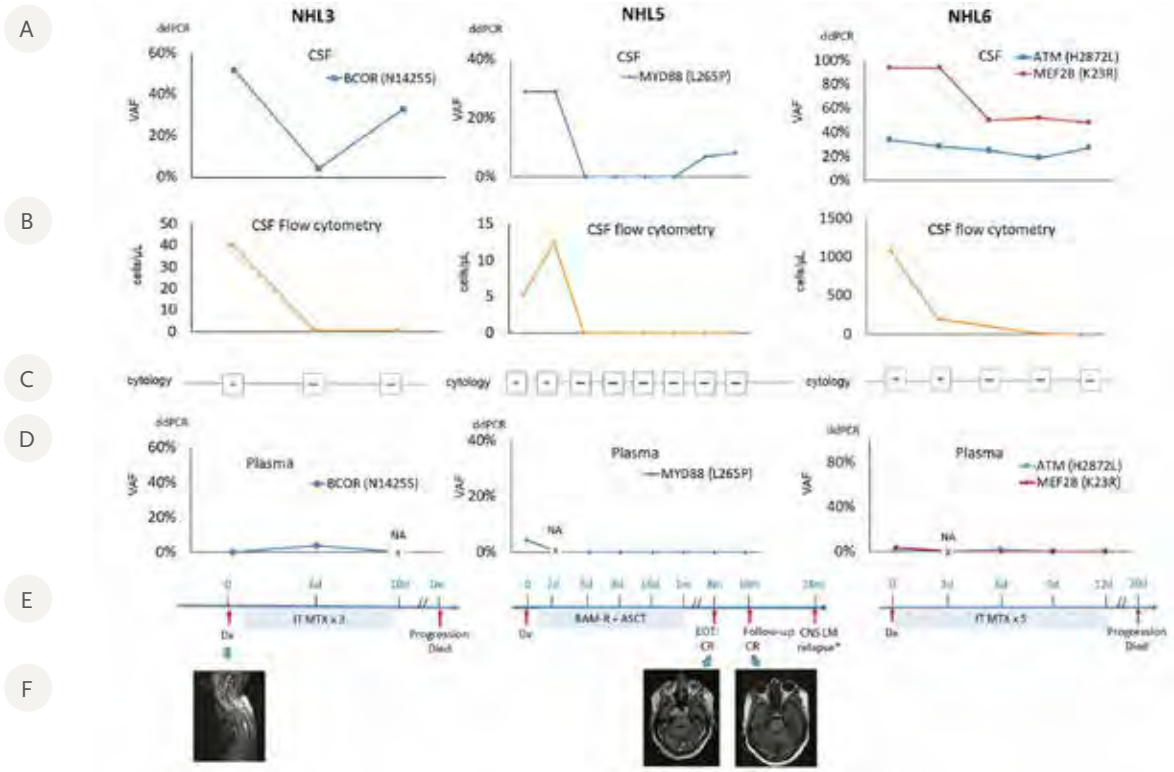


Figure: Cerebrospinal fluid (CSF) circulating tumor DNA (ctDNA) is more sensitive than flow cytometry (FC) to detect central nervous system (CNS) relapse and residual disease in CNS-restricted lymphomas. Bobillo et al, *Haematologica* 2020.

PI PAPER PICK

Jiménez I, Carabia J, Bobillo S, Palacio C, Abrisqueta P, Pagès C, Nieto JC, Castellví J, Martínez-Ricarte F, Escoda L, Perla C, Céspedes Torrez DH, Boix J, Purroy N, Puigdefàbregas L, Seoane J, Bosch F, Crespo M. Repolarization of tumor infiltrating macrophages and increased survival in mouse primary CNS lymphomas after XPO1 and BTK inhibition. *J Neurooncol.* 2020 Aug;149(1):13-25.

Bobillo S, Crespo M, Escudero L, Mayor R, Raheja P, Carpio C, Rubio-Perez C, Tazón-Vega B, Palacio C, Carabia J, Jiménez I, Nieto JC, Montoro J, Martínez-Ricarte F, Castellvi J, Simó M, Puigdefàbregas L, Abrisqueta P, Bosch F, Seoane J. Cell free circulating tumor DNA in cerebrospinal fluid detects and monitors central nervous system involvement of B-cell lymphomas. *Haematologica*. 2020. Epub ahead of print.

Carpio C, Bouabdallah R, Ysebaert L, Sancho JM, Salles G, Cordoba R, Pinto A, Gharibo M, Rasco D, Panizo C, Lopez-Martin JA, Santoro A, Salar A, Damian S, Martin A, Verhoef G, Van den Neste E, Wang M, Couto S, Carrancio S, Weng A, Wang X, Schmitz F, Wei X, Hege K, Trotter MWB, Risueño A, Buchholz TJ, Hagner PR, Gandhi AK, Pourdehnad M, Ribrag V. Avadomide monotherapy in relapsed/refractory DLBCL: safety, efficacy, and a predictive gene classifier. *Blood.* 2020 Mar 26;135(13):996-1007.

Muntañola A, Villacampa G, Hernández-Rivas JÁ, Alonso R, Mirás F, Osorio S, Baile M, Baltasar P, López Jiménez J, Hernandez-Rodriguez I, Valenciano S, Alfayate A, Gimeno E, Bárez A, Oliveira AC, Riaza R, Romero P, Delgado J, Yáñez L, Zabalza A, Torres A, Gómez-Roncero MI, Crespo M, Córdoba R, Mateos-Mazón JJ, Pérez S, Andreu R, Labrador J, Ruiz ME, Velasquez CA, Terol MJ, Santiago R, Vidal MJ, Campoy García F, Villalón L, Muiña BS, Soler JA, Seri C, Sánchez MJ, Cuesta A, Ramos R, Sánchez-Montalvá A, Ruiz-Camps I, González M, Abrisqueta P, Bosch F; of the GELLC (Grupo Español de Leucemia Linfática Crónica). Clinical characteristics and outcome of SARS-CoV-2 infection in admitted patients with chronic lymphocytic leukemia from a single European country. *Exp Hematol Oncol.* 2020 Dec 18;9(1):37.

GASTROINTESTINAL & ENDOCRINE TUMORS GROUP

Director Josep Tabernero Principal Investigator Teresa Macarulla Medical Oncologists and Clinical Research Fellows Daniel Alejandro Acosta, Guillem Argilés, Iosune Baraibar, Jaume Capdevila, Marc Diez, Elena Élez, Jorge Hernando, Javier Ros, Helena Verdaguer Translational Investigator Rodrigo A. Toledo Translational Graduate Student Carlota Arenillas Translational Technician Ana Belen Moreno Clinical Nurse Specialist Alexandre Sierra

STRATEGIC GOALS

- Discovery and validation of novel biomarkers in GI tumors.
- Development of relevant preclinical models (in vitro, in vivo with PDXs and organoids) with emphasis on the identification of predictive markers and mechanisms of primary and secondary resistance.
- Molecular characterization of GI diseases, in particular colorectal, gastric, pancreatic, biliary tract cancers and NETs. Study of targetable subtypes and tumor heterogeneity.
- Clonal evolution studies, with special emphasis in BRAF mutant tumors
- Use of liquid biopsy (ctDNA, Mutant Allele Fraction) to study disease evolution (GI tumors).
- Development of Early clinical research with innovative targets.
- Clinical research in late stage with more translational endpoints, focusing on the identification of prognostic/predictive biomarkers.
- Design, leadership and development of investigator-initiated trials (IIT), including Basket studies.
- Participation in multidisciplinary/multinational consortia and collaborative research programs of excellence.
- Validation of repurposed drugs or candidate drugs, in partnership with pharma companies or academic groups.
- Expansion of research lines in GI cancers including the study of microbiota & immunology and microenvironment.

HIGHLIGHTS

- Development of over 40 different projects (translational research) for GI cancer malignancies.
- We have advanced insights into prognostic and predictive factors for response and efficacy with targeted agents across various gastrointestinal malignancies (Scitron -Novartis, CIBERONC, ISCIII).
- Prospective studies in CRC homogeneous populations in 1st line treatment to study prognostic and predictive value of ctDNA and its correlation with tumor vascularization. Non-invasive methods (liquid biopsy and MRI) - AECC, TV3 Marató.
- New studies on MAF (Mutant Allele Fraction) of BRAFV600E in plasma as a tool for the therapeutic monitoring of patients with a poor prognosis
- Understanding the colorectal cancer microbiome: implications in therapy (OPTIMISTICC).
- Participation in EU Horizon 2020-funded projects and consortia including MoTriColor, IntraColor COLOSSUS, LEGACY, NOCANTHER, THRUST.
- Our group is a partner of many national and international consortia and networks including Cancer Core Europe (CCE), WIN, and CIBERONC
- Single cell profiling persistence to immunotherapy (Partner of Choice, AstraZeneca).
- ACRCelerate: Colorectal Cancer Stratified (ACCELERATOR CRUK).
- BioPrinted hydROgel MicrofluIdicS to mimic patient-specific tumor metastatic microenvironment (PROMISE, CaixaHealth).
- TuMICC: Understanding which mechanisms are utilized by tumor cells to resist therapy and identify patient specific resistance before initiating treatment (Grupos Coordinados, AECC).
- New study of combination of plasmonic photothermal therapy with optical monitoring as a complementary approach for colorectal cancer management (ICFO, within Barcelona Medical Photonic Network).

SUMMARY

VHIO's Gastrointestinal & Endocrine Tumors Group continues to play an essential role in developing molecular therapies against GI malignancies. We make important contributions to advancing insights into prognostic and predictive factors of response and potentiating precision medicine in oncology.

Our group pioneers transformative research of excellence and leads early phase clinical trials aimed at potentiating novel anti-cancer therapies, either as monotherapy or in combination, together with translational studies for biomarker analysis.

Importantly, we co-designed and led the BEACON study. Results showed that the doublet combination of a BRAF inhibitor and an EGFR inhibitor, improves overall survival and also increases objective response rates compared to standard of care in patients with BRAF V600E-mutant mCRC.

We have also made significant progress in validating and developing liquid biopsy technologies for the more effective, less invasive monitoring of cancer in real time. Moreover, our research has shown that genomic and transcriptomic profiling are both useful in guiding the more precise selection of therapies toward improved clinical outcomes for patients.

Our truly multidisciplinary team incorporates medical oncologists and clinical investigators, a translational researcher with expertise in biomarker discovery, a research nurse 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. We also work in close collaboration with other VHIO researchers and groups through our highly interactive and functional Task Forces in colorectal and pancreatic cancers

We have also participated in KEYNOTE-177; one of the highlighted studies featuring in Josep Tabernero's foreword to this year's report (page 9). The particular relevance of this study is that, for the very first time, the administration of immunotherapy as monotherapy has demonstrated superiority to standard of care in the first-line treatment of metastatic colorectal cancer.

Presented during the 2020 Annual Meeting of the American Society of Clinical Oncology (ASCO), and published in the *New England Journal of Medicine* (André T, Shiu KK, Kim TW, et al. *N Engl J Med.* 2020) results of this study could lead to paradigm shift in the treatment of these patients.

During 2020, the European Horizon 2020-supported NoCanTher Consortium reached a major milestone. Launched back in 2016, this project is powered by eleven European partners, including VHIO. Specifically, we completed work to initiate the project's clinical study and subsequently received approval from the necessary regulatory bodies. Leading the assessment and clinical development of magnetic nanoparticles for the treatment of locally advanced pancreatic cancer, this is the first time that this novel approach will be tested in the clinical setting.

Also, in pancreatic cancer, a novel strategy combining immunotherapy and chemotherapy for the treatment of metastatic disease has shown promising results. Data from the COMBAT trial suggest that the addition of chemotherapy could potentiate immunotherapy, which, up until now, has not been effective in treating pancreatic cancer.

The COMBAT investigators combined pembrolizumab that binds to and blocks PD-1 located on lymphocytes to help the immune system destroy cancer cells, with BL-8040, a CXCR4 antagonist, that enhances tumor T cell infiltration.

Finally, we received European Neuroendocrine Tumor Society (ENETS) Certification for excellence in treating neuroendocrine tumors. As the first Unit to do so in Spain, this accreditation jointly recognizes the Vall d'Hebron University Hospital and VHIO.

PI PAPER PICK

André T, Shiu KK, Kim TW, Jensen BV, Jensen LH, Punt C, Smith D, Garcia-Carbonero R, Benavides M, Gibbs P, de la Fouchardiere C, Rivera F, Elez E, Bendell J, Le DT, Yoshino T, Van Cutsem E, Yang P, Farooqui MZH, Marinello P, Diaz LA Jr; KEYNOTE-177 Investigators. Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer. *N Engl J Med.* 2020 Dec 3;383(23):2207-2218.

Shitara K, Van Cutsem E, Bang YJ, Fuchs C, Wyrwicz L, Lee KW, Kudaba I, Garrido M, Chung HC, Lee J, Castro HR, Mansoor W, Braghiroli MI, Karaseva N, Caglevic C, Villanueva L, Goekkurt E, Satake H, Enzinger P, Alsina M, Benson A, Chao J, Ko AH, Wainberg ZA, Kher U, Shah S, Kang SP, Tabernero J. Efficacy and Safety of Pembrolizumab or Pembrolizumab Plus Chemotherapy vs Chemotherapy Alone for Patients With First-line, Advanced Gastric Cancer: The KEYNOTE-062 Phase 3 Randomized Clinical Trial. *JAMA Oncol.* 2020 Oct 1;6(10):1571-1580.

Bockorny B, Semenisty V, Macarulla T, Borazanci E, Wolpin BM, Stemmer SM, Golan T, Geva R, Borad MJ, Pedersen KS, Park JO, Ramirez RA, Abad DG, Feliu J, Muñoz A, Ponz-Sarvise M, Peled A, Lustig TM, Bohana-Kashtan O, Shaw SM, Sorani E, Chaney M, Kadosh S, Vainstein Haras A, Von Hoff DD, Hidalgo M. BL-8040, a CXCR4 antagonist, in combination with pembrolizumab and chemotherapy for pancreatic cancer: the COMBAT trial. *Nat Med.* 2020 Jun;26(6):878-885.

Abou-Alfa GK, Macarulla T, Javle MM, Kelley RK, Lubner SJ, Adeva J, Cleary JM, Catenacci DV, Borad MJ, Bridgewater J, Harris WP, Murphy AG, Oh DY, Whisenant J, Lowery MA, Goyal L, Shroff RT, El-Khoueiry AB, Fan B, Wu B, Chamberlain CX, Jiang L, Gliser C, Pandya SS, Valle JW, Zhu AX. Ivosidenib in IDH1-mutant, chemotherapy-refractory cholangiocarcinoma (ClarIDHy): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study. *Lancet Oncol.* 2020 Jun;21(6):796-807.

GENITOURINARY, CNS TUMORS, SARCOMA & CANCER OF UNKNOWN PRIMARY SITE GROUP

Principal Investigator Joan Carles Medical Oncologists and Clinical Fellows Macarena Gonzalez, Joaquin Mateo, Rafael Morales, César Serrano, Cristina Suarez, Claudia Valverde, Maria Vieito Clinical Nurse Specialist Alexandre Sierra

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 chemotherapies.
- Conduct clinical trials at different stages of disease with emphasis on a histology-tailored design and multidisciplinary approach.
- Consolidate our biopsy program (mainly in bone), 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.
- 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).
- Develop new tools and techniques including liquid biopsy for our patients to more precisely tailor treatments against mCRPC, GIST and kidney cancer.

HIGHLIGHTS

- We have consolidated our Task Force and our Serum Bank in Prostate Cancer. This allows us to participate in different translational studies as leading the IRONMAN Project in Spain.
- Expansion of our Phase I program across all tumor types studied by our group.
- Fostered and developed new collaborations with different VHIO as well as external research groups.

SUMMARY

We are dedicated to advancing clinical and translational research against cancer, with extensive experience and expertise in treating various neoplasms. We design and develop clinical trials for genitourinary malignancies at different stages of disease in collaboration with urologists and radiation therapists.

During 2020 we continued to consolidate our expert Prostate Task Force. By closely connecting clinical and translational researchers at VHIO and the Vall d'Hebron Research Institute (VHIR), we have initiated translational projects focused on prostate cancer. We are also doing the same for kidney cancer in pursuit of similar goals in collaboration with other partners including the Biomedical Research Institute of Bellvitge (IDIBELL).

Over recent years, several advances have been reported in the more effective treatment of GU malignancies. Immunotherapy (IO) is proving increasingly important against bladder and kidney cancers. Concerning the latter, immune-based therapies in combination with others, or paired with antiangiogenics, are considered the new standard treatments for first-line therapy.

In bladder cancer immunotherapy has also been shown as superior to chemotherapy in second line and in first-line for ineligible patients. It has recently been shown that immunotherapy as maintenance after 4/6 cycles of chemotherapy in first-line improves progression-free survival (PFS) and overall survival (OS).

Our group –along with others- has observed that immunotherapy could also be effective for certain subgroups of patients with castration-resistant prostate cancer. We are currently participating in phase I studies to assess immune-based cancer medicines for the treatment of this patient population.

We have also participated in various clinical trials using checkpoint inhibitors for the adjuvant treatment of bladder and kidney cancers with high risk of recurrence. Working closely with our Vall d'Hebron University Hospital's Urology Department and other experts in high-risk tumors, we are currently running studies aimed at improving outcomes for patients with non-muscle- invasive bladder cancer.

We collaborate with various other renowned research centers including the Cleveland Clinic (Ohio, USA), University of California, San Francisco (California, USA). We also participate in studies carried out 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 expanded our translational research program in prostate cancer working alongside VHIO's Prostate Cancer Translational Research Group, led by Principal Investigator Joaquin Mateo (page 78).

Our main focus is metastatic castration-resistant prostate cancer and we are working on a project led by Joaquin, 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 US Department of Defense's (DoD) Congressionally Directed Medical Research Program. Additionally, we are participating in the IRONMAN project lead by the Memorial Sloan Kettering Cancer Center (MSKCC – New York, USA). Led by VHIO, we collect patients' reported outcomes in parallel with serum. This research is supported by Movember and the FERO Foundation.

We are also partnering with VHIO's Radiomics Group (page 108) headed by Raquel Perez-Lopez 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, radio-oncologist, radiologist and medical oncologist to establish a circuit for the systematic metastatic tissue acquisition from prostate cancer patients at our Hospital.

We have also expanded our avatar program for kidney cancer tumors in collaboration with IDIBELL and implanted more than 35 samples. Additionally, we 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, supported by TRANSCAN-2 ERA-NET, under the scope of the EU Framework Programme Horizon 2020.

In collaboration with other professionals in neurosurgery and radiation therapy, we lead and develop several multidisciplinary clinical studies and phase I trials in CNS tumors. Additionally, it is thanks to a project with our Gene Expression & Cancer Group led by Joan Seoane (page 72) that we continue to develop VHIO's translational research platform for glioblastoma. We analyze cfDNA in blood and cephaloraquidic liquid for assessing primary CNS tumors and metastases.

Our group also participates in a project directed by the European Organisation for Research and Treatment of Cancer (EORTC, Brussels, Belgium), against several tumor types, working on CNS tumors: *Cancer Patients for Efficient Clinical Trial Access* (SPECTA). The main objective is to screen patients and develop academic clinical trials based on molecular stratification. This initiative is supported by the European Cancer Research Fund (ECRF) and Walgreens Boots Alliance (WBA). We are also active at the national level in a medulloblastoma platform to better define and classify these cancers.

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). For 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 CSUR for the treatment of Sarcoma patients. This accreditation enables us to participate in the European References Network (ERN) for sarcoma tumors and other rare diseases.

In 2019, César Serrano he set up his own research group, VHIO's Sarcoma Translational Research (page 80). During this year we have consolidated different clinical trials with new drugs in GIST by leading and participating in phase I-II-III studies. As this report went to print, one of these studies led to the U.S. Food and Drug Administration's (FDA) January 2020 approval of Avapritinib for the treatment of adult patients harboring a platelet-derived growth factorreceptor alpha (PDGFRA) exon 18 mutation, including D842V mutations.

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 2020 we welcomed six fellows from in (5) and outside (1) of Spain for three-month short stays.

PI PAPER PICK

Mateo J, Porta N, Bianchini D, McGovern U, Elliott T, Jones R, Syndikus I, Ralph C, Jain S, Varughese M, Parikh O, Crabb S, Robinson A, McLaren D, Birtle A, Tanguay J, Miranda S, Figueiredo I, Seed G, Bertan C, Flohr P, Ebbs B, Rescigno P, Fowler G, Ferreira A, Riisnaes R, Pereira R, Curcean A, Chandler R, Clarke M, Gurel B, Crespo M, Nava Rodrigues D, Sandhu S, Espinasse A, Chatfield P, Tunariu N, Yuan W, Hall E, Carreira S, de Bono JS. Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial. *Lancet Oncol.* 2020 Jan;21(1):162-174. Clinical Trial.

Matos I, Martin-Liberal J, Garcia-Ruiz A, Hierro C, Ochoa de Olza M, Viaplana C, Azaro A, Vieito M, Braña I, Mur G, Ros J, Mateos J, Villacampa G, Berche R, Oliveira M, Alsina M, Elez E, Oaknin Ana, Munoz-Couselo E, Carles J, Felip E, Rodon J, Tabernero J, Dienstmann R, Perez-Lopez R, Garralda E. Capturing Hyperprogressive Disease with Immune-Checkpoint Inhibitors Using RECIST 1.1 Criteria. *Clin Cancer Res.* 2020 Apr 15;26(8):1846-1855.

Morales-Barrera R, Suárez C, González M, Valverde C, Serra E, Mateo J, Raventos C, 03 Maldonado X, Morote J, Carles J. The future of bladder cancer therapy: Optimizing the inhibition of the fibroblast growth factor receptor. *Cancer Treat Rev.* 2020 Jun; 86. Article 102000.

Fizazi K, Kramer G, Eymard JC, Sternberg CN, de Bono J, Castellano D, Tombal B, Whuelfing C, Liontos M, Carles J, Iacovelli R, Melichar B, Sverrisdottir A, Theodore C, Eyerabend S, Helissey C, Oudard S, Facchini G, Poole EM, Ozatilgan A, Geffriaud-Ricouard C, Bensfia S, de Wit R. Quality of life in patients with metastatic prostate cancer following treatment with cabazitaxel versus abiraterone or enzalutamide (CARD): an analysis of a randomised, multicentre, open-label, phase 4 study. *Lancet Oncol.* 2020 Nov;21(11):1513-1525.

GYNECOLOGICAL MALIGNANCIES GROUP

Principal Investigator Ana Oaknin Medical Oncologists Lorena Fariñas, Carmen García Durán, Francisco Grau

STRATEGIC GOALS

- Determine the best treatment approaches against advanced gynecologic malignancies through optimally designed international clinical trials.
- Contribute to early 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 take the lead on other clinical trials toward defining next generation treatment regimens:

- Ana Oaknin signed the FDA filing of dostarlimab (PD-1 inhibitor) in MSI-H recurrent endometrial cancer after successfully presenting the results of the clinical trial, included in the file. at the Society of Gyencologic Oncology's (SGO) 2019 Annual Meeting (Honolulu, Hawaii, March 16-19).
- Ana is the global lead of a phase III Investigator-Initiated Trial for first line metastatic cervical cancer (the BEATcc trial) running in USA, EU and Japan. She is also the European lead investigator of the EMPOWER trial, a phase III study aimed at testing cemiplimab in recurrent cervical cancer. Both of these trials promise potentially practice-changing data.
- She is also the lead investigator of the ATOMICC Trial to investigate the role of dostarlimab as maintenance therapy in locally advanced cervical cancer.

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 group 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 in gynecological oncology including the Gynecologic Cancer InterGroup (GCIG) for which we are appointed as the Spanish Representative serving on its Cervical Cancer and Phase II Trial Committees, the Gynecologic Oncology Group (GOG), as the Spanish clinical lead, as well as the European Network of Gynecological Oncology Trial Groups (ENGOT).

Our group contributes to the advancement of the treatment of gynecological malignancies. Over the past few years, we have participated in the development of a number of therapies that are now the current standard of care for different malignancies.

In 2020 we participated in several important clinical trials that have generated new and compelling data in gynecologic malignancies. As an example, we led the GARNET study. This trial includes the largest series of patients with endometrial cancer (EC) treated with immunotherapy; the anti-PD-1 agent, dostarlimab.

As this Scientific Report was being finalized, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion in February 2021, recommending dostarlimab for the treatment of patients with EC who have progressed to platinum therapy. Initial data that led to this approval was published in *JAMA Oncology* (Oaknin, A et al. *JAMA Oncol.* 2020).

While metastatic cervical cancer is a devastating disease, over recent years we have succeeded in expanding therapeutic approaches which have mainly been driven by immunotherapy. Moreover, we are working on other targeted agents such as neratinib that is showing promising results (Oaknin, A et al. *Gynecol Oncol.* 2020).

In addition, our Principal Investigator, Ana Oaknin, also serves on the Executive Board as Vice President for the *Grupo Español de Investigación en Cáncer de Ovario* – GEICO (the Spanish Ovarian Cancer Research Group); and as Faculty of the European Society for Medical Oncology's (ESMO) Annual Meeting's Gynecological Tumors Track, for which she was appointed as the Track Chair at the ESMO 2019 Congress, 27 September – 01 October (Barcelona, Spain), and Discussant of the Track's Presidential Symposium during which, the results of two Phase III trials were presented. Most recently, at the beginning of 2021, she was appointed as a Subject Editor of ESMO's Guidelines Committee.

PI PAPER PICK

Oaknin A, Tinker AV, Gilbert L, Samouëlian V, Mathews C, Brown J, Barretina-Ginesta MP, Moreno V, Gravina A, Abdeddaim C, Banerjee S, Guo W, Danaee H, Im E, Sabatier R. Clinical Activity and Safety of the Anti-Programmed Death 1 Monoclonal Antibody Dostarlimab for Patients With Recurrent or Advanced Mismatch Repair-Deficient Endometrial Cancer: A Nonrandomized Phase 1 Clinical Trial. *JAMA Oncol*. 2020 Oct 1;6(11):1–7.

Oaknin A, Friedman CF, Roman LD, D'Souza A, Brana I, Bidard FC, Goldman J, Alvarez EA, Boni V, ElNaggar AC, Passalacqua R, Do KTM, Santin AD, Keyvanjah K, Xu F, Eli LD, Lalani AS, Bryce RP, Hyman DM, Meric-Bernstam F, Solit DB, Monk BJ. Neratinib in patients with HER2-mutant, metastatic cervical cancer: Findings from the phase 2 SUMMIT basket trial. *Gynecol Oncol*. 2020 Oct;159(1):150-156.

Lheureux S, Oaknin A, Garg S, Bruce JP, Madariaga A, Dhani NC, Bowering V, White J, Accardi S, Tan Q, Braunstein M, Karakasis K, Cirlan I, Pedersen S, Li T, Fariñas-Madrid L, Lee YC, Liu ZA, Pugh TJ, Oza AM. EVOLVE: A Multicenter Open-Label Single-Arm Clinical and Translational Phase II Trial of Cediranib Plus Olaparib for Ovarian Cancer after PARP Inhibition Progression. *Clin Cancer Res.* 2020 Aug 15;26(16):4206-4215.

Makker V, Taylor MH, Aghajanian C, Oaknin A, Mier J, Cohn AL, Romeo M, Bratos R, Brose MS, DiSimone C, Messing M, Stepan DE, Dutcus CE, Wu J, Schmidt EV, Orlowski R, Sachdev P, Shumaker R, Casado Herraez A. Lenvatinib Plus Pembrolizumab in Patients With Advanced Endometrial Cancer. *J Clin Oncol.* 2020 Sep 10;38(26):2981-2992.

CLINICAL RESEARCH

HEREDITARY CANCER GENETICS GROUP

Principal Investigator Judith Balmaña Senior Scientists Orland Díez, Sara Gutiérrez Enríquez Post-Doctoral Fellow Sandra Bonache Graduate Students Ester Aguado, Joanna Domènech, Sara Hermosa, Alejandro Moles, Cristina Zamarreño Medical Oncologist Mara Cruellas Clinical Nurse Specialist Eduard Pérez Ballestero Genetic Counselors Estela Carrasco, Adrià López Auxiliary Clinician Carmen Aguilar Data Curator Sara Torres Project Manager Mònica Pardo

STRATEGIC GOALS

- 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 as a biomarker of homologous recombination repair deficiency (HRR-D) among non-BRCA 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).
- Improve the genetic diagnosis of HBOC.
- Identify cellular and genomic biomarkers as predictors of late toxicity after radiotherapy.

HIGHLIGHTS

- Prior to the COVID-19 pandemic lockdown we started a project to explore predictors of telegenetics' acceptance in hereditary cancer. In 2020 we investigated the impact of COVID-19 on the preference of telegenetics versus in-person visits. Our research included the predictive analysis of personality traits, and the opinion of health care providers in order to identify challenges in implementing e-health.
- 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.
- Recruitment of women with familial breast cancer to perform individualized breast cancer risk estimation with PRS analysis and non-genetic risk factors.
- We continue our clinical validation of the RAD51predict assay as a functional biomarker of homologous recombination repair deficiency and predictor of PARPi resistance.
- In collaboration with expert Spanish groups, we have participated in the creation of the first guide to standardize and improve the classification of *ATM* gene variants that increase the risk of breast or prostate cancer.
- We are leading research into the value of RAD51 foci in the interpretation of VUS in *BRCA1*, *BRCA2* and *PALB2* genes as part of one of the ERAPerMed project's work packages (granted to Violeta Serra, PI of VHIO's Experimental Therapeutics Group – page 70).
- In spite of the COVID-19 pandemic, we initiated the enrollment of patients in the RADprecise project and achieved 32% of the total expected inclusion in the breast cancer cohort of patients. 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

We focus on the clinical development of PARP inhibitors (PARPi) in early *gBRCA1/2* breast cancer, and novel combinations in the advanced setting. The consolidation of our collaboration with VHIO's Experimental Therapeutics Group (page 70), led by Violeta Serra, 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 progression. We have identified a functional biomarker for PARPi sensitivity that has been tested preclinically and in human samples, and are now collecting samples for a larger clinical validation.

Our group is also interested in unravelling the challenges of implementing the advances in diagnosis of hereditary cancer susceptibility and applying these insights to 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, as well as 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 genome- based cancer risk estimation and cancer-risk adapted approaches incorporating polygenic risk score (PRS) analysis. A longitudinal national-based registry of mutation carriers incorporates prospective data for the analysis of health outcomes.

We pursue our interest in the genetic epidemiology of hereditary breast and ovarian cancer (HBOC), led by one of our Senior Scientists, Sara Gutiérrez-Enríquez. This research has shed important light on the characterization of new pathogenic variants in HBOC genes, and provided discriminatory tools to interpret variants of uncertain significance in BRCA genes. We are devoted to deciphering the role of intronic, splicing, and missense variants in major HBOC genes and investigate the yield of long-read RNA-seq. Sara Gutiérrez-Enríquez is also independently leading research into predictive genetic and cellular markers for susceptibility to radiotherapy-induced clinical toxicity.

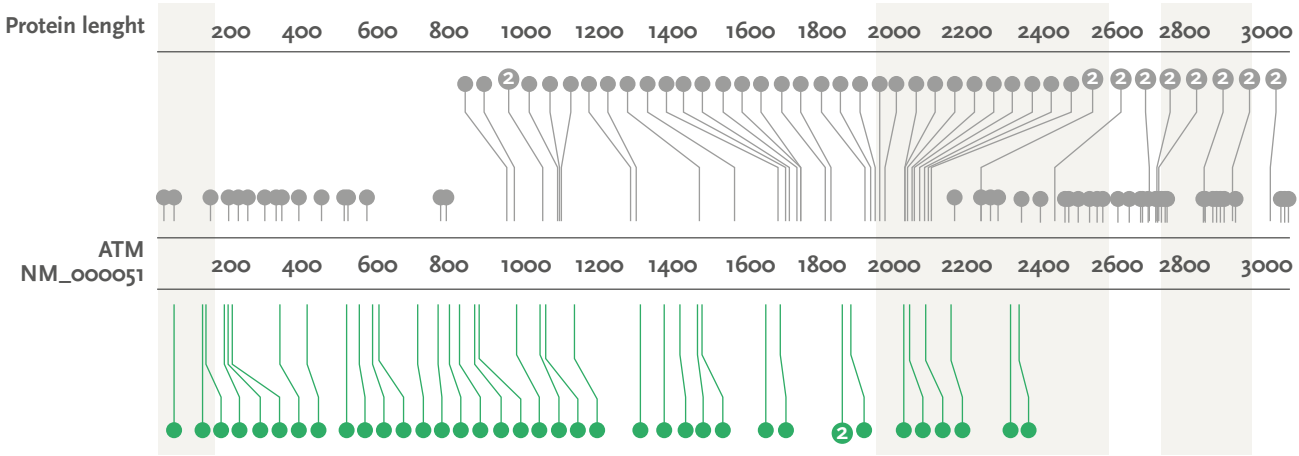


Figure: Missense germline variants along the ATM protein. Pathogenic missense variants (in grey) in A-T patients were obtained from the literature, LOVD and/or HGMD. Benign missense variants (in green) were present with a MAF greater than 0.05% in the GnomAD v2.1.1 control database.

PI PAPER PICK

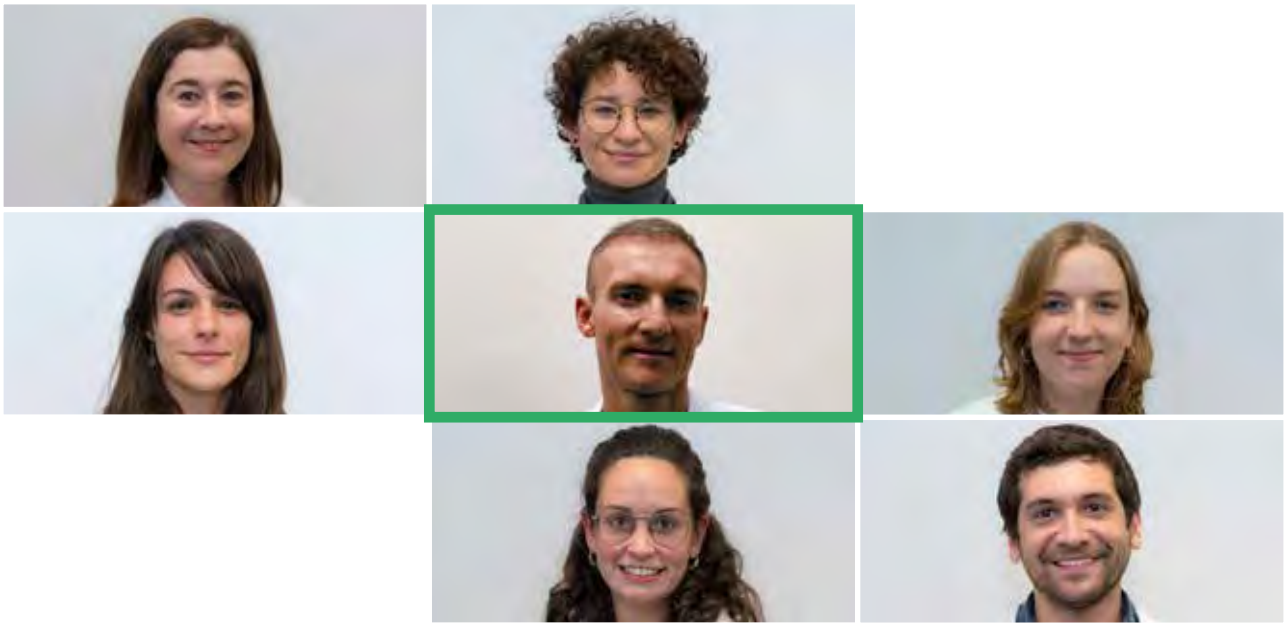
Feliubadaló L, Moles-Fernández A, Santamariña-Pena M, Sánchez AT, López-Novo A, Porras LM, Blanco A, Capellá G, de la Hoya M, Molina IJ, Osorio A, Pineda M, Rueda D, de la Cruz X, Diez O, Ruiz-Ponte C, Gutiérrez-Enríquez S, Vega A, Lázaro C. A Collaborative Effort to Define Classification Criteria for ATM Variants in Hereditary Cancer Patients. *Clin Chem.* 2020 Dec 6:hvaa250. Epub ahead of print.

Stjepanovic N, Villacampa G, Nead KT, Torres-Esquius S, Melis GG, Nathanson KL, Teule A, Brunet J, Y Cajal TR, Llort G, Dienstmann R, Rue M, Domchek SM, Balmaña J. Association of premenopausal risk-reducing salpingo-oophorectomy with breast cancer risk in BRCA1/2 mutation carriers: Maximising bias-reduction. *Eur J Cancer.* 2020 Jun;132:53-60.

Yang X, Leslie G, Doroszuk A,...Diez O,...Balmaña J,... Tischkowitz M. Cancer Risks Associated With Germline PALB2 Pathogenic Variants: An International Study of 524 Families. *J Clin Oncol.* 2020 Mar 1;38(7):674-685.

Yang X, Song H, Leslie G,...Diez O, Balmaña J,... Antoniou AC. Ovarian and Breast Cancer Risks Associated With Pathogenic Variants in RAD51C and RAD51D. *J Natl Cancer Inst.* 2020 Dec 14;112(12):1242-1250.

ONCOLOGY DATA SCIENCE (ODysSey) GROUP



Principal Investigator Rodrigo Dienstmann Biostatistician Guillermo Villacampa Biomedical Engineer Anna Pedrola Data Curators Raquel Comas, Magdalena Guardiola, Fiorella Ruiz, Cristina Viaplana, Carla Sanchez, Sara Torres

STRATEGIC GOALS

Facilitate clinical-molecular correlative studies at VHIO:

- Development and maintenance of clinical-molecular databases and decision-support software as resources for clinicians, molecular pathologists and translational investigators.
- Provide guidance to medical oncologists and cancer biologists regarding the design and interpretation of biomarker correlative studies, as well as the development and validation of omics-based tests that have a direct clinical application.

Promote evidence-based medicine:

- Continued medical education with standardized reports of genomic alterations and weekly Molecular Tumor Boards. We facilitate data exchange among a wide range of experts for the review of patients' medical histories and cancer molecular profiles in order to more precisely inform and guide treatment decisions.

Collaborative research on Big and Real-World Data:

- Encourage interactions among computational oncology scientists and preclinical-clinical researchers to promote the identification of cancer subtypes and druggable drivers.
- Generate large databases that allow the study of complex associations between tumor omics, drug sensitivities and patient outcome.

HIGHLIGHTS

- We have provided support to VHIO's investigators working on clinical and preclinical research. This has resulted in several impactful publications within our field, oral presentations at some of the most prestigious oncology conferences, as well as 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 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.
- Co-development of the Molecular Tumor Board portal (MTBP), a clinical decision support system for the selection of the most appropriate treatment for cancer patients based on genomics data, including clinical trial opportunities. This portal employs a variety of state-of-the-art tools to interpret the biological and clinical significance of tumor and germline alterations. The MTBP is regularly used by the Cancer Core Europe (CCE) Consortium's (page 175) Basket of Basket (BoB) trial, which is the first European multi-modular academic clinical trial in Europe. This study is set to significantly advance basket trial design by integrating molecular prescreening, the development of novel diagnostic tests including liquid biopsies, and assessing targeted therapies matched to patients who would be most likely to benefit from them.
  An open access version of our MTBP technology, developed under CCE's umbrella, is available at: http://mtbp.org.

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).

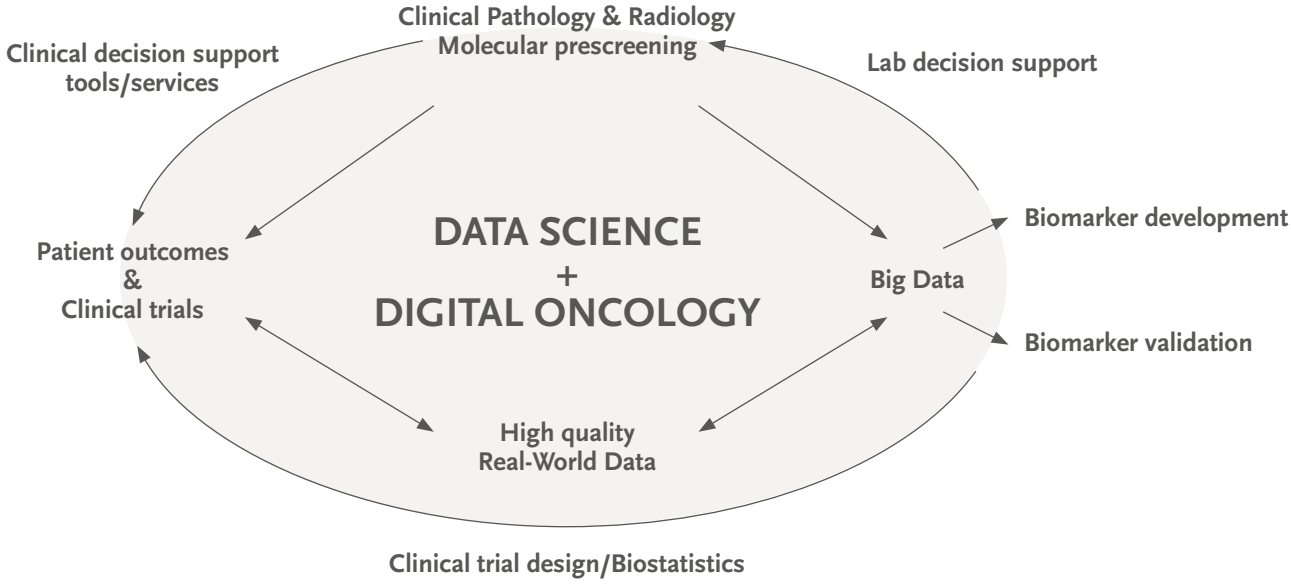
To analyze big and real-world data, we design and maintain comprehensive clinical-molecular databases and develop customized decision-support systems to researchers who have an interest in correlative analyses for hypothesis- generation and biomarker validation. We also provide assistance to investigators for the calculation of sample size, clinical trial design, and downstream statistical analyses.

Our team also participates in international multi-omic data analyses projects and fosters collaborative research in computational oncology. We 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.

In collaboration with Susana Aguilar, Jennifer Gonzalez, and VHIO's Cancer Genomics Group led by Ana Vivancos (page 116), Molecular Oncology Group, directed by Paolo Nuciforo (page 118), and Elena Garralda, PI of our Early Clinical Drug Development Group (page 92), and Director of VHIO's Research Unit for Molecular Therapy of Cancer (UITM) - CaixaResearch (page 133), we co-lead VHIO's in-house Molecular Prescreening Program - see page 140.

We have performed tumor molecular profiling in over 1,100 cancer patients as candidates for enrollment in clinical trials. In total, 151 patients were treated with biomarker-matched innovative therapies as a result of this effort.

Interpretation of next-generation sequencing tests and educating clinicians on emerging biomarkers is another of our priority areas, and genetic counseling alerts in case of pathogenic germline variants. 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 case of pathogenic germline variants.



PI PAPER PICK

Tamborero D, Dienstmann R, Rachid MH, Boekel J, Baird R, Braña I, De Petris L, Yachnin J, Massard C, Opdam FL, Schlenk R, Vernieri C, Garralda E, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium, Calvo F, Fröhling S, Eggermont A, Apolone G, Voest EE, Caldas C, Tabernero J, Ernberg I, Rodon J, Lehtiö J. Support systems to guide clinical decision-making in precision oncology: The Cancer Core Europe Molecular Tumor Board Portal. *Nat Med.* 2020;26(7):992-994.

Mosele F, Remon J, Mateo J, Westphalen CB, Barlesi F, Lolkema MP, Normanno N, Scarpa A, Robson M, Meric-Bernstam F, Wagle N, Stenzinger A, Bonastre J, Bayle A, Michiels S, Bièche I, Rouleau E, Jezdic S, Douillard JY, Reis-Filho JS, Dienstmann R, André F. Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group. *Ann Oncol.* 2020;S0923-7534(20):39971-3.

Wagner AH, Walsh B, Mayfield G, Tamborero D, Sonkin D, Krysiak K, Deu-Pons J, Duren RP, Gao J, McMurry J, Patterson S, Del Vecchio Fitz C, Pitel BA, Sezerman OU, Ellrott K, Warner JL, Rieke DT, Aittokallio T, Cerami E, Ritter DI, Schriml LM, Freimuth RR, Haendel M, Raca G, Madhavan S, Baudis M, Beckmann JS, Dienstmann R, Chakravarty D, Li XS, Mockus S, Elemento O, Schultz N, Lopez-Bigas N, Lawler M, Goecks J, Griffith M, Griffith OL, Margolin AA; Variant Interpretation for Cancer Consortium. A harmonized meta-knowledgebase of clinical interpretations of somatic genomic variants in cancer. *Nat Genet.* 2020;52(4):448-457.

Dienstmann R, Garralda E, Aguilar S, Sala G, Viaplana C, Ruiz-Pace F, González-Zorelle J, Grazia LoGiacco D, Ogbah Z, Ramos Masdeu L, Mancuso F, Fasani R, Jimenez J, Martinez P, Oaknin A, Saura C, Oliveira M, Balmaña J, Carles J, Macarulla T, Elez E, Alsina M, Braña I, Felip E, Tabernero J, Rodon J, Nuciforo P, Vivancos A. Evolving Landscape of Molecular Prescreening Strategies for Oncology Early Clinical Trials. *JCO Precis Oncol.* 2020 May 14;4:PO.19.00398.

RADIATION ONCOLOGY GROUP

Principal Investigator Jordi Giralt Radiation Oncologists Manel Altabas, Sergio Benavente, Alexandra Giraldo, Raquel Granado, Begoña Navalpotro, Xavier Maldonado, Soraya Mico, 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 combined radio-immunotherapy therapy.

HIGHLIGHTS

- Over 90% of our patients treated with radical radiotherapy have been treated using highly complex techniques.
- Treating patients using our Halcyon linac - the first ever to be installed in Spain.
- 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 group continues to participate as national representatives of radiotherapy in the International Society of Paediatric Oncology (SIOP) clinical trials 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.

In 2020 we have renewed three linacs thanks to a donation received from the Amancio Ortega Foundation. 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.

These include:

- 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 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 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 in very small volume (5-10 mm in diameter), requiring extremely precise techniques.

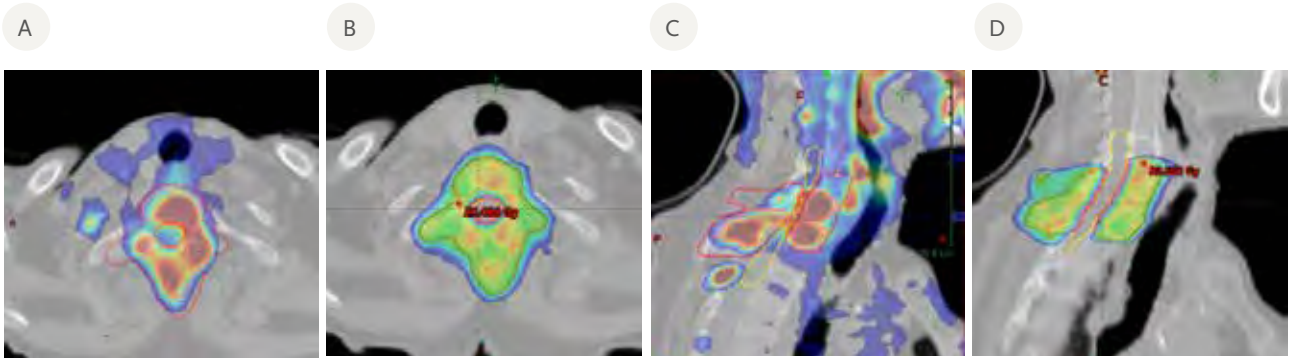


Figure: SBRT of a vertebral metastasis. In the upper images fusion of PET scan and planning CT. In B and D images dose distribution. Dose prescription of 24 Gy in 2 fractions.

