H.U.B
HÔPITAL UNIVERSITAIRE DE BRUXELLES
ACADEMISCH ZIEKENHUIS BRUSSEL

INSTITUT JULES BORDET INSTITUUT

Hôpital Erasme

Institut Jules Bordet Instituut

SCIENTIFIC REPORT

2025

For the years 2020-2024

ECI
Organisation of European Cancer Institutes – EEIG

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Foreword

J. Cimino,
M. Piccart
and
J.M. Hougardy

The Institut Jules Bordet (IJB) stands as a beacon of ambition, achievement, and interdisciplinary collaboration. Established 85 years ago, the IJB is now fully operational within its superb new infrastructure. The "New Bordet OECI-certified comprehensive cancer center" is seamlessly integrated into the academic campus of Université Libre de Bruxelles (ULB). With 250 beds dedicated to cancer care and an excellent setting, IJB maintains a steadfast commitment to providing the highest quality care and services for patients, their families, and all stakeholders in the fight against cancer. This commitment is a fundamental part of IJB's DNA, and all caregivers and dedicated research teams work together to address the challenges that cancer presents. Throughout its history, IJB has sought to remain at the forefront of work on developing strategies that will incorporate the latest discoveries and technological advances to fight cancer effectively.

Following a relocation that has brought it closer to the University's Medical Faculties and Laboratories, IJB has become a part of a dynamic hospital group with a significant impact on Brussels and Belgium. IJB is a cornerstone of Hôpital Universitaire de Bruxelles (H.U.B), a coalition bringing together three major institutions in Brussels: IJB, Hôpital Erasme, and HUDERF/UKZKF (Hôpital Universitaire Des Enfants Reine Fabiola / Universitair KinderZiekenhuis Koningin Fabiola). Integration within the H.U.B creates unique opportunities for the comprehensive cancer center to grow and build new synergies, shared values, a strong culture and its ambitions for innovation.

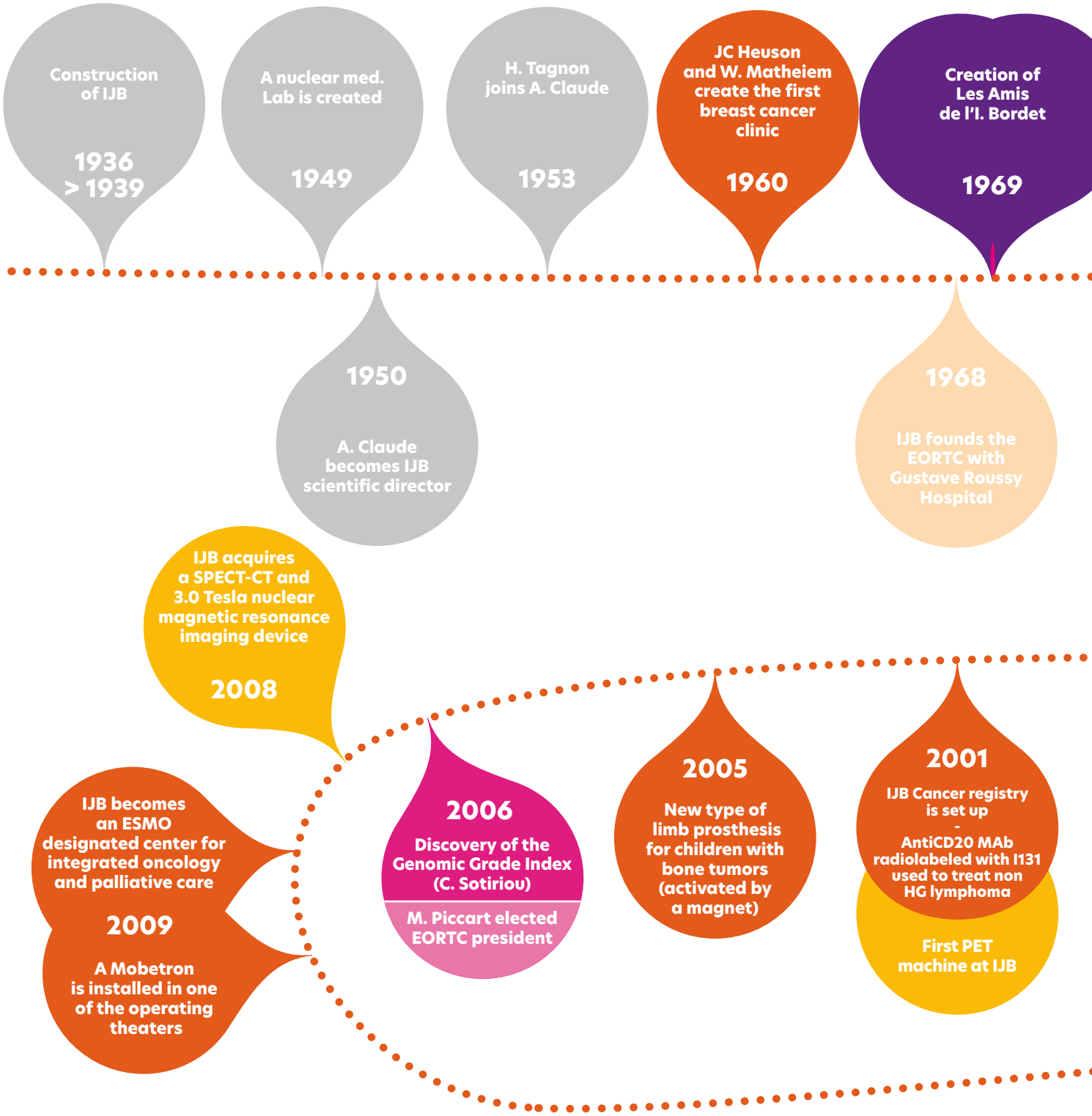
Alongside its role as a leader in cancer discovery within the medical sciences, IJB has also set a precedent for interdisciplinary work. It brings together healthcare researchers from diverse fields within medical and scientific oncology and accommodates several state-of-the-art technological platforms. This pioneering spirit of interdisciplinarity sets IJB apart, fostering an environment where innovative ideas and approaches can flourish. IJB now faces a series of challenges and opportunities as it enters a new era. A strategic research plan, aligned with its strategic medical plan, has highlighted 3 pillars:

1. *Transformative translational research*
2. *Highly specific biological targeting of cancer*
3. *Precision immunotherapy*

These strategic directions will create bridges between fundamental research in our laboratories and clinical applications, via a "dream team" consisting of clinician-researcher pairs. This initiative will enhance existing connections within H.U.B in the fields of neuroscience, the oncofertility clinic, cardiology, paediatric oncology, and other fields. Collaboration with the European Plotkin Institute for Vaccinology offers potential for development of anti-cancer vaccines. Strong ties have also been established with BioPark, a biomedical startup incubator originally founded by ULB.

Additional key areas for attention include building stronger bridges between our academic partners and the pharmaceutical industry, development of European networks of comprehensive cancer centers (especially through the European Organisation for the Research and Treatment of Cancer-EORTC, the Breast International Group-BIG, and the Oncodistinct Network), translational research, the sustainability of its technological platforms, a structural reorganisation to nurture a more dynamic and cross-disciplinary collaborative environment, renewal of its OECI certification, and exploitation of its biobanking and research discoveries. In this context, the "Association Jules Bordet" continues to play a crucial role, and we extend our heartfelt thanks to the association. The collective efforts of IJB's talented researchers, dedicated staff, and visionary leadership will undoubtedly continue to push the boundaries in the fight against cancer. IJB's tradition of excellence and its pioneering approach to interdisciplinary research make it a standout institution that is poised to make even greater contributions to medical science and society in the years to come.

With this ambition in mind, we pledge to ensure that IJB receives unwavering support from the H.U.B family and its co-founders, the City of Brussels and the Université Libre de Bruxelles. In the coming years we will showcase the exceptional quality of research together and carry it to the forefront of academic excellence.



The first 50 years of Institut Jules

1971 ERASMUS HOSPITAL is built

1972 First oncology out patient Unit.

1979 IJB = founder member of OECI

1985 IJB creates the first psycho-oncology UNIT

1970 Empirical antibiotics for febrile Neutropenia (J Klastersky)

Creation of the first cyta pheresis facility by P. Strijckmans

1977 IJB acquires a linear accelerator

1980 Intensive care unit is set up inside IJB

1988 Introduction of intra operative RT

1989 IJB opens the first pain clinic

1990 Creation of IJB "Data Center"

1994 IJB creates the first umbilical cord blood bank

1996 Creation of BIG with headquarters at IJB

1997 IJB introduces the sentinel lymph node technique - Pathology lab launches the HER2 FISH test

1999 IJB performs the first haplo-identical bone marrow transplant in a leukemia patient

s Bordet

- High quality translational research
- Innovation in cancer treatment
- High tech equipement
- International research initiatives

The Strategic Oncology Research plan for 2025-2027

In 2009 the Jules Bordet Cancer Center celebrated its 70th birthday and marked a number of its important contributions to the care of cancer patients and the implementation of effective cancer research infrastructure at the International level.

Its original small size (160 beds) partly accounts for its pioneering role in accelerating research through networking and its agility in building a close "in-house" collaboration between cancer disciplines.

Small hospital institutions, however, cannot survive the recent technological revolution in medicine that requires powerful, expensive equipment in the areas of radiology, surgery, radiotherapy, nuclear medicine, big data, artificial intelligence, omics dissection of tumours, telemedicine devices and so on…

In 2021, a new Institut Jules Bordet (IJB) with 250 beds opened its doors on the Erasme Campus of the Université Libre de Bruxelles (ULB), with the aim of being in a stronger position to meet today's challenges in cancer treatment and research.

A period of adaptation was required to become familiar with a new "ECOSYSTEM" (see below on page 4-5) and establish a new form of "GOVERNANCE" (see p94). After this, a retreat for oncology researchers working on the Erasme Campus was organised to define a strategic research plan for the 2024 to 2027 period; paediatric oncology research was not included in this first "brainstorming" process and its conclusions were endorsed by the heads of departments and by the new Governance leadership.

Given the increasing complexity of the oncology services landscape and the associated research structures in Europe and within Belgium, it is important for a comprehensive cancer center like the Institut Jules Bordet to prioritise its research domains in order to maintain or increase its competitiveness at the national and international levels.

The strategic research plan therefore makes a distinction between:

1. **Strategic pillars:** those are research domains in which the IJB benefits from a critical mass of researchers and/or modern technological platforms in its new environment - close to the Faculty of Medicine and its laboratories and to the academic Hôpital Erasme, where this should increase the likelihood of impactful discoveries that will improve patient care and outcomes.
2. **Transversal axis:** these are research areas that are a cohesive force for the cancer research community within H.U.B because many departments are able to contribute and/or directly benefit from their research output.
3. **Research columns:** these encompass promising research activities with the potential to "grow" and to become research pillars in the future.

Strategic Pillars 2025-2027

Transformative translational research in selected tumour types around selected topics

Highly specific biological targeting of cancer, encompassing
- ADCs
- Radiotheranostics

3 PILLARS

"Precision immunotherapy" = Optimisation of immunotherapeutic approaches aiming at an enhanced patient benefit vs risk

I. "Transformative" translational research:

This is research that builds a strong bridge between the clinic and the lab, where there is a plan to achieve "clinical utility" or to close a knowledge gap in cancer biology.

This ambitious goal requires "dream teams" that bring together dynamic clinical researchers who can launch proof of concept clinical trials and innovative laboratory researchers with a strong track record and a team leader position secured through a faculty (usually the Faculty of Medicine) or the "FNRS" (Fonds National de la Recherche Scientifique).

The IJB has a breast cancer dream team that is recognised internationally and continues to drive important TR projects with international ramifications. This will benefit from two new research antennas: one in epigenetics and the other in artificial intelligence.

Candidate "dream teams" on the horizon include a "lung cancer dream team", focused on the double-edged sword role of neutrophils, and a "melanoma dream team" which has tools to study malignant transformation and dissemination.

II. Highly specific biological targeting of cancer:

Building this pillar involves at least two departments: the Nuclear Medicine Department for innovative radiotheranostic approaches, and the Medical Oncology Department for improved tailoring of antibody drug conjugates.

The Nuclear Medicine Department, following IJB's move onto the Erasme campus, has grown tremendously and benefits from a GMP-accredited radiopharmacy.

After its pioneering work in Belgium with lutetium Dotatate in neuroendocrine tumours and lutetium-177 PSMA ligand therapy in prostate cancer, it is now exploring new indications for these theranostic approaches, such as actinium-225 Dotatate for multiple myeloma and lutetium-177-PSMA for triple-negative breast cancer.

It is also trying to explore ways to move away from a fixed dose of the isotope and to tailor dosimetry for each individual patient.

A new area of active research focuses on a new vector "FAPI" targeting cancer-associated fibroblasts, a key component of the tumour microenvironment: in line with the theranostic concept "first see, then treat what you see" the team is launching a number of imaging trials in several tumour types to be followed by therapeutic trials based on lutetium-177-FAPI and, in the future, astatine-211-FAPI (an α emitter).

The Medical Oncology Department has a track record in early clinical trials of antibody drug conjugates and continues to contribute actively towards their clinical development. It works in close collaboration with the Nuclear Medicine Department to improve tailoring of antibody-drug conjugates, a rapidly expanding family of new anti-cancer drugs that link potent cytotoxic molecules to antibodies targeting relevant tumour antigens in a wide range of tumour types.

An active area of research here involves exploiting molecular imaging to assess heterogeneity of antigen expression across the entire metastatic tumour burden and to link the degree of heterogeneity to tumour response, in an effort to reduce under-treatment and over-treatment. This research is most advanced in the field of ADCs targeting HER2.

III. Precision Immunotherapy: encompasses research initiatives aimed at improving the therapeutic index of cancer immunotargeting.

This third "pillar" involves a number of preclinical research programmes, focusing mainly on the double-edged sword represented by neutrophils in lung cancer, the potential role of T-lymphocytes in chronic lymphocytic leukaemia and the prognostic/predictive value of tertiary lymphoid structures in breast cancer.

On the other hand, several investigator-initiated trials are exploring and will continue to explore new combinations of immune therapies with the goal of increasing the proportion of patients who benefit from this treatment modality. Special areas of interest include gastroesophageal therapy with trials aiming to reverse anti-PD(L)1 resistance (initially in oesophageal cancer and cholangiocarcinomas), and exploration of stereotactic radiation in combination with an anti-PD(L)1 agent and an anti-CD73 monoclonal antibody in early luminal breast cancer.

Expansion of a patient cohort being monitored for immune therapy-related side effects who are undergoing serial blood tests and tissue biopsies is planned with the goal of identifying blood biomarkers predictive of severe toxicity.

Transversal Axis

1. **Artificial Intelligence to support « precision oncology »**
2. **Young talent career development**
3. **Expansion of core research facilities/ high tech equipment**
4. **Risk - adapted organ sparing**
5. **Evidence-based integrative medicine**

This comprises five domains: one has been a top priority for IJB's oncology surgeons for decades - namely risk-adapted organ sparing - which will continue to be a central area for attention, two developed thanks to valuable support from the "Association Jules Bordet" namely "Young talent career development" and "Expansion of core research facilities" and finally two quite new fields: "Artificial Intelligence" to support precision oncology and "Evidence-based integrative medicine".

An Artificial Intelligence (AI) Research Committee is currently being set up with the task of examining, improving and coordinating all AI-based research projects in Oncology. With support from the Scientific Board of the Association Jules Bordet, ambitious AI-based projects will be encouraged: the first one, "ARTEMIS", is strongly multidisciplinary and aims to improve quality of life for early breast cancer patients through improved systemic treatment tailoring. It is an ambitious project spanning 4-5 years and scheduled to start in 2025.

Psycho-oncology expertise at IJB has been recognised for decades and research in this field has been very active, with robust methodological approaches favouring randomisation with a "crossover" (that facilitates the patient's willingness to collaborate).

In view of IJB's interest in developing "integrative medicine", an approach that recognises the benefit of combining conventional/standard therapies with complementary therapies (such as acupuncture), there will be a need to develop research protocols extending beyond those for psycho-oncology to ensure that unconventional approaches are only promoted if they are demonstrated to be safe and effective.

Research columns

TO BE REINFORCED	TO BE CONSIDERED
Digital pathology	**Cancer complications (Cardiology, Neurology, Geriatrics etc.)**
Oncofertility	**Cancer vaccines (Plotkin Institute)**
Research «survivorship»	
Liquid Biopsy	
Cell therapies	
Aya Research	
Nursing Research	

Highlighted above are a number of promising research activities that could grow in the coming years, especially in light of the new research ecosystem on the Erasme Campus and the new modern equipment acquired with help from the "Association Jules Bordet".

Topics of particular relevance here include: oncofertility (already well developed by Hôpital Erasme), precision radiotherapy (using the MRI linac), cancer complications (building on the proximity of dynamic research teams in neuroscience/cardiology) or cancer vaccines (based on a potential collaboration with the Plotkin Institute).

Research in numbers

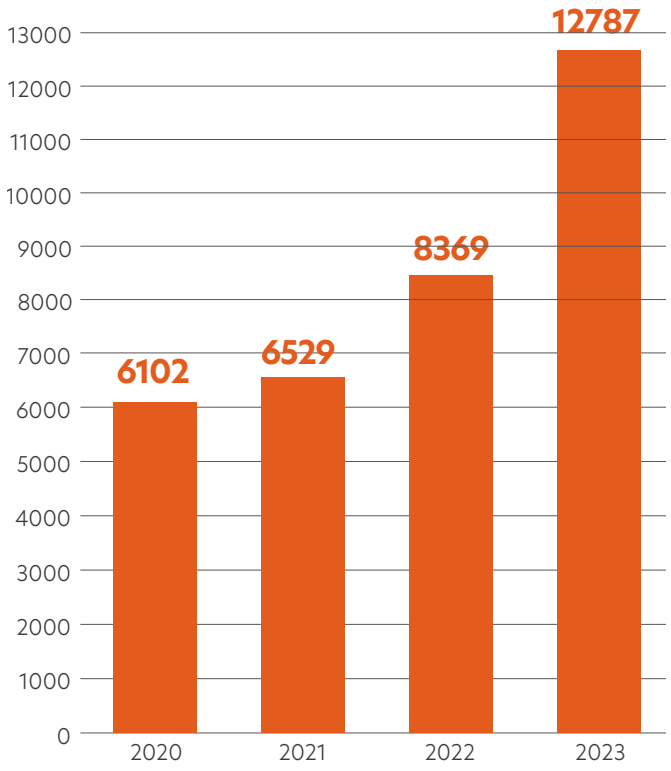
1. General data

Number of tumours recorded in Institut Jules Bordet's cancer registry annually:

On average, **2100** patients are diagnosed or treated with a new tumour incident

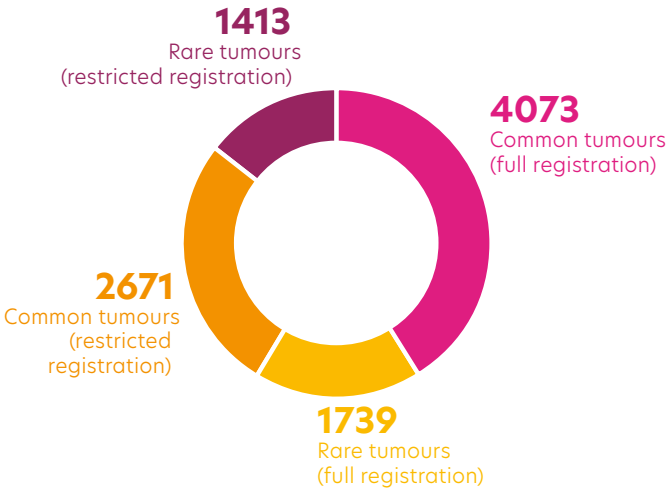
and about **4000** attended to at the Institute for a new tumour episode (including new relapse episodes).

Number of dicussions in multidisciplinary teams



The increase over 2023 is due to the fact that we have reached the exhaustiveness of the cases discussed in 2023 (prior to this, only billable cases were recorded at Hôpital Erasme)

Hospital cancer registry status (incidence year 2022-2023)

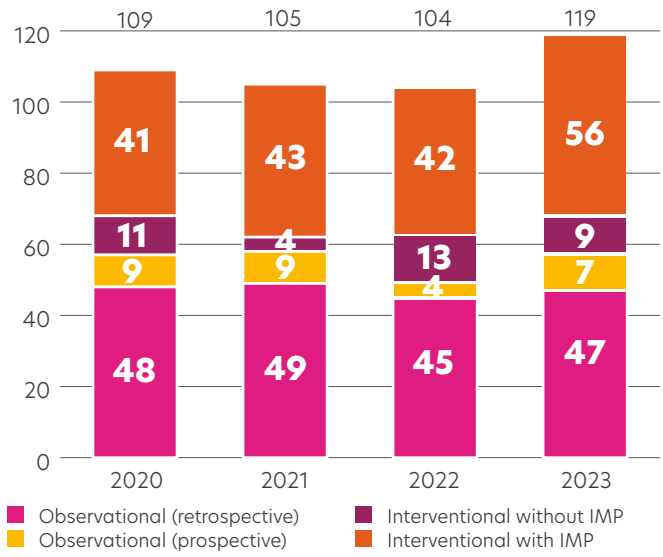


Full registration is done for incident tumours with therapeutic management in the institution (Bordet up to 2022, Bordet and Erasme from 2023).

Restricted registration is done for patients who have a tumour not treated in the institution for the primary episode (it can be a previous tumour for a tumour with full registration or a patient coming at the institution at the moment of the relapse, for instance).

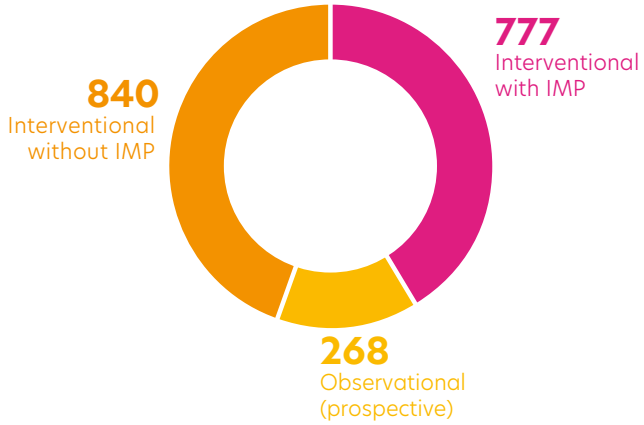
2. Research projects

More than 100 research projects receive ethics committee approval each year



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

Patients included in prospective trials 2021-2023



3. Research personnel

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, 238 professionals (199 FTEs) specifically dedicated to research.

12 Medical Senior Scientists

8 Medical Research Fellows

37 Postdoctoral Scientists

46 PhD Students

7 Technicians

27 Study (Nurse) Coordinators

8 Clinical Data Managers

7 Research Coordinators

5 Research Pharmacists

32 Experts in Clinical Trials Operations

3 Statisticians

11 Research IT

2 Quality Assurance & Control

4 Patients Collaboration

12 Finance/ Legal Support for Research

17 Administrative Support for Research

4. Finance & funding

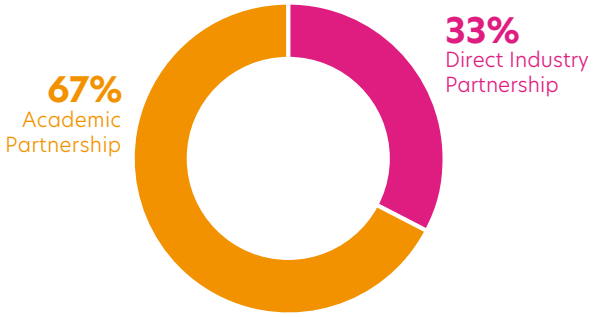
Budget

€19.9 MM Annual research budget

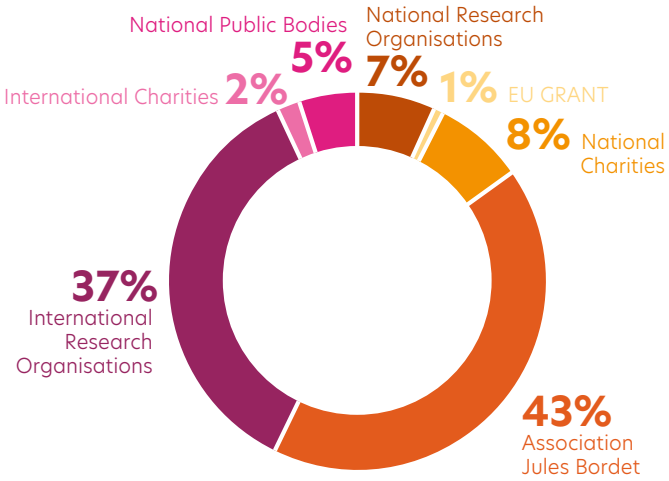
10% Percentage of Institut Jules Bordet's annual budget dedicated to research

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 type of partnership (2023)



Academic partnership funding breakdown by type of funder (2023)

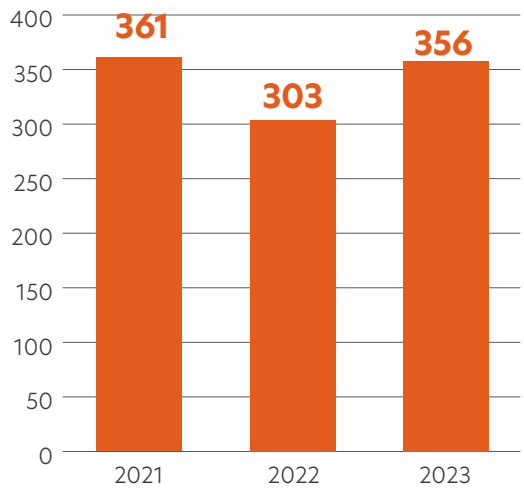


5. Publications

Budget

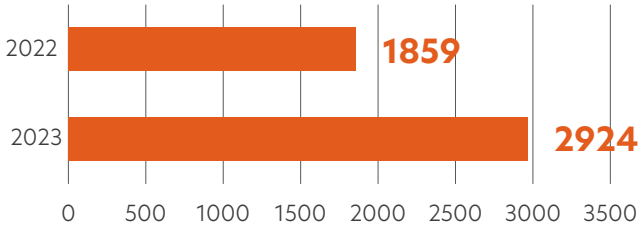
Scientific production in terms of publications is about 340 papers a year, with about 45 having an impact factor above 10

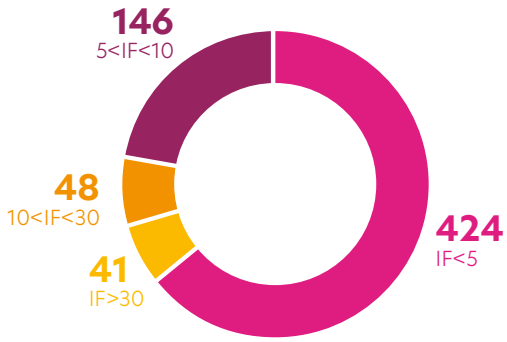
Number of publications



Impact factor sum and distribution 2022-2023

The sum of the impact factors for all the publications per year ranges between 1900 and 3000:





The 2023-2024 H.U.B Oncology Research Themes and Achievements

In line with the previous scientific report 2020-2022 of the Institut Jules Bordet, the 2023-2024 oncology research themes and achievements of the new "H.U.B" have been grouped into 4 major themes that encompass all H.U.B research activities, without an attempt at "prioritisation" : this is why the term "pillar" has now been replaced by "chapter", to avoid any confusion with the new strategic research plan 2025-2027 described previously, in which pillars refer to research domains with a greater likelihood of impactful discoveries.

1. Dissecting Tumour Heterogeneity

Improve our understanding of tumour heterogeneity by means of a transversal research team from the IJB research laboratories working to discover new biomarkers and/or new treatment targets.

2. Contributing to Precision Oncology

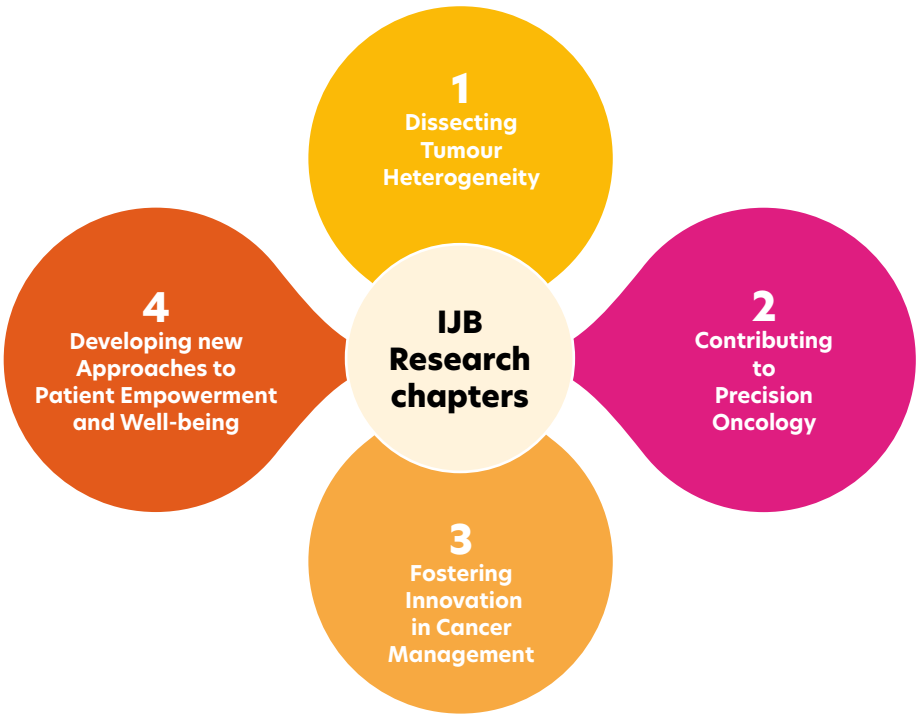
Focus on better ways to distinguish patients with poor versus good prognosis and patients who respond poorly or well to anticancer therapies: this is key to innovating cancer management. Investing in "omics" technologies, modern imaging techniques, and artificial intelligence can help us to avoid the under- or overtreatment of patients; in other words, our goal is to demonstrate the contribution of these tools to improved treatment personalisation in the fields of surgery, radiotherapy, and drug therapy.

3. Fostering Innovation in Cancer Management

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 immune-therapeutics. Similarly, contribute to the development of improved radiotherapy and surgical techniques as well as new radiotheranostic approaches.

4. Developing New Approaches to Patient Empowerment and Well-being

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



RESEARCH CHAPTERS

Chapter I • Dissecting Tumour Heterogeneity

The IJB laboratories were created by a previous generation of visionary clinicians working in three main areas – medical oncology, haematology and surgery (H. Tagnon, JC. Heuson, P. Stryckmans and F. Lejeune) – but also active in pathology and molecular biology (A. Claude, Nobel Prize Laureate). Their ambition was to contribute towards 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 benefit from the unprecedented development of new technologies, permitting a deeper exploration of the interactions between cancer cells and their microenvironment, as well as the potential mechanisms underlying resistance to anticancer therapies.

Using genomic, transcriptomic, epigenetic, and immunological tools, researchers are dissecting tumours and their environment, hoping to better understand tumour heterogeneity and to identify new clinically relevant biomarkers and/or new treatment targets.

At H.U.B, this preclinical and translational research is most developed in the areas of breast cancer, melanoma, gastrointestinal tumours, and haematological malignancies.

Many research projects at H.U.B focus on the tumor microenvironment (TME) in solid tumours and share the common goal of understanding how variation in this affects malignant growth and dissemination as well as patient response to treatment and clinical outcomes. The ultimate goal of such research is to identify and characterise the mechanisms that promote tumorigenesis and metastases as a basis for discovering exploitable targets for improved patient care and survival.

