INSTITUT
JULES BORDET

SCIENTIFIC REPORT 2020

For the years 2016 to 2019

ULB iris

OECI COMPREHENSIVE Cancer Centre

Table of Contents

Foreword

Dominique de Valeriola
General Medical Director

Institut Jules Bordet is a public and academic OECI*-certified comprehensive cancer center playing an important role in cancer care, research and education, both in Belgium and internationally. Entirely dedicated to adult cancer patients since its creation in 1939, it belongs to the City of Brussels and the Université Libre de Bruxelles.

Both translational and clinical research are part of the Institute's DNA, aiming to bring research discoveries to the patient's bedside quickly. The present 2016-2019 scientific report reflects the spirit of commitment and collaboration of the Institute's healthcare professionals, researchers, and administrative support teams and, above all, of the patients who trust our teams and volunteer to participate in clinical trials. A concerted and well-rewarded effort has been made during these recent years to build a stronger partnership with patients in developing our clinical trials, and to establish more efficient, centralised governance and operational support for our research activities.

For several decades, the Institut Jules Bordet has played a particularly strong role in promoting academic research by creating prestigious international research networks such as the European Organisation for Research and Treatment of Cancer (EORTC), the Breast International Group (BIG) and, more recently, the Oncodistinct Network.

All these achievements would never have been possible without funding from several organisations and the unconditional support of "Les Amis de l'Institut Bordet".

Looking to the future, a new Institut Jules Bordet is being built on the campus of the Université Libre de Bruxelles alongside other research laboratories and the general academic Erasmus Hospital. Comprising a total of 80.000 m^2, including state-of-the art equipment and technologies as well as 10.000 m^2 for cancer research activities alone, the Institute will increase its capacity from 160 to 250 beds and be entirely dedicated to cancer. The building is now entering the final stretch, with the move planned for the end of 2021.

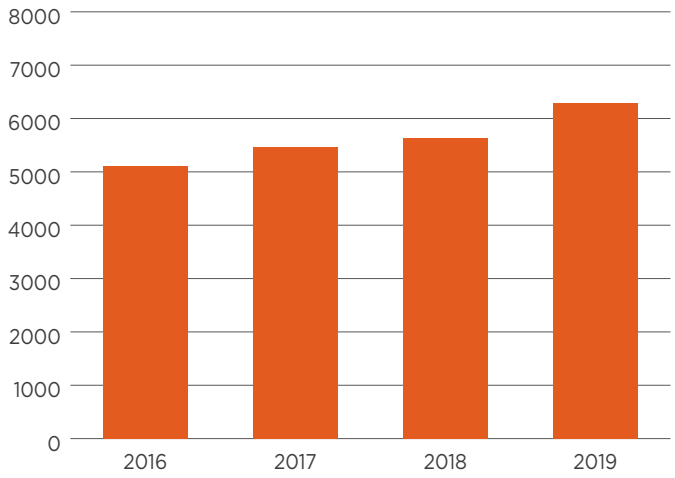
The new Institut Jules Bordet will offer a wide range of opportunities for our research teams and our existing and future academic and private partners, both in Belgium and abroad – all with the common aim to discover new strategies to fight cancer and its consequences for patients and their relatives!

Research in Numbers

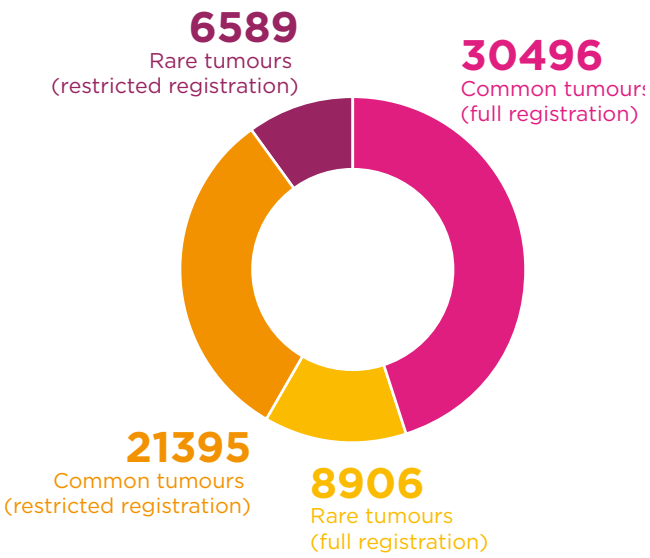
General data

On average, 2000 patients are diagnosed or treated with a new tumour incident and about 3700 are attended to at the Institute for a new tumour episode:

Dicussions in multidisciplinary teams

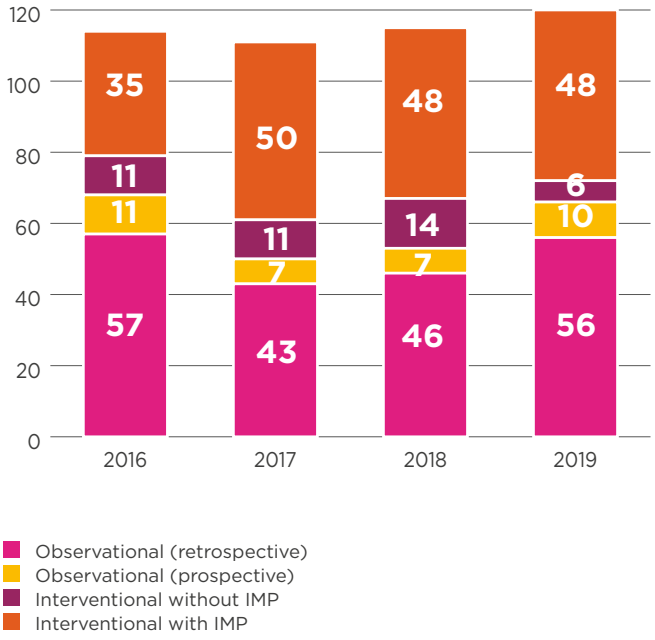


Hospital cancer registry status *(incidence years 2000-2018)*



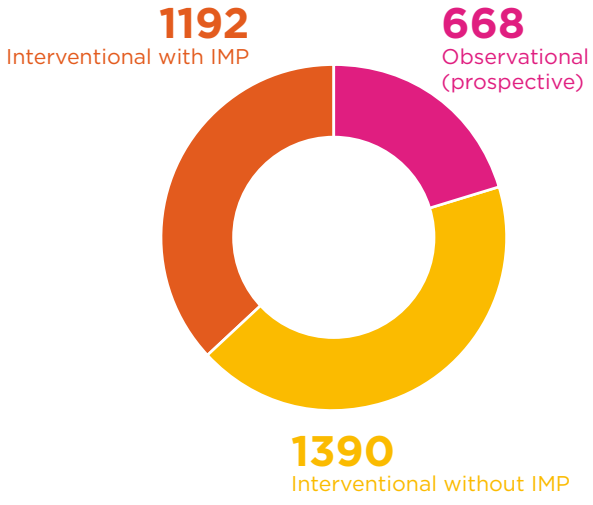
Research projects

Around 100 to 120 research projects are approved each year by the Ethics Committee:



Patients included in prospective trials 2016-2019

On average, about 800 new patients are included each year in prospective studies:



Research personnel

Institut Jules Bordet employs 1200 persons in total (972 FTEs), of which 237 are medical doctors (160 FTEs). Since research and care activities are closely integrated, every staff member is involved in research activities at various levels within the Institute. There are however 168 professionals (147 FTEs) specifically dedicated to research activities.

6 Medical Senior Scientists

6 Medical Research Fellows

26 Postdoctoral Scientists

21 PhD Students

15 Technicians

19 Study (Nurse) Coordinators

6 Clinical Data Managers

5 Research Coordinators

2 Research Pharmacists

24 Experts in Clinical Trials Operations

3 Statisticians

11 Research IT

14 Administrative Support for Research

10 Finance/Legal Support for Research

Finance & funding

BUDGET:

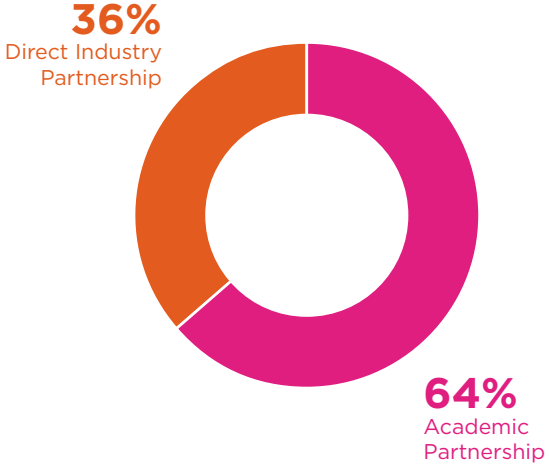
14,6 mio€ Annual research budget

9% of Institut Jules Bordet's annual budget dedicated to research

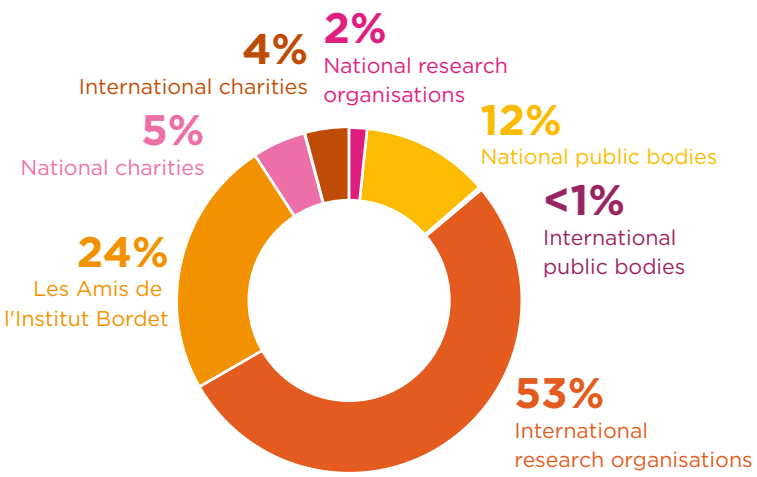
FUNDING:

Research funding comes both from non-commercial sources through donors, foundations and academic partnerships, and from commercial sources through collaboration with industry.

Total funding breakdown by types of partnership (2017-2019)



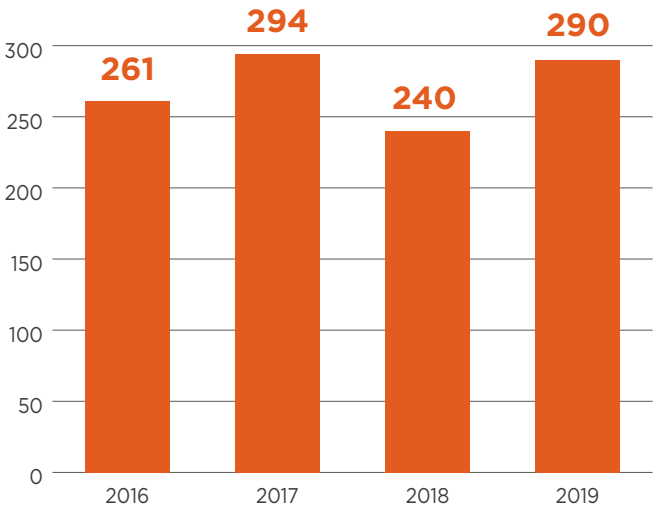
Academic partnership funding breakdown by types of funders (2017-2019)



Publications

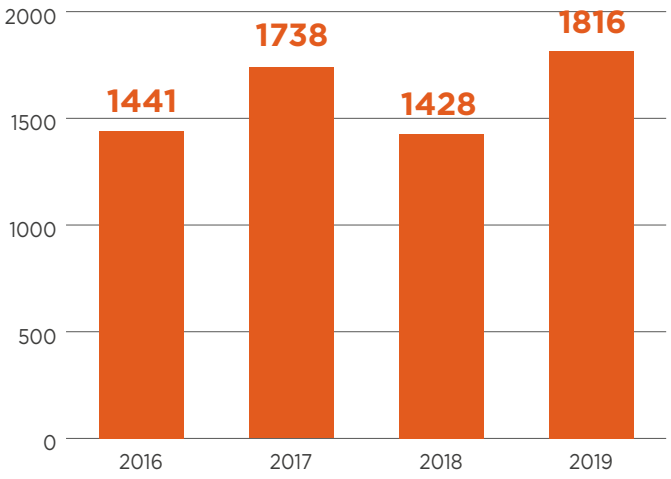
Scientific production in terms of publications is about 250-300 papers a year, with about 40 having an impact factor above 10:

Number of publications

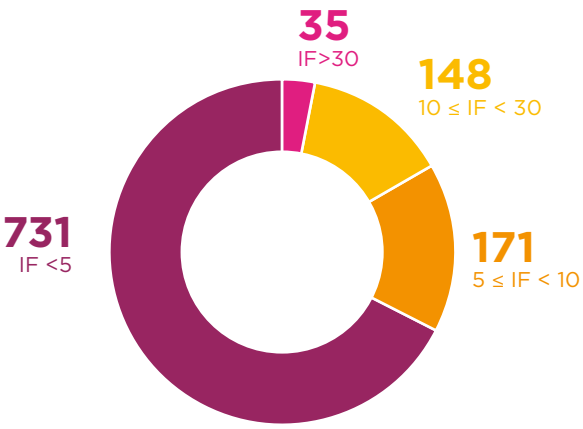


The sum of the impact factors for all the publications occurring per year ranges between 1428 and 1816:

Sum of impact factors



Impact factors distribution (2016-2019)



Find out more at research.bordet.be/

Strategic Vision

Martine J. Piccart-Gebhart, MD PhD
Scientific Director

The oncology landscape has changed rapidly during the last 15 to 20 years, and is characterised by a revolution in molecular diagnostics and imaging, the adoption of less mutilating surgeries, the spread of more accurate radiotherapy techniques, and the exponential growth of innovative anticancer drug treatments as well as supportive therapies.

While the Institut Jules Bordet has undoubtedly contributed to this progress at a national and international levels in its more than 80 years of existence, it no longer stands alone in the landscape of "modern oncology" in Belgium and belongs to a growing list of accredited cancer institutes across Europe.