PI PAPER PICK

Thomson DJ, Palma D, Guckenberger M, Balermpas P, Beitler JJ, Blanchard P, Brizel D, Budach W, Caudell J, Corry J, Corvo R, Evans M, Garden AS, Giralt J, Gregoire V, Harari PM, Harrington K, Hitchcock YJ, Johansen J, Kaanders J, Koyfman S, Langendijk JA, Le QT, Lee N, Margalit D, Mierzwa M, Porceddu S, Soong YL, Sun Y, Thariat J, Waldron J, Yom SS. Practice recommendations for risk-adapted head and neck cancer radiotherapy during the COVID-19 pandemic: An ASTRO-ESTRO consensus statement. *Radiother Oncol*. 2020 Oct;151:314-321.

Giralt J, Tao Y, Kortmann RD, Zasadny X, Contreras-Martinez J, Ceruse P, Arias de la Vega F, Lalla RV, Ozsahin EM, Pajkos G, Mazar A, Attali P, Bossi P, Vasseur B, Sonis S, Henke M, Bensadoun RJ. Randomized Phase 2 Trial of a Novel Clonidine Mucoadhesive Buccal Tablet for the Amelioration of Oral Mucositis in Patients Treated With Concomitant Chemoradiation Therapy for Head and Neck Cancer. *Int J Radiat Oncol Biol Phys*. 2020 Feb 1;106(2):320-328.

Rattay T, Seibold P, Aguado-Barrera ME, Altabas M, Azria D, Barnett GC, Bultijnck R, Chang-Claude J, Choudhury A, Coles CE, Dunning AM, Elliott RM, Farcy Jacquet MP, Gutiérrez-Enríquez S, Johnson K, Müller A, Post G, Rancati T, Reyes V, Rosenstein BS, De Ruysscher D, de Santis MC, Sperk E, Stobart H, Symonds RP, Taboada-Valladares B, Vega A, Veldeman L, Webb AJ, West CM, Valdagni R, Talbot CJ; REQUITE consortium. External Validation of a Predictive Model for Acute Skin Radiation Toxicity in the REQUITE Breast Cohort. *Front Oncol*. 2020 Oct 30;10:575909.

López-Campos F, Linares-Espinós E, Maldonado Pijoan X, Sancho Pardo G, Morgan TM, Martínez-Ballesteros C, Martínez-Salamanca J, Couñago F. Genetic testing for the clinician in prostate cancer. *Expert Rev Mol Diagn*. 2020 Sep;20(9):933-946.

CLINICAL RESEARCH

RADIOMICS GROUP

Principal Investigator Raquel Perez-Lopez Post-Doctoral Fellows Kinga Bernatowicz-Goma, Francesco Grussu PhD Students Alonso García, Marta Ligero Students Eric Delgado, Samantha Elizabeth Toinga

STRATEGIC GOALS

- Provide expertise in engineering and bioinformatics for the development and clinical qualification of quantitative imaging biomarkers for precision medicine to improve outcomes for cancer patients.
- Use functional imaging for optimizing drug development through clinical trials.
- Integrate radiomics and genomics in translational studies towards a deeper understanding of tumor evolution and mechanisms of resistance to anti-cancer therapies.
- Optimize and standardize imaging acquisition protocols.
- Develop and implement computational models for advanced image processing.

HIGHLIGHTS

- Our group participates in the European DART Consortium aiming to enhance novel clinical trial designs thanks to the support of the European Commission under the Horizon 2020 program.
- Raquel Perez-Lopez has been granted a CRIS Foundation Research Talent Award and a FERO Foundation Research Grant.
- We have developed and validated a combined CT-radiomics and clinical signature with predictive value of response to immunotherapy. This study has recently been published in *Radiology* (Ligero M et al. 2021).
- We have also developed a pipeline for semi-automatic robust quantification of residual tumor on the post-surgery MRI in patients with brain glioblastoma which published in *Scientific Reports* (Garcia-Ruiz A et al. 2020).
- We have designed a method for CT-radiomics standardization based on post-acquisition image processing and batch effect correction (Ligero M et al. *Eur Radiol.* 2020).
- The continued expansion of existing partnerships with other groups as well as new collaborative projects in order to increase the incorporation of imaging studies within translational research lines.

SUMMARY

Our Radiomics Group keeps growing; in 2020 Aina de Torner joined us to carry out her end-of-degree research project on CT-radiomics towards optimizing patient selection for immunotherapy in a selected population of lung cancer. Francesco Grussu also joined the team as our new Post-Doctoral Scientist. We are also pleased to announce that we are currently recruiting for additional new talents.

Over the past year, we have fostered further collaborations with additional leading imaging research groups including the Computing Vision Centre (CVC–*Universitat Autónoma de Barcelona*), and cutting-edge research centers including the Bellvitge Institute for Biomedical Research (IDIBELL), in Barcelona, the Netherlands Cancer Institute (NKI), Amsterdam, and the Cancer Research UK (CRUK) Cambridge Institute. In partnership, we have designed various projects for which we have applied for funding through national and international grants.

Continuing our collaboration with VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch led by Elena Garralda (pages 133-135), we have developed a CT-radiomics signature in order to better characterize response to immunotherapy (published in *Radiology*). Thanks to the support received through an AstraZeneca Proof of Concept Award, we have recently initiated the first prospective study of CT and multiparametric MRI-radiomics to quantify changes in tumor cellularity and vascularization as a biomarker of response to immune checkpoint inhibitors.

We are also delighted to report that the CRIS Cancer Foundation has awarded Raquel Perez-Lopez with a Research Talent Award. This will fuel her research aimed at improving cancer patient selection for immunotherapy and better understanding differential responses to immune-checkpoint inhibitors. We are also very grateful to the FERO Foundation for its support that will enable us to apply deep-learning models to medical imaging for a deeper understanding of tumor immunophenotypes.

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 the metrics derived from this new assay will have crucial applications as non-invasive biomarkers in cancer.

Thanks to the support received from the Carlos III Institute of Health (ISCIII) and the Prostate Cancer Foundation 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 has recently expanded to include breast cancer patients thanks to funding from *La Fundació La Marato de TV3* (PreciMet study).

Our group has established interdisciplinary partnerships with various VHIO groups to work together on several 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.

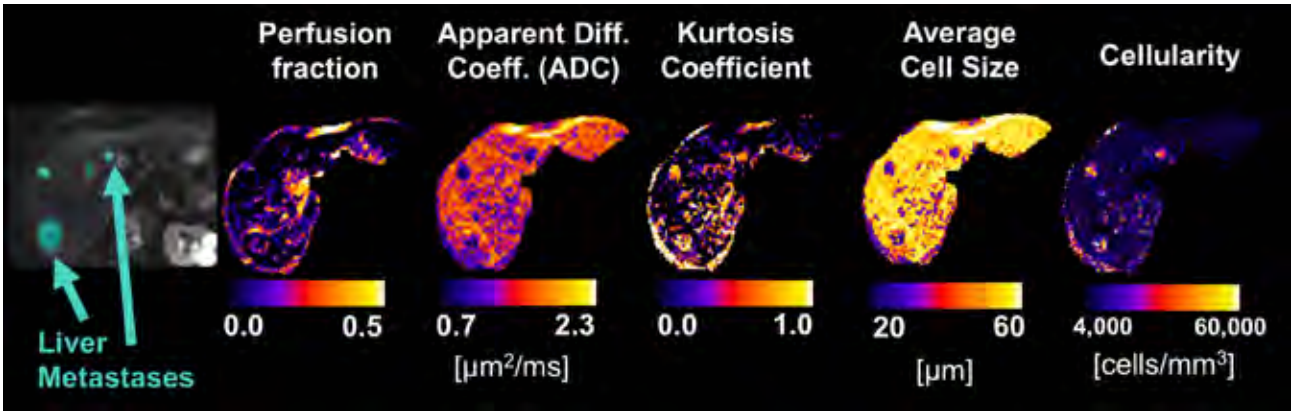


Figure: DW microstructural MRI metrics provide biological-specific metrics that offer sensitivity to tumorigenic processes in the liver such as metastases.

PI PAPER PICK

Ligero M, Jordi-Ollero O, Bernatowicz K, Garcia A, Delgado-Muñoz E, Leiva D, Mast R, Suarez C, Sala-Llonch R, Calvo N, Escobar M, Navarro-Martin A, Villacampa G, Dienstmann R, Perez-Lopez R. Minimizing acquisition-related radiomics variability by image resampling and batch effect correction to allow for large scale data analysis. *Eur Radiol*. 2020 Sep 9.

Garcia-Ruiz A, Naval-Baudin P, Ligero M, Pons-Escoda A, Bruna J, Plans G, Calvo N, Cos M, Majós C, Perez-Lopez R. Precise enhancement quantification in post-operative MRI as an indicator of residual tumor impact is associated with survival in patients with glioblastomas. *Sci Rep*. Dec 2020.

Pons A, Garcia A, Naval P, Cos M, Vidal N, Plans G, Bruna J, Perez-Lopez R, Majós C. Presurgical Identification of Primary Central Nervous System Lymphoma with Normalized Time-Intensity Curve: A Pilot Study of a New Method to Analyze DSC-PWI. *AJNR Am J Neuroradiol*. 2020 Oct;41(10):1816-1824.

Yap TA, O'Carrigan B, Penney MS, Lim JS, Brown JS, Miguel Luken MJ, Tunariu N, Perez-Lopez R, Nava Rodrigues D, Riisnaes R, Figueiredo I, Carreira S, Hare B, McDermott K, Khalique S, Williamson CT, Natrajan R, Pettitt SJ, Lord CJ, Banerji U, Pollard J, Lopez J, de Bono JS. Phase I Trial of First-in-Class ATR Inhibitor M6620 (VX-970) as Monotherapy or in Combination With Carboplatin in Patients With Advanced Solid Tumors. *J Clin Oncol*. 2020 Jun 22;JCO1902404.

CLINICAL RESEARCH

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 Associate Researcher Ramon Amat Post-Doctoral Fellow Caterina Carbonell Bioinformatician Joan Frigola

STRATEGIC GOALS

- Expansion of our translational thoracic cancer program in non-small-cell lung cancer, small-cell lung cancer and mesothelioma.
- Implementation of liquid biopsy determinations.
- Contribute to early drug development, targeted therapies and immunotherapy strategies for the treatment of thoracic and head and neck tumors.
- Advance precision medicine for lung cancer patients through translational research and the application of cutting-edge technologies and new approaches.
- Potentiate novel therapies including immunotherapeutic and targeted agents for the management of patients with thoracic and head and neck malignancies.
- Achieve a deeper understanding of intratumoral heterogeneity and its clinical implications.
- Further strengthen multidisciplinarity for optimal patient care.

HIGHLIGHTS

- Cooperation between our translational thoracic cancer genomics unit and our clinical team. By integrating genomics, molecular biology and clinical data, we aim to better understand lung cancer physiology and response to therapy.

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 group 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 we are also deeply committed to ameliorating clinical outcomes by working in close connectivity with professionals across other disciplines.

Precision medicine for the treatment advanced lung cancer is no longer an ambition. It is a guiding principle. We establish molecular determinants of disease in individual tumors and circulating-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 (page 133). We contribute to VHIO's early clinical drug development efforts, led by Elena Garralda (page 92), and also manage other less common thoracic malignancies including head and neck cancer, small-cell lung cancer, mesothelioma, thymoma and neuroendocrine tumors.

PI PAPER PICK

Frigola J, Navarro A, Carbonell C, Callejo A, Iranzo P, Cedrés S, Martinez-Marti A, Pardo N, Saoudi-Gonzalez N, Martinez D, Jimenez J, Sansano I, Mancuso FM, Nuciforo P, Montuenga LM, Sánchez-Cespedes M, Prat A, Vivancos A, Felip E, Amat R. Molecular profiling of long-term responders to immune checkpoint inhibitors in advanced non-small cell lung cancer. *Mol Oncol.* 2020 Dec 20. Epub ahead of print.

Paik PK, Felip E, Veillon R, Sakai H, Cortot AB, Garassino MC, Mazieres J, Viteri S, Senellart H, Van Meerbeeck J, Raskin J, Reinmuth N, Conte P, Kowalski D, Cho BC, Patel JD, Horn L, Griesinger F, Han JY, Kim YC, Chang GC, Tsai CL, Yang JC, Chen YM, Smit EF, van der Wekken AJ, Kato T, Juraeva D, Stroh C, Bruns R, Straub J, Johne A, Scheele J, Heymach JV, Le X. Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. *N Engl J Med.* 2020 Sep 3;383(10):931-943

Felip E, de Braud FG, Maur M, Loong HH, Shaw AT, Vansteenkiste JF, John T, Liu G, Lolkema MP, Selvaggi G, Giannone V, Cazorla P, Baum J, Balbin OA, Wang LV, Lau YY, Scott JW, Tan DS. Ceritinib plus Nivolumab in Patients with Advanced ALK-Rearranged Non-Small Cell Lung Cancer: Results of an Open-Label, Multicenter, Phase 1B Study. *J Thorac Oncol.* 2020 Mar;15(3):392-403.

Shaw AT, Bauer TM, de Marinis F, Felip E, Goto Y, Liu G, Mazieres J, Kim DW, Mok T, Polli A, Thurm H, Calella AM, Peltz G, Solomon BJ; CROWN Trial Investigators. First-Line Lorlatinib or Crizotinib in Advanced ALK-Positive Lung Cancer. *N Engl J Med.* 2020 Nov 19;383(21):2018-2029.

CORE TECHNOLOGIES

114 Bioinformatics Support Unit
116 Cancer Genomics Group
118 Molecular Oncology Group
120 Proteomics Group

Due to safety and logistical considerations brought about by the COVID-19 pandemic, and to reflect the reality of balancing those physically working in the lab and clinical settings, with those working from home, we had to rethink our approach to this year's Scientific Report photo shoot and set up. We translated this obstacle into opportunity*.

To be able to include as many group members as possible, and photograph our researchers and investigators without masks, we took each picture individually, at a distance, and in locations away from areas dedicated to the care of our cancer patients. Designed to depict the very familiar "Zoom" virtual meeting scenario, we were able to also include faculty who were homeworking at the time of each photo session, by inviting them to send their pictures from home.

* Considering certain logistical and spatial issues, we have unfortunately had to repeat pictures of some of our larger groups and units from VHIO's Scientific Report 2019 - as indicated in the corresponding pages.

BIOINFORMATICS SUPPORT UNIT

Principal Investigator José Fernández Navarro Bioinformatician Jonatan González Rodriguez

STRATEGIC GOALS

- Develop state-of-the-art pipelines and tools for the processing, analyses, and visualization of different omics datasets.
- Provide support, expertise and resources to VHIO's research groups.
- Establish collaborative research with other groups with a focus on advanced computational methods, machine learning, data analysis and visualization.
- Promote and drive digital transformation and best practices.

HIGHLIGHTS

- Provision of support and expertise to many PIs at VHIO. Projects range from processing to analysis and visualization of different omics datasets.
- Development of pipelines for the processing and analysis of genomic, transcriptomics, epigenomics and immuno-genomics datasets.
- The setting up of a highly scalable and advanced data processing structure in Amazon Cloud.
- In collaboration, we have defined and driven the configuration and acquisition of a high-performance computational cluster.
- Active involvement in several consortia and taskforces.
- Together with other VHIO PIs, we have applied for different grants to establish new research lines.

SUMMARY

VHIO's Bioinformatics Support Unit, led by José Fernández Navarro, promotes digital transformation and sets optimal standards and best-practices for the processing, analysis and visualization of omics datasets.

We provide support and expertise across multiple projects in collaboration with other investigators at VHIO including Joaquín Arribas, Héctor G. Palmer, Alena Gros, Joaquin Mateo, Ana Vivancos, Raquel Pérez-López, Rodrigo Toledo, and Sara Rodriguez, to name but a few. Projects range from mentorship, the development of pipelines and tools for the processing of multi-omics datasets, to the analysis, integration and visualization of omics datasets by applying machine learning and statistics.

We have also started to represent our Institute as a member of various consortia and taskforces, and have also developed state-of-the-art pipelines and tools for the processing of different omics using modern standards. In collaboration with other VHIO groups, we aim to establish our own research lines.

PI PAPER PICK

Chen WT, Lu A, Craessaerts K, Pavie B, Sala Frigerio C, Corthout N, Qian X, Laláková J, Kühnemund M, Voytyuk I, Wolfs L, Mancuso R, Salta E, Balusu S, Snellinx A, Munck S, Jurek A, Fernandez Navarro J, Saido TC, Huitinga I, Lundeberg J, Fiers M, De Strooper B. Spatial Transcriptomics and In Situ Sequencing to Study Alzheimer's Disease. *Cell*. 2020 Aug 20;182(4):976-991.e19.

Navarro JF, Croteau DL, Jurek A, Andrusivova Z, Yang B, Wang Y, Ogedegbe B, Riaz T, Støen M, Desler C, Rasmussen LJ, Tønjum T, Galas MC, Lundeberg J, Bohr VA. Spatial Transcriptomics Reveals Genes Associated with Dysregulated Mitochondrial Functions and Stress Signaling in Alzheimer Disease. *iScience*. 2020 Sep 15;23(10):101556.

Ortiz C, Navarro JF, Jurek A, Märtin A, Lundeberg J, Meletis K. Molecular atlas of the adult mouse brain. *Sci Adv*. 2020 Jun 26;6(26):eabb3446.

Yoosuf N, Navarro JF, Salmén F, Ståhl PL, Daub CO. Identification and transfer of spatial transcriptomics signatures for cancer diagnosis. *Breast Cancer Res*. 2020 Jan 13;22(1):6.

CANCER GENOMICS GROUP

Principal Investigator Ana Vivancos Post-Doctoral Fellows Alberto González, Miriam Sansó Specialized Technicians Deborah G. Lo Giacco, Judit Matito, Miriam Navarro, Zighereda Ogbah, Laia Ramos, Ginevra Caratu Bioinformaticians Francesco Mancuso, Marina Gómez, Maria Vila Technician Agatha Martín

STRATEGIC GOALS

- Develop and implement improved strategies for routine patient prescreening with a large pan-cancer panel in a setting of excellence.
- Provide cutting-edge applications in cancer genomics through the use of novel technologies and protocol development.
- Prioritize translational projects and partnerships that reinforce VHIO's renowned excellence in oncology.
- Implement the Guardant 360® DX test in liquid biopsy as the first laboratory in Europe to perform the assay from Guardant Health.

HIGHLIGHTS

- VHIO is a Founding Partner of the Cancer Core Europe Consortium (CCE - see page 175) 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 is appointed co-leader of the Consortium's Genomics Task Force and is responsible for the alignment of genomic testing across all member institutions.
- We have validated our 450 gene capture panel for mutations, Tumor Mutational Burden and for Copy Number Alterations to be used in our Molecular Prescreening Program (see page 140).
- In liquid biopsy, we developed Copy Number Alteration analysis through the use of shallow Whole Genome Sequencing to provide data along with our custom NGS test with Unique Molecular Identifiers (UMI) chemistry and envision that this will be our first disease tracking test in the clinical setting.
- Driven by our Advanced Molecular Diagnostics Program, supported by the FERO Foundation (page 122), VHIO is one of the few centers in Europe to run such a comprehensive prescreening program. Molecular profiling, performed in around 1100 patients each year as candidates for enrollment in our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch (page 133) early phase clinical trials, enables our teams to more precisely match an increasing number of individual patients to a particular study.

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 the development of novel, 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 three NextGen Sequencers; MiSeq, NextSeq and HiSeq2500, Illumina. We are also starting to work with Minion Oxford Nanopore technology.

Our Molecular Prescreening Program (page 140), is headed by Rodrigo Dienstmann, PI of VHIO's Oncology Data Science – ODysSey – Group (page 104), and co-led by our PI, Ana Vivancos, Paolo Nuciforo, PI of VHIO's Molecular Oncology Group (page 118), and Elena Garralda, who leads VHIO's Early Clinical Drug Development Group (page 92).

Our Advanced Molecular Diagnostics Program – DIAMAV (page 122), is supported by the FERO Foundation. 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, directed by Elena Garralda.

Patients' suitability for inclusion in any given clinical trial is assessed based on their respective genomic or pathologic profile. We have developed and routinely implemented several tests for our Molecular Prescreening 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), and our Copy Number Alterations panel, evaluating a 59 gene panel for genes with frequent gains or losses in cancer.

As a reflection of our dedication to excellence and quality in the services we provide, we have attained ISO 15189 flexible accreditation for our Amplicon-seq testing as well as for our 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 a number of translational research projects including the identification of mechanisms of resistance to targeted therapies, as well as predictive biomarkers for immunotherapeutics. Based on nanostring and RNA-seq technologies for the detection of an immune signature, we use the VIGex tool (see figure). Our group is particularly interested in liquid biopsy and RNA-based analysis of tumors for microenvironment profiling.

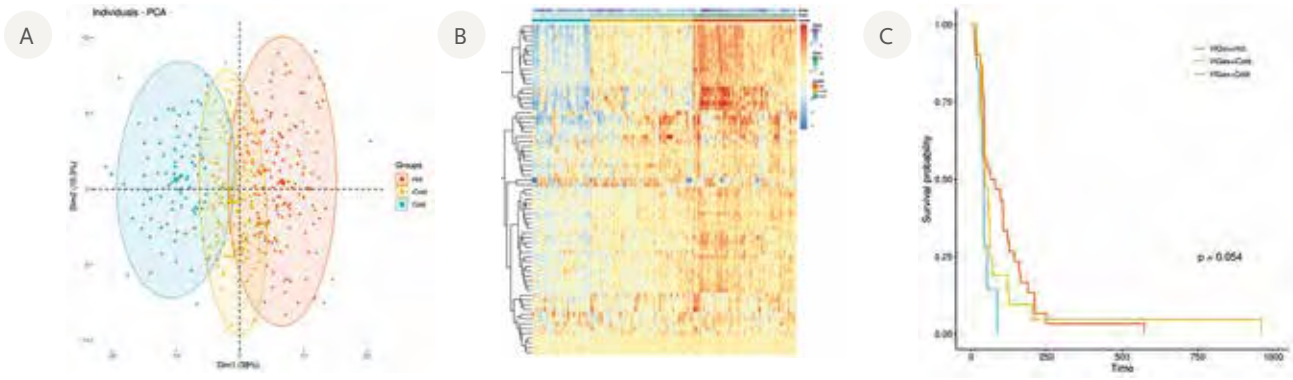


Figure: VIGex classification of 398 cancer metastatic samples according to nCounter (Nanostring) gene expression (69 immuno-related genes). Gene expression values were normalized to the geometric mean expression of 19 housekeeping genes, then log2-transformed and centred around mean. A) PCA showing the 3 clusters identified with PAM (partitioning around medoids) method (Hot, iCold and Cold). B) Heatmap showing relative gene expression and PCA values of the 69 immuno-related genes within Hot, iCold and Cold groups. C) Kaplan-Meier plot showing time to progression of the Hot, iCold and Cold groups of an independent cohort of 58 samples.

PI PAPER PICK

Dienstmann R, Garralda E, Aguilar S, Sala G, Viaplana C, Ruiz-Pace F, González-Zorelle J, Grazia LoGiacco D, Ogbah Z, Ramos Masdeu L, Mancuso F, Fasani R, Jimenez J, Martinez P, Oaknin A, Saura C, Oliveira M, Balmaña J, Carles J, Macarulla T, Elez E, Alsina M, Braña I, Felip E, Tabernero J, Rodon J, Nuciforo P, Vivancos A. Evolving Landscape of Molecular Prescreening Strategies for Oncology Early Clinical Trials. *JCO Precis Oncol.* 2020 May 14;4:PO.19.00398.

Capdevila J, Matos I, Mancuso FM, Iglesias C, Nuciforo P, Zafon C, Palmer HG, Ogbah Z, Muiños L, Hernando J, Villacampa G, Peña CE, Tabernero J, Brose MS, Schlumberger M, Vivancos A. Identification of Expression Profiles Defining Distinct Prognostic Subsets of Radioactive-Iodine Refractory Differentiated Thyroid Cancer from the DECISION Trial. *Mol Cancer Ther.* 2020 Jan;19(1):312-317.

MOLECULAR ONCOLOGY GROUP

Principal Investigator Paolo Nuciforo Attending Physicians Roberta Fasani, Sara Simonetti Laboratory Supervisor Jose Antonio Jiménez Laboratory Assistant Mª Ángeles Diaz Post-Doctoral Fellow Francisca Gallego PhD Student Garazi Serna Technicians Lidia Alonso, Eloy Garcia, Xavier Guardia, Paola Martinez, Stefania Napoli, Gertrudis Sánchez, Lidia Sánchez, César Javier Sevillano Student Ana Santamaria Lacuesta

STRATEGIC GOALS

- Discovery and validation of novel biomarkers using tissue-based technologies.
- Identification of targetable alterations as part of VHIO's Molecular Prescreening Program (page 140).
- Application of molecular pathology strategies to support early clinical drug development programs.
- Resolve spatial interaction of tumor-associated microbiota, tumor cells, and immune cells in the tumor microenvironment.
- Better define molecular target epidemiology to render treatment strategies more precise.
- Act as a central and local laboratory in clinical trials.
- Serve as a Core Facility for VHIO research programs.

HIGHLIGHTS

- Identification of Fusobacterium nucleatum as predictive biomarker of relapse after neoadjuvant chemo-radiotherapy in locally advanced rectal cancer (*Annals of Oncology* 2020).
- Development of KiQuant methodology for automated and reproducible Ki67 scoring in breast cancer.
- Pathology Task Force leader for the Cancer Core Europe Consortium - CCE (see page 175).

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 (PI Ana Vivancos, page 116), and Oncology Data Science - ODysSey Group (PI Rodrigo Dienstmann, page 104), we participate in our in-house Molecular Prescreening Program (page 140). We molecularly profile over 1500 patients per year as candidates for enrolment in early phase clinical trials at our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, directed by Elena Garralda (page 133).

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, including 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 contribution is reflected by several high-impact factor collaborative papers published throughout 2020.

Our team also continues to work both independently as well as in partnership to establish the impact of microbiome in colorectal cancer development and progression. In particular, we developed a *Fusobacterium nucleatum* diagnostic assay that permits the simultaneous visualization and quantification of bacteria within tumors. Using this assay we identified, for the very first time, *Fusobacterium nucleatum* as a biomarker of relapse in rectal cancer (*Annals of Oncology* 2020). We are also leading the FUSOMAP, a 3-year project funded by the *Mutua Madrileña* Foundation and *Instituto de Salud Carlos III* - ISCIII (Institute of Health Carlos III), to develop microbiota-based diagnostic and prognostic models by mapping intratumoral Fusobacterium and associated gut microbiota in early-stage colorectal cancer.

As a Core Facility we have provided support for approximately 340 clinical studies conducted at Vall d'Hebron, representing 72% of all currently open trials at our institution. Our involvement in clinical trials ranges from 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 2020, we performed more than 3000 molecular determinations on samples for patient inclusion in clinical trials, and over 19,000 tests to support basic and translation research. We have also served as the central laboratory of choice for 10 international studies, and successfully maintained the prestigious ISO15189 accreditation that endorses quality and competence.

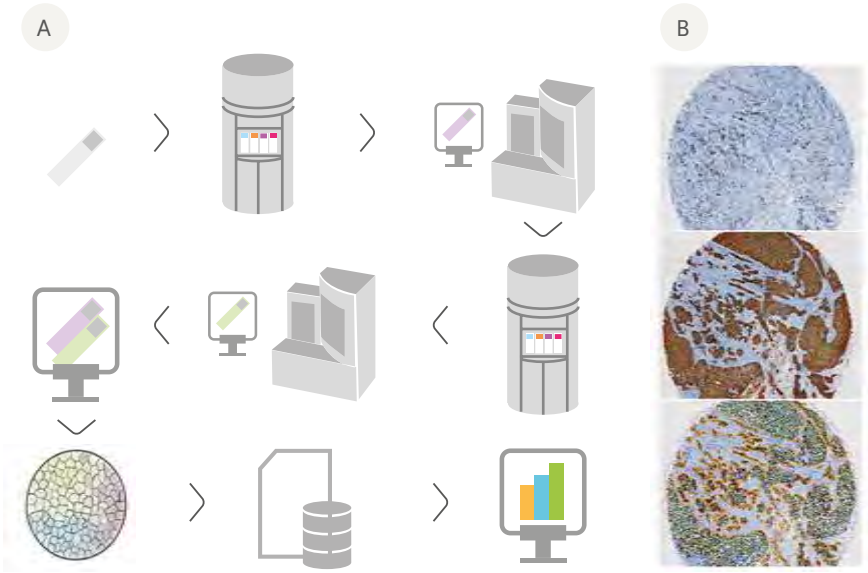


Figure: A) KiQuant workflow. B) A tumor core sequentially stained with Ki67 (top) and Pan-Keratin (middle). The two stainings are aligned into a single virtual digital image (bottom). Tumor region of interest are automatically identified by the Pan-Keratin-positive brown areas (dotted orange line). Green and red cells represent Ki67-negative and -positive nuclei, respectively.

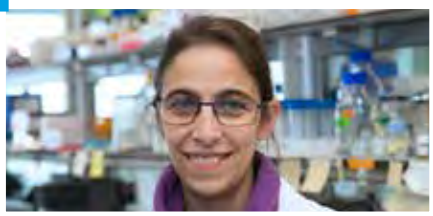
PI PAPER PICK

Serna G, Ruiz-Pace F, Hernando J, Alonso L, Fasani R, Landolfi S, Comas R, Jimenez J, Elez E, Bullman S, Tabernero J, Capdevila J, Dienstmann R, Nuciforo P. Fusobacterium nucleatum persistence and risk of recurrence after preoperative treatment in locally advanced rectal cancer. *Ann Oncol*. 2020 Oct;31(10):1366-1375.

Serna G, Simonetti S, Fasani R, Pagliuca F, Guardia X, Gallego P, Jimenez J, Peg V, Saura C, Eppenberger-Castori S, Ramon Y Cajal S, Terracciano L, Nuciforo P. Sequential immunohistochemistry and virtual image reconstruction using a single slide for quantitative KI67 measurement in breast cancer. *Breast*. 2020 Oct;53:102-110.

Dienstmann R, Garralda E, Aguilar S, Sala G, Viaplana C, Ruiz-Pace F, González-Zorelle J, Grazia LoGiacco D, Ogbah Z, Ramos Masdeu L, Mancuso F, Fasani R, Jimenez J, Martinez P, Oaknin A, Saura C, Oliveira M, Balmaña J, Carles J, Macarulla T, Elez E, Alsina M, Braña I, Felip E, Tabernero J, Rodon J, Nuciforo P, Vivancos A. Evolving Landscape of Molecular Prescreening Strategies for Oncology Early Clinical Trials. *JCO Precis Oncol*. 2020 May 14;4:PO.19.00398.

PROTEOMICS GROUP



Principal Investigator Francesc Canals Technicians Luna Martín, Anna Sabé

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.
- Contribute to mapping the Chromosome 16 proteome as part of the Human Proteome Project.

HIGHLIGHTS

- The provision of proteomic services to VHIO groups, oncology professionals at the Vall d'Hebron University Hospital (HUVH), and members belonging to the *ProteoRed-Instituto Salud Carlos III* network.
- Application of proteomic and phosphoproteomic screening to the characterization of CRC PDX models.
- Setting up mass spectrometry based analytical methods to monitor specific drugs in plasma and tumor tissue, to assess preliminary pharmacokinetics in preclinical mouse models.

SUMMARY

Our group serves as a Core Technology Platform. We provide state-of-the-art proteomic methodologies to investigators at VHIO, and incorporate new developments within the field to offer the very latest strategies and technologies in the field.

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.

Our group also develops MS based assays for marker proteins in FFPE tissue samples in order to provide accurate quantitative measurements that can translate in superior stratification compared with routine IHC scoring methods.

We have set up workflows for the proteomic and phosphoproteomic characterization of patient-derived xenograft (PDX) models of colorectal cancer. PDX constitute an ideal platform for the molecular characterization at the proteomic level of this tumor type.

Complementing genomic classification, we are exploring the suitability of this characterization as a tool for tumor subtype classification.

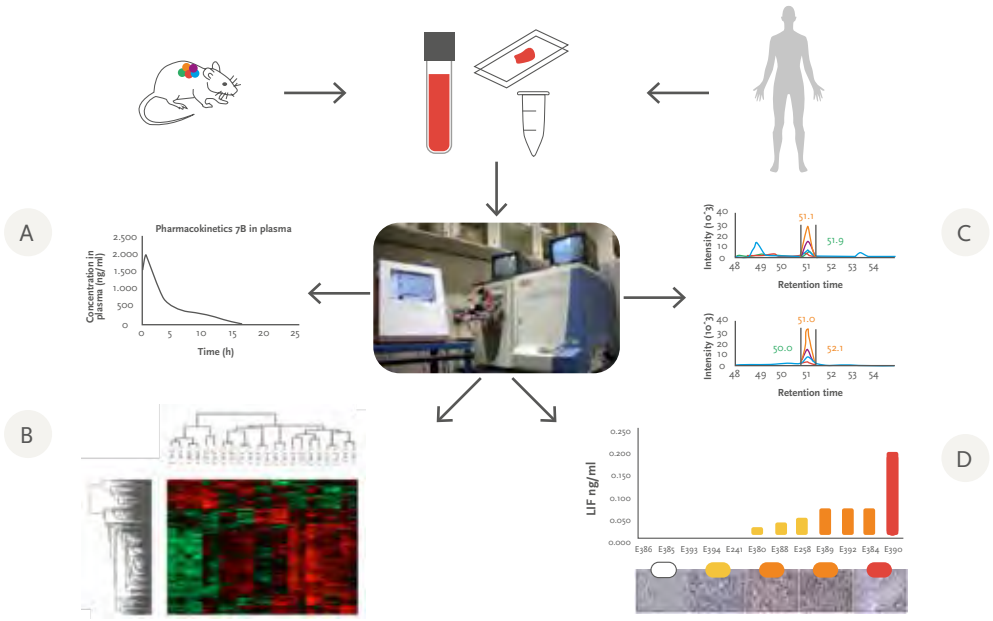


Figure: Proteomics in preclinical and translational research. Our laboratory provides mass spectrometry based analysis of plasma, tissue or FFPE samples for: A) monitoring small drugs in plasma or tissue of model animals for pharmacokinetic characterization. B) Profiling of total proteome and phosphoproteome of PDX tumor models to explore pathways involved in therapeutic response. C) targeted LCMS analysis and D) immune-MS analysis, to measure levels of biomarkers in clinical samples for patient stratification or treatment monitoring.

PI PAPER PICK

Simats A, Ramiro L, García-Berrocoso T, Briansó F, Gonzalo R, Martín L, Sabé A, Gill N, Penalba A, Colome N, Sánchez A, Canals F, Bustamante A, Rosell A, Montaner J. A mouse brain-based multi-omics integrative approach reveals potential blood biomarkers for ischemic stroke. *Mol Cell Proteomics.* 2020 Dec;19(12):1921-1935.

Vitali M , Casals E , Canals F , Colomé N , Puntes V. Simple spectroscopic determination of the hard protein corona composition in AuNPs: albumin at 75. *Nanoscale.* 2020 Aug 7;12(29):15832-15844.

Granado-Martínez P, Garcia-Ortega S, González-Sánchez E, McGrail K, Selgas R, Grueso J, Gil R, Naldaiz-Gastesi N, Rhodes AC, Hernandez-Losa J, Ferrer B, Canals F, Villanueva J, Méndez O, Espinosa-Gil S, Lizcano JM, Muñoz-Couselo E, García-Patos V, Recio JA. STK11 (LKB1) missense somatic mutant isoforms promote tumor growth, motility and inflammation. *Commun Biol.* 2020 Jul 9;3(1):366.

INSTITUTIONAL PROGRAMS

FERO Foundation: driving advanced molecular diagnostics against cancer

Headed by Rodrigo Dienstmann, Principal Investigator of VHIO's Oncology Data Science (ODysSey) Group (page 104), under the co-leadership of Ana Vivancos, Principal Investigator of VHIO's Cancer Genomics Group (page 116), Paolo Nuciforo, Principal Investigator of our Molecular Oncology Group (page 118), and Elena Garralda, who leads VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, as well as Early Clinical Drug Development (page 92), our **Molecular Prescreening Program** (page 118), is supported through our institutional **Advanced Molecular Diagnostics Program (DIAMAV)**, powered by one of our patrons and Institutional Supporters, the FERO Foundation (page 24).

Serving as a Core VHIO Service, 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. Additionally, this knowledge better guides our multidisciplinary teams to assess and establish patients' suitability for inclusion in early phase clinical trials led by VHIO's Research Unit for Molecular Therapy of Cancer (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, and continues to extend its enabling technologies and platforms to an increasing number of individuals. In 2020, our researchers and clinical investigators performed molecular profiling in over 1,100 cancer patients as potential candidates for inclusion in our clinical studies. In total, 150 patients were treated with biomarker-matched innovative therapies as a result of these efforts.

In short, this Program enables us to lead one of the few centers in Europe to run such a comprehensive program, 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, as well as develop cancer diagnostics for the early detection of disease.

"la Caixa" Foundation: advancing research and rendering anti-cancer medicines more precise

Cancer is the second leading cause of death globally, with around 18 million new cases diagnosed and more than 9.6 million cancer-related deaths each year. While cancer survival rates continue to improve, there are still many tumor types with no effective treatments. Clinical trials are crucial to identifying and developing novel therapies against cancer and are only possible at VHIO thanks to the continued support received from the "la Caixa" Foundation; one of our Institutional Supporters and Patrons (see pages 23-27).

Building on the successes of the two previous VHIO-"la Caixa" Institutional 3-year Programs, our **CaixaResearch Advanced Oncology Research Program** (2020-2023) launched this year to further spur the development of more potent and precise anti-cancer medicines, fortify existing research lines as well as initiate new projects to lead frontier research in some of the most relevant and rising focus fields in precision oncology; those areas showing particular promise in solving the multiple questions that stand in the way of more effectively combating cancer.

Marking the tenth anniversary of our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch -also supported by "la Caixa" Foundation (page 133), this program enables us to pursue our transformative research lines aimed at unpicking the complex role that the microbiome plays in cancer development, driving 'big data'-derived insights, developing and integrating cutting-edge platforms incorporating bioinformatics, biostatistics and machine learning applications in cancer prognosis and prediction, as well as harnessing the potential of Artificial Intelligence (AI) in the development of individually matched therapies.

In parallel with our plans to expand VHIO's portfolio of clinical trials performed at our Unit, that have led and/or contributed to the approval of some 30 anti-cancer agents by the U.S. Food and Drug Administration (FDA), our **CaixaResearch Advanced Oncology Research Program** will allow us to further 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 (page 92), Cancer Genomics (page 116), Molecular Oncology (page 118), Oncology Data Science (ODysSey – page 104) Groups, led by Elena Garralda, Ana Vivancos, Paolo Nuciforo, and Rodrigo Dienstmann, respectively.

Within the scope of this CaixaResearch Advanced Oncology Research Program, Elena Garralda's team has performed several clinical trials with patients selected 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.

The matched dedication of our clinical and translational investigators across all VHIO groups, as well as our Clinical Trial Office (page 130), headed by Marta Beltran, Clinical Trials Support Office, managed by Susana Muñoz, Clinical Research Oncology Nurses, spearhead by Nines Peñuelas, Clinical Research Oncology Pharmacy Unit –an additional Facility supported by the "la Caixa" Foundation, led by Maria Queralt Gorgas, and Quality & Processes Unit (page 142), led by Gemma Sala, has also made the past decade's total of over 1,300 Phase I plus Basket studies, and 1076 Phase II insightful studies possible. Over the last ten years more than 7,800 patients have been enrolled in clinical trials at VHIO.

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 BBVA Foundation 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 antitumor responses to develop more personalized and potent immune-based therapies and treatment strategies.

Represents 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.

Under the leadership of our Director, Josep Tabernero, CAIMI counts on the expertise of VHIO's 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 (UITM) - CaixaResearch (page 133), who heads up the program's clinical research, and Alena Gros, Principal Investigator of our Tumor Immunology and Immunotherapy Group (page 86), who leads its translational research.

These efforts also rely on our Molecular Prescreening Program (page 140), headed by Rodrigo Dienstmann, Principal Investigator of VHIO's Oncology Data Science (ODysSey) Group (page 104), under the co-leadership of Ana Vivancos, Principal by VHIO's Cancer Genomics Group (page 116), Paolo Nuciforo, Principal Investigator of our Molecular Oncology Group (page 118), and Elena Garralda.

Over the past two years, CAIMI has enabled the development of various translational projects linked to the early clinical development phases of immunotherapy. Just some focus areas include the development of cell-based therapies such as killer T cells for non-responders to current immunotherapies, characterizing hyperprogressive disease with immunotherapy to advance insights into this phenomenon, as well as establishing a radiomic signature to predict response to immunotherapy, led by Raquel Perez-Lopez, Principal Investigator of our Radiomics Group (page 108). Concerning the latter, we are now exploring how this correlates with the genomic evolution in patients.

Importantly, this year, Alena Gros and Elena Garralda's teams have worked together to finalize the clinical grade validations of tumor-infiltrating lymphocytes expansion for the treatment of certain cancer patients at the Vall d'Hebron University Hospital HUVH).

Most recently, Alena's group filed an investigational new drug (IND) application to the AEMPS Spanish Regulatory Agency towards treating patients with metastatic epithelial or immunotherapy refractory tumors with neoantigen-reactive TILs. By enriching for neoantigen-reactive lymphocytes, the aim is to fortify the efficacy of TIL therapy in epithelial cancers.

VHIO's TASK FORCES

VHIO's task forcing teams in multidisciplinary action (these two pictures were taken prior to the COVID-19 pandemic). The second picture depicts the launch of VHIO's renal task force, celebrated on World Kidney Cancer Day.

STRATEGIC GOALS

- Foster research collaborations in-house and with external partners, by providing the multidisciplinary forum for interaction between researchers other healthcare professionals in oncology.
- Update on funding opportunities (competitive and non-competitive), for the development, coordination, compilation, writing, and logistical management of new proposals.
- Create, maintain and standardize the necessary tools (CRF, informed consents, and databases), to optimize the development of ongoing research.
- Improve circuits in sampling, samples procedures, and data collection to spur research development.
- Identify the needs of the 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' & clinical needs and translate these into focused research opportunities.
- Central management of patients' data according to projects' pipelines and cohorts.

HIGHLIGHTS

- We have successfully maintained the activity of our task forces despite the COVID-19 pandemic through the digitalization of activities, and consolidated our task forcing model by increasing the number of participants and projects.

SUMMARY

Accelerating progress through team science, VHIO's multidisciplinary teams, coordinated by our VHIO's Scientific Area (page 144), also work together as established Task Forces that have been created 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, oncologists, pathologists, other MD disciplines, clinical research nurses, data curators as well as study coordinators, and project managers, among others.

Covering breast, colorectal, gastroesophageal, kidney, melanoma, neuroendocrine/rectal, pancreatic, prostate, and gynaecological cancers, as well as onco-imaging, VHIO's task forces regularly convene to synergize efforts, boost collaborations among groups and between specialists, and continuously revise patients and samples' circuits and ethics toward advancing cancer science and precision medicine.

The internal organization of each dedicated task force varies depending on its size, workflow, participants, and level of action. Each have an appointed Chair and are coordinated by an allocated project manager for the setting of agendas, writing of meeting minutes, follow up of action points/ tasks, and establishing alignments, interactions and synergies across our various task forces.

Illustrative of VHIO's commitment to team science in more effectively tackling the complexity of cancer malignancies, 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 Camps and other research institutions, actively contribute to the activities of our dedicated task forces.

We aim to create new task forces for pathologies that do not currently have specific, allocated task teams, as well as other transversal areas. In addition, we hope to set up a new task force devoted to patients, their families and caregivers, to further involve patients in our research, in alignment with ongoing policies and activities of the Vall d'Hebron University Hospital.

VHIO's TRANSVERSAL CLINICAL TRIALS CORE SERVICES & UNITS

130 Clinical Trials Office

133 Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch

136 Clinical Research Oncology Nurses

138 Clinical Research Oncology Pharmacy Unit

140 Molecular Prescreening Program

142 Quality & Processes Unit

Considering certain logistical and spatial issues, we have unfortunately had to repeat pictures of our larger transversal clinical trials core services and units from VHIO's Scientific Report 2019 - as indicated in within their respective pages.

VHIO'S TRANSVERSAL CLINICAL TRIALS CORE SERVICES & UNITS

CLINICAL TRIALS OFFICE

* For logistical issues brought about by the current COVID-19 pandemic, we are repeating pictures of some of our larger groups, services and units from our 2019 Scientific Report.

Director, Clinical Trials Office Marta Beltran Head, Start-Up Unit and Clinical Trials Liaison Silvia Perez Head, Data Entries Ignacio Carcela Head, Hematology Laura Segura Lead Study Coordinators Olga Padrós, Eulalia Aliende, Montse Moreno, Ester Serra, Sergi Recasens, Cristina Perez Leads, Data Entries David Alvarez, Gloria García, Eva Lázaro Study Coordinators Carlos Fernández, Maria Del Mar Suanes, Montse Hernández, Maribel Martinez, Marta Batista González, Enric Álvarez, Pol Gonzalez, Thaïs Miquel, Alba Meire, Maribel Martinez, Júlia Serra, Jordi Perera, Nuria Casado, Irati Fernandez, Berta Feliu, Raquel Madrenas, Alba Martinez, Sònia Martínez, Guillem Cunill, Gemma Mur, María López, Ana Matres, Raquel de la Torre, Alejandro Pardines, Albert Teixidó, Laura Saucedo, Eva Banús, Núria Farràs, Marina Coll, Joel Puig, Judit Pinteño, Mafalda Nunes, Júlia Sedó, Queralt Ferrer, Elena Sànchez, Josu Iraola, Danis Fernàndez, Magda Masana Data Entries Paula Chiquillo, Cristina Aguilar, Joana Pinyol, Asal Rinaldi, Laia Gregori, Jordina Lavall, Eva Marín, Sílvia Marín, Lidia Martinez De Arenzana, Carina Monclús, Helena Montanuy, Nuria Ortega, Eduard Solà, Samanta Bascuas, Nuria Clotet, Neus Iserte, Sergio Perez, Montserrat Pujades, Isabel Rico, Andrea Gomez, Jordi Romero, Gaudi Vall, Marta Vidigal, Rosa Romero, Pau Juhera, Xavier Perez, Inés Tejero, Alejandro Lahire, Marina Polo, Natàlia Écija, Alberto Rojo, Mireia Mira, Nestor Babon Clinical Trials' Assistants Nuria Carballo, Marc Palomar, Cristian Campderros

STRATEGIC GOALS

- Contribute to the development of novel therapies against cancer.
- 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.
- Appropriate management of the complexity of protocols which are increasingly demanding.
- We have provided tailored training for our staff in order to further improve the quality of our work and expand related skill sets.
- Implementation of new tools and procedures to increase the quality and efficiency of research.
- Reorganization of the clinical trials office to implement transversal work
- Reorganization during the Sars-CoV-2 pandemic to guarantee the continuity of treatments while maintaining quality standards.
- Adaptation of monitoring systems to achieve remote source data verification by 2021.

SUMMARY

Launched in 1997, our Clinical Trials Office incorporates experts conducting clinical trials at the Vall d'Hebron University Hospital's (HUVH) Medical Oncology Department, the Vall d'Hebron Barcelona Hospital Campus. Headed by VHIO's Director, Josep Tabernero, our team comprises study coordinators, data managers and administrative who coordinate phase I–IV clinical studies and also participate in several translational research projects at VHIO. 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, our personnel are managed by the Clinical Trials Office Director, Marta Beltran.

