ANNUAL REPORT .23

unicancer RESEARCH

Excellence and Innovation
in patients care

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REPORT .23

• ABOUT US

Leading academic clinical trial sponsor in France, **Unicancer is a major stakeholder in cancer research in France and in Europe.**

Its mission, to move research and treatments forward in a translational approach **using health data; Its ambition, to work to serve public health and benefit all patients**, with a special focus on rare cancer and cancer with poor prognosis and on specific populations, especially paediatric and geriatric.

EDITORIAL

A very eventful year, marked by scientific advancements and major medical innovations! This momentum is set against a backdrop of evolving epidemiology, with the number of cancer cases doubling between 1990 and 2023, including a 100% increase in women and a 90% increase in men. This situation compels and increasingly guides our actions to improve treatments and innovate for the benefit of cancer patients, now and always.

We are proud to have collectively mobilized the resources to implement this and achieve major successes.

With an increasingly refined, yet still imperfect, understanding of the intimate mechanisms of oncogenesis, our discipline and cancer care have entered a remarkable period, marked by significant progress in survival rates, as well as advancements in techniques and patient quality of life.

On one hand, local treatments have led to less invasive procedures, progress in minimally invasive surgery, and the advent of interventional radiology. On the other hand, biotechnology, since the discovery of the role of oncogenes in cancer development, now allows us to classify cancers in entirely new ways.

Finally, thanks to artificial intelligence and image analysis, tools are emerging that will enable us to classify tumor types even more precisely and assist molecular biology in making even more accurate diagnoses.
One of the major consequences of these numerous developments is the fragmentation of cancer pathology into a series of rare, specific diseases, which underpins the development of targeted therapies. This personalized approach to medicine prompts us to reflect, particularly on how to conduct clinical trials.

Our responsibility is to continuously improve treatments and innovate. Unicancer thus promotes the adoption of new clinical trial models and works to facilitate patient access to innovation.

In 2023, the Federation actively committed to ensuring patient access to molecular tests that allow for the genetic characterization of tumors, with a determination to secure standard reimbursement for BRCA-1 and BRCA-2 tests for breast, pancreatic, and ovarian cancers.

Une année très riche, marquée par des avancées scientifiques et des innovations médicales majeures ! Cette dynamique s'inscrit dans un contexte épidémiologique en évolution, avec un doublement du nombre de cas de cancers entre 1990 et 2023, dont une augmentation de 100% chez la femme et de 90% chez l'homme. Cette situation nous oblige et guide toujours davantage nos actions pour améliorer les traitements et innover au service des patients atteints de cancers, encore et toujours.

Nous sommes fiers d'avoir, collectivement, mobilisé les ressources pour le mettre en œuvre et obtenir des succès majeurs.

Avec la connaissance, de plus en plus fine mais encore imparfaite, des mécanismes intimes de l'oncogénèse, notre discipline et la prise en charge du cancer sont entrées dans une période formidable, avec des progrès majeurs enregistrés, en matière de survie mais aussi de techniques et de qualité de vie des patients.

Par les traitements locaux d'une part, vers une diminution de la lourdeur des gestes, les progrès de la chirurgie invasive et l'arrivée de la radiologie interventionnelle.D'autre part la biotechnologie, depuis la découverte du rôle des oncogènes dans le développement des cancers, nous sommes aujourd'hui capables de classer les cancers de manière totalement inédite.

Enfin, grâce à l'intelligence artificielle et l'analyse des images, des outils qui vont nous permettre de classer plus finement encore les types de tumeurs et d'aider la biologie moléculaire à établir des diagnostics encore plus précisément.
L'une des conséquences majeures de ces nombreuses évolutions se traduit par une fragmentation de la pathologie cancéreuse en une série de maladies rares, spécifiques, qui sous-tend le développement des thérapies ciblées. Cette approche personnalisée de la médecine nous invite à nous questionner, notamment dans la manière de conduire des essais cliniques.

Notre responsabilité est d'améliorer les traitements et d'innover, encore et toujours. Unicancer promeut ainsi l'adoption de nouveaux modèles d'essais cliniques et œuvre à faciliter l'accès à l'innovation pour les patients.