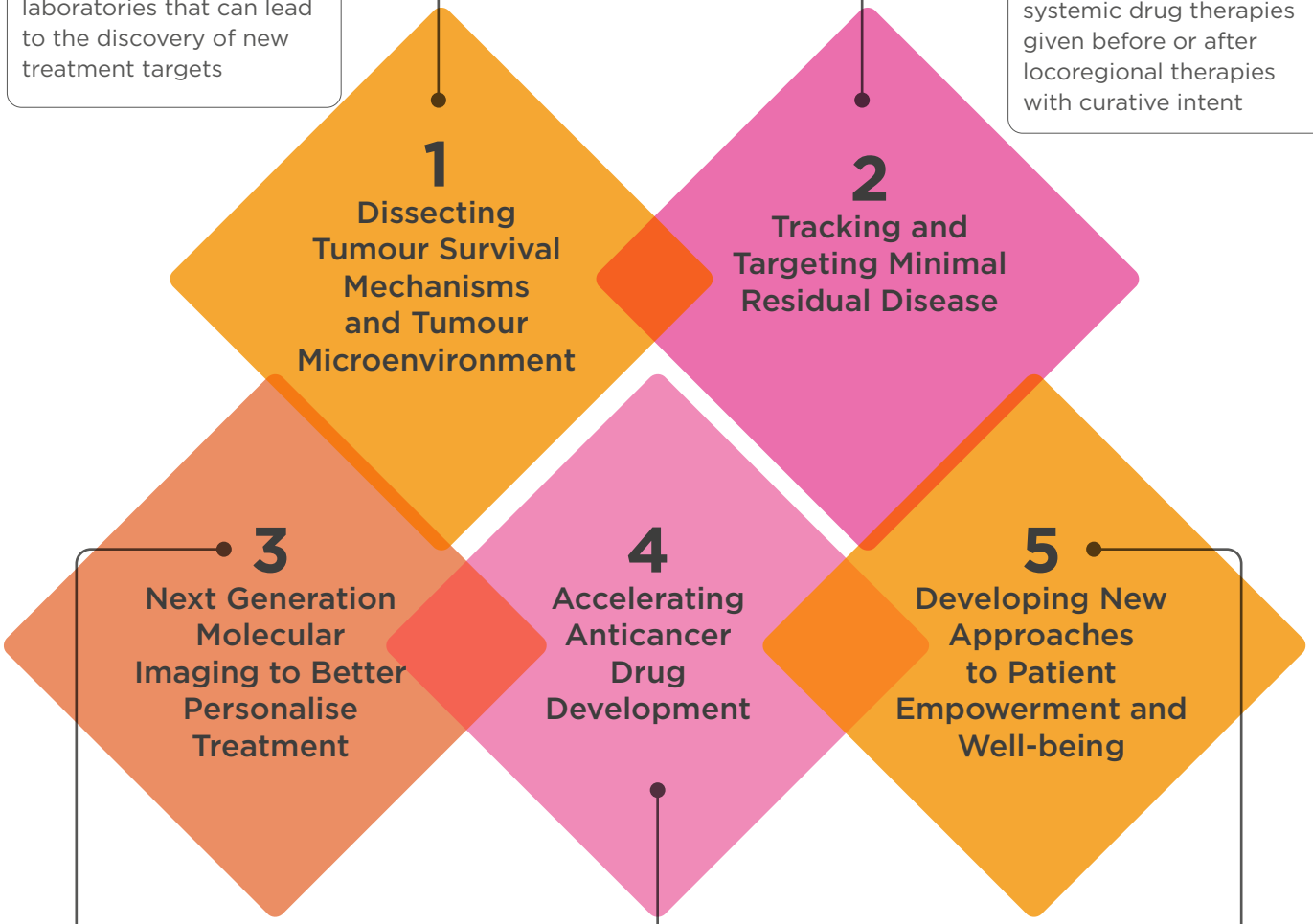
It became important to think how the Institut Jules Bordet could continue to play a leadership role in innovations along a patient's cancer path, from diagnosis to palliative care. It was also logical to build this plan for the future on a foundation of the Institute's strengths: its easy channels of communication and deep integration between its laboratories and its surgical, radiotherapy, medical oncology, imaging and pathology departments, and the support provided by "Les Amis de l'Institut Bordet," a philanthropic organisation able to finance research projects devoid of commercial interest.

With these cards in hand, the Institut Jules Bordet is uniquely positioned to prioritise the most critical needs of patients in its research agenda, which encompasses 5 pillars.

Research Pillars:

Improve understanding of the crosstalk between the tumour and its microenvironment, a transversal research theme of the Institut Jules Bordet research laboratories that can lead to the discovery of new treatment targets

Focus on better ways to diagnose and tackle minimal residual disease or the presence of occult cancer cells that escape not only locoregional therapies, but also systemic drug therapies given before or after locoregional therapies with curative intent



Invest in modern imaging techniques to avoid the under or overtreatment of patients; in other words, demonstrate the contribution of these tools to improved treatment personalisation in the fields of surgery, radiotherapy and drug therapy

Contribute to the important domain of new anticancer drug development, with an emphasis on novel partnership models with the pharmaceutical industry that reinforce academic freedom as well as the efficient conduct of proof-of-concept clinical trials with innovative designs, particularly in the field of immuno-therapeutics

Develop a portfolio of research initiatives centred on patient empowerment and wellbeing, not only during treatment, but also during the survivorship period and in the palliative context

Research Pillars

PILLAR I:

Dissecting Tumour Survival Mechanisms and Tumour Microenvironment

The Institut Jules Bordet laboratories were created by a previous generation of visionary clinicians active in 3 main domains– medical oncology, hematology and surgery (H. Tagnon, J.-C. Heuson, P. Stryckmans, F. Lejeune) – but also in pathology and molecular biology (A. Claude). Their ambition was to contribute to a better understanding of cancer at the cellular and molecular levels, as this knowledge would form the basis for improved patient treatment.

Today's researchers can count on the unprecedented development of new technologies to explore in greater depth the interactions between cancer cells and their microenvironment, as well as the potential mechanisms underlying resistance to anticancer therapies.

With the use of genomic, transcriptomic, epigenetic and immunological tools, researchers are dissecting tumour survival mechanisms and the tumour microenvironment, moving ever closer towards precision medicine.

At Institut Jules Bordet, this preclinical and translational research is mostly developed in the areas of breast cancer, melanoma, gastrointestinal tumours and haematological malignancies.

J.-C. HEUSON BREAST CANCER TRANSLATIONAL RESEARCH LABORATORY

> "Our goal is to better understand breast cancer biology and disease dissemination and progression. We aim to unravel the mechanisms associated with resistance to adjuvant and neoadjuvant therapies across the different breast cancer subtypes."

TEAM AND INFRASTRUCTURE

The laboratory is headed by an MD-PhD together with a senior scientist. The team includes 2 medical senior scientists, 6 postdoctoral scientists, 5 PhD students, 4 laboratory technicians, 1 research fellow, and 1 administrative assistant.

The laboratory is fully equipped with molecular and cellular biology equipment, including droplet digital PCR, single cell analysis, and spatial transcriptomics platforms. The laboratory has access to the sequencing core facility of the Université Libre de Bruxelles with a NovaSeq sequencer for high throughput next-generation sequencing (NGS) analyses. The laboratory has expertise in state-of-the-art bioinformatic analyses of several types of omics data, including single cell and spatial transcriptomic data.

AIMS

- Characterising breast cancer heterogeneity and immune landscapes within breast cancer subtypes, most notably lobular cancers and triple negative cancers (TNBC)
- Elucidating the mechanism of resistance to adjuvant and neoadjuvant therapies through integrated genome-wide molecular profiling of tumour cells and their microenvironment with spatial transcriptomics and single cell analysis
- Dissecting the paths leading to metastatic dissemination

MAIN PROJECTS

- Mapping tumour and immune cell architecture using spatial transcriptomics and single cell sequencing to gain novel insights into treatment resistance in TNBC
- Interrogating the impact of intratumour heterogeneity on disease recurrence in HER2-positive breast cancer by integrating spatial transcriptomics and single-cell sequencing
- A prospective tissue collection from patients with TNBC and HER2-positive disease undergoing neoadjuvant treatment is ongoing with the integration of single cell RNAseq and immune phenotyping in order to explore the impact of heterogeneity on treatment response

The link between the laboratory and international clinical research teams facilitates the laboratory's ambitious translational research projects, linked to

- **AURORA** (BIG)
- **(Neo)ALTTO** (BIG)
- **Zephir**, **Neorhea**, **Synergy**, **D-Beyond** (international trials sponsored by Institut Jules Bordet)

Françoise Rothé, Christos Sotiriou

RECENT ACHIEVEMENTS

- Identified novel molecular alterations associated with the metastatic progression of invasive lobular cancer and potential mechanisms of endocrine resistance, offering new paths for drug development in this setting
- Mapped the genomic alterations that characterise each of the TNBC molecular subtypes, opening new avenues to develop novel targeted therapeutic approaches for patients with TNBC
- Analysed metastatic dissemination through 2 different paths: primary-to-metastasis and daughter-to-daughter metastasis dissemination, namely parallel and cascade paths
- Associated the immune landscape of HER2-positive breast cancer and TNBC with clinical outcome and response to treatment
- Demonstrated that the use of RANK pathway inhibitors can prime poorly immunogenic luminal breast cancer for immunotherapy

SELECTED PUBLICATIONS
[1] [2] [3] [4] [5] [6] [7] [8] [9]

Find out more at bctl.bordet.be/

MOLECULAR IMMUNOLOGY LABORATORY

"Our goals are to understand how the composition, organisation and functionality of immune infiltrates in breast cancer are linked with response to treatment and long-term clinical outcome. We also aim to discover blood and tissue biomarkers that signal the onset of severe immune-related adverse effects in patients on immunotherapy."

TEAM AND INFRASTRUCTURE

The team includes 1 Head (PhD), 3 post-doctoral scientists, 3 PhD students, 3 technicians, 1 tissue analyst, and 2 trainees (per semester). The laboratory has expertise in all classical approaches for DNA, RNA, and protein analysis, immunophenotyping, flow cytometry, functional immunological assays, image analysis, confocal microscopy, and multiplex immune-histochemistry. In addition, 1 post-doc and 1 technician from an immuno-oncology company work 75% of their time in our laboratory on collaborative projects.

AIMS

- Characterise immune cell composition, balance and functionality in tumour-associated tertiary lymphoid structures (TLS) and their relation to treatment response and prognosis
- Compare the immune microenvironment in ductal carcinoma in situ (DCIS) to that which is characterised in invasive breast cancer.
- Identify biomarkers for immunotherapy-treated patients at a high risk of severe immune related toxicities
- Find a biomarker that accurately scores the level of activity of tumour infiltrating lymphocytes (TIL) and TLS

MAIN PROJECTS

- Ongoing prospective collection of fresh breast tumour samples at diagnosis for TIL and TLS characterization (currently more than 1400 breast cancer samples dating from 2012) and linkage with clinico-pathological parameters, including 5-year survival
- Collection of pre- and post-neoadjuvant paired biopsies for TIL immunophenotypic and functionality characterisation and their association with treatment benefit
- In-depth characterisation of T cells infiltrating DCIS (Université Catholique de Louvain-Institut de Duve)
- Blood and tissue monitoring of patients undergoing immune therapies with the goal of finding biomarkers predicting severe immune reactions.
- Correlating host immune responses in COVID-19 infected cancer patients, non-cancer patients and healthcare workers with disease severity

Soizic Garaud, Karen Willard-Gallo

RECENT ACHIEVEMENTS

- Recognised and characterised TLS in breast tumours
- Identified CXCL13 as a key chemokine for TIL recruitment and organisation in TLS
- Determined that the transcription factor FOXP1 plays an important role in regulating chemokine-mediated TIL recruitment
- Demonstrated that functional follicular helper T (Tfh) cells and functional B cells are key components of TIL infiltrates, with PD-1 Tfh TIL and germinal center B cell TIL characteristic of active TLS and a good clinical prognosis

SELECTED PUBLICATIONS
[10] [11] [12] [13] [14] [15] [16]

Find out more at miu.bordet.be/

ONCOLOGY AND EXPERIMENTAL SURGERY LABORATORY

> "Our goal is to contribute to the improved understanding of resistance to targeted therapies, with a longstanding focus on melanoma and a recent interest in preclinical models of solid tumour brain metastases."

TEAM AND INFRASTRUCTURE

The team includes 1 Head (PhD), 5 post-doctoral scientists, 1 PhD student, 5 technicians, and 1 administrative assistant. It has at its disposal 30 fully characterised melanoma cell lines, a cell bank of about 200 different tumour and normal tissue primary cultures and a nude mouse unit, which is now expanding with an immune-competent mouse subunit (AVATAR).

AIMS

- Develop model-based mechanistic studies of targeted therapeutics, exploring hypotheses of resistance in BRAF, NRAS or c-kit mutated melanomas
- Develop melanoma progression biomarkers
- Develop tools for prediction of drug resistance and sensitivity (kinome profiling)
- Explore ways to enhance radiotherapy effects with the use of radiosensitisers and targeted drug combinations

MAIN PROJECTS

- Exploration of Prohibitin antagonists alone or in combination with MAPK inhibitors as a new therapeutic strategy for melanoma
- TYRP1 as a prognostic marker in melanoma sentinel lymph nodes
- Phenotype switching in melanoma tumour tissues and patient survival
- Preclinical testing of innovative targeted drug combinations for brain metastases, with or without radiotherapy, that also includes the interaction of these treatments with astrocytes, pericytes and endothelial cells

RECENT ACHIEVEMENTS

- Patented the use of a p53 activator to restore sensitivity to MAPK pathway inhibitors
- Identified MITF / Bcl2 as the main resistance mechanism in NRAS- mutated melanoma
- Identified TYRP1 as a prognostic factor in metastatic melanoma
- Successfully developed an AVATAR mouse model, to be used for testing of immune checkpoint blockade + radiotherapy under a reactivated p53 background

Ahmad Awada, Ghanem Ghanem

SELECTED PUBLICATIONS
[17] [18]

Find out more at
loce.bordet.be/

EXPRIMENTAL HAEMATOLOGY LABORATORY

> "Our goal is to improve our understanding of the acute myeloid leukemia immune microenvironment as a potential way to discover innovative treatment targets."

TEAM

The laboratory comprises 1 laboratory Head (MD), 1 senior scientist, 1 postdoctoral scientist, and 4 PhD students.

AIMS

- Correlating the immune landscape of acute myeloid leukemia (AML) and more specifically the molecular profile and function of T-infiltrating lymphocytes with the risk of relapse of AML after standard treatment
- Identifying novel immune targets for the development of immunotherapeutic strategies

MAIN PROJECTS

- Confirm in a large AML patient cohort the preliminary observation of a correlation between the transcriptomic and methylation profile of CD3+ T cells isolated from patients and their risk of relapse with standard therapy
- Study how allogeneic transplantation impacts this immune profile
- Understand how differentially expressed miRNAs in AML mediate the communication between leukemia cells and TIL

RECENT ACHIEVEMENTS

- Developed first microRNA signatures of human CD4+ Tregs and CD8+ Tregs
- First circulating microRNA signatures in bone marrow and plasma of AML
- Correlated CD3+ T cell dysimmunity with AML relapse risk

SELECTED PUBLICATION
[19]

Find out more at
hemexp.bordet.be/

Philippe Lewalle

CLINICAL CELL THERAPY LABORATORY

"Our goal is to understand how mesenchymal stromal cells influence the tumour immune microenvironment. With a particular focus on chronic lymphocytic leukemia, we hope to identify new prognostic markers, therapeutic vectors or targets."

TEAM AND INFRASTRUCTURE

The laboratory comprises 1 Head (PhD), 3 post-doctoral scientists, 1 scientific collaborator, 3 PhD students and 1 technician. It has access to cellular culture and molecular biology facilities (including real-time PCR, fluorometer), flow cytometry (MACSQuant®) and Nanotrack analyser and ultracentrifuge for extracellular vesicle analysis.