Clinical Trials in Oncology

In 2020 we managed 2 phase 0, 169 Phase I, 26 Basket studies, 148 phase II, and 129 phase III clinical trials with active recruitment throughout the year (Figure I), with patient enrolment totaling at 1084 (Figure II). 178 new trials were initiated, including 7 post-authorization trials, and rollover studies. In addition, we continue to follow up patients who were recruited prior to 2020 and are still enrolled and receiving study treatment (more than 800 patients in total, and more than 1700 in follow -up).

Figure I: **Annual distribution of oncology clinical trials (Phase 0, I + Basket, II and III) and post authorization trials with active recruitment**

	2013	2014	2015	2016	2017	2018	2019	2020
Phase 0							1	2
Phase I & basket trials	75	83	106	129	137	161	162	195
Phase I Specific Tumor Type (STT)	29	36	32	44	45	53	59	79
Phase I Non Specific Tumor Type (NSTT)	46	47	68	71	75	86	80	90
Basket			6	14	17	22	23	26
Phase II STT trials	96	99	94	117	107	131	141	148
Phase III trials	61	64	89	108	111	107	121	129
Nº clinical trials	232	246	289	354	355	399	425	474
Post authorization & rollover trials		5	14	16	19	33	34	34

Figure II: **Annual recruitment of patients enrolled in oncology clinical trials (Phase 0, I + Baskets - II–III) and post authorization trials**

	2013	2014	2015	2016	2017	2018	2019	2020
Included in Phase 0							1	1
Included in Phase I & basket trials	345	303	370	453	445	508	499	521
Phase I Specific Tumor Type (STT)	107	79	79	84	80	110	124	178
Phase I Non Specific Tumor Type (NSTT)	238	224	262	301	289	334	303	307
Basket			29	68	76	64	72	36
Included in Phase II STT trials	257	302	327	333	323	361	337	230
Included in Phase III trials	241	166	282	343	328	329	285	332
Total of patients included	843	771	979	1129	1096	1198	1122	1084
Included in post authorization & rollover trials		20	56	50	80	184	164	156

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 leading reference in early clinical studies. As a reflection of our continued expansion as well as recognition of excellence, VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch directed by Elena Garralda (page 133), 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 respond to the specificities of each individual patient, each individual tumor, the requirements and selection criteria for inclusion in certain studies are also becoming more complex.

While we are dedicated to expanding our portfolio of trials in order to ultimately establish new treatment models with highly selective drugs, we continue to fine-tune patient selection criteria in order to best identify those patients who are most likely to benefit from novel therapies, including emerging immune-based therapies, tailored to individual patients' molecular 'measurements'.

Clinical Studies in Hematology

In 2020 we managed 39 Phase I, 36 phase II, and 45 phase III clinical trials with active recruitment throughout the year (Figure III) with patient enrolment totaling at 153 patients (Figure IV). 50 new trials were initiated, including 7 post-authorization trials, and rollover studies. In addition, we continue to follow up patients who were recruited prior to 2020 and are still enrolled and receiving study treatment (more than 122 patients in total, and more than 74 in follow-up).

Clinical research is spearhead by Francesc Bosch, Prinicipal Investigator of VHIO's Experimental Hematology Group - please see page 94 to discover more.

Figure III: **Annual distribution of hematology clinical trials (Phase I + Basket, II and III) and post authorization trials with active recruitment**

	2018	2019	2020
Phase I	25	31	39
Phase I Specific Disease	24	30	37
Phase I Non Specific Disease	1	1	2
Basket			
Phase II trials	28	24	36
Phase II Specific Disease	28	23	35
Phase II Non Specific Disease		1	1
Phase III trials	50	51	45
Phase III Specific Disease	50	51	42
Phase III Non Specific Disease			3
N° clinical trials	103	106	120
Post authorization & rollover trials	15	22	25

Figure IV: **Annual recruitment of patients enrolled in hematology clinical trials (Phase I + Baskets - II–III) and post authorization trials**

	2018	2019	2020
Included in Phase I	38	55	59
Specific Disease (SD)	37	55	56
Non Specific Disease (NSD)	1		3
Basket			
Included in Phase II trials	20	38	39
Specific Disease (SD)	20	38	39
Non Specific Disease (NSD)			
Included in Phase III trials	52	56	55
Specific Disease (SD)	52	56	51
Non Specific Disease (NSD)			4
Total of patients included	110	149	153
Included in post authorization & rollovers trials	1	6	38

The prestige of HUVH's Medical Oncology Department, led by VHIO's Director, Josep Tabernero, is increasingly recognized by pharmaceutical as well as biotechnology companies. It has also become a reference program and selected by the industry to carry out complex clinical trials for which the number of participating centers is highly restricted.

Clinical sites are selected based on the highest standards of quality 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. We have also conducted more than 10 Investigator-Initiated Trials (IITs) in oncology.

VHIO'S TRANSVERSAL CLINICAL TRIALS CORE SERVICES & UNITS

RESEARCH UNIT FOR MOLECULAR THERAPY OF CANCER (UITM) – CaixaResearch

* For logistical issues brought about by the current COVID-19 pandemic, we are repeating pictures of some of our larger groups, services and units from our 2019 Scientific Report.

Director Elena Garralda Co-Director Josep Tabernero Executive Team Marta Beltran, Elena Garralda, Ángeles Peñuelas, Gemma Sala Clinical Head Elena Garralda Associated Investigators Senior Cosultants: Judith Balmaña, Joan Carles, Elena Garralda, Enriqueta Felip, Teresa Macarulla, Ana Oaknin, Cristina Saura, Josep Tabernero Phase I Investigators: Daniel Acosta, Guzmán Alonso, Juan David Assaf, Iosune Baraibar, Irene Braña, Meritxell Bellet, Ana Callejo, Jaume Capdevila, Marta Capelan, Susana Cedrés, Marc Diez, Mª Elena Élez, Santiago Escrivá, Lorena Fariñas, Vladimir Galvao, Carmen Garcia, Patricia Gómez, Macarena González, Francisco Grau, Jorge Hernando, Patricia Iranzo, Alexandre Martínez, Joaquin Mateo, Rafael Morales, Alejandro Navarro, Eva Muñoz, Honey Oberoi, Mafalda Oliveira, Carolina Ortiz, Núria Pardo, Isabel Pimentel, Francisco Javier Ros, Omar Saavedra, Cesc Salvá, César Serrano, Cristina Suarez, Claudia Mª Valverde, Helena Verdaguer, María Vieito Clinical Trials Office Director Marta Beltran Start Up Unit Head Sílvia Pérez Data Entries Head Ignacio Carcela Study Coordinators Lead Coordinators Eulàlia Aliende, Montserrat Moreno Coordinators: Eva Banús, Guillem Cunill, Gemma Mur, Núria Farràs, María López, Ana Matres (Sponsor dedicated), Elena Martínez, Sonia Martinez (Sponsor dedicated), Aitana Almodóvar (Sponsor dedicated), Albert Teixidor (Sponsor dedicated), Joel Puig, Alejandro Pardines, Laura Saucedo Data Entries, Lead Data Entries Gloria García Data Entries Eva del Castillo (Personal externo), Andrea Gómez (Sponsor dedicated), Lidia Martinez, Gerard Orriols, Sergio Pérez, Montserrat Pujadas, Isabel Rico, Jordi Romero, Inés Tejero (Sponsor dedicated), Gaudí Vall, Marta Vidigal Clinical Trials Office Administrative Support Nuria Carballo, Marc Palomar Nursing Head Ángeles Peñuelas Nurse Coordinator Sonia Valverde Operational Research Nurses Irene Calzado, Begoña Fargas, Andrea Martínez Nurses María Ayala, Elena de Cabo, Margarida Marcos, Marta Mate, Isabel Muñoz, Tania Sánchez, Alba Silverio Nurses Assistants Mª Ascensión Clop, Alicia López Inventory Manager Cristina Resina UITM - CaixaResearch Administrative Support (Schedulers) Rosa Andújar, Laura Castejón, Mª Teresa Mendoza Clinical Director of the Clinical Research Oncology Pharmacy Unit Maria Queralt Gorgas Coordinator of the Clinical Research Oncology Pharmacy Unit Isabel Cidoncha Senior Pharmacists María Josep Carreras, Laura Maños Pharmacists Montserrat Carreres, Carla Esteban, Lorena García, Patricia García, Pablo Latorre, Javier Martínez, Pilar Rovira, Eugenia Serramontmany, Javier Varela Technicians Romina Bellini, Esther Carabantes, Bryan Cárdenas, Angelica Cely, Ismael Delgado, Rafael Diaz, Ariadna Jabalera, Roser Klimt, Susana Mulet, Isabel Pérez, Marta Pozo, Alan Thompson, Silvia Torralba, Alexandre Valle, Noemi Visus Data Entry Carmen Torres Secretary Isabel Mª Alerany

STRATEGIC GOALS

- Early clinical drug development and translational research led by UITM – CaixaResearch clinical investigators and VHIO researchers: expansion of our broad portfolio of promising novel anticancer therapies, across a balanced spectrum of studies, with special 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 UITM to VHIO's preclinical and translational projects. Our Unit also collaborates with the various 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 treatments 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 trials in immuno-oncology.
- We have expanded our expertise in drugs targeting developmental pathways, cell signaling (ERK, MET, FGFR, RET, NOTCH, NTRK), and immunotherapy (LAG3, TIGIT, OX40, CD40, IDO, arginase inhibitors and engineered antibodies).
- Developed by VHIO's Cancer Genomics Group (page 116), PI: Ana Vivancos, we benefit from applications for faster results including an n-Counter (Nanostring) platform, two digital PCR platforms (BEAMing Sysmex and ddPCR, BIO-RAD), and two NextGen Sequencers; MiSeq and HiSeq2500 (Illumina). We also co-develop customized molecular tests for VHIO's Molecular Prescreening Program (page 140): disease-oriented mutation panels for our NGS platforms.
- We have developed alliances with many pharma companies as the preferred site for testing their novel and most relevant therapies, including GlaxoSmithKline OCTC, Roche ImCORE, and AstraZeneca/MedImmune, Partners of Choice.
- We 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 in their tumors and a high probability of benefiting from the selected treatments. This is an academic study, endorsed by the Cancer Core Europe (CCE) Consortium (page 175), 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 to evaluate possible treatment options.
- We have started an advanced cell-based therapy program, and are participating in several pharma sponsored trials to evaluate the role of TIL therapy as well as exploring an academic TIL product in collaboration with Alena Gros, PI of VHIO's Tumor Immunology & Immunotherapy Group (page 86).
- In collaboration with several other VHIO groups, we head the VHIO - CaixaResearch Advanced Oncology Research Program (2020-2023), supported by the "la Caixa" Foundation (page 123).

"la Caixa" Foundation

SUMMARY

Inaugurated in June 2010, thanks to the support received from the "la Caixa" Foundation, the 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 m2 our Unit is located within the General Area of the Vall d'Hebron University Hospital (HUVH), the 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 rapidly establish itself as one of the few comprehensive facilities in Europe to rapidly transform latest discovery into benefits for patients.

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 diseases and how to treat them in an individualized way – getting the right therapy to the right patient at the right time. As the figures show, we are gradually doing so for an increasing number of patients.

This year has been particularly challenging due to the COVID 19 pandemic. All our efforts have focused on successfully maintaining our clinical research activities and continuing to include patients in our clinical trials. During 2020, our Unit participated in 195 ongoing phase I clinical trials, 26 of which are Basket trials (a 20% increase compared with 2019). Our facilities, coupled with our multidisciplinary clinical teams, enable us to continue to expand our portfolio of phase I studies. This year we opened 71 new trials; 4 as Baskets, with 521 patients enrolled.

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 also collaborate closely 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 140), that performs molecular analyses of patients' tumors to select the best possible treatment with the experimental therapeutics available. Thanks to our Cancer Genomics Group's (page 116), the development of existing applications for faster results including an n-Counter (Nanostring) platform, two digital PCR platforms (BEAMing Sysmex and ddPCR, BIO-RAD), and two NextGen Sequencers; MiSeq and HiSeq2500 (Illumina), enable us to drive faster and more precise mutational analyses of tumor suppressor genes as well as translocations and gene amplifications.

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.

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 team of Clinical Research Oncology Nurses led by Mª Angeles Peñuelas (page 136), pathologists from the Vall d'Hebron University Hospital's Molecular Pathology Department, radiologists and interventional radiologists, our Clinical Trials Office, directed by Marta Beltran (page 130), Database Management, Clinical Research Oncology Pharmacy Unit headed by Maria Queralt (page 138), our Quality & Processes Unit, managed by Gemma Sala (page 142), as well as many other healthcare specialists including dermatologists, cardiologists, and ophthalmologists.

VHIO'S TRANSVERSAL CLINICAL TRIALS CORE SERVICES & UNITS

CLINICAL RESEARCH ONCOLOGY NURSES

* For logistical issues brought about by the current COVID-19 pandemic, we are repeating pictures of some of our larger groups, services and units from our 2019 Scientific Report.

Nurse Supervisor Mª Angeles Peñuelas Nurse Supervisor's Assistant Juan Manuel Garcia Nurse Coordinators Cristina Casal, Sonia Valverde, Lydia Velez Nurses Maria Ayala, Andrea Caballero, Anna Maria Carro, Mª Elena De Cabo, Sandra Jara, Carla Junyent, Margarida Marcos, Marta Mate, Carmen Moina, Mireia Moral, Isabel Muñoz, Silvia Oliver, Silvia Puyalto, Tania Sanchez, Alba Silverio Operational Research Nurses Irene Cazaldo, Begoña Fargas, Andrea Martinez Nursing Assistants Alicia Lopez, Thalia Maldonado, Mª Ascension Martin, Ana Belen Ortiz, Cristina Resina

SUMMARY

Clinical trials in oncology are essential for the identification of novel, more effective targeted therapies against cancer as well as improving survival, side effect profiles and the quality of life of patients. Advances in oncology care and the development of more powerful anti-cancer medicines are driven by optimal processes in clinical trials.

Our expert clinical research oncology nurses assume a central role by undertaking a variety of roles including identifying trends in side effects, closely collaborating with multidisciplinary teams to develop and evaluate patient management, contributing to clinical studies by collating samples and quality data, as well as providing excellence in nursing care and symptom management for all patients enrolled in clinical trials.

While the COVID-19 pandemic naturally presented new challenges which demanded adaptive procedures, structures and where possible, our clinical teams and oncology nurses had, in many cases, to re-think conventional patient care.

With the safety of our patients as the highest priority, Angeles Peñuelas led her team in working tirelessly together with VHIO's medical oncologists and clinical investigators to swiftly establish adaptive circuits and approaches to ensure the optimal running of clinical studies, while delivering, as always, the highest levels of quality patient care. Newly introduced measures in response to COVID-19 –whenever/wherever possible- included remote monitoring as well as dispensation of medication for certain patients receiving orally administered therapies, and telematic clinical consultations.

VHIO's Clinical Research Oncology Nurses are specialized in molecular therapies and represent an important element of the multidisciplinary teams involved in the studies performed and coordinated at VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch and Clinical Trials Office, directed by Elena Garralda and Marta Beltran, respectively (see pages 133-130).

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 patients who receive the full range of expertise, guidance, and the necessary follow-up throughout the course of their participation in a clinical study. As importantly is the psychological support they provide, alongside the other superbly trained oncology care givers and specialists including psychologists.

Our nurses also provide patients and their families with the information and professional guidance they need to make fully informed decisions concerning their treatment options. In 2020, across the 474 actively recruiting trials in oncology patient enrollment totaled at 1084. Regarding clinical studies in hematology, across the 120 trials, a total of 153 patients were enrolled. Our clinical teams also continue to follow up patients that were recruited prior to 2020 who are still enrolled and receiving treatment.

As VHIO continues to expand its portfolio of clinical trials to ultimately establish novel treatments with highly selective drugs, and 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.

CLINICAL RESEARCH ONCOLOGY PHARMACY UNIT

* For logistical issues brought about by the current COVID-19 pandemic, we are repeating pictures of some of our larger groups, services and units from our 2019 Scientific Report.

Clinical Director of the Clinical Research Oncology Pharmacy Unit Maria Queralt Gorgas Coordinator of the Clinical Research Oncology Pharmacy Unit Isabel Cidoncha Senior Pharmacists María Josep Carreras, Laura Maños Pharmacists Montserrat Carreres, Carla Esteban, Lorena García, Patricia García, Pablo Latorre, Javier Martínez, Pilar Rovira, Eugenia Serramontmany, Javier Varela Technicians Romina Bellini, Esther Carabantes, Bryan Cárdenas, Angelica Cely, Ismael Delgado, Rafael Diaz, Ariadna Jabalera, Roser Klimt, Susana Mulet, Isabel Pérez, Marta Pozo, Alan Thompson, Silvia Torralba, Noemi Visus 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 studies treated with orally administered medicines to improve safety, compliance and the efficacy of these therapies.
- Provide instructions and indications to patients for orally administered therapies in phase II and III studies.
- Successful sponsor audits as well as inspections carried out by regulatory authorities.

"la Caixa" Foundation

HIGHLIGHTS

- Thanks to the support received from the "la Caixa" Foundation, we moved into our new facility, the Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch- Clinical Research Onco-Hematology Unit. Equipped with cutting edge technologies, it enables us to provide even higher quality pharmaceutical care and continue to meet all regulatory requirements.
- 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.

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. As noted in our highlights above, 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 this year. 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 2020 they managed drugs used in 591 active clinical trials in oncology & hematology, and 10,748 resupply deliveries/clinical trial supplies receptions. 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 2020 our dispensing staff actively participated in 240 pre-study visits, 245 initial visits, 1,850 monitoring visits, 180 close-out visits, and also successfully passed 5 audits, and 1 ISO inspection.

Additionally, 44,136 clinical trial drugs have been dispensed and validated by our pharmacists, 13,044 of which were for oral administration, 984 for IM/subcutaneous administration, and 30,108 for IV administration. A total of 204 Standardized Dispensing Procedures for clinical trials have been drawn up and we have performed 684 updates of these procedures due to subsequent amendments to protocols or pharmacy manuals. 156 storage temperature data reports have also been prepared by our dispensing team.

Preparations of cytostatics, monoclonal antibodies and other parenteral antitumor drugs for clinical trials totaled at 30,108. We also included 392 antineoplastic therapeutic schedules in our prescription software.

Our Pharmaceutical Care Program for patients enrolled in phase I clinical trials: we performed 1,248 visits, 348 screenings, 450 C1D1s, and 450 follow-ups, also compiling patient diaries and/or instructions for patients (in the absence of documentation provided by the respective sponsor).

We have also compiled 20 different diaries and 28 instruction manuals for patients enrolled in the phase I studies involving orally administered drugs by our preparation staff. We also prepared 24 diaries and 80 patient manuals for phase II and phase III clinical trials in 2020 for patients enrolled in all phase II and III studies involving orally administered drugs by our dispensing staff.

MOLECULAR PRESCREENING PROGRAM

FERO Foundation Advanced Molecular Diagnostics Program (DIAMAV)

Head of Program Rodrigo Dienstmann – Principal Investigator, VHIO's Oncology Data Science (ODysSey) Group– Co-leadership Ana Vivancos – Principal Investigator, VHIO's Cancer Genomics Group–, Paolo Nuciforo –Principal Investigator, VHIO's Molecular Oncology Group–, Elena Garralda –Director, VHIO's Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, Principal Investigator, VHIO's Early Clinical Drug Development Group– Program Coordinator Susana Aguilar Research Support Technician Jenifer Gonzalez

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 on emerging cancer biomarkers for precision cancer therapy.

HIGHLIGHTS

- VHIO is an active member of the 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), see page 140, catalyzes precision medicine at VHIO. Over the last decade, DIAMAV has provided access to advanced molecular diagnostics to more than 5,000 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), funded by the "la Caixa" Foundation (page 133) and directed by Elena Garralda, is led by Rodrigo Dienstmann (PI of Oncology Data Science – ODysSey – Group, page 104), and is based on the activity of VHIO's Cancer Genomics Group headed by Ana Vivancos (page 116), and Molecular Oncology Group directed by Paolo Nuciforo (page 118), in collaboration with our Early Clinical Drug Development Group also led by Elena Garralda (page 92).

The main objective of the program is to facilitate clinical implementation of emerging cancer biomarkers that help optimize the selection of therapies for patients being considered for enrolment in clinical trials. Our program guides clinicians in selecting novel anti-cancer treatments and facilitates 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 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 2020, we have performed tumor molecular profiling in over 1,100 cancer patients that are candidates for enrolment in clinical trials. In total, around 150 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.

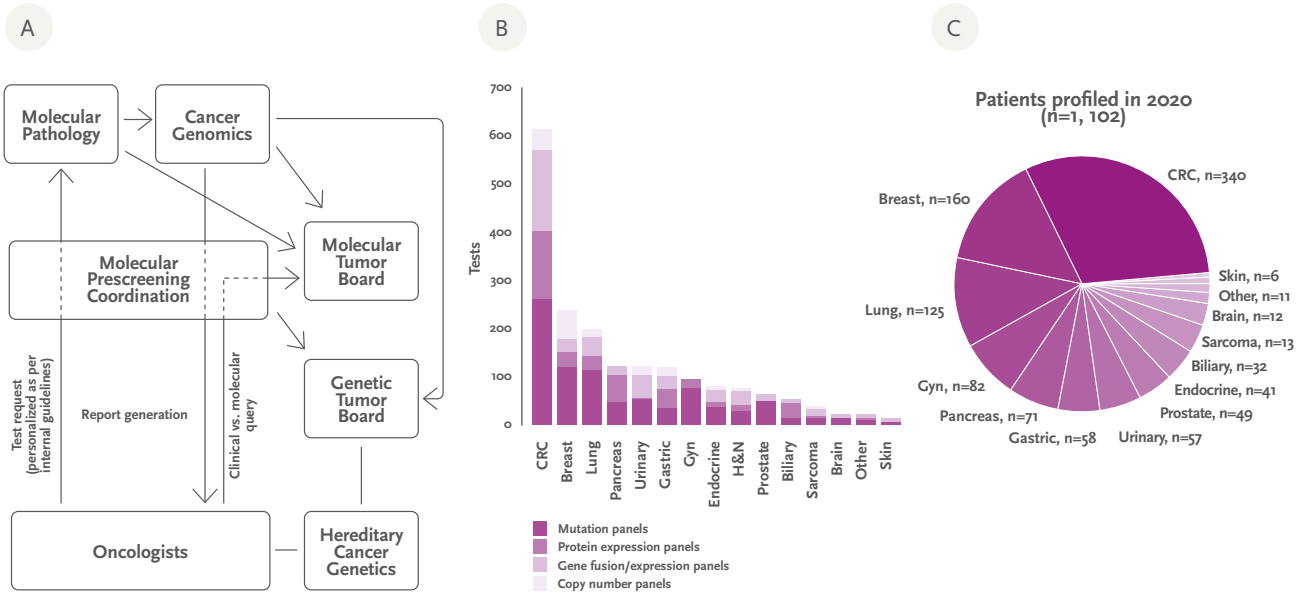


Figure: Molecular Prescreening Program at VHIO. (A) Interrelationship between Genomic and Molecular Pathology laboratories with clinical oncologists, and the functionality of the Prescreening Program. (B) Number of genomic and proteomic tests per tumor type. (C) Distribution of tumor types profiled in 2020.

PI PAPER PICK

Dienstmann R, Garralda E, Aguilar S, Sala G, Viaplana C, Ruiz-Pace F, González-Zorelle J, Grazia LoGiacco D, Ogbah Z, Ramos L, Mancuso F, Fasani R, Jimenez J, Martinez P, Oaknin A, Saura C, Oliveira M, Balmaña J, Carles J, Macarulla T, Elez E, Alsina M, Braña I, Felip E, Tabernero J, Rodon J, Nuciforo P, Vivancos A. Evolving landscape of molecular prescreening strategies for oncology early clinical trials. *JCO Precis Oncol.* 2020. 4:505-513.

VHIO'S TRANSVERSAL CLINICAL TRIALS CORE SERVICES & UNITS

QUALITY & PROCESSES UNIT

Director Gemma Sala Quality Managers Javier Fonts, Isabel González Quality Technician Miriam Artigas Sample Managers Alma Calahorro, Gerard Perez, David Vendrell Schedulers Rosa Andujar, Laura Castejon, Maria Teresa Mendoza

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) – CaixaReasearch (page 133).
- Develop and update Standard Work Procedures to standardize circuits, and provide all necessary trainings.

HIGHLIGHTS

- Clinical trials in oncology and hematology trials.

Our Unit collaborated in 500 active trials collectively enrolling a total of 1,200 patients. We have also monitored and managed over 200 patients receiving therapy each month, and successfully passed 18 audits and 1 inspection.

SUMMARY

Headed by Gemma Sala, formerly Director of VHIO's Clinical Trials Office (page 130), VHIO's Quality and Processes Unit was established this year, 2020, in order 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 management and schedulers

At VHIO we run numerous tasks related to clinical trials. It is therefore imperative that all these activities - and the personnel who perform them- are carried out by assuring optimal quality and excellence, and that the processes governing them are both homogeneous and the very best.

Quality is key to correctly performing clinical trials. Guaranteeing that all the current regulations of these studies be complied with is therefore essential. These homogeneous efforts follow Good Clinical Practice (GCP) guidelines, with the safety of patients as the top priority throughout.

SCIENTIFIC COORDINATION AREA

Head of Area Alejandro Piris Giménez Senior Project Managers Neus Bayó, Elena Chavarria, Javier Gonzalo, Josep Maria Miquel, Sandra Porta, Xenia Villalobos Clinical Senior Manager (Advanced Therapies) Silvia Martin-Lluesma Junior Project Managers (Task Forces) Cristina Molero (Gastroesophageal Cancer and GI non-CRC), Mireia Sanchís (Colorectal Cancer) Project Manager Technicians Berta Colldeforns (Junior), Nacho Sánchez (Junior), Isabel Vallvé (Senior) Masters Student Mireia Monrás

STRATEGIC GOALS

- Identify and promote new research opportunities involving academic and industry partners.
- Write, coordinate and manage scientific proposals.
- Manage, monitor and follow up institutional programs.
- Promote intramural research through education, networking and driving force.

HIGHLIGHTS

- In 2020, we maintained a good track record with a success rate of 29%, out of 205 grant (competitive) applications.
- This year, our Area managed more than 9.2 million EUR obtained from competitive funds.
- Our research support to VHIO groups has been recognized through our co-authorship of three publications - see our *Paper pick*.
- We supported the preparation and management of our Scientific Advisory Board (SAB) virtual meeting.
- Our Unit co-leads major EU consortia, including MoTriColor (H2020), page 177, COLOSSUS (H2020), page 175, the Basket of Baskets trial (Cancer Core Europe – CCE, page 175), and participates in numerous project boards and work packages. This year we compiled the CCE-DART project application, the first H2020 grant to be awarded to the Cancer Core Europe Consortium (see page 179), as well as the application for an ISCIII grant that will spur our cell-based therapy program led by VHIO's Elena Garralda and Alena Gros. This research focuses on TIL therapy targeting neoantigens for immune checkpoint blockade-resistant tumors.
- We have provided support to our Scientific Direction through the management of scientific data, documents and actions required for the elaboration and development of research proposals and projects at VHIO. In addtion, this year we received funding through a MINECO European Networks and Management grant to support the internationalization of our activities, expand our personnel, and organize educational and dissemination activities to improve our researchers' knowledge surrounding European funding programs.

AREA SUMMARY

VHIO's Scientific Coordination Area has consolidated itself as a Unit to support VHIO's Direction, Management, and research groups for the development of research proposals and programs, monitoring and follow up. We also provide support to our various Task Forces (page 126), that strengthen and promote multidisciplinary connectivity and spur joint research programs with other oncology teams at the Vall d'Hebron University Hospital, Vall d'Hebron Barcelona Hospital Campus (page 31).

Our managerial responsibilities include both financial and scientific support, as well as the implementation of institutional actions to various areas including education, ethics & regulatory issues, scientific dissemination, consortia and coordinated research. These cover competitive grant application processes, dissemination of national and international funding opportunities for our researchers, assessment of the preparation and writing of competitive project proposals, as well as the monitoring and coordination of awarded research projects.

We aim to optimize opportunities for the internationalization of groups through a personalized plan for VHIO groups, centralize ideas from taskforces and match selected research priorities with competitive calls, as well as support highly innovative technological project proposals to increase VHIO's success rate in terms of Innovative Medicines Initiative (IMI), and H2020 and Horizon Europe framework approved projects as coordinators and partners through the proactive search and evaluation of opportunities, as well as potentiate our area's organizational structure and optimize our project management processes.

PAPER PICK

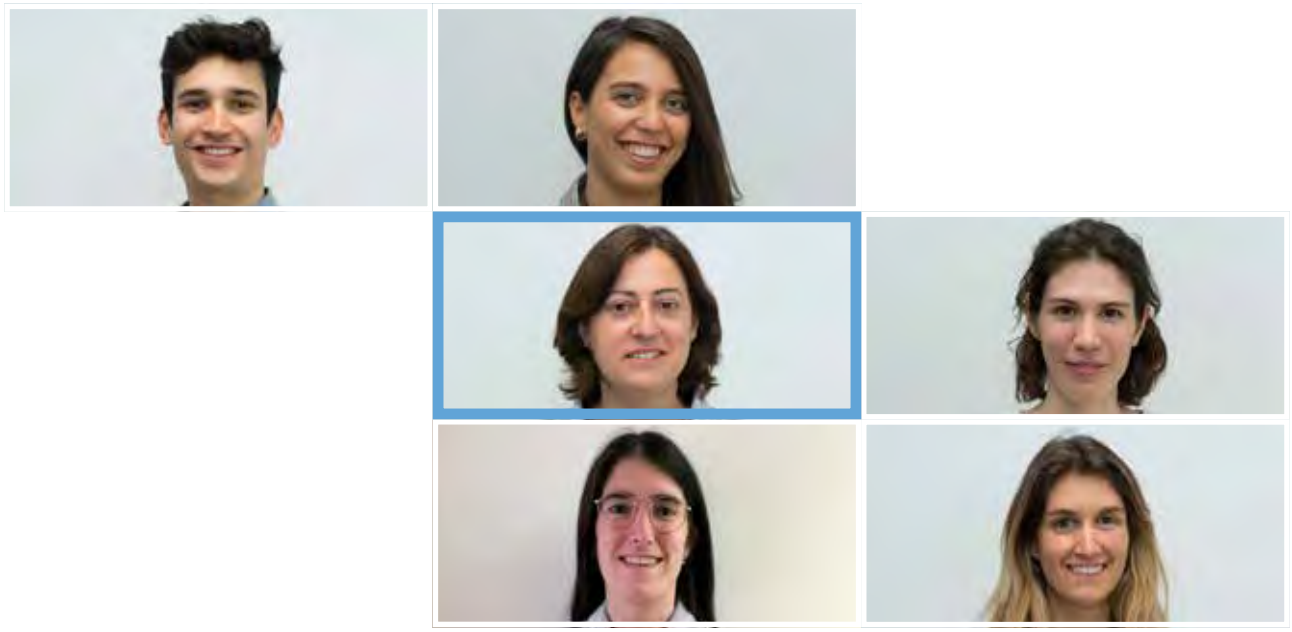
Tamborero D, Dienstmann R, Rachid MH, Boekel J, Baird R, Braña I, De Petris L, Yachnin J, Massard C, Opdam FL, Schlenk R, Vernieri C, Garralda E, Masucci M, Villalobos X, Chavarria E; Cancer Core Europe consortium, Calvo F, Fröhling S, Eggermont A, Apolone G, Voest EE, Caldas C, Tabernero J, Ernberg I, Rodon J, Lehtiö J. Support systems to guide clinical decision-making in precision oncology: The Cancer Core Europe Molecular Tumor Board Portal. *Nat Med.* 2020 Jul;26(7):992-994.

Cedrés S, Ponce-Aix S, Iranzo P, Callejo A, Pardo N, Navarro A, Martinez-Marti A, Gómez-Abecia S, Zucchiatti AC, Sansano I, Enguita AB, Miquel JM, Viaplana C, Dienstmann R, Paz-Ares L, Felip E. Analysis of mismatch repair (MMR) proteins expression in a series of malignant pleural mesothelioma (MPM) patients. *Clin Transl Oncol.* 2020 Aug;22(8):1390-1398.

van de Haar J, Hoes LR, Coles CE, Seamon K, Fröhling S, Jäger D, Valenza F, de Braud F, De Petris L, Bergh J, Ernberg I, Besse B, Barlesi F, Garralda E, Piris-Giménez A, Baumann M, Apolone G, Soria JC, Tabernero J, Caldas C, Voest EE. Caring for patients with cancer in the COVID-19 era. *Nat Med.* 2020 May;26(5):665-671.

VHIO'S SCIENTIFIC COORDINATION AREA

ACADEMIC CRO (VHIO - aCRO)



Unit Head Susana Muñoz Lead CRA and Project Manager Marta González Clinical Research Associates Ana Gainza, Darío López, Marta Pascual, Àgata Villanueva

AREA SUMMARY

VHIO's Academic Contract Research Organization (VHIO-aCRO), has extensive experience in conducting sponsored trials and investigator-initiated trials. We offer a complete package of start-to-end management services required to perform clinical trials and studies. Thanks to our multidisciplinary team, we can operate as a full service CRO in clinical studies from phase I to IV studies.

We also offer guidance to all researchers and sponsors on how to achieve the best experimental design and logistical advice in order to maximize their resources. With a team of 6 professionals, our Unit provides medical writing support, full regulatory activities, monitoring, project management, e-CRF creation, statistics, drug management, insurance management, and pharmacovigilance activities.

We seek to expand our Unit's structure with a clinical project manager and a CRA to be able to even more effectively manage current and future clinical trials, optimize CRO digital tools to allow for working remotely, as well as continue to bring out the best in each team member to enhance our newly created Facility.

STRATEGIC GOALS

- Clinical project management support to awarded R&D projects (European/Pharma funded), 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.
- Academic CRO for Investigator initiated trials.
- Academic CRO for pharmacy sponsored trials, when VHIO is involved in the development of the trial.

HIGHLIGHTS

- In 2020 our academic CRO successfully managed a number of major projects including COMBAT, TOPIC, IRONMAN, MONEO, among others. Most of these are led the Vall d'Hebron University Hospital (HUVH) oncology teams, at the Medical Oncology Department headed by Josep Tabernero, VHIO's Director.
- During 2020, we successfully met the regulatory requirements of all of our trials (first submissions and amendments).
- Our CRA team were able to monitor more than 150 patients in several hospitals throughout Spain.
- We managed clinical trials drug requirements in more than 25 national hospitals.
- We have also evidenced sufficient benefits to cover CRO activities for non-funded academic trials.

FULL LISTING OF ARTICLES PUBLISHED BY VHIO INVESTIGATORS IN 2020

Articles published by VHIO Investigators in 2020 with allocated Impact Factor (IF):

Enhancing global access to cancer medicines. Cortes, Javier; Perez-Garcia, Jose Manuel; Llombart-Cussac, Antonio; Curigliano, Giuseppe; El Saghir, Nagi S.; Cardoso, Fatima; Barrios, Carlos H.; Wagle, Shama; Roman, Javier; Harbeck, Nadia; Eniu, Alexandru; Kaufman, Peter A.; Tabernero, Josep; Garcia-Estevez, Laura; Schmid, Peter; Arribas, Joaquin. 2020. *CA Cancer J Clin.* 70(2): 105 - 124. IF: 292,278.

Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer. Hussain M; Mateo J; Fizazi K; Saad F; Shore N; Sandhu S; Chi KN; Sartor O; Agarwal N; Olmos D; Thiery-Vuillemin A; Twardowski P; Roubaud G; Özgüroglu M; Kang J; Burgents J; Gresty C; Corcoran C; Adelman CA; de Bono J; PROfound Trial Investigators. 2020. *N Engl J Med.* 383(24): 2345 - 2357. IF: 74,699.

Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer. André T; Shiu KK; Kim TW; Jensen BV; Jensen LH; Punt C; Smith D; Garcia-Carbonero R; Benavides M; Gibbs P; de la Fouchardiere C; Rivera F; Elez E; Bendell J; Le DT; Yoshino T; Van Cutsem E; Yang P; Farooqui MZH; Marinello P; Diaz LA Jr; KEYNOTE-177 Investigators. 2020. *N Engl J Med.* 383(23): 2207 - 2218. IF: 74,699.

First-Line Lorlatinib or Crizotinib in Advanced ALK-Positive Lung Cancer. Shaw AT; Bauer TM; de Marinis F; Felip E; Goto Y; Liu G; Mazieres J; Kim DW; Mok T; Polli A; Thurm H; Calella AM; Peltz G; Solomon BJ; CROWN Trial Investigators. 2020. *N Engl J Med.* 383(21): 2018 - 2029. IF: 74,699.

Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. Herbst RS; Giaccone G; de Marinis F; Reinmuth N; Vergnenegre A; Barrios CH; Morise M; Felip E; Andric Z; Geater S; Özgüroglu M; Zou W; Sandler A; Enquist I; Komatsubara K; Deng Y; Kuriki H; Wen X; McCleland M; Mocci S; Jassem J; Spigel DR. 2020. *N Engl J Med.* 383(14): 1328 - 1339. IF: 74,699.

Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. Paik PK; Felip E; Veillon R; Sakai H; Cortot AB; Garassino MC; Mazieres J; Viteri S; Senellart H; Van Meerbeeck J; Raskin J; Reinmuth N; Conte P; Kowalski D; Cho BC; Patel JD; Horn L; Griesinger F; Han JY; Kim YC; Chang GC; Tsai CL; Yang JC; Chen YM; Smit EF; van der Wekken AJ; Kato T; Juraeva D; Stroh C; Bruns R; Straub J; Johne A; Scheele J; Heymach JV; Le X. 2020. *N Engl J Med.* 383(10): 931 - 943. IF: 74,699.

Capmatinib in MET Exon 14-Mutated or MET-Amplified Non-Small-Cell Lung Cancer. Wolf, Juergen; Seto, Takashi; Han, Ji-Youn; Reguart, Noemi; Garon, Edward B.; Groen, Harry J. M.; Tan, Daniel S. W.; Hida, Toyoaki; de Jonge, Maja; Orlov, Sergey V.; Smit, Egbert F.; Souquet, Pierre-Jean; Vansteenkiste, Johan; Hochmair, Maximilian; Felip, Enriqueta; Nishio, Makoto; Thomas, Michael; Ohashi, Kadoaki; Toyozawa, Ryo; Overbeck, Tobias R.; de Marinis, Filippo; Kim, Tae-Min; Laack, Eckart; Robeva, Anna; Le Mouhaer, Sylvie; Waldron-Lynch, Maeve; Sankaran, Banu; Balbin, O. Alejandro; Cui, Xiaoming; Giovannini, Monica; Akimov, Mikhail; Heist, Rebecca S.; GEOMETRY Mono-1. 2020. *N Engl J Med.* 383(10): 944 - 957. IF: 74,699.

Efficacy of Selpercatinib in RET Fusion-Positive Non-Small-Cell Lung Cancer. Drilon, A.; Oxnard, G. R.; Tan, D. S. W.; Loong, H. H. F.; Johnson, M.; Gainor, J.; McCoach, C. E.; Gautschi, O.; Besse, B.; Cho, B. C.; Peled, N.; Weiss, J.; Kim, Y. -J.; Ohe, Y.; Nishio, M.; Park, K.; Patel, J.; Seto, T.; Sakamoto, T.; Rosen, E.; Shah, M. H.; Barlesi, F.; Cassier, P. A.; Bazhenova, L.; De Braud, F.; Garralda, E.; Velcheti, V.; Satouchi, M.; Ohashi, K.; Pennell, N. A.; Reckamp, K. L.; Dy, G. K.; Wolf, J.; Solomon, B.; Falchook, G.; Ebata, K.; Nguyen, M.; Nair, B.; Zhu, E. Y.; Yang, L.; Huang, X.; Olek, E.; Rothenberg, S. M.; Goto, K.; Subbiah, V. 2020. *N Engl J Med.* 383(9): 813 - 824. IF: 74,699.

Olaparib for Metastatic Castration-Resistant Prostate Cancer. de Bono J; Mateo J; Fizazi K; Saad F; Shore N; Sandhu S; Chi KN; Sartor O; Agarwal N; Olmos D; Thiery-Vuillemin A; Twardowski P; Mehra N; Goessl C; Kang J; Burgents J; Wu W; Kohlmann A; Adelman CA; Hussain M. 2020. *N Engl J Med.* 382(22): 2091 - 2102. IF: 74,699.

Pembrolizumab for Early Triple-Negative Breast Cancer. Schmid, Peter; Cortes, Javier; Pusztai, Lajos; McArthur, Heather; Kuemmel, Sherko; Bergh, Jonas; Denkert, Carsten; Park, Yeon Hee; Hui, Rina; Harbeck, Nadia; Takahashi, Masato; Foukakis, Theodoros; Fasching, Peter A.; Cardoso, Fatima; Untch, Michael; Jia, Liyi; Karantza, Vassiliki; Zhao, Jing; Aktan, Gursel; Dent, Rebecca; O'Shaughnessy, Joyce; Keynote-522 Investigators. 2020. *N Engl J Med.* 382(9): 810 - 821. IF: 74,699.

Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. Murthy RK; Loi S; Okines A; Paplomata E; Hamilton E; Hurvitz SA; Lin NU; Borges V; Abramson V; Anders C; Bedard PL; Oliveira M; Jakobsen E; Bachelot T; Shachar SS; Müller V; Braga S; Duhoux FP; Greil R; Cameron D; Carey LA; Curigliano G; Gelmon K; Hortobagyi G; Krop I; Loibl S; Pegram M; Slamon D; Palanca-Wessels MC; Walker L; Feng W; Winer EP. 2020. *N Engl J Med.* 382(7): 597 - 609. IF: 74,699.

Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer. Modi S; Saura C; Yamashita T; Park YH; Kim SB; Tamura K; Andre F; Iwata H; Ito Y; Tsurutani J; Sohn J; Denduluri N; Perrin C; Aogi K; Tokunaga E; Im SA; Lee KS; Hurvitz SA; Cortes J; Lee C; Chen S; Zhang L; Shahidi J; Yver A; Krop I; DESTINY-Breast01 Investigators. 2020. *N Engl J Med.* 382(7): 610 - 621. IF: 74,699.

Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial. Cortes J; Cescon DW; Rugo HS; Nowecki Z; Im SA; Yusof MM; Gallardo C; Lipatov O; Barrios CH; Holgado E; Iwata H; Masuda N; Otero MT; Gokmen E; Loi S; Guo Z; Zhao J; Aktan G; Karantza V; Schmid P; KEYNOTE-355 Investigators. 2020. *Lancet.* 396(10265): 1817 - 1828. IF: 60,392.

Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. Grosicki S; Simonova M; Spicka I; Pour L; Kriachok I; Gavriatopoulou M; Pylypenko H; Auner HW; Leleu X; Doronin V; Usenko G; Bahlis NJ; Hajek R; Benjamin R; Dolai TK; Sinha DK; Venner CP; Garg M; Gironella M; Jurczyszyn A; Robak P; Galli M; Wallington-Beddoe C; Radinoff A; Salogub G; Stevens DA; Basu S; Liberati AM; Quach H; Goranova-Marinova VS; Bila J; Katodritou E; Oliynyk H; Korenkova S; Kumar J; Jagannath S; Moreau P; Levy M; White D; Gatt ME; Facon T; Mateos MV; Cavo M; Reece D; Anderson LD Jr; Saint-Martin JR; Jeha J; Joshi AA; Chai Y; Li L; Peddagali V;

Arazy M; Shah J; Shacham S; Kauffman MG; Dimopoulos MA; Richardson PG; Delimpasi S. 2020. *Lancet*. 396(10262): 1563 - 1573. IF: 60,392.

Support systems to guide clinical decision-making in precision oncology: The Cancer Core Europe Molecular Tumor Board Portal. Tamborero D; Dienstmann R; Rachid MH; Boekel J; Baird R; Braña I; De Petris L; Yachnin J; Massard C; Opdam FL; Schlenk R; Vernieri C; Garralda E; Masucci M; Villalobos X; Chavarria E; Cancer Core Europe consortium; Calvo F; Fröhling S; Eggermont A; Apolone G; Voest EE; Caldas C; Tabernero J; Ernberg I; Rodon J; Lehtiö J. 2020. *Nat Med*. 26(7): 992 - 994. IF: 36,130.

BL-8040, a CXCR4 antagonist, in combination with pembrolizumab and chemotherapy for pancreatic cancer: the COMBAT trial. Bockorny B; Semenisty V; Macarulla T; Borazanci E; Wolpin BM; Stemmer SM; Golan T; Geva R; Borad MJ; Pedersen KS; Park JO; Ramirez RA; Abad DG; Feliu J; Muñoz A; Ponz-Sarvise M; Peled A; Lustig TM; Bohana-Kashtan O; Shaw SM; Sorani E; Chaney M; Kadosh S; Vainstein Haras A; Von Hoff DD; Hidalgo M. 2020. *Nat Med*. 26(6): 878 - 885. IF: 36, 130.

Caring for patients with cancer in the COVID-19 era. van de Haar J; Hoes LR; Coles CE; Seamon K; Fröhling S; Jäger D; Valenza F; de Braud F; De Petris L; Bergh J; Ernberg I; Besse B; Barlesi F; Garralda E; Piris-Giménez A; Baumann M; Apolone G; Soria JC; Tabernero J; Caldas C; Voest EE. 2020. *Nat Med*. 26(5): 665 - 671. IF: 36,130.

Durvalumab alone and durvalumab plus tremelimumab versus chemotherapy in previously untreated patients with unresectable, locally advanced or metastatic urothelial carcinoma (DANUBE): a randomised, open-label, multicentre, phase 3 trial. Powles T; van der Heijden MS; Castellano D; Galsky MD; Loriot Y; Petrylak DP; Ogawa O; Park SH; Lee JL; De Giorgi U; Bögemann M; Bamias A; Eigl BJ; Gurney H; Mukherjee SD; Fradet Y; Skoneczna I; Tsiatas M; Novikov A; Suárez C; Fay AP; Duran I; Necchi A; Wildsmith S; He P; Angra N; Gupta AK; Levin W; Bellmunt J; DANUBE study investigators. 2020. *Lancet Oncol*. 21(12): 1574 - 1588. IF: 33,752.

Neoadjuvant chemotherapy and nivolumab in resectable non-small-cell lung cancer (NADIM): an open-label, multicentre, single-arm, phase 2 trial. Provencio M; 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; Casarrubios M; Salas Antón C; Parra ER; Wistuba I; Calvo V; Laza-Briviesca R; Romero A; Massuti B; Cruz-Bermúdez A. 2020. *Lancet Oncol*. 21(11): 1413 - 1422. IF: 33,752.

Quality of life in patients with metastatic prostate cancer following treatment with cabazitaxel versus abiraterone or enzalutamide (CARD): an analysis of a randomised, multicentre, open-label, phase 4 study. Fizazi K; Kramer G; Eymard JC; Sternberg CN; de Bono J; Castellano D; Tombal B; Wülfing C; Liontos M; Carles J; Iacovelli R; Melichar B; Sverrisdóttir Á; Theodore C; Feyerabend S; Helissey C; Oudard S; Facchini G; Poole EM; Ozatilgan A; Geffriaud-Ricouard C; Bensfia S; de Wit R. 2020. *Lancet Oncol*. 21(11): 1513 - 1525. IF: 33,752.

A multivariable prognostic score to guide systemic therapy in early-stage HER2-positive breast cancer: a retrospective study with an external evaluation. Prat A; Guarneri V; Paré L; Griguolo G; Pascual T; Dieci MV; Chic N; González-Farré B; Frassoldati A; Sanfeliu E; Cejalvo JM; Muñoz M; Bisagni G; Brasó-Maristany F; Urso L; Vidal M; Brandes AA; Adamo B; Musolino A; Miglietta F; Conte B; Oliveira M; Saura C; Pernas S; Alarcón J; Llombart-Cussac A; Cortés J; Manso L; López R; Ciruelos E; Schettini F; Villagrasa P; Carey LA; Perou CM; Piacentini F; D'Amico R; Tagliafico E; Parker JS; Conte P. 2020. *Lancet Oncol*. 21(11): 1455 - 1464. IF: 33,752.