En 2023, la Fédération s'est engagée activement en faveur de l'accès des patients aux tests moléculaires qui permettent la caractérisation génétique des tumeurs, avec une détermination à obtenir un remboursement en droit commun des tests BRCA-1 et 2 pour les cancers du sein, du pancréas et de l'ovaire.

Pr. Jean-Yves BLAY
President

- **Sophie BEAUPÈRE**
- General Director

Vecteur d'excellence et d'agilité, Unicancer demeure le premier promoteur d'essais cliniques en oncologie au niveau européen et nous avons la volonté forte de donner une dimension internationale à nos actions, en participant activement aux projets européens et aux programmes et financements communautaires.

Parmi les chercheurs les plus cités en médecine clinique à l'échelle internationale, toutes disciplines confondues, la moitié des cancérologues sont membres du réseau Unicancer.

Les données de santé enfin sont un pilier de l'action d'Unicancer. Notre stratégie de la donnée repose sur le succès des travaux menés dans le cadre de notre entrepôt de données OncoDS lancé en 2023.

Nous souhaitons aller plus loin en consacrant toute l'énergie et les investissements nécessaires afin d'encourager un plus grand partage des données et des outils qui en permettent l'exploitation, et afin de garantir leur interopérabilité.

Nous sommes absolument convaincus que les données de santé concourent à l'amélioration de l'efficacité des traitements en intégrant pleinement les approches de médecine personnalisée et de précision que nous portons depuis plusieurs années.

Evolution exceptionnelle, l'intelligence artificielle va révolutionner les métiers de la recherche. Ces évolutions s'accompagnent ainsi de l'impérieuse nécessiter de former les professionnels de santé et de la recherche à l'utilisation de ces nouveaux outils, mais aussi de former et d'impliquer toujours davantage les patients dans la construction des protocoles de recherche.

2024 sera donc une année charnière, de concrétisation et de poursuite de ces efforts.
Dans un contexte institutionnel complexe, nous continuerons à tracer notre route, celle de l'accès pour tous à une prise en charge de qualité et aux innovations, et du soutien à l'engagement quotidien de nos professionnels et des associations de patients dans la lutte contre le cancer.

A vector of excellence and agility, Unicancer remains the leading sponsor of clinical trials in oncology at the European level, and we have a strong commitment to giving our actions an international dimension by actively participating in European projects and community programs and funding.

Among the most cited researchers in clinical medicine worldwide, across all disciplines, half of the oncologists are members of the Unicancer network.

Health data is, finally, a cornerstone of Unicancer's actions. Our data strategy is based on the success of the work carried out within our OncoDS data warehouse, launched in 2023. We aim to go further by dedicating all the necessary energy and investments to encourage greater data sharing and the tools that enable its exploitation, as well as ensuring their interoperability.

We are absolutely convinced that health data contributes to improving treatment efficacy by fully integrating the personalized and precision medicine approaches that we have been advocating for several years.

As an exceptional development, artificial intelligence will revolutionize research professions. These advancements also bring with them the imperative need to train healthcare and research professionals in the use of these new tools, and to increasingly involve patients in the development of research protocols.

2024 will therefore be a pivotal year, one of realization and continuation of these efforts.
In a complex institutional context, we will continue to forge our path ensuring access for all to quality care and innovations, and supporting the daily commitment of our professionals and patient associations in the fight against cancer.

EDITORIAL

Beginning of 2023, we presented a roadmap outlining our Directorate's ambitions for the coming years.

This strategic roadmap aims to coordinate our actions on major axes such as the evolution of methodologies and clinical research professions, the development of translational research, patient involvement, and national and international collaborations.

Developed with the input of group and project leaders and with strong team engagement, this roadmap was quickly deployed, launching significant projects throughout 2023.

In terms of competencies, we launched a feasibility study to establish a clinical research associate school by the fall of 2025. We aim to enhance the attractiveness of this little-known profession, which is essential for the smooth conduct of trials.

To better integrate and master new technologies—digital, omics—we have also developed partnerships with engineering schools. The goal is to advance even more rapidly in new clinical trial methodologies, relying on evidence-based medicine as well as adaptive trials, decentralized trials with virtual arms, and the integration of real-world data...