Dominique Bron, Basile Stamatopoulos, Laurence Lagneaux, Nathalie Meuleman

AIMS

- Investigate mechanisms by which mesenchymal stromal cells (MSC) mediate immunosuppressive effects and contribute to treatment resistance, particularly in chronic lymphocytic leukemia (CLL) (e.g., through Toll-like receptors and the production of extracellular vesicles)
- Exploit the mechanisms by which MSC exert immunosuppressive effects in the tumour microenvironment therapeutically

MAIN PROJECTS

- Dissect the immunosuppressive pathways of tumour-MSC
- Characterise the immunomodulatory potential of extracellular vesicles derived from MSC of different origins (e.g., bone marrow, adipose tissue, umbilical cord)
- Explore the feasibility of extracellular vesicles to deliver SiRNA and drugs for therapeutic targeting, starting with pancreatic cancer

RECENT ACHIEVEMENTS

- Demonstrated the existence of multiple leukemic clones within the same chronic lymphocytic leukemia patient
- Recognised the existence of a harmful crosstalk between cancer cells and MSC in CLL and multiple myeloma
- Demonstrated the impact of MSC extracellular vesicles on survival, gene expression and chemoresistance of CLL cells

SELECTED PUBLICATIONS
[20] [21] [22] [23]

Find out more at ltcc.bordet.be/

VIRAL ONCOGENESIS LABORATORY

"Our ultimate goal is to identify carriers of human T-cell lymphotropic virus type-1 (HTLV-1) at risk of aggressive adult T-cell leukemia. We develop molecular tools to improve treatment decision-making and identify novel treatment targets for adult T-cell leukemia."

TEAM AND INFRASTRUCTURE

The team is composed of 1 Head (PhD), 1 post-doctoral scientist, 1 post-doctoral scientist with expertise in bioinformatics, and 1 PhD student. The team is supported by technicians dedicated to animal experiments (Canada) and has access to the GIGA Institute's genomic platform (University of Liège).

Anne van den Broeke

AIMS

- Discover novel cancer drivers by pursuing our longitudinal exploration of virus-host transcriptional interactions in adult T-cell leukemia (ATL) induced by human T-cell leukemia virus and its corresponding animal model (BLV/bovine leukemia virus, cattle and sheep) from premalignant stages to full blown tumours; expand this research to humanised mouse models of infection
- Transform the basic research laboratory findings into novel NGS tools to improve the clinical management of HTLV-1 carriers and patients with aggressive ATL

MAIN PROJECTS

- Use of parallel genome and transcriptome NGS at the single cell level to track premalignant clones and uncover drivers of tumour evolution (with KU Leuven and University of Liège Microfluidics Facility)
- NGS clonality of Japanese HTLV-1 carriers to predict patients at risk of progression (Tokyo cohort, JSPFAD)
- Monitoring of leukemic clones in patients with ATL (from Belgium, France and UK) in order to measure therapeutic response and predict relapse

RECENT ACHIEVEMENTS

- Demonstrated that oncoretroviruses produce critical noncoding transcripts despite strong immune response (in bovine leukemia model)
- Discovered a novel mechanism of viral oncogenesis, namely an antisense-dependent cis-perturbation of host cancer drivers by HTLV-1 and BLV (in human malignancy and animal model)
- Developed a novel NGS clonality method to monitor patients with ATL (short-read Illumina & long-read Nanopore sequencing technologies)

SELECTED PUBLICATIONS
[24] [25]

PILLAR II:

Tracking and Targeting Minimal Residual Disease

Tracking and targeting minimal residual disease is now possible with liquid biopsy, immunomonitoring, and novel diagnosis and treatment approaches.

The liquid biopsy concept, exploited by haemato-oncologists for decades, is about to revolutionise the screening, treatment and follow-up of patients with solid tumours : circulating tumour DNA (ctDNA) detection and sequencing enable us to detect and molecularly characterise small disease burden in various malignancies, including breast cancer after therapy given with curative intent.

Institut Jules Bordet incorporates ctDNA assessments in most of its clinical research projects, but also as a tool to dissect the mechanism of early metastatic spread and to understand in greater depth the concept of tumour dormancy in breast cancer (see J.-C. Heuson BCTL Laboratory).

The perioperative period offers a window of opportunity to try to counteract the dissemination of cancer cells in the body and minimal residual disease growth through pharmacologic interventions that might favourably impact the host and the tumour microenvironment. This research theme is actively pursued by the Institut Jules Bordet's Anaesthesiology Department in collaboration with laboratories within and outside of Institut Jules Bordet.

PLASMA CIRCULATING TUMOUR DNA IN PRIMARY BREAST CANCER

TEAM AND INFRASTRUCTURE

The team is headed by a Medical Senior Scientist who is part of the J.-C. Heuson Breast Cancer Translational Research Laboratory (BCTL).

Michail Ignatiadis

AIM

- To identify associations between clinical outcome and plasma ctDNA detection in patients with early breast cancer

MAIN PROJECTS

- **SUCCESS** ctDNA study

In this project, serial plasma samples collected before and after the administration of adjuvant chemotherapy, and during follow-up from patients who have participated in the phase III **SUCCESS** trial, will be evaluated using state of the art ctDNA technology. Associations between ctDNA detection and clinical outcome will be performed.

- Institut Jules Bordet's ctDNA pilot study

State of the art ctDNA technology is being evaluated in serial plasma samples from breast cancer patients who have been treated with standard neoadjuvant chemotherapy at the Institut Jules Bordet. Correlations between ctDNA detection and clinical outcome will be performed.

The results from these projects will inform interventional trials using ctDNA to select high-risk patients for secondary adjuvant treatment strategies.

- A recent translational research study using data and samples from the phase III **NeoALTTO** trial demonstrated that among patients with HER2-amplified tumours who were treated with neoadjuvant paclitaxel and anti-HER2 therapy, those with HER2-enriched primary tumours and undetectable ctDNA at baseline had the highest pathological complete response rates. These patients are good candidates for chemotherapy de-escalation trials.

SELECTED PUBLICATIONS
[26] [27] [28] [29]

EXPLOITING THE PERIOPERATIVE PERIOD TO IMPROVE PATIENT OUTCOMES

> "Our goal is to manipulate the host's metabolism and the tumour microenvironment during the perioperative period. We aim to reduce cancer recurrences using cheap and safe medications able to antagonise inflammation and stress."

TEAM AND INFRASTRUCTURE

The team is headed by an anaesthesiologist working in collaboration with the Clinical Trials Support Unit, Institut Jules Bordet's Pathology Department, and research laboratories from the Katholieke Universiteit Leuven

Maher Khalife, Imane Bachir

AIM

Run proof of concept randomised clinical trials in the perioperative period of breast and colorectal cancers that will fuel the hypothesis of favourable host and tumour microenvironment changes induced by specific drugs (such as ketorolac and pregabalin)

In case the proof of concept phase is successful, move to a definitive practice-changing phase III study

MAIN PROJECTS

- **PRECOL**

Because of its highly innervated environment, colorectal cancer is probably the best candidate to investigate the neural pathway as a potential promoter of minimal residual disease growth after surgery. As a specific blocking drug for this model, pregabalin was chosen for its modulating properties on neuronal transmission, and its effects will be evaluated following presurgical administration.

- **B-KeSt I**

Breast cancer was chosen as a model to explore how the inflammatory pathway is involved in growth stimulation of minimal residual disease after surgery. Ketorolac, a non-steroidal anti-inflammatory agent, will be tested as a specific blocking drug.

RECENT ACHIEVEMENTS

Conducted a large retrospective study of intra-operative ketorolac that reduced the cumulative incidence of breast cancer distant metastases in obese women

SELECTED PUBLICATION
[30]

Find out more at
www.bordet.be/en/anesthesiology

PILLAR III:

Next Generation Molecular Imaging to Better Personalise Treatment

Institut Jules Bordet develops molecular imaging with or without omics support as a tool to:

- optimise locoregional therapy: surgery, external beam radiotherapy and radioembolisation;
- optimise systemic therapies by identifying early on (within 2 to 3 weeks) ineffective, and often toxic, anticancer drugs;
- understand and tackle oligometastatic and oligoresistant disease with multimodality treatment approaches;
- expand an ongoing, ambitious theranostics programme (e.g., the use of radiolabelled molecules to specifically target cancer cells disseminated in the body) for imaging and molecular radiotherapy.

Furthermore, Institut Jules Bordet

- is pursuing its longstanding efforts to build on imaging (e.g., sentinel node, MRI) for safe de-escalation of locoregional surgery and radiotherapy, resulting in fewer sequelae and improving patient quality of life
- will continue to build on the deep and unique collaboration that exists between its oncologists and nuclear medicine specialists; together they design and conduct proof of concept clinical trials in which early molecular imaging is used to "see" drug target expression or to stop ineffective (and often toxic) anticancer therapy several weeks ahead of morphological imaging (e.g., CT scan), and in which new multidisciplinary approaches are explored to cure oligometastatic disease or to improve control of oligoresistant disease
- in collaboration with the Vrije Universiteit Brussel (VUB), has the ambition to hold the premier position in radiotheranostics in Belgium, following the creation of the Brussels Radiotheranostic Platform, which includes a state of art facility for Good Manufacturing Practices (GMP) production and (pre)clinical testing of innovative radiotherasnostic compounds.

OPTIMISING LOCOREGIONAL THERAPY

> "Our goal is to develop less aggressive surgical procedures and better customised radiotherapy techniques that will enhance patient quality of life without compromising the chances of being cured."

TEAM AND INFRASTRUCTURE

The team is composed of surgeons and radiation oncologists who receive support from the Nuclear Medicine and Radiology Departments, as well as the Clinical Trials Support Unit.

AIMS

- Refine and expand sentinel node techniques to forego extensive nodal resection and its ensuing side effects in carefully selected patients
- Explore ways to replace surgical resection of the tumour through destruction via other means (such as ultrasound)
- Minimise the radiotherapy dose to healthy functional tissue while maximising the dose to the tumour

MAIN PROJECTS

- **ProCaLung** : a national quality assurance program of radiotherapy for stage III NSCLC patients entirely coordinated by Institut Jules Bordet
- A prospective trial using magnetic resonance imaging (MRI) to guide a needle for ultrasound destruction of early localised prostate cancer
- Standardisation of imaging techniques for quantitative evaluation of functional liver volume before and after stereotactic body radiation therapy (SBRT) or selective internal radiation therapy (SIRT) for the treatment of liver metastasis
- Study correlating dose distribution based on pre-treatment
- 99mTcmacroaggregated-albumin and post-treatment activity distribution of 90y microspheres, with the goal to improve the safety and efficacy of radioembolisation of liver tumours and metastasis
- Preoperative stereotactic radiotherapy in borderline resectable pancreatic cancer under immune therapy or not
- **MRI linac** : a linear accelerator with on-board, high-field MRI imaging, which takes into account daily anatomical changes and monitors the tumour position in realtime during radiotherapy, minimising the irradiation of healthy tissue. This MRI accelerator will be installed in the new Institut Jules Bordet in 2021, introducing the opportunity to undertake a large and novel research domain.

Patrick Flamen, Gabriel Liberale, Maria Bali

RECENT ACHIEVEMENTS

- Pioneered the sentinel node technique and intraoperative partial radiotherapy for early breast cancer (Mobetron) in Belgium, with an experience involving more than 1000 patients; 251 patients benefitted from Mobetron treatment in 2018-2019
- Introduced stereotactic radiotherapy for brain tumours and metastasis (Gamma Knife) (total of 294 in 2018-2019)

SELECTED PUBLICATION
[31]

IMPROVING SYSTEMIC ANTICANCER THERAPIES AND DEVELOPING SPECIFIC APPROACHES FOR OLIGORESISTANT DISEASES

"In advanced disease, our goal is to promptly recognise ineffective drug therapy, sparing patients its side-effects and society its financial cost. At the same time, we hope to extend the survival of patients with oligometastases or oligoprogressive disease."

TEAM AND INFRASTRUCTURE

The team is composed of dedicated medical oncologists, nuclear medicine specialists and radiation oncologists who are assisted by the Clinical Trials Support Unit to conduct multicentric randomised trials with high quality imaging and translational research.

AIMS

- Molecular imaging and ctDNA monitoring to detect response or resistance to anticancer therapy much earlier than with traditional morphological imaging like CT scan and MRI
- Assess tumour heterogeneity for improved selection of patients likely to benefit from anticancer drugs, especially antibody drug conjugates
- Diagnose oligometastatic disease and develop multimodality treatment approaches including, for example, stereotactic radiotherapy (SBRT), surgery, radiofrequency ablation or radioembolisation with or without immunotherapy, with the hope to improve survival
- Diagnose oligoresistant disease under systemic treatment and explore how SBRT of these few resistant lesions can extend progression-free-survival

MAIN PROJECTS

- **Regain** study to explore hyperselective radioembolisation as a potentially effective modality in patients with oligoprogressive liver metastases
- **Oligopro-Breast** study to evaluate SBRT as a potential way to pursue the same systemic therapy when oligoresistant disease is documented
- **Copernic** study to test the hypothesis in a randomised trial that ctDNA monitoring in first-line therapy of advanced colorectal cancer has clinical utility
- The ongoing **Oliver** project, an ambitious retrospective analysis of 600 patients operated for liver metastasis with curative intent, having the goal to produce an algorithm of clinical data, morphological, and functional imaging together with genomic biomarkers able to predict patients deriving clear benefit from this surgical approach

RECENT ACHIEVEMENTS

In colorectal cancer

- Correlated 4 distinct patterns of FDG-PET responses in advanced colorectal cancer with different clinical outcomes
- Improved prognostic stratification of advanced colorectal patients based on whole body metabolic tumour volume at baseline combined with early metabolic response

Robbe Van den Begin, Andrea Gombos, Erwin Woff, Alain Hendlisz, Géraldine Gebhart, Thomas Guiot

- Completed **PEPITA**, a single arm Belgian trial in early colorectal cancer evaluating FDG-PET response to 1 preoperative cycle of FOLFOX chemotherapy with the hypothesis that non-metabolic responders would not benefit from adjuvant FOLFOX given after surgery (N =240 patients currently being analysed)
- Completed **REGARD-C**, as a single arm trial in advanced colorectal cancer investigating how an early FDG-PET associated with cTDNA monitoring can identify patients unlikely to benefit from regorafenib (N = 141 patients)
- Completed **CORIOLAN** (N =50 pts), which failed to demonstrate that metabolic progression on FDG-PET during a 4-week "window" without treatment is correlated to patient survival in advanced disease

In breast cancer demonstrated that

- For women with early HER2-positive disease, FDG PET response after 6 weeks of preoperative anti-HER2 treatment predicts pathological complete response (**NEOALTTO**)
- For women with advanced HER2-positive disease, combining a HER2-PET with an early FDG-PET identifies women who will or will not benefit from the antibody drug conjugate T-DM1 (**ZEPHIR**)
- For women with advanced luminal disease, progression-free-survival is worse in women not showing a FDG-PET response after 2 weeks of exposure to exemestane and everolimus (**PEARL**)

SELECTED PUBLICATIONS
[32] [33] [34] [35] [36] [37]

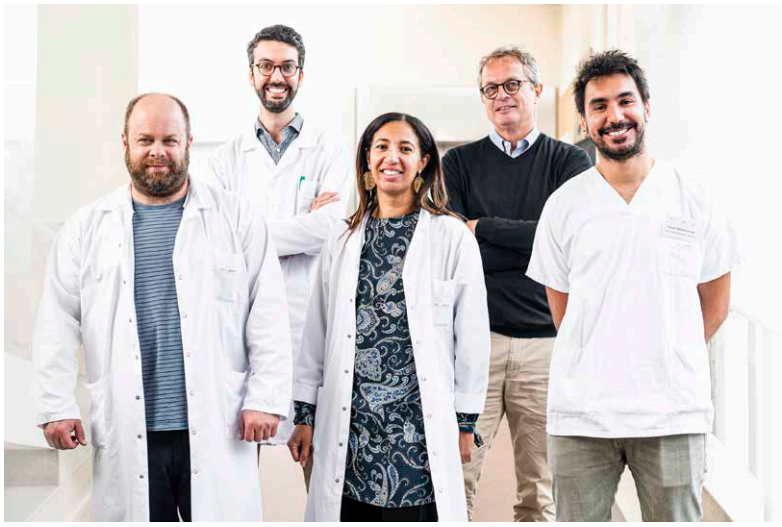
PUSHING FORWARD THERANOSTICS RESEARCH

> "Our goal is to expand the portofolio of radiotheranostics approaches as effective, personalised, and highly targeted anticancer therapies."