Trastuzumab emtansine plus atezolizumab versus trastuzumab emtansine plus placebo in previously treated, HER2-positive advanced breast cancer (KATE2): a phase 2, multicentre, randomised, double-blind trial. Emens LA; Esteva FJ; Beresford M; Saura C; De Laurentiis M; Kim SB; Im SA; Wang Y; Salgado R; Mani A; Shah J; Lambertini C; Liu H; de Haas SL; Patre M; Loi S. 2020. *Lancet Oncol*. 21(10): 1283 - 1295. IF: 33,752.

Dabrafenib plus trametinib in patients with BRAF(V600E)-mutated biliary tract cancer (ROAR): a phase 2, open-label, single-arm, multicentre basket trial. Subbiah, Vivek; Lassen, Ulrik; Elez, Elena; Italiano, Antoine; Curigliano, Giuseppe; Javle, Milind; de Braud, Filippo; Prager, Gerald W.; Greil, Richard; Stein, Alexander; Fasolo, Angelica; Schellens, Jan H. M.; Wen, Patrick Y.; Viele, Kert; Boran, Aislyn D.; Gasal, Eduard; Burgess, Paul; Ilankumaran, Palanichamy; Wainberg, Zev A. 2020. *Lancet Oncol*. 21(9): 1234 - 1243. IF: 33,752.

Ripretinib in patients with advanced gastrointestinal stromal tumours (INVICTUS): a double-blind, randomised, placebo-controlled, phase 3 trial. Blay JY; Serrano C; Heinrich MC; Zalcberg J; Bauer S; Gelderblom H; Schöffski P; Jones RL; Attia S; D'Amato G; Chi P; Reichardt P; Meade J; Shi K; Ruiz-Soto R; George S; von Mehren M. 2020. *Lancet Oncol*. 21(7): 923 - 934. IF: 33,752.

Avapritinib in advanced PDGFRA D842V-mutant gastrointestinal stromal tumour (NAVIGATOR): a multicentre, open-label, phase 1 trial. Heinrich MC; Jones RL; von Mehren M; Schöffski P; Serrano C; Kang YK; Cassier PA; Mir O; Eskens F; Tap WD; Rutkowski P; Chawla SP; Trent J; Tugnait M; Evans EK; Lauz T; Zhou T; Roche M; Wolf BB; Bauer S; George S. 2020. *Lancet Oncol*. 21(7): 935 - 946. IF: 33,752.

COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Garassino MC; Whisenant JG; Huang LC; Trama A; Torri V; Agustoni F; Baena J; Banna G; Berardi R; Bettini AC; Bria E; Brighenti M; Cadranel J; De Toma A; Chini C; Cortellini A; Felip E; Finocchiaro G; Garrido P; Genova C; Giusti R; Gregorc V; Grossi F; Grosso F; Intagliata S; La Verde N; Liu SV; Mazieres J; Mercadante E; Michielin O; Minuti G; Moro-Sibilot D; Pasello G; Passaro A; Scotti V; Solli P; Stroppa E; Tiseo M; Viscardi G; Voltolini L; Wu YL; Zai S; Pancaldi V; Dingemans AM; Van Meerbeeck J; Barlesi F; Wakelee H; Peters S; Horn L; TERAVOLT investigators. 2020. *Lancet Oncol*. 21(7): 914 - 922. IF: 33,752.

Ivosidenib in IDH1-mutant, chemotherapy-refractory cholangiocarcinoma (ClarIDHy): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study. Abou-Alfa GK; Macarulla T; Javle MM; Kelley RK; Lubner SJ; Adeva J; Cleary JM; Catenacci DV; Borad MJ; Bridgewater J; Harris WP; Murphy AG; Oh DY; Whisenant J; Lowery MA; Goyal L; Shroff RT; El-Khoueiry AB; Fan B; Wu B; Chamberlain CX; Jiang L; Gliser C; Pandya SS; Valle JW; Zhu AX. 2020. *Lancet Oncol*. 21(6): 796 - 807. IF: 33,752.

Rucaparib for patients with platinum-sensitive, recurrent ovarian carcinoma (ARIEL3): post-progression outcomes and updated safety results from a randomised, placebo-controlled, phase 3 trial. Ledermann JA; 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; O'Malley DM; Armstrong DK; Banerjee S; García-Donas J; Swisher EM; Cameron T; Maloney L; Goble S; Coleman RL. 2020. *Lancet Oncol*. 21(5): 710 - 722. IF: 33,752.

Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. Swain

SM; Miles D; Kim SB; Im YH; Im SA; Semiglazov V; Ciruelos E; Schneeweiss A; Loi S; Monturus E; Clark E; Knott A; Restuccia E; Benyunes MC; Cortés J; CLEOPATRA study group. 2020. *Lancet Oncol.* 21(4): 519 - 530. IF: 33,752.

Patient-reported outcomes following pembrolizumab or placebo plus pemetrexed and platinum in patients with previously untreated, metastatic, non-squamous non-small-cell lung cancer (KEYNOTE-189): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Garassino MC; Gadgeel S; Esteban E; Felip E; Speranza G; Domine M; Hochmair MJ; Powell S; Cheng SY; Bischoff HG; Peled N; Reck M; Hui R; Garon EB; Boyer M; Wei Z; Burke T; Pietanza MC; Rodríguez-Abreu D. 2020. *Lancet Oncol.* 21(3): 387 - 397. IF: 33,752.

Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial. Mateo J; Porta N; Bianchini D; McGovern U; Elliott T; Jones R; Syndikus I; Ralph C; Jain S; Varughese M; Parikh O; Crabb S; Robinson A; McLaren D; Birtle A; Tanguay J; Miranda S; Figueiredo I; Seed G; Bertan C; Flohr P; Ebbs B; Rescigno P; Fowler G; Ferreira A; Riisnaes R; Pereira R; Curcean A; Chandler R; Clarke M; Gurel B; Crespo M; Nava Rodrigues D; Sandhu S; Espinasse A; Chatfield P; Tunariu N; Yuan W; Hall E; Carreira S; de Bono JS. 2020. *Lancet Oncol.* 21(1): 162 - 174. IF: 33,752.

Ribociclib plus letrozole versus chemotherapy for postmenopausal women with hormone receptor-positive, HER2-negative, luminal B breast cancer (CORALLEEN): an open-label, multicentre, randomised, phase 2 trial. Prat A; Saura C; Pascual T; Hernando C; Muñoz M; Paré L; González Farré B; Fernández PL; Galván P; Chic N; González Farré X; Oliveira M; Gil-Gil M; Arumi M; Ferrer N; Montaño A; Izarzugaza Y; Llombart-Cussac A; Bratos R; González Santiago S; Martínez E; Hoyos S; Rojas B; Virizuela JA; Ortega V; López R; Céliz P; Ciruelos E; Villagrasa P; Gavilá J. 2020. *Lancet Oncol.* 21(1): 33 - 43. IF: 33,752.

First-in-Human Phase I Study of Iadademstat (ORY-1001): A First-in-Class Lysine-Specific Histone Demethylase 1A Inhibitor, in Relapsed or Refractory Acute Myeloid *Leukemia.* Salamero O; Montesinos P; Willekens C; Pérez-Simón JA; Pigneux A; Récher C; Popat R; Carpio C; Molinero C; Mascaró C; Vila J; Arévalo MI; Maes T; Buesa C; Bosch F; Somervaille TCP. 2020. *J Clin Oncol.* 38(36): 4260 - 4273. IF: 32,956.

Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2-, Node-Positive, High-Risk, Early Breast Cancer (monarchE). Johnston SRD; Harbeck N; Hegg R; Toi M; Martin M; Shao ZM; Zhang QY; Martinez Rodriguez JL; Campone M; Hamilton E; Sohn J; Guarneri V; Okada M; Boyle F; Neven P; Cortés J; Huober J; Wardley A; Tolaney SM; Cicin I; Smith IC; Frenzel M; Headley D; Wei R; San Antonio B; Hulstijn M; Cox J; O'Shaughnessy J; Rastogi P; monarchE Committee Members and Investigators. 2020. *J Clin Oncol.* 38(34): 3987 - 3998. IF: 32,956.

Brigatinib Versus Crizotinib in Advanced ALK Inhibitor-Naive ALK-Positive Non-Small Cell Lung Cancer: Second Interim Analysis of the Phase III ALTA-1L Trial. Camidge DR; Kim HR; Ahn MJ; Yang JCH; Han JY; Hochmair MJ; Lee KH; Delmonte A; García Campelo MR; Kim DW; Griesinger F; Felip E; Califano R; Spira A; Gettinger SN; Tiseo M; Lin HM; Gupta N; Hanley MJ; Ni Q; Zhang P; Popat S. 2020. *J Clin Oncol.* 38(31): 3592 - 3603. IF: 32,956.

Efficacy of Maintenance Olaparib for Patients With Newly Diagnosed Advanced Ovarian Cancer With a BRCA Mutation: Subgroup Analysis Findings From the SOLO1 Trial. DiSilvestro P; Colombo N; Scambia G; Kim BG; Oaknin A; Friedlander M; Lisyanskaya A; Floquet A; Leary A; Sonke GS; Gourley C; Banerjee S; Oza A; González-Martín A; Aghajanian CA; Bradley WH; Mathews CA; Liu J; Lowe ES; Bloomfield R; Moore KN. 2020. *J Clin Oncol.* 38(30): 3528 - 3537. IF: 32,956.

Patient-Centered Outcomes in ARIEL3, a Phase III, Randomized, Placebo-Controlled Trial of Rucaparib Maintenance Treatment in Patients With Recurrent Ovarian Carcinoma. 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; O'Malley DM; Armstrong DK; Banerjee S; García-Donas J; Swisher EM; Cella D; Meunier J; Goble S; Cameron T; Maloney L; Mörk AC; Bedel J; Ledermann JA; Coleman RL. 2020. *J Clin Oncol.* 38(30): 3494 - 3505. IF: 32,956.

Neratinib Plus Capecitabine Versus Lapatinib Plus Capecitabine in HER2-Positive Metastatic Breast Cancer Previously Treated With ≥ 2 HER2-Directed Regimens: Phase III NALA Trial. Saura C; Oliveira M; Feng YH; Dai MS; Chen SW; Hurvitz SA; Kim SB; Moy B; Delaloge S; Gradishar W; Masuda N; Palacova M; Trudeau ME; Mattson J; Yap YS; Hou MF; De Laurentiis M; Yeh YM; Chang HT; Yau T; Wildiers H; Haley B; Fagnani D; Lu YS; Crown J; Lin J; Takahashi M; Takano T; Yamaguchi M; Fujii T; Yao B; Bebchuk J; Keyvanjah K; Bryce R; Brufsky A; NALA Investigators. 2020. *J Clin Oncol.* 38(27): 3138 - 3149. IF: 32,956 .

Randomized Phase III Trial of Pegvorhyaluronidase Alfa With Nab-Paclitaxel Plus Gemcitabine for Patients With Hyaluronan-High Metastatic Pancreatic Adenocarcinoma. Van Cutsem E; Tempero MA; Sigal D; Oh DY; Fazio N; Macarulla T; Hitre E; Hammel P; Hendifar AE; Bates SE; Li CP; Hingorani SR; de la Fouchardiere C; Kasi A; Heinemann V; Maraveyas A; Bahary N; Layos L; Sahai V; Zheng L; Lacy J; Park JO; Portales F; Oberstein P; Wu W; Chondros D; Bullock AJ; HALO 109-301 Investigators. 2020. *J Clin Oncol.* 38(27): 3185 - 3194. IF: 32,956.

Lenvatinib Plus Pembrolizumab in Patients With Advanced Endometrial Cancer. Makker V; Taylor MH; Aghajanian C; Oaknin A; Mier J; Cohn AL; Romeo M; Bratos R; Brose MS; DiSimone C; Messing M; Stepan DE; Dutcus CE; Wu J; Schmidt EV; Orlowski R; Sachdev P; Shumaker R; Casado Herraez A. 2020. *J Clin Oncol.* 38(26): 2981 - 2992. IF: 32,956.

Pregnancy After Breast Cancer in Patients With Germline BRCA Mutations. Lambertini M; Ameye L; Hamy AS; Zingarello A; Poorvu PD; Carrasco E; Grinshpun A; Han S; Rousset-Jablonski C; Ferrari A; Paluch-Shimon S; Cortesi L; Senechal C; Miolo G; Pogoda K; Pérez-Fidalgo JA; De Marchis L; Ponzone R; Livraghi L; Estevez-Diz MDP; Villarreal-Garza C; Dieci MV; Clatot F; Berlière M; Graffeo R; Teixeira L; Córdoba O; Sonnenblick A; Luna Pais H; Ignatiadis M; Paesmans M; Partridge AH; Caron O; Saule C; Del Mastro L; Peccatori FA; Azim HA. 2020. *J Clin Oncol.* 38(26): 3012 - 3023. IF: 32,956.

PD-1 Blockade in Anaplastic Thyroid Carcinoma. Capdevila J; Wirth LJ; Ernst T; Ponce Aix S; Lin CC; Ramlau R; Butler MO; Delord JP; Gelderblom H; Ascierto PA; Fasolo A; Führer D; Hütter-Krönke ML; Forde PM; Wrona A; Santoro A; Sadow PM; Szpakowski S; Wu H; Bostel G; Faris J; Cameron S; Varga A; Taylor M. 2020. *J Clin Oncol.* 38(23): 2620 - 2627. IF: 32,956.

Intracranial Efficacy and Survival With Tucatinib Plus Trastuzumab and Capecitabine for Previously Treated HER2-Positive Breast Cancer With Brain Metastases in the HER2CLIMB Trial. Lin NU; Borges V; Anders C; Murthy RK; Paplomata E; Hamilton E; Hurvitz S; Loi S; Okines A; Abramson V; Bedard PL; Oliveira M; Mueller V; Zelnak A; DiGiovanna MP; Bachelot T; Chien AJ; O'Regan R; Wardley A; Conlin A; Cameron D; Carey L; Curigliano G; Gelmon K; Loibl S; Mayor J; McGoldrick

S; An X; Winer EP. 2020. *J Clin Oncol.* 38(23): 2610 - 2619. IF: 32,956.

Pembrolizumab or Placebo Plus Etoposide and Platinum as First-Line Therapy for Extensive-Stage Small-Cell Lung Cancer: Randomized, Double-Blind, Phase III KEYNOTE-604 Study. Rudin CM; Awad MM; Navarro A; Gottfried M; Peters S; Csoszi T; Cheema PK; Rodriguez-Abreu D; Wollner M; Yang JC; Mazieres J; Orlandi FJ; Luft A; Gümüs M; Kato T; Kalemkerian GP; Luo Y; Ebiana V; Pietanza MC; Kim HR; KEYNOTE-604 Investigators. 2020. *J Clin Oncol.* 38(21): 2369 - 2379. IF: 32 ,956.

HER2-Low Breast Cancer: Pathological and Clinical Landscape. Tarantino P; Hamilton E; Tolaney SM; Cortes J; Morganti S; Ferraro E; Marra A; Viale G; Trapani D; Cardoso F; Penault-Llorca F; Viale G; Andrè F; Curigliano G. 2020. *J Clin Oncol.* 38(17): 1951 - 1962. IF: 32,956.

Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non-Small-Cell Lung Cancer. Gadgeel S; Rodríguez-Abreu D; Speranza G; Esteban E; Felip E; Dómine M; Hui R; Hochmair MJ; Clingan P; Powell SF; Cheng SY; Bischoff HG; Peled N; Grossi F; Jennens RR; Reck M; Garon EB; Novello S; Rubio-Viqueira B; Boyer M; Kurata T; Gray JE; Yang J; Bas T; Pietanza MC; Garassino MC. 2020. *J Clin Oncol.* 38(14): 1505 - 1517. IF: 32,956.

Geographic and Ethnic Heterogeneity of Germline BRCA1 or BRCA2 Mutation Prevalence Among Patients With Metastatic Pancreatic Cancer Screened for Entry Into the POLO Trial. Golan, Talia; Kindler, Hedy L.; Park, Joon Oh; Reni, Michele; Macarulla, Teresa; Hammel, Pascal; Van Cutsem, Eric; Arnold, Dirk; Hochhauser, Daniel; McGuinness, David; Locker, Gershon Y.; Goranova, Teodora; Schatz, Philipp; Liu, Yu-Zhen; Hall, Michael J. 2020. *J Clin Oncol.* 38(13): 1442 - 1454. IF: 32,956.

Standard Anthracycline Based Versus Docetaxel-Capecitabine in Early High Clinical and/or Genomic Risk Breast Cancer in the EORTC 10041/BIG 3-04 MINDACT Phase III Trial. Delaloge S; Piccart M; Rutgers E; Litière S; van 't Veer LJ; van den Berkmortel F; Brain E; Dudek-Peric A; Gil-Gil M; Gomez P; Hilbers FS; Khalil Z; Knox S; Kuemmel S; Kunz G; Lesur A; Pierga JY; Ravdin P; Rubio IT; Saghatchian M; Smilde TJ; Thompson AM; Viale G; Zoppoli G; Vuylsteke P; Tryfonidis K; Poncet C; Bogaerts J; Cardoso F; MINDACT investigators and the TRANSBIG Consortium. 2020. *J Clin Oncol.* 38(11): 1186 - 1197. IF: 32,956.

Cancer Risks Associated With Germline PALB2 Pathogenic Variants: An International Study of 524 Families. Yang X; Leslie G; Doroszuk A; Schneider S; Allen J; Decker B; Dunning AM; Redman J; Scarth J; Plaskocinska I; Luccarini C; Shah M; Pooley K; Dorling L; Lee A; Adank MA; Adlard J; Aittomäki K; Andrulis IL; Ang P; Barwell J; Bernstein JL; Bobolis K; Borg Å; Blomqvist C; Claes KBM; Concannon P; Cuggia A; Culver JO; Damiola F; de Pauw A; Diez O; Dolinsky JS; Domchek SM; Engel C; Evans DG; Fostira F; Garber J; Golmard L; Goode EL; Gruber SB; Hahnen E; Hake C; Heikkinen T; Hurley JE; Janavicius R; Kleibl Z; Kleiblova P; Konstantopoulou I; Kvist A; Laduca H; Lee ASG; Lesueur F; Maher ER; Mannermaa A; Manoukian S; McFarland R; McKinnon W; Meindl A; Metcalfe K; Mohd Taib NA; Moilanen J; Nathanson KL; Neuhausen S; Ng PS; Nguyen-Dumont T; Nielsen SM; Obermair F; Offit K; Olopade OI; Ottini L; Penkert J; Pylkäs K; Radice P; Ramus SJ; Rudaitis V; Side L; Silva-Smith R; Silvestri V; Skytte AB; Slavin T; Soukupova J; Tondini C; Trainer AH; Unzeitig G; Usha L; van Overeem Hansen T; Whitworth J; Wood M; Yip CH; Yoon SY; Yussuf A; Zogopoulos G; Goldgar D; Hopper JL; Chenevix-Trench G; Pharoah P; George SHL; Balmaña J; et al.... 2020. *J Clin Oncol.* 38(7): 674 - 685. IF: 32,956.

Capivasertib Plus Paclitaxel Versus Placebo Plus Paclitaxel As First-Line Therapy for Metastatic Triple-Negative Breast Cancer: The PAKT Trial. Schmid, Peter; Abraham, Jacinta; Chan, Stephen; Wheatley, Duncan; Brunt, Adrian Murray; Nemsadze, Gia; Baird, Richard D.; Park, Yeon Hee; Hall, Peter S.; Perren, Timothy; Stein, Robert C.; Mangel, Laszlo; Ferrero, Jean-Marc; Phillips, Melissa; Conibear, John; Cortes, Javier; Foxley, Andrew; de Bruin, Elza C.; McEwen, Robert; Stetson, Daniel; Dougherty, Brian; Sarker, Shah-Jalal; Prendergast, Aaron; McLaughlin-Callan, Max; Burgess, Matthew; Lawrence, Cheryl; Cartwright, Hayley; Mousa, Kelly; Turner, Nicholas C. 2020. *J Clin Oncol.* 10;38(5):423-433. IF: 32,956.

Phase II Open-Label Study of Pembrolizumab in Treatment-Refractory, Microsatellite Instability-High/Mismatch Repair-Deficient Metastatic Colorectal Cancer: KEYNOTE-164. Le DT; Kim TW; Van Cutsem E; Geva R; Jäger D; Hara H; Burge M; O'Neil B; Kavan P; Yoshino T; Guimbaud R; Taniguchi H; Elez E; Al-Batran SE; Boland PM; Crocenzi T; Atreya CE; Cui Y; Dai T; Marinello P; Diaz LA; André T. 2020. *J Clin Oncol.* 38(1): 11 - 19. IF: 32,956.

RBMS1 Suppresses Colon Cancer Metastasis through Targeted Stabilization of Its mRNA Regulon. Yu J; Navickas A; Asgharian H; Culbertson B; Fish L; Garcia K; Olegario JP; Dermit M; Dodel M; Hanisch B; Luo Y; Weinberg EM; Dienstmann R; Warren RS; Mardakheh FK; Goodarzi H. 2020. *Cancer Discov.* 10(9): 1410 - 1423. IF: 29,497.

MYC Instructs and Maintains Pancreatic Adenocarcinoma Phenotype. Sodir NM; Kortlever RM; Barthet VJA; Campos T; Pellegrinet L; Kupczak S; Anastasiou P; Brown Swigart L; Soucek L; Arends MJ; Littlewood TD; Evan GI. 2020. *Cancer Discov.* 10(4): 588 - 607. IF: 29,497.

Efficacy and Determinants of Response to HER Kinase Inhibition in HER2-Mutant Metastatic Breast Cancer. Smyth LM; Piha-Paul SA; Won HH; Schram AM; Saura C; Loi S; Lu J; Shapiro GI; Juric D; Mayer IA; Arteaga CL; de la Fuente MI; Brufksy AM; Spanggaard I; Mau-Sorensen M; Arnedos M; Moreno V; Boni V; Sohn J; Schwartzberg LS; Gonzalez-Farre X; Cervantes A; Bidard FC; Gorelick AN; Lanman RB; Nagy RJ; Ulaner GA; Chandarlapaty S; Jhaveri K; Gavrila EI; Zimel C; Selcuklu SD; Melcer M; Samoila A; Cai Y; Scaltriti M; Mann G; Xu F; Eli LD; Dujka M; Lalani AS; Bryce R; Baselga J; Taylor BS; Solit DB; Meric-Bernstam F; Hyman DM. 2020. *Cancer Discov.* 10(2): 198 - 213. IF: 29,497.

Clinical portrait of the SARS-CoV-2 epidemic in European cancer patients. Pinato DJ; Zambelli A; Aguilar-Company J; Bower M; Sng C; Salazar R; Bertuzzi A; Brunet J; Mesia R; Segui E; Biello F; Generali D; Grisanti S; Rizzo G; Libertini M; Maconi A; Harbeck N; Vincenzi B; Bertulli R; Ottaviani D; Carbo A; Bruna R; Benafif S; Marrari A; Wuerstlein R; Carmona-Garcia MC; Chopra N; Tondini C; Mirallas O; Tovazzi V; Betti M; Provenzano S; Fotia V; Cruz CA; Dalla Pria A; D'Avanzo F; Evans JS; Saoudi-Gonzalez N; Felip E; Galazi M; Garcia-Fructuoso I; Lee AJX; Newsom-Davis T; Patriarca A; Garcia-Illescas D; Reyes R; Dileo P; Sharkey R; Wong YNS; Ferrante D; Marco-Hernandez J; Sureda A; Maluquer C; Ruiz-Camps I; Gaidano G; Rimassa L; Chiudinelli L; Izuzquiza M; Cabirta A; Franchi M; Santoro A; Prat A; Tabernero J; Gennari A. 2020. *Cancer Discov.* 10(10): 1465 - 1474. IF: 29,497.

Recognizing hypoxia in phaeochromocytomas and paragangliomas. Dahia PLM; Toledo RA. 2020. *Nat Rev Endocrinol.* 16(4): 191 - 192. IF: 28,800.

CTCF is dispensable for immune cell transdifferentiation but facilitates an acute inflammatory response. Stik G; Vidal E; Barrero M; Cuartero S; Vila-Casadesús M; Mendieta-Esteban J; Tian TV; Choi J; Berenguer C; Abad A; Borsari B; le Dily F; Cramer P; Marti-Renom MA; Stadhouders R; Graf T. 2020. *Nat Genet.* 52(7): 655 - 661. IF: 27,603.

Genome-wide association study identifies 32 novel breast cancer susceptibility loci from overall and

subtype-specific analyses. Zhang H; Ahearn TU; Lecarpentier J; Barnes D; Beesley J; Qi G; Jiang X; O'Mara TA; Zhao N; Bolla MK; Dunning AM; Dennis J; Wang Q; Ful ZA; Aittomäki K; Andrulis IL; Anton-Culver H; Arndt V; Aronson KJ; Arun BK; Auer PL; Azzollini J; Barrowdale D; Becher H; Beckmann MW; Behrens S; Benitez J; Bermisheva M; Bialkowska K; Blanco A; Blomqvist C; Bogdanova NV; Bojesen SE; Bonanni B; Bondavalli D; Borg A; Brauch H; Brenner H; Briceno I; Broeks A; Brucker SY; Brüning T; Burwinkel B; Buys SS; Byers H; Caldés T; Caligo MA; Calvello M; Campa D; Castelao JE; Chang-Claude J; Chanock SJ; Christiaens M; Christiansen H; Chung WK; Claes KBM; Clarke CL; Cornelissen S; Couch FJ; Cox A; Cross SS; Czene K; Daly MB; Devilee P; Diez O; et al....2020. *Nat Genet.* 52(6): 572 - 581. IF: 27,603.

A harmonized meta-knowledgebase of clinical interpretations of somatic genomic variants in cancer. Wagner AH; Walsh B; Mayfield G; Tamborero D; Sonkin D; Krysiak K; Deu-Pons J; Duren RP; Gao J; McMurry J; Patterson S; Del Vecchio Fitz C; Pitel BA; Sezerman OU; Ellrott K; Warner JL; Rieke DT; Aittokallio T; Cerami E; Ritter DI; Schriml LM; Freimuth RR; Haendel M; Raca G; Madhavan S; Baudis M; Beckmann JS; Dienstmann R; Chakravarty D; Li XS; Mockus S; Elemento O; Schultz N; Lopez-Bigas N; Lawler M; Goecks J; Griffith M; Griffith OL; Margolin AA; Variant Interpretation for Cancer Consortium. 2020. *Nat Genet.* 52(4): 448 - 457. IF: 27,603.

Fine-mapping of 150 breast cancer risk regions identifies 191 likely target genes. Fachal L; Aschard H; Beesley J; Barnes DR; Allen J; Kar S; Pooley KA; Dennis J; Michailidou K; Turman C; Soucy P; Lemaçon A; Lush M; Tyrer JP; Ghoussaini M; Moradi Marjaneh M; Jiang X; Agata S; Aittomäki K; Alonso MR; Andrulis IL; Anton-Culver H; Antonenkova NN; Arason A; Arndt V; Aronson KJ; Arun BK; Auber B; Auer PL; Azzollini J; Balmaña J; et al.... 2020. *Nat Genet.* 52(1): 56 - 73. IF: 27,603.

The Effective Targeting of KRAS G12C Elusiveness. Elez E; Tabernero J. 2020. *Cancer Cell.* 38(6): 785 - 787. IF: 26,602.

Metabolic Imaging Detects Resistance to PI3Ka Inhibition Mediated by Persistent FOXM1 Expression in ER(+) Breast Cancer. Ros S; Wright AJ; D'Santos P; Hu DE; Hesketh RL; Lubling Y; Georgopoulou D; Lerda G; Couturier DL; Razavi P; Pelossof R; Batra AS; Mannion E; Lewis DY; Martin A; Baird RD; Oliveira M; de Boo LW; Linn SC; Scaltriti M; Rueda OM; Bruna A; Caldas C; Brindle KM. 2020. *Cancer Cell.* 38(4): 516 - 516. IF: 26,602.

Safety and efficacy of nazartinib (EGF816) in adults with EGFR-mutant non-small-cell lung carcinoma: a multicentre, open-label, phase 1 study. Tan DS; Leighl NB; Riely GJ; Yang JC; Sequist LV; Wolf J; Seto T; Felip E; Aix SP; Jonnaert M; Pan C; Tan EY; Ko J; Moody SE; Kim DW. 2020. *Lancet Respir Med.* 8(6): 561 - 572. IF: 25,094.

Efficacy and Safety of Pembrolizumab or Pembrolizumab Plus Chemotherapy vs Chemotherapy Alone for Patients With First-line, Advanced Gastric Cancer: The KEYNOTE-062 Phase 3 Randomized Clinical Trial. Shitara K; Van Cutsem E; Bang YJ; Fuchs C; Wyrwicz L; Lee KW; Kudaba I; Garrido M; Chung HC; Lee J; Castro HR; Mansoor W; Braghiroli MI; Karaseva N; Caglevic C; Villanueva L; Goekkurt E; Satake H; Enzinger P; Alsina M; Benson A; Chao J; Ko AH; Wainberg ZA; Kher U; Shah S; Kang SP; Tabernero J. 2020. *JAMA Oncol.* 6(10): 1571 - 1580. IF: 24,799.

Characterization of the Cancer Spectrum in Men With Germline BRCA1 and BRCA2 Pathogenic Variants: Results From the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA). Silvestri V; Leslie G; Barnes DR; and the CIMBA Group; Agnarsson BA; Aittomäki K; Alducci E; Andrulis IL; Barkardottir RB; Barroso A; Barrowdale D; Benitez J; Bonanni B; Borg A; Buys SS; Caldés T; Caligo MA; Capalbo C; Campbell I; Chung WK; Claes KBM; Colonna SV; Cortesi L; Couch FJ; de la Hoya M; Diez O; et al.... 2020. *JAMA Oncol.* 6(8): 1218 - 1230. IF: 24,799.

Efficacy and Safety of Trastuzumab Emtansine Plus Capecitabine vs Trastuzumab Emtansine Alone in Patients With Previously Treated ERBB2 (HER2)-Positive Metastatic Breast Cancer: A Phase 1 and Randomized Phase 2 Trial. Cortés J; Diéras V; Lorenzen S; Montemurro F; Riera-Knorrenschild J; Thuss-Patience P; Allegrini G; De Laurentiis M; Lohrisch C; Oravcová E; Perez-Garcia JM; Ricci F; Sakaeva D; Serpanchy R; Šufliarský J; Vidal M; Irahara N; Wohlfarth C; Aout M; Gelmon K. 2020. *JAMA Oncol.* 6(8): 1203 - 1209. IF: 24,799.

Efficacy and Safety of Trifluridine/Tipiracil Treatment in Patients With Metastatic Gastric Cancer Who Had Undergone Gastrectomy Subgroup Analyses of a Randomized Clinical Trial.Ilson DH; Tabernero J; Prokharau A; Arkenau HT; Ghidini M; Fujitani K; Van Cutsem E; Thuss-Patience P; Beretta GD; Mansoor W; Zhavrid E; Alsina M; George B; Catenacci D; McGuigan S; Makris L; Doi T; Shitara K. 2020. *JAMA Oncol.* 6(1). IF: 24,799.

Clinical Activity and Safety of the Anti-Programmed Death 1 Monoclonal Antibody Dostarlimab for Patients With Recurrent or Advanced Mismatch Repair-Deficient Endometrial Cancer: A Nonrandomized Phase 1 Clinical Trial. Oaknin A; Tinker AV; Gilbert L; Samouëlian V; Mathews C; Brown J; Barretina-Ginesta MP; Moreno V; Gravina A; Abdeddaim C; Banerjee S; Guo W; Danaee H; Im E; Sabatier R. 2020. *JAMA Oncol.* 6(11): 1-7. IF: 24,799.

ESMO recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer. Miller RE; Leary A; Scott CL; Serra V; Lord CJ; Bowtell D; Chang DK; Garsed DW; Jonkers J; Ledermann JA; Nik-Zainal S; Ray-Coquard I; Shah SP; Matias-Guiu X; Swisher EM; Yates LR. 2020. *Ann Oncol.* 31(12): 1606 - 1622. IF: 18,274.

5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). Cardoso F; Paluch-Shimon S; Senkus E; Curigliano G; Aapro MS; André F; Barrios CH; Bergh J; Bhattacharyya GS; Biganzoli L; Boyle F; Cardoso MJ; Carey LA; Cortés J; El Saghir NS; Elzayat M; Eniu A; Fallowfield L; Francis PA; Gelmon K; Gligorov J; Haidinger R; Harbeck N; Hu X; Kaufman B; Kaur R; Kiely BE; Kim SB; Lin NU; Mertz SA; Neciosup S; Offersen BV; Ohno S; Pagani O; Prat A; Penault-Llorca F; Rugo HS; Sledge GW; Thomssen C; Vorobiof DA; Wiseman T; Xu B; Norton L; Costa A; Winer EP. 2020. *Ann Oncol.* 31(12): 1623 - 1649. IF: 18,274.

Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group. Mosele F; Remon J; Mateo J; Westphalen CB; Barlesi F; Lolkema MP; Normanno N; Scarpa A; Robson M; Meric-Bernstam F; Wagle N; Stenzinger A; Bonastre J; Bayle A; Michiels S; Bièche I; Rouleau E; Jezdic S; Douillard JY; Reis-Filho JS; Dienstmann R; André F. 2020. *Ann Oncol.* 31(11): 1491 - 1505. IF: 18,274.

Diagnosis and management of tropomyosin receptor kinase (TRK) fusion sarcomas: expert recommendations from the World Sarcoma Network. Demetri GD; Antonescu CR; Bjerkehagen B; Bovée JVMG; Boye K; Chacón M; Dei Tos AP; Desai J; Fletcher JA; Gelderblom H; George S; Gronchi A; Haas RL; Hindi N; Hohenberger P; Joensuu H; Jones RL; Judson I; Kang YK; Kawai A; Lazar AJ; Le Cesne A; Maestro R; Maki RG; Martín J; Patel S; Penault-Llorca F; Raut CP; Rutkowski P; Safwat A; Sbaraglia M; Schaefer IM; Shen L; Serrano C; Schöffski P; Stacchiotti S; Hall KS; Tap WD;

Thomas DM; Trent J; Valverde C; van der Graaf WTA; von Mehren M; Wagner A; Wardelmann E; Naito Y; Zalcberg J; Blay JY. 2020. *Ann Oncol.* 31(11): 1506 - 1517. IF: 18,274.

Fusobacterium nucleatum persistence and risk of recurrence after preoperative treatment in locally advanced rectal cancer. Serna G; Ruiz-Pace F; Hernando J; Alonso L; Fasani R; Landolfi S; Comas R; Jimenez J; Elez E; Bullman S; Meyerson M; Tabernero J; Capdevila J; Dienstmann R; Nuciforo P. 2020. *Ann Oncol.* 31(10): 1366 - 1375. IF: 18,274.

Phase I, first-in-human study of futibatinib, a highly selective, irreversible FGFR1-4 inhibitor in patients with advanced solid tumors. Bahleda R; Meric-Bernstam F; Goyal L; Tran B; He Y; Yamamiya I; Benhadji KA; Matos I; Arkenau HT. 2020. *Ann Oncol.* 31(10): 1405 - 1412. IF: 18,274.

Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. Curigliano G; Banerjee S; Cervantes A; Garassino M; Garrido P; Girard N; Haanen J; Jordan K; Lordick F; Machiels JP; Michielin O; Peters S; Tabernero J; Douillard JY; Pentheroudakis G; all Voting Panel members. 2020. *Ann Oncol.* 31(10): 1320 - 1335. IF: 18,274.

Clinical development of therapies targeting TGFß: current knowledge and future perspectives. Ciardiello D; Elez E; Tabernero J; Seoane J. 2020. *Ann Oncol.* 31(10): 1336 - 1349. IF: 18,274.

Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Argiles G; Tabernero J; Labianca R; Hochhauser D; Salazar R; Iveson T; Laurent-Puig P; Quirke P; Yoshino T; Taieb J; Martinelli E; Arnold D; ESMO Guidelines Committee. 2020. *Ann Oncol.* 31(10): 1291 - 1305. IF: 18,274.

Trifluridine/tipiracil plus bevacizumab in patients with untreated metastatic colorectal cancer ineligible for intensive therapy: the randomized 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; Kanehisa A; Egorov A; Aubel P; Amellal N; Moiseenko V. 2020. *Ann Oncol.* 31(9): 1160 - 1168. IF: 18,274.

JSCO-ESMO-ASCO-JSMO-TOS: international expert consensus recommendations for tumour-agnostic treatments in patients with solid tumours with microsatellite instability or NTRK fusions. Yoshino T; Pentheroudakis G; Mishima S; Overman MJ; Yeh KH; Baba E; Naito Y; Calvo F; Saxena A; Chen LT; Takeda M; Cervantes A; Taniguchi H; Yoshida K; Kodera Y; Kitagawa Y; Tabernero J; Burris H; Douillard JY. 2020. *Ann Oncol.* 31(7): 861 - 872. IF: 18,274.

Molecular correlates of response to capmatinib in advanced non-small-cell lung cancer: clinical and biomarker results from a phase I trial. Schuler M; Berardi R; Lim WT; de Jonge M; Bauer TM; Azaro A; Gottfried M; Han JY; Lee DH; Wollner M; Hong DS; Vogel A; Delmonte A; Akimov M; Ghebremariam S; Cui X; Nwana N; Giovannini M; Kim TM. 2020. *Ann Oncol.* 31(6): 789 - 797. IF: 18,274.

Phase I study of CC-90010, a reversible, oral BET inhibitor in patients with advanced solid tumors and relapsed/refractory non-Hodgkin's lymphoma. Moreno V; Sepulveda JM; Vieito M; Hernández-Guerrero T; Doger B; Saavedra O; Ferrero O; Sarmiento R; Arias M; De Alvaro J; Di Martino J; Zuraek M; Sanchez-Pérez T; Aronchik I; Filvaroff EH; Lamba M; Hanna B; Nikolova Z; Brana I. 2020. *Ann Oncol.* 31(6): 780 - 788. IF: 18,274.

Pembrolizumab plus chemotherapy as neoadjuvant treatment of high-risk, early-stage triple-negative breast cancer: results from the phase 1b open-label, multicohort KEYNOTE-173 study. Schmid P; Salgado R; Park YH; Muñoz-Couselo E; Kim SB; Sohn J; Im SA; Foukakis T; Kuemmel S; Dent R; Yin L; Wang A; Tryfonidis K; Karantza V; Cortés J; Loi S. 2020. *Ann Oncol.* 31(5): 569 - 581. IF: 18,274.

Antitumor activity of ipatasertib combined with chemotherapy: results from a phase Ib study in solid tumors. Isakoff SJ; Tabernero J; Molife LR; Soria JC; Cervantes A; Vogelzang NJ; Patel MR; Hussain M; Baron A; Argilés G; Conkling PR; Sampath D; Maslyar D; Patel P; Chan W; Gendreau S; Musib L; Xu N; Ma H; Lin K; Bendell J. 2020. *Ann Oncol.* 31(5): 626 - 633. IF: 18,274.

Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with intermediate and advanced/relapsed hepatocellular carcinoma: a TOS-ESMO initiative endorsed by CSCO, ISMPO, JSMO, KSMO, MOS and SSO. Chen, L.-T.; Martinelli, E.; Cheng, A.-L.; Pentheroudakis, G.; Qin, S.; Bhattacharyya, G.S.; Ikeda, M.; Lim, H.-Y.; Ho, G.F.; Choo, S.P.; Ren, Z.; Malhotra, H.; Ueno, M.; Ryoo, B.-Y.; Kiang, T.C.; Tai, D.; Vogel, A.; Cervantes, A.; Lu, S.-N.; Yen, C.-J.; Huang, Y.-H.; Chen, S.-C.; Hsu, C.; Shen, Y.-C.; Tabernero, J.; Yen, Y.; Hsu, C.-H.; Yoshino, T.; Douillard, J.-Y. 2020. *Ann Oncol.* 31(3): 334 - 351. IF: 18,274.

Genome-wide profiling of non-smoking-related lung cancer cells reveals common RB1 rearrangements associated with histopathologic transformation in EGFR-mutant tumors. Pros E; Saigi M; Alameda D; Gomez-Mariano G; Martinez-Delgado B; Alburquerque-Bejar JJ; Carretero J; Tonda R; Esteve-Codina A; Catala I; Palmero R; Jove M; Lazaro C; Patiño-Garcia A; Gil-Bazo I; Verdura S; Teulé A; Torres-Lanzas J; Sidransky D; Reguart N; Pio R; Juan-Vidal O; Nadal E; Felip E; Montuenga LM; Sanchez-Cespedes M. 2020. *Ann Oncol.* 31(2): 274 - 282. IF: 18,274.

Bevacizumab as adjuvant treatment of colon cancer: updated results from the S-AVANT phase III study by the GERCOR Group. André T; Vernerey D; Im SA; Bodoky G; Buzzoni R; Reingold S; Rivera F; McKendrick J; Scheithauer W; Ravit G; Fountzilas G; Yong WP; Isaacs R; Österlund P; Liang JT; Creemers GJ; Rakez M; Van Cutsem E; Cunningham D; Tabernero J; de Gramont A. 2020. *Ann Oncol.* 31(2): 246 - 256. IF: 18,274.

Cisplatin and 5-fluorouracil with or without epidermal growth factor receptor inhibition panitumumab for patients with non-resectable, advanced or metastatic oesophageal squamous cell cancer: a prospective, open-label, randomised phase III AIO/EORTC trial (POWER). Moehler M; Maderer A; Thuss-Patience PC; Brenner B; Meiler J; Ettrich TJ; Hofheinz RD; Al-Batran SE; Vogel A; Mueller L; Lutz MP; Lordick F; Alsina M; Borchert K; Greil R; Eisterer W; Schad A; Slotta-Huspenina J; Van Cutsem E; Lorenzen S. 2020. *Ann Oncol.* 31(2): 228 - 235. IF: 18,274.

Neutropenia and survival outcomes in metastatic colorectal cancer patients treated with trifluridine/tipiracil in the RECOURSE and J003 trials. Yoshino T; Cleary JM; Van Cutsem E; Mayer RJ; Ohtsu A; Shinozaki E; Falcone A; Yamazaki K; Nishina T; Garcia-Carbonero R; Komatsu Y; Baba H; Argilés G; Tsuji A; Sobrero A; Yamaguchi K; Peeters M; Muro K; Zaniboni A; Sugimoto N; Shimada Y; Tsuji Y; Hochster HS; Moriwaki T; Tran B; Esaki T; Hamada C; Tanase T; Benedetti F; Makris L; Yamashita F; Lenz HJ. 2020. *Ann Oncol.* 31(1): 88 - 95. IF: 18,274.

A phase I dose-escalation study of enzalutamide in combination with the AKT inhibitor AZD5363 (capivasertib) in patients with metastatic castration-resistant prostate cancer. Kolinsky, M.P.; Rescigno, P.; Bianchini, D.; Zafeiriou, Z.; Mehra, N.; Mateo, J.; Michalarea, V.; Riisnaes, R.; Crespo, M.; Figueiredo, I.; Miranda, S.; Nava Rodrigues, D.; Flohr, P.; Tunariu, N.; Banerji, U.; Ruddle, R.; Sharp, A.; Welti, J.; Lambros, M.; Carreira,

S.; Raynaud, F.I.; Swales, K.E.; Plymate, S.; Luo, J.; Tovey, H.; Porta, N.; Slade, R.; Leonard, L.; Hall, E.; de Bono, J.S. 2020. *Ann Oncol.* 31(5): 619 - 625. IF: 18,274.

Advanced Prostate Cancer with ATM Loss: PARP and ATR Inhibitors. Neeb A; Herranz N; Arce-Gallego S; Miranda S; Buroni L; Yuan W; Athie A; Casals T; Carmichael J; Rodrigues DN; Gurel B; Rescigno P; Rekowski J; Welti J; Riisnaes R; Gil V; Ning J; Wagner V; Casanova-Salas I; Cordoba S; Castro N; Fenor de la Maza MD; Seed G; Chandran K; Ferreira A; Figueiredo I; Bertan C; Bianchini D; Aversa C; Paschalis A; Gonzalez M; Morales-Barrera R; Suarez C; Carles J; Swain A; Sharp A; Gil J; Serra V; Lord C; Carreira S; Mateo J; de Bono JS. 2021. *Eur Urol.* 79(2): 200 - 211. Epub 2020 Nov 8. IF: 17,947.

Clinical outcome after progressing to frontline and second-line Anti-PD-1/PD-L1 in advanced urothelial cancer. Gómez de Liaño Lista A; van Dijk N; de Velasco Oria de Rueda G; Necchi A; Lavaud P; Morales-Barrera R; Alonso Gordoa T; Maroto P; Ravaud A; Durán I; Szabados B; Castellano D; Giannatempo P; Loriot Y; Carles J; Anguera Palacios G; Lefort F; Raggi D; Gross Goupil M; Powles T; Van der Heijden MS. 2020. *Eur Urol.* 77(2): 269 - 276. IF: 17,947.

Avadomide monotherapy in relapsed/refractory DLBCL: safety, efficacy, and a predictive gene classifier. Carpio C; Bouabdallah R; Ysebaert L; Sancho JM; Salles GA; Cordoba R; Pinto A; Gharibo M; Rasco D; Panizo C; Lopez-Martin JA; Santoro A; Salar A; Damian S; Martin Garcia-Sancho A; Verhoef G; Van Den Neste EW; Wang M; Couto S; Carrancio S; Weng A; Wang X; Schmitz F; Wei X; Hege KM; Trotter MWB; Risueno A; Buchholz T; Hagner PR; Gandhi AK; Pourdehnad M; Ribrag V. 2020. *Blood.* 135(13): 996 - 1007. IF: 17,543.

Venetoclax-obinutuzumab: harnessing complexity. Abrisqueta, Pau; Bosch, Francesc. 2020. *Blood.* 135(11): 789 - 790. IF: 17,543.

Arterial thrombosis in Philadelphia-negative myeloproliferative neoplasms predicts second cancer: a case-control study. De Stefano V; Ghirardi A; Masciulli A; Carobbio A; Palandri F; Vianelli N; Rossi E; Betti S; Di Veroli A; Iurlo A; Cattaneo D; Finazzi G; Bonifacio M; Scaffidi L; Patriarca A; Rumi E; Casetti IC; Stephenson CIM; Guglielmelli P; Elli EM; Palova M; Rapezzi D; Erez D; Gomez M; Wille K; Perez-Encinas M; Lunghi F; Angona A; Fox ML; Beggiato E; Benevolo G; Carli G; Cacciola R; McMullin MF; Tieghi A; Recasens V; Isfort S; Marchetti M; Griesshammer M; Alvarez-Larran A; Vannucchi AM; Rambaldi A; Barbui T. 2020. *Blood.* 135(5): 381 - 386. IF: 17,543.

Precision Therapy in RAS Mutant Colorectal Cancer. Dienstmann R; Connor K; Byrne AT. 2020. *Gastroenterology.* 158(4): 806 - 811. IF: 17,373.

Colorectal cancer residual disease at maximal response to EGFR blockade displays a druggable Paneth cell-like phenotype. Lupo B; Sassi F; Pinnelli M; Galimi F; Zanella ER; Vurchio V; Migliardi G; Gagliardi PA; Puliafito A; Manganaro D; Luraghi P; Kragh M; Pedersen MW; Horak ID; Boccaccio C; Medico E; Primo L; Nichol D; Spiteri I; Heide T; Vatsiou A; Graham TA; Élez E; Argiles G; Nuciforo P; Sottoriva A; Dienstmann R; Pasini D; Grassi E; Isella C; Bertotti A; Trusolino L. 2020. *Sci Transl Med.* 12(555). IF: 16,304.