We are also developing collaborations with community biologists, community and hospital pharmacists, and nurses. And, of course, with patients who have been at the heart of our co-construction strategy for clinical trials for several years:

we have developed a strategy and charter, training programs for patient representatives who help us design trials that are better accepted by patients and more aligned with their priorities, particularly in terms of supportive care.

They now routinely participate in the development of protocols, the review of study reports, project calls, especially European ones, etc.

Début 2023, nous avons présenté une feuille de route qui porte les ambitions de notre Direction pour les années à venir.

Cette roadmap stratégique a pour objectif de coordonner nos actions sur des axes majeurs que sont l'évolution des méthodologies et des métiers de la recherche clinique, le développement de la recherche translationnelle ou encore l'implication des patients et les collaborations nationales et internationales.

Elaborée avec les responsables de groupes et de projets et avec une forte mobilisation des équipes, cette feuille de route a pu être déployée rapidement avec des projets d'envergure lancés courant 2023.

Sur le volet des compétences, nous avons lancé une étude de faisabilité pour créer, à la rentrée 2025, une école d'attachés de recherche clinique. Nous souhaitons améliorer l'attractivité de ce métier méconnu qui est un maillon essentiel au bon déroulement des essais.

Pour mieux intégrer et maîtriser les nouvelles technologies - numériques, omiques -, nous avons également développé des partenariats avec des écoles d'ingénieurs. L'objectif est d'avancer encore plus rapidement sur les nouvelles méthodologies d'essais cliniques, s'appuyant sur « l'évidence-based medicine » mais aussi sur les essais adaptatifs, décentralisés, avec bras virtuels, ou encore l'intégration des données en vie réelle...

Pr. Muriel DAHAN
Director of Research
and Development

Nous développons aussi les collaborations avec les biologistes de ville, les pharmaciens de ville et hospitaliers, les infirmiers. Et bien sûr avec les patients qui sont depuis plusieurs années au cœur de notre stratégie de co-construction des essais cliniques :

nous avons élaboré une stratégie et une charte, des programmes de formation à destination des patients référents qui nous aident à concevoir des essais mieux acceptés par les patients et plus en phase avec leurs priorités, notamment en matière de soins de support.

Ils participent désormais en routine au développement des protocoles, à la relecture des rapports d'études, aux appels à projets notamment européens, etc.

Beata JUZYNA
Deputy Director of Research
and Development

Renforcer la présence d'Unicancer au niveau européen est une autre priorité tout comme notre positionnement national, sur les appels à projets, vis-à-vis des instances privées et publiques, ou encore en Outre-mer.

Pour renforcer nos liens sur le terrain, nous avons fait en 2023 un « Tour de France des CLCC », qui nous le pensons a été très apprécié, et qui a permis de créer des synergies, de partager les expertises au travers de groupes de travail sur les questions règlementaires, de pharmacovigilance, d'intelligence artificielle par exemple.

Toujours sur ce volet des collaborations, nous avons déployé une charte de labellisation d'études dont nous ne sommes pas promoteurs.

Strengthening Unicancer's presence at the European level is another priority, as is our national positioning on project calls with private and public bodies, including overseas.

To strengthen our ties on the ground, we conducted a "Tour de France of CLCCs" in 2023, which we believe was very well received, and which created synergies and shared expertise through working groups on regulatory issues, pharmacovigilance, artificial intelligence, for example.

In terms of collaborations, we have deployed a labeling charter for studies where we are not the promoters.

To anticipate future directions, we are also undertaking a forward-looking approach to anticipate innovations and developments in research and project calls.

This of course concerns translational research, which took a significant leap forward in 2023 with the almost systematic development of ancillary research for each clinical trial, but also our desire to simplify trial management by adapting resources and budgets to each phase, from inclusion to the follow-up of the last patient.

Our actions always aim for a single objective: to deploy our expertise and efforts to conceive and conduct the most relevant and efficient clinical trials—8 trials were launched in 2023 and 18 are expected to be implemented in 2024—and to contribute to the development of innovation and medical progress for the benefit of patients.

Afin d'anticiper les futures orientations, nous menons aussi une démarche prospective pour anticiper les innovations et évolutions de la recherche et des appels à projets.