I. THE BORDET CANCER RESEARCH LABORATORIES (BCRL)

- **EQUIPMENT/FACILITIES**
- **DESCRIPTION OF THE LABS**

- **BCTL** - Breast Cancer Translational Research Laboratory
- **GI** - Gastrointestinal Cancer Laboratory
- **LOCE** - Clinical and Experimental Oncology Laboratory
- **MIU** - Molecular Immunology Laboratory
- **LCIO** - Lung Cancer and Immuno-Oncology Laboratory
- **Onco Vir** - Onco-Virology Laboratory
- **LTCC** - Clinical Cell Therapy Laboratory
- **ACEE** - Applied Cancer Epigenomics and Epitranscriptomics Laboratory
- **MRI** - Physics & Radiophysics Laboratory

II. LABORATORIES ON THE ERASMUS CAMPUS INVOLVED IN TRANSLATIONAL CANCER RESEARCH BUT NOT INTEGRATED IN THE BCRL

- **Laboratory of Experimental Gastroenterology**
- **Research laboratory in Human reproduction**
- **Center of Human Genetics**
- **Skin Cancer Research Unit**

III. OTHER "ULB" LABORATORIES WITH A MORE BASIC CANCER RESEARCH ORIENTATION

- Stem Cell and Cancer Group, ULB (C. Blanpain)
- Laboratory of Cancer Epigenetics, ULB (F. Fuks)
- Institute of Medical Immunology (IMI), ULB (A. Marchant)
- Immunobiology (IBMM), ULB (E. Meylan, F. Andris, G. Oldenhove, O. Leo, S. Goriely)
- G-protein coupled receptors Laboratory, ULB (C. Gueydan)
- Laboratory of Computational Biology, ULB (M. Rooman)
- Molecular Virology, ULB (C. Van Lint)
- RNA Molecular Biology, ULB (D. Lafontaine)
- Metabolism of Phosphoinositides, ULB (D. Communi, I. Pirson)
- Control of Cell Proliferation and Cancer, KUL (G. Halder)
- Tumorigenesis using the zebrafish model, IRIBHM (V. Wittamer)
- Cancerology and Experimental Toxicology

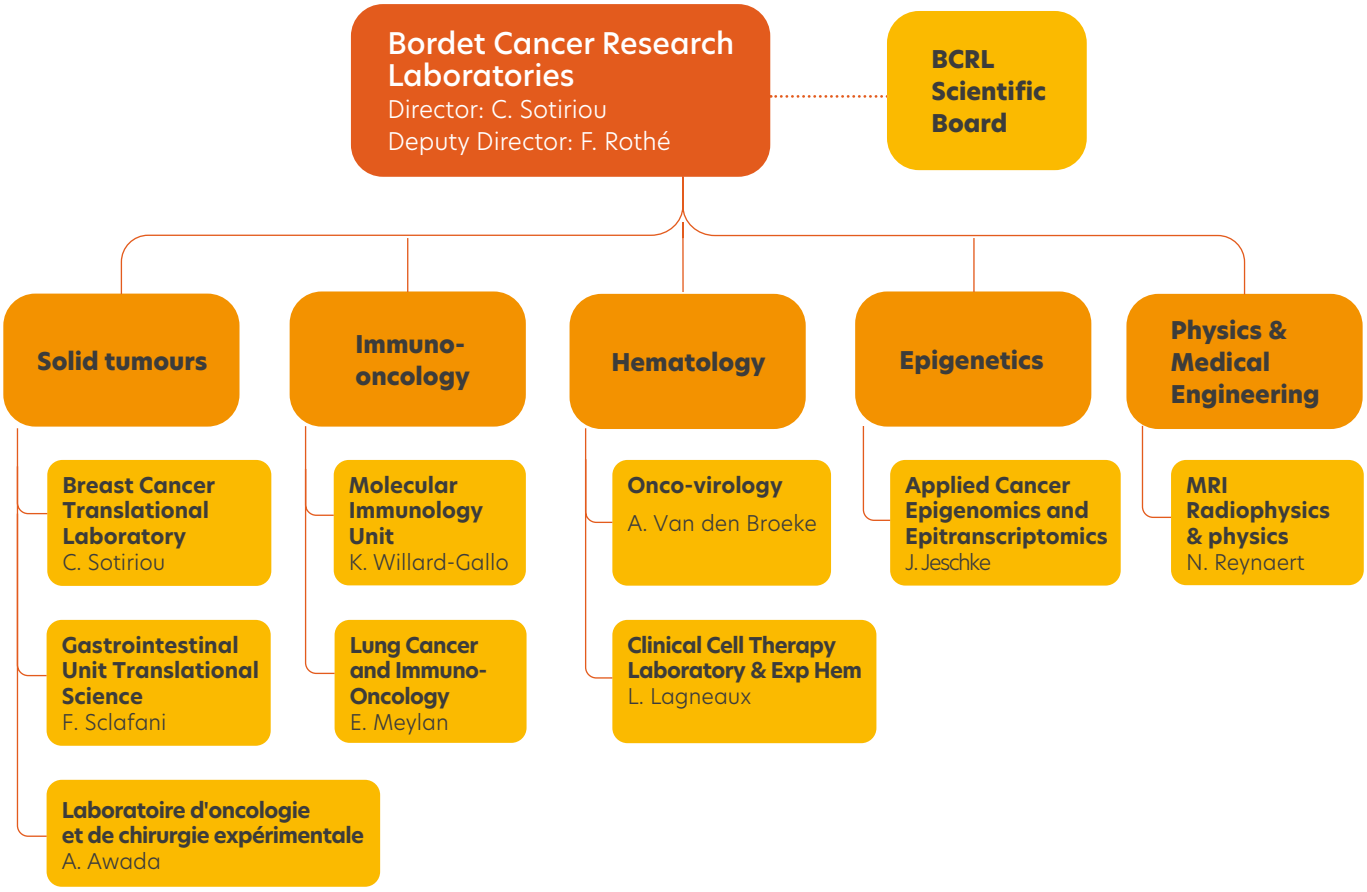
Bordet Cancer Research Laboratories (BCRL)

Bordet Cancer Research Laboratories (BCRL) bring all the laboratories dedicated to cancer research into a single entity (see figure below). This unification aims to enhance research excellence and professionalisation at the Institut Jules Bordet (IJB) by fostering research potential and scientific creativity through internal collaboration and also through partnerships with the Faculty of Medicine at ULB. The BCRL seeks to provide robust protection for IJB researchers, aiming to reduce redundancy and maintain efficiency in areas such as cost control and shared research platforms.

Currently, the BCRL comprises nine laboratories: LOCE – Clinical and Experimental Oncology Laboratory; GI – Gastrointestinal Laboratory; BCTL – Breast Cancer Translational Research Laboratory; Onco Vir – Onco-Virology Laboratory; LTCC – Clinical Cell Therapy Laboratory; MIU – Molecular Immunology Laboratory; LCIO – Lung Cancer and Immuno-Oncology Laboratory and recently the ACEE – Applied Cancer Epigenomics and Epitranscriptomics and MRI – Physics & Radiophysics Laboratory. These laboratories primarily focus on organ-specific translational and basic research, including breast, gastrointestinal (GI), melanoma, lung, and leukaemia cancers, immunology, and epigenetics. The epigenetics research is led by Jana Jeschke, a young and recently appointed Principal Investigator (PI) at the Faculty of Medicine.

The BCRL is committed to transformative translational research, highly specific biological targeting of cancer, and precision immunotherapy. This commitment is reflected in our alignment with the Institute's strategic research plan. A novel translational/basic research axis on brain metastasis and melanoma, utilising state-of-the-art technologies such as single-cell RNA sequencing, spatial transcriptomics, and mass spectrometry, will be led by Panagiotis Karras, a recently appointed PI at the Faculty of Medicine. We will continue to promote translational and basic research in immunology covering all tumour types and liaise with the European Plotkin Institute for Vaccinology, which has biosafety level 2 and 3 immunology and microbiology laboratories situated next to our Institute.

Finally, the development of artificial intelligence (AI) is another crucial axis of research, spearheaded by young post-doc Jennifer Dhont at the Physics and Radiophysics Laboratory. The AI research will commence with an ambitious breast cancer program that will be funded by the Association of Jules Bordet during a pilot phase, with plans to expand AI applications to other tumour types and broader applications.


Bordet Cancer Research Laboratories
Director: C. Sotiriou
Deputy Director: F. Rothé
BCRL Scientific Board
Solid tumours
Immuno-oncology
Hematology
Epigenetics
Physics & Medical Engineering
Breast Cancer Translational Laboratory
C. Sotiriou
Gastrointestinal Unit Translational Science
F. Sclafani
Laboratoire d'oncologie et de chirurgie expérimentale
A. Awada
Molecular Immunology Unit
K. Willard-Gallo
Lung Cancer and Immuno-Oncology
E. Meylan
Onco-virology
A. Van den Broeke
Clinical Cell Therapy Laboratory & Exp Hem
L. Lagneaux
Applied Cancer Epigenomics and Epitranscriptomics
J. Jeschke
MRI Radiophysics & physics
N. Reynaert

Equipment/Facilities of the BCRL

- Single cell analysis (10X Genomics Chromium platform)
- Spatial transcriptomics (10X Genomics Visium and Nanostring GeoMX platforms)
- NGS facility
- Epigenomics profiling platform
- Flow cytometry
- Multispectral IF imaging platform
- Confocal microscopy
- In vivo imaging facility (microPET, SPECT, MRI)
- Incucyte life-cell analysis platform
- 3D culture facility
- Mouse facility
- Bioinformatics facility

BREAST CANCER TRANSLATIONAL RESEARCH LABORATORY (BCTL)

"Our goal is to understand breast cancer biology better, assessing whether tumour heterogeneity and the tumour's immune microenvironment impact response to therapy and clinical outcome."

Team and infrastructure

The laboratory is headed by Christos Sotiriou MD, PhD. The team includes two senior scientists, four post-doctoral scientists in bioinformatics, 10 PhD students, four laboratory technicians, and one administrative assistant.

The laboratory has advanced molecular and cellular biology equipment, including droplet digital PCR, single-cell analysis, and spatial transcriptomics platforms. It has access to ULB's sequencing core facility, featuring a NovaSeq sequencer for high-throughput, next-generation sequencing (NGS) analyses. The laboratory excels in state-of-the-art bioinformatic analyses of various types of omics data, including single-cell and spatial transcriptomic data.

Aims

- To map tumour and stroma cell architecture and assess cell-to-cell interactions at an unparalleled level
- To portray the immune landscape, including immune cell composition and geographic localisation (TLS, TCR, and BCR repertoires)
- To assess how tumoral, stroma, and immune cell composition and organisation impact disease progression, response to therapy, and clinical outcome

Main projects

- Mapping tumour and immune cell architecture using spatial transcriptomics and single-cell sequencing to gain novel insights into treatment resistance in all breast cancer molecular subtypes
- Collecting tissue prospectively from patients with triple-negative breast cancer (TNBC) and HER2-positive disease undergoing neoadjuvant treatment: this activity is ongoing with the integration of single-cell RNAseq and immune phenotyping to explore the impact of heterogeneity on treatment response
- Mapping TNBC heterogeneity by leveraging spatial transcriptomics and artificial intelligence: moving towards optimised patient care
- Decoding metastatic breast cancer by integrating multi-omics data and artificial intelligence in the context of the AURORA study
- Analysing the impact of intra-tumour heterogeneity on low genomic risk breast cancer recurrence in the MINDACT study

F. Rothé, Ch. Sotiriou

The link between the laboratory and international clinical research teams facilitates the laboratory's ambitious translational research projects linked to AURORA (BIG), MINDACT (BIG, EORTC), (Neo)ALTTO (BIG), Zephir, Neorhea, Synergy, and NeoCheckRAY (international trials sponsored by IJB)

Recent achievements

- Developed a score predicting survival after neoadjuvant chemotherapy with targeted therapy in HER2+ breast cancer by incorporating B-cell repertoires.
- Identified five molecular subtypes of HER2 using deep learning and RNAseq with distinct clinical outcomes and response to therapies.
- Refined the TNBC molecular classification with potential clinical implications by incorporating spatial transcriptome and single-cell RNA sequencing.
- Identified cell states and immune subpopulations predicting pathological complete response to neoadjuvant chemotherapy with and without immunotherapy in TNBC.
- Mapped the tumour architecture of lobular breast cancer using spatial transcriptomics with potential clinical implications.

Selected publications

- Buisseret L, Bareche Y, Venet D, Girard E, Gombos A, Emonts P, Majjaj S, Rouas G, Serra M, Debien V, Agostinetto E, Garaud S, Willard-Gallo K, Larsimont D, Stagg J, Rothé F, Sotiriou C. The long and winding road to biomarkers for immunotherapy: a retrospective analysis of samples from patients with triple-negative breast cancer treated with pembrolizumab. **ESMO Open**. 2024 May;9(5):102964. doi: 10.1016.

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- Buisseret L, Loirat D, Aftimos P, Maurer C, Punie K, Debien V, Kristanto P, Eiger D, Goncalves A, Ghiringhelli F, Taylor D, Clatot F, Van den Mooter T, Ferrero JM, Bonnefoi H, Canon JL, Duhoux FP, Mansi L, Poncin R, Barthélémy P, Isambert N, Denis Z, Catteau X, Salgado R, Agostinetto E, de Azambuja E, Rothé F, Craciun L, Venet D, Romano E, Stagg J, Paesmans M, Larsimont D, Sotiriou C, Ignatiadis M, Piccart-Gebhart M. Paclitaxel plus carboplatin and durvalumab with or without oleclumab for women with previously untreated locally advanced or metastatic triple-negative breast cancer: the randomized SYNERGY phase I/II trial. Nat Commun. 2023 Nov 2;14(1):7018. doi: 10.1038/s41467-023-42744-y. Erratum in: **Nat Commun**. 2023 Dec 12;14(1):8223. doi: 10.1038.
- Joaquin Garcia A, Rediti M, Venet D, Majjaj S, Kammler R, Munzone E, Gianni L, Thürlimann B, Laáng I, Colleoni M, Loi S, Viale G, Regan MM, Buisseret L, Rothé F, Sotiriou C. Differential Benefit of Metronomic Chemotherapy Among Triple-Negative Breast Cancer Subtypes Treated in the IBCSG Trial 22-00. **Clin Cancer Res**. 2023 Dec 1;29(23):4908-4919. doi: 10.1158.

GASTROINTESTINAL CANCER LABORATORY (GI LAB)

“Our goal is to identify prognostic and predictive biomarkers for gastrointestinal cancers, and to translate our findings into applications for clinical practice. We also aim to elucidate the mechanisms underlying the immuno-resistance of colorectal cancers and to develop more effective immunomodulatory therapeutic strategies.”

Team and infrastructure

The laboratory is headed by Francesco Sclafani & Alain Hendlisz, and its team includes two PhD students (an MD and a biologist), two research fellows (MD), and one laboratory technician. The laboratory has access to techniques needed to analyse circulating biomarkers such as droplet digital (dd)PCR and multiplex ELISA immunoassays, and it manages a large biobank of prospectively collected plasma samples and other biological materials. Thanks to collaborations with a number of institutional, national, and international research teams, it has access to other research platforms, including genomics; single-cell and spatial transcriptomics; patient-derived xenografts and organoids; immunophenotyping and functional immunological assays; and gut microbiome analysis.

Aims

- To analyse the role of the tumour microenvironment and other immune-related biomarkers in mediating resistance to immunotherapy in mismatch repair proficient (pMMR)/microsatellite stable (MSS) colorectal cancer, and to evaluate the potential of immunomodulation strategies to revert immune resistance
- To characterise the prognostic and predictive value of circulating biomarkers such as tumour DNA and cytokines in early- and advanced-stage gastrointestinal cancer, and to translate these into practical tools for management decisions in clinical practice
- To elucidate the genomic mechanisms of oligoresistance/oligoprogression in gastrointestinal cancers treated with standard systemic therapy
- To identify prognostic/predictive tissue and radiomics biomarkers for rectal cancer patients treated with standard-of-care neoadjuvant therapy
- To elucidate mechanisms of response and resistance to multi-kinase inhibitors using in vitro models, organoids, and patient-derived xenografts
- To explore the prognostic/predictive value and biological correlates of early metabolic response to treatment in early-stage and advanced-stage colorectal cancer

Main projects

- Correlative biomarker studies on biological samples from “REGINA”: a phase II trial of neoadjuvant regorafenib in combination with nivolumab and short-course radiotherapy in stage II-III rectal cancer”

F. Sclafani

- Analysis of circulating biomarkers on plasma samples from patients enrolled in Chronos & Kairos (a prospective, sample collection study of patients with gastrointestinal cancer) and other prospective studies
- Analysis of the immune cell repertoire, and identification of prognostic/predictive immune-related tissue biomarkers and radiomics parameters in early-stage rectal cancer
- Study of changes in gene expression profiles after neoadjuvant chemotherapy and their impact on the outcome of patients with early-stage colon cancer enrolled in the PEPITA trial

Recent achievements

- Conducted the very first study looking at the dynamics of circulating tumour DNA in the neoadjuvant setting in colon cancer
- Launched the COPERNIC trial, a study aiming to shed light on the clinical utility of early dynamics of ctDNA in advanced colorectal cancer
- Built a unique platform for correlative biomarker analyses and co-clinical trials around the REGINA trial, to elucidate the determinants of the innate immuno-resistance of pMMR/MSS colorectal cancer and to develop effective immuno-modulatory therapeutic strategies in this setting
- Built the largest international real-world database of locally-advanced rectal cancer patients treated with total neoadjuvant therapy, to serve as a platform for correlative studies based on tissue biomarkers and radiomics

Selected publications

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FZ, Assaf I, Conti C, Gallio C, Benhima N, Bregni G, Gkolfakis P, Spagnolo V, Anthoine G, Liberale G, Moretti L, Martinive P, Hendlisz A, Demetter P, Sclafani F. PD-L1 Expression in Paired Samples of Rectal Cancer. **Cancers** (Basel). 2024 Jul 21;16(14):2606.

- Assaf I, Bregni G, Anthoine G, Aparicio T, Artru P, Abdelghani MB, Buyse M, Chibaudel B, Coart E, Diaz M, Evrard C, Geboes K, Ghiringhelli F, Puleo F, Raimbourg J, Vandamme T, Van den Eynde M, Hendlisz A, Sclafani F. Rationale and Design of the COPERNIC Trial: A Study of On-treatment ctDNA Changes in Chemo-refractory Colorectal Cancer Patients. **Clin Colorectal Cancer**. 2024 Sep 3:S1533-0028(24)00081-1.
- Assaf I, Fimereli D, Anthoine G, Fazio R, Daprà V, Audisio A, Bardiaux A, Telli TA, Vanhooren M, Saude-Conde R, Bregni G, Hendlisz A, Sclafani F. Prognostic Value of Circulating Cytokines in Chemorefractory Colorectal Cancer. **Cancers** (Basel). 2023 Dec 3;15(24):5823
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CLINICAL AND EXPERIMENTAL ONCOLOGY LABORATORY (LOCE)

“The Laboratory of Clinical and Experimental Oncology (LOCE) is dedicated to advancing cancer research by bridging the gap between fundamental biology and clinical applications. With a multidisciplinary approach, LOCE integrates both basic and applied research, focusing on translating laboratory discoveries into innovative treatments for cancer patients. The LOCE is a laboratory of the Faculty of Medicine at the Université Libre de Bruxelles (ULB).”

Team and infrastructure

LOCE is headed by Ahmad Awada (Director), with Fabrice Journe serving as the lab manager and Ghanem Ghanem as the past director. The core research team includes three post-doctoral scientists, six PhD students, six technicians, one data manager, and one administrative assistant. Together, this multidisciplinary team contributes diverse expertise in cancer biology, drug development, and clinical oncology.

LOCE has advanced technology and expert knowledge in several areas essential for preclinical and translational cancer research:

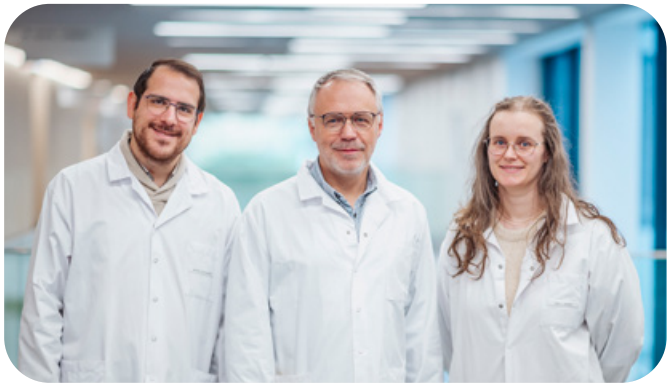
1. **Preclinical Drug Development:** The lab has specific expertise in animal experimentation. These models are crucial for evaluating drug efficacy and toxicity.
2. **Technological Platforms:**
   - **Cell Culture Platform:** LOCE’s cell culture facilities support both 2D and 3D cultures, enabling more accurate modelling of tumour environments. The lab also maintains a comprehensive cell banking system.
   - **Animal Platform:** The animal facility includes PDX models, allowing the study of cancer biology in a living system that recapitulates human tumour microenvironment.
   - **3D Tissue Bioprinting:** This innovative technology enables to print 3-dimensional tissues, creating more realistic tumour models for drug testing and mechanistic studies.

LOCE’s research is conducted in close collaboration with the respective clinical departments. This bench-to-bedside approach accelerates the translation of basic research findings into clinical applications.

Aims

LOCE’s primary mission is to deepen our understanding of cancer biology with the goal of developing more effective treatments. Our research focuses on:

1. **Identification of New Therapeutic Targets and Biomarkers:** The discovery of novel molecular targets is crucial for the development of new cancer therapies. Constantly searching for novel “druggable” targets—molecules or pathways in cancer cells that can be effectively targeted with new or existing drugs.



A. Najem, F. Journé, N. Kindt

2. **Mechanisms of Drug Resistance:** Cancer cells often develop resistance to therapies, which limits treatment success. Our research focus is to study the molecular mechanisms of resistance in the hope of identifying new strategies.
3. **Evaluation of Rationally Designed Combinatorial Strategies:** The lab explores innovative combinations of treatments.

Main projects

- A central focus of the LOCE is the study of brain metastases, particularly in the context of breast cancer. Brain metastasis is a significant and often lethal complication of advanced breast cancer and understanding the molecular drivers of this process is critical for developing more effective treatments. At LOCE, we are actively developing new preclinical models of brain metastasis that are designed to study the specific pathways and mechanisms by which breast cancer cells adapt and invade the brain.
- In parallel with this, we are investigating a novel class of drugs that target mitochondria. These mitochondrial-targeted therapies exploit the altered metabolism of melanoma cells, aiming to disrupt their energy production and induce apoptosis (programmed cell death). Our lab is deciphering the molecular mechanisms of a new class of these drugs, focusing on how they selectively affect cancer cells while sparing normal tissue. This research could offer a new avenue for treatment, particularly in drug-resistant cancers.
- Additionally, LOCE is dedicated to exploring the tumour microenvironment and phenotypic plasticity in regulating melanoma progression. We are specifically investigating how new microenvironmental factors

influence phenotype switching and the epithelial-to-mesenchymal transition (EMT). Phenotype switching refers to the cancer cells' ability to shift between different functional states, enabling adaptation to changing microenvironmental conditions and contributing to therapeutic resistance. By understanding the molecular cues that regulate these processes, we aim to identify new therapeutic strategies that can prevent metastasis and enhance treatment efficacy.

Recent achievements

- Cell bank set up for the storage and distribution of cancer cell lines, facilitating research collaborations and advancing drug development.
- Collaborations secured with two companies in Europe and the USA to commercialise the melanoma lines, including signature of two contracts, promoting further research and clinical applications.
- Humanised mouse model established to study the "abscopal effect" of radiotherapy, advancing our understanding of how localised radiation can induce systemic anti-tumour effects.
- Breast cancer (BC) cell lines developed that are specifically adapted to the brain microenvironment, enabling detailed comparison of gene expression profiles with human breast cancer brain metastases.
- It has been demonstrated that breast cancer brain metastases display greater infiltration by pro-tumoral macrophages compared to primary tumours, highlighting a potential target for therapeutic intervention.
- 2D and 3D melanoma models created, providing advanced platforms for studying melanoma progression, drug resistance, and treatment responses.
- A new class of mitochondrial-targeted agents (MTAs) identified, which target cancer cell mitochondria, disrupting energy production and promoting apoptosis, representing a promising therapeutic strategy across several cancer types.
- It has been demonstrated that bufalin, a bufadienolide isolated from toad venoms, exhibits potent antiproliferative activity against treatment-resistant melanoma cells, presenting a promising therapeutic candidate.
- Iron oxide nanoparticles have been developed which are designed to radiosensitise head and neck cancer cells, inducing ferroptosis and enhancing the efficacy of radiotherapy.

Selected publications

- Soumoy L, Genbauffe A, Mouchart L, Sperone A, Trelcat A, Mukeba-Harchies L, Wells M, Blankert B, Najem A, Ghanem G, Saussez S, Journe F. ATP1A1 is a promising new target for melanoma treatment and can be inhibited by its physiological ligand bufalin to restore targeted therapy efficacy. **Cancer Cell Int.** 2024 Jan 4;24(1):8. doi: 10.1186/s12935-023-03196-y.
- Mhaidly N, Journe F, Najem A, et al. Macrophage Profiling in Head and Neck Cancer to Improve Patient Prognosis and Assessment of Cancer Cell-Macrophage Interactions Using Three-Dimensional Coculture Models. **Int J Mol Sci.** 2023 Aug 15;24(16):12813. doi: 10.3390/ijms241612813.
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MOLECULAR IMMUNOLOGY LABORATORY (MIU)

“Our research aims to understand how the composition, organisation and functionality of the tumour’s immune microenvironment is linked with treatment responses (including immunotherapies) and long-term clinical outcomes. Another important goal is to identify early blood and tissue biomarkers that signal the onset of immune-related adverse events in patients treated with immunotherapies.”

Team and infrastructure

The team includes: one Laboratory head (PhD), one clinical scientist (MD/PhD), one post-doctoral scientist (PhD), three PhD students (two biologists, one clinician), one bioengineer tissue analyst, two technicians, three or four trainees (each semester, including biologists and clinicians).

The dedicated cytometry lab is equipped with a Navios flow cytometer for analysis and an Astrios cell sorter. Plans are currently underway to upgrade these machines in the coming year. The specialised tissue imaging lab is equipped with a BenchMark Ultra Automated IHC stainer, a BOND RX fully automated research stainer and a Vectra™ Polaris imager upgraded to process eight markers plus DAPI. There is also a current project to acquire a system for ultrahigh-plex spatial protein analysis.

The MIU lab has expertise in state-of-the-art approaches including flow cytometric analysis of cellular phenotypes, their functional or differentiation states and soluble factor expression including cytokines and chemokines, other functional immunological assays, DNA, RNA and protein analysis, immunohistochemistry and immunofluorescent image analysis using multiplex immunohistochemistry.

Our knowledge and training are used to investigate immune activities in human tumours with a particular focus on breast cancer. We perform analyses of fresh tissue homogenates on the day of surgery coupled with analyses of FFPE tissue blocks and relate these data to clinical-pathological parameters. We maintain, collaborate and provide training for other BCRL and academic labs that use the flow cytometry and image analysis platforms.

Aims

- The main focus of our fundamental/translational research projects is to study tumour infiltrating lymphocytes (TIL) and their organisation in tertiary lymphoid structures (TLS). Our goal is to understand their functionality, how they reflect an individual patient’s pro- or anti-tumour immune responses and how their presence and cellular composition is both prognostic and predictive, particularly for immunotherapy.
- The principal goal of our translational/clinical research is to identify a reliable blood biomarker(s) of severe immune-related adverse events in patients receiving immunotherapy. A major feature of this research is the longitudinal analysis of patients enrolled in the IJB-sponsored clinical trial entitled: Immunological variables associated to immune checkpoint inhibitor toxicity in cancer patients.

K. Willard-Gallo

Main projects

- A prospective collection of fresh breast cancer patient samples (including blood, biopsies/surgical tissues and ascites/pleural effusions) at diagnosis, following surgery and at relapse. These fresh tissues (currently >2000 breast cancer samples dating from 2012) together with the corresponding fixed tissue blocks are used for TIL and TLS characterisation and ascertaining their relationship to clinico-pathological parameters, including treatment responses and survival.
- Our data show that TIL and TLS are detected in both pre-malignant lesions and invasive breast cancer, with TLS characterised by the presence of specialised T follicular helper (Tfh) cells and B cells. Our current studies are focusing on the immune activities of CD4 and CD8 T cells together with B cells in TLS across breast cancer stages from ductal carcinoma in situ (DCIS) to metastatic disease. This research is designed to further our understanding of how their activities affect treatment responses and long-term clinical outcomes as well as their value as biomarkers.
- Blood and tissue monitoring of patients treated with immune checkpoint inhibitors with the goal of identifying biomarkers that predict severe immune reactions

Recent achievements

- Tumour-infiltrating T follicular helper (Tfh) cells identified and characterised, demonstrating their key role in orchestrating B-cell mediated TLS activities. Our first publication on this topic (2013) currently has 1034 citations and is considered a foundational study in the field. Our subsequent research determined that

the prevailing Tfh balance relative to regulatory cells within a TLS signalled effective anti-tumour immune responses in patients. Our current data (publication in final preparation) shows that tumours with active plus inactive TLS intrinsically create a tumour immune microenvironment conducive to TLS-directed anti-tumour immune responses in both types of TLS.

- Specialised CXCL13-producing Tfh TIL subpopulation identified, revealing the role of these cells in CXCR5+ TIL (including CD4 T cells, CD8 T cells and B cells) recruitment and organisation in TLS.
- It has been demonstrated that functionally active TLS are abundant in ductal carcinoma in situ of the breast and potentially play a role in invasive progression.
- Circulating Tfh cells identified as an early biomarker of toxicity in patients receiving immunotherapy.

Selected publications

- Padonou F, Vanhulst T, Langouo-Fontsa MD. Can we yet use tertiary lymphoid structures as predictive biomarkers for immunotherapy response in melanoma? **Curr Opin Oncol.** 2024 Mar 1;36(2):63-68. doi: 10.1097.
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LUNG CANCER & IMMUNO-ONCOLOGY LABORATORY (LCIO)

“In our laboratory, we want to understand how lung tumours grow and progress to lethal disease. Currently, we are studying the complex relationships between cancer cells and cells in the tumour microenvironment, focusing on tumour-associated neutrophils in primary tumours and in metastases. Although these cells are emerging as critical modulators of tumour growth and therapy efficacy, most of their regulation and pro- or anti-tumour functions are still to be discovered. Hopefully, a better knowledge of these innate immune cells will enable the development of new therapies to combat this malignancy.”

Team and infrastructure

Our laboratory is strategically located on two ULB research sites: in the new Institut Jules Bordet and in the Gosselies campus. This allows us to develop fundamental, preclinical and translational research. The laboratory has grown since the PI's move from Switzerland to Belgium in mid-2021, and it currently comprises two technicians, one PhD student, four post-docs and one part-time clinical oncologist). It is equipped with standard molecular and cell biology techniques and approaches. We have now started our translational research at the H.U.B using both archived specimens and tumours freshly obtained from the nearby surgery. Our exploratory research approaches should enable us to gradually obtain crucial information about the regulation and functions of neutrophils in non-small cell lung cancer.

Aims

- Catalyse our translational research to identify new neutrophil biology in human lung tumours
- Interrogate how the tumour impacts tumour-associated neutrophil phenotypes
- Dissect the mechanisms of neutrophil actions for tumour growth and therapy response
- Compare tumour-associated neutrophils in primary tumours and metastases

Main projects

- Interrogate the impact of short-chain fatty acids and fibre supplementation on tumour-associated neutrophils in lung adenocarcinoma (supported by FNRS MISU)
- Compare the phenotypes of tumour-associated neutrophils between lung adenocarcinoma, squamous cell carcinoma and distant metastases (supported by Télévie and PROTHER-WAL)
- Identify functionally different neutrophil subsets in tumours (supported by the Association Jules Bordet and the Actions de Recherche Concertées)

Recent achievements

- Tumour-supportive role identified for tumour-associated neutrophils in primary lung cancer
- Methodology defined for specific and efficient depletion of neutrophils in the mouse
- Altered glucose metabolism identified in tumour-associated neutrophils that contributes to their tumour-supporting capacity
- Mechanisms discovered that lead to prolonged neutrophil lifespan in tumours, and ways to counteract this phenomenon pharmacologically

E. Meylan, M. Brandao

Selected publications

- Bodac A, Mayet A, Rana S, Pascual J, Bowler AD, Roh V, Fournier N, Craciun L, Demetter P, Radtke F, Meylan E. Bcl-xL targeting eliminates ageing tumor-promoting neutrophils and inhibits lung tumor growth. **EMBO Molecular Medicine 2024** Jan;16(1):158-184. doi: 10.1038.
- Ancey P-B, Contat C, Boivin G, Sabatino S, Pascual J, Zangger N, Perentes JY, Peters P, Abel ED, Kirsch DG, Rathmell JC, Vozenin M-C, Meylan E. Glut1 expression in tumor-associated neutrophils promotes lung cancer growth and resistance to radiotherapy. **Cancer Research** 2021 May 1;81(9):2345-2357. doi: 10.1158.
- Contat C, Ancey P-B, Zangger N, Sabatino S, Pascual J, Escrig S, Jensen L, Goepfert C, Lanz B, Lepore M, Gruetter R, Rossier A, Berezowska S, Neppl C, Zlobec I, Clerc-Rosset S, Knott G, Rathmell JC, Abel ED, Meibom A, Meylan E. Combined deletion of Glut1 and Glut3 impairs lung adenocarcinoma growth. **eLife** 2020 Jun 23;9:e53618. doi: 10.7554..
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of neutrophils in mice. **Nature Communications** 2020 Jun 2;11(1):2762. doi: 10.1038/s41467-020-16596-9.