The IDH-TAU-EGFR triad defines the neovascular landscape of diffuse gliomas. Gargini R; Segura-Collar B; Herránz B; García-Escudero V; Romero-Bravo A; Núñez FJ; García-Pérez D; Gutiérrez-Guamán J; Ayuso-Sacido A; Seoane J; Pérez-Núñez A; Sepúlveda-Sánchez JM; Hernández-Laín A; Castro MG; García-Escudero R; Ávila J; Sánchez-Gómez P. 2020. *Sci Transl Med.* 12(527). IF: 16,304.

The International Association for the Study of Lung Cancer Global Survey on Molecular Testing in Lung Cancer. Smeltzer MP; Wynes MW; Lantuejoul S; Soo R; Ramalingam SS; Varella-Garcia M; Meadows Taylor M; Richeimer K; Wood K; Howell KE; Dalurzo ML; Felip E; Hollenbeck G; Kerr K; Kim ES; Mathias C; Pacheco J; Postmus P; Powell C; Tsuboi M; Wistuba II; Wakelee HA; Belani CP; Scagliotti GV; Hirsch FR. 2020. *J Thorac Oncol.* 15(9): 1434 - 1448. IF: 13,357.

Bintrafusp Alfa, a Bifunctional Fusion Protein Targeting TGF-ß and PD-L1, in Second-Line Treatment of Patients With NSCLC: Results From an Expansion Cohort of a Phase 1 Trial. Paz-Ares L; Kim TM; Vicente D; Felip E; Lee DH; Lee KH; Lin CC; Flor MJ; Di Nicola M; Alvarez RM; Dussault I; Helwig C; Ojalvo LS; Gulley JL; Cho BC. 2020. *J Thorac Oncol.* 15(7): 1210 – 1222. IF: 13,357.

Final Overall Survival and Other Efficacy and Safety Results From ASCEND-3: Phase II Study of Ceritinib in ALKi-Naive Patients With ALK-Rearranged NSCLC. Nishio M; Felip E; Orlov S; Park K; Yu CJ; Tsai CM; Cobo M; McKeage M; Su WC; Mok T; Scagliotti GV; Spigel DR; Viraswami-Appanna K; Chen Z; Passos VQ; Shaw AT. 2020. *J Thorac Oncol.* 15(4): 609 - 617. IF: 13,357.

Ceritinib plus Nivolumab in Patients with Advanced ALK-Rearranged Non-Small Cell Lung Cancer: Results of an Open-Label, Multicenter, Phase 1B Study. Felip E; de Braud FG; Maur M; Loong HH; Shaw AT; Vansteenkiste JF; John T; Liu G; Lolkema MP; Selvaggi G; Giannone V; Cazorla P; Baum J; Balbin OA; Wang LV; Lau YY; Scott JW; Shao-Weng Tan D. 2020. *J Thorac Oncol.* 15(3): 392 - 403. IF: 13,357.

Evolution and Clinical Impact of EGFR Mutations in Circulating Free DNA in the BELIEF Trial. Molina-Vila MA; Stahel RA; Dafni U; Jordana-Ariza N; Balada-Bel A; Garzón-Ibáñez M; García-Peláez B; Mayo-de-Las-Casas C; Felip E; Fontecedro AC; Gautschi O; Peters S; Massutí B; Palmero R; Aix SP; Carcereny E; Früh M; Pless M; Popat S; Cuffe S; Bidoli P; Kammler R; Roschitzki-Voser H; Tsourti Z; Karachaliou N; Rosell R; results from the European Thoracic Oncology Platform (ETOP) BELIEF trial. 2020. *J Thorac Oncol.* 15(3): 416 - 425. IF: 13,357.

TGFß promotes widespread enhancer chromatin opening and operates on genomic regulatory domains. Guerrero-Martínez JA; Ceballos-Chávez M; Koehler F; Peiró S; Reyes JC. 2020. *Nat Commun.* 11(1): 6196 - 6196. IF: 12,121.

Circulating tumour DNA from the cerebrospinal fluid allows the characterisation and monitoring of medulloblastoma. Escudero, L.; Llort, A.; Arias, A.; Diaz-Navarro, A.; Martínez-Ricarte, F.; Rubio-Perez, C.; Mayor, R.; Caratù, G.; Martínez-Sáez, E.; Vázquez-Méndez, É.; Lesende-Rodríguez, I.; Hladun, R.; Gros, L.; Ramón y Cajal, S.; Poca, M.A.; Puente, X.S.; Sahuquillo, J.; Gallego, S.; Seoane, J. 2020. *Nat Commun.* 11(1): 5376 - 5376. IF: 12,121.

ITGB3-mediated uptake of small extracellular vesicles facilitates intercellular communication in breast cancer cells. Fuentes P; Sesé M; Guijarro PJ; Emperador M; Sánchez-Redondo S; Peinado H; Hümmer S; Ramón Y Cajal S. 2020. *Nat Commun.* 11(1): 4261 - 4261. IF: 12,121.

Multiple low dose therapy as an effective strategy to treat EGFR inhibitor-resistant NSCLC tumours. Fernandes Neto JM; Nadal E; Bosdriesz E; Ooft SN; Farre L; McLean C; Klarenbeek S; Jurgens A; Hagen H; Wang L; Felip E; Martinez-Marti A; Vidal A; Voest E; Wessels LFA; van Tellingen O; Villanueva A; Bernards R. 2020. *Nat Commun.* 11(1): 3157 - 3157. IF: 12,121.

Phenotypic changes of HER2-positive breast cancer during and after dual HER2 blockade. Brasó-Maristany F; Griguolo G; Pascual T; Paré L; Nuciforo P; Llombart-Cussac A; Bermejo B; Oliveira M; Morales S; Martínez N; Vidal M; Adamo B; Martínez O; Pernas S; López

R; Muñoz M; Chic N; Galván P; Garau I; Manso L; Alarcón J; Martínez E; Gregorio S; Gomis RR; Villagrasa P; Cortés J; Ciruelos E; Prat A. 2020. *Nat Commun.* 11(1): 385 - 385. IF: 12,121.

Genomics of lethal prostate cancer at diagnosis and castration resistance. Mateo J; Seed G; Bertan C; Rescigno P; Dolling D; Figueiredo I; Miranda S; Nava Rodrigues D; Gurel B; Clarke M; Atkin M; Chandler R; Messina C; Sumanasuriya S; Bianchini D; Barrero M; Petremolo A; Zafeiriou Z; Fontes MS; Perez-Lopez R; Tunariu N; Fulton BA; Jones R; McGovern UB; Ralph C; Varughese M; Parikh O; Jain S; Elliott T; Sandhu S; Porta N; Hall E; Yuan W; Carreira S; de Bono JS. 2020. *J Clin Invest.* 130(4): 1743 - 1751. IF: 11,864.

Ovarian and Breast Cancer Risks Associated With Pathogenic Variants in RAD51C and RAD51D. Yang X; Song H; Leslie G; Engel C; Hahnen E; Auber B; Horváth J; Kast K; Niederacher D; Turnbull C; Houlston R; Hanson H; Loveday C; Dolinsky JS; LaDuca H; Ramus SJ; Menon U; Rosenthal AN; Jacobs I; Gayther SA; Dicks E; Nevanlinna H; Aittomäki K; Pelttari LM; Ehrencrona H; Borg Å; Kvist A; Rivera B; Hansen TVO; Djursby M; Lee A; Dennis J; Bowtell DD; Traficante N; Diez O; Balmaña J; Gruber SB; Chenevix-Trench G; kConFab Investigators; Jensen A; Kjær SK; Høgdall E; Castéra L; Garber J; Janavicius R; Osorio A; Golmard L; Vega A; Couch FJ; Robson M; Gronwald J; Domchek SM; Culver JO; de la Hoya M; Easton DF; Foulkes WD; Tischkowitz M; Meindl A; Schmutzler RK; Pharoah PDP; Antoniou AC. 2020. *J Natl Cancer Inst.* 112(12): 1242 - 1250. IF: 11,577.

HER2-Enriched Subtype and ERBB2 Expression in HER2-Positive Breast Cancer Treated with Dual HER2 Blockade. Prat A; Pascual T; De Angelis C; Gutierrez C; Llombart-Cussac A; Wang T; Cortés J; Rexer B; Paré L; Forero A; Wolff AC; Morales S; Adamo B; Brasó-Maristany F; Vidal M; Veeraraghavan J; Krop I; Galván P; Pavlick AC; Bermejo B; Izquierdo M; Rodrik-Outmezguine V; Reis-Filho JS; Hilsenbeck SG; Oliveira M; Dieci MV; Griguolo G; Fasani R; Nuciforo P; Parker JS; Conte P; Schiff R; Guarneri V; Osborne CK; Rimawi MF. 2020. *J Natl Cancer Inst.* 112(1): 46 - 54. IF: 11,577.

Cdk9 and H2Bub1 signal to Clr6-CII/Rpd3S to suppress aberrant antisense transcription. Sansó M; Parua PK; Pinto D; Svensson JP; Pagé V; Bitton DA; MacKinnon S; Garcia P; Hidalgo E; Bähler J; Tanny JC; Fisher RP. 2020. *Nucleic Acids Res.* 48(13): 7154 - 7168. IF: 11,501.

Hierarchical chromatin organization detected by TADpole. Soler-Vila P; Cuscó P; Farabella I; Di Stefano M; Marti-Renom MA. 2020. *Nucleic Acids Res.* 48(7): 39 - 39. IF: 11,501.

Hyperprogression and Immunotherapy: Fact, Fiction, or Alternative Fact? Adashek, J.J.; Subbiah, I.M.; Matos, I.; Garralda, E.; Menta, A.K.; Ganeshan, D.M.; Subbiah, V. 2020. *Trends in Cancer.* 181 - 191. IF: 11,093.

Personalized cancer therapy prioritization based on driver alteration co-occurrence patterns. Mateo L; Duran-Frigola M; Gris-Oliver A; Palafox M; Scaltriti M; Razavi P; Chandarlapaty S; Arribas J; Bellet M; Serra V; Aloy P. 2020. *Genome Med.* 12(1): 78 - 78. IF: 10,675.

Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial. Male C; Lensing AWA; Palumbo JS; Kumar R; Nurmeev I; Hege K; Bonnet D; Connor P; Hooimeijer HL; Torres M; Chan AKC; Kenet G; Holzhauer S; Santamaría A; Amedro P; Chalmers E; Simioni P; Bhat RV; Yee DL; Lvova O; Beyer-Westendorf J; Biss TT; Martinelli I; Saracco P; Peters M; Kállay K; Gauger CA; Massicotte MP; Young G; Pap AF; Majumder M; Smith WT; Heubach JF; Berkowitz SD; Thelen K; Kubitza D; Crowther M; Prins MH; Monagle P; EINSTEIN-Jr Phase 3 Investigators. 2020. *Lancet Haematol.* 7(1): e18-e27. IF: 10,406.

Palbociclib and Trastuzumab in HER2-Positive Advanced Breast Cancer: Results from the Phase II SOLTI-1303 PATRICIA Trial. Ciruelos EM; Villagrasa P; Pascual T; Oliveira M; Pernas S; Paré L; Escrivá-de-Romaní S; Manso L; Adamo B; Martínez de Dueñas E; Cortés J; Vázquez S; Perelló A; Garau I; Melé M; Martínez Jañez N; Montaño A; Bermejo B; Morales S; Echarri MJ; Vega E; González-Farré B; Martínez D; Galván P; Canes J; Nuciforo P; Gonzàlez Farré X; Prat A. 2020. *Clin Cancer Res.* 26(22): 5820 - 5829. IF: 10,107.

Phase Ib Dose-escalation/Expansion Trial of Ribociclib in Combination With Everolimus and Exemestane in Postmenopausal Women with HR(+), HER2(-) Advanced Breast Cancer. Bardia A; Modi S; Oliveira M; Cortés J; Campone M; Ma BBY; Dirix LY; Weise A; Hewes B; Diaz-Padilla I; Han Y; Deshpande P; Samant T; Rodriguez Lorenc CK; He W; Su F; Chavez-MacGregor M. 2020. *Clin Cancer Res.* 26(24): 6417 - 6428. IF: 10,107.

Gastrointestinal Stromal Tumor: Challenges and Opportunities for a New Decade. Serrano C; George S. 2020. *Clin Cancer Res.* 26(19): 5078 - 5085. IF: 10,107.

A Phase Ib/II Study of the BRAF Inhibitor Encorafenib Plus the MEK Inhibitor Binimetinib in Patients with BRAF(V600E/K) -mutant Solid Tumors. Sullivan RJ; Weber JS; Patel SP; Dummer R; Carlino MS; Tan DS; Lebbe C; Siena S; Élez E; Wollenberg L; Pickard M; Sandor V; Ascierto PA. 2020. *Clin Cancer Res.* 26(19): 5102 - 5112. IF: 10,107.

First-in-Human Study of AT13148, a Dual ROCK-AKT Inhibitor in Patients with Solid Tumors. McLeod R; Kumar R; Papadatos-Pastos D; Mateo J; Brown J; Ingles Garces AH; Ruddle R; Decordova SA; Jueliger S; Ferraldeschi R; Maiques O; Sanz-Moreno V; Jones P; Traub S; Halbert G; Mellor S; Swales KE; Raynaud FI; Garrett MD; Banerji U. 2020. *Clin Cancer Res.* 26(18): 4777 - 4784. IF: 10,107.

EVOLVE: A Multicenter Open-Label Single-Arm Clinical and Translational Phase II Trial of Cediranib Plus Olaparib for Ovarian Cancer after PARP Inhibition Progression. Lheureux S; Oaknin A; Garg S; Bruce JP; Madariaga A; Dhani NC; Bowering V; White J; Accardi S; Tan Q; Braunstein M; Karakasis K; Cirlan I; Pedersen S; Li T; Fariñas-Madrid L; Lee YC; Liu ZA; Pugh TJ; Oza AM. 2020. *Clin Cancer Res.* 26(16): 4206 - 4215. IF: 10,107.

TCR Repertoire Changes during TIL Expansion: Clonal Selection or Drifting? Lozano-Rabella M; Gros A. 2020. *Clin Cancer Res.* 26(16): 4177 - 4179. IF: 10,107.

Capivasertib, an AKT Kinase Inhibitor, as Monotherapy or in Combination with Fulvestrant in Patients with AKT1 (E17K)-Mutant, ER-Positive Metastatic Breast Cancer. Smyth LM; Tamura K; Oliveira M; Ciruelos EM; Mayer IA; Sablin MP; Biganzoli L; Ambrose HJ; Ashton J; Barnicle A; Cashell DD; Corcoran C; de Bruin EC; Foxley A; Hauser J; Lindemann JPO; Maudsley R; McEwen R; Moschetta M; Pass M; Rowlands V; Schiavon G; Banerji U; Scaltriti M; Taylor BS; Chandarlapaty S; Baselga J; Hyman DM. 2020. *Clin Cancer Res.* 26(15): 3947 - 3957. IF: 10,107.

Patient-Derived Organoids from Multiple Colorectal Cancer Liver Metastases Reveal Moderate Intra-patient Pharmacotranscriptomic Heterogeneity. Bruun J; Kryeziu K; Eide PW; Moosavi SH; Eilertsen IA; Langerud J; Røsok BI; Totland MZ; Brunsell TH; Pellinen T; Saarela J; Bergsland CH; Palmer HG; Brudvik KW; Guren T; Dienstmann R; Guren MG; Nesbakken A; Bjørnbeth BA;

Sveen A; Lothe RA. 2020. *Clin Cancer Res.* 26(15): 4107 - 4119. IF: 10,107.

Genetic Alterations in the PI3K/AKT Pathway and Baseline AKT Activity Define AKT Inhibitor Sensitivity in Breast Cancer Patient-derived Xenografts. Gris-Oliver A; Palafox M; Monserrat L; Brasó-Maristany F; Òdena A; Sánchez-Guixé M; Ibrahim YH; Villacampa G; Grueso J; Parés M; Guzman M; Rodriguez O; Bruna A; Hirst CS; Barnicle A; de Bruin EC; Reddy A; Schiavon G; Arribas J; Mills GB; Caldas C; Dienstman R; Prat A; Nuciforo P; Razavi P; Scaltriti M; Turner NC; Saura C; Davies BR; Oliveira M; Serra V. 2020. *Clin Cancer Res.* 26(14): 3720 - 3731. IF: 10,107.

Phase I Study of TAK-659, an Investigational, Dual SYK/FLT3 Inhibitor, in Patients with B-Cell Lymphoma. Gordon LI; Kaplan JB; Popat R; Burris HA; Ferrari S; Madan S; Patel MR; Gritti G; El-Sharkawi D; Chau I; Radford JA; Perez de Oteyza J; Luigi Zinzani P; Iyer S; Townsend W; Karmali R; Miao H; Proscurshim I; Wang S; Wu Y; Stumpo K; Shou Y; Carpio C; Bosch F. 2020. *Clin Cancer Res.* 26(14): 3546 - 3556. IF: 10,107.

Multiparametric MR-PET Imaging Predicts Pharmacokinetics and Clinical Response to GDC-0084 in Patients with Recurrent High-Grade Glioma. Ellingson BM; Yao J; Raymond C; Nathanson DA; Chakhoyan A; Simpson J; Garner JS; Olivero AG; Mueller LU; Rodon J; Gerstner E; Cloughesy TF; Wen PY. 2020. *Clin Cancer Res.* 26(13): 3135 - 3144. IF: 10,107.

BRAF-Mutant Transcriptional Subtypes Predict Outcome of Combined BRAF, MEK, and EGFR Blockade with Dabrafenib, Trametinib, and Panitumumab in Patients with Colorectal Cancer. Middleton G; Yang Y; Campbell CD; André T; Atreya CE; Schellens JHM; Yoshino T; Bendell JC; Hollebecque A; McRee AJ; Siena S; Gordon MS; Tabernero J; Yaeger R; O'Dwyer PJ; De Vos F; Van Cutsem E; Millholland JM; Brase JC; Rangwala F; Gasal E; Corcoran RB. 2020. *Clin Cancer Res.* 26(11): 2466 - 2476. IF: 10,107.

Patient-Reported Outcomes from the Phase III Randomized IMmotion151 Trial: Atezolizumab + Bevacizumab versus Sunitinib in Treatment-Naïve Metastatic Renal Cell Carcinoma. Atkins MB; Rini BI; Motzer RJ; Powles T; McDermott DF; Suarez C; Bracarda S; Stadler WM; Donskov F; Gurney H; Oudard S; Uemura M; Lam ET; Grüllich C; Quach C; Carroll S; Ding B; Zhu Q; Piault-Louis E; Schiff C; Escudier B. 2020. *Clin Cancer Res.* 26(11): 2506 - 2514. IF: 10,107.

Design and Conduct of Early Clinical Studies of Immunotherapy: Recommendations from the Task Force on Methodology for the Development of Innovative Cancer Therapies 2019 (MDICT). Smoragiewicz M; Adjei AA; Calvo E; Tabernero J; Marabelle A; Massard C; Tang J; de Vries EGE; Douillard JY; Seymour L; task force on Methodology for the Development of Innovative Cancer Therapies. 2020. *Clin Cancer Res.* 26(11): 2461 - 2465. IF: 10,107.

Capturing Hyperprogressive Disease with Immune-Checkpoint Inhibitors Using RECIST 1.1 Criteria. Matos I; Martin-Liberal J; Garcia-Ruiz A; Hierro C; Ochoa de Olza M; Viaplana C; Azaro A; Vieito M; Brana I; Mur G; Ros J; Mateos J; Villacampa G; Berché R; Oliveira M; Alsina M; Élez E; Oaknin A; Muñoz-Couselo E; Carles J; Felip E; Rodon J; Tabernero J; Dienstmann R; Perez-Lopez R; Garralda E. 2020. *Clin Cancer Res.* 26(8): 1846 - 1855. IF: 10,107.

First-in-Human Phase I Study to Evaluate the Brain-Penetrant PI3K/mTOR Inhibitor GDC-0084 in Patients with Progressive or Recurrent High-Grade Glioma. Wen, Patrick Y.; Cloughesy, Timothy F.; Olivero, Alan G.; Morrissey, Kari M.; Wilson, Timothy R.; Lu, Xuyang; Mueller, Lars U.; Coimbra, Alexandre F.; Ellingson, Benjamin M.; Gerstner, Elizabeth; Lee, Eudocia Q.; Rodon, Jordi. 2020. *Clin Cancer Res.* 26(8): 1820 - 1828. IF: 10,107.

Epigenetic EGFR Gene Repression Confers Sensitivity to Therapeutic BRAFV600E Blockade in Colon Neuroendocrine Carcinomas. Capdevila J; Arqués O; Hernandez Mora JR; Matito J; Caratu 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. 2020. *Clin Cancer Res.* 26(4): 902 - 909. IF: 10,107.

Evaluation of the Predictive Role of Tumor Immune Infiltrate in Patients with HER2-Positive Breast Cancer Treated with Neoadjuvant Anti-HER2 Therapy without Chemotherapy. De Angelis C; Nagi C; Hoyt CC; Liu L; Roman K; Wang C; Zheng Y; Veeraraghavan J; Sethunath V; Nuciforo P; Wang T; Tsimelzon A; Mao S; Hilsenbeck SG; Trivedi MV; Cataldo ML; Pavlick A; Wolff AC; Weigelt B; Reis-Filho JS; Prat A; Gutierrez C; Osborne CK; Rimawi MF; Schiff R. 2020. *Clin Cancer Res.* 26(3): 738 - 745. IF: 10,107.

Impact of Prior Bevacizumab Treatment on VEGF-A and PlGF Levels and Outcome Following Second-Line Aflibercept Treatment: Biomarker Post Hoc Analysis of the VELOUR Trial. Van Cutsem E; Paccard C; Chiron M; Tabernero J. 2020. *Clin Cancer Res.* 26(3): 717 - 725. IF: 10,107.

Phase Ia Study of Anti-NaPi2b Antibody-Drug Conjugate Lifastuzumab Vedotin DNIB0600A in Patients with Non-Small Cell Lung Cancer and Platinum-Resistant Ovarian Cancer. Gerber DE; Infante JR; Gordon MS; Goldberg SB; Martín M; Felip E; Martinez Garcia M; Schiller JH; Spigel DR; Cordova J; Westcott V; Wang Y; Shames DS; Choi Y; Kahn R; Dere RC; Samineni D; Xu J; Lin K; Wood K; Royer-Joo S; Lemahieu V; Schuth E; Vaze A; Maslyar D; Humke EW; Burris HA. 2020. *Clin Cancer Res.* 26(2): 364 - 372. IF: 10,107.

Lucitanib for the Treatment of HR(+)/HER2(-) Metastatic Breast Cancer: Results from the Multicohort Phase II FINESSE Study. Hui R; Pearson A; Cortés J; Campbell C; Poirot C; Azim HA; Fumagalli D; Lambertini M; Daly F; Arahmani A; Pérez-Garcia J; Aftimos P; Bedard PL; Xuereb L; Scheepers ED; Vicente M; Goulioti T; Loibl S; Loi S; Pierrat MJ; Turner NC; Andre F; Curigliano G. 2020. *Clin Cancer Res.* 26(2): 354 - 363. IF: 10,107.

Randomized Phase 0/I Trial of the Mitochondrial Inhibitor ME-344 or Placebo Added to Bevacizumab in Early HER2-Negative Breast Cancer. Quintela-Fandino M; Morales S; Cortés-Salgado A; Manso L; Apala JV; Muñoz M; Gasol Cudos A; Salla Fortuny J; Gion M; Lopez-Alonso A; Cortés J; Guerra J; Malón D; Caleiras E; Mulero F; Mouron S. 2020. *Clin Cancer Res.* 26(1): 35 - 45. IF: 10,107.

Nivolumab and sunitinib combination in advanced soft tissue sarcomas: a multicenter, single-arm, phase Ib/II trial. Martin-Broto J; Hindi N; Grignani G; Martinez-Trufero J; Redondo A; Valverde C; Stacchiotti S; Lopez-Pousa A; D'Ambrosio L; Gutierrez A; Perez-Vega H; Encinas-Tobajas V; de Alava E; Collini P; Peña-Chilet M; Dopazo J; Carrasco-Garcia I; Lopez-Alvarez M; Moura DS; Lopez-Martin JA. 2020. *J Immunother Cancer.* Nov;8(2):e001561. IF: 9,913.

A first-in-human phase 1 dose escalation study of spartalizumab (PDR001), an anti-PD-1 antibody, in patients with advanced solid tumors. Naing A; Gainor JF; Gelderblom H; Forde PM; Butler MO; Lin CC; Sharma S; Ochoa de Olza M; Varga A; Taylor M; Schellens JHM; Wu H; Sun H; Silva AP; Faris J; Mataraza J; Cameron S; Bauer TM. 2020. *J Immunother Cancer.* Mar;8(1):e000530 IF: 9,913.

Transient exposure to miR-203 enhances the differentiation capacity of established pluripotent stem cells. Salazar-Roa M; Trakala M; Álvarez-Fernández M; Valdés-Mora F; Zhong C; Muñoz J; Yu Y; Peters TJ; Graña-Castro O; Serrano R; Zapatero-Solana E; Abad M; Bueno MJ; de Cedrón MG; Fernández-Piqueras J; Serrano M; Blasco MA; Wang DZ; Clark SJ; Izpisua-Belmonte JC; Ortega S; Malumbres

M. 2020. *EMBO J.* 39(16): e104324. IF: 9,889.

The anti-cancer drug ABTL0812 induces ER stress-mediated cytotoxic autophagy by increasing dihydroceramide levels in cancer cells. Muñoz-Guardiola P; Casas J; Megías-Roda E; Solé S; Perez-Montoyo H; Yeste-Velasco M; Erazo T; Diéguez-Martínez N; Espinosa-Gil S; Muñoz-Pinedo C; Yoldi G; Abad JL; Segura MF; Moran T; Romeo M; Bosch-Barrera J; Oaknin A; Alfón J; Domènech C; Fabriàs G; Velasco G; Lizcano JM. *Autophagy.* 1 - 18. IF: 9,770.

Association of Pathologic Complete Response with Long-Term Survival Outcomes in Triple-Negative Breast Cancer: A Meta-Analysis. Huang M; O'Shaughnessy J; Zhao J; Haiderali A; Cortés J; Ramsey SD; Briggs A; Hu P; Karantza V; Aktan G; Qi CZ; Gu C; Xie J; Yuan M; Cook J; Untch M; Schmid P; Fasching PA. 2020. *Cancer Res.* 80(24): 5427 - 5434. IF: 9,727.

Association of Genomic Domains in BRCA1 and BRCA2 with Prostate Cancer Risk and Aggressiveness. Patel VL; Busch EL; Friebel TM; Cronin A; Leslie G; McGuffog L; Adlard J; Agata S; Agnarsson BA; Ahmed M; Aittomäki K; Alducci E; Andrulis IL; Arason A; Arnold N; Artioli G; Arver B; Auber B; Azzollini J; Balmaña J; et al. 2020. *Cancer Res.* 80(3): 624 - 638. IF: 9,727.

Epigenetic SMAD3 Repression in Tumor-Associated Fibroblasts Impairs Fibrosis and Response to the Antifibrotic Drug Nintedanib in Lung Squamous Cell Carcinoma. Ikemori R; Gabasa M; Duch P; Vizoso M; Bragado P; Arshakyan M; Luis IC; Marín A; Morán S; Castro M; Fuster G; Gea-Sorli S; Jauset T; Soucek L; Montuenga LM; Esteller M; Monso E; Peinado VI; Gascon P; Fillat C; Hilberg F; Reguart N; Alcaraz J. 2020. *Cancer Res.* 80(2): 276 - 290. IF: 9,727.

Pharmacological disruption of the Notch transcription factor complex. Lehal R; Zaric J; Vigolo M; Urech C; Frismantas V; Zangger N; Cao L; Berger A; Chicote I; Loubéry S; Choi SH; Koch U; Blacklow SC; Palmer HG; Bornhauser B; González-Gaitán M; Arsenijevic Y; Zoete V; Aster JC; Bourquin JP; Radtke F. 2020. *Proc Natl Acad Sci U S A.* 117(28): 16292 - 16301. IF: 9,412.

Evaluation of Pathologic Complete Response as a Surrogate for Long-Term Survival Outcomes in Triple-Negative Breast Cancer. Huang M; O'Shaughnessy J; Zhao J; Haiderali A; Cortes J; Ramsey S; Briggs A; Karantza V; Aktan G; Qi CZ; Gu C; Xie J; Yuan M; Cook J; Untch M; Schmid P; Fasching PA. 2020. *J Natl Compr Canc Netw.* 18(8): 1096 - 1104. IF: 9,316.

Role of POLE and POLD1 in familial cancer. Mur P; García-Mulero S; Del Valle J; Magraner-Pardo L; Vidal A; Pineda M; Cinnirella G; Martín-Ramos E; Pons T; López-Doriga A; Belhadj S; Feliubadaló L; Munoz-Torres PM; Navarro M; Grau E; Darder E; Llort G; Sanz J; Ramón Y Cajal T; Balmana J; Brunet J; Moreno V; Piulats JM; Matías-Guiu X; Sanz-Pamplona R; Aligué R; Capellá G; Lázaro C; Valle L. 2020. *Genet Med.* 22(12): 2089 - 2100. IF: 8,904.

Polygenic risk scores and breast and epithelial ovarian cancer risks for carriers of BRCA1 and BRCA2 pathogenic variants. Barnes DR; Rookus MA; McGuffog L; Leslie G; Mooij TM; Dennis J; Mavaddat N; Adlard J; Ahmed M; Aittomäki K; Andrieu N; Andrulis IL; Arnold N; Arun BK; Azzollini J; Balmaña J; et al.... 2020. *Genet Med.* 22(10): 1653 - 1666. IF: 8,904.

The promise of selective MET inhibitors in non-small cell lung cancer with MET exon 14 skipping. Salgia R; Sattler M; Scheele J; Stroh C; Felip E. 2020. *Cancer Treat Rev.* 87: 102022 - 102022. IF: 8,885.

The future of bladder cancer therapy: Optimizing the inhibition of the fibroblast growth factor receptor. Morales-Barrera R; Suárez C; González M; Valverde C; Serra E; Mateo J; Raventos C; Maldonado X; Morote J; Carles J. 2020. *Cancer Treat Rev.* 86: 102000 - 102000. IF: 8,885.

Contextualizing pertuzumab approval in the treatment of HER2-positive breast cancer patients. Cortés J; Ciruelos E; Pérez-García J; Albanell J; García-Estévez L; Ruiz-Borrego M; Espinosa R; Gallegos I; González S; Álvarez I; Llombart A. 2020. *Cancer Treat Rev.* 83: 101944 - 101944. IF: 8,885.

Kidney cancer PDOXs reveal patient-specific pro-malignant effects of antiangiogenics and its molecular traits. Moserle L; Pons R; Martínez-Lozano M; Jiménez-Valerio GA; Vidal A; Suárez C; Trilla E; Jiménez J; de Torres I; Carles J; Senserrich J; Aguilar S; Palomero L; Amadori A; Casanovas O. 2020. *EMBO Mol.* Med. 12(12): e11889. IF: 8,821.

Tumors defective in homologous recombination rely on oxidative metabolism: relevance to treatments with PARP inhibitors. Lahiguera Á; Hyroššová P; Figueras A; Garzón D; Moreno R; Soto-Cerrato V; McNeish I; Serra V; Lazaro C; Barretina P; Brunet J; Menéndez J; Matias-Guiu X; Vidal A; Villanueva A; Taylor-Harding B; Tanaka H; Orsulic S; Junza A; Yanes O; Muñoz-Pinedo C; Palomero L; Pujana MÀ; Perales JC; Viñals F. 2020. *EMBO Mol.* Med. 12(6): e11217. IF: 8,821.

Immunosuppressive Mediators Impair Proinflammatory Innate Lymphoid Cell Function in Human Malignant Melanoma. Ercolano G; Garcia-Garijo A; Salomé B; Gomez-Cadena A; Vanoni G; Mastelic-Gavillet B; Ianaro A; Speiser DE; Romero P; Trabanelli S; Jandus C. 2020. *Cancer Immunol Res.* 8(4): 556 - 564. IF: 8,728.

Posttransplant cyclophosphamide after allogeneic hematopoietic cell transplantation mitigates the immune activation induced by previous nivolumab therapy. Nieto JC; Roldán E; Jiménez I; Fox L; Carabia J; Ortí G; Puigdefàbregas L; Gallur L; Iacoboni G; Raheja P; Pérez A; Bobillo S; Salamero O; Palacio C; Valcárcel D; Crespo M; Bosch F; Barba P. 2020. *Leukemia.* 34(12): 3420 - 3425. IF: 8,665.

UGT1A1 genotype influences clinical outcome in patients with intermediate-risk acute myeloid leukemia treated with cytarabine-based chemotherapy. Díaz-Santa J; Rodríguez-Romanos R; Osca G; Pratcorona M; Garrido A; Coll R; Moret C; Escoda L; Tormo M; Heras I; Arnan M; Vives S; Salamero O; Lloveras N; Bargay J; Sampol A; Cruz D; Garcia A; Quiñones T; Esteve J; Sierra J; Gallardo D; on the behalf of CETLAM Group. 2020. *Leukemia.* 34(11): 2925 - 2933. IF: 8,665.

Outcome of older (=70 years) APL patients frontline treated with or without arsenic trioxide-an International Collaborative Study. Kayser S; Rahmé R; Martínez-Cuadrón D; Ghiaur G; Thomas X; Sobas M; Guerci-Bresler A; Garrido A; Pigneux A; Gil C; Raffoux E; Tormo M; Vey N; de la Serna J; Salamero O; Lengfelder E; Levis MJ; Fenaux P; Sanz MA; Platzbecker U; Schlenk RF; Adès L; Montesinos P. 2020. *Leukemia.* 34(9): 2333 - 2341. IF: 8,665.

Obinutuzumab plus fludarabine and cyclophosphamide in previously untreated, fit patients with chronic lymphocytic leukemia: a subgroup analysis of the GREEN study. Bosch F; Cantin G; Cortelezzi A; Knauf W; Tiab M; Turgut M; Zaritskey A; Merot JL; Tausch E; Trunzer K; Robson S; Gresko E; Böttcher S; Foà R; Stilgenbauer S; Leblond V. 2020. *Leukemia.* 34(2): 441 - 450. IF: 8,665.

Clinical and Pathological Characterization of Lynch-Like Syndrome. Picó MD; Castillejo A; Murcia Ó; Giner-Calabuig M; Alustiza M; Sánchez A; Moreira L; Pellise M; Castells A; Carrillo-Palau M; Ramon Y Cajal T; Gisbert-Beamud A; Llort G; Yagüe C; López-Fernández A; Alvarez-Urturi C; Cubiella J; Rivas L; Rodríguez-Alcalde D; Herraiz M; Garau C; Dolz C; Bujanda

L; Cid L; Povés C; Garzon M; Salces I; Ponce M; Hernández-Villalba L; Alenda C; Balaguer F; Soto JL; Jover R. 2020. *Clin Gastroenterol Hepatol.* 18(2): 368-374.e1. IF: 8,549.

Quality of colonoscopy is associated with adenoma detection and post-colonoscopy 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; Fernandez AL; 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. 2020. *Clin Gastroenterol Hepatol.* IF: 8,549.

Comparison of next-generation sequencing (NGS) and next-generation flow (NGF) for minimal residual disease (MRD) assessment in multiple myeloma. Medina A; Puig N; Flores-Montero J; Jimenez C; Sarasquete ME; Garcia-Alvarez M; Prieto-Conde I; Chillon C; Alcoceba M; Gutierrez NC; Oriol A; Rosinol L; Bladè J; Gironella M; Hernandez MT; Gonzalez-Calle V; Cedena MT; Paiva B; San-Miguel JF; Lahuerta JJ; Mateos MV; Martinez-Lopez J; Orfao A; Gonzalez M; Garcia-Sanz R. 2020. *Blood Cancer J.* 10(10): 108 - 108. IF: 8,023.

Multiple myeloma and SARS-CoV-2 infection: clinical characteristics and prognostic factors of inpatient mortality. Martínez-López J; Mateos MV; Encinas C; Sureda A; Hernández-Rivas JÁ; Lopez de la Guía A; Conde D; Krsnik I; Prieto E; Riaza Grau R; Gironella M; Blanchard MJ; Caminos N; Fernández de Larrea C; Senin MA; Escalante F; de la Puerta JE; Giménez E; Martínez-Barranco P; Mateos JJ; Casado LF; Bladé J; Lahuerta JJ; de la Cruz J; San-Miguel J. 2020. *Blood Cancer J.* 10(10): 103 - 103. IF: 8,023.

Molecular profiling of immunoglobulin heavy-chain gene rearrangements unveils new potential prognostic markers for multiple myeloma patients. Medina A; Jiménez C; Sarasquete ME; González M; Chillón MC; Balanzategui A; Prieto-Conde I; García-Álvarez M; Puig N; González-Calle V; Alcoceba M; Cuenca I; Barrio S; Escalante F; Gutiérrez NC; Gironella M; Hernández MT; Sureda A; Oriol A; Bladé J; Lahuerta JJ; San Miguel JF; Mateos MV; Martínez-López J; Calasanz MJ; García-Sanz R. 2020. *Blood Cancer J.* 10(2): 14 - 14. IF: 8,023.

The proapoptotic gene interferon regulatory factor-1 mediates the antiproliferative outcome of paired box 2 gene and tamoxifen. Wang, Shixiong; Somisetty, Venkata S.; Bai, Baoyan; Chernukhin, Igor; Niskanen, Henri; Kaikkonen, Minna U.; Bellet, Meritxell; Carroll, Jason S.; Hurtado, Antoni. 2020. *Oncogene.* 39(40): 6300 - 6312. IF: 7,971.

LOXL2-mediated H3K4 oxidation reduces chromatin accessibility in triple-negative breast cancer cells. Cebrià-Costa JP; Pascual-Reguant L; Gonzalez-Perez A; Serra-Bardenys G; Querol J; Cosín M; Verde G; Cigliano RA; Sanseverino W; Segura-Bayona S; Iturbide A; Andreu D; Nuciforo P; Bernado-Morales C; Rodilla V; Arribas J; Yelamos J; de Herreros AG; Stracker TH; Peiró S. 2020. *Oncogene.* 39(1): 79 - 121. IF: 7,971.

Emerging PD-1 and PD-1L inhibitors-associated myopathy with a characteristic histopathological pattern. Matas-García A; Milisenda JC; Selva-O'Callaghan A; Prieto-González S; Padrosa J; Cabrera C; Reguart N; Castrejón N; Solé M; Ros J; Trallero-Araguas E; Antoniol MN; Vila-Pijoan G; Grau JM. 2020. *Autoimmun Rev.* 19(2): 102455 - 102455. IF: 7,767.

Critical role of interleukin (IL)-17 in inflammatory and immune disorders: An updated review of the evidence focusing in controversies. Ruiz de Morales JMG; Puig L; Daudén E; Cañete JD; Pablos JL; Martín AO; Juanatey CG; Adán A; Montalbán X; Borruel N; Ortí G; Martín EH; García-Vidal C; Morales CV; Vázquez VM; González-Gay MÁ. 2020. *Autoimmun Rev.* 19(1): 102429 - 102429. IF: 7,767.

Liquid biopsies for diagnosing and monitoring primary tumors of the central nervous system. Le Rhun E; Seoane J; Salzet M; Soffietti R; Weller M. 2020. *Cancer Lett.* 480: 24 - 28. IF: 7,360.

Chromosome fragility in the buccal epithelium in patients with Fanconi anemia. Ramírez MJ; Minguillón J; Loveless S; Lake K; Carrasco E; Stjepanovic N; Balmaña J; Català A; Mehta PA; Surrallés J. 2020. *Cancer Lett.* 472: 1 - 7. IF: 7,360.

High risk of thrombosis in patients with advanced lung cancer harboring rearrangements in ROS1. Muñoz-Unceta N; Zugazagoitia J; Manzano A; Jiménez-Aguilar E; Olmedo ME; Cacho JD; Oliveira J; Dómine M; Ortega-Morán L; Aguado C; Luna AM; Fernández L; Pérez J; Font C; Salvador C; Corral J; Benítez G; Ros S; Biosca M; Calvo V; Martínez J; Sánchez-Cánovas M; López R; Sereno M; Mielgo X; Aparisi F; Carmona M; Carrión R; Ponce-Aix S; Soares M; Martínez-Salas I; García-Morillo M; Juan-Vidal O; Blasco A; Muñoz AJ; Paz-Ares L; Grupo de trombosis y cáncer SEOM. 2020. *Eur J Cancer.* 141: 193 - 198. IF: 7,275.

AXL is a predictor of poor survival and of resistance to anti-EGFR therapy in RAS wild-type metastatic colorectal cancer. Cardone C; Blauensteiner B; Moreno-Viedma V; Martini G; Simeon V; Vitiello PP; Ciardiello D; Belli V; Matrone N; Troiani T; Morgillo F; Zito Marino F; Dentice M; Nappi A; Boccaccino A; Antoniotti C; Cremolini C; Pietrantonio F; Prager GW; Normanno N; Maiello E; Argiles G; Elez E; Signoriello G; Franco R; Falcone A; Tabernero J; Sibilia M; Ciardiello F; Martinelli E. 2020. *Eur J Cancer.* 138: 1 - 10. IF: 7,275.

Immune checkpoint inhibitors: a physiology-driven approach to the treatment of coronavirus disease 2019. Di Cosimo S; Malfettone A; Pérez-García JM; Llombart-Cussac A; Miceli R; Curigliano G; Cortés J. 2020. *Eur J Cancer.* 135: 62 - 65. IF: 7,275.

Association of premenopausal risk-reducing salpingo-oophorectomy with breast cancer risk in BRCA1/2 mutation carriers: Maximising bias-reduction. Stjepanovic N; Villacampa G; Nead KT; Torres-Esquius S; Melis GG; Nathanson KL; Teule A; Brunet J; Y Cajal TR; Llort G; Dienstmann R; Rue M; Domchek SM; Balmaña J. 2020. *Eur J Cancer.* 132: 53 - 60. IF: 7,275.

CheckMate 171: A phase 2 trial of nivolumab in patients with previously treated advanced squamous non-small cell lung cancer, including ECOG PS 2 and elderly populations. Felip E; Ardizzoni A; Ciuleanu T; Cobo M; Laktionov K; Szilasi M; Califano R; Carcereny E; Griffiths R; Paz-Ares L; Duchnowska R; Garcia MA; Isla D; Jassem J; Appel W; Milanowski J; Van Meerbeeck JP; Wolf J; Li A; Acevedo A; Popat S. 2020. *Eur J Cancer.* 127: 160 - 172. IF: 7,275.

Clinical progression is associated with poor prognosis whatever the treatment line in metastatic castration resistant prostate cancer: The CATS international database. Delanoy N; Hardy-Bessard AC; Efstathiou E; Le Moulec S; Basso U; Birtle A; Thomson A; Krainer M; Guillot A; De Giorgi U; Hasbini A; Daugaard G; Bahl A; Chowdhury S; Caffo O; Beuzeboc P; Spaeth D; Eymard JC; Fléchon A; Alexandre J; Helissey C; Butt M; Priou F; Lechevallier E; Deville JL; Gross-Goupil M; Morales R; Thiery-Vuillemin A; Gavrikova T; Barthélémy P; Sella A; Fizazi K; Ferrero JM; Laguerre B; Thibault

C; Hans S; Oudard S. 2020. *Eur J Cancer*. 125: 153 - 163. IF: 7,275.

Results from the primary analysis of a 30 patient extension of the GATTO study, a phase Ib study combining the anti-MUC1 Gatipotuzumab (GAT) with the anti-EGFR Tomuzotuximab (TO) or Panitumumab in patients with refractory solid tumors. Macchini, M.; Garralda, E.; Fiedler, W.; Del Conte, G.; Rolling, C.; Kebenko, M.; Klinghammer, K.F.; Ahrensfath, I.; Habel, B.; Baumeister, H.; Zurlo, A.; Ochsenreiter, S. 2020. *Eur J Cancer*. 138: 5 - 6. IF: 7,275.

Genome wide association study of acute radiation toxicity and quality of life in breast cancer patients – results from the REQUITE cohort study. Rattay, T.; Veal, C.D.; Azria, D.; Chang-Claude, J.; Davidson, S.; Dunning, A.; de Ruysscher, D.; Fachal, L.; Gutierrez-Enriquez, S.; Lambin, P.; Rancati, T.; Rosenstein, B.S.; Seibold, P.; Sperk, E.; Symonds, R.P.; Vega, A.; Veldeman, L.; Webb, A.J.; West, C.M.L.; Talbot, C.J.; REQUITE Study Group. 2020. *Eur J Cancer*. 138: 12 - 12. IF: 7,275.

Nine-year survival outcome of neoadjuvant lapatinib with trastuzumab for HER2-positive breast cancer (NeoALTTO, BIG 1-06): final analysis of a multicentre, open-label, phase 3 randomised clinical trial. Nuciforo, P.; Townend, J.; Saura, C.; de Azumbaja, E.; Hilbers, F.; Manukyants, A.; Werutsky, G.; Bliss, J.; Moebus, V.; Colleoni, M.; Aspitia, A.M.; Di Cosimo, S.; Van dooren, V.; Kroep, J.; Ferro, A.; Cameron, D.; Gelber, R.; Piccart-Gebhart, M.; Huober, J. 2020. *Eur J Cancer*. 138: 15 - 16. IF: 7,275.

Unique clinico-biological, genetic and prognostic features of adult early T cell precursor acute lymphoblastic *Leukemia*. Genescà E; Morgades M; Montesinos P; Barba P; Gil C; Guàrdia R; Moreno MJ; Martínez-Carballeira D; García-Cadenas I; Vives S; Ribera J; González-Campos J; González-Gil C; Zamora L; Ramírez JL; Díaz-Beya M; Mercadal S; Artola MT; Cladera A; Tormo M; Bermúdez A; Vall-Llovera F; Martínez P; Amigo ML; Monsalvo S; Novo A; Cervera M; García-Guiñon A; Juncà J; Ciudad J; Orfao A; Ribera JM. 2020. *Haematologica*. 105(6): 294 - 297. IF: 7,116.

Impact of cytogenetic abnormalities on outcomes of adult Philadelphia-negative acute lymphoblastic leukemia after allogeneic hematopoietic stem cell transplantation: a study by the Acute Leukemia Working Committee of the Center for International Blood and Marrow Transplant Research. Lazaryan A; Dolan M; Zhang MJ; Wang HL; Kharfan-Dabaja MA; Marks DI; Bejanyan N; Copelan E; Majhail NS; Waller EK; Chao N; Prestidge T; Nishihori T; Kebriaei P; Inamoto Y; Hamilton B; Hashmi SK; Kamble RT; Bacher U; Hildebrandt GC; Stiff PJ; McGuirk J; Aldoss I; Beitinjaneh AM; Muffly L; Vij R; Olsson RF; Byrne M; Schultz KR; Aljurf M; Seftel M; Savoie ML; Savani BN; Verdonck LF; Cairo MS; Hossain N; Bhatt VR; Frangoul HA; Abdel-Azim H; Al Malki M; Munker R; Rizzieri D; Khera N; Nakamura R; Ringdén O; van der Poel M; Murthy HS; Liu H; Mori S; De Oliveira S; Bolaños-Meade J; Elsawy M; Barba P; et al.... 2020. *Haematologica*. 105(5): 1329 - 1338. IF: 7,116.

Daratumumab displays in vitro and in vivo anti-tumor activity in models of B-cell non-Hodgkin lymphoma and improves responses to standard chemo-immunotherapy regimens. Vidal-Crespo A; Matas-Céspedes A; Rodriguez V; Rossi C; Valero JG; Serrat N; Sanjuan Pla A; Menéndez P; Roué G; López-Guillermo A; Giné E; Campo E; Colomer D; Bezombes C; Lammerts van Bueren J; Chiu C; Doshi P; Pérez-Galán P. 2020. *Haematologica*. 105(4): 1032 - 1041. IF: 7,116.