Cela concerne bien sûr la recherche translationnelle, qui a pris un véritable essor en 2023 avec le développement presque systématique de recherches ancillaires pour chaque essai clinique, mais aussi notre volonté de simplifier la gestion des essais en adaptant par exemple les moyens et budgets à chaque phase, de l'inclusion jusqu'au suivi du dernier patient.

Nos actions visent comme toujours un seul et même objectif : déployer notre expertise et nos efforts pour imaginer et conduire les essais cliniques les plus pertinents et performants – 8 essais ont été lancés en 2023 et 18 devraient être mis en œuvre en 2024 - et contribuer à développer l'innovation et le progrès médical au bénéfice des patients.

EDITORIAL

The ability to mobilize health data is one of the challenges of the decade and is at the heart of the France 2030 strategy.

2023 will be remembered as a key year with the announcement of the winners of the call for projects for the creation and consolidation of hospital data warehouses. The ambition is significant—to equip every hospital with a data warehouse so that all establishments can communicate with each other using interoperable databases—and it is part of an open science approach, on a national, European, and international scale. **Winner of the first wave of the call for projects, our OncoDS project aims to create an infrastructure dedicated to data sharing based on networking 12 local warehouses from Cancer Control Centers.** A central infrastructure will allow the creation of multicentric cohorts on research questions but also enhance the management of the establishments and further advance the anticipation and management of care pathways.

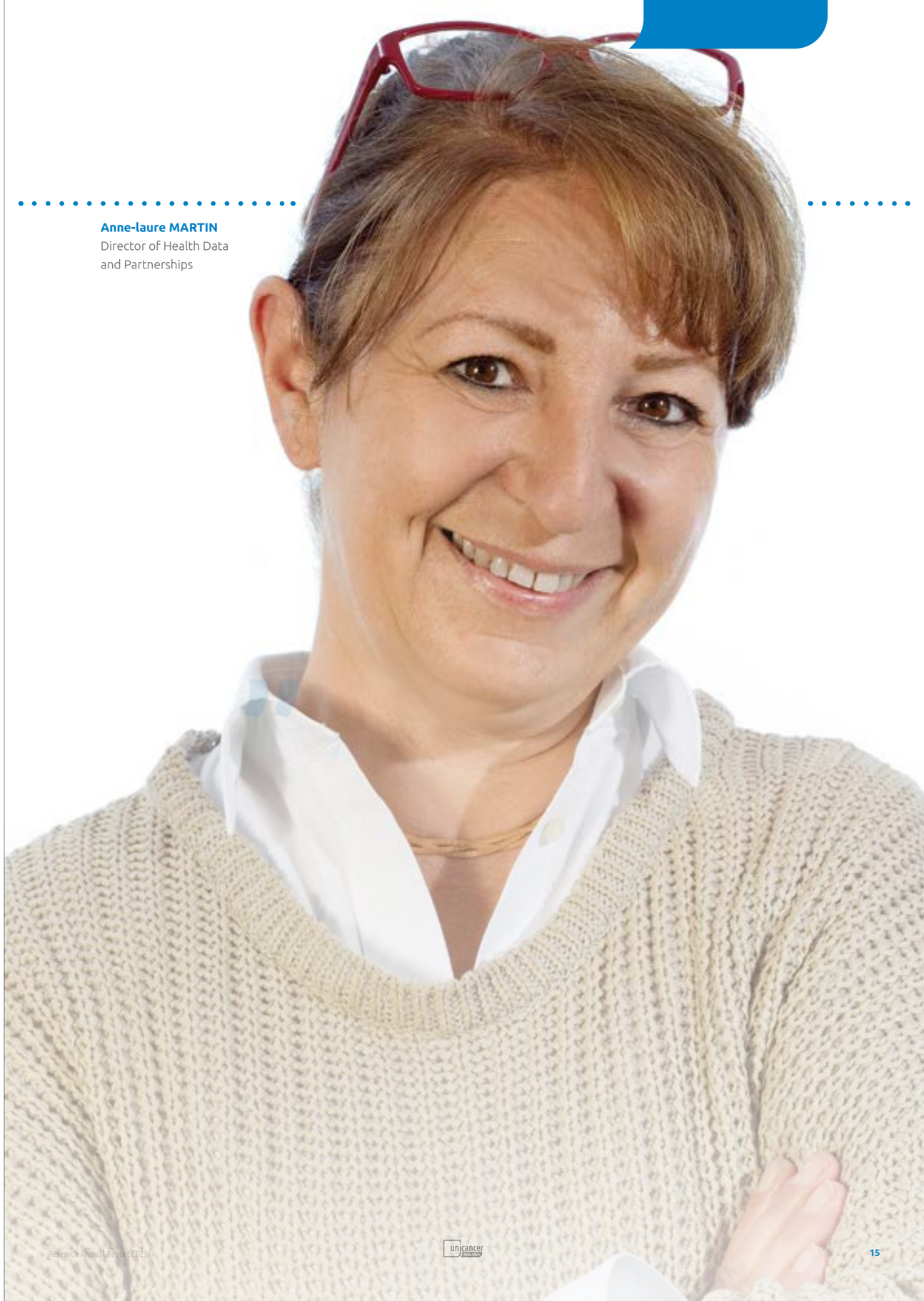
2023 is also a fruitful year for the development of new methodologies applied to clinical research. Health data is indeed a powerful tool enabling clinical research on indications where conducting "classic randomized" trials, the gold standard of proof, is not feasible: niche indications are increasingly common in oncology in the era of molecular biology. External control arms, synthetic arms, or even digital twins are new tools that should enable us to accelerate and amplify research.