- Faget J, Groeneveld S, Boivin G, Sankar M, Zangger N, Garcia M, Guex N, Zlobec I, Steiner L, Piersigilli A, Xenarios I, Meylan E.Neutrophils and Snail orchestrate the establishment of a pro-tumor microenvironment in lung cancer. **Cell Reports** 2017 Dec 12;21(11):3190-3204. doi: 10.1016.

ONCO-VIROLOGY LABORATORY

“Our goal is to improve how to identify asymptomatic HTLV-1 carriers at high risk of progression to aggressive adult T-cell leukemia (ATL), to develop molecular tools to advance treatment decision-making for ATL, and to identify novel treatment targets. We aim to track tumour evolution in viral cancers by developing novel cutting-edge NGS technologies.”

Team and infrastructure

The team is headed by Anne Van den Broeke, a DVM-PhD and comprises two post-doctoral scientists, two PhD students, and a technician. The team is supported by technicians dedicated to animal experiments (USASK, Canada) and has access to the GIGA Institute’s genomic platform (University of Liège).

Aims

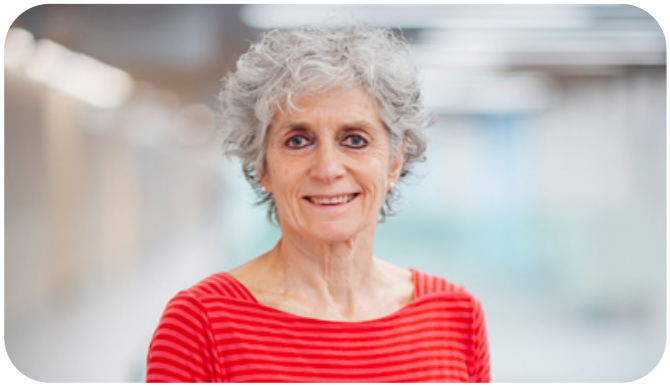
- To study clonal heterogeneity and tumour evolution through longitudinal exploration of clonal landscapes and virus-host interactions in Human T-cell leukemia virus (HTLV-1) induced Adult T-cell leukemia (ATL) and its corresponding animal model (BLV, bovine leukemia virus, cattle and sheep), from early premalignant stages to full-blown tumours
- To transform basic laboratory research findings into novel NGS tools to improve the clinical management of asymptomatic carriers of HTLV-1, patients with aggressive ATL, and patients affected by human papillomavirus (HPV)-associated oropharyngeal cancers

Main projects

- Use of cutting-edge NGS technologies to explore tumour heterogeneity, track the rare premalignant ancestor clone, and uncover drivers of tumour evolution and oncogenic switching. To achieve these goals, creation of a catalogue of somatic alterations in primary tumours (SNVs and SVs), development of novel dual-tracing targeted single-cell NGS tools and custom high-throughput microfluidics
- Analysis of clonality and single-cell NGS of HTLV-1 asymptomatic carriers to identify patients at high risk of progression to aggressive ATL (Tokyo cohort, JSPFAD, Japan)
- Use of long-read NGS technologies to assess HPV genomic integration as a biomarker of aggressiveness, prognosis, and therapeutic response in patients with HPV-positive head and neck squamous cell carcinoma (HNSCC)

Recent achievements

- It has been demonstrated that NGS clonality enables the identification of HTLV-1 carriers at high risk of progression to aggressive ATL. System of clonality metrics created (Viral Clonality Evenness score, VCE) that outperforms the current predictive biomarker. Implementation of VCE in clinics will (i) reassure a significant proportion of infected individuals and (ii) guide early preemptive intervention of high-risk asymptomatic carriers to avoid progression to treatment-resistant disease.
- VCE validated as a novel diagnostic classifier to discriminate between patients with indolent ATL from asymptomatic carriers, addressing the limitations of the Shimoyama classification, which has remained unchanged since 1991 (Institut Necker cohort, Paris, France).
- Novel long-read Oxford Nanopore NGS method validated for identification of clonally expanded precursor/malignant cells and sequencing of the entire viral genome at the tumour-specific genomic integration site
- Genomic landscape of BLV-induced B-cell leukemia/lymphoma unravelled, revealing recurrent aneuploidies and mutational hotspots; clonal and sub-clonal mutational signatures discovered in patients with ATL, as well as the significance of these signatures in defining an unfavourable indolent subtype
- Novel cutting-edge single-cell NGS approaches developed (a dual-tracing scTarget-seq tool and a high-throughput droplet microfluidic approach) for tumour heterogeneity and precursor tracing



A. Van den Broeke

Selected publications

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- Marçais A, Lhermitte L, Artesi M, Laurent C, Durkin K, Hahaut V, Rosewick N, Suarez F, Sibon D, Cheminant M, Avettand-Fenoel V, Bruneau J, Georges M, Pique C, Van den Broeke A+, Asnafi V+, Hermine O+ Targeted deep sequencing reveals clonal and subclonal mutational signatures in Adult T-cell leukemia/lymphoma and defines an unfavorable indolent subtype, **Leukemia** 2021, 35:764-776; doi: 10.1038/s41375-020-0900-3 +joint last author.

CLINICAL CELL THERAPY LABORATORY (LTCC)

“Our goal is to understand clonal heterogeneity and the interaction between leukemic cells and their immune and stromal microenvironments. With a particular focus on chronic lymphocytic leukemia and multiple myeloma, we hope to identify new prognostic markers and discover innovative treatment targets.”

Team and infrastructure

The laboratory is headed by Laurence Lagneaux (PhD) and comprises one medical senior scientist (MD, PhD), one senior scientist (PhD), one scientific collaborator (MS), six Ph.D. students, and one technician. It has access to cellular culture and molecular biology facilities (including real-time PCR, fluorometer), multiplex ELISA system (Bioplex 200), flow cytometry (MACSQuant®), Nanotrack analyser, and ultracentrifuge for extracellular vesicle analysis.

Aims

- To decipher the immune landscape of haematological malignancies:
  - Crosstalk between chronic lymphocytic leukemia (CLL) and the immune microenvironment via extracellular vesicles
  - Study of the TCR repertoire in CLL to highlight common antigens stimulating the disease in different patients
  - Multiple myeloma (MM) mesenchymal stromal cell interactions with immune cells in the microenvironment
  - Identification of immune evasion mechanisms based on sialoglycan interactions with the immunoregulatory Siglec receptors expressed by immune cells
- To understand the clonal heterogeneity and origin of leukemic cells
  - To study their immunoglobulin structure to highlight the antigens that stimulate the disease
  - To study the epitranscriptomic modifiers in CLL in order to highlight new prognostic markers and new therapeutic targets
- To investigate mechanisms by which mesenchymal stromal cells (MSC) and their extracellular vesicles mediate immunosuppressive effects and to discover novel immune targets for the development of immunotherapeutic strategies

Main projects

- Dissecting the crosstalk between malignant cells and their microenvironment (e.g., MSC, immune cells) and investigating their different methods of communication (e.g., via extracellular vesicles, via microRNA)

L. Lagneaux, B. Stamatopoulos

- Studying the immunosuppressive microenvironment in MM: role of bone marrow-mesenchymal cell (BM-MSC) glycosylation
- Deciphering the clonal heterogeneity of T cells in CLL using next-generation sequencing of T cell receptors (TCR) in order to identify relevant CLL-associated antigens
- Predicting epitope and modelling of antibody-antigen structure to discover CLL-stimulating antigens

Recent achievements

- Demonstrated the feasibility of using extracellular vesicles to deliver siRNA and drugs for therapeutic targeting, starting with pancreatic cancer (1)
- Showed evidence of the existence of harmful crosstalk between cancer cells and MSC in CLL and MM
- Bioinformatic tools developed to discover similar 3D motif across proteins (2)
- Participated in whole-genome sequencing study in CLL identifying the role of non-coding mutations (3)
- Demonstrated the impact of MSC extracellular vesicles on survival, gene expression, and chemoresistance of CLL cells
- Deciphered age-related changes in human bone marrow mesenchymal stromal cells (4)
- Established microRNA profiling of CLL extracellular vesicles by small RNA sequencing
- Highlighted the contribution of endothelial progenitors in the osteogenic potential of MSC via extracellular vesicle liberation
- Developed a new cellular therapy to treat jaw osteonecrosis in MM patients (5)

Selected publications

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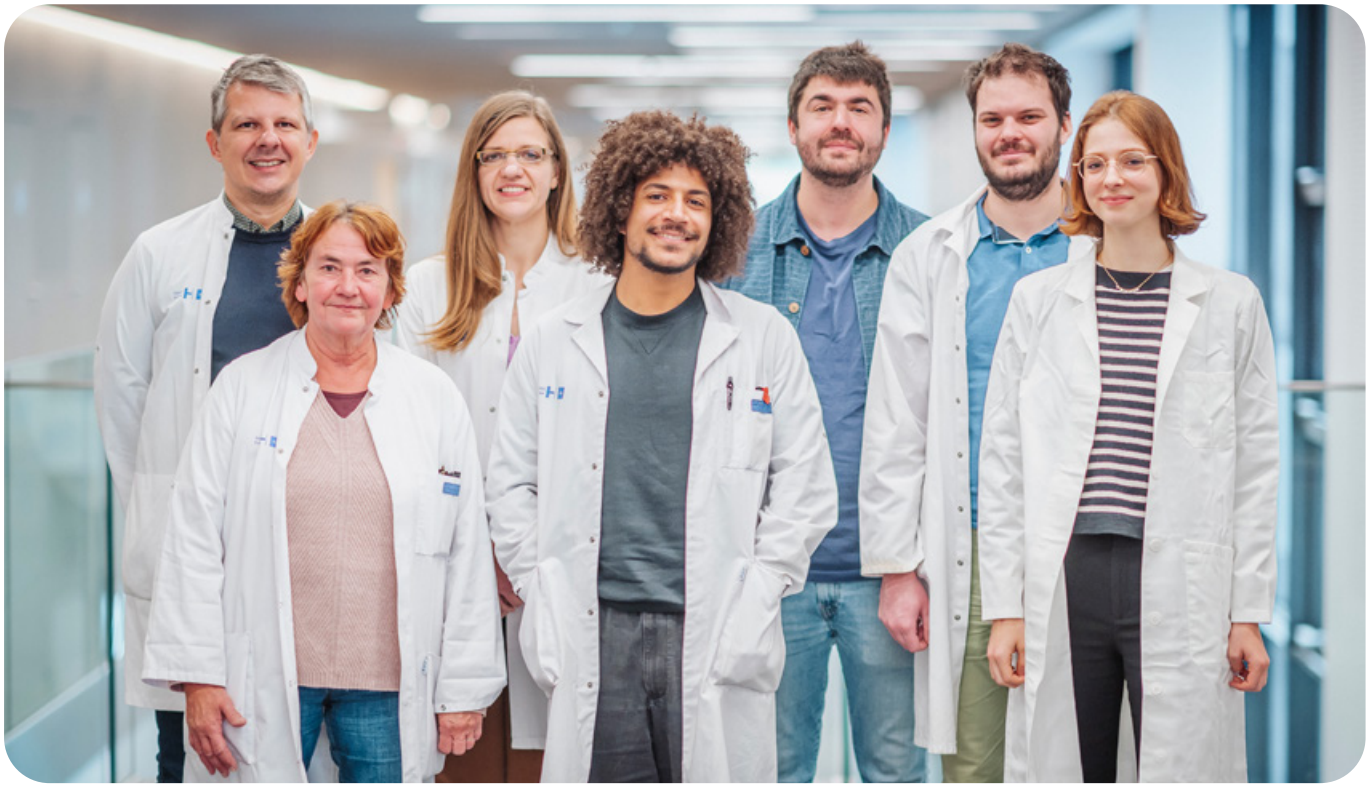
- Robbe P, Ridout KE, Vavoulis DV, Dréau H, Kinnersley B, Denny N, CH.U.Bb D, Appleby N, Cutts A, Cornish AJ, Lopez-Pascua L, Clifford R, Burns A, Stamatopoulos B, Cabes M, Alsolami R, Antoniou P, Oates M, Cavalieri D; Genomics England Research Consortium; CLL pilot consortium; Gibson J, Prabhu AV, Schwessinger R, Jennings D, James T, Maheswari U, Duran-Ferrer M, Carninci P, Knight SJL, Månsson R, Hughes J, Davies J, Ross M, Bentley D, Strefford JC, Devereux S, Pettitt AR, Hillmen P, Caulfield MJ, Houlston RS, Martín-Subero JI, Schuh A. Whole-genome sequencing of chronic lymphocytic leukemia identifies subgroups with distinct biological and clinical features. **Nat Genet**. 2022 Nov;54(11):1675-1689. doi: 10.1038.



APPLIED CANCER EPIGENOMICS AND EPITRANSCRIPTOMICS LABORATORY (ACEE)

"The goal of our research is to understand how changes in the chemical modifications that occur in DNA and RNA in cancer contribute to the progression and therapy resistance of this disease and to utilise these changes to identify new biomarkers and therapeutic targets for improved diagnosis and treatment of cancer patients."

Team and infrastructure

The ACEE team, led by Jana Jeschke, is comprised of two postdoctoral researchers, two PhD students, one technician, and one trainee. The laboratory is well-equipped with essential equipment for studying DNA/RNA modifications and proteins at both the molecular and cellular levels. It also features advanced equipment for epigenomic and epitranscriptomic profiling, including Oxford Nanopore sequencing technology. The team's expertise lies in establishing and manipulating pre-clinical cancer models using genetic and pharmacologic tools to investigate the role of DNA and RNA modification machineries in cancer progression and cancer drug resistance. To understand the molecular mechanisms behind the phenotypes observed in these models and to probe their relevance in human tumours, the ACEE team develops state-of-the-art technologies and bioinformatic tools for mapping DNA and RNA modifications in human cancer biopsies.

Aims

- Map DNA and RNA modifications in pre-clinical cancer models and human tumour biopsies
- Search epigenomic and epitranscriptomic maps to identify changes in DNA and RNA modifications in cancer
- Study the role of epigenomic and epitranscriptomic alterations in cancer progression and therapy resistance
- Explore epigenomic and epitranscriptomic alterations as new biomarkers or therapeutic targets to improve the diagnosis and treatment of cancer

Main projects

- Establish new technologies for transcriptome-wide mapping of m6A mRNA modification at both the bulk (e.g. Oxford Nanopore) and single-cell (e.g. scMeRIP-seq) levels that are applicable to human tumours
- Develop bioinformatic pipelines for the analysis of data generated with new m6A mapping technologies
- Identify changes of m6A in human breast tumours with direct RNA sequencing and explore their value as disease biomarkers
- Generate in vitro and in vivo models to study the role of m6A and its machinery in tumour development and progression
- Study the role of m6A in breast cancer heterogeneity and drug resistance using single-cell m6A mapping in preclinical models and human biopsies of breast cancer
- Investigate the role of epitranscriptomic gene regulation in the tumour microenvironment

J. Jeschke

Recent achievements

- Obtained an ERC Starting Grant
- Identified the widespread downregulation of FTO m6A RNA demethylase in breast and other epithelial cancers
- Established m6A-RIPseq for transcriptome-wide mapping of m6A and applied it to preclinical models of breast cancer to show that m6A is enriched at transcripts of several oncogenic pathways including Wnt signalling
- Generated various in vitro and in vivo models to demonstrate that downregulation of FTO promotes EMT-mediated progression and sensitivity to Wnt inhibitors in breast cancer
- Developed a new bioinformatics pipeline for Infinium MethylationEPIC data processing
- Co-authored a research article that identified DNA methylation-based markers of breast cancer risk in blood
- Co-authored a review article that highlights the challenges of investigating RNA modifications beyond m6A and offers insights into how to overcome them
- Contributed a written testimonial to a series in the Journal of Experimental Medicine that highlights the experiences of women scientists in starting their independent research labs
- Edited the "Cancer Biology" section for the March 2023 edition of the "Current Opinion in Oncology" journal

Selected publications

- Campbell, C., Funk, M.C., Hattori, Y., Hu, W., Jeschke, J., Lau, C.M., Ling, G.S., Liu, S., Llorens-Rico, V., Nemes, E. Women in STEM becoming independent: The journey to independence is an immensely gratifying odyssey. **Journal of Experimental Medicine**, 2024. 221(7), e20240842.
- Chung, F. F.-L., Maldonado, S. G., Nemc, A., Bouaoun, L., Cahais, V., Cuenin, C., Salle, A., Johnson, T., Ergüner, B., Laplana, M., Datlinger, P., Jeschke, J., Weiderpass, E., Kristensen, V., Delaloge, S., Fuks, F., Risch, A., Ghantous, A., Plass, C., Bock, C., Kaaks, R., & Herceg, Z.. Buffy coat signatures of breast cancer risk in a prospective cohort study. **Clinical Epigenetics**, 2023 15(1), 102.
- Bizet, M., Defrance, M., Calonne, E., Bontempi, G., Sotiriou, C., Fuks, F., & Jeschke, J. Improving Infinium MethylationEPIC data processing: re-annotation of enhancers and long noncoding RNA genes and benchmarking of normalization methods. **Epigenetics**, 2022. 17(13), 2434-2454.
- Penning, A., Jeschke, J., & Fuks, F. Why novel mRNA modifications are so challenging and what we can do about it. **Nature reviews**. 2022. Molecular cell biology, 23(6), 385-386.
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- Jeschke, J. Editorial: Advances in cancer detection and diagnosis: from liquid biopsies and molecular biomarkers to opportunistic intratumoral bacteria. **Current opinion in oncology**, 2023. 35(2), 114.

MRI PHYSICS & RADIOPHYSICS LABORATORY

"Established in 2020, the MRI Physics and Radiophysics Laboratory combines clinical and basic research to develop novel treatment modalities and optimise existing clinical workflows across multiple departments and laboratories. Our goal is to improve patient clinical outcomes."

Collaborative Research Environment

The laboratory fosters close collaboration with the departments of Nuclear Medicine, Radiology and Radiotherapy, and the BCRL (Brussels Center for Radiotherapy Research). This interdisciplinary environment allows us to leverage wide-ranging expertise and pursue diverse research topics.

We have also strong collaborations with:

- **Nuclear Molecular Imaging & CT (NuMix) Unit of CMMI-ULB:** Led by our co-director, this unit facilitates further research opportunities.
- **Advanced Theranostics in Oncology (Atheno) Unit:** Collaborating on theranostics projects.

ORILAB: Imaging Core Facility

The laboratory coordinates H.U.B's core imaging facility, ORILAB. This facility performs quality control and medical review of images for prospective clinical trials. Between 2020 and 2023, ORILAB has provided services to 16 academic and industry-sponsored clinical trials.

Team and infrastructure

Our team comprises a Director (Nick Reynaert), a co-director (PhD), six senior scientists (two PhDs and four MScs), five postdoctoral scientists (PhDs), eight PhD students, and one administrative assistant.

Advanced Facilities

The laboratory is equipped with cutting-edge technology:

- Computational Units: Dedicated CPU and GPU-based units for big data analysis and deep learning experiments.
- Radiobiology Unit Development: We are currently developing a unit for assessing the radiobiology of BNCT (Boron Neutron Capture Therapy) and FLASH therapy.
- 3D Printing Platform: Featuring four printers with different technologies for diverse applications.

Main Research Projects

- A. **Data Science and Artificial Intelligence Research Unit:** Initiating several projects aiming to enhance patient care (see "Pillar II" for details).

S. Penninckx, H. Levillain, N. Reynaert, J. Dhont

- B. **Optimising Radiotherapy Techniques:** Integrating multimodality imaging into precision radiotherapy approaches (MR-Linac, Theranostics: 68-Gallium/177-Lutetium PRRT and PSMA, etc.).
- C. **EORTC Collaboration:** Our director serves as the physicist responsible for the Radiotherapy Quality Assurance/Radiation Oncology Science Council (RTQA/ROSC) group at EORTC, actively contributing to radiotherapy-related clinical studies in Europe.
- D. **FLASH Radiotherapy Research:** Utilising zebrafish models to understand the FLASH effect for potential clinical applications. The team is studying new tools for robust dosimetry in FLASH conditions, an important step for clinical implementation of the technology. This is performed via characterisation of the response of existing ionisation chambers in close collaboration with academic (Darmouth Heath Center) and industrial (IBA Dosimetry, IntraOp) collaborators. Additionally, a joint research project with KU Leuven has resulted in the development of a brand-new type of ionisation chamber for FLASH dosimetry. Our prototype is characterised by Monte-Carlo simulation and tested in clinical conditions within the Institute. The preliminary results are very promising.
- E. **Radiobiology Collaborations:** Partnering with various entities on radiobiology research:
    - A. Brussels RadioTheranostics Platform (BRTP)
    - B. Numix CMMI-ULB
    - C. Atheno
    - D. SCK-CEN (focusing on kidney toxicity in PRRT)

- F. **3D Printing Applications:**
    - A. Bolus materials for radiotherapy
    - B. Phantoms for nuclear medicine and radiology
    - C. Simulations for surgical interventions
- G. **Proton and Hadrontherapy Project (D-CAF):** Collaborating with IBA on modelling new detectors for carbon ion beams.
- H. **Boron Neutron Capture Therapy (BNCT) Development:** developing BNCT technology.
- I. **European Theranostics Consortia** Participating in two European consortiums focused on novel theranostics approaches (in collaboration with H.U.B's Nuclear Medicine Department). The corresponding EU grant applications were successfully submitted by Hugo Levillain.

Recent achievements

- Established data science and 3D printing platforms within the BCRL.
- Signed a letter of intent with Neutron Therapeutics for co-installing a BNCT facility next to IJB: unfortunately, this project had to be abandoned due to financial difficulties affecting Neutron therapeutics.
- Secured funding from two European grants, one FNRS grant, and one Télévie grant.

Selected publications

- Mileva M, Marin G, Levillain H, Artigas C, Van Bogaert C, Marin C, Danieli R, Deleporte A, Picchia S, Stathopoulos K, Jungels C, Vanderlinden B, Paesmans M, Ameye L, Critchi G, Taraji-Schiltz L, Velghe C, Wimana Z, Bali M, Hendlisz A, Flamen P, Karfis I. Prediction of 177Lu-DOTATATE PRRT Outcome Using Multimodality Imaging in Patients with Gastroenteropancreatic Neuroendocrine Tumors: Results from a Prospective Phase II LUMEN Study. **J Nucl Med**. 2024 Feb 1;65(2):236-244. doi: 10.2967.
- Lombardo E, Dhont J, Page D, Garibaldi C, Künzel LA, Hurkmans C, Tijssen RHN, Paganelli C, Liu PZY, Keall PJ, Riboldi M, Kurz C, Landry G, Cusumano D, Fusella M, Placidi L. Real-time motion management in MRI-guided radiotherapy: Current status and AI-enabled prospects. **Radiother Oncol**. 2024 Jan; 190:109970. doi: 10.1016.
- Danieli R, Stella M, Leube J, Tran-Gia J, Marin C, Uribe CF, Vanderlinden B, Reynaert N, Flamen P, Levillain H. Quantitative 177Lu SPECT/CT imaging for personalized dosimetry using a ring-shaped CZT-based camera. **EJNMMI Phys**. 2023 Oct 18;10(1):64. doi: 10.1186.
- Penninckx S, Martinive P, Mirjolet C. Radiation-activated nanoparticles: Which combination to optimize radiosensitization? **Cancer Radiother**. 2023 Sep;27(6-7):494-498. doi: 10.1016.
- Burghelea M, Bakkali Tahiri J, Dhont J, Kyndt M, Gulyban A, Szkitsak J, Bogaert E, van Gestel D, Reynaert N. Results of a multicenter 4D computed tomography quality assurance audit: Evaluating image accuracy and consistency. **Phys Imaging Radiat Oncol**. 2023 Aug 14; 28:100479. doi: 10.1016.

II. LABORATORY OF EXPERIMENTAL GASTROENTEROLOGY

"The Laboratory of Experimental Gastroenterology aims to develop translational and basic research in digestive diseases. Our lab is in close relationship with the department of Gastroenterology, Hepatopancreatology and Digestive Oncology at H.U.B, and is led by Christophe Moreno. Our lab is subdivided into three units: the digestive oncology group (lead: Jean-Luc Van Laethem), the liver research group (lead: Eric Trépo), and the IBD group (lead: Denis Franchimont)."

A. The digestive oncology Group/Unit within the ULB Laboratory of Experimental Gastroenterology (LGE) is led by Jean-Luc Van Laethem, MD, PhD and Tatjana Arsenijevic, PhD. The research team is composed of:

- three senior researchers (Tatjana Arsenijevic, Anne Demols, MD, PhD, Jean-Luc Van Laethem)
- one postdoctoral researcher (Christelle Bouchart, MD, PhD)
- five PhD. students (Julie Navez, MD, Kosta Stosic, BSc, Oier Azurmendi Senar, Bioinformatics, Jawad Tarfouss, BSc and Rita Saude Conde, MD)
- two technicians (Eric Quertinmont, Vjola Tafçiu)

Aims

- to identify generic and specific genes associated with the clinical behaviour of pancreatobiliary cancers and the benefit of/resistance to different therapies;
- to correlate molecular subtyping classification to histo-morphological patterns, focusing on immune infiltrate and stromal components assessed by spatial transcriptomics
- to evaluate the pathological/histological effects of neoadjuvant treatments in borderline resectable PDAC patients, focusing on the components of the tumour microenvironment (TME), especially Cancer Associated Fibroblasts (CAF) and their impact on resistance to treatment.
- to explore molecular subgroups in depth and perform pathway enrichment analysis in order to identify new possible druggable targets;
- to decipher the molecular landscape of vascular and retroperitoneal surgical margins by transcriptomic and genomic analyses in order to understand and better characterise vascular and retroperitoneal invasiveness.
- to integrate the molecular characterisation into clinical trials in neoadjuvant therapy for pancreatic cancer (correlation with molecular profile, dynamic imaging monitoring and pathological response/pattern after tumour resection (window trials)).

E. Trépo, Ch. Moreno, J.L. Van Laethem

Main projects

- STEREOPAC TRANS study (multimodal (clinical, radiological and histo-molecular) evaluation of the response to neoadjuvant treatments (chemo only vs chemo-radio therapy) in patients with borderline resectable pancreatic adenocarcinoma (PDAC)
- FAPI-PANC study: influence and integration of 68Ga-FAPI PET Imaging on the staging of borderline resectable pancreatic ductal adenocarcinoma patients: a prospective ancillary substudy from the STEREOPAC clinical trial.
- A multimodal and translational evaluation of predicting the surgical resection margins in patients undergoing curative-intent pancreatectomy for pancreatic cancer
- Glycation stress as a novel therapeutic target in gemcitabine-resistant pancreatic cancer
- Evaluation of tumour heterogeneity in pancreatic cancer and its impact on molecular classification and therapeutic purpose
- Study of the intratumoral heterogeneity of the extrahepatic cholangiocarcinoma and its implications in resistance to treatment

Recent achievements

- Showed in a pilot cohort of 50 borderline resectable PDAC patients that the addition of iHD-SBRT to mFOLFIRINOX leads to a significant enrichment shift towards PDAC tumour and stroma transcriptomic signatures associated with better prognosis.
- Published the results of OPTIMIZE-1 study aiming to test the safety, immunomodulation and antitumour activity of mitazalimab, a human CD40 agonistic IgG1 antibody,

with modified mFOLFIRINOX, in chemotherapy-naïve patients with metastatic pancreatic ductal adenocarcinoma: demonstrated manageable safety and encouraging activity, warrant continued development in a phase 3 randomised, controlled trial.

- Contributed to the discovery of intra-ductal heterogeneity in PDAC and identified a new ΔNp63-expressing basal cell type in human pancreatic ducts.
- Found, in collaboration with ULg, that resistance to Gemcitabine in PDAC is connected to methylglyoxal stress and heat shock response that can be modulated using potent methylglyoxal scavengers, such as metformin and aminoguanidine.

Selected publications

- Jean-Luc Van Laethem, Ivan Borbath, Hans Prenen, Karen Paula Geboes, Aurélien Lambert, Emmanuel Mitry, Philippe Alexandre Cassier, Jean-Frédéric Blanc, Lorenzo Pilla, Jaime Feliu Batlle, Mercedes Rodriguez Garrote, Roberto Antonio Pazo-Cid, Inmaculada Gallego, Karin Enell Smith, Peter Ellmark, Yago Pico de Coaña, Sumeet Vijay Ambarkhane, Teresa Macarulla.Combining CD40 agonist mitazalimab with mFOLFIRINOX in previously untreated metastatic pancreatic ductal adenocarcinoma (OPTIMIZE-1): a single-arm, multicentre phase 1b/2 study. **The Lancet Oncology**, 2024.
- Christelle Bouchart, Oier Azurmendi Senar, Julie Navez, Laurine Verset, Anaïs Boisson, Matthieu Hein, Kosta Stosic, Eric Quertinmont, Vjola Tafciu, Shulin Zhao, Léo Mas, Nicky D'Haene, Dirk Van Gestel, Luigi Moretti, Ilse Rooman, Vincent Detours, Jean-Baptiste Bachet, Pieter Demetter, Karen Willard-Gallo, Rémy Nicolle, Tatjana Arsenijevic, Jean-Luc Van Laethem. Favorable histo-molecular remodeling of pancreatic ductal adenocarcinoma after Total Neoadjuvant Therapy including Stereotactic Body Radiotherapy. **BioRxiv** 2024.04.30.591890
- Michiels E, Madhloum H, Van Lint S, Messaoudi N, Kunda R, Martens S, Giron P, Olsen C, Lefesvre P, Dusetti N, El Mohajer L, Tomasini R, Hawinkels LJ, Ahsayni F, Nicolle R, Arsenijevic T, Bouchart C, Van Laethem JL, Rooman I. High-resolution and quantitative spatial analysis reveal intra-ductal phenotypic and functional diversification in pancreatic cancer. **J Pathol**. 2024 Jan;262(1):76-89. doi: 10.1002/path.6212. Epub 2023 Oct 16.
- B, D'Haene N, Azurmendi Senar O, Arsenijevic T, Lambert F, Peulen O, Van Laethem JL, Bellahcène A. Resistance to Gemcitabine in Pancreatic Cancer Is Connected to Methylglyoxal Stress and Heat Shock Response. Crake R, Gasmi I, Dehaye J, Lardinois F, Peiffer R, Maloujahmoum N, Agirman F, Koopmansch. **Cells**. 2023 May 17;12(10):1414. doi: 10.3390/cells12101414. PMID: 37408249; PMCID: PMC10217245.
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B. The liver research group within the Laboratory of Experimental Gastroenterology (LGE) is led by Christophe Moreno and Eric Trépo. The liver research team comprises:

- three senior researchers (Eric Trépo, Thierry Gustot, Christophe Moreno)
- two postdoctoral researchers (Lukas Otero Sanchez, Ahmed Arslan)
- two PhD students (Clélia Galvanin, Alia Hadefi)
- two technicians (Eric Quertinmont, Vjola Tafçiu)

We have access to approximately 150 liver biopsy/liver resection procedures annually. We manage a substantial DNA/plasma/tissue biobank from liver disease patients (>6000 liver related samples). This biobank has been established since 1999 and continues to grow.

Aims

- To unravel the genetic architecture of liver tumours, particularly hepatocellular carcinoma (HCC)
- To explore gene-environment interactions in the context of HCC
- To develop and apply artificial intelligence models for predicting HCC development and better understand the early steps of liver carcinogenesis
- To integrate genetic/genomic and clinical information for improved risk prediction and patient stratification.

Main projects

- GENIAL project: A European collaborative effort (13 partners, 2023-2028) funded under the Horizon Europe programme, aiming to better understand the early steps of alcohol-related HCC (ALD-HCC). Eric Trépo serves as the coordinator for this project (https://cordis.europa.eu/project/id/101096312).
- Transcriptomics and prognostic modelling in liver cirrhosis and cancer
- Artificial intelligence applications in systemic treatment for HCC

Recent achievements

- Conducted the first GWAS in alcohol-related cirrhosis, identifying PNPLA3, TM6SF2, and MBOAT7 as key risk loci
- Performed the first GWAS focused specifically on ALD-HCC, identifying variants in the WNT3A-WNT9A region as a novel susceptibility locus
- Contributed to the development of an AI model that estimates gene signature expression associated with progression-free survival in HCC patients treated with

atezolizumab-bevacizumab

- Identified a spectrum of driver mechanisms and cisplatin resistance pathways in paediatric liver tumours

Selected publications

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RESEARCH LABORATORY IN HUMAN REPRODUCTION

“With significant advances in oncological treatments, improving the long-term quality of life for young cancer survivors has become a research priority, including the possibility of conception after remission. Our goal is to enhance the management of reproductive issues in cancer patients and to offer them a personalised, efficient, and safe fertility preservation procedure based on their individual context. .”

Team and infrastructure

The Research laboratory of Human Reproduction is headed by Isabelle Demeestere. The team includes two senior scientists, two lab technicians, one data manager, six PhD students, one post-doc and several master's students. It has all the expertise and equipment required for assessing all aspects of gametogenesis in human and mice, including culture rooms, molecular or immunohistological equipment, and has also access to several technical platforms at ULB (flow cytometry, confocal and electronic microscopy, transcriptomics or proteomics platforms and animal facilities).