Health-related quality of life associated with trifluridine/tipiracil in heavily pretreated metastatic gastric cancer: results from TAGS. Tabernero J; Alsina M; Shitara K; Doi T; Dvorkin M; Mansoor W; Arkenau HT; Prokharau A; Ghidini M; Faustino C; Gorbunova V; Zhavrid E; Nishikawa K; Ando T; Yalçin S; Van Cutsem E; Sabater J; Skanji D; Leger C; Amellal N; Ilson DH. 2020. *Gastric Cancer*. 23(4): 689 - 698. IF: 7,088.

Urelumab alone or in combination with rituximab in patients with relapsed or refractory B-cell lymphoma. Timmerman J; Herbaux C; Ribrag V; Zelenetz AD; Houot R; Neelapu SS; Logan T; Lossos IS; Urba W; Salles G; Ramchandren R; Jacobson C; Godwin J; Carpio C; Lathers D; Liu Y; Neely J; Suryawanshi S; Koguchi Y; Levy R. 2020. *Am J Hematol*. 95(5): 510 - 520. IF: 6,973.

Second cancers in MPN: Survival analysis from an international study. Marchetti M; Ghirardi A; Masciulli A; Carobbio A; Palandri F; Vianelli N; Rossi E; Betti S; Di Veroli A; Iurlo A; Cattaneo D; Finazzi G; Bonifacio M; Scaffidi L; Patriarca A; Rumi E; Casetti IC; Stephenson C; Guglielmelli P; Elli EM; Palova M; Rapezzi D; Erez D; Gomez M; Wille K; Perez-Encinas M; Lunghi F; Angona A; Fox ML; Beggiato E; Benevolo G; Carli G; Cacciola R; McMullin MF; Tieghi A; Recasens V; Isfort S; Pane F; De Stefano V; Griesshammer M; Alvarez-Larran A; Vannucchi AM; Rambaldi A; Barbui T. 2020. *Am J Hematol*. 95(3): 295 - 301. IF: 6,973.

Simple spectroscopic determination of the hard protein corona composition in AuNPs: Albumin at 75%. Vitali M; Casals E; Canals F; Colomé N; Puntes V. 2020. *Nanoscale*. 12(29): 15832 - 15844. IF: 6,895.

Molecular subtypes and the evolution of treatment management in metastatic colorectal cancer. Martini G; Dienstmann R; Ros J; Baraibar I; Cuadra-Urteaga JL; Salva F; Ciardiello D; Mulet N; Argiles G; Tabernero J; Elez E. 2020. *Ther Adv Med Oncol*. 12: 1758835920936089. IF: 6,852.

Practical considerations in the use of regorafenib in metastatic colorectal cancer. Loupakis F; Antonuzzo L; Bachet JB; Kuan FC; Macarulla T; Pietrantonio F; Xu RH; Taniguchi H; Winder T; Yuki S; Zeng S; Bekaii-Saab T. 2020. *Ther Adv Med Oncol*. 12: 1758835920956862. IF: 6,852.

Towards a cancer mission in Horizon Europe: recommendations. Berns A; Ringborg U; Celis JE; Heitor M; Aaronson NK; Abou-Zeid N; Adami HO; Apostolidis K; Baumann M; Bardelli A; Bernards R; Brandberg Y; Caldas C; Calvo F; Dive C; Eggert A; Eggermont A; Espina C; Falkenburg F; Foucaud J; Hanahan D; Helbig U; Jönsson B; Kalager M; Karjalainen S; Kásler M; Kearns P; Kärre K; Lacombe D; de Lorenzo F; Meunier F; Nettekoven G; Oberst S; Nagy P; Philip T; Price R; Schüz J; Solary E; Strang P; Tabernero J; Voest E. 2020. *Mol Oncol*. 14(8): 1589 - 1615. IF: 6,574.

Trastuzumab Emtansine Plus Non-Pegylated Liposomal Doxorubicin in HER2-Positive Metastatic Breast Cancer (Thelma): A Single-Arm, Multicenter, Phase Ib Trial. López-Miranda E; Pérez-García JM; Di Cosimo S; Brain E; Ravnik M; Escrivá-de-Romaní S; Vidal M; Gligorov J; Borštnar S; Calabuig L; Sampayo-Cordero M; Malfettone A; Llombart-Cussac A; Suter TM; Cortés J. 2020. *Cancers (Basel)*. 12(12). IF: 6,126.

Hereditary Leiomyomatosis and Renal Cell Cancer Syndrome in Spain: Clinical and Genetic Characterization. Sánchez-Heras AB; Castillejo A; García-Díaz JD; Robledo M; Teulé A; Sánchez R; Zúñiga Á; Lastra E; Durán M; Llort G; Yagüe C; Ramon Y Cajal T; López San Martin C; López-Fernández A; Balmaña J; Robles L; Mesa-Latorre JM; Chirivella I; Fonfria M; Perea Ibañez R; Castillejo MI; Escandell I; Gomez L; Berbel P; Soto JL. 2020. *Cancers (Basel)*. 12(11). IF: 6,126.

TSPAN1: A Novel Protein Involved in Head and Neck Squamous Cell Carcinoma Chemoresistance. Garcia-Mayea Y; Mir C; Carballo L; Castellvi J; Temprana-Salvador J; Lorente J; Benavente S; García-Pedrero JM; Allonca E; Rodrigo JP; LLeonart ME. 2020. *Cancers (Basel)*. 12(11). IF: 6,126.

CDK4/6 Inhibitors in Hormone Receptor-Positive Metastatic Breast

Cancer: Current Practice and Knowledge. de Melo Gagliato D; C Buzaid A; Perez-Garcia JM; Llombart A; Cortes J. 2020. *Cancers (Basel)*. 12(9). IF: 6,126.

Phase II Clinical Trial of Pembrolizumab in Patients with Progressive Metastatic Pheochromocytomas and Paragangliomas. Jimenez C; Subbiah V; Stephen B; Ma J; Milton D; Xu M; Zarifa A; Akhmedzhanov FO; Tsimberidou A; Habra MA; Rodon Anhert J; Fu S; Naing A. 2020. *Cancers (Basel)*. 12(8). IF: 6,126.

Presenting Features and Early Mortality from SARS-CoV-2 Infection in Cancer Patients during the Initial Stage of the COVID-19 Pandemic in Europe. Pinato DJ; Lee AJX; Biello F; Seguí E; Aguilar-Company J; Carbó A; Bruna R; Bower M; Rizzo G; Benafif S; Carmona C; Chopra N; Cruz CA; D'Avanzo F; Evans JS; Galazi M; Garcia-Fructuoso I; Dalla Pria A; Newsom-Davis T; Ottaviani D; Patriarca A; Reyes R; Sharkey R; Sng CCT; Wong YNS; Ferrante D; Scotti L; Avanzi GC; Bellan M; Castello LM; Marco-Hernández J; Mollà M; Pirisi M; Ruiz-Camps I; Sainaghi PP; Gaidano G; Brunet J; Tabernero J; Prat A; Gennari A. 2020. *Cancers (Basel)*. 12(7). IF: 6,126.

Molecular Features of Metaplastic Breast Carcinoma: An Infrequent Subtype of Triple Negative Breast Carcinoma. González-Martínez S; Pérez-Mies B; Carretero-Barrio I; Palacios-Berraquero ML; Perez-García J; Cortés J; Palacios J. 2020. *Cancers (Basel)*. 12(7): 1 - 13. IF: 6,126.

Comprehensive Constitutional Genetic and Epigenetic Characterization of Lynch-Like Individuals. Dámaso E; González-Acosta M; Vargas-Parra G; Navarro M; Balmaña J; Ramon Y Cajal T; Tuset N; Thompson BA; Marín F; Fernández A; Gómez C; Velasco À; Solanes A; Iglesias S; Urgel G; López C; Del Valle J; Campos O; Santacana M; Matias-Guiu X; Lázaro C; Valle L; Brunet J; Pineda M; Capellá G. 2020. *Cancers (Basel)*. 12(7). IF: 6,126.

Effect of Baseline Characteristics on Cabazitaxel Treatment Duration in Patients with Metastatic Castration-Resistant Prostate Cancer: A Post Hoc Analysis of the Compassionate Use/Expanded Access Programs and CAPRISTANA Registry. Malik Z; Di Lorenzo G; Pichler A; De Giorgi U; Hitier S; Ecstein-Fraisse E; Ozatilgan A; Carles J. 2020. *Cancers (Basel)*. 12(4). IF: 6,126.

Safety of Aflibercept in Metastatic Colorectal Cancer: A Literature Review and Expert Perspective on Clinical and Real-World Data. Muro K; Salinardi T; Singh AR; Macarulla T. 2020. *Cancers (Basel)*. 12(4). IF: 6,126.

Pharmacological Modulation of SAMHD1 Activity by CDK4/6 Inhibitors Improves Anticancer Therapy. Castellví M; Felip E; Ezeonwumelu IJ; Badia R; Garcia-Vidal E; Pujantell M; Gutiérrez-Chamorro L; Teruel I; Martínez-Cardús A; Clotet B; Riveira-Muñoz E; Margelí M; Ballana E. 2020. *Cancers (Basel)*. 12(3). IF: 6,126.

The Second Generation Antibody-Drug Conjugate SYD985 Overcomes Resistances to T-DM1. Nadal-Serrano M; Morancho B; Escrivá-de-Romaní S; Morales CB; Luque A; Escorihuela M; Espinosa Bravo M; Peg V; Dijcks FA; Dokter WHA; Cortés J; Saura C; Arribas J. 2020. *Cancers (Basel)*. 12(3). IF: 6,126.

The Spectrum of FANCM Protein Truncating Variants in European Breast Cancer Cases. Figlioli G; Kvist A; Tham E; Soukupova J; Kleiblova P; Muranen TA; Andrieu N; Azzollini J; Balmaña J; Barroso A; Benítez J; Bertelsen B; Blanco A; Bonanni B; Borg Å; Brunet J; Calistri D; Calvello M; Chvojka S; Cortesi L; Darder E; Valle JD; Diez O; et al.... 2020. *Cancers (Basel)*. 12(2). IF: 6,126.

Pitfalls in assessing stromal tumor infiltrating lymphocytes (sTILs) in breast cancer. Kos, Z.; Roblin, E.; Kim, R.S.; Michiels, S.; Gallas, B.D.; Chen, W.; van de Vijver, K.K.; Goel, S.; Adams, S.; Demaria, S.; Viale, G.; Nielsen, T.O.; Badve, S.S.; Symmans, W.F.; Sotiriou, C.; Rimm, D.L.; Hewitt, S.; Denkert, C.; Loibl, S.; Luen, S.J.; Bartlett, J.M.S.; Savas, P.; Pruneri, G.; Dillon, D.A.; Cheang, M.C.U.; Tutt, A.; Hall, J.A.; Kok, M.; Horlings, H.M.; Madabhushi, A.; van der Laak, J.; Ciompi, F.; Laenkholm, A.-V.; Bellolio, E.; Gruosso, T.; Fox, S.B.; Araya, J.C.; Floris, G.; Hudecek, J.; Voorwerk, L.; Beck, A.H.; Kerner, J.; Larsimont, D.; Declercq, S.; Van den Eynden, G.; Pusztai, L.; Ehinger, A.; Yang, W.; AbdulJabbar, K.; Yuan, Y.; Singh, R.; Hiley, C.; Bakir, M.; Lazar, A.J.; Naber, S.; Wienert, S.; Castillo, M.; Curigliano, G.; Dieci, M.-V.; André, F.; Swanton, C.; Reis-Filho, J.; Sparano, J.; Balslev, E.; Chen, I.-C.; Stovgaard, E.I.S.; Pogue-Geile, K.; Blenman, K.R.M.; Penault-Llorca, F.; Schnitt, S.; Lakhani, S.R.; Vincent-Salomon, A.; Rojo, F.; Braybrooke, J.P.; Hanna, M.G.; Soler-Monsó, M.T.; Bethmann, D.; Castaneda, C.A.; Willard-Gallo, K.; Sharma, A.; Lien, H.-C.; Fineberg, S.; Thagaard, J.; Comerma, L.; Gonzalez-Ericsson, P.; Brogi, E.; Loi, S.; Saltz, J.; Klaushen, F.; Cooper, L.; Amgad, M.; Moore, D.A.; Salgado, R.; Hyytiäinen, A.; Hida, A.I.; Thompson, A.; Lefevre, A.; Gown, A.; Lo, A.; Sapino, A.; Moreira, A.M.; Richardson, A.; Vingiani, A.; Bellizzi, A.M.; Guerrero, A.; Grigoriadis, A.; Garrido-Castro, A.C.; Cimino-Mathews, A.; Srinivasan, A.; Acs, B.; Singh, B.; Calhoun, B.; Haibe-Kans, B.; Solomon, B.; Thapa, B.; Nelson, B.H.; Ballesteroes-Merino, C.; Criscitiello, C.; Boeckx, C.; Colpaert, C.; Quinn, C.; Chennubhotla, C.S.; Solinas, C.; Drubay, D.; Sabanathan, D.; Peeters, D.; Zardavas, D.; Höflmayer, D.; Johnson, D.B.; Thompson, E.A.; Perez, E.; ElGabry, E.A.; Blackley, E.F.; Reisenbichler, E.; Chmielik, E.; Gaire, F.; Lu, F.-I.; Azmoudeh-Ardalan, F.; Peale, F.; Hirsch, F.R.; Acosta-Haab, G.; Farshid, G.; Broeckx, G.; Koeppen, H.; Haynes, H.R.; McArthur, H.; Joensuu, H.; Olofsson, H.; Cree, I.; Nederlof, I.; Frahm, I.; Brcic, I.; Chan, J.; Ziai, J.; Brock, J.; Weseling, J.; Giltnane, J.; Lemonnier, J.; Zha, J.; Ribeiro, J.; Lennerz, J.K.; Carter, J.M.; Hartman, J.; Hainfellner, J.; Le Quesne, J.; Juco, J.W.; van den Berg, J.; Sanchez, J.; Cucherousset, J.; Adam, J.; Balko, J.M.; Saeger, K.; Siziopikou, K.; Sikorska, K.; Weber, K.; Steele, K.E.; Emancipator, K.; El Bairi, K.; Allison, K.H.; Korski, K.; Buisseret, L.; Shi, L.; Kooreman, L.F.S.; Molinero, L.; Estrada, M.V.; Van Seijen, M.; Lacroix-Triki, M.; Sebastian, M.M.; Balancin, M.L.; Mathieu, M.-C.; van de Vijver, M.; Rebelatto, M.C.; Piccart, M.; Goetz, M.P.; Preusser, M.; Khojasteh, M.; Sanders, M.E.; Regan, M.M.; Barnes, M.; Christie, M.; Misialek, M.; Ignatiadis, M.; de Maaker, M.; Van Bockstal, M.; Harbeck, N.; Tung, N.; Laudus, N.; Sirtaine, N.; Burchardi, N.; Ternes, N.; Radosevic-Robin, N.; Gluz, O.; Grimm, O.; Nuciforo, P.; et al... 2020. *NPJ Breast Cancer*. 6: 17 - 17. IF: 6,000.

Application of a risk-management framework for integration of stromal tumor-infiltrating lymphocytes in clinical trials. Hudecek, J.; Voorwerk, L.; van Seijen, M.; Nederlof, I.; de Maaker, M.; van den Berg, J.; van de Vijver, K.K.; Sikorska, K.; Adams, S.; Demaria, S.; Viale, G.; Nielsen, T.O.; Badve, S.S.; Michiels, S.; Symmans, W.F.; Sotiriou, C.; Rimm, D.L.; Hewitt, S.M.; Denkert, C.; Loibl, S.; Loi, S.; Bartlett, J.M.S.; Pruneri, G.; Dillon, D.A.; Cheang, M.C.U.; Tutt, A.; Hall, J.A.; Kos, Z.; Salgado, R.; Kok, M.; Horlings, H.M.; Hyytiäinen, A.; Hida, A.I.; Thompson, A.; Lefevre, A.; Lazar, A.J.; Gown, A.; Lo, A.; Sapino, A.; Madabhushi, A.; Moreira, A.; Richardson, A.; Vingiani, A.; Beck, A.H.; Bellizzi, A.M.; Guerrero, A.; Grigoriadis, A.; Ehinger, A.; Garrido-Castro, A.; Vincent-Salomon, A.; Laenkholm, A.-V.; Sharma, A.; Cimino-Mathews, A.; Srinivasan, A.; Acs, B.; Singh, B.; Calhoun, B.; Haibe-Kans, B.; Solomon, B.; Thapa, B.; Nelson, B.H.; Gallas, B.D.; Castaneda, C.; Ballesteros-Merino, C.; Criscitiello, C.; Boeckx, C.; Colpaert, C.; Quinn, C.; Chennubhotla, C.S.; Swanton, C.; Solinas, C.; Hiley, C.; Drubay, D.; Bethmann, D.; Moore, D.A.; Larsimont, D.; Sabanathan, D.; Peeters, D.; Zardavas, D.; Höflmayer, D.; Johnson, D.B.; Thompson, E.A.; Brogi, E.; Perez, E.; ElGabry, E.A.; Stovgaard, E.S.; Blackley, E.F.; Roblin, E.; Reisenbichler, E.; Bellolio, E.; Balslev, E.; Chmielik, E.; Gaire, F.; Andre, F.; Lu, F.-I.; Azmoudeh-Ardalan, F.; Rojo, F.; Gruosso, T.; Ciompi, F.; Peale, F.; Hirsch, F.R.; Klauschen, F.; Penault-Llorca, F.; Acosta Haab, G.; Farshid, G.; van den Eynden, G.; Curigliano, G.; Floris, G.; Broeckx, G.; Gonzalez-Ericsson; Koeppen, H.;

Haynes, H.R.; McArthur, H.; Joensuu, H.; Olofsson, H.; Lien, H.-C.; Chen, I.-C.; Cree, I.; Frahm, I.; Brcic, I.; Chan, J.; Ziai, J.; Brock, J.; Wesseling, J.; Giltnane, J.; Kerner, J.K.; Thagaard, J.; Braybrooke, J.P.; van der Laak, J.A.W.M.; Lemonnier, J.; Zha, J.; Ribeiro, J.; Lennerz, J.K.; Carter, J.M.; Saltz, J.; Hartman, J.; Hainfellner, J.; Quesne, J.L.; Juco, J.W.; Reis-Filho, J.; Sanchez, J.; Sparano, J.; Cucherousset, J.; Araya, J.C.; Adam, J.; Balko, J.M.; Saeger, K.; Siziopikou, K.; Willard-Gallo, K.; Weber, K.; Pogue-Geile, K.L.; Steele, K.E.; Emancipator, K.; AbdulJabbar, K.; El Bairi, K.; Blenman, K.R.M.; Allison, K.H.; Korski, K.; Pusztai, L.; Comerma, L.; Buisseret, L.; Cooper, L.A.D.; Shi, L.; Kooreman, L.F.S.; Molinero, L.; Estrada, M.V.; Lacroix-Triki, M.; Al Bakir, M.; Sebastian, M.M.; van de Vijver, M.; Balancin, M.L.; Dieci, M.V.; Mathieu, M.-C.; Rebelatto, M.C.; Piccart, M.; Hanna, M.G.; Goetz, M.P.; Preusser, M.; Khojasteh, M.; Sanders, M.E.; Regan, M.M.; Barnes, M.; Christie, M.; Misialek, M.; Ignatiadis, M.; van Bockstal, M.; Castillo, M.; Amgad, M.; Harbeck, N.; Tung, N.; Laudus, N.; Sirtaine, N.; Burchardi, N.; Ternes, N.; Radosevic-Robin, N.; Gluz, O.; Grimm, O.; Nuciforo, P.; et al.... 2020. *NPJ Breast Cancer.* 6: 15 - 15. IF: 6,000.

Report on computational assessment of Tumor Infiltrating Lymphocytes from the International Immuno-Oncology Biomarker Working Group. Amgad M; Stovgaard ES; Balslev E; Thagaard J; Chen W; Dudgeon S; Sharma A; Kerner JK; Denkert C; Yuan Y; AbdulJabbar K; Wienert S; Savas P; Voorwerk L; Beck AH; Madabhushi A; Hartman J; Sebastian MM; Horlings HM; Hudecek J; Ciompi F; Moore DA; Singh R; Roblin E; Balancin ML; Mathieu MC; Lennerz JK; Kirtani P; Chen IC; Braybrooke JP; Pruneri G; Demaria S; Adams S; Schnitt SJ; Lakhani SR; Rojo F; Comerma L; Badve SS; Khojasteh M; Symmans WF; Sotiriou C; Gonzalez-Ericsson P; Pogue-Geile KL; Kim RS; Rimm DL; Viale G; Hewitt SM; Bartlett JMS; Penault-Llorca F; Goel S; Lien HC; Loibl S; Kos Z; Loi S; Hanna MG; Michiels S; Kok M; Nielsen TO; Lazar AJ; Bago-Horvath Z; Kooreman LFS; van der Laak JAWM; Saltz J; Gallas BD; Kurkure U; Barnes M; Salgado R; Cooper LAD; International Immuno-Oncology Biomarker Working Group. 2020. *NPJ Breast Cancer.* 6: 16 - 16. IF: 6,000.

Histological Subtypes and Response to PD-1/PD-L1 Blockade in Advanced Urothelial Cancer: A Retrospective Study. Miller NJ; Khaki AR; Diamantopoulos LN; Bilen MA; Santos V; Agarwal N; Morales-Barrera R; Devitt M; Nelson A; Hoimes CJ; Shreck E; Assi H; Gartrell BA; Sankin A; Rodriguez-Vida A; Lythgoe M; Pinato DJ; Drakaki A; Joshi M; Isaacsson Velho P; Hahn N; Liu S; Alonso Buznego L; Duran I; Moses M; Jain J; Murgic J; Barata P; Tripathi A; Zakharia Y; Galsky MD; Sonpavde G; Yu EY; Lyman GH; Grivas P. 2020. *J Urol.* 204(1): 63 - 69. IF: 5,925.

Practice Recommendations for Risk-Adapted Head and Neck Cancer Radiation Therapy During the COVID-19 Pandemic: An ASTRO-ESTRO Consensus Statement. Thomson, David J.; Palma, David; Guckenberger, Matthias; Balermpas, Panagiotis; Beitler, Jonathan J.; Blanchard, Pierre; Brizel, David; Budach, Wilfred; Caudell, Jimmy; Corry, June; Corvo, Renzo; Evans, Mererid; Garden, Adam S.; Giralt, Jordi; Gregoire, Vincent; Harari, Paul M.; Harrington, Kevin; Hitchcock, Ying J.; Johansen, Jorgen; Kaanders, Johannes; Koyfman, Shlomo; Langendijk, J. A.; Le, Quynh-Thu; Lee, Nancy; Margalit, Danielle; Mierzwa, Michelle; Porceddu, Sandro; Soong, Yoke Lim; Sun, Ying; Thariat, Juliette; Waldron, John; Yom, Sue S. 2020. *Int J Radiat Oncol Biol Phys.* 107(4): 618 - 627. IF: 5,859.

Randomized Phase 2 Trial of a Novel Clonidine Mucoadhesive Buccal Tablet for the Amelioration of Oral Mucositis in Patients Treated With Concomitant Chemoradiation Therapy for Head and Neck Cancer. Giralt J; Tao Y; Kortmann RD; Zasadny X; Contreras-Martinez J; Ceruse P; Arias de la Vega F; Lalla RV; Ozsahin EM; Pajkos G; Mazar A; Attali P; Bossi P; Vasseur B; Sonis S; Henke M; Bensadoun RJ. 2020. *Int J Radiat Oncol Biol Phys.* 106(2): 320 - 328. IF: 5,859.

New therapeutic approaches to overcoming resistant EGFR exon 20 alterations. Li AM; Boichard A; Felip E; Kurzrock R. 2020. *Crit Rev Oncol Hematol.* 151: 102990 - 102990. IF: 5,833.

First-in-human Phase 1 open label study of the BET inhibitor ODM-207 in patients with selected solid tumours. Ameratunga M; Braña I; Bono P; Postel-Vinay S; Plummer R; Aspegren J; Korjamo T; Snapir A; de Bono JS. 2020. *Br J Cancer.* 123(12): 1730 - 1736. IF: 5,791.

Phase 1 study of mTORC1/2 inhibitor sapanisertib (TAK-228) in advanced solid tumours, with an expansion phase in renal, endometrial or bladder cancer.Voss MH; Gordon MS; Mita M; Rini B; Makker V; Macarulla T; Smith DC; Cervantes A; Puzanov I; Pili R; Wang D; Jalal S; Pant S; Patel MR; Neuwirth RL; Enke A; Shou Y; Sedarati F; Faller DV; Burris HA 3rd. 2020. *Br J Cancer.* 123(11): 1590 - 1598. IF: 5,791.

First-in-human, dose-escalation, phase 1 study of anti-angiopoietin-2 LY3127804 as monotherapy and in combination with ramucirumab in patients with advanced solid tumours. Martin-Liberal J; Hollebecque A; Aftimos P; Jungels C; Martin-Romano P; Rodon J; Kremer JD; Zhang W; Bendell J. 2020. *Br J Cancer.* 123(8): 1235 - 1243. IF: 5,791.

Repurposing anticancer drugs for COVID-19-induced inflammation, immune dysfunction, and coagulopathy. Saini KS; Lanza C; Romano M; de Azambuja E; Cortes J; de Las Heras B; de Castro J; Lamba Saini M; Loibl S; Curigliano G; Twelves C; Leone M; Patnaik MM. 2020. *Br J Cancer.* 123(5): 694 - 697. IF: 5,791.

Imatinib in combination with phosphoinositol kinase inhibitor buparlisib in patients with gastrointestinal stromal tumour who failed prior therapy with imatinib and sunitinib: a Phase 1b, multicentre study. Gelderblom H; Jones RL; George S; Valverde Morales C; Benson C; Jean-Yves Blay; Renouf DJ; Doi T; Le Cesne A; Leahy M; Hertle S; Aimone P; Brandt U; Schöffski P. 2020. *Br J Cancer.* 122(8): 1158 - 1165. IF: 5,791.

Transcriptional response to metal starvation in the emerging pathogen Mycoplasma genitalium is mediated by Fur-dependent and -independent regulatory pathways. Martínez-Torró C; Torres-Puig S; Monge M; Sánchez-Alba L; González-Martín M; Marcos-Silva M; Perálvarez-Marín A; Canals F; Querol E; Piñol J; Pich OQ. 2020. *Emerg Microbes Infect.* 9(1): 5 - 19. IF: 5,776.

Pembrolizumab for the treatment of programmed death-ligand 1-positive advanced carcinoid or pancreatic neuroendocrine tumors: Results from the KEYNOTE-028 study. Mehnert JM; Bergsland E; O'Neil BH; Santoro A; Schellens JHM; Cohen RB; Doi T; Ott PA; Pishvaian MJ; Puzanov I; Aung KL; Hsu C; Le Tourneau C; Hollebecque A; Élez E; Tamura K; Gould M; Yang P; Stein K; Piha-Paul SA. 2020. *Cancer.* 126(13): 3021 - 3030. IF: 5,742.

Preclinical Activity of PI3K Inhibitor Copanlisib in Gastrointestinal Stromal Tumor. García-Valverde A; Rosell J; Serna G; Valverde C; Carles J; Nuciforo P; Fletcher JA; Arribas J; Politz O; Serrano C. 2020. *Mol Cancer Ther.* 19(6): 1289 - 1297. IF: 5,615.

A Phase I Study of LY3009120, a Pan-RAF Inhibitor, in Patients with Advanced or Metastatic Cancer. Sullivan, Ryan J.; Hollebecque, Antoine; Flaherty, Keith T.; Shapiro, Geoffrey I.; Ahnert, Jordi Rodon; Millward, Michael J.; Zhang, Wei; Gao, Ling; Sykes, Amanda; Willard, Melinda D.; Yu, Danni; Schade, Andrew E.; Crowe, KrisAnne; Flynn, Daniel L.; Kaufman, Michael D.; Henry, James R.; Peng, Sheng-Bin; Benhadji, Karim A.; Conti, Ilaria; Gordon, Michael S.; Tiu, Ramon V.;

Hong, David S. 2020. *Mol Cancer Ther.* 19(2): 460 - 467. IF: 5,615.

Identification of Expression Profiles Defining Distinct Prognostic Subsets of Radioactive-Iodine Refractory Differentiated Thyroid Cancer from the DECISION Trial. Capdevila J; Matos I; Mancuso FM; Iglesias C; Nuciforo P; Zafon C; Palmer HG; Ogbah Z; Muinos L; Hernando J; Villacampa G; Peña CE; Tabernero J; Brose MS; Schlumberger M; Vivancos A. 2020. *Mol Cancer Ther.* 19(1): 312 - 317. IF: 5,615.

The role of eosinophil morphology in distinguishing between reactive eosinophilia and eosinophilia as a feature of a myeloid neoplasm. Goasguen JE; Bennett JM; Bain BJ; Brunning R; Zini G; Vallespi MT; Tomonaga M; Locher C; International Working Group on Morphology of MDS. 2020. *Br J Haematol*. 191(3): 497 - 504. IF: 5,518.

Acute myeloid leukemia with NPM1 mutation and favorable European LeukemiaNet category: outcome after preemptive intervention based on measurable residual disease. Bataller A; Oñate G; Diaz-Beyá M; Guijarro F; Garrido A; Vives S; Tormo M; Arnan M; Salamero O; Sampol A; Coll R; Vall-Llovera F; Oliver-Caldés A; López-Guerra M; Pratcorona M; Zamora L; Villamon E; Roué G; Blanco A; Nomdedeu JF; Colomer D; Brunet S; Sierra J; Esteve J; Grupo Cooperativo Para el Estudio y Tratamiento de las Leucemias Agudas y Mielo. 2020. *Br J Haematol*. 191(1): 52 - 61. IF: 5,518.

Single-agent daratumumab in patients with relapsed and refractory multiple myeloma requiring dialysis: results of a Spanish retrospective, multicentre study. Cejalvo MJ; Legarda M; Abella E; Cabezudo E; Encinas C; García-Feria A; Gironella M; Iñigo B; Martín J; Ribas P; Ruíz MÁ; González Y; Vicuña I; Ramírez Á; Fernández P; de la Rubia J. 2020. *Br J Haematol*. IF: 5,518.

Micronuclei, dmin chromosomes and MYC amplifications as a singular presentation of myeloid malignancies. Montoro MJ; Rivero E; Teixidó M; Rodriguez Y; Chávez C; Salamero O; Navarrete M; Talavera E; Ortega M; Valcárcel D. 2020. *Br J Haematol*. 191(1): 19 - 22. IF: 5,518.

Clinical outcome and prognostic factors of patients with Richter syndrome: real-world study of the Spanish Chronic Lymphocytic Leukemia Study Group (GELLC). Abrisqueta P; Delgado J; Alcoceba M; Oliveira AC; Loscertales J; Hernández-Rivas JA; Ferrà C; Cordoba R; Yáñez L; Medina A; Motlló C; Iacoboni G; Villacampa G; González M; Bosch F. 2020. *Br J Haematol*. 190(6): 854 - 863. IF: 5,518.

Checkpoint inhibitors in AML: are we there yet? Ghosh, A.; Barba, P.; Perales, M.-A. 2020. *Br J Haematol*. 188: 159 - 167. IF: 5,518.

MYC, MYCL, and MYCN as therapeutic targets in lung cancer. Massó-Vallés D; Beaulieu ME; Soucek L. 2020. *Expert Opin Ther Targets.* 24(2): 101 - 114. IF: 5,473.

Phase I/IIa, open-label, multicentre study to evaluate the optimal dosing and safety of ODM-203 in patients with advanced or metastatic solid tumours. Bono P; Massard C; Peltola KJ; Azaro A; Italiano A; Kristeleit RS; Curigliano G; Lassen U; Arkenau HT; Hakulinen P; Garratt C; Ikonen T; Mustonen MVJ; Rodon JA. 2020. *ESMO Open*. 5(6): e001081. IF: 5,329.

First-line PARP inhibitors in ovarian cancer: summary of an ESMO Open - Cancer Horizons round-table discussion. Banerjee S; Gonzalez-Martin A; Harter P; Lorusso D; Moore KN; Oaknin A; Ray-Coquard I. 2020. *ESMO Open*. 5(6): e001110. IF: 5,329.

Clinical research disruption in the post-COVID-19 era: will the pandemic lead to change? Lorusso D; Ray-Coquard I; Oaknin A; Banerjee S. 2020. *ESMO Open*. 5(5): e000924. IF: 5,329.

Oncological care organisation during COVID-19 outbreak. Onesti CE; Rugo HS; Generali D; Peeters M; Zaman K; Wildiers H; Harbeck N; Martin M; Cristofanilli M; Cortes J; Tjan-Heijnen V; Hurvitz SA; Berchem G; Tagliamento M; Campone M; Bartsch R; De Placido S; Puglisi F; Rottey S; Müller V; Ruhstaller T; Machiels JP; Conte P; Awada A; Jerusalem G. 2020. *ESMO Open*. 5(4). IF: 5,329.

Effect of trifluridine/tipiracil in patients treated in RECOURSE by prognostic factors at baseline: an exploratory analysis. Tabernero J; Argiles G; Sobrero AF; Borg C; Ohtsu A; Mayer RJ; Vidot L; Moreno Vera SR; Van Cutsem E. 2020. *ESMO Open*. 5(4). IF: 5,329.

Phase I, open-label, multicentre study of buparlisib in combination with temozolomide or with concomitant radiation therapy and temozolomide in patients with newly diagnosed glioblastoma. Wen PY; Rodon JA; Mason W; Beck JT; DeGroot J; Donnet V; Mills D; El-Hashimy M; Rosenthal M. 2020. *ESMO Open*. 5(4). IF: 5,329.

ESMO Management and treatment adapted recommendations in the COVID-19 era: Lung cancer. Passaro A; Addeo A; Von Garnier C; Blackhall F; Planchard D; Felip E; Dziadziuszko R; de Marinis F; Reck M; Bouchaab H; Peters S. 2020. *ESMO Open*. 5(Suppl 3). IF: 5,329.

ESMO Management and treatment adapted recommendations in the COVID-19 era: Breast Cancer. de Azambuja E; Trapani D; Loibl S; Delaloge S; Senkus E; Criscitiello C; Poortman P; Gnant M; Di Cosimo S; Cortes J; Cardoso F; Paluch-Shimon S; Curigliano G. 2020. *ESMO Open*. 5(Suppl 3): e000793. IF: 5,329.

First-line and second-line treatment of patients with metastatic pancreatic adenocarcinoma in routine clinical practice across Europe: a retrospective, observational chart review study. Taieb J; Prager GW; Melisi D; Westphalen CB; D'Esquermes N; Ferreras A; Carrato A; Macarulla T. 2020. *ESMO Open*. 5(1). IF: 5,329.

Immunotherapy in Breast Cancer: Current Practice and Clinical Challenges. de Melo Gagliato D; Buzaid AC; Perez-Garcia J; Cortes J. 2020. *Biodrugs*. 34(5): 611 - 623. IF: 5,313.

Immune-related hepatitis related to checkpoint inhibitors: Clinical and prognostic factors. Riveiro-Barciela M; Barreira-Díaz A; Vidal-González J; Muñoz-Couselo E; Martínez-Valle F; Viladomiu L; Mínguez B; Ortiz-Velez C; Castells L; Esteban R; Buti M. 2020. *Liver Int.* 40(8): 1906 - 1916. IF: 5,175.

Analysis of KRAS, NRAS, BRAF, PIK3CA and TP53 mutations in a large prospective series of locally advanced rectal cancer patients. Sclafani F; Hulkki Wilson S; Cunningham D; Gonzalez De Castro D; Kalaitzaki E; Begum R; Wotherspoon A; Capdevila J; Glimelius B; Roselló S; Thomas J; Tait D; Brown G; Oates J; Chau I. 2020. *Int J Cancer.* 146(1): 94 - 102. IF: 5,145.

Characterization of a Cytomegalovirus-Specific T Lymphocyte Product Obtained Through a Rapid and Scalable Production Process for Use in Adoptive Immunotherapy. Grau-Vorster, Marta; Lopez-Montanes, Maria; Canto, Ester; Vives, Joaquim; Oliver-Vila, Irene; Barba, Pere; Querol, Sergi; Rudilla, Francesc. 2020. *Front Immunol.* 11: 271. IF: 5,085.

Deep Sequencing of B Cell Receptor Repertoires From COVID-19 Patients Reveals Strong Convergent Immune

Signatures. Galson JD; Schaetzle S; Bashford-Rogers RJM; Raybould MIJ; Kovaltsuk A; Kilpatrick GJ; Minter R; Finch DK; Dias J; James LK; Thomas G; Lee WJ; Betley J; Cavlan O; Leech A; Deane CM; Seoane J; Caldas C; Pennington DJ; Pfeffer P; Osbourn J. 2020. *Front Immunol.* 11: 605170 - 605170. IF: 5,085.

Association of Bevacizumab Plus Oxaliplatin-Based Chemotherapy With Disease-Free Survival and Overall Survival in Patients With Stage II Colon Cancer: A Secondary Analysis of the AVANT Trial. Chibaudel B; Henriques J; Rakez M; Brenner B; Kim TW; Martinez-Villacampa M; Gallego-Plazas J; Cervantes A; Shim K; Jonker D; Guerin-Meyer V; Mineur L; Banzi C; Dewdney A; Dejthevaporn T; Bloemendal HJ; Roth A; Moehler M; Aranda E; Van Cutsem E; Tabernero J; Schmoll HJ; Hoff PM; André T; de Gramont A. 2020. *JAMA Netw Open.* 3(10): 2020425 - 2020425. IF: 5,032.

Activity of Platinum-Based Chemotherapy in Patients With Advanced Prostate Cancer With and Without DNA Repair Gene Aberrations. Schmid S; Omlin A; Higano C; Sweeney C; Martinez Chanza N; Mehra N; Kuppen MCP; Beltran H; Condeduca V; Vargas Pivato de Almeida D; Cotait Maluf F; Oh WK; Tsao CK; Sartor O; Ledet E; Di Lorenzo G; Yip SM; Chi KN; Bianchini D; De Giorgi U; Hansen AR; Beer TM; Pernelle L; Morales-Barrera R; Tucci M; Castro E; Karalis K; Bergman AM; Le ML; Zürrer-Härdi U; Pezaro C; Suzuki H; Zivi A; Klingbiel D; Schär S; Gillessen S. 2020. *JAMA Netw Open.* 3(10): e2021692. IF: 5,032.

The PALBONET Trial: A Phase II Study of Palbociclib in Metastatic Grade 1 and 2 Pancreatic Neuroendocrine Tumors (GETNE-1407). Grande E; Teulé A; Alonso-Gordoa T; Jiménez-Fonseca P; Benavent M; Capdevila J; Custodio A; Vera R; Munarriz J; La Casta A; Díez JJ; Gajate P; Molina-Cerrillo J; Matos I; Cristóbal EM; Ruffinelli JC; Palacios J; García-Carbonero R. 2020. *Oncologist.* 25(9): 745 - 745. IF: 5,025.

The McCAVE Trial: Vanucizumab plus mFOLFOX-6 Versus Bevacizumab plus mFOLFOX-6 in Patients with Previously Untreated Metastatic Colorectal Carcinoma (mCRC). Bendell JC; Sauri T; Gracián AC; Alvarez R; López-López C; García-Alfonso P; Hussein M; Miron ML; Cervantes A; Montagut C; Vivas CS; Bessudo A; Plezia P; Moons V; Andel J; Bennouna J; van der Westhuizen A; Samuel L; Rossomanno S; Boetsch C; Lahr A; Franjkovic I; Heil F; Lechner K; Krieter O; Hurwitz H; McCAVE Study Group. 2020. *Oncologist.* 25(3): e451-e459. IF: 5,025.

Phase Ib Study of Combination Therapy with MEK Inhibitor Binimetinib and Phosphatidylinositol 3-Kinase Inhibitor Buparlisib in Patients with Advanced Solid Tumors with RAS/RAF Alterations. Bardia A; Gounder M; Rodon J; Janku F; Lolkema MP; Stephenson JJ; Bedard PL; Schuler M; Sessa C; LoRusso P; Thomas M; Maacke H; Evans H; Sun Y; Tan DSW. 2020. *Oncologist.* 25(1): 160 - 169. IF: 5,025.

Real-World Delivery of Rucaparib to Patients with Ovarian Cancer: Recommendations Based on an Integrated Safety Analysis of ARIEL2 and Study 10. Drew Y; Kristeleit RS; Oaknin A; Ray-Coquard I; Haris NM; Swisher EM. 2020. *Oncologist.* 25(1): 109 - 119. IF: 5,025.

Immuno-priming durvalumab with bevacizumab in HER2-negative advanced breast cancer: a pilot clinical trial. Quintela-Fandino M; Holgado E; Manso L; Morales S; Bermejo B; Colomer R; Apala JV; Blanco R; Muñoz M; Caleiras E; Iranzo V; Martinez M; Dominguez O; Hornedo J; Gonzalez-Cortijo L; Cortes J; Gasol Cudos A; Malon D; Lopez-Alonso A; Moreno-Ortíz MC; Mouron S; Mañes S. 2020. *Breast Cancer Res.* 22(1): 124 - 124. IF: 4,988.

Phase 2 study of buparlisib (BKM120), a pan-class I PI3K inhibitor, in patients with metastatic triple-negative breast cancer. Garrido-Castro AC; Saura C; Barroso-Sousa R; Guo H; Ciruelos E; Bermejo B; Gavilá J; Serra V; Prat A; Paré L; Céliz P; Villagrasa P; Li Y; Savoie J; Xu Z; Arteaga CL; Krop IE; Solit DB; Mills GB; Cantley LC; Winer EP; Lin NU; Rodon J. 2020. *Breast Cancer Res.* 22(1): 120 - 120. IF: 4,988.

Effect of body mass index on response to neo-adjuvant therapy in HER2-positive breast cancer: an exploratory analysis of the NeoALTTO trial. Di Cosimo S; Porcu L; Agbor-Tarh D; Cinieri S; Franzoi MA; De Santis MC; Saura C; Huober J; Fumagalli D; Izquierdo M; Piccart M; Daidone MG; de Azambuja E. 2020. *Breast Cancer Res.* 22(1): 115 - 115. IF: 4,988.

Haplotype analysis of the internationally distributed BRCA1 c.3331_3334delCAAG founder mutation reveals a common ancestral origin in Iberia. Tuazon AMA; Lott P; Bohórquez M; Benavides J; Ramirez C; Criollo A; Estrada-Florez A; Mateus G; Velez A; Carmona J; Olaya J; Garcia E; Polanco-Echeverry G; Stultz J; Alvarez C; Tapia T; Ashton-Prolla P; Vega A; Lazaro C; Tornero E; Martinez-Bouzas C; Infante M; De La Hoya M; Diez O; Browning BL; Rannala B; Teixeira MR; Carvallo P; Echeverry M; Carvajal-Carmona LG; Brazilian Familial Cancer Network; COLUMBUS Consortium. 2020. *Breast Cancer Res.* 22(1): 108 - 108. IF: 4,988.

Phase 1 study of capmatinib in MET-positive solid tumor patients: Dose escalation and expansion of selected cohorts. Bang YJ; Su WC; Schuler M; Nam DH; Lim WT; Bauer TM; Azaro A; Poon RTP; Hong D; Lin CC; Akimov M; Ghebremariam S; Zhao S; Giovannini M; Ma B. 2020. *Cancer Sci.* 111(2): 536 - 547. IF: 4,966.

Clinical Predictive Model of Multidrug Resistance in Neutropenic Cancer Patients with Bloodstream Infection Due to Pseudomonas aeruginosa. Gudiol C; Albasanz-Puig A; Laporte-Amargós J; Pallarès N; Mussetti A; Ruiz-Camps I; Puerta-Alcalde P; Abdala E; Oltolini C; Akova M; Montejo M; Mikulska M; Martín-Dávila P; Herrera F; Gasch O; Drgona L; Paz Morales H; Brunel AS; García E; Isler B; Kern WV; Morales I; Maestro-de la Calle G; Montero M; Kanj SS; Sipahi OR; Calik S; Márquez-Gómez I; Marin JI; Gomes MZR; Hemmatti P; Araos R; Peghin M; Del Pozo JL; Yáñez L; Tilley R; Manzur A; Novo A; Carratalà J; IRONIC Study Group. 2020. *Antimicrob Agents Chemother.* 64(4). IF: 4,904.

A Mouse Brain-based Multi-omics Integrative Approach Reveals Potential Blood Biomarkers for Ischemic Stroke. Simats A; Ramiro L; García-Berrocoso T; Briansó F; Gonzalo R; Martín L; Sabé A; Gill N; Penalba A; Colome N; Sánchez A; Canals F; Bustamante A; Rosell A; Montaner J. 2020. *Mol Cell Proteomics.* 19(12): 1921 - 1935. IF: 4,870.

Genetic Profile and Functional Proteomics of Anal Squamous Cell Carcinoma: Proposal for a Molecular Classification. Trilla-Fuertes L; Ghanem I; Gámez-Pozo A; Maurel J; G-Pastrián L; Mendiola M; Peña C; López-Vacas R; Prado-Vázquez G; López-Camacho E; Zapater-Moros A; Heredia V; Cuatrecasas M; García-Alfonso P; Capdevila J; Conill C; García-Carbonero R; Ramos-Ruiz R; Fortes C; Llorens C; Nanni P; Fresno Vara JÁ; Feliu J. 2020. *Mol Cell Proteomics.* 19(4): 690 - 700. IF: 4,870.

Practice recommendations for risk-adapted head and neck cancer radiotherapy during the COVID-19 pandemic: An ASTRO-ESTRO consensus statement. Thomson DJ; Palma D; Guckenberger M; Balermpas P; Beitler JJ; Blanchard P; Brizel D; Budach W; Caudell J; Corry J; Corvo R; Evans M; Garden AS; Giralt J; Gregoire V; Harari PM; Harrington K; Hitchcock YJ; Johansen J; Kaanders J; Koyfman S; Langendijk JA; Le QT; Lee N; Margalit D; Mierzwa M; Porceddu S; Soong YL; Sun Y; Thariat

J; Waldron J; Yom SS. 2020. *Radiother Oncol.* 151: 314 - 321. IF: 4,856.

Impact of non-adherence to radiotherapy on 1-year survival in cancer patients in Catalonia, Spain. Borras JM; Font R; Solà J; Macia M; Tuset V; Arenas M; Eraso A; Verges R; Farré N; Pedro A; Mollà M; Algara M; Solé JM; Mira M; Espinàs JA. 2020. *Radiother Oncol.* 151: 200 - 205. IF: 4,856.

Treatment of brain metastases in small cell lung cancer: Decision-making amongst a multidisciplinary panel of European experts. Putora PM; Fischer GF; Früh M; Califano R; Faivre-Finn C; Van Houtte P; McDonald F; Nestle U; Dziadziuszko R; Le Pechoux C; Ramella S; Belderbos J; Slotman BJ; Troost EGC; Peeters S; Widder J; Pöttgen C; Reck M; Blackhall F; Cappuzzo F; Besse B; Novello S; Garrido P; Felip E; O'Brien M; Paz Ares L; de Marinis F; Westeel V; De Ruysscher D. 2020. *Radiother Oncol.* 149: 84 - 88. IF: 4,856.

Compliance and tolerability of short-course radiotherapy followed by preoperative chemotherapy and surgery for high-risk rectal cancer - Results of the international randomized RAPIDO-trial. van der Valk MJM; Marijnen CAM; van Etten B; Dijkstra EA; Hilling DE; Kranenbarg EM; Putter H; Roodvoets AGH; Bahadoer RR; Fokstuen T; Ten Tije AJ; Capdevila J; Hendriks MP; Edhemovic I; Cervantes AMR; de Groot DJA; Nilsson PJ; Glimelius B; van de Velde CJH; Hospers GAP; Collaborative investigators. 2020. *Radiother Oncol.* 147: 75 - 83. IF: 4,856.

Commentary: SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China. Di Cosimo S; Porcu L; Malfettone A; Cortés J; Miceli R. 2020. *Front Oncol.* 10: 1223 - 1223. IF: 4,848.