TEAM AND INFRASTRUCTURE

The team is composed of nuclear medicine specialists, medical physicists, biologists and a doctor in biomedical sciences with expertise in radiopharmacy. The latter directs a preclinical laboratory (in vitro, in vivo and ex vivo) dedicated to the radiobiology of radiotheranostics and radiotherapy as well as the evaluation of new radiotracers, and will coordinate the fully GMP- compliant clinical radiopharmaceuticals production unit in the new Institut Jules Bordet.

Increasing collaboration with the VUB is expected as a result of the recently created "Brussels Radiotheranostics Platform" that will bring together the preclinical and clinical expertise of the 2 teams.



Bruno Vanderlinden, Carlos Artigas, Zena Wimana, Patrick Flamen, Ivan Duran Derijckere

AIMS

- Generate innovative radiotheranostics for bench to bedside use
- Understand the radiobiological dynamics
- Identify radioresistance biomarkers

PROJECTS

- Understanding the radiobiology of peptide receptor radionuclide therapy with 177 Lu-Dotatate
- Developing an imaging biomarker for immunotherapy monitoring, namely a Granzyme B specific PET-tracer (currently in preclinical testing)

RECENT ACHIEVEMENTS

Institut Jules Bordet has been a major protagonist of the radiotheranostic approach:

- ^{68}Ga/^{177}Lu-Dotatate for neuroendocrine tumours (the **LUMEN** STUDY)
- ^{99}mTc-MAA/^{90}Y-microspheres for radioembolization of liver tumours
- ^{89}Zr/^{90}Y-rituximab for CD-20 positive lymphomas
- ^{99}mTc-MDP/^{223}Radium (alpha emitter) for therapy of bone metastasis
- ^{68}Ga/^{177}Lu-PSMA (under development) for therapy of prostate cancer

SELECTED PUBLICATIONS
[38] [39]

PILLAR IV:

Accelerating Anticancer Drug Development

The Institut Jules Bordet has a long tradition of active involvement in new anticancer drug development, from the birth of the EORTC within its walls in the early 1960s, the establishment of a phase I/II clinical trials unit in the late 1970s, the set-up of the Breast International Group (BIG) in the mid-1990s, to the recent creation of the Oncodistinct clinical trials network in 2015. The Institut has also increasingly focussed on developing and leading innovative immunotherapeutic approaches tested in academic trials for breast, genito-urinary, and gastro-intestinal malignancies that are financially supported by pharmaceutical companies and academic funders.

The initially small phase I/II unit has grown over decades into a large Clinical Trials Support Unit (CTSU), the governance and structure of which are explained later.

The CTSU assists researchers in academia and industry to develop and conduct their clinical trials. More than 1500 patients were enrolled in CTSU-managed trials, mainly multicentric ones, between 2016 and 2019.

BIG became a separate legal entity from Institut Jules Bordet in 1999, but Institut Jules Bordet played a crucial role by housing and providing infrastructure for the organisation for many years. Without this support, BIG would not have grown as it did. Moreover, Martine Piccart as a co-founder and chair, ensured that BIG developed into a respected international scientific organisation. BIG Headquarters moved outside of Institut Jules Bordet in 2016, but close links remain, as several large academic-led breast cancer trials, including ones for registration, are run with the support of the CTSU.

CONDUCTING CLINICAL TRIALS WITH RIGOUR AND PATIENT ENGAGEMENT

> "Our goal is to accompany patients engaged in a clinical trial by ensuring their safety and respecting the highest professional standards."

The role of the Clinical Trials Conduct Unit (CTCU) is to conduct clinical studies in a professional manner, in compliance with European Directives, applicable regulations and Good Clinical Practice. These clinical studies are carried out in collaboration with pharmaceutical companies and/or academic partners. The Institut Jules Bordet also implements its own clinical studies. The clinical studies conducted at the Institut Jules Bordet are coordinated by CTCU research physicians and teams. These doctors are responsible for monitoring patients and collecting data.

TEAM AND INFRASTRUCTURE

The team is led by 1 medical senior scientist and 1 operational head, and comprises 17 study coordinators (including 13 study nurses), 6 clinical data managers, 1 pathology samples coordinator, 1 quality assurance manager, 1 administrative & start-up coordinator, and 1 administrative assistant.

It has at its disposal 5 pharmacokinetic dedicated beds, a biosafety level 2 pharmaceutical facility, and an aphereris unit.

An Intensive Care Unit of 7 beds fully dedicated to cancer patients is also available.

AIMS

- To play a leadership role in precision medicine trials (genotype driven)
- To actively participate in the clinical development of antibody-drug conjugates, given the close collaboration with the nuclear medicine department, which has expertise in targeted molecular imaging
- To take part in clinical trials involving immune-oncologic combinations, including trials of new vaccines, oncolytic viruses and CART-T cells
- To pursue active collaboration with academic research networks such as the international EORTC, IBCSG, and BIG, and national organisations such as BSMO and BHS, and to develop original, academic proof of concept early clinical trials sponsored by Institut Jules Bordet
- To enhance further quality assurance of all clinical procedures in order to become an ISO-accredited clinical trials unit

PROJECTS

- Finalise the steps needed to activate **Rosaline**, a proof of concept (synthetic lethality based on loss of E-cadherin and ROS1 inhibition) neoadjuvant trial for lobular breast cancers testing endocrine therapy and entrectinib, entirely designed in-house and approved by Roche

Philippe Aftimos, Michel Dubuisson

- Expand the in-house NGS panel (to be able to track copy number changes and fusion genes)
- Continue recruitment in the institutional molecular screening programme for rare cancers
- Pursue the development of SOPs needed to obtain the Unit's full accreditation
- Improve patient recruitment in tumours other than breast and genito-urinary cancers by using a tool that helps to match patients to clinical trials

RECENT ACHIEVEMENTS

- Between 2016 and 2019, managed 316 patients enrolled in phase I/Ib clinical trials (yearly accrual around 80) and 864 enrolled in phase I-II/II/III clinical trials (yearly accrual ranging between 200 and 250)
- Completed the programme allowing electronic reporting of adverse events
- Implemented a rapid on-site evaluation procedure (ROSE) for research biopsies in collaboration with the pathology and radiology departments

SELECTED PUBLICATIONS
[40] [41] [42] [43] [44] [45] [46] [47] [48] [49] [50] [51] [52] [53] [54] [55] [56] [57] [58]

Find out more at ctcu.bordet.be/ trials.bordet.be/

DESIGNING AND SPONSORING ACADEMIC CLINICAL TRIALS FOR INNOVATIVE IMMUNOTHERAPEUTIC APPROACHES

"Our goal is to expand the proportion of patients who will benefit from immunotherapy in the form of durable responses or even cures and to identify biomarkers predictive of clinical benefit."

TEAM AND INFRASTRUCTURE

The team includes radiation oncologists, medical oncologists and surgeons working in close collaboration with pathologists, radiologists, nuclear medicine specialists and the Institut Jules Bordet laboratories. They work closely with the CTSU to develop their innovative proof of concept phase II trials.

AIMS

- Discover highly active novel combinations of immunotherapeutic agents – such as PD(L)1 inhibitors associated with drugs targetting the tumour microenvironment, or immunotherapeutic drugs combined with stereotactic radiotherapy or chemotherapy – in order to transform "cold" tumours into "hot" ones
- Improve patient selection through biomarker research

MAIN PROJECTS

- The **SYNERGY** trial, a randomised phase II trial developed in-house (N=150 pts) and testing the addition of an anti CD73 monoclonal antibody (Mab) to chemotherapy with an anti-PD-L1 immune checkpoint inhibitor as first-line therapy for patients with metastatic triple negative breast cancer across 21 institutions in 2 countries
- The **NEOCHECKRAY** trial, a randomised neoadjuvant phase II trial developed in-house for high risk luminal B cancers, run in collaboration with Institut Curie (Paris) completed accrual in its safety running phase and will reopen soon to compare adding an anti PD-L1 Mab alone or combined with an anti CD73 Mab to a chemotherapy backbone associated with stereotactic RT delivered on the primary tumour
- The hope is to reach a high rate of eradication, or complete or almost complete eradication, of the primary breast cancer
- The **AURA** trial addresses the question of optimal treatment strategy in patients with a non-metastatic bladder cancer. All patients, whether they are considered cisplatin eligible or not, benefit from an anti PD-L1 Mab alone or combined with different chemotherapy regimens in the neoadjuvant context. The objectives are to increase rates of pathological complete response and to identify genomic or molecular biomarkers to facilitate the selection of patients for perioperative therapy
- **NEOPAC** is investigating a neoadjuvant regimen for pancreatic cancer that combines FOLFIRINOX chemotherapy with an anti PD1 agent and stereotactic radiotherapy

Laurence Buisseret, Alexandre Peltier, Vincent Donckier, Thierry Gil, Alex de Caluwe

- In hepatocellular carcinoma, after the demonstration that Selective Internal Radiation Therapy (SIRT or Yttrium 90 labeled microspheres embolisation in the hepatic artery) promotes cytotoxic T-cell and NK cell infiltrates, the plan is to explore the combination of a PD(L)1 inhibitor and SIRT
- Active translational research built into the above trials will take place, for the most part, in the Institut Jules Bordet laboratories (e.g., RNA sequencing, ctDNA measurements, IHC multiplex of the immune microenvironment)

RECENT ACHIEVEMENTS

Successfully launched 3 Institut Jules Bordet sponsored clinical trials of novel immune approaches (see above), the result of strong in-house multidisciplinary collaborations, close interactions of clinicians with the Institut Jules Bordet laboratories and with pharmaceutical companies in order to obtain their new drugs and financial support

SUPPORTING AND PARTICIPATING IN THE BIG NETWORK

"Our goal is to accelerate the discovery of curative treatments for breast cancer by reducing duplication and fragmentation of efforts, facilitating international collaboration and promoting a win-win partnership model between academia and the pharmaceutical industry."

TEAM AND INFRASTRUCTURE

Today the Breast International Group (BIG) is composed of over 55 academic research groups from around the world. Its headquarters, located close to Institut Jules Bordet, comprises 45 staff members, and reports to a board of directors and general assembly of members.

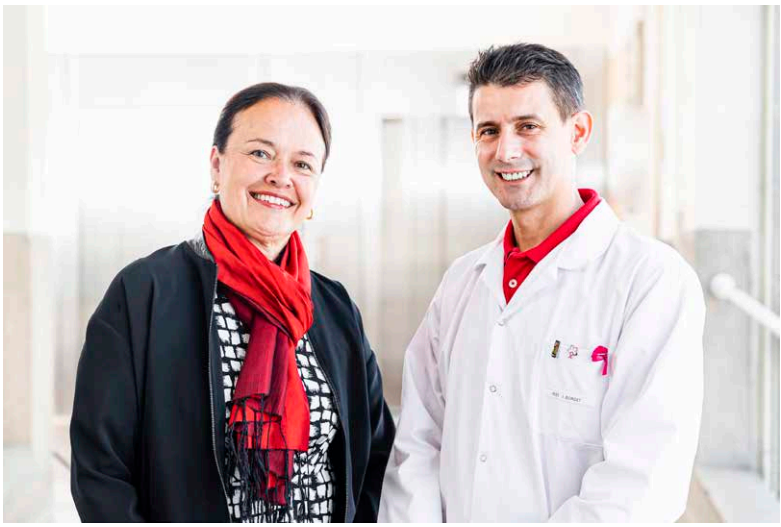
The headquarters staff work closely with BIG's member groups to develop, support and run clinical trials and research programmes. Many of its pivotal (adjuvant) trials are conducted in co-partnership with the Institut Jules Bordet's CTSU, which has acquired unique expertise in managing international registration trials.

AIMS

- Contribute to more effective, but also better individualised adjuvant treatment strategies for breast cancer
- Markedly accelerate the conduct of practice-changing adjuvant clinical trials through worldwide collaboration (involving not only Europe but also North America, Latin America, Asia, Australasia and the Middle East) and according to a model that preserves academic freedom
- Promote clinical trials addressing questions devoid of commercial interest that serve breast cancer patients' needs
- Improve the molecular understanding of the lethal evolution of the disease via metastatic spread with the hope to find new strategies to counteract this

MAIN PROJECTS (IN COLLABORATION WITH THE CLINICAL TRIALS SUPPORT UNIT)

- Coordinating the first worldwide, large adjuvant trial to explore adding a PD-L1 inhibitor to chemotherapy in triple negative breast cancer (**ALEXANDRA / IMpassion 030** trial)
- Setting up an international, academic BIG trial exploring chemotherapy de-escalation in selected patients with HER2-positive hormone receptor negative early breast cancer (**DECRESCENDO**)
- Conducting **AURORA**, an ambitious translational research programme aimed at understanding the clonal evolution of metastatic breast cancer in 1000 women from across 12 European countries; the study compares molecular data from primary and metastatic biopsies, collects plasma 6-monthly for ctDNA analysis, and follows patients for up to 10 years



Martine J. Piccart-Gebhart, Evandro de Azambuja

RECENT ACHIEVEMENTS

- Reported the 9-year update of the **MINDACT** trial results proving the clinical utility of the 70-gene signature MammaPrint® to identify which women with hormone receptor-positive early breast cancer might safely forego adjuvant chemotherapy in the future (leading group : EORTC)
- Contributed to the worldwide registration of pertuzumab given in addition to trastuzumab and adjuvant chemotherapy on the basis of the **APHINITY** trial and the benefit demonstrated for node-positive patients with HER2 positive breast cancer (leading group : Institut Jules Bordet)
- Completed patient recruitment in the **OLYMPIA** trial investigating the addition of olaparib to standard adjuvant therapy for BRCA1-2 mutation carriers diagnosed with high risk early breast cancer (results in late 2020)

SELECTED PUBLICATIONS
[59] [60] [61] [62] [63] [64] [65] [66] [67] [68] [69] [70]

Find out more at bigagainstbreastcancer.org/

LEADING THE ONCODISTINCT NETWORK

> "Our goal is to accelerate oncology drug development with closer attention paid to patients' essential needs."