Aims

- To investigate the mechanisms leading to gonadotoxicity of standard and new cancer drugs
- To develop innovative and safe fertility preservation strategies using pharmacoprotective approaches
- To investigate the impact of patient characteristics such as age or gene mutations on reproductive outcomes

Main projects

- Assessing miRNas therapeutics as a potential pharmacoprotective approach to reduce chemotherapy-induced gonadal damage and optimising surface-engineered gold nanoparticles to efficiently and specifically deliver miRNAs in the ovary and testis
- Analysing the landscape of the chemotherapy-induced microenvironmental alterations in the human ovary, including more specifically modifications occurring in the extracellular matrix network organisation as well as the oxidative stress and inflammation responses by integrating multi-omics approaches.
- Evaluating the impact of BReast CAncer (BRCA) gene mutations on oocyte quality by assessing the ageing process and DNA repair response to chemotherapy.
- Evaluating the relevance of Anti-Mullerian Hormone (AMH) as biomarkers of chemotherapy-induced ovarian damage in a prepubertal population

The link between the laboratory and national and international oncological centers facilitates its participation in ambitious clinical research trials such as **POSITIVE** (BIG-IBCSG), **NeoALTTO** (BIG), **AHL2011** (CHU Dijon- GELA), **CHANCE** and **FAMHOPE** (multi-centre trials sponsored by the H.U.B)

I. Demeestere

Recent achievements

- Identified miRNAs involved in the ovarian response to chemotherapy and provided evidence that miRNAs replacement therapy is an attractive approach for reducing damage.
- Provided insights into the mechanism of gonadotoxicity through signalling pathways involved in follicular activation (Hippo and PI3K/AKT)
- Demonstrated using an in-vitro model that germline BRCA mutations do not increase the risk of chemotherapy-induced ovarian damage when exposed to chemotherapy (carboplatin – paclitaxel).
- Reported reassuring data on the safety and efficiency of the ovarian stimulation protocol for fertility preservation in breast cancer patients.

Selected publications

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- Grosbois J., Devos M., Demeestere I. Implications of non-physiological ovarian primordial follicle activation for fertility preservation. **Endocrine Reviews**. 2020 ;41(6); bnaa020.
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CENTER OF HUMAN GENETICS

“Our goal is to increase hereditary cancer risk diagnosis rate and identify individuals at high genetic risk to develop tailored preventive strategies and help to personalise pharmacologic cancer treatment.”

Team and infrastructure

The ULB Center of Human Genetics is headed by Guillaume SMITS MD, PhD. The two senior oncogeneticists are T'KINT DE ROODENBEKE, Daphné MD (Institut Bordet) and VANDERNOOT, Isabelle MD, PhD (Erasme, IRIS, IRIS Sud, CHU St Pierre, Chirec, Ambroise Paré and Tivoli hospitals.

The clinical team includes 18 members, the laboratory team consists of 40 scientists and eight administrative assistants and quality staff.

The Genetics Center offers an integrated medical genetics analysis and consultation activity, approved by the Ministry of Health and reimbursed by NIHDI. In addition, the Genetics Center is engaged in ongoing research and teaching activities in genetics.

In addition to oncogenetic activity, the service offers consultations and tests that cover all ages of life: PGD, preconception, prenatal, paediatric and adult.

The Genetics Center works closely with many departments of the Bordet Institute and provides hereditary oncogenetic consultations in all H.U.B, IRIS, IRIS Sud, CHU St Pierre, Chirec, Ambroise Paré and Tivoli hospitals.

The (ISO15189 accredited) laboratory has advanced molecular and cellular biology equipment, including a sequencer for high-throughput next-generation sequencing (NGS) analyses and long-read sequencing. The laboratory excels in state-of-the-art clinical bioinformatic analyses of various types of genomics data.

Aims

- To evaluate the **c**linical **u**tility of **p**olygenic risk **s**cores (PRS) in a genetic counselling setting and to evaluate clinical feasibility of analysing lyse gene panel, PRS and promotor methylation by means of long-read sequencing (**CUPS project**).
- To evaluate detection of structural variants by long read sequencing (**LRS SV project**).
- To evaluate whether genetic screening for HBOC genes in the general population is feasible or desirable (**KOTK project**).
- To evaluate the performance of NIPT for cancer detection (**CAN HEAL project**).
- To develop accessible and affordable tests to advance early detection of heritable cancers in European regions (**HERLIPSY project**).

I. Vandernoot, F. Wilkin, G. Smits, D. t'Kint de Roodenbeke

- To achieve early detection of cancer in carriers of the TP53 germline mutation (**TP53-BE project**).
- To implement a diagnostic path for genetic predisposition screening in the routine diagnostic work-up of paediatric cancer patients (**DHECIPR project**).
- To investigate whether salpingectomy with delayed oophorectomy is non-inferior to the current standard salpingo-oophorectomy for the prevention of tubo-ovarian cancer among individuals at high inherited risk (**TUBA WISP II project**).

Main projects

- **CUPS project**

  First objective: to evaluate the feasibility and clinical utility of applying PRS in individuals referred to oncogenetic testing, with no pathogenic monogenic variant found (target group), using BOaDICEA v6 model.

  Secondary objective: to estimate the feasibility of using the genome skimming technique in routine (low-pass genome-wide long read sequencing + enrichment for cancer predisposition genes + promotor methylation)

  Target group: women referred to oncogenetic testing according to established criteria (Eisinger score or equivalent), with no pathogenic variant found.
- **LRS SV project**

  Characterisation of complex structural variants when suspected in the HBOC panel or in the exome in clinical routine by LRS. Results allow re-classification into pathological or likely pathological variant (class V or IV).
- **KOTK project**

  Kom op tegen Kanker (KOTK) proposes to evaluate

if genetic screening for HBOC genes in the general population is feasible or desirable.

The Belgian College of Genetics is working to bring together data from the eight Belgian centers in order to help KOTK reach its conclusions.

- **CAN HEAL project**

  A prospective study on NIPT and Cancer detection (patients recruited through pregnancy NIPT screening results).

  The aims are:

  To evaluate the performance of NIPT for cancer detection.

  To compare NIPT platforms.

  To characterise the type of genomic aberrations in NIPT results that are linked to a cancer (type).

  To investigate whether an incidental finding of cancer via NIPT is associated with an improved patient outcome (cancer stage, GA at diagnosis, start of treatment, outcome).

  To design and facilitate the implementation of guidelines for the downstream clinical management of NIPT results presenting a suspicion of cancer.

- **HERLIPSY project**

  Assistance in recruiting, storing and sending samples in the context of colorectal cancers and rare paediatric oncogenetic syndromes. On process, the number of potential patients was shared with Sciensano.

- **DHECIPR project:**

  Diagnosing HEreditary predisposition syndromes for Childhood cancer: Implementation in clinical practice).

  Target group: all patients with (pre)malignant tumour or haematologic disease diagnosed < 18 yrs that requires treatment or follow-up.

Recent achievements

- Deployment of Oxford Nanopore long read sequencing technology.
- Acquisition of Promethion 24.
- Acquisition of High-performance computing server.
- More than 10 patients with a structural variant in HBOC gene characterised with Oxford Nanopore long read sequencing technology.
- Deployment of SNP arrays technology and BODICEA CanRisk Software for HBOC PRS use in clinical routine.

Selected publications

- L, Badoer C, Smits G, Vandernoot I, T Kint de Roodenbeke D. POT1 tumour predisposition: a broader spectrum of associated malignancies and proposal for additional screening program. Baptista Freitas M, Desmyter **Eur J Hum Genet**. 2024.
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- Joris S, Denys H, Collignon J, Rasschaert M, T Kint de Roodenbeke D, Duhoux FP, Canon JL, Tejpar S, Mebis J, Decoster L, Aftimos P, De Grève J. Efficacy of olaparib in advanced cancers with germline or somatic mutations in BRCA1, BRCA2, CHEK2 and ATM, a Belgian Precision tumor-agnostic phase II study. **ESMO Open 2023**.
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SKIN CANCER RESEARCH UNIT

“We strive to achieve a better clinical and scientific understanding of skin cancer in order to prevent it, diagnose it, treat it and manage it better.”

Team and infrastructure

The Skin Cancer Clinic and Research Unit is headed by Professor Véronique del Marmol, MD, PhD (Head of the Department of Dermatology of the H.U.B) and Professor Mariano Suppa, MD, PhD (Director of the Clinic of Dermato-Oncology). The medical team also includes five senior physicians (three experts in dermato-oncology, two experts in dermato-surgery), 12 junior physicians and three PhD candidates.

The Unit is equipped with all the key equipment required for non-invasive skin imaging, and these are used in strong clinical, research and teaching activities at both national and international levels. The Unit's international recognition in the field of dermato-oncology is partly based on this and partly on its continuous research investment in skin cancer prevention and risk factors, which will lead to genomic and epigenetic studies in the near future.

Aims of the unit

- To perform early diagnosis, offer adequate treatment and guarantee optimal management of skin cancer
- To produce research in the field of non-invasive skin imaging, as well as skin cancer prevention and risk factors
- To participate in the main European networks designing skin cancer guidelines
- To perform translational research based on a biobank including biological samples from patients (skin, blood and saliva)

Main projects

- Non-invasive skin imaging studies on: (i) the diagnostic performance of non-invasive skin imaging for different types of skin cancer, including basal cell carcinoma, squamous cell carcinoma, and melanoma; (ii) the monitoring of non-invasive treatments for skin cancer; (iii) the addition of artificial intelligence to the human eye for the diagnosis of skin cancer; and (iv) a comprehensive explanation of the link between dermoscopy and histopathology. Our PhD candidate working in this field is Dr Clément LENOIR (PhD jointly supervised by ULB and University of Barcelona).
- Non-invasive skin imaging and translational studies to better understand the field of cancerisation (actinic keratosis and squamous cell carcinoma) and the mechanisms of keratinocyte carcinogenesis. These will include in-vivo skin imaging on patients, the use of artificial intelligence, the gathering of blood/skin samples, and the conduct of genetic studies. These projects are based on the idea that cellular atypia can be objectively defined and quantified with a non-invasive in-vivo approach in three dimensions by using line-field confocal optical coherence tomography (LC-OCT) associated with artificial intelligence (we trained a Deep Learning algorithm to segment keratinocyte nuclei from 3D LC-OCT images).1 Our PhD candidate working in in this field is Dr Carmen ORTE CANO.
- Epidemiological and translational studies to produce new evidence on skin cancer risk factors: in particular these studies will be based on a new registry (EUropean Skin CAncer risk factors Platform, EUSCAP) which we have recently developed and which now includes over 750 patients in Belgium. We anticipate that the data produced by this project will help in better identifying specific risky subpopulations (e.g. multiple basal cell carcinomas). The next step will be to study these risky subpopulations from a genetic and epigenetic point of view, by comparing them with control groups. Our PhD candidate working in this field is Dr Katharina WUNDERLICH.
- Collaborations for our research projects are planned with the department of Prof Josep MALVEHY and Susan PUIG (University of Barcelona) and the labs of Prof Cedric BLANPAIN and Prof Ievgeniia PASTUSHENKO (ULB).

V. Del Marmol, M. Suppa

Recent achievements

- Paved the way for the use of artificial intelligence in association with LC-OCT, the newest and most promising tool in the field of non-invasive skin imaging.1-2
- Established as a leader in non-invasive skin imaging in Europe by producing a range of scientific evidence in this field (16 papers in the last 18 months.

- Created a new European registry (EUropean Skin CAncer risk factors Platform, EUSCAP) in order to investigate skin cancer risk factors in Europe.18-19

Selected publications

- Wunderlich K, Suppa M, Lipski J, Deworme V, Wambreuse A, Njimi H, White J, Gaide O; Euromelanoma Working Group; Gandini S, Del Marmol V. EUSCAP: A Euromelanoma project to investigate skin cancer risk factors in Europe. **J Eur Acad Dermatol Venereol**. 2024 Jun;38(6):e515-e517. doi: 10.1111/jdv.19710. PMID: 38069540
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Chapter II • Contribution to "Precision Oncology"

There is significant heterogeneity in the risk of developing cancer, and this heterogeneity extends to cancer patients themselves, who show markedly different outcomes despite receiving identical histopathological diagnoses and identical therapies. The "one size fits all" approach to screening and treatment as applied today in most circumstances is therefore largely unsatisfactory.

"Precision oncology" is rapidly reshaping cancer care, and this ambitious goal is pursued by most comprehensive cancer centers nowadays: it means exploiting modern technologies in order to better individualise cancer screening, diagnosis, and treatment in the fields of surgery, radiotherapy, and medical oncology.

H.U.B has launched precision oncology initiatives in these fields at national and international levels, using modern tools such as genotyping, liquid biopsies, molecular imaging with FDG-PET, MRI-Linac, radiomics, and artificial intelligence algorithms. H.U.B's ambition is to upgrade the efficiency of this research by creating a "learning healthcare system" through the use of artificial intelligence and big data analysis.

- **THE EU MYPEBS TRIAL**
- **CIRCULATING TUMOUR DNA, SINGLE-CELL MULTI-OMICS**
- **NUCLEAR IMAGING TEAM WORKING HAND IN HAND WITH MEDICAL ONCOLOGISTS**
- **ONCOLOGIC IMAGING**
- **PRECISION MEDICAL ONCOLOGY**
- **PRECISION RADIOTHERAPY**
- **PRECISION SURGERY**
- **PRECISION NEUROONCOLOGY**
- **CREATION OF A LEARNING HEALTH CARE SYSTEM WITH THE HELP OF A DATA SCIENCE RESEARCH TEAM**

USING A RISK-STRATIFIED STRATEGY TO IMPROVE OUTCOMES FROM STANDARD BREAST CANCER SCREENING: THE EU MYPEBS TRIAL

Team and infrastructure

This EU-funded, international, multi-centre study involves a 27-partner consortium and six recruiting countries. The Unicancer network of cancer centers (France) is the sponsor, and IJB is the national coordinator for 10 Belgian sites (Principal Investigator: Jean-Benoît Burrion). MyPeBS in Belgium is supported by the "Fondation Contre le Cancer".

Aims

- Risk-stratified breast cancer screening (BCS), integrating both personal and familial variables and a polygenic risk score (PRS), is a promising strategy that may improve current BCS outcomes.
- Real-time risk assessment and real-world implementation are some of the main challenges for such an approach.
- MyPeBS is a European research project that aims to assess the effectiveness and feasibility of a risk-stratified BCS programme that is based on the individual risk of developing breast cancer.

Main projects

- At the core of MyPeBS is a trial in which eligible women aged 40-70 are randomised 1:1 between continuing standard BCS as recommended in their participating country/region or switching to risk-stratified BCS, where BCS schedule and modalities are adapted to the individual predicted 5-year risk of invasive BC (IBC).
- The primary endpoint is 4-year incidence of stage 2 and higher BC.
- The 5-year IBC risk is estimated using a BCSC-derived or Tyrer-Cuzick risk score and centrally-determined PRS313 (saliva sample), adjusted for national BC incidence.

Recent achievements

- The last participant was recruited on July 14, 2023, bringing the total number of women recruited to 53,143. The follow up period is 4 years. The final analysis will take place in July 2027. Among the first 16,550 women randomised, 36% were estimated to be at low risk (<1% risk of IBC at 5 years), 29% at average risk, and 35% at high (34%) or very high risk (1%) (>1.67% and >6% risk, respectively) of developing IBC. Only 2.5% of DNA extractions were not usable for genotyping, due to insufficient DNA concentration or quality; and 98.8% of the eligible DNA samples were successfully genotyped. Median turnover time from saliva sampling to risk result availability was 11 weeks. This preliminary achievement shows that real-time BC risk assessment based on a large set of polymorphisms, on family, screening and hormonal history, and on breast density is feasible within organised screening programmes. Participants so far represent different strata of the general population with some over-representation of highly educated participants.

J.B. Burrion

Selected publications

- Belgium contributed 2,192 patients to the EU MyPePS trial.

CIRCULATING TUMOUR DNA, SINGLE-CELL MULTI-OMICS

Team and infrastructure

Michail Ignatiadis is the director of the breast medical oncology clinic. His research team is part of the J.-C. Heuson Breast Cancer Translational Research Laboratory (BCTL).

M. Ignatiadis

Circulating tumour DNA

Aim

- To explore the clinical validity and utility of circulating tumour DNA (ctDNA) for breast cancer diagnosis and monitoring of early disease.

Projects

- 1. Developed a ctDNA assay for breast cancer diagnosis based on patterns of plasma cell-free DNA fragmentation. We are comparing plasma from healthy women and women with breast cancer enrolled in several trials, (project ongoing).
- 2. Identified associations between plasma ctDNA detection using the SAGASignTM personalised assay and clinical outcome in patients with early breast cancer enrolled in the Neocheckray study. This is a randomised phase 2 trial of neoadjuvant chemotherapy + stereotactic radiotherapy +/- durvalumab +/- oleclumab in luminal B breast cancer. The project will start in September 2024.
- 3. Demonstrated the clinical utility of ctDNA monitoring for treatment escalation in high-risk ER+/HER2- early breast cancer in the context of the Treat ctDNA elacestrant study. This is an investigator-initiated, phase 3, randomised trial being conducted by the EORTC breast cancer group (study chair Dr Ignatiadis) with an education grant from Menarini/Stemline. The study started in December 2023 and will open in 120 sites in >10 European countries. High-risk, ER+/HER2- patients that have completed at least one and up to seven years of endocrine therapy will be screened using the personalised SignateraTM assay every 6 months for up to 5 years. Patients that are ctDNA-positive will undergo imaging to exclude the presence of loco-regional or distant recurrence. Patients with a negative imaging work-up will be randomised 1:1 to continue the same endocrine therapy they had at the time of ctDNA detection versus an oral selective estrogen receptor degrader, elacestrant for 2 years. Patients in both arms will be followed up with an intensive imaging work-up every 4 months (provided by the study). It is expected that approximately 2000 patients will be screened in order to randomise 220. The primary objective of the study is to demonstrate that elacestrant can improve distant-metastasis free survival compared to standard of care endocrine therapy.

Single-cell multi-omics

Aim

- To understand transcriptomic and epigenomic changes induced by targeted agents using single cell RNA-seq & ATAC-seq in pre and post treatment samples.

Projects

- To understand transcriptomic and epigenomic changes induced in tumour, immune and stromal cells by endocrine therapy in combination with the ROS1 inhibitor entrectinib in lobular breast cancer. We are conducting this project in the context of the phase 2, neoadjuvant, Rosaline study, (project ongoing).

Achievements

- **We studied associations between plasma ctDNA detection using the RaDaR™ personalised assay and clinical outcome in patients with early breast cancer enrolled in the NeoRHEA study**. This is a phase 2 trial involving 4 months of neoadjuvant endocrine treatment in combination with the CDK4/6 inhibitor palbociclib in luminal breast cancer. Of 100 patients enrolled, 78 patients and 302 plasma samples were successfully profiled by the RaDaR assay. The number of variants targeted by the assay ranged between 7-48 (median = 25). The median estimated variant allele fraction for ctDNA positive samples was 0.02% (range 0.0009%-0.91%). A total of 42/76 patients were ctDNA positive at baseline (BL), 4/76 at C1D28, 4/75 at Surgery and 0/75 at End of Study. Out of 78 patients, 68% were postmenopausal, 78% had cT2 and 69% cN0 tumours, 20% had multifocal/multicentric tumours, 18% had histological grade 3 tumours, 76% had complete cell cycle arrest (CCCA) and 34% RCB 3 at surgery. ctDNA detection at BL was higher in histological grade 3 tumours ($p = 0.03$), lower in multifocal/multicentric tumours ($p = 0.01$), higher in RCB III tumours, ($p = 0.01$) but was not associated with CCCA. With a median follow-up of 3.8 years (range 1-5 years), 4 patients developed distant and one patient locoregional recurrences.

ctDNA detection after one month of treatment (logrank p = 0.02) was associated with worse BCFS, but not at baseline (p = 0.59) nor at surgery (p = 0.67). The above results have been presented at ASCO 2023 annual meeting

- **We studied transcriptomic and epigenomic changes induced in tumor, immune and stroma cells by endocrine therapy and the CDK4/6 inhibitor palbociclib in the NeoRHEA study using single-nuclei RNA & ATAC sequencing.** Analyses were performed on pre- and post- treatment (four months of palbociclib and endocrine therapy) tumour samples from breast cancer patients enrolled in the NeoRHEA trial. Down-regulation of E2F targets and G2M checkpoint proliferation-related genes post treatment was observed in tumor, endothelial and T-cells. GSEA based on genes residing in the differentially accessible peaks revealed similar results suggesting that the observed gene expression changes are associated with altered chromatin accessibility. Moreover, decrease in CD8+/CD103+ tissue-resident memory cells was observed post-treatment. Multiplex immunohistochemistry validated these findings. Treatment with palbociclib and endocrine therapy diminishes adaptive anti-tumour immunity by decreasing T-cell proliferation and the presence of tissue-resident memory T-cells.

Selected publications

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NUCLEAR IMAGING TEAM WORKING HAND IN HAND WITH MEDICAL ONCOLOGISTS

"In addition to its extensive involvement in innovative radiotheranostic approaches the Nuclear Medicine Department works closely with the medical oncology department to develop imaging biomarkers that can be helpful in selecting patients likely to benefit or not from expensive anticancer drugs and evaluating response as early as possible. This collaboration started with the frequently quoted Zephir 01 trial which revealed significant heterogeneity in HER2 expression across the metastatic tumour burden and its correlation with response to TDM1 in HER2 positive breast cancer."

Team

The team involves enthusiastic nuclear medicine specialists (C. Artigas, E. Woff, G. Gebhart, P. Flamen, and medical oncologists (M. Piccart, E. Agostinetto, S. Lobo Martins, Ph. Aftimos and A. Hendlisz) and benefits from the support of the CTC.

Projects

Current projects are mainly focusing on HER2 imaging as a prognostic / predictive tool for therapy with HER2-directed antibody drug conjugates

- **Hermia:** this prospective trial, sponsored by Abscint, will evaluate, in metastatic breast cancer patients (all subtypes) the diagnostic performance of a relatively new HER2 imaging tracer – namely 68Ga-ABSO11 – which is a single domain antibody able to bind HER2 very fast.
- **Zephir 02:** this prospective academic clinical trial, sponsored by H.U.B and financially supported by Roche, will test the hypothesis that HER2 imaging (using zirconium trastuzumab) can identify patients with HER2 amplified BC likely to respond to TDM1 after progression on trastuzumab-deruxtecan. It will be based on imaging predictive criteria previously determined in the Zephir 01 trial.
- **Galilee:** this prospective academic clinical trial, under advanced negotiation with Daiichi-Sankyo and AstraZeneca – will test the hypothesis that HER2 imaging (based on the Abscint tracer) – can identify patients with "HER2 zero" metastatic breast cancer who derive a meaningful clinical benefit from Trastuzumab-deruxtecan
- **OASIS:** this recently selected EU-project, coordinated by Institut Gustave Roussy, aims at a better understanding of mechanisms of resistance to antibody drug conjugates (ADCs). The H.U.B teams will be in charge of the work package relative to HER2 directed ADCs.

Achievements

- PSMA PET/CT for Response Assessment and Overall Survival Prediction in Patients with Metastatic Castration-Resistant Prostate Cancer Treated with Androgen Receptor Pathway Inhibitors.
- Phergain trial investigated the potential of metabolic imaging (FDG-PET) to identify candidates for chemotherapy deescalation in human epidermal growth factor receptor 2 (HER2)-positive, invasive, operable breast cancer. Primary endpoint disease-free survival and secondary preplanned analysis of the optimal [18F] FDG PET/CT Cutoff for Pathologic Complete Response were published in 2024.
- Zephir trial: the primary endpoint was published in 2024, namely the ability of HER2 PET/CT to predict, before initiation of treatment, tumour lesions unlikely to respond anatomically to T-DM1.

S. Labo Martins, G. Gebhart, E. Agostinetto, E. Woff

Selected publications

- Geraldine Gebhart, Marleen Keyaerts, Thomas Guiot, Patrick Flamen, Manuel Ruiz-Borrego, Agostina Stradella, Begoña Bermejo, Santiago Escriva-de-Romani, Lourdes Calvo Martínez, Nuria Ribelles, María Fernandez-Abad, Cinta Albacar, Marco Colleoni, Laia Garrigos, Manuel Atienza de Frutos, Florence Dalenc, Aleix Prat, Frederik Marmé, Peter Schmid, Khaldoun Kerrou, Sofia Braga, Petra Gener, Miguel Sampayo-Cordero, Javier Cortés, José Manuel Pérez-García and Antonio Llombart-Cussac. Optimal [18F] FDG PET/CT Cutoff for Pathologic Complete Response in HER2-Positive Early Breast Cancer Patients Treated with Neoadjuvant Trastuzumab and Pertuzumab in the PHERGain Trial. **Journal of Nuclear Medicine** May 2024, 65 (5)
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ONCOLOGIC IMAGING

Artificial intelligence to improve patient management

Research by the department of oncologic imaging is principally focused on artificial intelligence approaches and several projects have been grouped around three main axes:

1. Development of AI-based tools for body composition analysis
2. AI-based approaches for acceleration of magnetic resonance sequences
3. AI-based tools for treatment response evaluation

M. Bali

1. Development of AI-based tools for body composition analysis

In-house AI-based tools for automated whole-body composition analysis (BCA) have been developed. This achievement has been the result of both internal (institutional Data Science team) and external collaborations (scientific collaboration with the University of Duisburg-Essen) led by Dr. Riccardo De Angelis:

i. Feasibility of using in-house automated BCA in a paediatric population

Project realised in collaboration with the radiology department of the HUDERF Children's Hospital which demonstrated the feasibility of automatically calculating the different compartments using an automated AI-based tool developed in-house. The results have been submitted for publication.

ii. BCA of patients with high-grade soft-tissue sarcoma of the extremities

Project realised as part of the external collaboration with the SHIP group of R. Hosch and Dr. Nensa. We performed the external validation of the "Body and Organs Analyser" (BOA), their newly-developed AI-based software for automated BCA prior to its public release. The results of this project have demonstrated the association between different adipose-related compartments (i.e., visceral and intramuscular adipose tissue), obtained from CT Thoracic images, with overall survival and progression-free survival in soft-tissue sarcoma patients (master thesis of M. Rombaut).

iii. Relationship between BCA and the mesopancreas

The radiological features of the mesopancreas calculated in subjects with no known pancreatic pathologic conditions were correlated with BCA: linear relationships were observed between the volume and density of the mesopancreas and body composition. (The manuscript has been submitted).

All these projects have been successfully selected for poster or oral presentations at internationally-recognised radiological conferences such as the European Congress of Radiology (ECR) 2024 and the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) 2024.

2. AI-based approaches to accelerate magnetic resonance sequences

A global trend is to accelerate and optimise magnetic resonance imaging (MRI) sequences through the use of AI approaches without any loss in terms of image quality and diagnostic certainty. The final aim is to increase accessibility to MR scanners, especially for cancer patients who need MR investigation for treatment decision purposes.

This axis of research mainly relies on a scientific collaboration with the MR scanner manufacturer Siemens, thanks to the Master Agreement for scientific collaboration. Testing and validation have been conducted of prototypes for several MR sequences in different settings. Three main projects have each focused on comparing deep-learning accelerated diffusion-weighted imaging (DWI) sequences with conventional DWI. These comparisons were made for liver and pancreas (master thesis of Dr. Menez), breast (master thesis of Dr. Petersbourg) and prostate DWI (master thesis of Dr. Venetis). These three studies have shown that the use of deep-learning accelerated DWI sequences reduced the acquisition time by 30 to 40% without compromising overall image quality or diagnostic accuracy. These results have been presented at ECR (European Congress of Radiology) and/or ESGAR. (European Society of Gastrointestinal and Abdominal Radiology) and are undergoing a peer-reviewed publication process.

Acceleration of MR sequences was also achieved thanks to an internal collaboration with the data science team (K. Brou Boni). In particular, the acceleration and denoising of breast DWI with a 70% reduction of acquisition time was achieved with no compromise in terms of image quality. These results have been submitted for oral presentation at the European Society of Breast Imaging (EUSOBI). Parallel projects for prostate DWI using the same approach are ongoing and aim to (i) accelerate and denoise prostate DWI and (ii) correct for geometric distortion of prostate DWI using morphological T2-weighted images.

3. AI-based tools for treatment response evaluation

This research line focuses on the comparison between conventional and AI-based approaches for the evaluation of tumour response. In this framework, Dr. Casale's PhD project, in collaboration with Dr Sclafani of the Medical Oncology Department will attempt to evaluate the prognostic and predictive value of AI-based quantitative imaging derived parameters in patients with locally advanced rectal cancer who are undergoing neo-adjuvant treatment.

Selected publications

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PRECISION MEDICAL ONCOLOGY

Team and infrastructure

Investigators at the CTCU are principal investigators for multi-institutional programmes that provide molecular screening for patients with metastatic breast cancer (AURORA: NCT02102165) and other solid tumours (GeNeo: NCT04641676) and target-oriented clinical trials.

Their work is supported by the Pathology Department's sequencing machines (Illumina and Thermofisher).

Aim

- To offer tools to H.U.B patients to identify genomic targets in their tumours and to actively participate in clinical trials of new drugs directed at these genomic alterations

Projects

- Expansion of GeNeo with the GeNeo 2 investigator-initiated trial that will allow comprehensive genomic profiling to be implemented locally.
- Leadership of the Belgian DRUP-like initiative in collaboration with Pharma.be, Sciensano and SPF Santé to provide molecular-guided targeted therapies for patients on an agnostic basis
- A further increase in the size of our NGS panels, with implementation of Comprehensive Genomic Profiling.
- Continuing discussions with government and industry stakeholders for a framework of access to molecular-guided therapeutic options

Recent achievements

- Initiated a portfolio of clinical trials covering a wide range of genomic alterations, including ERBB2-3, EGFR, HRD genes, RET fusions, PTEN mutations, PIK3CA mutations, NF1 mutations, FGFR1-3 fusions, CCNE amplification, and MET amplification, among others
- Expanded the size and number of available NGS panels in the Pathology Department in order to be able to identify all classes of genomic alterations (SNVs, indels, CNVs, and gene rearrangements)
- Launched the second phase of the Breast International Group's molecular screening programme (AURORA), focused on metastatic lobular cancers, triple-negative breast cancer, and late relapses (> 10 years)
- Co-created the Belgian Molecular Tumour Board to facilitate patient referrals across the whole of Belgium
- Initiated pharma-sponsored liquid biopsy trials for patients at high risk of relapse and for patients with metastatic disease and progression on standard therapies
- Co-authored the guidelines for molecular tumour boards together with the ESMO Precision Medicine WG

N. D'haene, Ph. Aftimos

Selected publications

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PRECISION RADIOTHERAPY

Team and infrastructure

The Radiotherapy Department, led by Ph. Martinive, and the Medical Physics Department, led by Nick Reynaert, work together to deliver cutting-edge cancer treatments. Our mission is to provide highly targeted, personalised radiation therapy using the latest innovations in the field.

Our facility features four state-of-the-art linear accelerators (Linacs), fully equipped with advanced technologies such as Image-Guided Radiotherapy (IGRT), Intensity-Modulated Radiotherapy (IMRT), Volumetric Modulated Arc Therapy (VMAT), and Surface Guidance for precise patient positioning. Two of these Linacs are enhanced with 6D tables, allowing sub-millimeter accuracy in treatment delivery. Complementing our equipment is the MRI-Linac, dedicated to online adaptive radiotherapy. This technology enables real-time adjustments to treatment plans to accommodate changes in tumour shape, size, or position during therapy sessions.

We collaborate closely with the Neurosurgery Department to offer high-precision radiosurgery with the Gamma Knife, providing advanced treatment options for patients with brain tumours. Additionally, we offer brachytherapy for prostate, gynaecologic, and skin cancers, and intra-operative radiotherapy (IORT) for small, localised breast cancers. IORT allows us to minimise the discomfort and toxicity associated with external beam radiotherapy, offering a more targeted approach.

Our dedicated team includes 11 radiation oncologists, supported by eight resident doctors in training, ensuring continuous professional development and innovation. The Medical Physics Department consists of 12 physicists and engineers, playing a crucial role in treatment planning and ensuring the highest levels of precision and safety. Our team of 30 highly skilled Radiation Therapists (RTTs) ensures accurate and efficient delivery of treatments, providing expert care to our patients every day.

Together, this multidisciplinary team and advanced infrastructure allow us to offer individualised, high-precision cancer treatments while maintaining a focus on patient comfort and outcomes.

Projects

- **Lung tumor: ProCaLung**

The ProCaLung project aims to improve treatment standardisation and quality for locally advanced non-small-cell lung cancer (NSCLC). This project is sponsored by the College of Radiotherapy and coordinated by Institut Jules Bordet. ProCalung provides a centralised peer review process for the radiation treatment of mediastinal node-positive, locally advanced NSCLC in Belgian radiation oncology departments.