Cell Plasticity-Related Phenotypes and Taxanes Resistance in Castration-Resistant Prostate Cancer. Jiménez N; Reig Ò; Montalbo R; Milà-Guasch M; Nadal-Dieste L; Castellano G; Lozano JJ; Victoria I; Font A; Rodriguez-Vida A; Carles J; Suárez C; Domènech M; Sala-González N; Fernández PL; Rodríguez-Carunchio L; Díaz S; Prat A; Marín-Aguilera M; Mellado B. 2020. *Front Oncol.* 10: 594023 - 594023. IF: 4,848.

External Validation of a Predictive Model for Acute Skin Radiation Toxicity in the REQUITE Breast Cohort. Rattay T; Seibold P; Aguado-Barrera ME; Altabas M; Azria D; Barnett GC; Bultijnck R; Chang-Claude J; Choudhury A; Coles CE; Dunning AM; Elliott RM; Farcy Jacquet MP; Gutiérrez-Enríquez S; Johnson K; Müller A; Post G; Rancati T; Reyes V; Rosenstein BS; De Ruysscher D; de Santis MC; Sperk E; Stobart H; Symonds RP; Taboada-Valladares B; Vega A; Veldeman L; Webb AJ; West CM; Valdagni R; Talbot CJ; REQUITE consortium. 2020. *Front Oncol.* 10: 575909 - 575909. IF: 4,848.

Therapy-Induced Modulation of the Tumor Microenvironment: New Opportunities for Cancer Therapies. Benavente S; Sánchez-García A; Naches S; LLeonart ME; Lorente J. 2020. *Front Oncol.* 10: 582884 - 582884. IF: 4,848.

Five microRNAs in Serum Are Able to Differentiate Breast Cancer Patients From Healthy Individuals. Feliciano A; González L; Garcia-Mayea Y; Mir C; Artola M; Barragán N; Martín R; Altés A; Castellvi J; Benavente S; Ramón Y Cajal S; Espinosa-Bravo M; Cortés J; Rubio IT; LLeonart ME. 2020. *Front Oncol.* 10: 586268 - 586268. IF: 4,848.

Patient-reported outcomes in a phase 2 study comparing atezolizumab alone or with bevacizumab vs sunitinib in previously untreated metastatic renal cell carcinoma. Pal SK; McDermott DF; Atkins MB; Escudier B; Rini BI; Motzer RJ; Fong L; Joseph RW; Oudard S; Ravaud A; Bracarda S; Suárez C; Lam ET; Choueiri TK; Ding B; Quach C; Hashimoto K; Schiff C; Piault-Louis E; Powles T. 2020. *BJU Int.* 126(1): 73 - 82. IF: 4,806.

Full donor chimerism without graft-versus-host disease: the key factor for maximum benefit of pre-emptive donor lymphocyte infusions (pDLI). Feliu J; Potter V; Grimaldi F; Clay J; Floro L; Saha C; Barber L; Orti G; Alnagar AA; Garcia-Muñoz R; Kenyon M; Krishnamurthy P; de Lavallade H; Raj K; McLornan D; Pagliuca A; Mufti GJ. 2020. *Bone Marrow Transplant.* 55(3): 562 - 569. IF: 4,725.

Choice of second-line systemic therapy in stage IV small cell lung cancer (SCLC) - A decision-making analysis amongst European lung cancer experts. Früh M; Panje CM; Reck M; Blackhall F; Califano R; Cappuzzo F; Besse B; Novello S; Garrido P; Felip E; O'Brien M; Paz Ares L; de Marinis F; Westeel V; De Ruysscher D; Putora PM. 2020. *Lung Cancer.* 146: 6 - 11. IF: 4,702.

Impact of lorlatinib on patient-reported outcomes in patients with advanced ALK-positive or ROS1-positive non-small cell lung cancer. Peters S; Shaw AT; Besse B; Felip E; Solomon BJ; Soo RA; Bearz A; Gadgeel SM; Lin CC; Kao S; Seto T; Masters ET; Abbattista A; Clancy JS; Thurm H; Reisman A; Peltz G; Ross Camidge D. 2020. *Lung Cancer.* 144: 10 - 19. IF: 4,702.

PD-1 blockade in recurrent or metastatic cervical cancer: Data from cemiplimab phase I expansion cohorts and characterization of PD-L1 expression in cervical cancer. Rischin D; Gil-Martin M; González-Martin A; Braña I; Hou JY; Cho D; Falchook GS; Formenti S; Jabbour S; Moore K; Naing A; Papadopoulos KP; Baranda J; Fury W; Feng M; Stankevich E; Li J; Yama-Dang NA; Yoo SY; Lowy I; Mathias M; Fury MG. 2020. *Gynecol Oncol.* 159(2): 322 - 328. IF: 4,623.

Neratinib in patients with HER2-mutant, metastatic cervical cancer: Findings from the phase 2 SUMMIT basket trial. Oaknin A; Friedman CF; Roman LD; D'Souza A; Brana I; Clement-Bidard F; Goldman J; Alvarez EA; Boni V; ElNaggar AC; Passalacqua R; Do KTM; Santin AD; Keyvanjah K; Xu F; Eli LD; Lalani AS; Bryce RP; Hyman DM; Meric-Bernstam F; Solit DB; Monk BJ. 2020. *Gynecol Oncol.* 159(1): 150 - 156. IF: 4,623.

The effect of age on efficacy, safety and patient-centered outcomes with rucaparib: A post hoc exploratory analysis of ARIEL3, a phase 3, randomized, maintenance study in patients with recurrent ovarian carcinoma. Colombo N; Oza AM; Lorusso D; Aghajanian C; Oaknin A; Dean A; Weberpals JI; Clamp AR; Scambia G; Leary A; Holloway RW; Gancedo MA; Fong PC; Goh JC; O'Malley DM; Armstrong DK; Banerjee S; García-Donas J; Swisher EM; Meunier J; Cameron T; Maloney L; Goble S; Bedel J; Ledermann JA; Coleman RL. 2020. *Gynecol Oncol.* 159(1): 101 - 111. IF: 4,623.

Phase II study of pembrolizumab efficacy and safety in women with recurrent small cell neuroendocrine carcinoma of the lower genital tract. Frumovitz M; Westin SN; Salvo G; Zarifa A; Xu M; Yap TA; Rodon AJ; Karp DD; Abonofal A; Jazaeri AA; Naing A. 2020. *Gynecol Oncol.* 158(3): 570 - 575. IF: 4,623.

Pharmacokinetic Drug-Drug Interaction of Apalutamide, Part 1: Clinical Studies in Healthy Men and Patients with Castration-Resistant Prostate Cancer. Duran I; Carles J; Bulat I; Hellemans P; Mitselos A; Ward P; Jiao J; Armas D; Chien C. 2020. *Clin Pharmacokinet.* 59(9): 1135 - 1148. IF: 4,604.

Zanubrutinib for the treatment of MYD88 wild-type Waldenström macroglobulinemia: a substudy of the phase 3 ASPEN trial. Dimopoulos M; Sanz RG; Lee HP; Trneny M; Varettoni M; Opat S; D'Sa S; Owen RG; Cull G; Mulligan S; Czyz J; Castillo JJ; Motta M; Siddiqi T; Gironella Mesa M; Granell Gorrochategui M; Talaulikar D; Zinzani PL; Askari E; Grosicki S; Oriol A; Rule S; Kloczko J; Tedeschi A; Buske C; Leblond V; Trotman J; Chan WY; Michel J; Schneider J; Tan Z; Cohen A; Huang J;

Tam CS. 2020. *Blood Adv.* 4(23): 6009 - 6018. IF: 4,584.

Extra copies of MYC, BCL2, and BCL6 and outcome in patients with diffuse large B-cell lymphoma. Sermer D; Bobillo S; Dogan A; Zhang Y; Seshan V; Lavery JA; Batlevi C; Caron P; Hamilton A; Hamlin P; Horwitz S; Joffe E; Kumar A; Matasar M; Noy A; Owens C; Moskowitz A; Palomba ML; Straus D; von Keudell G; Rodriguez-Rivera I; Falchi L; Zelenetz A; Yahalom J; Younes A. 2020. *Blood Adv.* 4(14): 3382 - 3390. IF: 4,584.

Reduced intensity conditioning for acute myeloid leukemia using melphalan- vs busulfan-based regimens: a CIBMTR report. Zhou Z; Nath R; Cerny J; Wang HL; Zhang MJ; Abdel-Azim H; Agrawal V; Ahmed G; Al-Homsi AS; Aljurf M; Alkhateeb HB; Assal A; Bacher U; Bajel A; Bashir Q; Battiwalla M; Bhatt VR; Byrne M; Cahn JY; Cairo M; Choe H; Copelan E; Cutler C; Damlaj MB; DeFilipp Z; De Lima M; Diaz MA; Farhadfar N; Foran J; Freytes CO; Gerds AT; Gergis U; Grunwald MR; Gul Z; Hamadani M; Hashmi S; Hertzberg M; Hildebrandt GC; Hossain N; Inamoto Y; Isola L; Jain T; Kamble RT; Khan MW; Kharfan-Dabaja MA; Kebriaei P; Kekre N; Khera N; Lazarus HM; Liesveld JL; Litzow M; Liu H; Marks DI; Martino R; Mathews V; Mishra A; Murthy HS; Nagler A; Nakamura R; Nathan S; Nishihori T; Olin R; Olsson RF; Palmisiano N; Patel SS; Patnaik MM; Pawarode A; Perales MA; Politikos I; Popat U; Rizzieri D; Sandmaier BM; Savani BN; Seo S; Shah NN; Uy GL; Valcárcel D; Verdonck LF; Waller EK; Wang Y; Weisdorf D; Wirk B; Wong E; Yared JA; Saber W. 2020. *Blood Adv.* 4(13): 3180 - 3190. IF: 4,584.

Early Modulation of Circulating MicroRNAs Levels in HER2-Positive Breast Cancer Patients Treated with Trastuzumab-Based Neoadjuvant Therapy. Di Cosimo S; Appierto V; Pizzamiglio S; Silvestri M; Baselga J; Piccart M; Huober J; Izquierdo M; de la Pena L; Hilbers FS; de Azambuja E; Untch M; Pusztai L; Pritchard K; Nuciforo P; Vincent-Salomon A; Symmans F; Apolone G; de Braud FG; Iorio MV; Verderio P; Daidone MG. 2020. *Int J Mol Sci.* 21(4). IF: 4,556.

Helpful Criteria When Implementing NGS Panels in Childhood Lymphoblastic *Leukemia*. Vega-Garcia N; Benito R; Esperanza-Cebollada E; Llop M; Robledo C; Vicente-Garcés C; Alonso J; Barragán E; Fernández G; Hernández-Sánchez JM; Martín-Izquierdo M; Maynou J; Minguela A; Montaño A; Ortega M; Torrebadell M; Cervera J; Sánchez J; Jiménez-Velasco A; Riesco S; Hernández-Rivas JM; Lassaletta Á; Fernández JM; Rives S; Dapena JL; Ramírez M; Camós M; On Behalf Of The Group Of Leukemia Of The Spanish Society Of Pediatric Hematolog. 2020. *J Pers Med.* 10(4). IF: 4,433.

Clinical implications of intratumor heterogeneity: challenges and opportunities. Ramon y Cajal, Santiago; Sese, Marta; Capdevila, Claudia; Aasen, Trond; De Mattos-Arruda, Leticia; Diaz-Cano, Salvador J.; Hernandez-Losa, Javier; Castellvi, Josep. 2020. *J Mol Med (Berl).* 98(2): 161 - 177. IF: 4,427.

How a Barcelona Post-Acute Facility became a Referral Center for Comprehensive Management of Subacute Patients With COVID-19. Inzitari M; Udina C; Len O; Ars J; Arnal C; Badani H; Davey V; Risco E; Ayats P; de Andrés AM; Mayordomo C; Ros FJ; Morandi A; Cesari M. 2020. *J Am Med Dir Assoc.* 21(7): 954 - 957. IF: 4,367.

Structural and Biophysical Insights into the Function of the Intrinsically Disordered Myc Oncoprotein. Beaulieu ME; Castillo F; Soucek L. 2020. *Cells.* 9(4). IF: 4,366.

Blocking Myc to Treat Cancer: Reflecting on Two Decades of Omomyc. Massó-Vallés D; Soucek L. 2020. *Cells.* 9(4). IF: 4,366.

Treatment with daratumumab in patients with relapsed/refractory AL amyloidosis: a multicentric retrospective study and review of the literature. Lecumberri R; Krsnik I; Askari E; Sirvent M; González-Pérez MS; Escalante F; Pradillo V; Tamariz LE; Cánovas V; Alegre A; Gironella M; González-García ME; Infante MS; Lakhwani S; Martínez-Bilbao C; Dourdil V; Ramírez-Payer Á; Sarrá J; Cibeira MT. 2020. *Amyloid.* 27(3): 163 - 167. IF: 4,323.

Cerebrospinal fluid circulating tumour DNA as a liquid biopsy for central nervous system malignancies. Escudero L; Martínez-Ricarte F; Seoane J. 2020. *Curr Opin Neurol.* 33(6): 736 - 741. IF: 4,207.

Clinical and Translational Challenges in Thyroid Cancer. Hernando J; Ros J; Arroyo A; Capdevila J. 2020. *Curr Med Chem.* 27(29): 4806 - 4822. IF: 4,184.

STK11 (LKB1) missense somatic mutant isoforms promote tumor growth, motility and inflammation. Granado-Martínez P; Garcia-Ortega S; González-Sánchez E; McGrail K; Selgas R; Grueso J; Gil R; Naldaiz-Gastesi N; Rhodes AC; Hernandez-Losa J; Ferrer B; Canals F; Villanueva J; Méndez O; Espinosa-Gil S; Lizcano JM; Muñoz-Couselo E; García-Patos V; Recio JA. 2020. *Commun Biol.* 3(1): 366 - 366. IF: 4,165.

Rivaroxaban for treatment of pediatric venous thromboembolism. An Einstein-Jr phase 3 dose-exposure-response evaluation. Young G; Lensing AWA; Monagle P; Male C; Thelen K; Willmann S; Palumbo JS; Kumar R; Nurmeev I; Hege K; Bajolle F; Connor P; Hooimeijer HL; Torres M; Chan AKC; Kenet G; Holzhauer S; Santamaría A; Amedro P; Beyer-Westendorf J; Martinelli I; Massicotte MP; Smith WT; Berkowitz SD; Schmidt S; Price V; Prins MH; Kubitza D; EINSTEIN-Jr. Phase 3 Investigators. 2020. *J Thromb Haemost.* 18(7): 1672 - 1685. IF: 4,157.

Incorporating traditional and emerging biomarkers in the clinical management of metastatic colorectal cancer: an update. Baraibar I; Ros J; Mulet N; Salvà F; Argilés G; Martini G; Cuadra JL; Sardo E; Ciardiello D; Tabernero J; Élez E. 2020. *Expert Rev Mol Diagn.* 20(7): 653 - 664. IF: 4,096.

Brain Penetration of Lorlatinib: Cumulative Incidences of CNS and Non-CNS Progression with Lorlatinib in Patients with Previously Treated ALK-Positive Non-Small-Cell Lung Cancer. Bauer TM; Shaw AT; Johnson ML; Navarro A; Gainor JF; Thurm H; Pithavala YK; Abbattista A; Peltz G; Felip E. 2020. *Target Oncol.* 15(1): 55 - 65. IF: 4,036.

(1)H NMR serum metabolomic profiling of patients at risk of cardiovascular diseases performing stress test. Lema C; Andrés M; Aguadé-Bruix S; Consegal M; Rodriguez-Sinovas A; Benito B; Ferreira-Gonzalez I; Barba I. 2020. *Sci Rep.* 10(1): 17838 - 17838. IF: 3,998.

Efficacy of eribulin for metastatic breast cancer based on localization of specific secondary metastases: a post hoc analysis. O'Shaughnessy J; Cortes J; Twelves C; Goldstein LJ; Alexis K; Xie R; Barrios C; Ueno T. 2020. *Sci Rep.* 10(1): 11203 - 11203. IF: 3,998.

An electronic alert system increases screening for hepatitis B and C and improves management of patients with haematological disorders. Riveiro-Barciela, Mar; Gubern, Paula; Roade, Luisa; Abrisqueta, Pau; Jose Carreras, Maria; Farriols, Anna; Bosch, Francesc; Esteban, Rafael; Buti, Maria. 2020. *Sci Rep.* 10(1): 3038. IF: 3,998.

The sacral chordoma margin. Radaelli, S.; Fossati, P.; Stacchiotti, S.; Akiyama, T.; Asencio, J. M.; Bandiera, S.; Boglione, A.; Boland, P.; Bolle, S.; Bruland, O.; Brunello, A.; Bruzzi, P.; Campanacci, D.; Cananzi, F.; Capanna, R.; Casadei, R.; Cordoba, A.; Court, C.; Dei Tos, A.

P.; DeLaney, T. F.; De Paoli, A.; De Pas, T. M.; Desai, A.; Di Brina, L.; Donati, D. M.; Fabbri, N.; Fiore, M. R.; Frezza, A.; Gambarotti, M.; Gasbarrini, A.; Georg, P.; Grignani, G.; Hindi, N.; Hug, E. B.; Jones, R.; Kawai, A.; Krol, A. D.; Le Grange, F.; Luzzati, A.; Marquina, G.; Martin-Benlloch, J. A.; Mazzocco, K.; Navarria, F.; Navarria, P.; Parchi, P. D.; Patel, S.; Pennacchioli, E.; Petrongari, M. G.; Picci, P.; Pollock, R.; Porcu, L.; Quagliuolo, V; Sangalli, C.; Scheipl, S.; Scotto, G. M.; Spalek, M.; Steinmeier, T.; Timmermann, B.; Trama, A.; Uhl, M.; Valverde, C.; Varga, P. P.; Verges, R.; Weber, D. C.; Zoccali, C.; Casali, P. G.; Sommer, J.; Gronchi, A. 2020. *Eur J Surg Oncol.* 46(8): 1415 - 1422. IF: 3,959.

Predicting Survival after Allogeneic Hematopoietic Cell Transplantation in Myelofibrosis: Performance of the Myelofibrosis Transplant Scoring System (MTSS) and Development of a New Prognostic Model. Hernández-Boluda JC; Pereira A; Alvarez-Larran A; Martín AA; Benzaquen A; Aguirre L; Mora E; González P; Mora J; Dorado N; Sampol A; García-Gutiérrez V; López-Godino O; Fox ML; Reguera JL; Pérez-Encinas M; Pascual MJ; Xicoy B; Parody R; González-Pinedo L; Español I; Avendaño A; Correa JG; Vallejo C; Jurado M; García-Cadenas I; Osorio S; Durán MA; Sánchez-Guijo F; Cervantes F; Piñana JL. 2020. *Biol Blood Marrow Transplant.* 26(12): 2237 - 2244. IF: 3,853.

A Personalized Prediction Model for Outcomes after Allogeneic Hematopoietic Cell Transplant in Patients with Myelodysplastic Syndromes. Nazha A; Hu ZH; Wang T; Lindsley RC; Abdel-Azim H; Aljurf M; Bacher U; Bashey A; Cahn JY; Cerny J; Copelan E; DeFilipp Z; Diaz MA; Farhadfar N; Gadalla SM; Gale RP; George B; Gergis U; Grunwald MR; Hamilton B; Hashmi S; Hildebrandt GC; Inamoto Y; Kalaycio M; Kamble RT; Kharfan-Dabaja MA; Lazarus HM; Liesveld JL; Litzow MR; Majhail NS; Murthy HS; Nathan S; Nishihori T; Pawarode A; Rizzieri D; Sabloff M; Savani BN; Schachter L; Schouten HC; Seo S; Shah NN; Solh M; Valcárcel D; Vij R; Warlick E; Wirk B; Wood WA; Yared JA; Alyea E; Popat U; Sobecks RM; Scott BL; Nakamura R; Saber W. 2020. *Biol Blood Marrow Transplant.* 26(11): 2139 - 2146. IF: 3,853.

Potential Survival Benefit for Patients Receiving Allogeneic Hematopoietic Stem Cell Transplantation after Nivolumab Therapy for Relapse/Refractory Hodgkin Lymphoma: Real-Life Experience in Spain. Martínez C; Carpio C; Heras I; Ríos-Herranz E; Buch J; Gutierrez A; Romero S; Zeberio I; García-García I; Rodriguez-Izquierdo A; Alonso R; Bargay J; Barrenetxea C; Domingo-Doménech E; de Haro ME; Palomera L; García-Sanz R; Spanish Group of Lymphoma and Bone Marrow Transplantation (GELTAMO). 2020. *Biol Blood Marrow Transplant.* 26(8): 1534 - 1542. IF: 3,853.

Analysis of Cell Subsets in Donor Lymphocyte Infusions from HLA Identical Sibling Donors after Allogeneic Hematopoietic Cell Transplant. Ortí G; Palacio-Garcia C; García-Cadenas I; Sanchez-Ortega I; Jimenez MJ; Azqueta C; Villacampa G; Ferrà C; Parody R; Martino R; Bosch F; Querol S; Valcárcel D. *Biol Blood Marrow Transplant.* IF: 3,853.

The Role of Donor Lymphocyte Infusion (DLI) in Post-Hematopoietic Cell Transplant (HCT) Relapse for Chronic Myeloid Leukemia (CML) in the Tyrosine Kinase Inhibitor (TKI) Era. Schmidt S; Liu Y; Hu ZH; Williams KM; Lazarus HM; Vij R; Kharfan-Dabaja MA; Ortí G; Wiernik PH; Weisdorf D; Kamble RT; Herzig R; Wirk B; Cerny J; Bacher U; Chaudhri NA; Nathan S; Farhadfar N; Aljurf M; Gergis U; Szer J; Seo S; Hsu JW; Olsson RF; Maharaj D; George B; Hildebrandt GC; Agrawal V; Nishihori T; Abdel-Azim H; Alyea E; Popat U; Sobecks R; Scott BL; Holter Chakrabarty J; Saber W. 2020. *Biol Blood Marrow Transplant.* 26(6): 1137 - 1143. IF: 3,853.

Prospective Randomized Study Comparing Myeloablative Unrelated Umbilical Cord Blood Transplantation versus HLA-Haploidentical Related Stem Cell Transplantation for Adults with Hematologic Malignancies. Sanz J; Montoro J; Solano C; Valcárcel D; Sampol A; Ferrá C; Parody R; Lorenzo I; Montesinos P; Ortí G; Hernández-Boluda JC; Balaguer-Roselló A; Guerreiro M; Carretero C; Sanz GF; Miguel A; Piñana JL. 2020. *Biol Blood Marrow Transplant.* 26(2): 358 - 366. IF: 3,853.

Real-world survival outcomes of heavily pretreated patients with refractory HR+, HER2-metastatic breast cancer receiving single-agent chemotherapy-a comparison with MONARCH 1. Rugo HS; Dieras V; Cortes J; Patt D; Wildiers H; O'Shaughnessy J; Zamora E; Yardley DA; Carter GC; Sheffield KM; Li L; Andre VAM; Li XI; Frenzel M; Huang YJ; Dickler MN; Tolaney SM. 2020. *Breast Cancer Res Treat.* 184(1): 161 - 172. IF: 3,831.

Real-world effectiveness of dual HER2 blockade with pertuzumab and trastuzumab for neoadjuvant treatment of HER2-positive early breast cancer (The NEOPETRA Study). González-Santiago S; Saura C; Ciruelos E; Alonso JL; de la Morena P; Santisteban Eslava M; Gallegos Sancho MI; de Luna A; Dalmau E; Servitja S; Ruiz Borrego M; Chacón JI. 2020. *Breast Cancer Res Treat.* 184(2): 469 - 479. IF: 3,831.

Vitamin D analogues exhibit antineoplastic activity in breast cancer patient-derived xenograft cells. Ferronato MJ; Nadal SM; Arenas Lahuerta EJ; Morales CB; Paolillo G; Martinez-Sabadell AA; Mascaró M; Vitale C; Fall Y; Arribas J; Facchinetti MM; Curino AC. *J Steroid Biochem Mol Biol.* 105735 - 105735. IF: 3,813.

Palbociclib combined with endocrine therapy in heavily pretreated HR+/HER2(-) advanced breast cancer patients: Results from the compassionate use program in Spain (PALBOCOMP). Manso L; Hernando C; Galán M; Oliveira M; Cabrera MA; Bratos R; Rodríguez CA; Ruiz-Borrego M; Blanch S; Llombart-Cussac A; Delgado-Mingorance JI; Álvarez-Busto I; Gallegos I; González-Cortijo L; Morales S; Aguirre E; Hernando BA; Ballesteros A; Alés-Martínez JE; Reboredo C; Oltra A; González-Cao M; Santisteban M; Malón D; Echeverría I; García-Garre E; Vega E; Servitja S; Andrés R; Robles CE; López R; Galve E; Echarri MJ; Legeren M; Moreno F. 2020. *Breast.* 54: 286 - 292. IF: 3,754.

Sequential immunohistochemistry and virtual image reconstruction using a single slide for quantitative KI67 measurement in breast cancer. Serna G; Simonetti S; Fasani R; Pagliuca F; Guardia X; Gallego P; Jimenez J; Peg V; Saura C; Eppenberger-Castori S; Ramon Y Cajal S; Terracciano L; Nuciforo P. 2020. *Breast.* 53: 102 - 110. IF: 3,754.

Cancer Surveillance Guideline for individuals with PTEN hamartoma tumour syndrome. Tischkowitz M; Colas C; Pouwels S; Hoogerbrugge N; PHTS Guideline Development Group; European Reference Network GENTURIS. 2020. *Eur J Hum Genet.* 28(10): 1387 - 1393. IF: 3,657.

Guidelines for the Li-Fraumeni and heritable TP53-related cancer syndromes. Frebourg T; Bajalica Lagercrantz S; Oliveira C; Magenheim R; Evans DG; European Reference Network GENTURIS. 2020. *Eur J Hum Genet.* 28(10): 1379 - 1386. IF: 3,657.

Neratinib plus capecitabine for the treatment of advanced HER2-positive breast cancer. Oliveira M; Garrigós L; Assaf JD; Escrivá-de-Romaní S; Saura C. 2020. *Expert Rev Anticancer Ther.* 20(9): 731 - 741. IF: 3,573.

Comprehensive Characterization of the Mutational Landscape in Localized Anal Squamous Cell Carcinoma. Trilla-Fuertes L; Ghanem I; Maurel J; G-Pastrián L; Mendiola M; Peña C; López-Vacas R; Prado-Vázquez G; López-Camacho E; Zapater-Moros A; Heredia V; Cuatrecasas M; García-Alfonso P; Capdevila J; Conill C; García-Carbonero R; Heath KE; Ramos-Ruiz R; Llorens C; Campos-Barros Á; Gámez-Pozo A; Feliu

J; Vara JÁF. 2020. *Transl Oncol.* 13(7): 100778 - 100778. IF: 3,558.

Homologous Recombination Repair Deficiency and the Immune Response in Breast Cancer: A Literature Review. Pellegrino B; Musolino A; Llop-Guevara A; Serra V; De Silva P; Hlavata Z; Sangiolo D; Willard-Gallo K; Solinas C. 2020. *Transl Oncol.* 13(2): 410 - 422. IF: 3,558.

Clinical Activity of Afatinib in Patients With Non-Small-Cell Lung Cancer Harboring Uncommon EGFR Mutations: A Spanish Retrospective Multicenter Study. Moran T; Taus A; Arriola E; Aguado C; Dómine M; Rueda AG; Calles A; Cedrés S; Viñolas N; Isla D; Palmero R; Sereno M; Diaz V; Juan O; Marsé R; Martorell PM; Sánchez Torres JM; Study Group for the Uncommon EGFR Mutations in Spain. 2020. *Clin Lung Cancer.* 21(5): 428-436.e2. IF: 3,550.

A phase 1b study of the MET inhibitor capmatinib combined with cetuximab in patients with MET-positive colorectal cancer who had progressed following anti-EGFR monoclonal antibody treatment. Delord JP; Argilés G; Fayette J; Wirth L; Kasper S; Siena S; Mesia R; Berardi R; Cervantes A; Dekervel J; Zhao S; Sun Y; Hao HX; Tiedt R; Vicente S; Myers A; Siu LL. 2020. *Invest New Drugs.* 38(6): 1774 - 1783. IF: 3,525.

Phase 1b/2a study of galunisertib, a small molecule inhibitor of transforming growth factor-beta receptor I, in combination with standard temozolomide-based radiochemotherapy in patients with newly diagnosed malignant glioma. Wick A; Desjardins A; Suarez C; Forsyth P; Gueorguieva I; Burkholder T; Cleverly AL; Estrem ST; Wang S; Lahn MM; Guba SC; Capper D; Rodon J. 2020. *Invest New Drugs.* 38(5): 1570 - 1579. IF: 3,525.

A randomized, phase 2 study of deoxyuridine triphosphatase inhibitor, TAS-114, in combination with S-1 versus S-1 alone in patients with advanced non-small-cell lung cancer. Yamamoto N; Hayashi H; Planchard D; Morán T; Gregorc V; Dowell J; Sakai H; Yoh K; Nishio M; Cortot AB; Benhadji KA; Soni N; Huang J; Makris L; Cedres S. 2020. *Invest New Drugs.* 38(5): 1588 - 1597. IF: 3,525.

Clinical characteristics and outcome of SARS-CoV-2 infection in admitted patients with chronic lymphocytic leukemia from a single European country. Muntañola A; Villacampa G; Hernández-Rivas JÁ; Alonso R; Mirás F; Osorio S; Baile M; Baltasar P; López Jiménez J; Hernandez-Rodriguez I; Valenciano S; Alfayate A; Gimeno E; Bárez A; Oliveira AC; Riaza R; Romero P; Delgado J; Yáñez L; Zabalza A; Torres A; Gómez-Roncero MI; Crespo M; Córdoba R; Mateos-Mazón JJ; Pérez S; Andreu R; Labrador J; Ruiz ME; Velasquez CA; Terol MJ; Santiago R; Vidal MJ; Campoy García F; Villalón L; Muiña BS; Soler JA; Seri C; Sánchez MJ; Cuesta A; Ramos R; Sánchez-Montalvá A; Ruiz-Camps I; González M; Abrisqueta P; Bosch F; of the GELLC (Grupo Español de Leucemia Linfática Crónica). 2020. *Exp Hematol Oncol.* 9(1): 37 - 37. IF: 3,492.

Risk factors and outcome of COVID-19 in patients with hematological malignancies. Piñana JL; Martino R; García-García I; Parody R; Morales MD; Benzo G; Gómez-Catalan I; Coll R; De La Fuente I; Luna A; Merchán B; Chinea A; de Miguel D; Serrano A; Pérez C; Diaz C; Lopez JL; Saez AJ; Bailen R; Zudaire T; Martínez D; Jurado M; Calbacho M; Vázquez L; Garcia-Cadenas I; Fox L; Pimentel AI; Bautista G; Nieto A; Fernandez P; Vallejo JC; Solano C; Valero M; Espigado I; Saldaña R; Sisinni L; Ribera JM; Jimenez MJ; Trabazo M; Gonzalez-Vicent M; Fernández N; Talarn C; Montoya MC; Cedillo A; Sureda A; Infectious Complications Subcommittee of the Spanish Hematopoietic Stem Cell Tr. 2020. *Exp Hematol Oncol.* 9: 21 - 21. IF: 3,492.

A pediatric regimen for adolescents and young adults with Philadelphia chromosome-negative acute lymphoblastic leukemia: Results of the ALLRE08 PETHEMA trial. Ribera, Josep-Maria; Morgades, Mireia; Montesinos, Pau; Tormo, Mar; Martinez-Carballeira, Daniel; Gonzalez-Campos, Jose; Gil, Cristina; Barba, Pere; Garcia-Boyero, Raimundo; Coll, Rosa; Pedreno, Maria; Ribera, Jordi; Mercadal, Santiago; Vives, Susana; Novo, Andres; Genesca, Eulalia; Hernandez-Rivas, Jesus-Maria; Bergua, Juan; Amigo, Maria-Luz; Vall-Llovera, Ferran; Martinez-Sanchez, Pilar; Calbacho, Maria; Garcia-Cadenas, Irene; Garcia-Guinon, Antoni; Sanchez-Sanchez, Maria-Jose; Cervera, Marta; Feliu, Evarist; Orfao, Alberto; Spanish Soc Hematology. 2020. *Cancer Med.* 9(7): 2317 - 2329. IF: 3,491.

VITAL phase 2 study: Upfront 5-fluorouracil, mitomycin-C, panitumumab and radiotherapy treatment in nonmetastatic squamous cell carcinomas of the anal canal (GEMCAD 09-02). Feliu J; Garcia-Carbonero R; Capdevila J; Guasch I; Alonso-Orduna V; Lopez C; Garcia-Alfonso P; Castanon C; Sevilla I; Cerezo L; Conill C; Quintana-Angel B; Sanchez ME; Ghanem I; Martin-Richard M; Lopez-Gomez M; Leon A; Caro M; Fernandez T; Maurel J. 2020. *Cancer Med.* 9(3): 1008 - 1016. IF: 3,491.

The microproteome of cancer: From invisibility to relevance. Merino-Valverde I; Greco E; Abad M. 2020. *Exp Cell Res.* 392(1): 111997 - 111997. IF: 3,383.

Presurgical identification of primary central nervous system lymphoma with normalized time-intensity curve: A pilot study of a new method to analyze DSC-PWI. Pons-Escoda, A.; Garcia-Ruiz, A.; Naval-Baudin, P.; Cos, M.; Vidal, N.; Plans, G.; Bruna, J.; Perez-Lopez, R.; Majos, C. 2020. *Am J Neuroradiol.* 41(10): 1816 - 1824. IF: 3,381.

Can we cure oligometastatic disease? A practical point of view. Pérez-García J; Cortez P; Gion M; Cortés J. 2020. *Curr Opin Oncol.* 32(6): 568 - 574. IF: 3,336.

Progress in the management of endometrial cancer (subtypes, immunotherapy, alterations in PIK3CA pathway): data and perspectives. Oaknin A; León-Castillo A; Lorusso D. 2020. *Curr Opin Oncol.* 32(5): 471 - 480. IF: 3,336.

Global Gene Expression Characterization of Circulating Tumor Cells in Metastasic Castration-Resistant Prostate Cancer Patients. León-Mateos L; Abalo A; Casas H; Anido U; Rapado-González Ó; Vieito M; Suárez-Cunqueiro M; Gómez-Tato A; Abal M; López-López R; Muinelo-Romay L. 2020. *J Clin Med.* 9(7). IF: 3,303.

Safety and preliminary signs of efficacy with the combination of pembrolizumab plus oxaliplatin and S-1 in Japanese gastric cancer patients. Alsina M; Smyth EC. 2020. *Ann Transl Med.* 8(24): 1696 - 1696. IF: 3,297.

Hitting the brakes on autophagy for overcoming acquired resistance in triple negative breast cancer. Bellio C; Villanueva J. 2020. *Ann Transl Med.* 8(14): 848 - 848. IF: 3,297.

Repolarization of tumor infiltrating macrophages and increased survival in mouse primary CNS lymphomas after XPO1 and BTK inhibition. Jiménez I; Carabia J; Bobillo S; Palacio C; Abrisqueta P; Pagès C; Nieto JC; Castellví J; Martínez-Ricarte F; Escoda L; Perla C; Céspedes Torrez DH; Boix J; Purroy N; Puigdefàbregas L; Seoane J; Bosch F; Crespo M. 2020. *J Neurooncol.* 149(1): 13 - 25. IF: 3,267.

Diagnostic delay and outcome in immunocompetent patients with primary central nervous system lymphoma in Spain: a multicentric study. Velasco R; Mercadal S; Vidal N; Alañá M; Barceló MI; Ibáñez-Juliá MJ; Bobillo S; Caldú Agud R; García Molina E; Martínez P; Cacabelos P; Muntañola A; García-Catalán G; Sancho JM; Camro I; Lado T; Erro ME; Gómez-Vicente L; Salar A; Caballero AC; Solé-Rodríguez M; Gállego Pérez-Larraya J; Huertas N;

Estela J; Barón M; Barbero-Bordallo N; Encuentra M; Dlouhy I; Bruna J; Graus F; GELTAMO and GENOSEN group. 2020. *J Neurooncol.* 148(3): 545 - 554. IF: 3,267.

A Phase Ib/II, open-label, multicenter study of INC280 (capmatinib) alone and in combination with buparlisib (BKM120) in adult patients with recurrent glioblastoma. van den Bent M; Azaro A; De Vos F; Sepulveda J; Yung WKA; Wen PY; Lassman AB; Joerger M; Tabatabai G; Rodon J; Tiedt R; Zhao S; Kirsilae T; Cheng Y; Vicente S; Balbin OA; Zhang H; Wick W. 2020. *J Neurooncol.* 146(1): 79 - 89. IF: 3,267.

Association of Consensus Molecular Subtypes and Molecular Markers With Clinical Outcomes in Patients With Metastatic Colorectal Cancer: Biomarker Analyses From LUME-Colon 1. Lenz HJ; Argiles G; Yoshino T; Tejpar S; Ciardiello F; Braunger J; Salnikov AV; Gabrielyan O; Schmid R; Höfler J; Kitzing T; Van Cutsem E.2020. *Clin Colorectal Cancer.* IF: 3,245.

Current Options for Third-line and Beyond Treatment of Metastatic Colorectal Cancer. Spanish TTD Group Expert Opinion. Fernandez-Montes, Ana; Gravalos, Cristina; Pericay, Carles; Safont, M. Jose; Benavides, Manuel; Elez, Elena; Garcia-Alfonso, Pilar; Garcia-Paredes, Beatriz; Carrato, Alfredo; Aranda, Enrique. 2020. *Clin Colorectal Cancer.* 19(3): 165 - 177. IF: 3,245.

Atezolizumab in the treatment of metastatic triple-negative breast cancer. Pérez-García J; Soberino J; Racca F; Gion M; Stradella A; Cortés J. 2020. Expert *Opin Biol Ther.* 20(9): 981 - 989. IF: 3,224.

The role of PIGF blockade in the treatment of colorectal cancer: overcoming the pitfalls. Macarulla T; Montagut C; Sánchez-Martin FJ; Granja M; Verdaguer H; Sastre J; Tabernero J. 2020. *Expert Opin Biol Ther.* 20(1): 15 - 22. IF: 3,224.

Phase II randomized trial of capecitabine with bevacizumab and external beam radiation therapy as preoperative treatment for patients with resectable locally advanced rectal adenocarcinoma: long term results. Salazar R; Capdevila J; Manzano JL; Pericay C; Martínez-Villacampa M; López C; Losa F; Safont MJ; Gómez-España A; Alonso-Orduña V; Escudero P; Gallego J; García-Paredes B; Palacios A; Biondo S; Grávalos C; Aranda E; Spanish Cooperative Group for the Treatment of Digestive Tumors (TTD). 2020. *BMC Cancer.* 20(1): 1164 - 1164. IF: 3,150.

Clinical value of next generation sequencing of plasma cell-free DNA in gastrointestinal stromal tumors. Serrano C; Vivancos A; López-Pousa A; Matito J; Mancuso FM; Valverde C; Quiroga S; Landolfi S; Castro S; Dopazo C; Sebio A; Virgili AC; Menso MM; Martín-Broto J; Sansó M; García-Valverde A; Rosell J; Fletcher JA; George S; Carles J; Arribas J. 2020. *BMC Cancer.* 20(1): 99 - 99. IF: 3,150.

Recommendations for screening, monitoring, prevention, and prophylaxis of infections in adult and pediatric patients receiving CAR T-cell therapy: a position paper. Los-Arcos I; Iacoboni G; Aguilar-Guisado M; Alsina-Manrique L; Díaz de Heredia C; Fortuny-Guasch C; García-Cadenas I; García-Vidal C; González-Vicent M; Hernani R; Kwon M; Machado M; Martínez-Gómez X; Maldonado VO; Pla CP; Piñana JL; Pomar V; Reguera-Ortega JL; Salavert M; Soler-Palacín P; Vázquez-López L; Barba P; Ruiz-Camps I. 2020. *Infection.* 1 - 17. IF: 3,040.

Feasibility of thiotepa addition to the fludarabine-busulfan conditioning with tacrolimus/sirolimus as graft vs host disease prophylaxis. Fox ML; García-Cadenas I; Pérez AM; Villacampa G; Piñana JL; Ortí G; Montoro J; Roldán E; Bosch Vilaseca A; Martino R; Salamero O; Saavedra S; Hernandez-Boluda JC; Esquirol A; Sierra J; Sanz J; Solano C; Bosch F; Barba P; Valcarcel D. 2020. *Leuk Lymphoma.* 61(8): 1823 - 1832. IF: 2,969.

Nomogram for Estimating Overall Survival in Patients With Metastatic Pancreatic Cancer. Goldstein D; Von Hoff DD; Chiorean EG; Reni M; Tabernero J; Ramanathan RK; Botteman M; Aly A; Margunato-Debay S; Lu B; Louis CU; McGovern D; Lee CK. 2020. *Pancreas.* 49(6): 744 - 750. IF: 2,920.

Landscape of Health-Related Quality of Life in Patients With Early-Stage Pancreatic Cancer Receiving Adjuvant or Neoadjuvant Chemotherapy: A Systematic Literature Review. Macarulla T; Hendifar AE; Li CP; Reni M; Riess H; Tempero MA; Dueck AC; Botteman MF; Deshpande CG; Lucas EJ; Oh DY. 2020. *Pancreas.* 49(3): 393 - 407. IF: 2,920.

Liposomal Irinotecan + 5-FU/LV in Metastatic Pancreatic Cancer: Subgroup Analyses of Patient, Tumor, and Previous Treatment Characteristics in the Pivotal NAPOLI-1 Trial. Macarulla Mercadé T; Chen LT; Li CP; Siveke JT; Cunningham D; Bodoky G; Blanc JF; Lee KH; Dean A; Belanger B; Wang-Gillam A. 2020. *Pancreas.* 49(1): 62 - 75. IF: 2,920.

Necrotizing fasciitis in haematological patients: a different scenario. Albasanz-Puig A; Rodríguez-Pardo D; Pigrau C; Lung M; Roldan E; Corona PS; Almirante B; Ruiz-Camps I. 2020. *Ann Hematol.* 99(8): 1741 - 1747. IF: 2,904.

The Value of Case Reports in Systematic Reviews from Rare Diseases. The Example of Enzyme Replacement Therapy (ERT) in Patients with Mucopolysaccharidosis Type II (MPS-II). Sampayo-Cordero M; Miguel-Huguet B; Malfettone A; Pérez-García JM; Llombart-Cussac A; Cortés J; Pardo A; Pérez-López J. 2020. *Int J Environ Res Public Health.* 17(18). IF: 2,849.

Long duration of immunotherapy in a STK11 mutated/KRAS wild-type non-small cell lung cancer patient. Domingues I; Perez SC; Callejo A; Vivancos A; Martinez-Marti A; Felip E. 2020. *Pulmonology.* 26(1): 49 - 50. IF: 2,778.

The role of ipilimumab after anti-PD-1 treatment: two case reports and a literature review. Ros-Montañá J; Saoudi-Gonzalez N; Ortiz-Velez C; Muñoz-Couselo E. 2020. *Melanoma Res.* 30(2): 209 - 212. IF: 2,750.

Latest progress in molecular biology and treatment in genitourinary tumours. González-Del-Alba A; Arranz JÁ; Bellmunt J; Maroto JP; Fernández-Calvo O; Valderrama BP; González-Billalabeitia E; Méndez-Vidal MJ; Cassinello J; Romero-Laorden N; Climent MÁ; Puente J; Peláez I; Lázaro-Quintela M; Gallardo E; Suárez C. 2020. *Clin Transl Oncol.* 22(12): 2175 - 2195. IF: 2,737.

Study of the Spanish Society of Medical Oncology (SEOM) on the access to oncology drugs and predictive biomarkers in Spain. Rodríguez-Lescure A; de la Peña FA; Aranda E; Calvo A; Felip E; Garrido P; Vera R. 2020. *Clin Transl Oncol.* 22(12): 2253 - 2263. IF: 2,737.

Analysis of mismatch repair (MMR) proteins expression in a series of malignant pleural mesothelioma (MPM) patients. Cedrés S; Ponce-Aix S; Iranzo P; Callejo A; Pardo N; Navarro A; Martinez-Marti A; Gómez-Abecia S; Zucchiatti AC; Sansano I; Enguita AB; Miquel JM; Viaplana C; Dienstmann R; Paz-Ares L; Felip E. 2020. *Clin Transl Oncol.* 22(8): 1390 - 1398. IF: 2,737.

Updated guidelines for predictive biomarker testing in advanced non-small-cell lung cancer: a National Consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology. Garrido P; Conde E; de Castro J; Gómez-Román JJ; Felip E; Pijuan L; Isla D; Sanz J; Paz-Ares L; López-Ríos F. 2020. *Clin Transl Oncol.* 22(7): 989 - 1003. IF: 2,737.

A spotlight on cancer researchers in Spain: new paradigms and disruptive

ideas. Ramón Y Cajal S; Sancho P; Soucek L; Peinado H; Abad M; Valiente M; Efeyan A; Pardo J; Quesada V; Jimeno J; Duque PM; Antón A; Varela I; Schuhmacher AJ. 2020. *Clin Transl Oncol.* 22(6): 798 - 801. IF: 2,737.

SEOR recommendations on the use of protons. Lloret-Saez-Bravo M; Giralt-L de Sagredo J; Contreras-Martinez J; Ferrer-Albiach C. 2020. *Clin Transl Oncol.* 22(6): 795 - 797. IF: 2,737.

Treatment options beyond immunotherapy in patients with wild-type lung adenocarcinoma: a Delphi consensus. Isla D; de Castro J; García-Campelo R; Lianes P; Felip E; Garrido P; Paz-Ares L; Trigo JM. 2020. *Clin Transl Oncol.* 22(5): 759 - 771. IF: 2,737.

A retrospective, multicenter study of the efficacy of lapatinib plus trastuzumab in HER2-positive metastatic breast cancer patients previously treated with trastuzumab, lapatinib, or both: the Trastyvere study. Gavilá J; De La Haba J; Bermejo B; Rodríguez-Lescure Á; Antón A; Ciruelos E; Brunet J; Muñoz-Couselo E; Santisteban M; Rodríguez Sánchez CA; Santaballa A; Sánchez Rovira P; García Sáenz JÁ; Ruiz-Borrego M; Guerrero-Zotano AL; Huerta M; Cotes-Sanchís A; Lao Romera J; Aguirre E; Cortés J; Llombart-Cussac A. 2020. *Clin Transl Oncol.* 22(3): 420 - 428. IF: 2,737.

SEOM clinical guidelines in hereditary breast and ovarian cancer (2019). González-Santiago S; Ramón Y Cajal T; Aguirre E; Alés-Martínez JE; Andrés R; Balmaña J; Graña B; Herrero A; Llort G; González-Del-Alba A; SEOM Hereditary Cancer Working Group. 2020. *Clin Transl Oncol.* 22(2): 193 - 200. IF: 2,737.

SEOM clinical guideline thyroid cancer (2019). Gallardo E; Medina J; Sánchez JC; Viúdez A; Grande E; Porras I; Ramón Y Cajal T; Trigo J; Iglesias L; Capdevila J. 2020. *Clin Transl Oncol.* 22(2): 223 - 235. IF: 2,737.

SEOM clinical guideline for the management of immune-related adverse events in patients treated with immune checkpoint inhibitors (2019). Majem M; García-Martínez E; Martinez M; Muñoz-Couselo E; Rodriguez-Abreu D; Alvarez R; Arance A; Berrocal A; de la Cruz-Merino L; Lopez-Martin JA. 2020. *Clin Transl Oncol.* 22(2): 213 - 222. IF: 2,737.

SEOM clinical guidelines for cervical cancer (2019). de Juan A; Redondo A; Rubio MJ; García Y; Cueva J; Gaba L; Yubero A; Alarcón J; Maximiano C; Oaknin A. 2020. *Clin Transl Oncol.* 22(2): 270 - 278. IF: 2,737.