THE TEAM AND INFRASTRUCTURE

Twenty-five cancer hospitals or departments across 8 countries have signed the ONCODISTINCT consortium agreement. They include academic and non-academic centers with expertise in early or late-phase clinical trials, sharing a common enthusiasm for innovation in clinical trial methodology.

The network functions with a steering committee and rotating data centers under Institut Jules Bordet's coordination, and benefits from the input of a patient advisory panel.

AIMS

- Address unmet medical needs such as brain metastases, rare tumours, oligometastases, and inflammatory breast cancer
- Conduct proof of concept studies with innovative designs, as well as biomarker driven trials
- Accelerate the conduct of phase I-II-III trials alongside new collaboration models with pharmaceutical and biotechnology companies

MAIN PROJECTS

- Four clinical trials are up and running: 1 basket trial exploring the activity of abemaciclib upon resistance to platinum-based chemotherapy in 4 tumours types (**MIME**), and 3 trials testing the addition of immune checkpoint inhibitors to cytotoxic chemotherapy in inflammatory breast cancer (**Pelican**), bladder cancer (**Aura**) and rectal cancer; 2 of the 4 trials are managed by the CTSU.
- **Brainstorm**, an ambitious programme aiming to diagnose brain metastases earlier and to improve therapies across 5 tumour types is now open for accrual. The programme foresees periodic MRI screening in asymptomatic patients and biosample tracking for molecular analyses (plasma, spinal fluid, metastasis outside the brain or, if possible, in the brain) at diagnosis of CNS involvement and under treatment.
- Three other ONCODISTINCT studies are currently being set-up, 1 investigating brain metastases from HER2-positive breast cancer, 1 in stage II-III rectal cancer and 1 in metastatic cholangiocarcinoma. Two are managed by the CTSU.

Ahmad Awada, Nuria Kotecki

RECENT ACHIEVEMENTS

- Designed and launched the aforementioned clinical studies
- Activated working groups focussing on ONCODISTINCT areas of interest and a patient advisory panel. The network is developing a translational research group and a junior faculty group.

Find out more at oncodistinct.net/

PILLAR V:

Developing New Approaches to Patient Empowerment and Well-being

The Institut Jules Bordet has worked for many years at accompanying patients for the duration of their cancer journey. The patient-centered approach, as it is implemented in care, is embedded in the way our researchers design and lead research.

Institut Jules Bordet has reinforced its international reputation through pivotal clinical trials studying the management of febrile neutropenia, establishing the Multinational Association of Supportive Care in Cancer (MASCC), and being among the first to set up an Intensive Care Unit (ICU) fully dedicated to cancer patients. At a national level it has played an important role in supporting Belgian legislation on euthanasia.

This pillar comprises 5 domains:

- Research on oncological complications, including infectious diseases and intensive care
- Psycho-oncology and supportive care research
- Geronto-oncological research
- Nursing research
- Patient involvement and empowerment

RESEARCH IN ONCOLOGICAL COMPLICATIONS

> "Our goal is to minimise the cancer patient's risk of death as a result of anticancer treatment complications."

TEAM AND INFRASTRUCTURE

Institut Jules Bordet's ICU, fully dedicated to cancer patients, comprises 7 beds, 3 full time physicians, 10 nurses and 1 research nurse.

Institut Jules Bordet's Infectious Disease Team comprises 3 full time physicians, 1 research nurse and 1 administrative assistant.

AIMS

- Provide state-of-the art treatment of febrile neutropenia, sepsis, acute respiratory failure, tumour lysis syndrome, and severe complications of targeted therapies and immune therapies, as well as constantly re-assess the rates of success and failure in managing these complications
- Benchmark clinical outcomes of Institut Jules Bordet cancer patients experiencing severe complications with the ones of other European cancer centers and departments
- Participate in international clinical trials testing new intensive care approaches or new antimicrobial, antiviral and antifungal agents

MAIN PROJECTS

For the ICU Team

- Epidemiological landscape of ICU infectious complications at Institut Jules Bordet
- The impact of inflammation on lung cancer clinical outcomes
- Immunotoxicity in the ICU
- Outcome of respiratory syncytial virus (RSV) infections in the ICU
- Guidelines for cancer patients in the ICU

For the Infectious Disease Team

- Active participation in 3 international phase III trials for cytomegalovirus (CMV) and Influenza A infections
- Recruitment in two phase II trials focussing on fungal infections
- Monitoring the ambulatory treatment of patients with low-risk febrile neutropenia
- Prospective monitoring of cultures obtained in high-risk patients with haematological cancers in order to detect multidrug resistant pathogens earlier and adapt empirical antibiotic therapy accordingly
- Role of PET scan imaging in cancer patients with fever of unknown origin
- Prospective monitoring of all care givers and other staff in the Institut Jules Bordet's haematology subunit for COVID-19 in order to reduce the risk of viral transmission to severely immunocompromised patients

Angela Loizidou, Vito Fontana, Anne-Pascale Meert

RECENT ACHIEVEMENTS

- Observed that the main cause of infections among patients undergoing transplantation (163 engraftment procedures in the last 3 years for leukemia, lymphoma and multiple myeloma) is endogenous bacterial flora
- Showed that in patients with a low to moderate risk of febrile neutropenia, a reduced dosing of G-CSF (tevagrastim, 2 injections) is not superior to no prophylaxis in a randomised trial of 112 patients

SELECTED PUBLICATIONS
[71] [72] [73] [74] [75] [76]

PSYCHO-ONCOLOGY AND SUPPORTIVE CARE RESEARCH

"Our goal is to preserve, restore or enhance the quality of life of cancer patients all along their journey (from diagnosis to end of life). In parallel we aim to enhance the communication skills of Institut Jules Bordet healthcare professionals, hoping to improve patient wellbeing and satisfaction."

TEAM AND INFRASTRUCTURE

The team is composed of 3 psychiatrists and 9 psychologists fully dedicated to cancer patients and their relatives, and to the physicians and nurses caring for them.

The Acute Supportive Care Unit comprises 2 physicians, and 15 nurses responsible for 8 beds.

AIMS

- Develop psychological interventions supported by written manuals and assess their efficacy on cancer patients and their relatives at different stages of the disease, and using rigorous methodologies (such as randomisation between early versus late intervention)
- Develop communication skills training programmes for cancer physicians to avoid burnout and to improve their wellbeing, and consequently improve patients' satisfaction with their medical care and compliance with their physicians' advice
- Develop supportive care interventions allowing better control of pain, mucositis, skin toxicities, sleep disturbances

MAIN PROJECTS

Programmes to

- regulate anxiety at the beginning of the survivorship period
- improve emotional regulation in patients with metastatic disease and in patients who have exhausted active cancer treatment options
- improve communication between cancer patients and their children
- develop communication skills addressing uncertainty and hope
- launch multidisciplinary interventions aimed at improving the decision-making process regarding therapeutic limitations for patients with advanced cancer hospitalised in Institut Jules Bordet's Acute Supportive Care Unit

Darius Razavi, Annie Drowart, Isabelle Libert, Yves Libert, Aurore Liénard

RECENT ACHIEVEMENTS

- Developed dyadic interventions aimed at improving communications between patients and caregivers
- Developed interventions that support smoking cessation in cancer patients
- Organised periodic training sessions for oncologists designed to improve their communication skills
- Created a Unit in charge of laser therapy to alleviate mucositis symptoms as well as hand and foot syndrome
- Demonstrated the beneficial effects of cannabinoids in cancer patients (including pain control)

Find out more at www.bordet.be/en/psychooncology

GERONTO-ONCOLOGIC RESEARCH

> "Our goal is to offer the best possible cancer care to older patients, taking into account their degree of frailty and their comorbidities."

TEAM AND INFRASTRUCTURE

Four leading physicians (1 geriatrician, 1 medical oncologist and 2 haemato-oncologists), and 1 fully dedicated nurse supported by members of the psycho-oncology team (including a neuro-psychologist) constitute this group.

Lissandra Dal Lago, Thierry Pepersack, Dominique Bron

AIMS

- With the use of validated tools, avoid overtreatment and undertreatment of the geriatric cancer population
- Develop new tools or refine existing ones in order to improve prognostic estimations, with a particular focus on the role of neurocognition
- Design or join clinical trials exploring alternative treatment regimens to chemotherapy or "softer" chemotherapy regimens
- Participate in real-world evidence phase IV initiatives focussing on the elderly cancer population

MAIN PROJECTS

- Evaluate a systematic pre-treatment geriatric screening on patient outcome
- Assess the feasibility of a computer-based geriatric assessment
- Explore a checkpoint inhibitor alone or combined with vinblastine in older patients with Hodgkin lymphoma and comorbidities
- Explore a checkpoint inhibitor in combination with rituximab, gemcitabine, oxaliplatin as an alternative to high dose chemotherapy for aggressive non-Hodgkin lymphoma in first relapse
- Immunomodulatory cytokines release through bone marrow mesenchymal stromal cells: examine the role of aging and their impact on the development of lymphoproliferative disorders

RECENT ACHIEVEMENTS

- Completed recruitment of the Belgian **COMPASS** trial in which different geriatric screening methods with newly diagnosed multiple myeloma patients are compared
- Completed recruitment of the **MCL R2 ELDERLY** study comparing 2 treatment schemes in elderly patients with mantle cell lymphoma

SELECTED PUBLICATIONS
[77] [78]

NURSING RESEARCH

> "Our goal is to improve patients' quality of life and adherence to treatment through evidence-based symptom management and early recognition of potentially severe complications."

TEAM AND INFRASTRUCTURE

Each Institut Jules Bordet unit has 1 nurse specifically interested in nursing research and who is a member of the Nursing Research Committee.

Patrick Crombez

AIMS

Improve nursing practices by implementing well-established processes:

- Identify a "Nursing Sensitive Patient Outcome" (e.g., catheter-related infections)
- Search for evidence-based guidelines describing how to best manage the problem
- Implement these guidelines in the Units
- Evaluate the impact of this change in nursing care on patients' well being

MAIN PROJECTS

- Identification of risk factors associated with falling among elderly patients and implementation of evidence-based preventive measures
- Systemic assessment of opioid-induced constipation and early implementation of adequate measures
- Early recognition of signs of neutropenic sepsis and rapid nursing intervention to enable documentation and antibiotic start within 1 hour (ongoing)
- Study of the feasibility of implementing state of the art palliative care interventions in a general oncology ward (in planning phase)

RECENT ACHIEVEMENTS

- Implemented a way to fix endotracheal tubes during long-term artificial ventilation that avoids spontaneous extubation
- Implemented a tool to improve communications between healthcare professionals in each Institut Jules Bordet unit

PATIENT INVOLVEMENT AND EMPOWERMENT

> "Our goals are to involve patients in order to increase the quality of our research and make projects more patient-centric while reducing inequalities in cancer care in a multicultural society."

TEAM AND INFRASTRUCTURE

The team includes 1 coordinator in research promotion and patient partnerships (PhD), 1 anthropologist, a group of 5 to 8 patient-partners, and clinical research professionals (collaborations)

AIMS

- Improve clinical and translational research by promoting patient involvement in studies through collaborations and the co-creation of projects
- Empower patients by developing innovative communication materials
- Guarantee optimal cancer care to migrants and ethnic minorities, including participation in clinical trials
- Train health care professionals on migrants' health and cultural issues

MAIN PROJECTS

- Research on patient involvement: coordination of the OECI Collaboration for Good Practices with Patients (CGPP) working group, which develops methodologies to launch, support and evaluate patient involvement initiatives in European cancer centers
- Communication about clinical research: development of tools and media solutions to engage patients in research
- Identification of risk factors for non-adherence to cancer therapy in migrants with haematological malignancies
- Comparison of incidence and mortality rates according to migration patterns in patients with haematological malignancies
- Development of a strategic plan to provide linguistically and culturally competent cancer care at Institut Jules Bordet

Patrick Miqueu, Sandra Michiels

RECENT ACHIEVEMENTS

- Created the PISARO group, the first Belgian patient advisory group in research (2018). The group gives insightful advice on research protocols and helps in the development of patient information documents and consent forms
- Developed a decision aid to support cancer patients' decision-making about clinical trial participation (**IREN**). This project received the Pfizer Oncology Award in 2016 and the Detournay & Damman-Latrique Cancer Research Grant in 2017
- Launched a new version of the Institut Jules Bordet's website (2017), integrating the various activities of a university hospital, and illustrating to patients and public the continuum between care and research
- Created a cross-cultural study subgroup within the Multinational Association of Supportive Care in Cancer (MASCC)
- Systematically recorded ethnolinguistic data for every new patient cared for at Institut Jules Bordet

New facilities will bring new opportunities for research

In 2021, the Institut Jules Bordet laboratories will be integrated into the Anderlecht campus of the Université Libre de Bruxelles (ULB), close to the academic general Hospital Erasme and the laboratories of the ULB Faculty of Medicine. New opportunities and developments will materialise:

◆ Creation of a new laboratory dedicated to the radiobiology of radionuclide therapies and external beam radiotherapy (EBRT). This unit will

- be supported by micro-imaging and micro-irradiation modalities
- perform preclinical studies in vitro on cell lines, in vivo on small animal models (mice and rats), and ex vivo on biological samples (tissues)
- have its micro-irradiation component belong to the Brussels Radiotheranostics Platform currently under construction in collaboration with the VUB
- pursue 3 major research themes:

Improving knowledge about the effect of ionising irradiation

- Stereotactic RT and its abscopal effects
- The effect of radionuclide therapies and more specifically of radiotheranostics

Evaluating novel treatment combinations involving ionising irradiation through radionuclide therapies and EBRT

- Combination with targeted therapies
- Combination with immunotherapies
- Combination with radiosensitising therapies

Monitoring the use of new radiotheranostics, EBRT protocols, contrast products and imaging sequences in the context of molecular and functional imaging

◆ Reinforcement of the already existing collaboration between the J.-C. Heuson BC laboratory (C. Sotiriou) and the ULB Cancer Research Center, most notably the laboratories of Cédric Blanpain (cancer initiation, development and metastasis) and François Fuks (cancer epigenetics)

◆ Integration of the current Experimental Haematology Laboratory into a Cancer Immunology Laboratory that will unite all the expertise in immunotherapeutic translational research across solid and haematological malignancies and develop fundamental research in cancer immunology in close collaboration with the Gosselies and the Erasme immunology research laboratories

Find out more at www.bordet.be/index.php/en/bordet-new

Organisation of Research

Since its creation, Institut Jules Bordet has always been a major actor in clinical and translational research. Over several decades, a few departments, very active in their respective fields, developed extensive expertise and specific skills in research activities, spanning from the design of ambitious scientific projects to proficiency in operational management.