ProCaLung is currently active in 19 out of 24 radiation oncology departments in Belgium, including both academic and non-academic settings and centres across the different

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regions. Of these 19 centres, 13 are actively including patients, amounting to a total of 100 patients currently submitted to the centralised peer review process. With 15 patients included, the Institut Jules Bordet is the forerunner among the participants.

The preliminary analysis of the 100 patients focuses on two major topics: the quality of diagnostic reports for establishing the radiotherapy treatment plan and the peer review process of radiation treatment plans. The first of these is intended to assess the quality of PET-CT, E(B)US and other diagnostic reports. These reports are used to evaluate whether the information received by the radiation oncologist (RO) is sufficient for radiotherapy treatment planning. We identified from this preliminary analysis that in up to 44% of cases, diagnostic reports are of varying quality, which can lead to issues in identifying the right targets (lymph nodes to irradiate). The second set of analyses focuses purely on the peer review aspect of the treatment plans. Looking at target definition (i.e., which nodes to irradiate?), only 71% of treatment plans complied with ProCaLung-guidelines. For target delineation (i.e., which volume (around/of) the lymph node should be treated?), the macroscopic volume (i.e., GTV) contours did not conform with guidelines in 40% of cases and the microscopic extensions (i.e., CTV) did not conform in 81% of patients. These observations highlight the continuing need for centralised peer review.

Supported by these preliminary results, ProCaLung-project is continuing over a longer period of time to allow for better standardisation of treatment planning in Belgian radiation oncology departments. We recently negotiated the extension of the project's run time with our partners so that we can continue including patients for at least another year, up to and including the summer of 2025.

- **Pancreatic cancer: STEREOPAC trial**

We developed and evaluated an innovative high-dose isotoxic stereotactic body radiotherapy technique, called iHD-SBRT, integrated into a total neoadjuvant treatment (TNT) sequence with FOLFIRINOX (FFX) chemotherapy for pancreatic cancer. In a preliminary prospective cohort of 39 patients with localised pancreatic adenocarcinoma, we confirmed for the first time the feasibility and safety of adding iHD-SBRT to this treatment sequence. We also

investigated the placement of intra-tumoral fiducial markers via endoscopic ultrasound, a necessary step for high-dose pancreatic SBRT, and introduced a new quality score to optimise their insertion for better iHD-SBRT delivery. Our results showed no significant difference in post-operative complications following pancreaticoduodenectomy between patients treated with TNT including iHD-SBRT and those treated with conventional chemoradiotherapy. Overall, this TNT-iHD-SBRT approach demonstrated promising oncological outcomes compared to a retrospective cohort treated with standard chemoradiotherapy. In parallel, the translational study on a 50 human PDAC samples treated with FFX alone or in combination with iHD-SBRT demonstrated that inclusion of ablative SBRT within a TNT strategy induces favourable stromal, metabolic and molecular remodelling, unlike FFX alone. This research led to the Belgian nationwide randomised phase II trial, STEREOPAC (NCT05083247), conducted by the Radiotherapy-Oncology Department (Christelle Bouchart), the Hepato-Biliary-Pancreatic Surgery Department (Julie Navez) and the Gastrointestinal Medical Oncology Department (Jean-Luc Van Laethem). The trial, which is currently recruiting in 17 Belgian centres, aims to confirm that TNT including iHD-SBRT improves both R0 resection rates and prognosis (DFS as a co-primary endpoint) for borderline resectable PDAC. Additionally, the ongoing ancillary studies, STEREOPAC-TRANS and FAPI-PANC, will further explore the translational results and refine patient selection for current pancreatic cancer treatments.

- **Metastatic prostate cancer: StereoBed trial**

Salvage radiotherapy is the standard treatment for biochemical recurrence (BCR) after radical prostatectomy. Up to now this involved numerous treatment sessions (20 to 35 fractions) with a significant time investment from patients (4 to 7 weeks). To reduce the treatment burden for patients, we will investigate a stereotactic treatment regimen in five sessions using modern high-precision RT with daily image guidance, which shows favourable results in single-arm phase II trials. StereoBed is a multi-centre, randomised seamless phase II/III study comparing SBRT with standard RT on the prostate bed. A total of 284 patients will be randomised in 13 Belgian centres. A preliminary study demonstrated dosimetric feasibility, and inclusion in the prospective trial is on track to begin in Q4 2024.

- **Precision radiotherapy for oligometastatic disease**

Stereotactic radiotherapy has emerged as an effective and well-tolerated local treatment for metastases in different organs. However, the impact of this on subsequent disease course in different forms of oligometastatic disease is still under study. We are participating in the EORTC-ESTRO project OligoCare, to collect real-world evidence for oligometastatic breast, prostate, colorectal and non-small cell lung cancer. For other oligometastatic tumours, we contribute to the OligoRare randomised trial. Finally, we have a special interest in oligoprogressive, estrogen receptor-positive breast cancer. Based on previously treated patients, we found that irradiating oligoprogressive metastases yielded an additional next-systemic treatment-free survival of 9.2 months (95%CI: 8.0-10.4 months). We aim to confirm this in the multicenter Oligopro-Breast trial, while testing circulating tumour DNA as a predictive marker to select the right patients for this approach.

Selected publications

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PRECISION SURGERY

Team

Surgery: Gabriel Liberale, Ali Bohlok, Antoine El Asmar, Charif Khaled, Sophie Vankerckhove, Vincent Donckier

Pathology: Denis Larsimont, Laurine Verset, Myriam Remmelink

Immuno-oncology: Leila Hosseinzadeh, Etienne Meylan

Infrastructure

- The team has access to translational research experts in the BCTL.

Aims

- The development of distant metastases represents the main cause of mortality in patients with solid tumours. Surgery could be curative in some patients with isolated or oligo-metastases. Currently, however, due to the lack of accurate clinical selection criteria, most of the patients undergoing surgery for metastatic disease recur postoperatively, including a significant proportion with rapid and diffuse relapses. There is therefore a major need to better adapt oncosurgical management to individual tumour profiles to reduce the risk of futile interventions.

Projects

- A focus on the tumour microenvironment or histopathological growth pattern (HGP) of metastases as a marker of tumour biology. Having established the reproducibility and prognostic value of distinct HGP in liver and peritoneal metastases, we are extending our research to include colorectal pulmonary metastases. We are currently investigating in greater detail the nature and extent of immunoinflammatory infiltrates in these different tumour microenvironments (using multiplex).
- Development of a model of colorectal liver metastases (LM) in mice, with the same objective: using two different colorectal cancer cell clones, we have established distinct models of desmoplastic and replacement-type LM. Under these conditions, we characterise the tumour microenvironment in these different patterns, with a particular focus on immune cells infiltrates. We are specifically studying the role of neutrophils using pre-implantation depletion protocols.
- Investigating how drug therapy and radiotherapy could modulate the microenvironment of LM and how these interventions could alter tumour progression.
- Validating and extending our initial data from patients undergoing operations for colorectal peritoneal metastases (PM): first, by collecting an extended series of samples from these patients from a large, multi-centre, international biobank. Second, by evaluating if similar patterns could be identified in peritoneal metastases of ovarian origin.

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- Evaluating the prognostic role of epigastric lymph node (ELN) in patients with PM
- Characterising peritoneal lesions of patients with PM using artificial intelligence to improve the quality of surgery and decrease postoperative morbidity/mortality.
- Prospectively evaluating the clinical use of the HGP of colorectal PM to select patients who are candidates for surgery.

Recent achievements

- In liver metastases of several cancer types (including colorectal, breast and melanoma), we observed that the tumour microenvironment as described by the HGP is a strong predictor of the benefit of surgery. We showed that postoperative outcomes are significantly better in patients with desmoplastic HGP (e.g., metastasis surrounded by a fibrous rim and presence of immune cells) than in those with replacement HGP (e.g. when cancer cells infiltrate the liver parenchyma, associated with no or minimal immune infiltrate). We recently identified a distinct HGP in colorectal pulmonary metastases and in PM, associated with a similar prognostic impact.
- In colorectal and ovarian PM, we described ELN as a new lymphatic pathway for systemic dissemination. Moreover, we reported the prognostic impact of these when they are involved.

Selected publications

- Bohlok A, Richard F, Lucidi V, El Asmar A, Demetter P, Craciun L, Larsimont D, Hendlisz A, Van Laethem JL, Dirix L, Desmedt C, Vermeulen P, Donckier V. Histopathological growth pattern of liver metastases as an independent marker of metastatic behavior in different primary cancers. **Front Oncol** 2023; 13:1260880.
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- El Asmar A, Vouche M, Pop F, Polastro L, Chintinne M, Veys I, Donckier V, Liberale G. Deep epigastric lymph nodes implication in patients' recurrence pattern after cytoreductive surgery in ovarian peritoneal metastases. **Eur J Surg Oncol** 2023; 49:106911.
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PRECISION NEUROONCOLOGY

Team

Surgery: Florence Lefranc, Olivier De Witte et al.

Radiology: Niloufar Sadeghi et al.

Isotopes: Gil Leurquin et al.

Oncology: Sylvie Luce and Nuria Kotecki

Neurology: Lorenzo Ferlini

Radiotherapy: Philippe Martinive and Christine Collen

Radiosurgery by Gamma Knife: Florence Lefranc, Philippe Martinive, Christine Collen et al.

Pathology: Laetitia Lebrun and Isabelle Salmon

Laboratory of Neuroanatomy and of Translational Neuroimagery (CRCN): Xavier De Tiège and Sara Goffinet

Harvey Cushing Center of psychologists: Annie Haquet and Lisa Delisse

Infrastructure

The H.U.B team has access to translational research experts with the CRCN and the Institut Bordet and thanks to the ANOCEF and EORTC collaborations.

Aims

- Brain tumours are most frequently malignant, comprising 50% gliomas (primary brain tumours) and 50% metastases.
- Our multidisciplinary group therefore aims to try to offer the best care in the context of primary and secondary brain tumours.

Projects

- Malignant gliomas remain a challenge because of their infiltrative characteristics, eloquent location and resistance to conventional treatment. This is the reason why we are initiating an international Phase III randomised trial ("Strateglio") together with the ANOCEF to evaluate early treatment intensification with temozolomide in adults with a glioblastoma. A total of 500 patients will be included. This study is supported by the Fonds Erasme.
- Some glioblastoma patients are long-term survivors. This is the reason why we are involved in the EORTC study named ETERNITY (see recent achievements).
- The commonest adult intracranial neoplasms are meningiomas. We recently presented the first meta-analysis and systematic review of the association between breast cancer and meningioma (ref 5). In collaboration with the ANOCEF we are starting an epidemiological study in Belgium and in France to collect clinical data from patients with meningiomas who perform a mammo test or have breast cancer. We are also collecting pathological data relating to these two diseases.
- We are actively involved in the BrainStorm study concerning brain metastases.

S. Schuind, O. De Witte, F. Lefranc

Recent achievements

- Proposed an improved imaging modality to perform the least aggressive but safe resection of gliomas.
- Reported several characteristics of long-term survivors treated for a malignant glioma.
- Showed that old molecules together with a targeted strategy could be of interest in late line treatment for malignant gliomas.
- Presented the first meta-analysis and systematic review of tfhe association between breast cancer and meningioma.

Selected publications

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- Seliger C, Oppong FB, Lefranc F, Chinot O, Stupp R, Nabors B, Gorlia T, Weller M; EORTC Brain Tumor Group.

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- Degeneffe A, De Maertelaer V, De Witte O, Lefranc F. The Association Between Meningioma and Breast Cancer: A Systematic Review and Meta-analysis. **JAMA Netw Open**. 2023 Jun 1;6(6):e2318620. doi: 0.1001/jamanetworkopen.2023.18620.PMID: 37326990; PMCID: PMC10276307
- Martins-Branco D, Nader-Marta G, Gombos A, Barthelemy P, Goncalves A, Borcoman E, Clatot F, Holbrechts S, De Maio D'Esposito E, Cheymol C, Vanhaudenarde V, Duhoux FP, Duhem C, Decoster L, Denys H, Lefranc F, Canon JL, Clement PM, Gligorov J, Paesmans M, Kindt N, Awada A, Kotecki N. BrainStorm: a multicenter international study to tackle CNS metastases in solid tumors. **Nat Med**. 2023 Dec;29(12):2981-2982. doi: 10.1038/s41591-023-02595-y. PMID: 37857713.

CREATING A LEARNING HEALTHCARE SYSTEM THROUGH THE USE OF ARTIFICIAL INTELLIGENCE AND BIG DATA ANALYSIS

"Artificial intelligence and big data are omnipresent in the current medical research landscape and are slowly but surely being introduced into clinical practice.

At IJB, a data science research team has been created in the Department of Medical Physics, which is fully dedicated to the development and clinical implementation of artificial intelligence and big data.

The ambition of the data science experts is to bridge the different disciplines within the Institute and to enable and perform modern data analysis, generating evidence with the aim of improving patient care."

A. DATA SCIENCE BOARD
B. IMPLEMENTING DATA FARMING TO ENABLE BIG DATA ANALYSIS
C. ARTIFICIAL INTELLIGENCE APPLICATIONS TO OPTIMISE CLINICAL WORKFLOW
D. APPLIED IMAGE AND DATA ANALYSIS TO PERSONALISE TREATMENT AND IMPROVE PATIENT OUTCOMES

Team and infrastructure

The Data Science & AI Research Unit includes two data science experts, four PhD students and one research coordinator, headed by Nick Reynaert. The team's infrastructure consists of both CPU-based and GPU-based computational units to perform big data analysis and deep learning experiments.

A. DATA SCIENCE BOARD

Aims

- To support current and future artificial intelligence and data science projects throughout H.U.B in the field of cancer, to standardise workflows and to ensure high-quality research.

Main projects

- CPC Artificial Intelligence

The CPC Artificial Intelligence will play a crucial role in ensuring the responsible and ethical use of AI technologies within H.U.B, while also maintaining high standards for research involving AI. The committee will evaluate proposals for AI projects to ensure that they comply with ethical standards and regulations and with the hospital's quality standards and research objectives, assessing the purpose, methodology, and potential impact on patients and staff. The committee will also be involved in educating all healthcare and research staff about the ethical use of AI, promoting awareness and understanding of its implications. In this way, the committee will support current and future AI and data science projects throughout H.U.B, standardising the workflow, and ensuring high-quality research.

J. Dhont

B. IMPLEMENTING DATA FARMING TO ENABLE BIG DATA ANALYSIS

Aims

- To collect real-world, high-quality data for the development of prediction models based on applied treatment parameters, recorded toxicities, and patient outcomes, and to apply these models in clinical decision support systems for personalised treatment.

Main projects

- Lu177-PSMA registry

The Lu117-PSMA registry collects real-world data obtained along the clinical pathway of metastatic chemo-resistant prostate cancer patients receiving 177Lu-PSMA radioligand therapy. The main purpose of the registry is to support the identification of predictive biomarkers for patient stratification and for treatment optimisation. The registry was constructed by a multidisciplinary team with expertise in nuclear medicine, medical physics and data

science, and contains 240 clinically relevant data elements standardised to a common nomenclature and data model. So far, the registry has obtained a 100% patient participation rate, resulting in the inclusion of 183 patients in 12 months, indicating strong patient engagement and support for the project. The registry is currently being extended to include several Belgian centres.

- IJB Breast Cancer Research Database

The IJB Breast Cancer Research Database will consist of a structured, multimodal real-world database including clinical, treatment and follow-up data, imaging metadata and digital pathology for all breast cancer patients newly diagnosed and treated at IJB from 2008 to 2018, which will then be progressively extended. This database will be used for all developments in ARTEMIS (see later in section D), but will also be made available for any current and future research projects focusing on breast cancer to accelerate breakthroughs. The database will be constructed by the Data Science & AI Research Unit, supported by the Information Management Unit (UGI) and different units (Infrastructure and Data Warehouse) within the Department of Information Technology (IT). IJB's Data Protection Officer will be involved to ensure strict adherence to all personal data privacy regulations. An initial estimate of the number of patients who will be included in the first phase of the database is 1400.

C. ARTIFICIAL INTELLIGENCE APPLICATIONS TO OPTIMISE THE CLINICAL WORKFLOW AND SUPPORT CLINICAL TRIAL DATA ANALYSIS

Aims

- To automate (parts of) the clinical workflow in the Radiotherapy and Nuclear Medicine Department by safely implementing both commercial artificial intelligence applications and those developed in-house. Artificial intelligence tools will also be developed to interpret clinical trial data and improve research efficiency and quality.

Main projects

- AI-based Fast Dose Calculation and Delivery Reconstruction, an Elekta research agreement concerning the MR-Linac Unit Monte Carlo (MC) dose calculation is the gold standard in terms of precision, but it is too slow to be used routinely in clinical practice. This study aims to develop a deep learning dose calculation that mimics MC accuracy in a matter of seconds. We may link the results to MC to calculate the dose in a fraction of the current time and speed up the segment shape and the weight optimisation process. In addition, Elekta Linacs currently log delivery data at a frequency of 40ms. We will use these data to estimate the dose received by the patient. This will be combined with online MR imaging. By synchronising online imaging and the estimated dose delivered, one can assess the accumulated treatment dose and treatment course.
- MR-only radiotherapy planning with synthetic CT While MR provides excellent soft-tissue imaging, CT is still essential for providing electron density information for dose planning, which MR images cannot deliver. Establishing an MRI-only workflow in radiotherapy depends on the ability to convert MRI intensities to obtain attenuation properties. Many different methods have been proposed in the literature to solve this problem, often referred to as synthetic CT generation. With the emergence of deep learning, these methods have recently undergone significant changes. Accuracy and generation speed have dramatically increased. Generative Adversarial Networks (GAN) have provided a new impetus, with their ability to learn to generate any data distribution. Our goal is to improve the generalisability of MRI-to-CT synthesis using GAN. This process is capable of dealing with the image variability problem in clinical practice, where changes occur in image acquisition parameters or, for instance, following machine replacement.
- AI for radiotherapy target optimisation in early-stage breast cancer We aim to optimise clinical target volume delineation for post-operative elective radiotherapy in early-stage breast cancer through an evidence-based and personalised approach. Our optimisation will focus on both the selection of lymph node levels to be included in the target volume, and their respective geometric definitions in comparison to the current European guidelines. An AI-based tool for automatic lymph node level delineation will be developed in collaboration with the European Institute of Oncology in Milan, using federated learning. We anticipate that this tool will not only support the clinical treatment workflow, but also accelerate our research on lymphatic progression patterns and target volume optimisation. More specifically, we will apply the auto-delineation tool to the PET-CT images of a large cohort of breast cancer patients with PET-positive locoregional lymph node lesions for two purposes: (1) to map the geometrical distribution of positive lymph nodes with respect to the current delineation guidelines, to validate coverage per level with respect to patient-specific clinicopathological factors, and (2) to collect spatial lymphatic progression patterns in order to build a probabilistic model that can quantify the risk of microscopic involvement in each level, given patient-specific clinicopathological factors.
- Automatic biomarker quantification in digital pathology This project involves development of a toolbox to perform automatic analysis of digital pathology datasets using artificial intelligence. The toolbox will include algorithms for automatic image segmentation, detection and biomarker quantification, increasing analysis efficiency and eliminating inter-observer variability. A first pilot project includes the analysis of the multi-timepoint immunohistochemistry data collected in the Neo-CheckRay trial. The long-term aim is to make the toolbox applicable across cancer types as well as for different staining methods.

Selected publications

- Hurkmans C, Bibault JE, Clementel E, Dhont J, van Elmpt W, Kantidakis G, Andratschke N. Assessment of bias in scoring of AI-based radiotherapy segmentation and planning studies using modified TRIPOD and PROBAST guidelines as an example. **Radiother Oncol.** 2024 May;194:110196. doi: 10.1016/j.radonc.2024.110196. Epub 2024 Mar 2.
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D. APPLIED IMAGE AND DATA ANALYSIS TO PERSONALISE TREATMENT AND IMPROVE PATIENT OUTCOMES

Aims

- To personalise the treatment of patients across different departments through the analysis of multi-modality data collected in the context of clinical trials and enriched with real-world data

Achievements

- 18F-FDG PET/CT-based imaging score for clinical decision support in advanced chemorefractory metastatic colorectal cancer
- In collaboration with Alain Hendlisz and Erwin Woff, a prediction model for patient outcome was developed to stratify patients, using data collected through the clinical trials REGARD, SoMore and Coriolan. The model was validated using real-world data.

Main projects

- ARTEMIS: Artificial intelligence for tailoring in early breast cancer – individual systemic therapy

ARTEMIS, in strong collaboration with the Breast cancer Translational Research Laboratory JC Heuson and several departments of Institut Jules Bordet, aims to facilitate safe systemic neo-/adjuvant treatment de-escalation in the three major breast cancer subtypes through the integration of artificial intelligence (AI) and digital pathology. The main objective is to develop an intelligent clinical decision support system, utilising deep reinforcement learning and self-supervised AI methods on digital pathology data for patient-specific neo-/adjuvant treatment recommendations. The system aims to predict pathological complete response and risk of recurrence, benchmarked against existing methods, and to use explainability methods to increase trust on the part of clinical end-users. The second objective focuses on uncovering novel biomarkers for early breast cancer through an array of explainable AI methods employed on the models developed under the main objective, to enhance understanding of disease heterogeneity and mechanisms. The strength of ARTEMIS lies in its multidisciplinary collaboration and a substantial repository of high-quality patient data, exceeding 6000 individuals, collected from randomised clinical trials, routine clinical practice, and cancer registries.

- Prediction of prostate cancer risk using machine learning

This project involves development of a machine learning model to predict individual prostate cancer risk from clinical data and the MRI radiology report. This risk prediction is intended to reduce the number of futile prostate biopsies in low risk individuals. The project, in collaboration with Dr. Romain Diamand from the Department of Urology, uses an international database of over 4000 individuals.

Chapter III • Fostering Innovation in Cancer Management

Providing cutting-edge treatment options has always been in the DNA of IJB. Many of these innovative therapeutics are delivered within the Clinical Trials Conduct Unit (CTCU) in collaboration with industry for pharma-sponsored clinical trials, academic collaborative groups for academic trials, and the Academic Trials Promoting Team (ATPT)/Clinical Trials Centre (CTC) for H.U.B-sponsored academic trials. The scope of activity of the CTCU encompasses medical oncology (breast, gastrointestinal, genito-urinary, gynaecological, sarcomas, and rare tumours), radiation oncology, and haematology. Members of the CTCU are study coordinators (early phase and later-phase clinical trials), data managers (including an imaging officer), a tissue officer, an administrative team, a start-up coordinator, an operational head, and a quality manager drafting the standard operating procedures while working to get the unit accredited by 2026. The CTCU team is managing the Novel Treatment Unit (NTU) in concert with the Nursing Department. The NTU is an inpatient unit of 12 beds, where patients are hospitalised for first-in-human therapies, studies requiring multiple PK blood draws, or procedures requiring overnight stays. Biosafety level 2 accreditation allows studies to be conducted with viral agents and cellular therapies.

A protocol review committee (PRC) is responsible for selecting the protocols to be implemented within H.U.B according to three criteria: innovation, unmet need, and feasibility. The principal investigators are selected on the basis of expertise. Recruitment of patients is intra-institutional and inter-institutional via a network of referring physicians. The creation of the "national" molecular tumour board (MTB) has facilitated the accumulation of patients with rare genomic alterations across Belgium and has increased the visibility of H.U.B in the field of precision medicine.

H.U.B has recently acquired an MR-Linac, thanks to support from "Association Jules Bordet": this modern machine increases the precision needed for radiotherapy delivery using a daily MRI-based, online adaptive procedure, and it will be prioritised as a means of exploring new radiotherapeutic approaches to cancer management.

H.U.B also features a modern radiotheranostic center with a fully 6MP-compliant clinical radiopharmaceutical production unit. It will produce and test new radiotheranostics within well-designed clinical trials in close collaboration with medical oncologists and has the ambition to become a "radiotheranostic centre of excellence"

H.U.B has also invested in a vast GMP Unit (UTCH) in its new building in order to take up the challenge of new cellular and gene immunotherapies. After a pause in the early 2000s linked to diagnoses of secondary leukemia in treated children, the optimisation of vectors and genetic manipulation techniques have facilitated a new clinical boom in the field of gene therapies. Chimeric Antigen Receptor (CAR) T-cell therapy is undoubtedly driving a revolution in cancer treatment. The recent successes of CAR T-cell therapy in the fight against haematological malignancies have led to a considerable increase in interest in the field of cellular immunotherapy.

INNOVATIVE CANCER THERAPIES PRIORITISED AT H.U.B

TEAMS AND INFRASTRUCTURES

- The CTCU and CTC clinical research units play a pivotal role in the implementation, conduct and analysis of the innovative clinical trials run at IJB/H.U.B. Some of these trials are initiated within the BIG or OncoDistinc networks, and a number of them are centrally managed by the CTC.
- The Academic Promoting Team gives advice and support to young investigators interested in designing innovative academic trials for which H.U.B will be the sponsor.
- The cell therapy platform is an entity meeting GMP standards for the collection, processing (including the selection, expansion, and freezing of cells), control, storage, and delivery of several types of cells, including haematopoietic stem cells, mesenchymal cells, lymphocytes, and dendritic cells. The new Cellular Therapy Unit built in H.U.B/IJB is equipped with four independent clean rooms, five laminar flows, four incubators, two temperature-controlled freezing devices, four -80°C freezers, and 35 nitrogen tanks containing human body material. It includes three banks accredited by the FAMHP (Federal Agency for Medicines and Health Products):
    - The haematopoietic stem cell bank
    - The cell bank for therapeutic purposes
    - The ULB umbilical cord blood bank
- As explained above, H.U.B now hosts a modern radiotheranostic center with a GMP radiopharmacy laboratory.

MAIN PROJECTS

Besides precision oncology (see Chapter 2), four axes of development are currently being prioritised:

- Cell therapies
- Immunotherapy beyond PD-1 / PDL1 immune checkpoint blockers
- Theranostics
- MR-Linac for individualised radiotherapy

- **CELL THERAPIES**
- **IMMUNOTHERAPY BEYOND PD-1/PDL1 IMMUNE CHECKPOINT BLOCKERS**
- **RADIOTHERANOSTICS**
- **MRI-GUIDED ADAPTIVE RADIOTHERAPY AND FLASH RADIOTHERAPY**
- **CONTRIBUTING TO ACADEMIC-LED RESEARCH WITHIN THE BIG AND ONCO-DISTINCT NETWORKS**

CELL THERAPIES

Team

CTU: one medical director, one lab director, one Quality Manager, one administrative assistant, five technicians.

Apheresis Unit: one medical director, one Quality Manager, one administrative assistant, four nurses.

Aims

- As part of its strategic development plan as an O.E.C.I. (Organisation of European Cancer Institutes) accredited comprehensive cancer center, H.U.B has decided to make cell therapy a priority.
- Initially, Cell therapy Units (CTUs) distribute only cell therapy preparations (CTP) that are not medicinal products but are covered by tissue/cell regulations, such as haematopoietic stem cells (HSC) for transplantation. However, many CTUs and tissue banks, such as the one at H.U.B, are now engaged in processes to improve their professional practices and participate in biomedical research protocols aiming to evaluate the clinical interest of therapeutic products derived from cell or tissue engineering, formerly classified as CTP and now considered as ATMPs. Nowadays, It is of major importance to develop expertise and obtain the necessary accreditations to perform immune and gene cellular therapies since several Belgian academic laboratories are working on the optimisation of new CAR-T cells and on CAR-T cells against new antigens. It is critical for the H.U.B to be able to collaborate in this academic network.
- Since July 2022 H.U.B is recognised as Belgian accredited center for cell therapies reimbursed by the National Institute for Health and Disability Insurance (NIHDI, known as INAMI in French). Currently two pharmaceutical companies have obtained NIHDI reimbursement from the Belgian authorities for their cellular products (Novartis and Gilead). Gilead selected and certified H.U.B for the use of their car-T cells. We were also selected by Vertex Crispr therapeutic as one of the two Belgian centers for gene therapy in haemoglobinopathies.
- Attractiveness to pharmaceutical and biotechnology firms is based on the ability to demonstrate our skills and expertise during center selection audits. The interlocutors at all levels (medical, paramedical, nursing) must therefore be trained, credible, and competent and must demonstrate that we have an integrated strategy with close collaboration between apheresis, the bank and the clinic which results in a unique, clear and standardised care pathway that is convincing for our sponsors.

Projects

- Our belief in the scientific, medical and financial value of the "point of care" approach is strongly anchored. A recent meeting with the "Federal Center of Expertise" KCE has strengthened our resolution even more, since the members of the KCE are convinced that the academic development of ATMPs must be financially supported and encouraged by the public authorities. They are preparing a recommendation for the authorities, meeting academic stakeholders in the field and comparing with what is already done in other European countries. It is indeed absolutely necessary for academic institutions to adopt an innovative and entrepreneurial stance if we want to be able to offer optimal treatment to as many patients as possible. The development of on-site academic production of CAR-T cells could bypass some of the disadvantages of the pharmaceutical companies' centralised model. Authorised on-site production platforms will allow shorter administration times at a reasonable production cost for national health systems and will maintain pressure on the extreme costs demanded by "Big Pharma". It is also important that academic centers take an interest in pathologies and situations that are not financially attractive to large pharmaceutical groups. These developments, however, must be carefully designed so as not to compromise the safety and efficacy of the products, as well as ensuring faster access for the patient. Despite the challenges to deliver high quality products, there are definite advantages of academic cell therapy GMP facilities over industrial ones:
    1. Close proximity between starting material procurement facility and treatment site, resulting in a shorter "vein to vein" time.
    2. Lower cost of manufacturing due to savings on workforce, shipments and cold chain logistics, utilisation of hospital resources and services.
    3. Utilisation of hospital internal laboratories for in-process and product release testing (i.e. microbiology, haematology, flow cytometry).
    4. Higher likelihood of obtaining transparency concerning the real cost of these treatments.

L. Lewalle

We have started a collaboration with Miltenyi biotech, and hope to develop the "point of care" production of Car-T cells using their CliniMACS Prodigy equipment.

Recent achievements

✓ Cell therapy protocol at Institut Jules Bordet-H.U.B

Company	Protocol	Strategy	Subject	Patient n°/ Cell Units	Start -End
Johnson & Johnson (Janssens)	Cartitude	CAR-T cell against the BCMA antigen	Myeloma		June 2024 (under initiation)
BioNtech	BNT211-02	CAR-T anti CLDN6 & CLDN6 RNA-LPX	Male adult patients with relapsed or refractory CLDN6-positive testicular or extragonadal germ cell tumours after prior salvage therapy	-	September 2024 (under initiation)
Miltenyi Biomedecine	DALY-2-EU	CAR-T anti-CD19 + anti-CD20 Tandem	Diffuse Large B cell Lymphoma Recurrent or refractory	2	2023 →
T-Knife	TK-8001-01	TCR-T anti MAGE-A1	Solid Tumours MAGE-A1 (Melanoma etc.)	(one pat planned)	2022 →
BMS	KarMMa-9	CAR-T anti-BCMA, Idecabtagene Vicleucel with Lenalidomide maintenance versus Lenalidomide maintenance therapy	Multiple Myeloma who Have Suboptimal Response After Autologous Stem Cell Transplantation	(one pat planned)	2023 →
Quell Therapeutics	QEL-001	Autologous CAR-Treg anti-HLA.A2 in HLA-A2/ A28neg patients that have received an HLA-A2pos liver transplant	hepatic transplantation	-	2022 →

Selected publications

- Sallman DA, Kerre T, Havelange V, Poiré X, Lewalle P, Wang ES, Brayer JB, Davila ML, Moors I, Machiels JP, Awada A, Alcantar-Orozco EM, Borissova R, Braun N, Dheur MS, Gilham DE, Lonez C, Lehmann FF, Flament A. CYAD-01, an autologous NKG2D-based CAR T-cell therapy, in relapsed or refractory acute myeloid leukaemia and myelodysplastic syndromes or multiple myeloma (THINK): haematological cohorts of the dose escalation segment of a phase 1 trial. **Lancet Haematol**. 2023 Mar;10(3):e191-e202. doi: 10.1016/S2352-3026(22)00378-7. Epub 2023 Feb 7.PMID: 36764323
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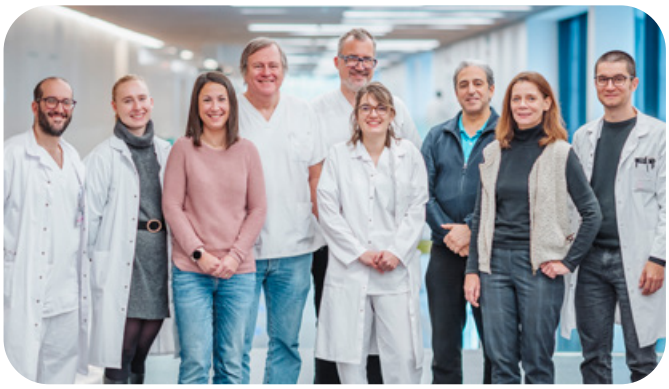


IMMUNOTHERAPY BEYOND PD-1/PD-L1 IMMUNE CHECKPOINT BLOCKERS

Aims

- To develop combinations of immunotherapeutic strategies to enhance the anti-tumour immune response using new immunomodulatory drugs alone or with other treatment modalities such as immunogenic radiation therapy in order to counteract resistance to immune checkpoint inhibitors and expand the proportion of patients who will ultimately benefit from these novel treatment combinations.