SEOM clinical guideline for treatment of kidney cancer (2019). Lázaro M; Valderrama BP; Suárez C; de-Velasco G; Beato C; Chirivella I; González-Del-Alba A; Laínez N; Méndez-Vidal MJ; Arranz JA. 2020. *Clin Transl Oncol.* 22(2): 256 - 269. IF: 2,737.

Final Overall Survival Analysis of the SOGUG Phase 2 MAJA Study: Maintenance Vinflunine Versus Best Supportive Care After First-Line Chemotherapy in Advanced Urothelial Carcinoma. Bellmunt Molins J; García-Donas Jiménez J; Valderrama BP; Virizuela Echaburu JA; Hernando-Polo S; Climent Durán MÁ; Villa-Guzmán JC; Arranz Arija JÁ; Ostiategui ML; Milagro NL; González-Del-Alba A; González BM; Díaz EG; Gauna DC; Santasusana MD; Herranz UA; Del Muro Solans XG; Pérez-Gracia JL; Vázquez JP; Morales-Barrera R; Pous AF. 2020. *Clin Genitourin Cancer.* 18(6): 452 - 460. IF: 2,695.

High absolute lymphocyte counts are associated with longer overall survival in patients with metastatic breast cancer treated with eribulin-but not with treatment of physician's choice-in the EMBRACE study. Miyoshi Y; Yoshimura Y; Saito K; Muramoto K; Sugawara M; Alexis K; Nomoto K; Nakamura S; Saeki T; Watanabe J; Perez-Garcia JM; Cortes J. 2020. *Breast Cancer.* 27(4): 706 - 715. IF: 2,695.

Correlation of the tumour-stroma ratio with diffusion weighted MRI in rectal cancer. Zunder SM; Perez-Lopez R; de Kok BM; Raciti MV; van Pelt GW; Dienstmann R; Garcia-Ruiz A; Meijer CA; Gelderblom H; Tollenaar RA; Nuciforo P; Wasser MN; Mesker WE. 2020. *Eur J Radiol.* 133: 109345 - 109345. IF: 2,687.

A new targeted treatment for patients with a germlineBRCAmutation: olaparib in pancreatic cancer. Verdaguer, Helena; Acosta, Daniel; Macarulla, Teresa. 2020. *Future Oncol.* 16(33): 2691 - 2700. IF: 2,660.

Infigratinib in patients with advanced cholangiocarcinoma with FGFR2 gene fusions/translocations: the PROOF 301 trial. Makawita S; K Abou-Alfa G; Roychowdhury S; Sadeghi S; Borbath I; Goyal L; Cohn A; Lamarca A; Oh DY; Macarulla T; T Shroff R; Howland M; Li A; Cho T; Pande A; Javle M. 2020. *Future Oncol.* 16(30): 2375 - 2384. IF: 2,660.

FIGHT-302: first-line pemigatinib vs gemcitabine plus cisplatin for advanced cholangiocarcinoma with FGFR2 rearrangements. Bekaii-Saab TS; Valle JW; Cutsem EV; Rimassa L; Furuse J; Ioka T; Melisi D; Macarulla T; Bridgewater J; Wasan H; Borad MJ; Abou-Alfa GK; Jiang P; Lihou CF; Zhen H; Asatiani E; Féliz L; Vogel A. 2020. *Future Oncol.* 16(30): 2385 - 2399. IF: 2,660.

SOLTI-1503 PROMETEO TRIAL: combination of talimogene laherparepvec with atezolizumab in early breast cancer. Pascual T; Cejalvo JM; Oliveira M; Vidal M; Vega E; Ganau S; Julve A; Zamora E; Miranda I; Delgado A; Bermejo B; la Cruz-Merino L; Juan M; Ferrero-Cafiero JM; Canes J; Gonzalez X; Villagrasa P; Prat A. 2020. *Future Oncol.* 16(24): 1801 - 1813. IF: 2,660.

Atypical patterns of response and progression in the era of immunotherapy combinations. Ferrara R; Matos I. 2020. *Future Oncol.* 16(23): 1707 - 1713. IF: 2,660.

- NUC-1031/cisplatin versus gemcitabine/cisplatin in untreated locally advanced/metastatic biliary tract cancer (NuTide:121). McNamara MG; Goyal L; Doherty M; Springfeld C; Cosgrove D; Sjoquist KM; Park JO; Verdaguer H; Braconi C; Ross PJ; Gramont A; Zalcberg JR; Palmer DH; Valle JW; Knox JJ. 2020. *Future Oncol.* 16(16): 1069 - 1081. IF: 2,660.

TROPiCS-02: A Phase III study investigating sacituzumab govitecan in the treatment of HR+/HER2- metastatic breast cancer. Rugo HS; Bardia A; Tolaney SM; Arteaga C; Cortes J; Sohn J; Marmé F; Hong Q; Delaney RJ; Hafeez A; André F; Schmid P. 2020. *Future Oncol.* 16(12): 705 - 715. IF: 2,660.

nextMONARCH: Abemaciclib Monotherapy or Combined With Tamoxifen for Metastatic Breast Cancer. Hamilton E; Cortes J; Ozyilkan O; Chen SC; Petrakova K; Manikhas A; Jerusalem G; Hegg R; Huober J; Chapman SC; Lu Y; Hardebeck MC; Bear MM; Johnston EL; Martin M. 2020. *Clin Breast Cancer.* IF: 2,647.

Population pharmacokinetics and covariate analysis of Sym004, an antibody mixture against the epidermal growth factor receptor, in subjects with metastatic colorectal cancer and other solid tumors. Alifrangis L; Schoemaker R; Skartved NJ; Hald R; Montagut C; Kopetz S; Tabernero J; Kragh M; Wade JR. 2020. *J Pharmacokinet Pharmacodyn.* 47(1): 5 - 18. IF: 2,461.

Treatment of Frail Older Adults and Elderly Patients With Philadelphia Chromosome-negative Acute Lymphoblastic Leukemia: Results of a Prospective Trial With Minimal Chemotherapy. Ribera JM; García O; Chapchap EC; Gil C; González-Campos J; Barba P; Amigo ML; Moreno MJ; Lavilla E; Alonso N; Bergua JM; Tormo M;

Ribera J; Sierra M; Martínez-Carballeira D; Mercadal S; Hernández-Rivas JM; Vall-Llovera F; Genescà E; Cladera A; Novo A; Abella E; García-Cadenas I; Monteserín C; Bermúdez A; Piernas S; Montesinos P; López JL; García-Guiñón A; Serrano A; Martínez MP; Olivares M; López A; Serrano J; PETHEMA Group, Spanish Society of Hematology. 2020. *Clin Lymphoma Myeloma Leuk.* 20(8): 513 - 513. IF: 2,298.

Prognosis Assessment of Early-Stage Chronic Lymphocytic Leukemia: Are We Ready to Predict Clinical Evolution Without a Crystal Ball? Gonzalez-Gascon-y-Marin, Isabel; Munoz-Novas, Carolina; Figueroa, Inigo; Hernandez-Sanchez, Maria; Rodriguez-Vicente, Ana-Eugenia; Quijada-Alamo, Miguel; Perez-Carretero, Claudia; Moreno, Carol; Collado, Rosa; Espinet, Blanca; Puiggros, Anna; de las Heras, Natalia; Bosch, Francesc; Hernandez, Jose-Angel; Grp Espanol Leucemia Linfatica; Grp Cooperativo Espanol Citogenet. 2020. *Clin Lymphoma Myeloma Leuk.* 20(8): 548 - 548. IF: 2,298.

Prognostic value of the neutrophil/lymphocyte ratio in enteropancreatic neuroendocrine tumors. Grenader T; Pavel ME; Ruszniewski PB; Cwikla JB; Phan AT; Raderer M; Sedlácková E; Cadiot G; Wolin EM; Capdevila J; Wall L; Rindi G; Truong Thanh XM; Caplin ME; CLARINET Study Group. 2020. *Anticancer Drugs.* 31(3): 216 - 222. IF: 2,260.

Acute myeloid leukemia with inv(3)(q21.3q26.2)/t(3;3)(q21.3;q26.2): Study of 61 patients treated with intensive protocols. Sitges M; Boluda B; Garrido A; Morgades M; Granada I; Barragan E; Arnan M; Serrano J; Tormo M; Miguel Bergua J; Colorado M; Salamero O; Esteve J; Benavente C; Pérez-Encinas M; Coll R; Martí-Tutusaus JM; Brunet S; Sierra J; Ángel Sanz M; Montesinos P; Ribera JM; Vives S; PETHEMA, CETLAM cooperative groups. 2020. *Eur J Haematol.* 105(2): 138 - 147. IF: 2,220.

A randomized double-blind phase II study evaluating the role of maintenance therapy with cabozantinib in high-grade uterine sarcoma after stabilization or response to doxorubicin ± ifosfamide following surgery or in metastatic first line treatment (EORTC62113). Ray-Coquard I; Hatcher H; Bompas E; Casado A; Westermann A; Isambert N; Casali PG; Pratap S; Stark D; Valverde C; Anand A; Huizing M; Floquet A; Lindner L; Hermes B; Seddon B; Coens C; Jones R; Reed N. 2020. *Int J Gynecol Cancer.* 30(10): 1633 - 1637. IF: 2,095.

Patient-reported outcomes at discontinuation of anti-angiogenesis therapy in the randomized trial of chemotherapy with bevacizumab for advanced cervical cancer: an NRG Oncology Group study. Chase, Dana; Huang, Helen Q.; Monk, Bradley J.; Ramondetta, Lois Michelle; Penson, Richard T.; Gil, Karen; Landrum, Lisa M.; Leitao, Mario; Oaknin, Ana; Huh, Warner K.; Pulaski, Heather L.; Robison, Katina; Guntupalli, Saketh R.; Richardson, Debra; Salani, Ritu; Sill, Michael W.; Wenzel, Lari B.; Tewari, Krishnansu Sujata. 2020. *Int J Gynecol Cancer.* 30(5): 596 - 601. IF: 2,095.

A randomized phase III trial of platinum chemotherapy plus paclitaxel with bevacizumab and atezolizumab versus platinum chemotherapy plus paclitaxel and bevacizumab in metastatic (stage IVB), persistent, or recurrent carcinoma of the cervix: the BEATcc study (ENGOT-Cx10/GEICO 68-C/JGOG1084/GOG-3030). Grau JF; Farinas-Madrid L; Oaknin A. 2020. *Int J Gynecol Cancer.* 30(1): 139 - 143. IF: 2,095.

Tackling the Biological Diversity in Early Triple-Negative Breast Cancer. Oliveira M; Saura C. 2020. *Breast Care (Basel).* 15(3): 205 - 207. IF: 2,029.

Quality of life of patients with metastatic pancreatic adenocarcinoma initiating first-line chemotherapy in routine practice. Laquente B; Macarulla T; Bugés C; Martín M; García C; Pericay C; Merino S; Visa L; Martín T; Pedraza M; Carnero B; Guardeño R; Verdaguer H; Mut A; Vilanova D; García A. 2020. *BMC Palliat Care.* 19(1): 103 - 103. IF: 2,015.

Impact of the number of prior chemotherapy regimens on outcomes for patients with metastatic breast cancer treated with eribulin: A post hoc pooled analysis. Cortes J; Twelves C. 2020. *Breast J.* 26(7): 1347 - 1351. IF: 1,991.

Transcriptome-wide association study of breast cancer risk by estrogen-receptor status. Feng H; Gusev A; Pasaniuc B; Wu L; Long J; Abu-Full Z; Aittomäki K; Andrulis IL; Anton-Culver H; Antoniou AC; Arason A; Arndt V; Aronson KJ; Arun BK; Asseryanis E; Auer PL; Azzollini J; Balmaña J; Barkardottir RB; Barnes DR; Barrowdale D; Beckmann MW; Behrens S; Benitez J; Bermisheva M; Bialkowska K; Blanco A; Blomqvist C; Boeckx B; Bogdanova NV; Bojesen SE; Bolla MK; Bonanni B; Borg A; Brauch H; Brenner H; Briceno I; Broeks A; Brüning T; Burwinkel B; Cai Q; Caldés T; Caligo MA; Campbell I; Canisius S; Campa D; Carter BD; Carter J; Castelao JE; Chang-Claude J; Chanock SJ; Christiansen H; Chung WK; Claes KBM; Clarke CL; GEMO Study Collaborators; EMBRACE Collaborators; GC-HBOC study Collaborators; Couch FJ; Cox A; Cross SS; Cybulski C; Czene K; Daly MB; de la Hoya M; De Leeneer K; Dennis J; Devilee P; Diez O; et al.... 2020. *Genet Epidemiol.* 44(5): 442 - 468. IF: 1,954.

Breast cancer during pregnancy: matched study of diagnostic approach, tumor characteristics, and prognostic factors. Reyes, E.; Xercavins, N.; Saura, C.; Espinosa, M.; Gil, A.; Cordoba, O. 2020. *Tumori.* 106(5): 378 - 387. IF: 1,707.

Autoimmune haemolytic anaemias: A retrospective study of 93 patients. Gutiérrez Jomarrón I; López Rubio M; Morado Arias M; Arrizabalaga B; de la Iglesia S; Beneitez D; Sáez MI; Cervera A; Recasens V; Herrera A; Villegas AM; Grupo Español de Eritropatología. 2020. *Med Clin (Barc).* 154(9): 331 - 337. IF: 1,635.

Toxicities from immunotherapy: From clinical trials to real-world clinical practice. Riveiro-Barciela M; Trallero-Araguás E; Martínez-Valle F; Vall d'Hebrón Group for the study of Immunotherapy immune-related adverse events; Vall d'Hebrón Committee for management of Immunotherapy immune-related adverse. 2020. *Med Clin (Barc).* 155(12): 541 - 547. IF: 1,635.

Clinico-biological characteristics of patients with myelofibrosis: an analysis of 1,000 cases from the Spanish Registry of Myelofibrosis. Pastor-Galán I; Hernández-Boluda JC; Correa JG; Alvarez-Larrán A; Ferrer-Marín F; Raya JM; Ayala R; Velez P; Pérez-Encinas M; Estrada N; García-Gutiérrez V; Fox ML; Payer A; Kerguelen A; Cuevas B; Durán MA; Ramírez MJ; Gómez-Casares MT; Mata-Vázquez MI; Mora E; Martínez-Valverde C; Arbelo E; Angona A; Magro E; Antelo ML; Somolinos N; Cervantes F; en representación del Grupo Español de Enfermedades Mieloproliferativas Filadelf. 2020. *Med Clin (Barc).* 155(4): 152 - 158. IF: 1,635.

Update of the Spanish registry of haemoglobinopathies in children and adults. Bardón Cancho EJ; García-Morín M; Beléndez C; Velasco P; Benéitez D; Ruiz-Llobet A; Berrueco R; Argilés B; Cervera Á; Salinas JA; Vecilla C; Gondra A; Vallés G; Murciano T; Bermúdez M; Cela E; en representación del grupo de trabajo de Eritropatología de la Sociedad Español. 2020. *Med Clin (Barc).* 155(3): 95 - 103. IF: 1,635.

Genetic counsellors in a multidisciplinary model of clinical genetics and hereditary cancer. López-Fernández, A.; Serra-Juhé, C.; Balmaña, J.; Tizzano, E.F. 2020. *Med Clin (Barc).* 155(2): 77 - 81. IF: 1,635.

Management of iron deficiency in various clinical conditions and the role of intravenous iron: Recommendations of the Spanish Erythropathology Group of the Spanish Society of Haematology

and Haemotherapy. García Erce JA; Altés A; López Rubio M; Remacha AF; en representación del Grupo Español de Eritropatología de la Sociedad Española de Hematología y Hemoterapia; Otros componentes del Grupo Español de Eritropatología de la Sociedad Española de Hematología y Hemoterapia. 2020. *Rev Clin Esp.* 220(1): 31 - 42. IF: 1,304.

Identification of Enhancer-Promoter Contacts in Embryoid Bodies by Quantitative Chromosome Conformation Capture (4C). Tian TV; Vidal E; Graf T; Stik G. 2020. *J Vis Exp.* (158). IF: 1,163.Use of micafungin as antifungal prophylaxis in patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT) in Spain (GETH-MIC). López-Sánchez C; Valcárcel D; Gómez V; López-Jiménez J; Serrano D; Rubio V; Solano C; Vázquez L; Ruiz I; Grupo Español de Trasplante Hematopoyético (GETH). 2020. *Rev Esp Quimioter.* 33(2): 110 - 115. IF: 1,132.

The economic burden of metastatic breast cancer in Spain. Bermejo de Las Heras B; Cortes Ramon Y Cajal J; Galve Calvo E; de la Haba Rodriguez J; Garcia Mata J; Moreno Anton F; Pelaez Fernandez I; Rodriguez-Lescure A; Rodriguez Sanchez CA; Ruiz-Borrego M; Remak E; Barra M; Rivero M; Soto Alvarez J. 2020. *Eur J Hosp Pharm.* 27(1): 19 - 24. IF: 0,892.

Articles published by VHIO Investigators in 2020 in journals with no Impact Factor (IF) allocated at the time of publication of this Scientific Report:

Inclusion of non-inferiority analysis in superiority-based clinical trials with single-arm, two-stage Simon's design. Sampayo-Cordero M; Miguel-Huguet B; Pérez-García J; Páez D; Guerrero-Zotano ÁL; Garde-Noguera J; Aguirre E; Holgado E; López-Miranda E; Huang X; Malfettone A; Llombart-Cussac A; Cortés J. 2020. *Contemp Clin Trials Commun.* 20: 100678 - 100678.

Hepatocellular carcinoma with tumor thrombus extends to the right atrium and portal vein: A case report. Gomez-Puerto, Diego; Mirallas, Oriol; Vidal-Gonzalez, Judit; Vargas, Victor. 2020. *World J Hepatol.* 12(11).

Assessment of the psychosocial and economic impact according to sex in non-small cell lung cancer patients: an exploratory longitudinal study. Viñolas NN; Garcia-Campelo R; Majem M; Carcereny E; Isla D; Gonzalez-Larriba JL; Coves J; De-Castro J; Domine M; Lianes P; Artal A; Remon J; Felip E; Garrido P. 2020. *BMC Psychol.* 8(1): 123 - 123.

Paraneoplastic cerebellar degeneration diagnosed by anti-Yo determination in a young woman with early breast cancer. Mirallas O; Rezqallah Arón MA; Saoudi Gonzalez N; Escrivá-de-Romaní S. 2020. *BMJ Case Rep.* 13(8).

Radium-223 Within the Evolving Treatment Options for Metastatic Castration-resistant Prostate Cancer: Recommendations from a European Expert Working Group. O'Sullivan JM; Carles J; Cathomas R; Gomez-Iturriaga A; Heinrich D; Kramer G; Ost P; van Oort I; Tombal B. 2020. *Eur Urol Oncol.* 3(4): 455 - 463.

Actualización de las recomendaciones para la determinación de biomarcadores predictivos en el carcinoma de pulmón de célula no pequeña avanzado. Consenso Nacional de la Sociedad Española de Anatomía Patológica y de la Sociedad Española de Oncología Médica. López-Ríos F; Paz-Ares L; Sanz J; Isla D; Pijuan L; Felip E; Gómez-Román JJ; de Castro J; Conde E; Garrido P. 2020. *Rev Esp Patol.* 53(3): 167 - 181.

Back-to-back discovery, co-precision, and prevention. Casadei B; Tabernero J. 2020. *Eur Heart J Qual Care Clin Outcomes.* 6(2): 98 - 99.

Phase 1 Study of Molibresib (GSK525762), a Bromodomain and Extra-Terminal Domain Protein Inhibitor, in NUT Carcinoma and Other Solid Tumors. Piha-Paul SA; Hann CL; French CA; Cousin S; Braña I; Cassier PA; Moreno V; de Bono JS; Harward SD; Ferron-Brady G; Barbash O; Wyce A; Wu Y; Horner T; Annan M; Parr NJ; Prinjha RK; Carpenter CL; Hilton J; Hong DS; Haas NB; Markowski MC; Dhar A; O'Dwyer PJ; Shapiro GI. 2020. *JNCI Cancer Spectr.* 4(2): pkz093.

Cancer Treatment and Research During the COVID-19 Pandemic: Experience of the First 6 Months. de Las Heras B; Saini KS; Boyle F; Ades F; de Azambuja E; Bozovic-Spasojevic I; Romano M; Capelan M; Prasad R; Pattu P; Massard C; Portera C; Saini ML; Singh BP; Venkitaraman R; McNally R; Leone M; Grande E; Gupta S. 2020. *Oncol Ther.* 8(2): 171 - 182.

Recommendations of the Spanish Rheumatology Society for Primary Antiphospholipid Syndrome. Part I: Diagnosis, Evaluation and Treatment. Cáliz Cáliz R; Díaz Del Campo Fontecha P; Galindo Izquierdo M; López Longo FJ; Martínez Zamora MÁ; Santamaría Ortiz A; Amengual Pliego O; Cuadrado Lozano MJ; Delgado Beltrán MP; Carmona Ortells L; Cervantes Pérez EC; Díaz-Cordovés Rego G; Garrote Corral S; Fuego Varela C; Martín López M; Nishishinya B; Novella Navarro M; Pereda Testa C; Sánchez Pérez H; Silva-Fernández L; Martínez Taboada VM. 2020. *Reumatol Clin.*

Recommendations of the Spanish Rheumatology Society for Primary Antiphospholipid Syndrome. Part II: Obstetric Antiphospholipid Syndrome and Special Situations. Cáliz Cáliz R; Díaz Del Campo Fontecha P; Galindo Izquierdo M; López Longo FJ; Martínez Zamora MÁ; Santamaria Ortiz A; Amengual Pliego O; Cuadrado Lozano MJ; Delgado Beltrán MP; Ortells LC; Pérez ECC; Rego GD; Corral SG; Varela CF; López MM; Nishishinya B; Navarro MN; Testa CP; Pérez HS; Silva-Fernández L; Taboada VMM.2020. *Reumatol Clin.*

Evolving Landscape of Molecular Prescreening Strategies for Oncology Early Clinical Trials. Dienstmann R; Garralda E; Aguilar S; Sala G; Viaplana C; Ruiz-Pace F; González-Zorelle J; Grazia LoGiacco D; Ogbah Z; Ramos Masdeu L; Mancuso F; Fasani R; Jimenez J; Martinez P; Oaknin A; Saura C; Oliveira M; Balmaña J; Carles J; Macarulla T; Elez E; Alsina M; Braña I; Felip E; Tabernero J; Rodon J; Nuciforo P; Vivancos A. 2020. *JCO Precis Oncol.* 4: 505 - 513.

Clinical Outcomes in Patients With Colon Cancer With Microsatellite Instability of Sporadic or Familial Origin Treated With Adjuvant FOLFOX With or Without Cetuximab: A Pooled Analysis of the PETACC8 and N0147 Trials. Zaanan A; Shi Q; Taieb J; Alberts SR; Meyers JP; Smyrk TC; Julie C; Zawadi A; Tabernero J; Mini E; Goldberg RM; Folprecht G; Van Laethem JL; Le Malicot K; Sargent DJ; Laurent-Puig P; Sinicrope FA. 2020. *JCO Precis Oncol.* 4

Advanced Colorectal Cancer Orthotopic Patient-Derived Xenograft Models for Cancer and Stem Cell Research. Chicote I; Cámara JA; Palmer HG. 2020. *Methods Mol Biol.* 2171: 321 - 329.

Grade I meningioma with disseminated bone disease: A rare clinical phenomenon. Mirallas, O.; Marmolejo, D.; Valdivia, A.; Vieito, M. 2020. *BMJ Case Rep.* 13(4).

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. VHIO would therefore like to express its immense gratitude to its following supporters, funding entities and agencies:

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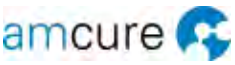


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CONSORTIA

As a reflection of VHIO's expertise in preclinical, translational and clinical research in oncology, we participated in the following Consortia of excellence in 2020.

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
Supported by EU's Horizon 2020 Framework Programme, 2020 celebrated the launch of **Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART) Consortium** (page 179) – also listed here under *New consortia – officially launched in 2020.* Coordinated by VHIO, this innovative project will harness and incorporate powerful cutting-edge technologies, methods and platforms, to spur the design, development, and ringing in of a new generation of data rich, dynamic studies in oncology.

This project has received funding from the European Union's Horizon 2020 framework programme research under grant agreement No: 965397.

Announced at the beginning of 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, the UK, 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 14 leading clinical investigators and researchers spanning 8 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 strives to both 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 **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

Intracolor

Initiated in 2016, **INTRACOLOR** (Evolution of resistant clones to novel target-directed drugs in colorectal tumors: a genetic and epigenetic study of intratumoural heterogeneity dynamics), is supported by EU Horizon 2020 funding and led by VHIO.
Running in parallel with MoTriColor's clinical trials, it incorporates 6 of MoTriColor's members to test novel targeted therapies for mCRC, each matched to distinctive gene expression signatures.
Representing a comprehensive framework for translational research, emerging molecular data is prospectively integrated in preclinical models and proof-of-concept clinical trials in mCRC. This project is carried out in collaboration with SPECTAcolor–Screening Platform for Efficient Clinical Trials Access in Colorectal Cancer, which is an initiative of the EORTC, supported by Alliance Boots.
www.motricolor.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 643638.

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 spearhead by INCLIVA Health Research Institute (Spain), in partnership with 10 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 outcomes by applying personalized medicine at the three levels of prevention. This consortium will seek to implement a personalized medicine strategy at the first level of prevention, improve early gastric cancer detection at the second level of prevention, and improve 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 14 partners from 6 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 will play a decisive role in 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.

Spurred by Horizon 2020's European Union funding for Research and Innovation funding, **MoTriColor** (Molecularly guided Trials with specific treatment strategies in patients with advanced newly molecular defined subtypes of Colorectal cancer), led by VHIO, is powered by 8 clinical research centers of excellence, spanning Spain, Italy, The Netherlands and Belgium, as well as a European organization in cancer research and a diagnostic/prognostic SME.
Dedicated to conducting multi-center early phase clinical trials to establish the anti-tumor activity of novel experimental therapies for patients with metastatic or advanced colorectal cancer, patients are stratified based on their gene expression profiles according to recently established predictive signatures.
This pioneering approach aims at identifying sensitivity of individual patients to the proposed experimental therapies towards ultimately developing more precise anti-cancer therapies for these patients.
www.motricolor.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 635342.

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 forward step in utilizing nanoparticles than can better target and more precisely combat cancer cells.
It 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 apprach and provide preliminary data on its efficacy in humans and aim 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 **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

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 genetic profiling of patients suffering from advanced colorectal cancer.
https://www.eortc.org/blog/category/spectacolor

RADprecise - Personalized radiotherapy: Incorporating cellular response to irradiation in personalized treatment planning to minimize radiation toxicity, is supported by funding received through ERAPerMed's co-funded Joint Translational Call 2018 and was founded in 2019 by 7 leading organizations from Spain, Italy, Germany and France. This 3-year project will render radiotherapy more precise by incorporating data from finely tuned predictive models to pre-identify toxicity based on insights from multiple biomarkers of radiosensitivity in individual patients.
Led by colleagues at the German Cancer Research Center (DKFZ), Germany, project partners will apply findings at the clinical level by integrating a treatment planning system. Using parametric models and machine learning, clinical investigators from academia and health research, in collaboration with small and medium enterprises as well as patient advocates, will apply new biological data as well as readily available genomic information to develop models that can more precisely envisage adverse effects from radiotherapy to be validated in independent samples.
www.erapermed.eu

This project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No. 779282

The Spanish Association against Cancer (AECC), and the *Institute of Health Carlos III* (ISCIII) through the *ERA-NET: Aligning national/regional translational cancer research activities* awarded VHIO with two **TRANSCAN-2** projects funded by the EU's Horizon 2020 framework program in 2017.
Supported through the TRANSCAN Joint Translational Call on *Minimally and non-invasive methods for early detection and/or progression of cancer*, the first will establish non-invasive prognostic markers for resected early-stage non-small cell lung cancer (NSCLC) by assessing the role of circulating and exosomal miRNAs and free circulating DNA (fcDNA); as well as characterize blood-based tumor-educate platelets (TEPs) for the evaluation of patients treated with immune checkpoint inhibitors using novel sequencing technologies.
The second project will focus on the early detection of relapse in advanced colon cancer patients by longitudinally following a personalized molecular signature by liquid biopsy. This proof-of-concept, prospective, multi-center study will primarily seek to evaluate the clinical feasibility of tracking tumor progression by dynamically detecting a molecular and personalized signature from a blood test.
www.transcanfp7.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 643638.

Announced in 2018, one of the U.S. **Department of Defense's (DoD) Innovative Minds in Prostate Cancer (IMPaCT)** Awards funds a three-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 Centre–CNIO (Madrid, Spain), and the University of Washington (USA).
Aimed at more precisely gauging response in patients to standard therapies, the team seeks to develop new, more effective and tailored treatment strategies, as well as design 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.
https://cdmrp.army.mil/pcrp

Worldwide Innovative Networking in personalized cancer medicine

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 39 leading organizations representing all stakeholders in personalized cancer medicine covering 21 countries and 4 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

NEW CONSORTIA – officially launched in 2020

The EU-funded **Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART), coordinated by VHIO**), is carried out in collaboration with other leading experts from within Cancer Core Europe Consortium. 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 will further enhance 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.cancercoreeurope.eu

This project has received funding from the European Union's Horizon 2020 framework programme research under grant agreement No: 965397.

The main objective of the EU-supported **EURAMED rocc-n-roll** project: *EURopeAn MEDical application and Radiation prOteCtion Concept: strategic research agenda aNd ROadmap interLinking to heaLth and digitisation 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 will work 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 will analyze 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.
www.cordis.europa.eu/project/id/899995

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No: 899995.

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).
Comprised of six other partners - CIC bioGUNE, IQS, CNRS, INSERM, Anaxomics Biotech, and VHIO, the investigators will 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 that will then be validated through xenoinjerts.
www.poctefa.eu/ayudas-de-estado-y-minimis

The project has been co-financed 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.

The **ERA-PerMed-supported RAD51predict Consortium**, is coordinated by VHIO and centers on patient stratification based on DNA repair functionality for precision cancer medicine. Consisting of five partners: the University Clinic of Giessen and Marburg (Germany), Institut Gustave Roussy (IGR)-INSERM U981, Villejuif (France), German Breast Group Forschungs GmbH, Neu-Isenburg (Germany), Université Laval (CHUQ), Quebec (Canada), and VHIO, along with six other collaborators, will further investigate the RAD51 *in vitro* diagnostic test to predict those patients who would be most likely to benefit from therapy with PARP inhibitors (PARPi).
Aimed at enabling the more precise and faster identification of patients with breast and this test has been developed to better guide the stratification of patients to clinical trials to evaluate the efficacy of PARPi across additional tumor types including prostate and endometrial cancers.
www.erapermed.isciii.es

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

The **SCITRON** *Consorcio público-privado de Investigación Científica y Translacional en Oncología* (Consortium for Scientific Translational Research in Oncology) is a scientific program established in collaboration with Novartis in 2017 as a new model of R&D collaboration. This initiative connects expertise 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

Launched by Roche in 2016, the **imCORE - immunotherapy Centres of Research Excellence Network** - a 27 partner-strong network aims to advance discovery in cancer immunotherapy, connect internationally renowned scientific and clinical experts in immune-based therapeutic strategies in oncology, and collaborate 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 research 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 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 2017 VHIO underwent evaluation for accreditation of the CERCA Institute of Research Centres of Catalunya (*Institució CERCA–Centres de Recerca de Catalunya*) for the period 2013–2016.
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.
www.cerca.cat/en/

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.
https://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.

Similarly, 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*. Our Research Management is also endorsed by ISO 9001 Certification.

NEW FUNDING AND PROJECTS IN 2020

For a complete listing of all our current supporters and funding sources see section Funding & Consortia (pages 172-181).

INSTITUTIONAL SUPPORTERS

VHIO patrons (more information see pages 23-27)

Departament de Salut: Budgetary support
Departament d'Empresa i Coneixement: Budgetary support

VHIO's CELLEX Building & Infrastructure

Advanced Molecular Diagnostics Program (DIAMAV), and other VHIO investigators, groups and projects

Research Unit for Molecular Therapy of Cancer (UITM) - CaixaResearch, and CaixaResearch Advanced Oncology Research Program

Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI)

INTERNATIONAL SUPPORT

H2020-SC1-2020-Lump-Sum-RTD – International Consortium – Ref: 965397
Building Data Rich Clinical Trials — CCE_DART
Consortium leader VHIO: Elena Garralda
Early Clinical Drug Development Group

NFRP-2019-2020– International Consortium – Ref: 899995
European Medical application and radiation protection concept: strategic research agenda and roadmap interlinking to health and digitisation aspects — EURAMED rocc-n-roll
PI VHIO: Jordi Giralt
Radiation Oncology Group
Granted to Joaquín Mateo
Prostate Cancer Translational Research Group

Interreg – POCTEFA – International Consortium* – Ref: EFA360/19
Red cooperativa franco-española para el análisis de proteinopatías y el desarrollo de terapias individualizadas en cánceres hematológicos (Proteoblood)
PI VHIO: David Valcarcel
Experimental Hematology Group

Clinical Unit Visit
Granted to Herminia Fernandes
Mentor: Teresa Macarulla
Gastrointestinal & Endocrine Tumors Group

Clinical Unit VisitTranslational/Clinical Research Fellowship
Impact of microbiota on breast cancer prognosis and treatment efficacy
Granted to Andri Papakonstantinou
Mentor: Mafalda Oliveira
Breast Cancer & Melanoma Group

Breast Cancer Research Foundation Grant – Ref: BCRF20-008
Novel therapies against HER2-positive breast tumors: targeting oncogene-induced senescence and the immune system
PI: Joaquín Arribas
Growth Factors Group

* Co-funded by European Regional Development Fund/European Social Fund

NATIONAL FUNDING

AGAUR
Agència de Gestió d'Ajuts Universitaris i de Recerca

Ajuts Producte destinats a l'obtenció de prototipus i a la valorització i transferència dels resultats d'investigació generada per equips de recerca de Catalunya* – Ref: 2019PROD00045
PARPiPRED, test diagnòstic que facilita la medicina personalitzada en el tractament del càncer
PI VHIO: Violeta Serra
Experimental Therapeutics Group

Ajuts per a projectes de valorització i transferència de coneixement desenvolupats per innovadors en estades en entitats del sistema de recerca i innovació de Catalunya* – Ref: 2019 INNOV 00028
ONIRIA: Mastering Cell Dormancy to Fight Cancer
Granted to Teresa Tarragó
Project Director: Héctor G. Palmer
Stem Cells & Cancer Group

Ajuts per a la incorporació de personal investigador postdoctoral al sistema català de ciència i tecnologia dins del programa Beatriu de Pinós – Ref: 2019 BP 00182
Improving patient Selection for immunotherapy: Multi-Omics signature of Response Evaluation (ISeeMORE)
Granted to Kinga Bernatowicz
Project Director: Raquel Perez-Lopez
Radiomics Group
Co-funded by H2020 Programme under Marie Sklodowska-Curie COFUND Grant Agreement (BP3, Ref: 801370)

Ajuts per a la contractació de personal investigador novell – FI Predoctoral – Ref: 2020 FI_B 00584
Functional impact assessment of variants of unknown clinical significance of hereditary breast and ovarian cancer predisposition genes
Granted to Joanna Domenech
Project Director: Sara Gutierrez Enríquez
Hereditary Cancer Genetics Group

Ajuts per a la contractació de personal investigador novell – FI Predoctoral – Ref: 2020 FI_B 00774
Redirection of T cells against HER2-driven tumors
Granted to Macarena Román
Project Director: Joaquín Arribas
Growth Factors Group

Generalitat de Catalunya

DEPARTAMENT DE SALUT
Projectes de recerca i innovació per a la prevenció i tractament de la malaltia Covid-19 – Ref: SLD019/20/00001
MSC1, an anti-LIF therapeutic antibody, as a potential treatment for CoVid19
PI: Joan Seoane
Gene Expression & Cancer Group

PREMI ICS TRAJECTORIA INVESTIGADORA
Josep Tabernero
Gastrointestinal & Endocrine Tumors Group

Proyectos I+D+i Retos de Investigación. Categoria JIN – Ref: PID2019-108008RJ-I00
Proteínas de fusión BRD-NUT en el carcinoma de línea media NUT: del diagnóstico al tratamiento
PI: Tian Tian
Chromatin Dynamics in Cancer Group

Proyectos I+D+i Retos Colaboración – Ref: RTC2019-007067-1
Estrategias para incrementar el potencial clínico de inhibidores de MYC: identificación de biomarcadores, sinergias y nuevas indicaciones
PI: Laura Soucek
Mouse Models of Cancer Therapies Group

Europa Redes y Gestores – Ref: ECT2020-000827
Creación de VHIOSfera Europa: área pionera en la dinamización de Propuestas Internacionales Competitivas en Oncología de Precisión
PI: Alejandro Piris

Ayudas para Contratos Ramon y Cajal – Ref: RYC2019-026576-I
Granted to Jose Antonio Seoane

* Co-funded by European Regional Development Fund/European Social Fund

Ayudas Contratos Juan de la Cierva Formación – Ref: FJC2019-041005-I
Granted to Lidia Mateo
Project Director: Joan Seoane
Gene Expression & Cancer Group

Ayudas Contratos Juan de la Cierva Formación – Ref: FJC2019-039770-I
Granted to Alberto Gonzalez-Medina
Project Director: Ana Vivancos
Cancer Genomics Group

Ayudas contratos Predoctorales para la formación de doctores FPI – Ref: PRE2019-088051
Granted to Alba Escriche
Project Director: Maria Abad
Cellular Plasticity & Cancer Group

FINANCIACIÓN EXTRAORDINARIA DE PROYECTOS DE INVESTIGACIÓN SOBRE EL SARS-COV-2 Y LA ENFERMEDAD COVID-19 – Ref: COV20/00324
Functional characterization of SARS-CoV-2 T and B cell long-lasting Immunity in immunosuppressed patients developing SARS-CoV-2 infection (COV-Immunity)
Granted to Oriol Bestard (IDIBELL)
PI VHIO subcontracted: Alena Gros
Tumor Immunology & Immunotherapy Group

VHIO projects managed through the *Instituto de Investigación Sanitaria Acreditdo Institut de Recerca* (Accredited Research Institute - Vall d'Hebron)

Proyectos de Investigación Clínica Independiente – Ref: ICI20/00076
Next generation TIL therapy targeting neoantigens for immune checkpoint blockade-resistant tumors*
PI: Elena Garralda
Early Clinical Drug Development Group

Proyectos de Investigación en Salud – Ref: PI20/00892
Developing new therapeutic strategies to overcome CDK4/6 resistance in oestrogen receptor positive breast cancer*
PI: Violeta Serra/Meritxell Bellet
Experimental Therapeutics Group

Proyectos de Investigación en Salud – PI20/00897
Targeting dormant tumor cells as a new strategy to fight cancer*
PI: Héctor G. Palmer
Stem Cells & Cancer Group

Proyectos de Investigación en Salud – PI20/00968
Identification and validation of sensitivity signatures and mechanisms of resistance and response to targeted therapies and immunotherapy in patients with advanced colorectal cancer*
PI: Josep Tabernero/Elena Élez
Gastrointestinal & Endocrine Tumors Group

Proyectos de Investigación en Salud – PI20/00987
Chromosome instability and tumor immune infiltration as determinants of lung cancer metastatic potential*
PI: Enriqueta Felip
Thoracic Tumors & Head and Neck Cancer Group

Proyectos de Investigación en Salud – PI20/01274
Deciphering the mechanisms of response and clonal evolution in high-risk chronic lymphocyticleukemia treated with highly specific BTK inhibitors*
PI: Francesc Bosch
Experimental Hematology Group

Proyectos de Investigación en Salud – PI20/00898
Pancreatic cancer and alterations in DNA damage response genes: analysis of predictive biomarkers and mechanisms of resistance to platinum-based chemotherapy and PARP inhibitors*
PI: Teresa Macarulla
Gastrointestinal & Endocrine Tumors Group

Proyectos de Investigación en Salud – PI20/00895
Investigating the mechanisms of resistance to RET-inhibitors in endocrine tumors*
PI: Jaume Capdevila
Gastrointestinal & Endocrine Tumors Group

Proyectos de Investigación en Salud – PI20/00881
Clonal Hematopoiesis of Indeterminate Potential in Cancer Patients: Impact on Immune Dysfunction, Treatment Response and Therapy Related Malignancies
PI: David Valcarcel*
Experimental Hematology Group

Proyectos de Investigación en Salud – PI20/00889
FUSOMAP: Development of microbiota-based diagnostic and prognostic models by mapping intratumoral Fusobacterium and associated gut microbiota in early-stage colorectal cancer*
PI: Paolo Giovanni Nuciforo
Molecular Oncology Group

Proyectos de Investigación en Salud – PI20/01112
Moving liquid biopsy toward clinical implementation: Study of the molecular origin of cell-free tumor DNA release into the bloodstream*
PI: Ana Vivancos
Cancer Genomics Group

Proyectos de Investigación en Salud* – PI20/00558
Exploiting senescence in a two-step approach to treat advanced Prostate Cancer*
PI: Nicolás Herranz
Prostate Cancer Translational Research Group

Contratos Miguel SERVET Tipo II* – CPII20/00020
Granted to Alena Gros
Tumor Immunology & Immunotherapy Group

Ayudas para la Intensificación de la Actividad Investigadora* – INT20/00042
Granted to Judith Balmaña
Hereditary Cancer Genetics Group

Ayudas para Contratos Predoctorales de Formación en Investigación en Salud* – FI20/00188
Granted to Alejandro Martínez-Sabadell
Project Director: Joaquín Arribas
Growth Factors Group

Ayudas para Contratos Predoctorales de Formación en Investigación en Salud* – FI20/00274
Granted to Fabio Giuntini
Project Director: Laura Soucek
Mouse Models of Cancer Therapies Group

Ayudas para Contratos Predoctorales de Formación en Investigación en Salud* – IMP/00009
Granted to David Gomez Peregrina
Project Director: César Serrano
Sarcoma Translational Research Group

IMPaCT* – FI20/00275
Medicina Genómica

FUNDACIÓN MUTUAMADRILEÑA

Convocatoria para Adjudicación de Ayudas para Proyectos de Investigación en Salud
Desarrollo de modelos diagnósticos y pronósticos basados en la infección intratumoral por Fusobacterium y microbiota intestinal asociada en el cáncer colorectal localizado, en el área de Oncologia
PI: Paolo Giovanni Nuciforo
Molecular Oncology Group

"la Caixa" Foundation

Ayudas Predoctorales InPhinit Incoming
Granted to Judit Diaz
Project Director: Alena Gros
Tumor Immunology & Immunotherapy Group

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* Co-funded by European Regional Development Fund/European Social Fund

PRIVATE FUNDING

"la Caixa" Foundation

CaixaImpulse Consolidate
PI: Violeta Serra
Experimental Therapeutics Group

Caixa Health Research Grant - NATIONAL CONSORTIUM
BioPrinted hydROgel MicrofluIdicS to mimic patient-specific tumor metastasic micrenvironment-PROMISE
PI VHIO: Elena Élez
Gastrointestinal & Endocrine Tumors Group

Junior Leader Incoming
Granted to Irene Casanova
Project Director: Joaquín Mateo
Prostate Cancer Translational Research Group
Co-funded by H2020 Programme under Marie Sklodowska-Curie Grant Agreement (Ref: 801370)

Ayudas Predoctorales InPhinit Retaining
Granted to Alex Mur
Mentor: Héctor G. Palmer
Stem Cells & Cancer Group

fundación fero
Investigando por un futuro sin cáncer

Beca FERO en Investigación Oncológica Traslacional
Unraveling the tumor immunotherapy with deep-learning based radiogenomics
PI: Raquel Perez-Lopez
Radiomics Group

Proyectos FERO-GHD en Cáncer de Mama
ctDNA in breast milk for early detection of pregnancy associated breast cancer
PI: Cristina Saura/Miriam Sansó
Breast Cancer & Melanoma Group

Estudios biofísicos y bio-informáticos de los complejos proteicos HER2-Pertuzumab en presencia del Trastuzumab innovador vs biosimilar
PI: Javier Cortés
Breast Cancer & Melanoma Group

TNBC Tumores inmunológicamente inflamados
PI: Javier Cortés
Breast Cancer & Melanoma Group

Análisis de las imágenes de Tomografía Computarizada (TAC) para identificar susceptibles de responder a inmunoterapia
PI: Raquel Perez-Lopez
Radiomics Group

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Contra el Cáncer

Grupos Coordinados AECC- NATIONAL CONSORTIUM
Tumor microenvironment-derived factors in localized colon cancer: clinical impact and therapeutic implications
PI VHIO: Héctor G. Palmer
Stem Cells & Cancer Group

LAB AECC
Leveraging the AR-DDR interaction in de-novo metastatic prostate cancer towards precision combination therapies with PARP inhibitors.
PI: Joaquin Mateo
Prostate Cancer Translational Research Group

INNOVA AECC
First-in-class small drug activators of TET2 for the treatment of cancer
PI: Héctor G. Palmer
Stem Cells & Cancer Group

Ideas Semilla
Dormancy and autophagy: decoding the molecular mechanism that mediates cancer drug resistance
PI: Isabel Puig
Stem Cells & Cancer Group

Clínico Senior AECC
Molecular landscape of resistance to KIT/PDGFRA inhibition in gastrointestinal stromal tumors
Granted to César Serrano
Project Director Joan Carles Galcerán
Genitourinary, CNS & Sarcoma Tumors Group

Investigador AECC
Characterisation of fusion protein BRD-NUT in NUT midline carcinoma: from diagnosis to treatment
Granted to Tian Tian
Project Director Sandra Peiró
Chromatin Dynamics in Cancer Group

Investigador AECC
Tumor DNA repair functionality and immunologic profile as predictive and prognostic biomarkers for cancer precision medicine
Granted to Alba Llop
Project Director Violeta Serra
Experimental Therapeutics Group

Postdoc AECC
Study of the impact of LIF and the tumor microenvironment on the immunomodulation of brain metastasis
Granted to Ester Bonfill
Project Director Joan Seoane
Gene Expression & Cancer Group

Programa Joves i Ciència. Premio Pedrera Talents
Granted to Iosune Baraibar
Co-Mentors: Joan Seoane and Elena Élez
Gastrointestinal & Endocrine Tumors Group and Gene Expression and Cancer Group

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Beca SEOM para Proyectos de Investigación de Oncología Médica relacionados con Medicina Nuclear
Desarrollo de un sistema de cuantificación volumétrica de carga tumoral mediante estudios con PET 68Ga-DOTATOC con valor pronóstico y predictivo de respuesta a 177Lu-DOTATATE en pacientes con tumores neuroendocrinos gastroenteropancreáticos
PI: Jaume Capdevila
Gastrointestinal & Endocrine Tumors Group

Fundación CRIS. Programa CRIS Talento Clínico
Personalized REsponse Imaging biomarker for Cancer immunotherapy
PI: Raquel Perez-Lopez
Radiomics Group

BECA GETNE
Estudio de la microbiota, de Fusobacterium Nucleatum y de la correlación con las vías de los receptores de TOLL-LIKE en tumores neuroendocrinos de intestino delgado
PI: Jaume Capdevila
Gastrointestinal & Endocrine Tumors Group

Premio Chiara Giorgetti
Identificación de pacientes con cáncer de mama metastásico sensibles a los inhibidores de PARP: estudio en pacientes con variantes hereditarias de significado incierto y en nuevos genes implicados en la recombinación homóloga
PI: Judith Balmaña
Hereditary Cancer Genetics Group

Vyda GEIS
DIVAS-DIssecting VAsculas Sarcomas
PI: Claudia Valverde
Genitourinary, CNS & Sarcoma Tumors Group


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