La capacité à mobiliser les données de santé est un des enjeux de la décennie et est au cœur de la stratégie France 2030.

2023 restera comme une année clef avec l'annonce des lauréats de l'appel à projets pour la constitution et la consolidation d'entrepôts de données hospitaliers. L'ambition est grande - doter chaque hôpital d'un entrepôt de données pour que tous les établissements puissent communiquer entre eux sur la base de données interopérables - et s'intègre dans une démarche de science ouverte, à l'échelle nationale mais aussi européenne et internationale. Lauréat de la première vague de l'appel d'offre, notre projet OncoDS vise à créer une infrastructure dédiée au partage de données qui s'appuie sur la mise en réseau de 12 entrepôts locaux des Centres de Lutte Contre le Cancer. Une infrastructure centrale permettra de constituer des cohortes multicentriques sur des questions de recherche mais aussi d'enrichir le pilotage des établissements et d'aller plus loin dans l'anticipation et la gestion des parcours de soin.

2023 est également une année riche par les travaux conduits pour le développement de nouvelles méthodologies appliquées à la recherche clinique. Les données de santé sont en effet un outil puissant permettant d'envisager la recherche clinique sur des indications où la conduite d'essais dits "classiques randomisés", gold standard de l'apport de preuve, ne sont pas réalisables : les indications de niche, sont en effet une situation de plus en plus fréquente en cancérologie à l'ère de la biologie moléculaire. Bras contrôles externes, bras synthétiques, voire jumeaux numériques sont autant de nouveaux outils qui doivent nous permettre d'accélérer et d'amplifier la recherche.

Anne-laure MARTIN
Director of Health Data and Partnerships



Other uses, such as the development of algorithmic models integrating Artificial Intelligence, should provide tools to assist in diagnosis and medical and therapeutic decision-making.

The databases and warehouses from programs led by Unicancer over the past 10 years (ESME, CANTO), thanks to the richness and quality of the data they contain, constitute a decisive ground for engaging collaborations with companies specializing in this field. Assistance in interpreting radiological images, and aiding diagnosis through the reading and interpretation of digitized pathology slides represent a crucial challenge and issue for the oncology of tomorrow with a clear objective: to improve diagnosis and patient care. Of course, these developments must be carried out under controlled conditions and with the exercise of human oversight behind every device incorporating artificial intelligence.

D'autres usages tels que le développement de modèles algorithmiques intégrant l'Intelligence Artificielle doit permettre d'apporter des outils d'aide au diagnostic et à la décision médicale et thérapeutique.