Projects

- Based on the very interesting observation in the Neo-CheckRay trial (sponsored by IJB) of a significantly enhanced response at surgery for patients with PDL1 negative tumours with the combination of 3x8 Gy stereotactic RT and immunotherapy (details: see below), the team is currently working on the design of a phase III trial that would confirm the efficacy of this innovative combination strategy.

Achievements

- NEO-CHECKRAY is an academic neoadjuvant randomised trial sponsored by IJB that aims to transform the immune cold luminal B breast cancer, characterised by a high risk of late relapses, into a disease that is more responsive to immunotherapy. To achieve this, immunogenic radiation therapy to the primary tumour (3x8 Gy using an SBRT technique) and an anti-CD73 (oleclumab) to decrease the production of immunosuppressive adenosine are combined with chemotherapy and durvalumab. In NEO-CHECKRAY, patients were randomised to one of three arms: 1) chemotherapy with 3x8 Gy radiation therapy (RT) to the primary tumour; 2) chemotherapy + RT + durvalumab or 3) the latter regimen with the addition of oleclumab. The feasibility and safety of the third arm had been previously demonstrated in a safety run-in including six patients and these results were published in the Journal of Immunotherapy for Cancer in 2023. In the phase II randomised trial, 145 patients were randomised and 135 were evaluable for the primary endpoint. The primary and secondary endpoints were presented at ESMO in 2024: RCB (residual cancer burden) 0/1 and pCR (pathological complete response) rates were increased in both immunotherapy arms. Interestingly, the pCR gain was far more pronounced in the PD-L1 negative subgroup: an absolute increase of 29.5%-30.8% in pCR rate was seen. This result suggests that the approach of combining immunogenic 3x8 Gy radiation therapy may be most effective in PD-L1 negative breast cancer.
- The SYNERGY trial, which tested the addition of oleclumab (anti-CD73) to carboplatin-paclitaxel and durvalumab as first line therapy for metastatic TNBC, was stopped early by the IDMC after randomisation of 127 patients based on identical clinical benefit rates of 42% that crossed the futility boundary. This randomised trial was initiated and sponsored by IJB following the translational discovery of the poor prognosis associated with the overexpression of CD73 in this disease. CD73 is responsible for the generation of immunosuppressive adenosine in the tumour microenvironment. The clinical results of the SYNERGY were published in 2023. In-depth analyses of tumour and blood biosamples, including single cell RNAseq, are ongoing. Of note, samples from the SYNERGY trial have been included in the IMMUcan Consortium making it possible to generate molecular (RNAseq, WES) and cellular profiling (IF, IMC) data of the tumour and its microenvironment (https://immucan.eu). The goal is to better understand the mechanisms associated with response and resistance and to identify predictive biomarkers and novel treatment strategies.
- Several grants have been secured for the translational research projects associated with the two clinical trials.

L. Buisseret, A. De Caluwé

Selected publications

- Buisseret, L., Loirat, D., Aftimos, P., Maurer, C., Punie, K., Debien, V., Kristanto, P., Eiger, D., Goncalves, A., Ghiringhelli, F., Taylor, D., Clatot, F., van den Mooter, T., Ferrero, J. M., Bonnefoi, H., Canon, J. L., Duhoux, F. P., Mansi, L., Poncin, R., ... Piccart-Gebhart, M. Paclitaxel plus carboplatin and durvalumab with or without oleclumab for women with previously untreated locally advanced or metastatic triple-negative breast cancer: the randomized SYNERGY phase I/II trial. **Nature Communications**, (2023). 14(1). https://doi.org/10.1038/s41467-023-42744-y
- De Caluwe, A., Romano, E., Poortmans, P., Gombos, A., Agostinetto, E., Marta, G. N., Denis, Z., Drisis, S., Vandekerkhove, C., Desmet, A., Philippson, C., Craciun, L., Veys, I., Larsimont, D., Paesmans, M., van Gestel, D., Salgado, R., Sotiriou, C., Piccart-Gebhart, M., Buisseret, L. First-in-human study of SBRT and adenosine pathway blockade to potentiate the benefit

of immunochemotherapy in early-stage luminal B breast cancer: results of the safety run-in phase of the Neo-CheckRay trial. **Journal for ImmunoTherapy of Cancer**, (2023). 11(12), e007279. https://doi.org

- Alex De Caluwe, Isabelle Desmoulins, Kim Cao, Vincent Remouchamps, Adinda Baten, Eleonore Longton, Karine Peignaux, Guilherme Nader Marta, Luca Arecco, Elisa Agostinetto, Paulus Kristanto, Xavier Catteau, Denis Larsimont, Roberto Salgado, Philip Poortmans, Christos Sotiriou, Martine Piccart, Michail Ignatiadis, Emanuela Romano, Laurence Buisseret. LBA10 Primary endpoint results of the Neo-CheckRay phase II trial evaluating stereotactic body radiation therapy (SBRT) +/- durvalumab (durva) +/- oleclumab (ole) combined with neo-adjuvant chemotherapy (NACT) for early-stage, high risk ER+/HER2- breast cancer (BC). **Annals of Oncology**, Volume 35, S1205

RADIOTHERANOSTICS

"We have everything on hand that is needed to support, promote and implement radiotheranostic research at the highest level."

Team and infrastructure

The multidisciplinary team (composed of nuclear medicine specialists, medical physicists, biologists, pharmacists and technologists) has expanded since 2020, with the arrival of new recruits, including a full time radiopharmacist for the fully GMP-Compliant clinical radiopharmaceuticals production unit.

The move to the new facility prompted the inauguration of the first radiotheranostic centre of excellence in Belgium. This opens the door to new collaborations with academia and industry.

G. Gebhart, Z. Wimana, P. Flamen, W. Delbart, I. Karfis, C. Artigas, H. Levillain

Aims

- To generate innovative radiotheranostics for bench-to-bedside use
- To offer a fully integrated solution to produce and test radiotheranostics in phase 1-2 studies for third parties
- To understand radiobiological dynamics
- To identify biomarkers of radioresistance

Projects

Preclinical & translational

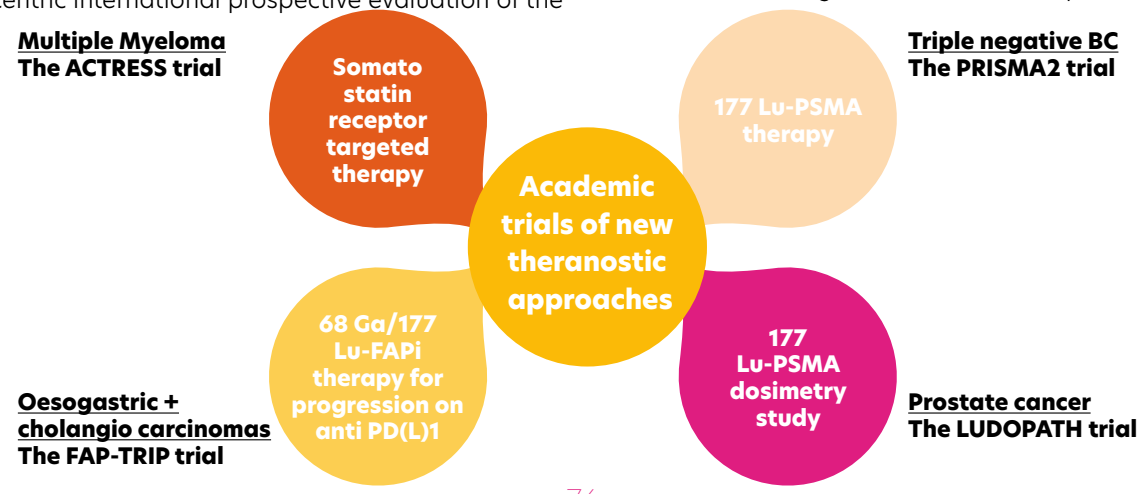
- Preclinical development and evaluation of innovative radiopharmaceuticals targeting the tumour microenvironment for clinical translation
- Identification of highly expressed molecules on tumour samples from advanced metastatic ovarian cancer patients as candidate targets for radionuclide therapy (in collaboration with the study center for nuclear energy (SCK CEN)

Imaging

- Prognostic added value of FDG-PET in patients treated with Lu-PSMA.
- Multicentric international prospective evaluation of the prognostic value of dual imaging (FDG & DOTATATE) in patients with neuroendocrine tumours (sponsored by Australia).
- Establishing criteria for the use of DOTA-SSTR PET imaging in the assessment of treatment response in collaboration with KUL.
- Establishing semi-automatic segmentation methods in DOTA-SSTR PET imaging.
- ^{68}Ga-FAPI imaging studies (as preliminary step prior to 177Lu-FAPI treatment) for
  - ✓ Gliobastoma
  - ✓ Liver metastasis from colorectal cancer

Theranostics

- Launching academic clinical trials of new theranostic approaches
- The below figure summarises four academic trials ready to be launched that will explore theranostic strategies for six tumour types: multiple myeloma, triple-negative breast cancer, oesophagogastric as well as cholangiocarcinomas and prostate cancer.



Of note, the last trial (^{177}Lu PSMA radioligand therapy) will explore lutetium-177 dosimetry as a predictive biomarker of response in metastatic prostate cancer patients treated with the already established PSMA radioligand therapy.

Recent achievements

Preclinical & translational

- Set-up of a preclinical and translational laboratory dedicated to the investigation of radiotheranostics in oncology (laboratory for Advancing Theranostics in Nuclear Oncology – ATheNO)

Imaging

- The value of PSMA PET/CT in the European Association of Urology Biochemical Prostate Cancer relapse classification.
- Completion of the Prisma 1 trial, a descriptive, prospective, single-centre pilot imaging study that assessed PSMA expression via PET/CT imaging in metastatic lesions of TNBC patients pre-identified on 18F-FDG PET/CT in order to evaluate the feasibility of molecular radionuclide therapy in refractory and relapsing TNBC using the radiolabelled targeting peptide in preparation for the future Prisma 2 therapeutic trial.
- Completion of the SCARLET trial (NCT04379817), demonstrating the value of somatostatin receptor (SSTR) imaging as a PET companion diagnostic tool to select multiple myeloma patients for radionuclide therapy (manuscript in preparation)

Theranostic

- Partial qualification of the GMP radiopharmacy lab (full qualification expected in early 2025)

Two EU grants were recently approved, thanks to the hard work of Hugo Levillain.

They are supported by the Innovative Health Initiative Joint Undertaking (IHI JU) under grant agreements No [101173001] and [101172788] respectively. The JU receives support from the European Union's Horizon Europe research and innovation program and COCIR.

1. "Accelerate.EU", co-coordinated by the Institute Jules Bordet and IBA, is a European initiative focused on transforming theranostics through targeted alpha-therapies with astatine-211. The consortium integrates diagnostics with the enhanced cytotoxic effects of alpha particles to provide precise tumour radiation while minimising side effects. Key objectives include developing theranostic solutions for challenging cancers such as triple-negative breast cancer, glioblastoma, and pancreatic cancer, and establishing a sustainable EU manufacturing infrastructure for astatine-211. The co-clinical approach, incorporating concurrent clinical and preclinical studies, adds a breakthrough dimension to theranostics. In its coordinating role, the Institute Jules Bordet's nuclear medicine and medical physics department will also support preclinical studies and the phase-1 clinical trial in triple-negative breast cancer, including efforts on dosimetry and the co-clinical approach.

2. "Thera4Care", co-coordinated by Università Cattolica del Sacro Cuore and GE Healthcare, is a European consortium aimed at advancing radiotheranostic tools for precision health. It will standardise the production and delivery of radiotheranostics, particularly those based on Terbium-161, and develop diagnostic and therapeutic ligands for diseases such as ovarian cancer, sarcoma, and glioblastoma. The Institute Jules Bordet's nuclear medicine and medical physics departments, as key beneficiaries, will contribute to preclinical studies, AI, and dosimetry developments.

Co-funded by the European Union

innovative health initiative

Selected publications

- Mileva M, Marin G, Levillain H, Artigas C, Van Bogaert C, Marin C, Danieli R, Deleporte A, Picchia S, Stathopoulos K, Jungels C, Vanderlinden B, Paesmans M, Ameye L, Critchi G, Taraji-Schiltz L, Velghe C, Wimana Z, Bali M, Hendlisz A, Flamen P, Karfis I. Prediction of 177Lu-DOTATATE PRRT Outcome Using Multimodality Imaging in Patients with Gastroenteropancreatic Neuroendocrine Tumors: Results from a Prospective Phase II LUMEN Study. J Nucl Med. 2024 Feb 1;65(2):236-244.
- Chan DL, Hayes AR, Karfis I, Conner A, Mileva M, Bernard E, Schembri G, Navalkissoor S, Gnanasegaran G, Pavlakis N, Marin C, Vanderlinden B, Flamen P, Roach P, Caplin ME, Toumpanakis C, Bailey DL. [18F]FDG PET/CT-Avid Discordant Volume as a Biomarker in Patients with Gastroenteropancreatic Neuroendocrine Neoplasms: A Multicenter Study. J Nucl Med. 2024 Feb 1;65(2):185-191.
- Chan DL, Hayes AR, Karfis I, Conner A, Furtado O'Mahony L, Mileva M, Bernard E, Roach P, Marin G, Pavlakis N, Schembri G, Gnanasegaran G, Marin C, Vanderlinden B, Navalkissoor S, Caplin ME, Flamen P, Toumpanakis C, Bailey DL.Dual [68Ga]DOTATATE and [18F]FDG PET/CT in patients with metastatic gastroenteropancreatic neuroendocrine neoplasms: a multicentre validation of the NETPET score. Br J Cancer. 2023 Feb;128(4):549-555.
- Delbart W, Karabet J, Marin G, Penninckx S, Derrien J, Ghanem GE, Flamen P, Wimana Z. Understanding the Radiobiological Mechanisms Induced by 177Lu-DOTATATE in Comparison to External Beam Radiation Therapy. Int J Mol Sci. 2022 Oct 15;23(20):12369. doi: 10.3390/ijms232012369.

MRI-GUIDED ADAPTIVE RADIOTHERAPY AND FLASH RADIOTHERAPY

Aims

- To develop and test novel radiotherapy approaches in order to further increase the therapeutic ratio in clinical radiation oncology. To this end, complementary strategies are explored, from the determination of biomarkers for the personalisation of radiotherapy to utilising MRI guidance to maximise precision and adapt to the temporal changes of the target tissue and the development of FLASH radiotherapy, a novel delivery modality.
- Magnetic Resonance Imaging (MRI) offers superior tissue contrast, and functional MRI adds a biological dimension to this. Integration of MRI in radiotherapy treatment is possible with the Unity MR-linac, a novel treatment machine that associates a high-precision linac with MR imaging of diagnostic quality. We aim to develop the implementation of MRI throughout the radiotherapy pathway: MRI-based planning instead of CT simulation; online daily adaptation to anatomical variations during treatment; and tailoring treatment to individual tumour characteristics based on MRI biomarkers.
- FLASH radiotherapy (RT) is an emerging technology that involves the ultra-fast delivery of ionising radiation at dose-rates several thousand times higher than the ones currently used in routine clinical practice. While a similar tumour cell killing efficacy was reported in both conventional and FLASH-RT, in vivo studies have shown that the latter limits radiation-induced damage in healthy tissues. This reduction of normal tissue toxicity enables FLASH-RT to overcome one of the main limitations of modern RT. It has the potential to revolutionise radiation oncology by becoming a standard in future clinical practice. Although the FLASH effect has been reported in a wide variety of animal models, unknown factors limit the rapid translation of this technology to clinical practice. We aim to determine the optimal biological and physical parameters needed to induce the FLASH effect using preclinical models, and to bring FLASH to clinical practice within a prospective trial.
- In the context of innovative radiotherapy, we also refer to the chapters "Immunotherapy beyond PD-1/PD-L1 immune checkpoint blockers" and "Precision Radiotherapy".

Projects

Multiple projects in MRI-guided radiotherapy are ongoing:

- The MINORA project comprises the implementation and validation of MRI as the cornerstone of radiotherapy simulation and planning. Synthetic CTs generated by dedicated MRI sequences are compared with standard care in a prospective patient population. Further, 4-dimensional MRI sequences will be benchmarked against MR-linac cine imaging allowing personalised respiratory motion management. Finally, we evaluated the dosimetric precision of MRI bulk density planning in 40 patients, comparing to a deformed CT benchmark.

R. Van den Begin, S. Penninckx, A. Gulyban, A. Desmet, N. Jullian, C. Bouchart

- International collaboration within the MR linac consortium and the Momentum study:
  - We launched an international survey among all Unity users under the name GLOBAL-MRI to inquire about operational details, in order to establish benchmarks for centres that are developing their activity.
  - We have participated in the development of a global consensus protocol for the treatment planning of MR-guided SBRT of pancreatic tumours, the manuscript of which has now been published.
- Within a PhD thesis, daily functional MRI is explored as a tool to identify patients with rectal cancer who will benefit from neoadjuvant radiotherapy dose-escalation:
  - Dynamic evolution of IVIM-DWI in rectal cancer patients treated with short course RT: in 20 patients, the inter- and intra-fractional dynamic evolution of the diffusion coefficient (D) and perfusion fraction (p-frac) is under investigation to identify a potential biomarker predictive of pathological response.
  - The PILLAR study evaluates the repeatability and reproducibility of these biomarkers in a population of healthy volunteers and patient tumours to establish Quality-Assurance recommendations for functional MRI study in oncology.
  - These different studies led to the development of the PRECHOICE prospective trial, integrating IVIM-DWI, metabolomics and 53BP1 DNA foci to establish a predictive model to personalise neoadjuvant rectal cancer treatment.
- Finally, the MR-linac is the ideal platform to participate in multicenter clinical studies on high-precision radiotherapy. In 2024 we will open trials on high-risk prostate cancer, locally advanced pancreatic cancer and cholangiocarcinoma.

For FLASH-RT, two preclinical PhD theses were launched last year, and we prepare a randomised trial.

- One thesis aims to study the impact of beam structure (physical parameters specific to irradiation) on the induction of the FLASH effect. This study is based on numerical simulations and is validated by in vivo experiments on zebrafish models.
- The second thesis aims at validating the observation of the FLASH effect on our clinical electron accelerator using murine models. The latter study will pave the way for the start-up of LANCE trial at the Institut Jules Bordet.
- The LANCE trial is a multi-centre randomised Phase II study of FLASH radiotherapy versus standard of care radiotherapy in patients with localised Cutaneous Squamous Cell Carcinoma (cSCC) or Basal Cell Carcinoma (BCC). The aims of the study are to describe and compare the toxicity and efficacy of high dose rate radiotherapy (FLASH therapy) to conventional radiotherapy (according to the standard guidelines per lesion size) through a randomised Phase II selection study. Small (T1) lesions will be exposed to a single 22Gy dose of radiation, while a fractionated 5 x 6Gy schedule will be used for the treatment of large (T2) lesions.

Selected publications

- Grimbergen G, Eijkelenkamp H, Snoeren LMW, Bahij R, Bernchou U, van der Bijl E, Heerkens HD, Binda S, Ng SSW, Bouchart C, Paquier Z, Brown K, Khor R, Chuter R, Freear L, Dunlop A, Mitchell RA, Erickson BA, Hall WA, Godoy Scripes P, Tyagi N, de Leon J, Tran C, Oh S, Renz P, Shessel A, Taylor E, Intven MPW, Meijer GJ. Treatment planning for MR-guided SBRT of pancreatic tumors on a 1.5 T MR-Linac: A global consensus protocol. **Clin Transl Radiat Oncol**. 2024; 47:100797.
- Mokhtari A, Casale R, Salahuddin Z, Paquier Z, Guiot T, Woodruff HC, Lambin P, Van Laethem JL, Hendlisz A, Bali MA. Development of Clinical Radiomics-Based Models to Predict Survival Outcome in Pancreatic Ductal Adenocarcinoma: A Multicenter Retrospective Study. **Diagnostics** (Basel). 2024;14(7):712.
- Bouchart C, Navez J, Borbath I, Geboes K, Vandamme T, Closset J, Moretti L, Demetter P, Paesmans M, Van Laethem JL. Preoperative treatment with mFOLFIRINOX (or Gemcitabine/Nab-paclitaxel) +/- isotoxic high-dose Stereotactic Body Radiation Therapy (iHD-SBRT) for borderline resectable pancreatic adenocarcinoma (the STEREOPAC trial): study protocol for a randomised comparative multicentre phase II trial. **BMC Cancer** 2023; 23 (1), 1-13
- Schoenauen L, Stubbe FX, Van Gestel D, Penninckx S, Heuskin AC. C. elegans: A potent model for high-throughput screening experiments investigating the FLASH effect. **Clin Transl Radiat Oncol**. 2023; 45:100712.
- Paquier Z, Chao SL, Bregni G, Sanchez AV, Guiot T, Dhont J, Gulyban A, Levillain H, Sclafani F, Reynaert N, Bali MA. Pre-trial quality assurance of diffusion-weighted MRI for radiomic analysis and the role of harmonisation. **Phys Med**. 2022 Nov; 103:138-146

CONTRIBUTING TO ACADEMIA-LED RESEARCH WITHIN THE BIG NETWORK

Many IJB staff are founders and/or committee members of collaborative groups / networks such as BIG, EORTC, IBCSG, OncoDistinct, actively promoting and empowering collaborative academic research internationally.

“Our goal is to facilitate breast cancer research at the international level by encouraging cooperation between members and other academic networks, and collaborating with but working independently from the pharmaceutical industry.”

Team and infrastructure

Today the Breast International Group (BIG) is composed of almost 60 academic research groups from around the world. Its headquarters, comprising about 45 staff members, report to a Board of Directors and a general assembly of members.

The headquarters staff works 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 IJB's CTC, which has acquired unique expertise in managing international registration trials over the last two decades.

E. de Azambuja, M. Piccart

Aims

- To contribute to more effective, but also more individualised adjuvant treatment strategies for breast cancer
- To 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), according to a model that preserves academic freedom
- To promote clinical trials addressing questions devoid of commercial interest that serve breast cancer patients' needs
- To improve the molecular understanding of the lethal evolution of the disease via metastatic spread with the hope of finding new strategies to counteract this

Main projects (in collaboration with the Clinical Trials Centre)

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

Progress report of the research conducted by the BIG network and involving IJB:

- The Alexandra / Impassion trials was prematurely stopped by the Independent Data Monitoring Committee after inclusion of 2199 (out of 2300 planned) patients, based on a planned interim and futility analysis – with invasive disease-free survival events in 141 (12.8%) patients treated with atezolizumab-chemotherapy and 125 (11.4%) with chemotherapy alone (median follow-up 32 months) the final stratified invasive disease-free survival hazard ratio was 1.11 (95% CI 6.87 – 1.42), p=0.38). The absence of benefit from adding atezolizumab to adjuvant chemotherapy directly informs optimal management of stage II/III triple negative breast cancer, namely that surgery should no longer be performed as initial treatment in this setting because it denies patients the opportunity to benefit from preoperative immunotherapy. A manuscript has been published to JAMA.
- DECRESCENDO was terminated early due to slow recruitment that led to financial support withdrawal. Among 139 patients enrolled, 131 patients underwent surgery, with 113 (86%) achieving pCR/RCB 0, 10 (8%) RCB 1, and 8 (6%) RCB ≥2. PAM50 subtype was successfully determined in 124 patients (insufficient material or non-contributive test in seven patients). Of these, among patients who achieved pCR/RCB 0 (n=107) the most represented PAM50 subtype was the HER2-enriched one (n=87, 81%) followed by the basal-like (n=13, 12%) and luminal-A (n=7, 7%) subtypes.

Selected publications

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- Ignatiadis M, Bailey A, McArthur H, El-Abed S, de Azambuja E, Metzger O, Chui SY, Dieterich M, Perretti T, Shearer-Kang E, Molinero L, Steger GG, Jassem J, Lee SC, Higgins M, Zarba J, Schmidt M, Gomez H, Guerrero Zotano A, Moscetti L, Chiu J, Munzone E, Ben-Baruch NE, Bajetta E, Ohno S, Im SA, Werutsky G, Gal-Yam EN, Gonzalez Farre X, Tseng LM, Jacot W, Gluz O, Shao Z, Shparyk Y, Zimina A, Winer E, Cameron DA, Viale G, Saji S, Gelber R, Piccart M. Adjuvant Atezolizumab for Early Triple-Negative Breast Cancer: The ALEXANDRA/IMpassion030 Randomized Clinical Trial. JAMA. 2025 Jan 30:e2426886.

CONTRIBUTING TO ACADEMIA-LED RESEARCH WITHIN THE ONCODISTINCT NETWORK

“Our goal is to accelerate oncology drug development, paying closer attention to patients’ needs.”

Team and infrastructure

Twenty-seven cancer hospitals or departments across 8 countries have signed the ONCODISTINCT consortium agreement. These include academic and non-academic centres with expertise in early or late-phase clinical trials, sharing a common enthusiasm for innovation in clinical trial methodology in the era of molecular oncology.

The network has a steering committee, a coordination team implementing the decisions of the Steering Committee and rotating data centres with an operational team conducted by coordinator managing all activities of the network based at IJB.

Aims

- To address unmet medical needs such as brain metastases, rare tumours, oligometastases, and inflammatory breast cancer
- To conduct proof-of-concept studies with innovative designs, as well as biomarker driven trials
- To accelerate the conduct of phase I-II-III trials alongside new collaboration models with pharmaceutical and biotechnology companies
- To develop new models of clinical research organisation such as the “spider’s web” model: this consists in setting up a permanent collaboration in form of a master agreement between all participating centres, with the aim of reducing the administrative burden related to clinical trials and facilitate access to biomarker-driven clinical trials regardless of country borders.
- To encourage academic research within our network with the creation of a bi-annual Oncodistinct grant.

Main projects

Five prospective clinical trials are up and running, of which four are managed by the CTSU:

- **REGINA**, testing the combination of neoadjuvant regorafenib in combination with nivolumab and short-course radiotherapy in intermediate-risk stage II/III rectal cancer (Oncodistinct 009)
- **BRAINSTORM**, aiming to constitute a brain metastases research platform to tackle the challenge of CNS metastases in solid tumours, including an analysis of ctDNA in the CSF of patients with CNS metastases (Oncodistinct 006)
- **CHANCES**, (first-in-human) evaluating an anti CD43 IDH5301 alone or in combination with chemotherapy and trastuzumab (Oncodistinct 011)

N. Kotecki

- **COPERNIC**, A study of on-treatment ctDNA changes in chemo-refractory colorectal cancer patients (Oncodistinct 012)
- **SHAPERS**, Efficacy and safety of short-course radiotherapy (SCRT) versus total neoadjuvant therapy in older patients with locally advanced rectal cancer: a multicentre, open-label, randomised pragmatic clinical trial (Oncodistinct 013)

Two multicentric retrospective studies are ongoing and sponsored by IJB:

- **ALINE**, ReAl-world cLINical outcomes of patients with Estrogen receptor-positive, HER2negative advanced breast cancer.
- **TNT**, REAL-WORLD RETROSPECTIVE STUDY OF TNT (total neoadjuvant therapy) FOR RECTAL CANCER

Recent achievements

- Oncodistinct is in the course of becoming an independent AISBL based at IJB
- Oncodistinct selected its new fellowship candidate who will start at the end of 2024

Selected publications

- Martins-Branco D, Nader-Marta G, Gombos A, Barthelemy P, Goncalves A, Borcoman E, Clatot F, Holbrechts S, De Maio D’Esposito E, Cheymol C, Vanhaudenarde V, Duhoux FP, Duhem C, Decoster L, Denys H, Lefranc F, Canon JL, Clement PM, Gligorov J, Paesmans M, Kindt N, Awada A, Kotecki N. BrainStorm: a multicenter international study to tackle CNS metastases in solid tumors. **Nat Med.** 2023 Dec;29(12):2981-2982. doi: 10.1038/s41591-023-02595-y. PMID: 37857713.

Chapter IV • Developing New Approaches to Patient Empowerment and Well-being

IJB has worked for many years to accompany patients throughout their cancer journey. This patient-centered approach, implemented in care, is embedded in the way our researchers design and lead research.

IJB 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. Today, IJB / H.U.B recognises that research is not only about researchers. Through various initiatives, researchers are involving patient-partners, patient-experts, artists, and others to explore new ways of caring for patients, as well as respecting and valuing the work of healthcare professionals.

This pillar comprises five domains:

1. *Research on oncological complications, including infectious diseases and intensive care*
2. *Research on psycho-oncology and supportive care*
3. *Nursing research*
4. *Survivorship clinic including oncofertility research (see the chapter I on the lab of Human reproduction)*
5. *Patient involvement and empowerment*

- **RESEARCH INTO ONCOLOGICAL COMPLICATIONS**
- **RESEARCH INTO PSYCHO-ONCOLOGY AND SUPPORTIVE CARE**
- **NURSING RESEARCH**
- **SURVIVORSHIP CLINIC**
- **PATIENT INVOLVEMENT AND EMPOWERMENT**

RESEARCH INTO ONCOLOGICAL COMPLICATIONS

“Our goal is to minimise the cancer patient’s risk of death as a result of anticancer treatment complications.”

Team and infrastructure

Five emergency rooms dedicated to oncological emergencies

Eight beds dedicated to short hospital admissions for the management of acute complications

Infectious disease team comprising one full-time physician, one part-time physician, one full-time resident, one research nurse, and one administrative assistant.

Aims

- To 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 to continuously re-assess the rates of success and failure in managing these complications
- To provide specialised care and uniform management for patients presenting with immunotherapy toxicity
- To benchmark clinical outcomes of IJB cancer patients experiencing severe complications with those in other European cancer centres and departments
- To participate in international clinical trials testing new intensive care approaches or new antimicrobial, antiviral, and antifungal agents
- To rapidly recognise infectious complications (including febrile neutropenia), prescribe optimal antibiotherapy and limit the use of antibiotics to infectious indications

Main projects

For the Oncological Emergency and Internal Medicine Team

- “Immunological variables associated to ICI toxicity in cancer patients”
- “Sarcoidosis and Sarcoid-like reaction associated with immune checkpoint inhibitors or MAP Kinase inhibitors”
- “Impact of irAEs on survival in NSCLC”
- “Immune checkpoint inhibition in kidney transplant recipients” (prospective study)
- “Impact of short-term corticosteroid treatment for ICI-renal toxicity” (prospective study)
- “Retrospective study of ICI-induced colitis”
- “Topicals steroids for low grade ICI-induced colitis” (prospective)
- “Retrospective study of ICI-induced muscle toxicity”

A. Georgala, B. Grigoriu, A.P. Meert, L. Wolff, A. Loizidou

- “Prospective study of autoimmune endocrine disease-related antibodies before the start of ICI therapy”
- “Type 1 diabetes and ICI”

For the Infectious Disease Team

- COVID-19: Immune response in patients with cancer receiving mRNA vaccination against SARS-CoV-2 (I-SPARC study)
- A Phase 2, open-label, randomised, safety, pharmacokinetic and efficacy study of voriconazole inhalation powder compared to voriconazole tablets in subjects with acute invasive pulmonary aspergillosis (TFF-V2-001 study)
- A phase 2b, randomised, double-blind, placebo-controlled study evaluating the effects of EDP-938 in adult haematopoietic cell transplant recipients with acute respiratory syncytial virus infection of the upper respiratory tract (EDP938-103 study)
- A phase III, adjudicator-blinded, randomised study to evaluate the efficacy of safety of treatment with olorofim versus treatment with Ambisome® followed by standard of care (SOC) in patients with invasive fungal disease cause by Aspergillus species (OASIS study)
- Global point of prevalence survey of antimicrobial consumption and resistance (GLOBAL-PPS study)
- Azole-echinocandin combination therapy for invasive aspergillosis: a randomised pragmatic superiority trial (IA-DUET study)
- ECDC prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals (ECDC study)

Recent achievements

Annual surveillance of antimicrobial ecology and antibacterial resistance / Sciensano reporting tools: our results are in line with national data and confirm the rise of multi-drug-resistant microorganisms.