Over time, a need arose to create more synergies between these different structures and to avoid inefficient duplication of efforts. The idea was to endow Institut Jules Bordet with an efficient research organisation able to conduct complex research.

In 2016, Institut Jules Bordet officially established its new research infrastructure.

The purpose of this reshuffle included the following:

- Promote excellence and professionalisation of research activities
- Stimulate scientific creativity
- Address OECI standards
- Develop and maintain a competitive position in clinical research at the Belgian and international levels
- Ensure efficiency for cost control
- Implement appropriate legal and contractual protection for Institut Jules Bordet and its researchers

Governance

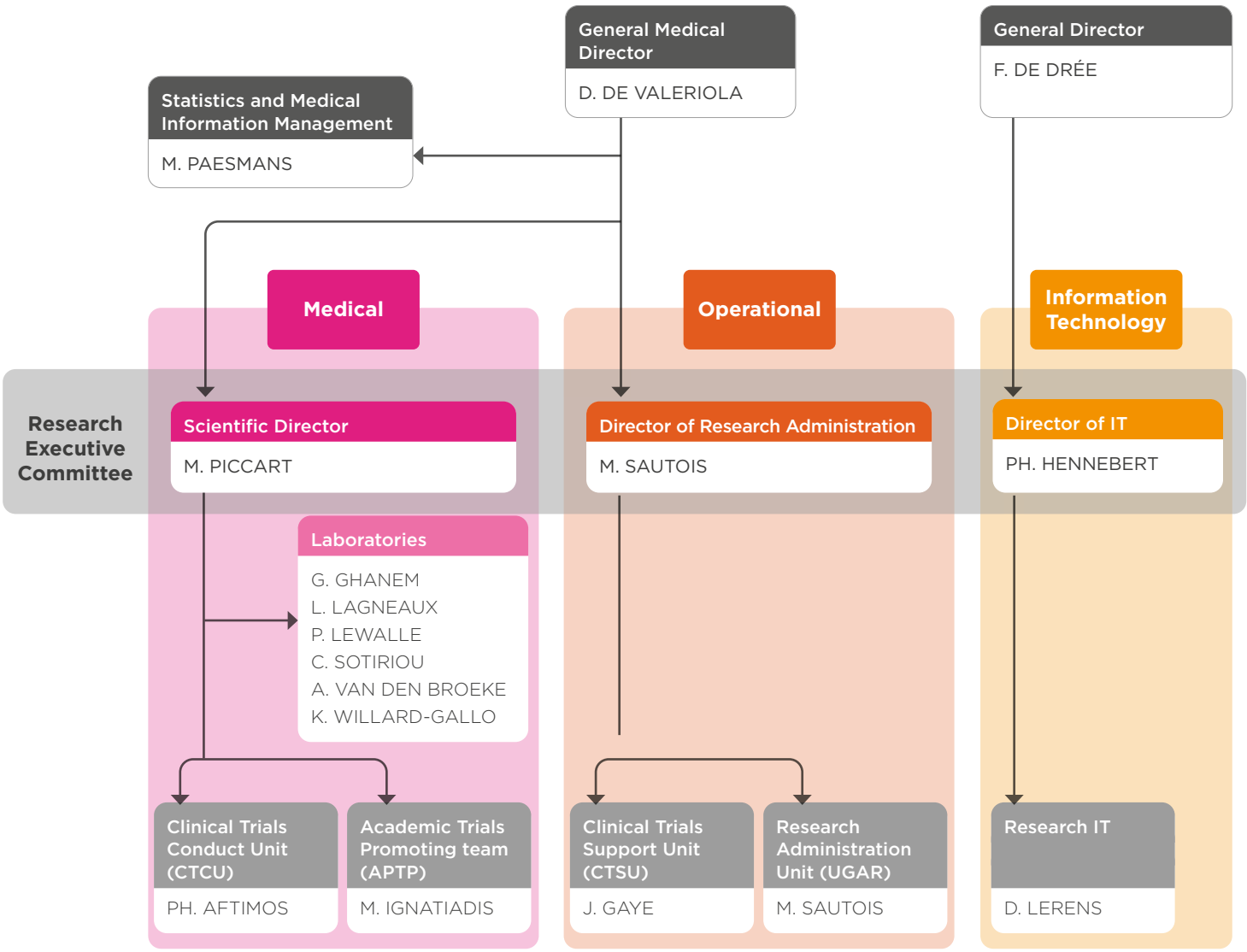
Successful research projects require strong collaboration between medical, scientific and operational teams. Institut Jules Bordet organises and conducts research by gathering scientific, medical, operational and information technology (IT) skills and expertise from all departments.

Research activities are now organised through 3 main structures working in close collaboration:

- A medical and scientific team, responsible for the development of new research projects and clinical trials, the enrollment and follow-up of patients, data collection and analysis, and the publication of the results in collaboration with the statistical team
- An operational team supporting the set-up and conduct of the research projects and clinical trials, in compliance with all legal and regulatory obligations and ensuring administrative and financial follow-up
- A specific team dedicated to IT for research

Julie Gaye, Marielle Sautois, Philippe Hennebert, Marianne Paesmans

RESEARCH ORGANIGRAMME



Institut Jules Bordet participates in many clinical trials with external sponsors, both from the pharmaceutical industry and academia, but also runs its own academic trials, many of them being international interventional trials with investigational medicinal products.

With its dedicated structures, Institut Jules Bordet can efficiently carry out clinical trial sponsors' responsibilities

Working in close collaboration with the above, specific decision-making bodies ensure the good governance of research activities:

INSTITUT JULES BORDET RESEARCH BOARD

The Institut Jules Bordet Research Board is composed of the Scientific Director, the General Medical Director, the General Director, the Director of Research Administration, the Heads of the Medical and Research departments, the IT Director and the Information Management Unit Director. This board carries out the following missions at the institutional level

- Defines research strategy and budget
- Analyses research activity reporting and processes

RESEARCH EXECUTIVE BOARD

The Research Executive Board is composed of individuals specialised in the operational aspects of research activities and meets on a very regular basis. This board manages global research operations and resources

- At site level: external sponsorship (pharma or academic)
- At sponsor level: Institut Jules Bordet sponsorship (academic) or service provider

PROJECT REVIEW COMMITTEES

Beyond these strategic and operational boards, some specific committees are in place that aim to optimise, stimulate and streamline the procedures related to the assessment and set-up of research projects.

Protocol Review Committees (PRC)

These committees aim to assess in an efficient and timely manner the clinical trial proposals coming from Institut Jules Bordet's medical departments that involve external sponsors

Committee for Clinical Research Optimisation

This committee aims to assess and provide strong scientific support to the research projects proposed by Institut Jules Bordet's study chairs. These projects, sponsored in-house, can be retrospective or prospective and may include human biological material.

Tumour Board

Biobanking activities are regulated by the Tumour Board, a scientific advisory committee. The Tumour Board takes decisions about the facilities, equipment, implementation of guidelines on best practices and, above all, the distribution and sharing of samples and data. The Board is a multidisciplinary team, including pathologists, biostatisticians, researchers and clinicians, and faces a crucial ethical challenge: improving and maintaining the trust of patients, clinicians, researchers and industry, and across academic medical networks.

Ethics Committee

Institut Jules Bordet's Ethics Committee is an independent body whose role includes:

- Prior to implementation, giving an opinion on all research projects for experimentation on humans, including interventional trials but also observational studies and retrospective research projects
- Monitoring and advising on ethical aspects of hospital care practices
- Assisting in decision-making on ethical aspects of individual cases

Research Support Units

RESEARCH ADMINISTRATION UNIT

The Research Administration Unit is a centralised unit set up to manage research. Its principal missions related to research projects are the following:

- Budgetary evaluation and financial monitoring of the projects conducted at Institut Jules Bordet
- Legal and contractual management
- Coordination of human and operational resources

CLINICAL TRIALS SUPPORT UNIT

The Clinical Trials Support Unit (CTSU) assists researchers from academia and industry in the development and conduct of phase I, II and III clinical trials:

- in early disease (neoadjuvant, adjuvant) and advanced disease (locally, metastatic)
- for all cancer types
- for all treatment and diagnostic modalities

CTSU can manage a clinical study from A to Z or can collaborate with partners on specific activities. CTSU activities include:

CLINICAL STUDY MANAGEMENT
operational coordination, communication

MEDICAL AND SCIENTIFIC EXPERTISE
clinical study design, medical oversight

CONTRACT MANAGEMENT
legal expertise, financial management

REGULATORY AFFAIRS
submissions in EU, regulatory compliance

PHARMACOVIGILANCE
safety reporting, adverse events oversight

STATISTICS
clinical study design and methodology, analysis plan, data analysis, publication

SITES MONITORING
site initiation visits, on- and off-site visits

DATA MANAGEMENT
ECRF design, data quality control

CENTRAL IMAGING
standardisation, collection, experts review

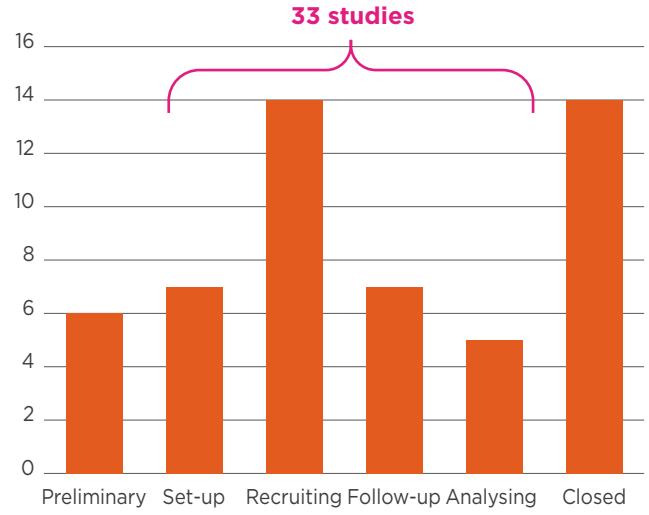
BIOSAMPLES MANAGEMENT
standardisation, collection, analysis

INFORMATION TECHNOLOGY
development and maintenance of software, users support

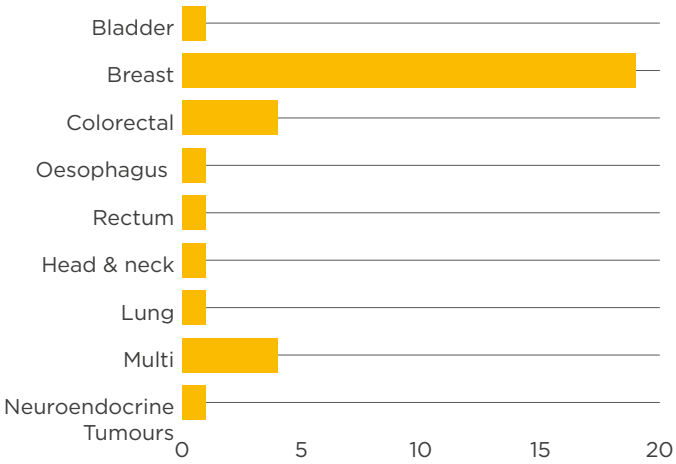
CTSU in numbers (31/12/2019)

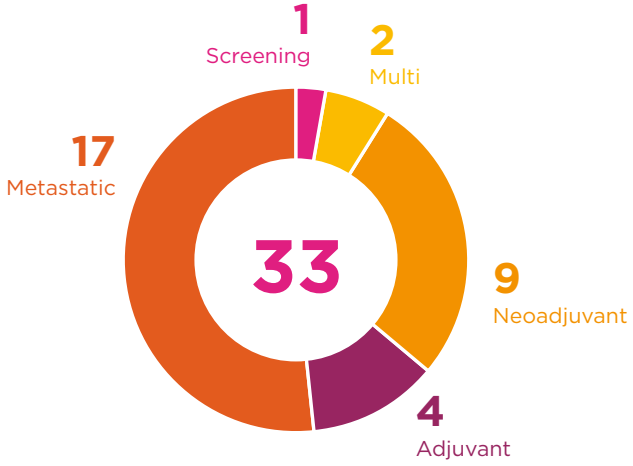
Number of trials operationally managed by the CTSU

23 trials sponsored by Institut Jules Bordet, 10 as a service provider for academic or pharmaceutical partners.

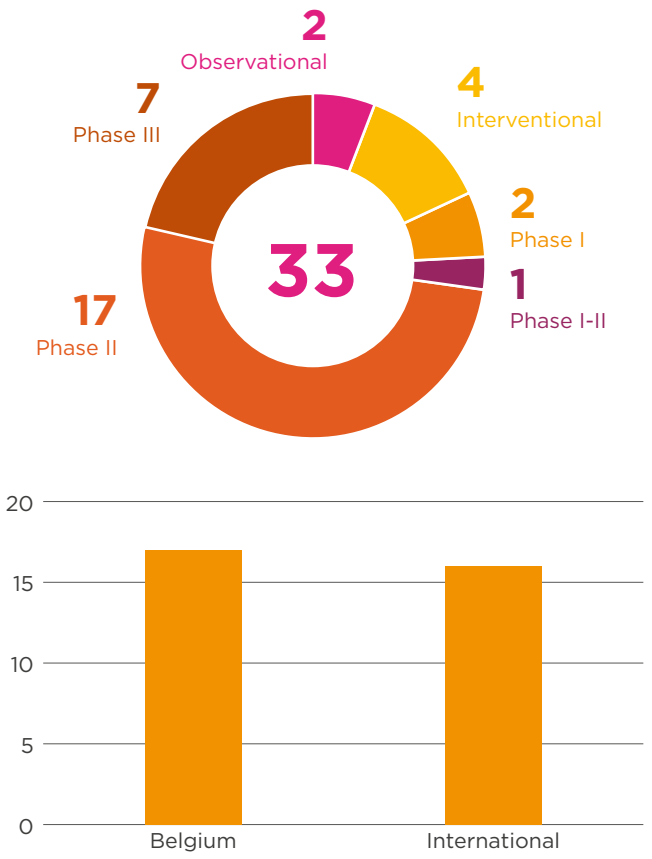


Cancer types and settings of the trials managed by the CTSU





National/International trials and phases of the trials managed by the CTSU



Find out more at ctsu.bordet.be

CLINICAL RESEARCH INFORMATICS

The Clinical Research Informatics team provides and maintains the computerised systems for the CTSU and other research activities, and develops software solutions for research activities when the Institute acts as trial coordinator or sponsor (e.g., tools for electronic data capture, safety databases, registration of patients into trials, biotracking or for the imaging core lab).