- A prospective, multicenter, observational study in hospitalised patients suffering from infections and treated with ZAVICEFTA (ceftazidime/avibactam) under actual conditions of use (OZAVIE)
- An open-label single-arm phase IIb study of F901318 as treatment of invasive fungal infections caused by Lomentospora prolificans, Scedosporium spp., Aspergillus spp. and other resistant fungi in patients lacking suitable alternative treatment options (FORMULA-OLS): the results are encouraging in this challenging setting.
- Development of a dedicated clinic for management of immunotoxicities: next steps will consist in finalising protocols for the diagnosis / management of immunotherapy toxicities, organising a multidisciplinary immunotoxicity consultation and encouraging clinical research in this field.

Selected publications

- T. Berghmans, M. Brandão, M. Ilzkovitz, A.-P. Meert. Complications sévères des traitements systémiques du patient cancéreux thoracique (complications hors infections et urgences respiratoires) Severe complications of systemic treatment in thoracic oncology. **Rev Mal Respir** 2024 ; 41:317–324. https://doi.org/10.1016/j.rmr.2024.02.014.
- Blum TG, Morgan RL, Durieux V, Chorostowska-Wynimko J, Baldwin DR, Boyd J, Faivre-Finn C, Galateau-Salle F, Gamarra F, Grigoriu B, Hardavella G, Hauptmann M, Jakobsen E, Jovanovic D, Knaut P, Massard G, McPhelim J, Meert AP, Milroy R, Muhr R, Mutti L, Paesmans M, Powell P, Putora PM, Rawlinson J, Rich AL, Rigau D, de Ruysscher D, Sculier JP, Schepereel A, Subotic D, Van Schil P, Tonia T, Williams C, Berghmans T. European Respiratory Society guideline on various aspects of quality in lung cancer care. **Eur Respir J**. 2023 Feb 16;61(2):2103201. doi: 10.1183/13993003.03201-2021.
- Lemiale V, Mabrouki A, Miry L, Mokart D, Pène F, Kouatchet A, Mayaux J, Bruneel F, Perez P, Meert AP, Moreau AS, Benoit D, Darmon M, Zafrani L, Clere-Jehl R; Groupe de Recherche en Réanimation Respiratoire du patient d'Onco-hématologieSepsis-associated coagulopathy in onco-hematology patients presenting with thrombocytopenia: a multicentric observational study. **Leuk Lymphoma**. 2023 Jan;64(1):197-204. doi: 10.1080/10428194.2022.2136971. Epub 2022 Oct 28
- Berghmans T, Meert AP. [Respiratory cancer diseases: Which role for intensive care?]. **Rev Mal Respir**. 2023 Feb 28: S0761-8425(23)00088-8. doi: 10.1016/j.rmr.2023.02.004
- Candice Gueuning; Lieveke Ameye; Angela Loizidou; Bogdan Grigoriu; Anne-Pascale Meert. PARIS score for evaluation of probability of SARS-CoV2 infection in cancer patients. **Supportive Care in Cancer** 2021https://doi.org/10.1007/s00520-022-07199-9,

RESEARCH INTO PSYCHO-ONCOLOGY AND SUPPORTIVE CARE

“Our goal is to preserve, restore, and enhance quality of life for cancer patients and their families throughout their journey, from diagnosis to end of life. Simultaneously, we strive to improve the communication skills of IJB healthcare professionals to improve patient well-being and satisfaction.”

Team and infrastructure

The Psycho-Oncology sector consists of 12.5 psychologists, one neuropsychologist, 0.7 psychiatrist, and one postgraduate psychiatrist, all fully dedicated to supporting cancer patients, their families, and the healthcare professionals caring for them.

The Acute Supportive Care Unit comprises one anaesthetist, one general practitioner specialised in palliative care, one senior oncologist, one nurse specialised in supportive care, and 0.5 nurse trained in research methodologies. This mobile team offers specialised supportive care consultations and provides comprehensive supportive care throughout all hospital departments.

Y. Libert, A. Liénard, I. Merckaert

Aims

- To develop psychological interventions supported by written manuals and to assess their efficacy for cancer patients and their relatives at different stages of the disease, using rigorous methodologies (i.e. randomised controlled studies assessed with validated self-report questionnaires, objective lab-based testing and everyday life measures)
- To develop specific psychological interventions supported by written manuals and to assess their efficacy on the psychological resilience of adolescents and young adults with cancer (AYAc) at the start of their cancer journey, using rigorous methodologies (i.e. randomised controlled study assessed with validated self-report questionnaires, objective lab-based testing and everyday life measures)
- To develop communication skills training programs for IJB healthcare professionals to prevent burnout and to improve their wellbeing, and consequently to improve patients’ satisfaction with their medical care and compliance with healthcare professionals’ advice.
- To develop studies that improve understanding among cancer patients and their relatives of the difficulties encountered throughout the course of the disease (such as cognitive fatigue and advanced care planning)
- To develop supportive care interventions allowing better control of pain, mucositis, skin toxicities, and sleep disturbances

Main projects

Several new projects have been launched:

- Re-Boost: A randomised controlled trial of an intensive, ecologically boosted group intervention focused on emotion regulation for cancer patients in the early survivorship period
- e-Motion: A randomised study assessing the efficacy of an intensive, ecologically boosted group intervention to promote emotional regulation in patients with metastatic cancer
- Efficacy of a parenting support intervention to improve communication between patients with advanced cancer and their adolescent children
- Cognitive fatigue and its associated factors in women with breast cancer
- Cross-sectional, observational study of patients with advanced cancer and their primary caregivers’ willingness to communicate about advanced care planning
- Frequencies, types, and predictors of early and late code status documentation among patients managed by a dedicated supportive care team
- A qualitative retrospective analysis of the euthanasia process and relational dynamics in a comprehensive cancer care centre
- A longitudinal randomised controlled multi-centre study assessing the efficacy of a brief and ecologically resilience boosted online group-based psychosocial intervention scheduled in the early treatment period of adolescents and young adults (AYAs) with cancer.
- Participation in the scientific development and supervision of the Early Together trial, a prospective randomised phase 3 trial on early Integration of palliative care for metastatic uveal melanoma patients (conducted in Institut Curie (Paris) and Centre Antoine Lacassagne (Nice)).

Recent achievements

- Development and evaluation of the efficacy of a communication skills training program focused on addressing uncertainty and hope (one published paper).
- Publication of two recent scoping reviews on advanced care planning in cancer care (two published papers, two PhDs ongoing).
- Publication of one scoping review on psychological interventions targeting patients with metastatic cancer with prolonged life expectancies (one published paper, one PhD. ongoing).
- Publication of one review on ways to support parenting in patients with cancer and co-parents, from research to practice (one published paper, one PhD. ongoing).
- Enhancement of emotion regulation in breast cancer patients during the early survivorship period by developing and assessing the efficacy of a brief, ecologically boosted group intervention (one published paper and three ongoing).
- Completion of a retrospective study on the frequencies, types, and predictors of early and late code status documentation among deceased patients managed by a dedicated supportive care team in a comprehensive cancer center (one submitted paper).
- Investigation of psychological factors associated with clinical fear of cancer recurrence in breast cancer patients in the early survivorship period (one published paper).
- Development and assessment of the efficacy of a support intervention aimed at improving communication between parents and their children dealing with parental cancer (one published paper, one PhD. ongoing).
- Co-authorship of the "Communication with Patients and Significant Others in Cancer Care: ESMO Clinical Practice Guidelines," published by the European Society for Medical Oncology.

Selected publications

- Klastersky J, Libert I, Libert Y, Echterbille MA. A new comprehensive and stratified concept for supportive care in cancer patients. **Curr Opin Oncol**. 2024 Jul 1;36(4):206-210. doi: 10.1097.
- Libert Y, Langhendries C, Choucroun L, Merckaert I. Interventions aiming to improve advance care planning uptake in oncology: a scoping review of recent randomized controlled trials. **Curr Opin Oncol**. 2024 Jul 1;36(4):233-247. doi: 10.1097.
- Libert Y, Choucroun L, Razavi D, Merckaert I. Advance care planning in oncology: a scoping review and some recommendations. **Curr Opin Oncol**. 2023 Jul 1;35(4):261-275. doi: 10.109.
- Merckaert I, Waroquier P, Caillier M, Verkaeren O, Righes S, Liénard A, Libert Y, Kristanto P, Razavi D. Improving emotion regulation in breast cancer patients in the early survivorship period: Efficacy of a brief ecologically boosted group intervention. **Psychooncology**. 2023 Apr;32(4):597-609. doi: 10.1002.
- Stiefel F, Bourquin C, Salmon P, Achtari Jeanneret L, Dauchy S, Ernstmann N, Grassi L, Libert Y, Vitinius F, Santini D, Ripamonti CI; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Communication and support of patients and caregivers in chronic cancer care: ESMO Clinical Practice Guideline. **ESMO Open**. 2024 Jul;9(7):103496. doi: 10.1016/j.esmoop.2024.103496. Epub 2024 Jun 18. PMID: 39089769; PMCID: PMC11360426.

NURSING RESEARCH

“Our goal is to improve patients’ outcomes and quality of life, through implementation of evidence-based nursing interventions and to contribute to symptom management as well as to ensure early recognition of potentially severe complications.”

Team and infrastructure

Any nurse with a clinical question and an interest in nursing research may consult the Nursing Research Unit.

Aims

Improve nursing practices by implementing well-established processes and contributing in response to qualitative research questions.

- 1. Identify “Nursing Sensitive Patient Outcomes” (e.g. symptom management)
- 2. Search for evidence-based guidelines/data describing how to best prevent and/or manage the problem
- 3. Implement these guidelines in care units
- 4. Evaluate the impact of this change in nursing care on patients’ outcomes

Main projects

- Inventory of evidence-based nursing assessment and management of side effects in oncology.
- Implementation of hypnosis for symptoms according to evidence from the literature.
- Implementation of systematic assessment of peripheral neuropathy in high-risk patients in the ambulatory anti-cancer treatment setting (day clinic).
- Exploration of reasons for emergency visits and re-admission of patients.
- Collaboration in the development of a multidisciplinary integrative oncology program.
- Collaboration in the development of an adapted programme of care for AYA patients.

P. Crombez

Recent achievements

- Use of photobiomodulation (Laser) in the treatment of early signs of peripheral neuropathy (RCT in progress).
- Qualitative study of patients’ reported experiences with advice and well-being nursing care (in progress): a patient partnership approach.
- Literature review of efficient complementary strategies for symptom relief in oncology.
- Review and implementation of helpful tools used to respond to needs of AYA patients.

Selected publications

- Crombez P. Le leadership infirmier : la signification et le contenu. **CancerCare**. 2023 ; Vol1, Num 1.
- Decock N, Friganovic A, Kurtovic B, Oomen B, Crombez P, Willems C. Temper the Specialist Nurses Heterogeneity in the Interest of Quality Practice and Mobility-18 EU Countries Study. **Healthcare** (Basel). 2022 Feb 25;10(3):435. doi: 10.3390/healthcare10030435. PMID: 35326913; PMCID: PMC8953535.

SURVIVORSHIP CLINIC

“Our goal is to accelerate recovery from the side effects of therapies given with ‘curative intent’, so that patients can return to a ‘normal life’ and regain autonomy.”

Team and infrastructure

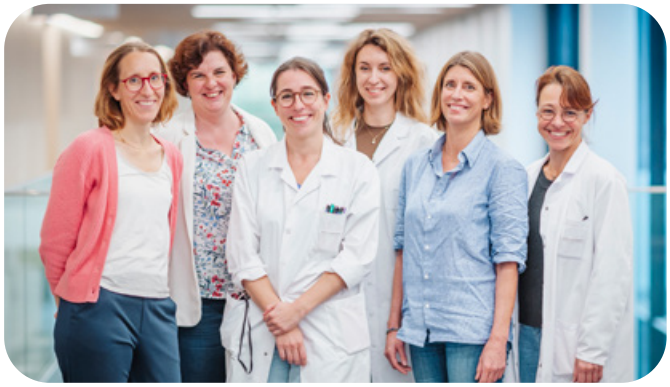
This programme is called RESTART and is the responsibility of one medical oncologist, Laura Polastro, assisted by a nurse.

Aims

- To identify the specific needs of breast and pelvic gynaecological cancer patients in the 3 months following completion of primary therapy given with a curative intent (e.g., surgery +/- radiotherapy +/- chemotherapy +/- endocrine therapy)
- To develop a physical rehabilitation programme with the help of physiotherapists
- To organise educational workshops for “eligible” patients that will allow them to actively participate in their recovery

Recent achievements

- The RESTART survivorship program has been up and running for breast cancer patients since early 2022 and will begin in mid-2024 for pelvic gynaecological cancers.
- Since 2022, more than 230 patients participated in the RESTART program. The feasibility of the Restart programme in breast cancer has been demonstrated and the RESTART 2.0 study began in 2024. The aim of the study is to measure the impact of the programme on the quality of life, the rate of return to work and levels of physical activity among participants.
- A pilot trial, “PRINTEMPS,” was launched for young cancer patients (< 40 years), who suffer from intense fatigue after treatment. The study offers multidisciplinary care with coaching, psychological interventions, and physical activity. A first goal is to determine its feasibility. The trial is ongoing.



L. Polastro, M.A. Echterbille, A. Wolfromm, Y. Stepanishyna, V. De Wilde, F. Bustin

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 one coordinator (PhD) in research promotion and patient partnerships, one anthropologist, one patient-expert, a group of patient-partners and two intercultural mediators

Aims

- To improve clinical and translational research by promoting patient involvement in studies through collaborations and co-creation of projects
- To pursue the training of patient-partners, integrate patient-experts, and open the hospital to other professionals and skills (artists, coaches, sociologists etc.).
- To guarantee optimal cancer care for migrants and ethnic minorities, including participation in clinical trials
- To train health care professionals on migrants’ health and cultural issues

Main projects

- Conduct 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, and co-chairing the BBMRI.be Stakeholder Involvement group.
- Communicate about clinical research: develop tools and media solutions to engage patients in research
- Conduct a retrospective study assessing patterns of imatinib use across patients treated for a Chronic Myeloid Leukemia (CML) in Belgium between 2004 and 2016
- Conduct a study to identify risk factors for non-adherence to oral cancer therapy and compare associated factors in both native and migrant populations - MADESIO mixed method study
- Develop a strategic plan to provide linguistically and culturally competent cancer care

Recent achievements

- B.CaRe project: An 18-month collaborative project gathering ESP-ULB researchers, patient advocates (Association Travail et Cancer), and front-line healthcare professionals (Maison médicale Le Noyer) through an innovative multidisciplinary, co-creation research approach to improve the resilience of the cancer community. In the context of the crisis in the health system, the project explored various paths of investigation to “re-humanise” oncology care pathways and improve the resilience of the cancer care model and the quality of life of all cancer stakeholders (caregivers, patients, and families).

A. Nguyen , S. Michiels

- Quantitative step of MADESIO study: Enrollment of 117 patients in a questionnaire-based study measuring adherence to oral anticancer drugs and identifying factors associated with low adherence, comparing one group of 53 native patients and a group of 64 migrant patients.
- Qualitative step of MADESIO study: Conducting semi-structured interviews with 13 non-French-speaking patients in order to explore the meaning they give to their illness and their experience of oral therapy
- Two-year follow-up measurement of adherence and persistence with Imatinib in a Belgian cohort of 1196 patients diagnosed with CML between 2004 and 2016.
- BEIS, an innovative nursing research project: Development and exploration of a new service offer, in collaboration with specialised nurses in cosmetic care and well-being, a patient expert and a group of 12 patient partners. A research project co-created with the patients to improve the department of cosmetic nursing care and determine the impact of this nursing service on the self-esteem / image of patients during cancer treatments.
- “PISARO”, the patient advisory group in research, celebrating its 3rd anniversary, 15 meetings between trained patient-partners and researchers, 10 full research project evaluations, five training sessions in clinical research for patient-partners, and four communication documents

- Two Intercultural mediators recruited to remove linguistic and cultural barriers to accessing high-quality care

Selected publications

- Cornillon J., Crocchiolo R., Dubois V., Guidicelli, G., Jorge-Cordeiro D., Meunier M-C., Michiels S., Timmermans A., Villemonteix J., Yakoub-Agha I., Ahmad I. Unrelated donor selection for allogeneic hematopoietic stem cell transplantation: Guidelines from the Francophone Society of Bone Marrow Transplantation and Cellular Therapy (SFGM-TC), Bulletin du Cancer Volume 111, Issue 2, **Supplement,2024**, Pages S1-S13.
- Michiels S, Tricas-Sauras S, Salaroli A, Bron D, Lewalle P, Vanschoenbeek K, Poirel HA, Kirakoya-Samadoulougou F. Imatinib Adherence and Persistence in Patients with Chronic Myeloid Leukemia in Belgium: Evidence from Real-World Data. **Patient Prefer Adherence**. 2024 Sep 25;18:1991-2006. doi: 10.2147/PPA.S472478. PMID: 39345760; PMCID: PMC11439344.
- Bron D, De Leval L, Michiels S, Wittnebel S; EuroBloodNet for rare diseases. Hepatosplenic T-cell lymphoma: treatment challenges. **Curr Opin Oncol.** 2021 Sep 1;33(5):406-411. doi: 10.1097.
- Michiels S, Tricas-Sauras S, Dauvrin M, Bron D, Kirakoya-Samadoulougou F. A mixed method study design to explore the adherence of haematological cancer patients to oral anticancer medication in a multilingual and multicultural outpatient setting: The MADESIO protocol. **PLoS One**. 2021 Jun 24;16(6):e0253526. doi: 10.1371/journal.pone.0253526.
- Dubois V, Amokrane K, Crocchiolo R, Fort M, Guillaume N, Kennel A, **Michiels S**, Ralazamahaleo M, Rouzaire PO, Yakoub-Agha I, Faucher C.) [Definition and standardization of histocompatibility requests depending on patient course and donor type: Guidelines from the Francophone Society of Bone Marrow Transplantation and Cellular Therapy (SFGM-TC) and the Francophone Society of Histocompatibility and Immunogenetics (SFHI)]. Bull Cancer. 2021 Dec;108(12S):S45-S52. French. doi: 10.1016/j.bulcan.2021.01.024. **Epub** 2021 May 7. PMID: 33966883.

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.

With the number of clinical trials and research projects increasing significantly throughout IJB, and having identified the need for professional support in their set-up and conduct, in 2016 IJB officially established a new centralised research infrastructure by reorganising its existing structures.

The purpose of this organisation, active for over eight years, is to stimulate scientific creativity through efficient medical and scientific support to researchers on the one hand and, on the other hand, to provide professional support to clinical research by centralising and harmonising the administrative, operational, contractual, and financial management.

The IJB's research organisation is now part of the H.U.B's overall research organisation, a network within which the scope and methods of collaboration have been further expanded.

The administrative and operational support structures for research now form a single H.U.B Clinical Trials Centre (CTC).

The teams responsible for conducting clinical trials in the field, following-up and monitoring the progress of patients participating in clinical studies remain part of a Clinical Trials Conduct Unit (CTCU) fully dedicated to oncology.

Governance

M. Ignatiadis, L. Buisseret, J. Cimino, M. Piccart, N. Kotecki, Ph. Aftimos, J. Gaye, M. Sautois, Ph. Hennebert

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

Research activities are organised through two 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.

As part of its integration into the H.U.B, research at IJB is overseen by a **Research Steering Committee (RSC)**

made up of key representatives from research at the three hospitals. The H.U.B RSC is composed of:

The General Medical Director

The Clinical Director of Research

The Administrative Director of Research

The Deputy Administrative Director of Research

The Academic Director of Research

The three Scientific Directors: Oncology, Paediatrics, Transversal

Three members, each from one of these 3 sectors (validated by the medical council)

The permanent guests are:

The Vice-Rector for Research (U.L.B.)

The Vice-Dean for Research (U.L.B.)

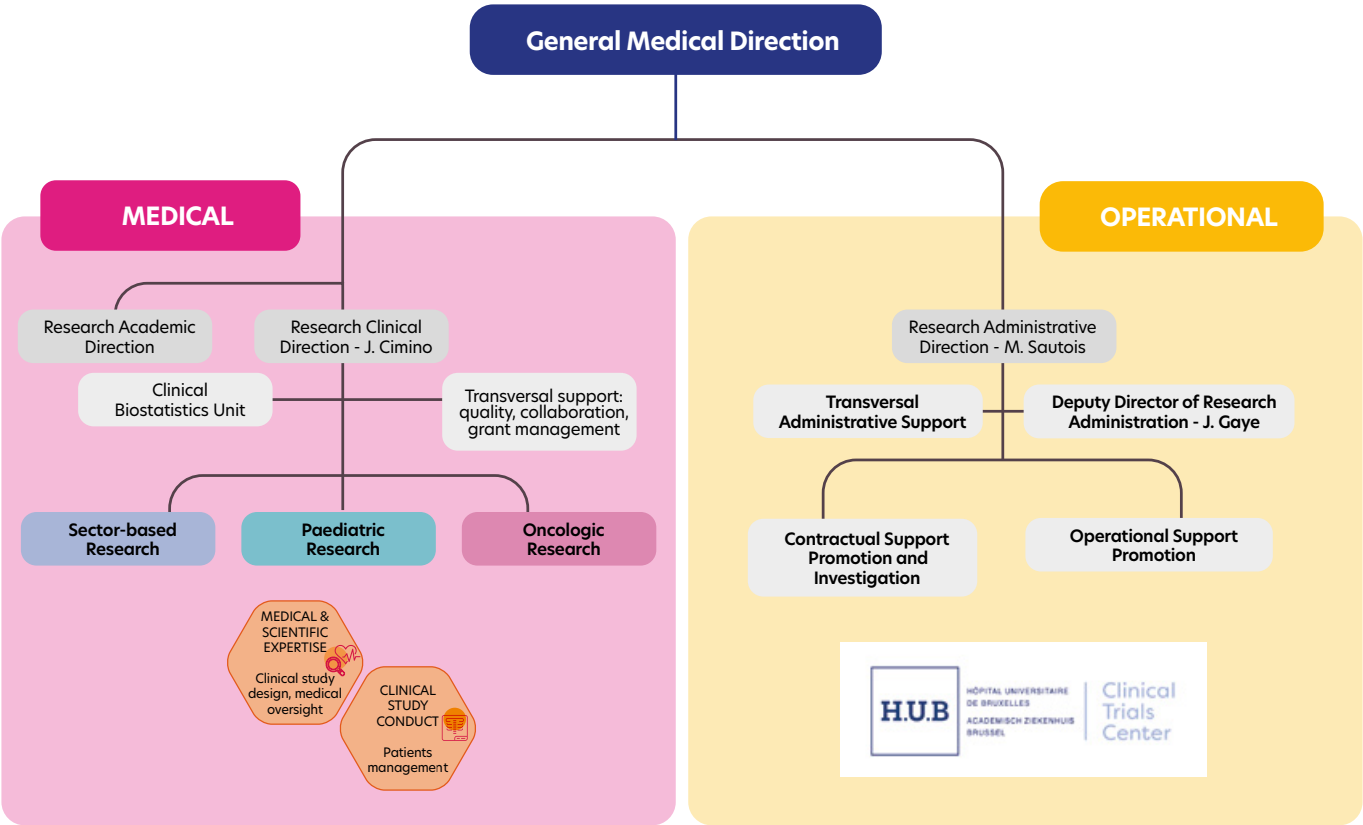
The Chairman of the H.U.B Ethics Committee

The scientific representatives of the main support funds: Association Jules Bordet, Fonds Erasme, Kids Foundation

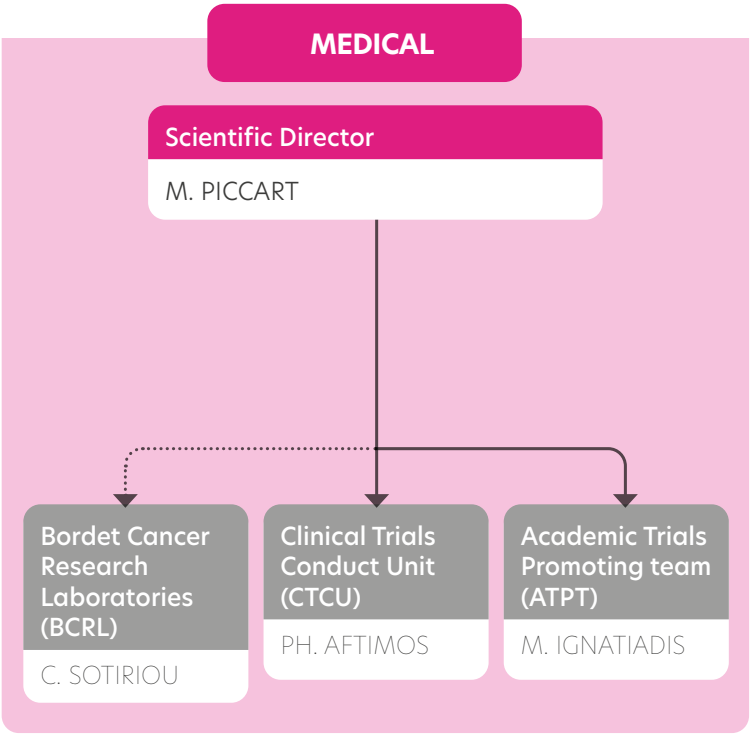
The Research Steering Committee is both a strategic and operational body with the power to take high-level decisions on all research activities.

As an integrated cancer center, the IJB also has a governance body dedicated to oncology, the Comprehensive Cancer Center (CCC) Board. In practice, the Board delegates strategic and operational research issues to committees dedicated to oncologic research. The CCC Board receives regular reports on oncology research activities.

H.U.B Research Organigram



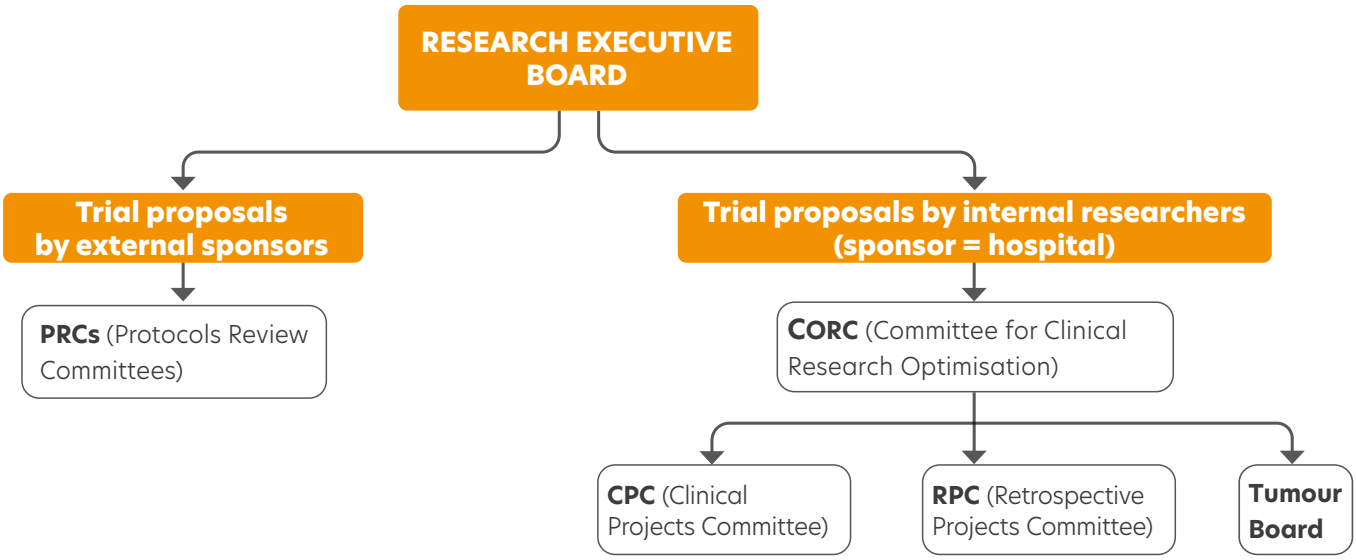
Oncologic Research



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, IJB can efficiently carry out the responsibilities of a clinical trial sponsor.

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



Research Executive Board Oncology

The Research Executive Board Oncology 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 the site level: external sponsorship (pharma or academic)
- At the sponsor level: IJB sponsorship (academic) or service provider.

Project Review Committees

Beyond this executive board, which aim to optimise, stimulate, and streamline the procedures related to the assessment and set-up of oncologic research projects, some specific committees are in place:

- **Protocol Review Committees (PRC)**

  These committees aim to assess in an efficient and timely manner the clinical trial proposals coming from IJB's medical departments and 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 IJB's study chairs. These projects, sponsored in-house, can be retrospective (RPC) or prospective (CPC) 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**

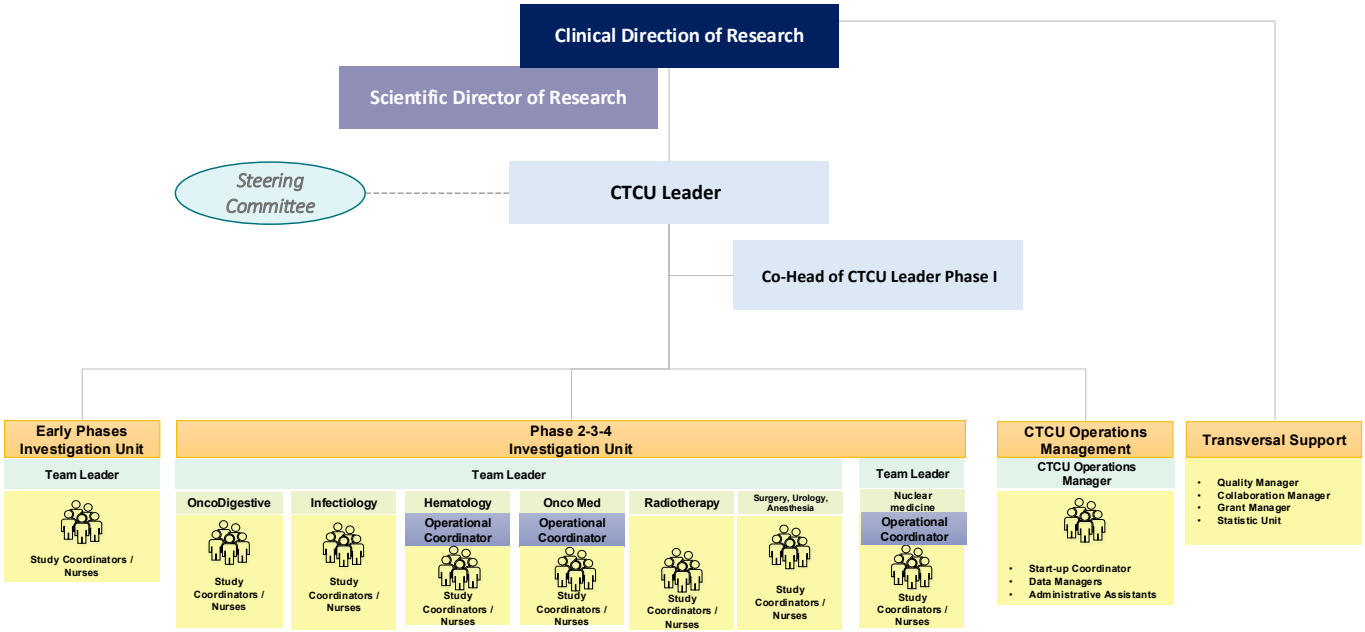
  IJB's Ethics Committee is an independent body whose role includes:

  - 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

Clinical Trials Conduct Unit

The **Clinical Trials Conduct Unit (CTCU)** is an entity dedicated to the management and coordination of clinical trials, specialised in oncology research. Over the past forty years, the foundations of this research unit have evolved steadily to become the CTCU, which plays a central role in the advancement of cancer treatments, facilitating access to the latest therapeutic innovations for oncology patients, ensuring their safety and supporting the hope of a future in which cancer is a better understood and treated disease.



Mission and objectives

The main mission of the CTCU is to coordinate clinical trials in the field of oncology, ensuring that they are conducted to the highest professional, ethical and scientific standards in compliance with European Directives, applicable regulations and Good Clinical Practice (GCP).

Team, infrastructure and expertise

The CTCU's team of more than thirty people, representing all oncology specialisations (Oncodigestive, Haematology, Radiotherapy, Nuclear Medecine, Infectiology, Medical Oncology, Surgery, Urology, Anesthesia) is made up of specialist oncology physicians and investigators, Study Coordinators (nurses or research assistants), data managers (including an Imaging DM), a Quality Manager and a management team with administrative support, all experts in ensuring that clinical trials in oncology are conducted with rigor and commitment.

Since March 2023, the Study Coordinators have also been working closely with the nurses in the NTU - B17 **(Novel Treatments Unit)**, which provides 12 single rooms for the care and treatment of patients included in an early clinical trial phase. The Intensive Care Unit, next door to the NTU, also provides added value in terms of safety.

Impact and contributions

The CTCU has made a significant contribution to improving cancer treatment by participating in early- and late-stage clinical trials and international multicenter studies, and has helped to develop innovative new therapies that have changed patients' lives.

Today, the CTCU continues to play a key role by collaborating with Huderf and Erasme within the H.U.B to standardise procedures. It plays a leading role in "Precision Medicine" trials (genotype-based). It is actively involved in the clinical development of ADC (Antibody-drug conjugate), given the close collaboration with the Nuclear Medicine Department, which has expertise in targeted molecular imaging. It is involved in clinical trials involving immuno-oncology combinations, including trials of new vaccines, oncolytic viruses and CART-T cells. It maintains active collaboration with academic research networks such as the EORTC, IBCSG, BIG and national organisations such as the BSMO and BHS, and develops early academic proof-of-concept clinical trials sponsored by the IJB.

Clinical Trials Centre

The H.U.B. **Clinical Trials Centre (CTC)** is a support service for commercial and academic clinical research conducted within the H.U.B. Its mission is to provide professional assistance to clinical research by centralising and harmonising the administrative, contractual, financial and operational management (e.g. data management, monitoring, regulatory affairs) of clinical trials.

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

PROJECT MANAGEMENT:
Operational coordination, communication.

LEGAL MANAGEMENT:
Legal expertise, financial management.

FINANCIAL MANAGEMENT:
Budget control&reporting.
Sites fees budgeting and negociations.

REGULATORY AFFAIRS:
EU submissions, regulatory compliance.

PHARMACOVIGILANCE:
Safety reporting, adverse events oversight.

SITE MONITORING:
Site initiation visits, on- and off-site visits.

DATA MANAGEMENT:
eCRF design, data quality control.

IT RESEARCH:
Development and maintenance of software, users support.

QUALITY ASSURANCE:
Ensures that clinical processes are conducted in accordance with Good Clinical Practice, guidelines and external partner's contracts in place.

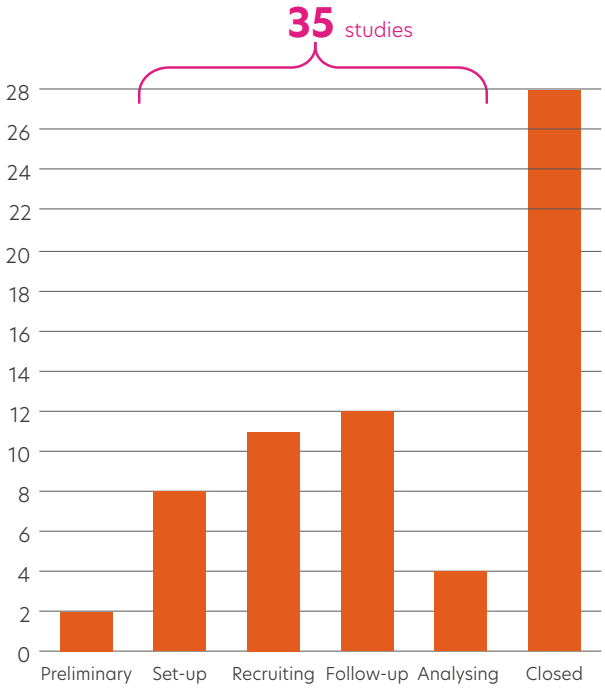
The CTC assists researchers from academia and industry in the development and conduct of phase I, II, and III clinical trials:

- In early disease (neoadjuvant, adjuvant) and advanced disease (locally, metastatic).
- For all cancer types.
- For all treatment and diagnostic modalities.

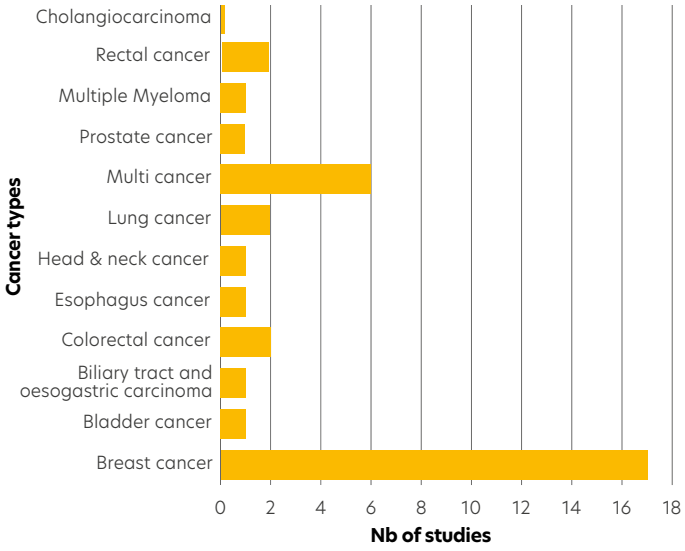
CTC Oncology in numbers (30/10/2024)

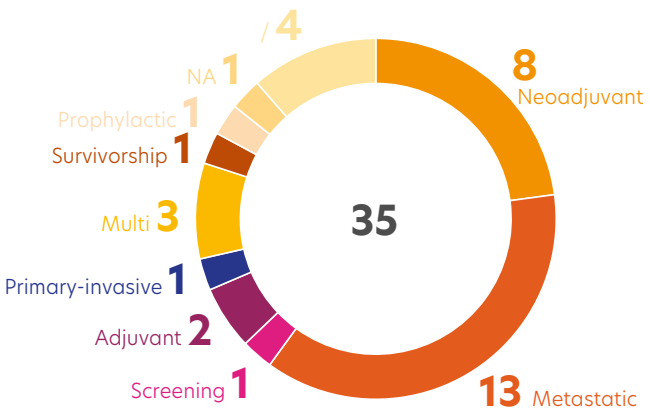
Number of trials operationally managed by the CTC.

24 trials sponsored by Institut Jules Bordet, 10 as a service provider for academic or pharmaceutical partners, 1 as national coordinator.

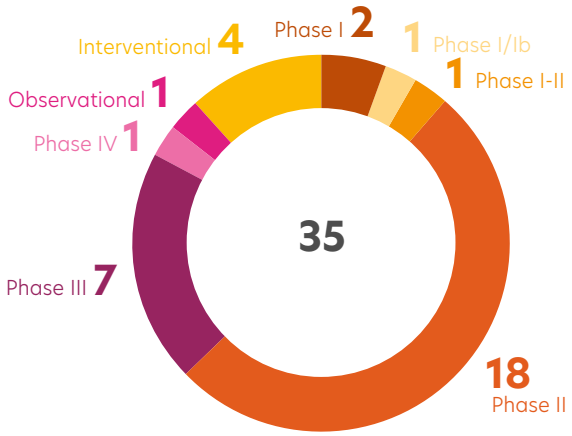


Cancer types and settings of the trials managed by the CTC

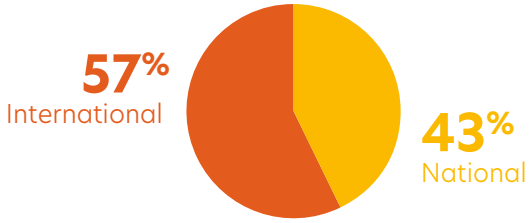




National/International trials and phases of the trials managed by the CTC



International vs National studies



Find out more at CTC.bordet.be

Registry Management Unit

The Registry Management Unit provides support to 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 relating to 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 and care quality evaluation tool. Since it includes all incident tumours since 1 January 2000, now encompassing more than 45,000 records, it is regularly used to plan studies as well as to conduct retrospective research by identifying patients and providing a core dataset for investigators. It is presently limited to data about the primary tumour episode, but the process of extending it to include data on relapses for breast cancer or for rare tumours is ongoing. For breast cancer tumour incidents between 1 January 2000 and 31 December 2010, the whole history of the disease including description of all relapses (local, regional, distant) and subsequent treatments is available.
- An analysis and reporting mission related to the Institute's activities, in particular by developing and maintaining a data warehouse (partially shared with the finances department).

Projects include:

- Identifying and documenting all data sets collected for each clinical project sponsored by the Institute, including retrospective projects, and making them available to the wider community of researchers
- Achieving early identification of new patients with rare tumours in order to help clinicians improve the therapeutic management of these cases and developing a specific registry for rare tumours, facilitating research among these patients
- Linking 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.

Clinical Biostatistics Unit (CBU)

The Clinical Biostatistics Unit (CBU) is a multidisciplinary team that collaborates with all Departments and Research Units within the H.U.B. The CBU provides researchers and clinicians with essential expertise for designing and conducting studies, from formulating research questions to presenting and interpreting study results. This includes assistance with protocol development, preparing submissions for ethics committees, field implementation, data encoding and storage, and statistical analysis using software like R, SAS, or JMP. With years of experience, the CBU has supported numerous projects in the medical field, collaborating with researchers, clinicians, public health organizations, and pharmaceutical companies. The CBU works closely with medical teams, researchers, and other stakeholders in clinical research to support the design, analysis, and interpretation of data from clinical studies and research projects, ensuring reliable and actionable results. As a crucial driver of biostatistics support at the H.U.B., the CBU plays an essential role in advancing research objectives and strategies. Key tasks include:

- Collaborating with stakeholders to design and plan the methodological aspects of clinical studies, including the development of study protocols, selection of appropriate statistical methods, and determining sample size and randomisation techniques.
- Providing expert advice to clinicians and researchers on statistical considerations for clinical trials and research projects, especially regarding variables of interest.
- Validating the selection and format of data to be collected, as well as database design, and overseeing complex statistical analyses to extract meaningful results from clinical data.
- Ensuring the quality, reliability, and interpretability of statistical results by managing missing, aberrant, and usable data.
- Safeguarding the integrity of data, ensuring compliance with security and confidentiality standards.
- Actively contributing to the writing and revision of scientific articles, particularly by validating statistical analyses and the interpretation of results.
- Assisting with the preparation of reports for ethics committees, regulatory bodies, and funding applications.
- Developing research programs within the unit and supervising researchers, including doctoral students and postdoctoral fellows.
- Offering continuing education in biostatistics and data analysis to H.U.B. researchers through training and teaching initiatives.
- Promoting academic and industrial collaboration by delivering high-quality methodological and statistical services.
- Representing biostatistics research at the H.U.B. in consultation councils, advising various working or study groups.
- Contributing to the dissemination of research findings at conferences, seminars, and other scientific events.

Academic Trials Promoting Team

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

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

Tumour Bank and Pathology Department Expertise

The Tumour Bank of IJB 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 have been added to tissue collections. More than 25 000 tissue samples and whole blood fractions are available, provided by more than 11 000 patients.

The Tumour Bank is completely integrated into the Pathology Department of the Brussels University Hospital, enabling full and accurate analysis of tumours by pathologists prior to sample preservation and delivery. It also forms an integral part of the Belgian Virtual Tumorbank (BVT) of the Belgian Cancer Registry, and of two European biobanks: the BBMRI –ERIC and ESBB (European, Middle Eastern & African Society for Biopreservation and Biobanking).

A robust system for sample quality control exists and enables numerous research projects to be supported every year. The Tumour Bank has been ISO 9001 certified since 2012 and is actively working to implement the ISO 20387 biobanking accreditation program. The quality of the tumour samples is very satisfactory and adapted to a large panel of next-generation technologies.

The Pathology Department of the Brussels University Hospital is a key partner in all of IJB's and Erasmus Hospital's translational research projects. Since his creation, in 2022, this department (fusion of the Pathology Department of IJB and Erasmus Hospital) has invested time and energy to maintain full BELAC accreditation (ISO 15189) and large offers in molecular pathology with, for example, 2 platforms for NGS, an essential tool for tumor molecular characterization and precision medicine.

Furthermore, this department remains deeply involved in the quality testing of all clinically relevant biomarkers.

The Tumour Bank and Pathology Department partnership offers to the research community digital pathology expertise (2 Hamamatsu scanners), including artificial intelligence projects (Visiopharm) and tissue laser microdissection techniques (Zeiss).

Research Grant Management

The advancement of scientific oncology research relies on participation in national, European, and international project calls. To improve the visibility of these opportunities and available funding, streamline submission processes, and enhance the management of ongoing and future applications, Dr. David Bergemann, Grant Manager, has established a centralised system for reviewing funding requests for research projects. This initiative aims to support researchers throughout the submission process, maximizing their chances of success and ensuring effective follow-up. By harmonising the preparation of proposals, offering critical reviews, ensuring project eligibility, tracking ongoing research, and guaranteeing timely availability of necessary documents for applications and reports, this system has significantly improved the efficiency of research funding submissions.

From 2022 to 2024, IJB researchers have been awarded highly prestigious research grants provided by the organisations listed hereafter.

Funders Name

- Association Jules Bordet
- 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 Kisane
- Fondation Lambeau-Marteaux
- Innoviris
- Het Antikankerfonds
- KCE
- Octobre Rose
- Plan National Cancer
- Télévie (FNRS)

Collaborations

National and International Collaborations

National collaborations

- ANOCEF (Association de Neuro Onologues d'Expression Françaises)
- ALWB
- AFMV
- AZ Groeninge Kortijk
- AZ Sint Marteen
- AZ Turnhout
- BAPCOC
- BBMRI
- Belgian Cancer Registry (BCR)
- BioCINBIOS
- Belgian Society of Medical Oncology (BSMO)
- Cancer et Psychologie asbl
- Centre Hospitalier Universitaire Ambroise Paré
- CHR Verviers
- CHU Erasme
- CHU Sart Tilman
- Cliniques de l'Europe
- Cliniques Universitaires St Luc
- D-CAF MecaTech
- ELCWP (European Lung Cancer Working Party)
- EORTC
- Hopital Erasme
- ESICM (European Society Intensive Care Medicine)
- GIGA-Cancer, Metastasis Research Laboratory
- Grrr-OH (Groupe de recherche en Réanimation Respiratoire en Onco-Hématologie)
- GZA Hospitals Sint-Augustinus
- Hôpital civil Marie Curie (Charleroi)
- IBA (Louvain-La-Neuve)
- IRIBHM
- iTeos Therapeutics
- KU Leuven
- Nine-i multinational network (Caring for critically ill immunocompromised patients)
- Siensano
- UCL
- UCL – MIRO Laboratory (Louvain-La-Neuve)
- ULB
- UNamur – Laboratory URBC
- University of Antwerp
- University of Ghent
- University of Liège
- University of Mons
- UZ Brussel
- VUB

European Collaborations

CARG (Cancer Aging Research Group)
ERS (European Respiratory Society)
SRLF (Société de reanimation de langue française)
EHA SWG (European Hematology Association)
Eurobloodnet
ESC (European Society of Cardiology)
IBCSG
Oncodistinct

- Austria:
  - Vienna (MedAustron Centre)
- Finland:
  - Helsinki (Helsinki General Hospital)
- France:
  - Paris (Institut Imagine, Institut Pasteur, Institut Gustave Roussy, Institut Curie)
  - Rennes (Université de Rennes, CHU)
  - Strasbourg (University of Strasbourg)
  - Dijon (Center Georges Francois Leclerc)
  - Brest (Université de Bretagne Occidentale)
- Germany
  - Hamburg (University of Hamburg)
  - Regensburg (Universität Regensburg)
- Greece (University of Crete)
- Italy:
  - Cagliari (University Hospital in Sardinia)
- Latvia:
  - Riga (Latvian Biomedical Research and Study Centre)
- Luxembourg (TIME, LIH):
  - Institut National du Cancer (INC)
- Netherlands:
  - Amsterdam (NKI)
  - Eindhoven (Philips)
  - Rotterdam (Erasmus MC)
  - Maastricht (Maastricht University)
- Slovenia:
  - Ljubjana (Cosylab)
- Spain:
  - Barcelona (Vall d'Hebron Institute of Oncology)
  - Murcia (University of Murcia)
  - Josep Carreras Leukaemia Research Institute (IJC), Barcelona, Catalonia, Spain
- Switzerland (SIB, ISREC, SIOG, University of Lausanne)
- Sweden:
  - Stockholm (Karolinska Institute and University Hospital)
- United Kingdom:
  - London (Guy's Hospital)
  - Cambridge (Wellcome Trust Sanger Institute)
  - Oxford (Institute of Molecular Medicine, University of Oxford

Collaborations outside Europe

- Canada:
  - Montreal (Lady Davis Institute, Jewish General Hospital, McGill University)
  - Montreal (CR-CHUM, Université de Montréal)
  - Saskatoon (USASK)

- China:
  - Wuhan (College of Chemistry and Molecular Sciences, Wuhan University)
  - Beijing (Chinese PLA General Hospital)

- Israel (The Weizmann Institute of Science)

- Japan:
  - Kumamoto (University of Kumamoto)
  - Tokyo (University of Tokyo)

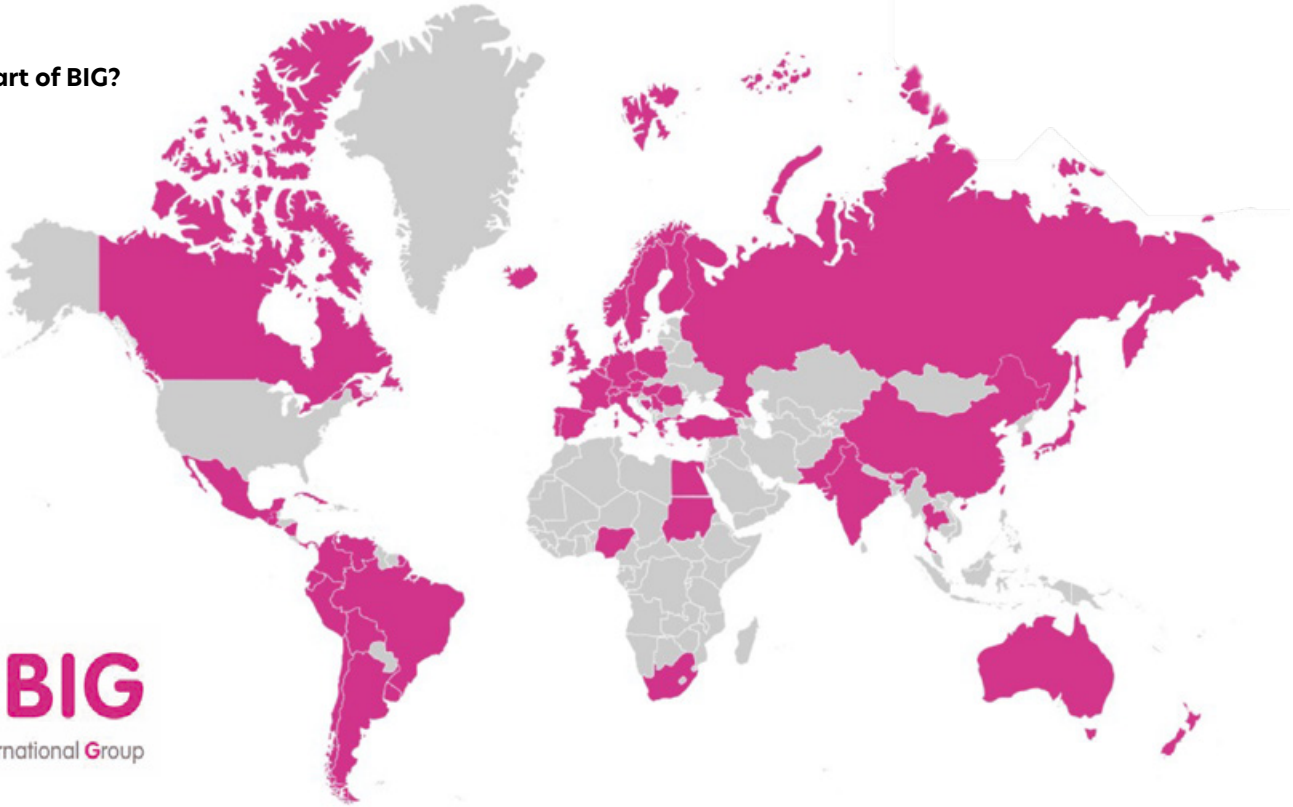
- United Kingdom:
  - London (Institute of Cancer Research)

- USA (NCI, NIH):
  - Baltimore (Sydney Kimmel Cancer Center, John Hopkins University - National Institute on Aging)
  - Boston (Harvard Medical School and Broad Institute of MIT and Harvard, Neutron Therapeutics)
  - Massachusetts (MIT)
  - New York (Albert Einstein College of Medicine, Montefiore Medical Center)
  - Texas (MD Anderson Cancer Center)
  - Washington (McDonnell Genome Institute)
  - Yale (Yale University)
  - Cincinnati (Rieveschl Laboratories for Mass Spectrometry, Department of Chemistry, University of Cincinnati, OH)
  - North Carolina (Duke University)

Participation in trials of international academic research groups

- Alexandra/IMPASSION (BIG/EORTC)
- AURORA (BIG)
- EudraCT
- IMMUCAN SPECTA (EORTC)
- IRAES
- I-SPARC
- MINDACT (EORTC/BIG)
- NEO ALTTO/ALTTO (BIG)
- Aphinity (BIG)
- Olympia (BIG)
- RELEVIUM
- LYSA
- IFM
- HOVON
- SASCIA
- Treat ctDNA (EORTC)
- DECRESCENDO
- TOUCH
- POSITIVE
- OligoCare (EORTC/ESTRO)
- OligoRare (EORTC/ESTRO)

Who is part of BIG?



BIG
Breast International Group

- BIG = ± **60** academic research groups
- It is the **largest international network of collaborative academic research groups** dedicated to breast cancer research
- Covering ± **70** countries on 6 continents
- Running large multinational trials, such as HERA, (Neo)ALTTO, MINDACT, APHINITY, OLYMPIA, PALLAS, ALEXANDRA/Impassion 030 among others

Who is part of ONCODISTINCT?

ONCODISTINCT NETWORK

- **27** cancer centers and university hospitals in **10** countries
- Multidisciplinary and pragmatic Network in Europe and beyond
- Running international trials in solid tumours such as AURA, BRAINSTORM, REGINA and CHANCES (first phase 1 Oncodistinct study)

Funding

Association Jules Bordet

For more than 50 years, cancer research at Institut Jules Bordet has been inseparable from the Jules Bordet Association (formerly "Les Amis de l'Institut Bordet"). As the Institute's first private donor, the Association has raised near 200 million euros in the past half a century, allowing the Institute to achieve a tremendous number of Belgian, European, and even world firsts in the research and treatment of cancer.

Concentrating its activity exclusively on the Institute, the Association is situated at the heart of the fight against cancer. This strategy allows the Association to identify the Institute's needs and to follow the results of its contributions as closely as possible.

True to its mission, the Jules Bordet Association has already provided 18 million euros to support research activities in the New Bordet, including nearly 15.5 million euros to acquire state-of-the-art research equipment.

As the Institute enters a new chapter in its history, the Association has also decided to set up a scientific committee to meet the expectations of this new environment. This committee is composed of scientists internationally recognised for their expertise in oncology and should enable the Association to help develop major breakthrough projects that will make a difference in the fight against cancer.

Jules Bordet Association Scientific Committee: Prof. Wolf Hervé Fridman (President), Prof. Yvan de Launoit (Vice-President); Prof. Eric Deutsch, Prof. Eric Gilson, Prof. Samra Turajlic, Prof. Niels Halama, Prof. Alberto Mantovani, Prof. Daniela Thommen, Prof. Elisabete Weiderpass.

A. Cambier

Research Grants

During the 2020-2024 period our researchers have been awarded highly prestigious research grants by the organisations listed below.

Name of Funder:

- AntiCancer Fund
- Association Jules Bordet
- Belgian Society of Medical Oncology (BSMO)
- Breast Cancer Research Foundation (BCRF - USA)
- European Society of Medical Oncology (ESMO)
- D-CAF MecaTech (in partnership with IBA)
- Erasmus, MC
- Fonds de la Recherche Scientifique - FNRS
- Fonds Ariane
- Fonds Barsy-Laffut
- Fondation ARC pour la Recherche Contre le Cancer
- Fondation FOCA
- Fondation Bekales
- Fondation Jaumotte-Demoulin
- Fondation Lambeau-Marteaux
- Fonds Yvonne Boël
- Fonds d'encouragement à la recherche (FER)
- Fonds Emile Defay
- Fonds Gaston Ithier
- Fondation Kisane
- Fondation Contre le Cancer
- Fondation Cancer Luxembourg
- FRS CDR Grant
- Het Antikankerfonds
- IBS
- Innoviris (Region Bruxelles-Capitale) BBM
- Intergroupe Francophone du Myélome (IFM)
- Iris-Research Fund - King Baudouin Foundation
- KULeuven
- Octobre Rose
- Plan National Cancer
- Région Wallonne
- Rising Tides
- Télévie (FNRS)
- TRANSCAN
- WALInnov
- WBHealth

Visiting Research Fellows (2020-2024)

Country	Name
Argentina	Maria Florencia Illia
Belgium	Karim Gourari
Belgium	Imane Bachir
Belgium	Sebastien Pennickx
Belgium	Christelle Bouchart
Belgium	Madeline Michel
Belgium	Morgane Cogels
Belgium	Tycho de Bakker
Belgium	Thomas Descamps
Brazil	Rafael Caparica
Brazil	Guilherme Nader Marta
Canada	Florence Perrault
China	Yan Jia
France	Kevin Brou Boni
France	Marion Panhaleux
France	Veronique Debien
Greece	George Garefalakis
Greece	Chrysanthi Iliadi
Greece	Andreas Papagiannis
Italy	Alessandro Audision
Italy	Rachele Danieli
Italy	Roberto Casale
Italy	Silvia Camera
Italy	Andrea Pretta
Italy	Elena Trevisi
Italy	Chiara Tomassi
Italy	Elisa Agostinetto
Italy	Flavia Jacobs
Italy	Chiara Molinelli
Italy	Ottavia Amato
Italy	Luca Arecco
Lebanon	Irene Assaf
Lebanon	Antoine El Asmar
Mexico	Grace Gattas
Nigeria	Ajayi Obazee Olugbende
North Macedonia	Magdalena Mileva
Philippines	Jessa Gilda Pandy
Portugal	Filipa Rodrigues Sousa
Portugal	Diogo Martins Branco
Portugal	Soraia Lobo Martins
Portugal	Joana Nunes Gonçalves
Portugal	Ana Rita Freitas
Romania	Marcela Carausu
Romania	Alexandra Stanciu
Saudi Arabia	Hamza Alghamdi
Spain	Ester Vicastillo Paredes
Spain	Raquel Juarez
Turkey	Tugba Akin Telli
Turkey	Arçay Ozturk Ayca
Turkey	Sule Mine Ozturk
USA	Edgar Cardenas
Yemen	Ahmed Shagera Qaid

Awards

2020

- Anaïs Boisson, honourable mention in the 2020 Akoya LinkedIn Usergroup image competition.
- Mattia Rediti – ASCO 2020: "2020 ASCO Annual Meeting Merit Award".
- Soizic Garaud, winner of the 2020 Akoya LinkedIn Usergroup image competition .
- Stamatopoulos Basile - Prix Bekales: "The light chain IgV3-21 defines a new poor prognostic subgroup in chronic lymphocytic leukemia".
- Christelle Bouchart - Belgian Week of Gatroenterology (BWG): Prix de la meilleure présentation orale (BGDO).
- Laurence Buisseret – Fondation contre le Cancer: Mandats en Recherche Translationnelle et Clinique.
- Elisa Agostinetto: ESMO Immuno-Oncology Merit award for the abstract "Cardiotoxicity of immune checkpoint inhibitors: a meta-analysis of randomised clinical trials" at ESMO Immuno-Oncology Congress 2020.

2021

- Bouland Cyril – Prix du Spécialiste de l'année.
- Marcela Carausu - ESMO Research Fellowship: "Interrogating triple-negative breast cancer heterogeneity and its microenvironment at the single-cell level".
- Noémie Thomas, Award recipient of the EACR-Akoya Spatial Phenotyping Award.
- Francesco Sclafani - Fondation contre le Cancer: Mandats en Recherche Translationnelle et Clinique.
- Christelle Bouchart - Belgian Week of Gastroenterology (BWG): Prix de la meilleure présentation orale (Working Group of Digestive Pathology).
- Elisa Agostinetto: ASCO Merit Award for the abstract "The prognostic performance of PREDICT+ in patients (pts) with HER2-positive (HER2+) early-stage breast cancer" at ASCO Congress 2021.

2022

- Martine Piccart – AACR Annual Meeting 2022 – Victoria's Secret Global Fund for Women's Cancers 2022 Meritorious Awards, in Partnership with Pelotonia and AACR.
- Laetitia Collet - ESMO Research Fellowship: "Molecular characterisation of intratumour heterogeneity and tumour microenvironment in high grade serous ovarian cancer and BRCA1/2 mutant breast cancers using spatial transcriptomics".
- Mattia Rediti – ESMO Congress 2022, "ESMO Merit Travel Grant": "Identification of biologically-driven HER2-positive breast cancer subgroups associated with prognosis after adjuvant trastuzumab in the ALTTO trial".
- XiaoXiao Wang - ESMO Congress 2022 "Best Poster Award": "Spatial transcriptomics reveals substantial heterogeneity in TNBC tumour and stroma compartments with potential clinical implications".
- Zelda Paquier (PhD student) - BHPA 2022 – Young scientist award.
- Rachele Danieli (PhD student) - BELNUC 2022 – Medical Physics best oral presentation.
- Elisa Agostinetto: Award "Premio Marzia Galli Kienle 2022" for the paper "Cardiotoxicity of immune checkpoint inhibitors: a meta-analysis of randomised clinical trials" published in European Journal of Cancer, 2021 (award ceremony in June 2022) Diogo Martins Branco: Clinical Scholar Award - San Antonio Breast Cancer Symposium (2022): "Ki-67 index after neoadjuvant endocrine therapy as a prognostic biomarker in patients with HR+/HER2- early breast cancer: a systematic review and meta-analysis".
- Guilherme Nader Marta: 2022 ASCO Conquer Cancer Merit Award. American Society of Clinical Oncology. Project: Impact of cancer diagnosis, stage, and systemic therapies on immunogenicity after COVID-19 vaccination in patients with cancer: A systematic review and meta-analysis.

2023

- Elisa Agostinetto: ASCO Merit Award for the abstract "Clinico-molecular characteristics associated with outcome in breast cancer patients treated with CDK4/6 inhibitors: results from the AURORA (BIG 14-01) Molecular Screening Initiative", ASCO 2023.
- Elisa Agostinetto: Gilead BeLux Breast Cancer Research Award for the project "Single-nuclei RNA-seq and ATAC-seq analysis in ROSALINE, a phase II, neoadjuvant study of targeting ROS1 in combination with endocrine therapy in invasive lobular carcinoma of the breast", February 2023.
- Guilherme Nader Marta: 2023 ASCO Conquer Cancer Award - Endowed Young Investigator Award in memory of Evelyn H. Lauder. American Society of Clinical Oncology. Project: Lutetium-177-PSMA for pretreated metastatic triple negative breast cancer (PRISMA-2).
- Guilherme Nader Marta: ESMO Breast Cancer 2023 - Best Poster Award (Biomarkers and translational research and precision medicine). Project: Circulating tumour DNA for predicting recurrence in patients with operable breast cancer: a systematic review and meta-analysis.
- Guilherme Nader Marta: ESMO Breast Cancer 2023 - Merit Award. Project: Circulating tumour DNA for predicting recurrence in patients with operable breast cancer: a systematic review and meta-analysis.
- Christelle Bouchart - Prix de la Fondation Fernand Hirsch (Gastro-entérologie, AMUB, ULB).
- Morgane Cogels: Award for Best Poster at ImmunoRAD - Paris.

2024

- Luca Arecco: ASCO Conquer Cancer Merit Award "Impact of hormone receptor status and tumour subtypes on clinical behaviour and outcomes of breast cancer in young BRCA carriers".
- Martine Piccart : Lobby Awards 2024 "When inspiring leadership meets exemplarity".
- Elisa Agostinetto: ESMO Breast Merit award/Travel grant for the abstract "Characteristics and outcomes of young breast cancer patients harboring BRCA pathogenic variants according to histologic subtype" at ESMO Breast Congress 2024.
- Alex De Caluwé – Belgian Society of Radiation Oncology (Bestro): Award for Best PhD thesis (Bestro Spring Meeting).
- Christelle Bouchart - Belgian Week of Gatroenterology (BWG): Prix de la meilleure présentation orale (BGDO).

Young talent career development

- PhD Thesis of Rafael Caparica entitled "Stress, adrenergic activation and breast cancer"; Defense presented on 24/05/2023 at Université Libre de Bruxelles (U.L.B) – Promotor – Evandro de Azambuja
- PhD Thesis of Maria Alice Franzoi entitled "Investigating the impact of overweight and obesity on breast cancer patients CDK4/6 inhibitors and endocrine therapy"; Defence presented on 12/03/2024 at Université Libre de Bruxelles (U.L.B) – Promotor – Evandro de Azambuja
- Christelle Bouchart - **Obtention du grade de Doctorat en Sciences Médicales**; ULB – année académique 2023-2024 - Dissertation originale intitulée: "*Contribution à l'étude de la radiothérapie stéréotaxique et de son impact immuno-moléculaire dans le traitement des adénocarcinomes pancréatiques localisés*" Promoteurs: Pr L. Moretti & J-L. Van Laethem

Publications 2023-2024

2023

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