More generally, the Clinical Research Informatics team provides software tools for operational activities that are susceptible to being used for research activities too. The core of these tools is the electronic health record, developed in-house, in which information is stored as HL7 CDA documents in order to combine textual and structured information. It makes use of "clinical building blocks" editable in various contexts (for instance for multidisciplinary team meetings or for discharge reports) and covering previous cancer treatments, biomarkers and comorbidities. On all electronic health records, queries can be run, including full-text searches with the integration of queries on other linked repositories (the tumour data bank, the chemotherapy prescription database and the cancer registry).

Projects include to:

- better collect structured and coded toxicities
- provide a digital workflow for tracing all activities linked to a clinical project from study design to publication
- develop a tool allowing to convert data from the electronic health record into e-case report form data (laboratory values and toxicity reports)
- gather patient-reported outcomes through smartphone applications and websites

Marianne Paesmans, Ionna Laios, Evandro de Azambuja, Ligia Craciun, Michail Ignatiadis, Denis Larsimont

INFORMATION MANAGEMENT UNIT

The Information Management Unit provides support to the clinical departments and the Institute as a whole.

This unit carries out the following missions:

- An epidemiological mission, by developing, managing and operating the hospital cancer registry as well as the clinical data related multidisciplinary oncological consultations. In doing so, it contributes actively to the Belgian Cancer Registry and makes the hospital's cancer registry available as a research support tool and care quality evaluation tool. Because it includes all incident tumours since 1 January 2000, now including about 40 000 records, it is regularly used to plan studies as well as to conduct retrospective studies by identifying patients and providing a core dataset to the investigators. It is presently limited to data about the primary tumour episode, but the process of extending it to collect data on relapses for breast cancer or for rare tumours is ongoing.
- An analysis and reporting mission related to the Institute's activities, in particular by developing and maintaining a data warehouse
- An oncological clinical research mission in terms of methodology and statistics (single-centre and multicentre research, centralised at the Institut Jules Bordet and elsewhere, including contribution to clinical projects and meta-analyses). This mission involves collaboration with the CTSU and participation in the various Project Review Committees.

Projects include to:

- identify and document all data sets collected for each clinical project sponsored by the Institute, including retrospective projects, and to make them available to the wider community of researchers
- achieve early identification of new patients with rare tumours in order to help clinicians improve the therapeutic management of these cases and to develop a specific registry for rare tumours, facilitating research on these patients
- link the cancer registry with other data sources. The goal for this last project is to be able to link a medical treatment or a medical investigation to a record in the cancer registry.

ACADEMIC TRIALS PROMOTING TEAM

The Academic Trials Promoting Team (ATPT) promotes and initiates new academic studies sponsored by Institut Jules Bordet.

The physicians comprising the ATPT design new clinical studies, supported by the extensive experience of the Institut Jules Bordet's statisticians for the methodology, statistical considerations and conduct of their projects. The ATPT and statisticians work closely with the CTSU throughout the study conduct

TUMOUR BANK AND PATHOLOGY DEPARTMENT EXPERTISE

The Tumour Bank provides cancer researchers with a diverse selection of high-quality biospecimens and derivatives, comprehensively annotated with clinical data; these materials are used to identify diagnostic molecular markers, prognostic indicators and therapeutic targets.

Samples and clinical data supplied by the Tumour Bank are handled in accordance with the highest ethical standards and in strictest compliance with all applicable rules and regulations.

Tumour and adjacent normal tissues from donors are available in snap frozen or formalin fixed paraffin embedded formats. More recently matched biofluid sets are added to tissue collections. More than 25 000 tissue samples and whole blood fractions are available, provided by more than 10 000 patients.

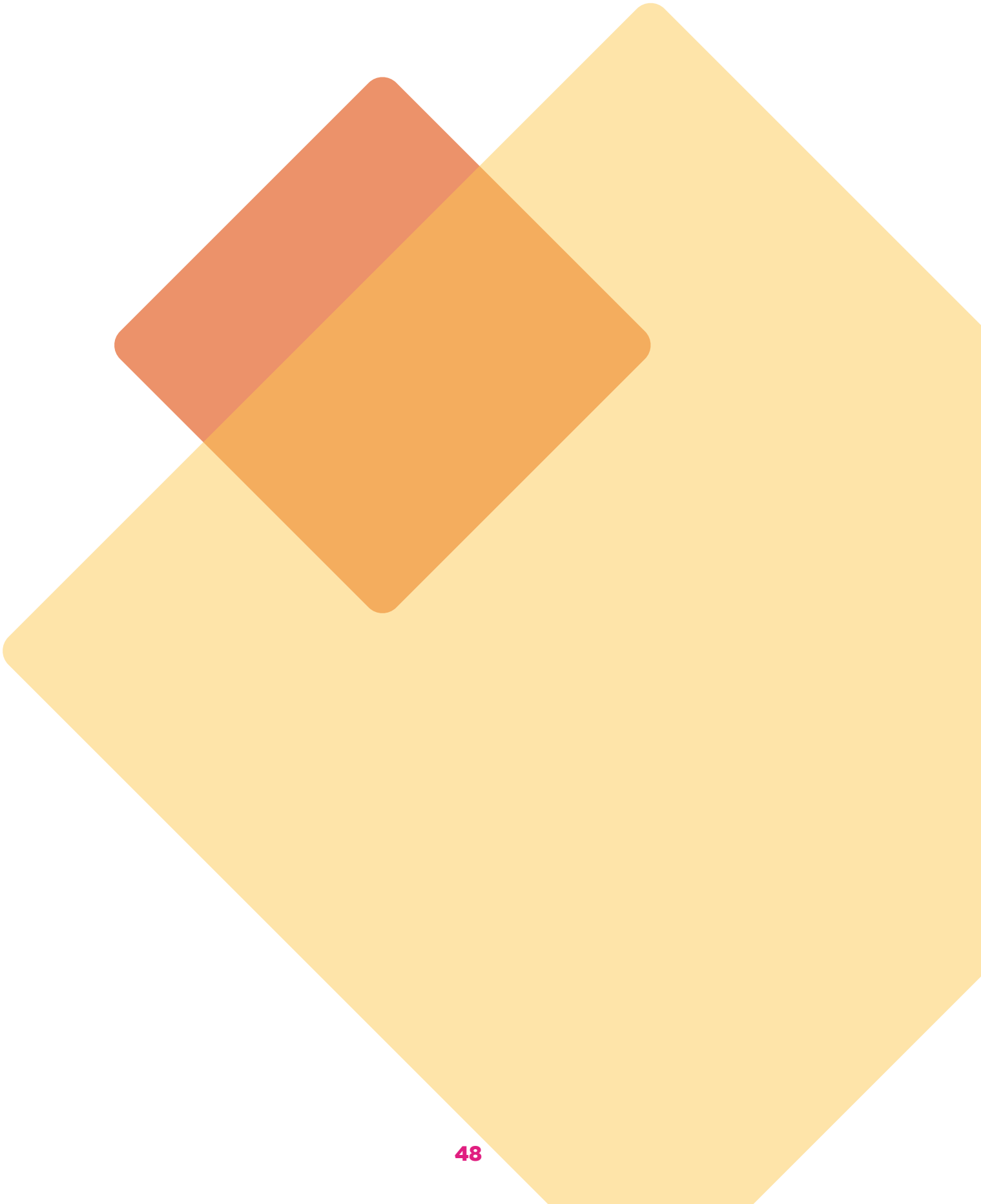
The Tumour Bank is completely integrated into the Pathology Department, enabling full and accurate analysis of tumours by pathologists prior to sample preservation. It also forms an integral part of other Belgian biobanks – the Cancer Register Virtual Catalogue, BWB (Wallonia-Brussels BioBank) and of 2 European biobanks: the BBMRI and ESBB.

A robust system for the sample quality control exists and enables us to support numerous research projects every year. The Tumour Bank has been ISO 9001 certified since 2012 – a guarantee of quality. The quality of our tumour samples is very satisfactory and adapted to a large panel of next-generation technologies.

The Pathology Department is a key partner in all of Institut Jule Bordet's translational research projects. Since 2009, it has invested time and energy to obtain full BELAC accreditation (ISO 15189) and remains deeply involved in quality testing of all clinically relevant biomarkers (e.g., PD(L)1 and many others).

It is also responsible for Institut Jules Bordet's NGS platform, an essential tool for tumour molecular characterisation and precision medicine.

Collaborations



NATIONAL AND INTERNATIONAL COLLABORATIONS

National Collaborations

ULB
Antwerp University
Ghent University
KU Leuven
Mons University
Namur Research Institute
UCL
ULg
VUB

European Collaborations

Czech Republic
France
Paris
- Gustave Roussy
- Institut Curie
- University René Descartes
- Institut Pasteur
- Hôpital St-Louis

Rennes
Strasbourg
Germany
- Hamburg
- Regensburg
- Freiburg

Greece
- University of Crete

Italy (I. Nationale Tumori Milan)
- Rome
- Pisa
- Aosta

Latvia (Riga)
Luxembourg
Norway (Bergen)
Spain (Vall d'Hebron – Barcelona)
Sweden (Karolinska)
Switzerland (Lausanne)
The Netherlands
- Groningen
- Rotterdam
- Amsterdam (NKI)

UK
- London / Oxford / Cambridge
- Newcastle

Collaborations outside Europe

Australia – Sydney
Canada
- Montreal (McGill)
- Saskatoon

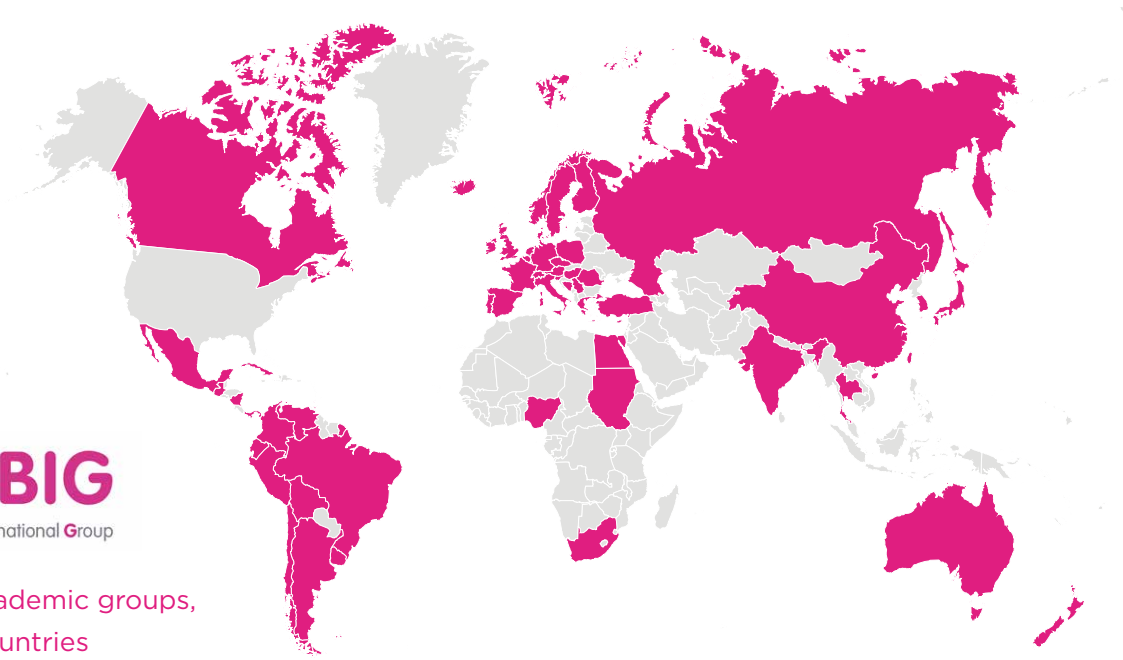
Japan
- Tokyo
- Nagasaki
- Kumamoto

Lebanon
Marocco
USA
- Yale
- MD Anderson
- NCI
- Johns Hopkins University

PARTICIPATION IN TRIALS OF INTERNATIONAL ACADEMIC RESEARCH GROUPS:

BIG
EORTC / ESTRO
IBCSG
SIOP
MEDSIR
MASCC
SIOG
EHA SWG

WHO IS PART OF BIG?



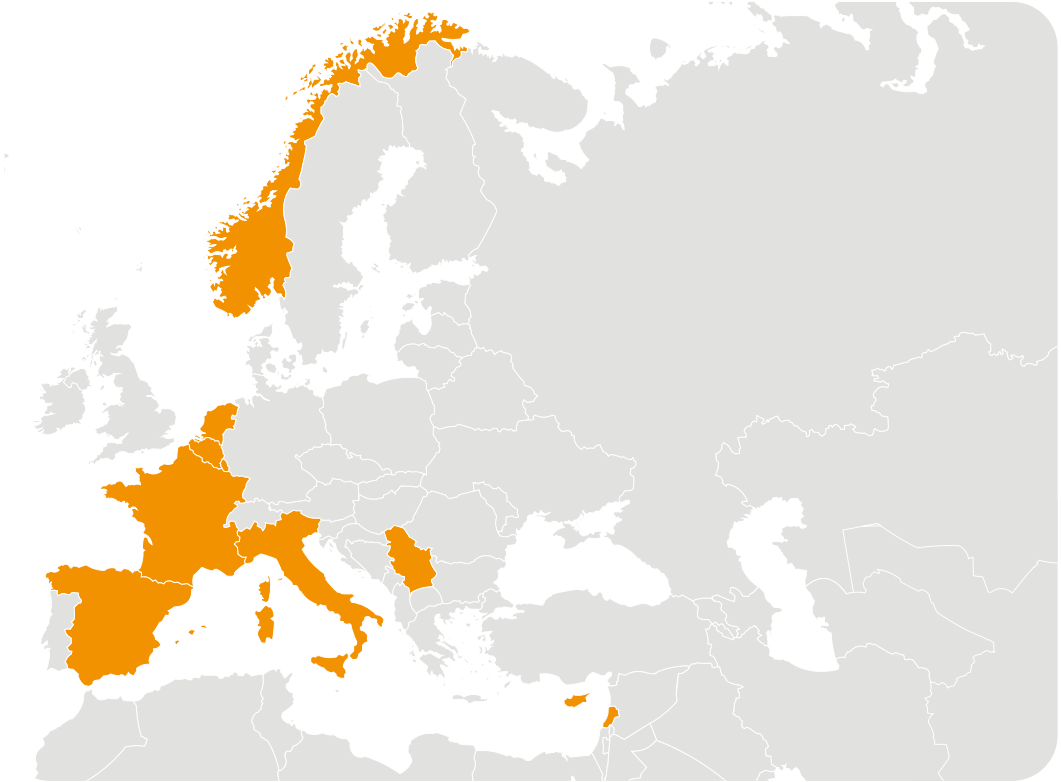
BIG
Breast International Group

56 academic groups,
60 countries

WHO IS PART OF ONCODISTINCT ?

ONCODISTINCT NETWORK

26 sites in
10 countries



Funding

Les Amis de l'Institut Bordet

'LES AMIS DE L'INSTITUT BORDET', THE INSTITUTE'S NO. 1 PRIVATE DONOR

For more than 50 years, Les Amis de l'Institut Bordet ("Les Amis") have been financing research at the Institute.

As the Institute's largest private sector donor, they support dozens of innovative research projects every year, enabling patients to benefit from cutting-edge treatments.

The money raised – more than 100 million euros since their creation – is given directly to the Institute's doctors and researchers, without any overheads or wasted energy.

All the projects financed are validated by leading international experts.

'The projects submitted to "Les Amis" are of high quality, as confirmed by the assessments of international experts. Thanks to their support, researchers can develop innovative, ambitious and significant projects for the institution.' Professor Fridman, scientific adviser of "Les Amis".

While "Les Amis" have made research their number one priority, such research would be inconceivable without the extraordinary technological advances now available. The association therefore also helps the Institute acquire the latest generation of medical equipment essential to its researchers.

"Les Amis" are also committed to the future, creating a number of fellowships to support promising young researchers. The first 'Young Talent Grant', which allows promising young doctors to launch their own research activities by freeing them from clinical duties on a part-time basis, was awarded to Dr Laurence Buisseret to work on new biomarkers in immunotherapy.

The Institute will soon be moving into a new building currently under construction in Anderlecht – a fabulous project that will reinforce its role as a leading oncology centre in Belgium and abroad. "Les Amis" hope to accompany the Institute in this incredible adventure and, with the help of their generous donors, meet the new challenges they will face!

Les Amis de l'Institut Bordet asbl

Find out more at amis-bordet.be

> "Without the constant support of "Les Amis", the Institut Jules Bordet would never have been able to establish itself as one of the world's leading cancer centres. Over the past few decades, almost every piece of state-of-the-art infrastructure, new technology or research team has been funded in whole or in part by "Les Amis".

Dr Dominique de Valeriola,
General Medical Director of the Institut Jules Bordet

Ariane Cambier
General Secretary of
"Les Amis de l'Institut Bordet"

Research Grants

From 2016 to 2019, our researchers have been awarded highly prestigious research grants provided by the organisations listed below.

Funders Name
Breast Cancer Research Foundation
Belgian Society of Medical Oncology
European Society of Medical Oncology
Fonds de la Recherche Scientifique-FNRS
Fondation ARC pour la Recherche sur le Cancer
Fondation Cancer Luxembourg
Fondation Contre le Cancer
Fondation Roi Baudouin
Fonds Ariane
Fonds Barsy-Laffut
Fonds Yvonne Boël
Fonds Gaston Ithier
Fondation Lambeau-Marteaux
Het Anti-Kankerfonds
Plan National Cancer
Télévie (FNRS)
WALInnov

Visiting Medical Research Fellows (2016-2019)

Country	Name
Belgium	DURAN DERIJCKERE Ivan
Brazil	CAPARICA Rafael
Brazil	EIGER Daniel
Brazil	FRANZOI Maria Alice
Brazil	PONDE Noam
Canada	MARTEL Samuel
Canada	PLOUZNIKOFF Nicolas
Germany	MAURER Christian
Italy	CAMERA Silvia
Italy	DE ANGELIS Claudia
Italy	GIACOMO Bregini
Italy	LAMBERTINI Matteo
Italy	POGGIO Francesca
Liban	BHOLOK Ali
Portugal	BRANDAO Mariana
Turkey	TUGBA AKIN Telli

Awards

2016

- **CTCU** (Clinical Trial Conduct Unit) of Institut Jules Bordet - The Pfizer Oncology Award for the project *Dynamic perspective for patient information: How improving informed consent (IC) process/understanding using 3D film or cartoon material.*
- **Dragan T.** – ESO Best Clinical Case Award
- Stamapoulos B.- AMGEN award for the best oral presentation of the Annual Meeting of the Belgian Hematological Society, La Hulpe, Belgium
- **Stamatopoulos B.** - Prize for poster presentation – 21st Annual EHA CongressCopenhagen, Denmark
- **Van Damme M.** - Prize for poster presentation and oral presentation – 31st General Meeting of Belgian Haematological Society, La Hulpe, Belgium

2017

- **Buisseret L.** - 2nd prize of the Belgian Society of Medical Oncology: BSMO Junior Awards for a scientific presentation: *Clinical significance of CD73 expression in triple-negative breast cancer from the BIG 02-98 adjuvant phase III clinical trial*
- **Martinez Chanza N.** - 1st prize for best clinical case, Journées Onco-Urologie Médicale: *Carcinome urothélial et syndrome de lynch; un défaut de réparation de l'ADN*
- **Piccart M.** - St Gallen International Breast Cancer Award Winner, 15th St.Gallen Breast Cancer Conference
- **Stamatopoulos B.** - Prize for poster presentation – 22nd EHA Annual Congress, Madrid, Spain
- **Stamapoulos B.**- UK CLL's Hamblin Prize awarded to the best paper published in 2017 by a researcher affiliated with a UK-based group
- **Stamapoulos B.**- Bekalès Foundation prize awarded to a young researcher (under age 40) who has made a significant contribution to the field of leukemia
- **Woff E.** - 1st prize for the best oral presentation in the category of Best Scientific Awards" of the 18th Symposium of the Belgian Society of Nuclear Medicine

2018

- **Bouchart Ch.** - I3health-ULB Best Student Award for the Certificate of Higher Education in Translational Medicine
- **CTCU** (Clinical Trials Conduct Unit) of Institut Jules Bordet - Syneos Site Appreciation Award
- **Piccart M.** - Fondation ARC Leopold Griffuel Award (Association pour la Recherche sur le Cancer, Paris,)
- **Piccart M.** - KNAW Bob Pinedo Cancer Care Award (Cancer Center Amsterdam, University Medical Centers)
- **Van den Begin R.** -Prize of the Belgian Society of Radiation Oncology for the best PhD presentation

2019

- **Bron D.** -Prix Jean Teghem awarded by the CEPULB-Université Inter-Ages to reward a person distinguished by remarkable work in the field of popular science or lifelong education
- **Lagneaux L, Meuleman N and Crompot E** - Bekalès Foundation prize awarded to a research team demonstrating a significant contribution to the field of leukemia
- **Michiels S.** -Patient Centricity Award ("PACE") Award of Belgian Hematology Society (BHS) for MADESIO, *Project of multicultural support for adherence of migrants and ethnic minorities with hematological cancer*
- **Woff E.** - 2nd prize for the best oral presentation in the category "Best Scientific Awards" of the 19th Symposium of the Belgian Society of Nuclear Medicine

Publications 2016-2019

2016-2019 (Selected Papers)

J.-C. HEUSON BREAST CANCER TRANSLATIONAL RESEARCH LABORATORY

[1] **Y. Bareche, D. Venet, M. Ignatiadis, P. Aftimos, M. Piccart, F. Rothe, C. Sotiriou.** *Unravelling triple-negative breast cancer molecular heterogeneity using an integrative multiomic analysis.* Ann Oncol 29(4) (2018) 895-902.

[2] **Y. Bareche, L. Buisseret,** T. Gruosso, E. Girard, **D. Venet, F. Dupont, C. Desmedt, D. Larsimont,** M. Park, **F. Rothe,** J. Stagg, **C. Sotiriou.** *Unraveling triple-negative breast cancer tumour microenvironment heterogeneity: towards an optimized treatment approach.* J Natl Cancer Inst (2019).

[3] **I. Bozovic-Spasojevic, D. Zardavas, S. Brohee, L. Ameye, D. Fumagalli, F. Ades, E. de Azambuja, Y. Bareche, M. Piccart, M. Paesmans, C. Sotiriou.** *The Prognostic Role of Androgen Receptor in Patients with Early-Stage Breast Cancer: A Meta-analysis of Clinical and Gene Expression Data.* Clin Cancer Res 23(11) (2017) 2702-2712.

[4] **D. Brown,** D. Smeets, B. Szekely, **D. Larsimont,** A.M. Szasz, P.Y. Adnet, **F. Rothe,** G. Rouas, Z.I. Nagy, Z. Farago, A.M. Tokes, M. Dank, G. Szentmartoni, N. Udvarhelyi, G. Zoppoli, L. Pusztai, **M. Piccart,** J. Kulka, D. Lambrechts, **C. Sotiriou, C. Desmedt.** *Erratum: Phylogenetic analysis of metastatic progression in breast cancer using somatic mutations and copy number aberrations.* Nat Commun 8 (2017) 15759.

[5] **L. Buisseret,** S. Pommey, B. Allard, **S. Garaud,** M. Bergeron, I. Cousineau, **L. Ameye,** Y. Bareche, **M. Paesmans,** J.P.A. Crown, A. Di Leo, S. Loi, **M. Piccart-Gebhart, K. Willard-Gallo, C. Sotiriou,** J. Stagg. *Clinical significance of CD73 in triple-negative breast cancer: multiplex analysis of a phase III clinical trial.* Ann Oncol 29(4) (2018) 1056-1062.

[6] **C. Desmedt,** G. Zoppoli, G. Gundem, G. Pruneri, **D. Larsimont,** M. Fornili, D. Fumagalli, **D. Brown, F. Rothe,** D. Vincent, N. Kheddoumi, **G. Rouas,** S. Majjaj, S. Brohee, P. Van Loo, P. Maisonneuve, **R. Salgado,** T. Van Brussel, D. Lambrechts, R. Bose, O. Metzger, C. Galant, F. Bertucci, **M. Piccart-Gebhart,** G. Viale, E. Biganzoli, P.J. Campbell, **C. Sotiriou.** *Genomic Characterization of Primary Invasive Lobular Breast Cancer.* J Clin Oncol 34(16) (2016) 1872-81.

[7] **D. Fumagalli, D. Venet, M. Ignatiadis, H.A. Azim, Jr., M. Maetens, F. Rothe, R. Salgado,** I. Bradbury, L. Pusztai, N. Harbeck, H. Gomez, T.W. Chang, M.A. Coccia-Portugal, S. Di Cosimo, **E. de Azambuja,** L. de la Pena, P. Nuciforo, J.C. Brase, J. Huober, J. Baselga, **M. Piccart,** S. Loi, **C. Sotiriou.** *RNA Sequencing to Predict Response to Neoadjuvant Anti-HER2 Therapy: A Secondary Analysis of the NeoALTTO Randomized Clinical Trial.* JAMA Oncol 3(2) (2017) 227-234.

[8] **B. Nguyen, D. Venet, M. Lambertini, C. Desmedt, R. Salgado,** H.M. Horlings, **F. Rothe, C. Sotiriou.** *Imprint of parity and age at first pregnancy on the genomic landscape of subsequent breast cancer.* Breast Cancer Res 21(1) (2019) 25.

[9] **B. Nguyen, I. Veys, S. Leduc, Y. Bareche, S. Majjaj,** D.N. Brown, B. Boeckx, D. Lambrechts, **C. Sotiriou, D. Larsimont, C. Desmedt.** *Genomic, transcriptomic, epigenetic, and immune profiling of mucinous breast cancer.* J Natl Cancer Inst 111(7) (2019) 742-746.

MOLECULAR IMMUNOLOGY LABORATORY

[10] **L. Buisseret, C. Desmedt, S. Garaud,** M. Fornili, X. Wang, G. Van den Eyden, **A. de Wind,** S. Duquenne, **A. Boisson,** C. Naveaux, **F. Rothe,** S. Rorive, C. Decaestecker, **D. Larsimont, M. Piccart-Gebhart,** E. Biganzoli, **C. Sotiriou, K. Willard-Gallo.** *Reliability of tumour-infiltrating lymphocyte and tertiary lymphoid structure assessment in human breast cancer.* Mod Pathol 30(9) (2017) 1204-1212.

[11] C. Gu-Trantien, **K. Willard-Gallo.** *PD-1(hi)CXCR5(-)CD4(+) TFH Cells Play Defense in Cancer and Offense in Arthritis.* Trends Immunol 38(12) (2017) 875-878.

[12] C. Mascaux, M. Angelova, A. Vasaturo, J. Beane, K. Hijazi, **G. Anthoine,** B. Buttard, **F. Rothe, K. Willard-Gallo, A. Haller,** V. Ninane, A. Burny, **J.P. Sculier,** A. Spira, J. Galon. *Immune evasion before tumour invasion in early lung squamous carcinogenesis.* Nature 571(7766) (2019) 570-575.

[13] **G. Noel, M. Langouo Fontsa, K. Willard-Gallo.** *The impact of tumour cell metabolism on T cell-mediated immune responses and immuno-metabolic biomarkers in cancer.* Semin Cancer Biol 52(Pt 2) (2018) 66-74.

[14] **C. Solinas,** M. Ceppi, **M. Lambertini,** M. Scartozzi, **L. Buisseret, S. Garaud, D. Fumagalli, E. de Azambuja, R. Salgado, C. Sotiriou, K. Willard-Gallo, M. Ignatiadis.** *Tumour-infiltrating lymphocytes in patients with HER2-positive breast cancer treated with neoadjuvant chemotherapy plus trastuzumab, lapatinib or their combination: A meta-analysis of randomized controlled trials.* Cancer Treat Rev 57 (2017) 8-15.

[15] **C. Solinas, N.M. Chanza, A. Awada,** M. Scartozzi. *The immune infiltrate in prostate, bladder and testicular tumours: An old friend for new challenges.* Cancer Treat Rev 53 (2017) 138-145.

[16] **C. Solinas, D. Marcoux, S. Garaud, J.R. Vitoria, G. Van den Eynden, A. de Wind, P. De Silva, A. Boisson, L. Craciun, D. Larsimont, M. Piccart-Gebhart, V. Detours, D. t'Kint de Roodenbeke, K. Willard-Gallo.** *BRCA gene mutations do not shape the extent and organization of tumour infiltrating lymphocytes in triple negative breast cancer.* Cancer Lett 450 (2019) 88-97.

ONCOLOGY AND EXPERIMENTAL SURGERY LABORATORY

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Abbreviations

AML:	acute myeloid leukemia
ATL:	adult T-cell leukemia
ATPT:	Academic Trials Promoting Team
BCTL:	Breast Cancer Translational Research Laboratory
BIG:	Breast International Group
ctDNA:	circulating tumour DNA
CTCU:	Clinical Trials Conduct Unit
CTSU:	Clinical Trials Support Unit
CT scan:	computerized tomography scan
EBRT:	external beam radiotherapy
EORTC:	European Organisation for Research and Treatment of Cancer
FDG-PET:	fluorodeoxyglucose (FDG)-positron emission tomography (PET)
HER2:	human epidermal growth factor receptor 2
HTLV-1:	human T-cell lymphotropic virus type-1
GMP:	Good Manufacturing Practice
ICU:	Intensive Care Unit
MSC:	mesenchymal stromal cells
MRI:	magnetic resonance imaging
NGS:	next generation sequencing
OECI:	Organisation of European Cancer Institutes
PCR:	polymerase chain reaction
PET:	positron emission tomography
SBRT:	stereotactic body radiation therapy
SIRT:	selective Internal radiation therapy
TIL:	tumour infiltrating lymphocytes
TLS:	tertiary lymphoid structures
TNBC:	triple negative breast cancer

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