Les bases de données et entrepôts des programmes conduits par Unicancer depuis 10 ans maintenant (ESME, CANTO), par la richesse et la qualité des données qu'ils contiennent, constituent un terreau décisif pour engager des collaborations avec des sociétés spécialisées dans ce domaine. L'aide à l'interprétation des images radiologiques, l'aide au diagnostic par la lecture et l'interprétation des lames digitalisées d'anatomopathologie représentent un défi et un enjeu crucial pour la cancérologie de demain avec un objectif clair : améliorer le diagnostic et la prise en charge au bénéfice des patients. Bien sûr ces évolutions devront se faire dans des conditions maîtrisées et avec l'exercice de la garantie humaine derrière chaque dispositif embarquant de l'intelligence artificielle.

In summary, the objective is the same across all programs (ESME, ODH, CANTO), tools (ConSoRe), and infrastructures (WeShare) that we implement: to access quality data, further exploit this data, and pose research questions open to all use cases, particularly concerning care pathways, city-hospital coordination, the impact of cancer and treatments on patients' lives, post-cancer, and exploring the socio-economic aspects of the disease and its management, and to align with public health policies by offering effective tools for evaluating treatments and care.

This period is exciting: we are bringing to fruition everything that has been envisioned for years. Oncology is a true laboratory of innovations, whether we are talking about personalized medicine or the contributions of AI or machine learning. Our role at the Data & Partnerships Department is to support our researchers and the CLCCs in this capacity and willingness to mobilize data that has and will have an impact on patient care, diagnosis, service organization, care pathways, professions, and training.

2024 will be a pivotal year, positioning data at the service of research methodology, physicians, and patients, and at the heart of the prospective approach launched in 2023 to envision the oncology of tomorrow.

De façon synthétique, l'objectif est le même dans tous les programmes (ESME, ODH, CANTO), outils (ConSoRe), infrastructures (WeShare), que nous mettons en œuvre : accéder à des données de qualité, aller plus loin dans l'exploitation de ces données, poser des questions de recherche s'ouvrant à tous les cas d'usage notamment sur les parcours de soin, l'articulation ville-hôpital, le retentissement du cancer et des traitements sur la vie du patient, l'après-cancer, explorer les aspects socio-économiques de la maladie et de sa prise en charge, s'inscrire dans les politiques de santé publique en proposant des outils performants pour l'évaluation des traitements et des prises en charge.

Cette période est enthousiasmante: nous sommes en train de concrétiser tout ce qui a été imaginé depuis des années. L'oncologie est un vrai laboratoire d'innovations, que l'on parle de médecine personnalisée ou d'apport de l'IA ou du machine learning. Notre rôle à la Direction Data & Partenariats est d'accompagner nos chercheurs et les CLCC dans cette capacité et cette volonté à mobiliser les données qui ont et vont avoir un impact sur la prise en charge des patients, le diagnostic, l'organisation des services, les parcours de soin, les métiers et la formation.

2024 sera une année charnière positionnant les données au service de la méthodologie de recherche, des médecins et des patients, et au cœur de la démarche prospective lancée en 2023 pour imaginer la cancérologie de demain.

2023 UNICANCER KEY FIGURES

unicancer

Unicancer is ISO 9001 certified for its clinical research activity

12 248
PATIENTS
included in Unicancer R&D sponsored-clinical trials of which **9642** in MyPeBS

181 000
PATIENTS
registered in the ESME, CANTO and ODH database

8
NEWLY INITIATED CLINICAL TRIALS

104
ONGOING CLINICAL TRIALS
for the Unicancer R&D department, including **50** recruiting trials

198
INVESTIGATIONAL SITES INVOLVED*
(public hospitals, private clinics, comprehensive cancer centres), including **32** Abroad

** The French general practitioners, gynaecologists and radiologists who contributed to the MyPeBS recruitment in 2019 are not included in this number.*

UNICANCER RESEARCH PRIORITIES AND CHALLENGES

Over 2022-2023, this commitment is seen in three strategic priorities answering to the main challenges of oncology in the 21st Century:

1 UNDERSTAND AND ERADICATE CANCER

Faced with a polymorphic, progressive and sometimes so-called chronic disease, Unicancer uses an integrated and comprehensive approach.
From research into risk factors through the development and evaluation of new therapies, to post-cancer mental health and welfare care, and investing especially in:

- **Development** of early phase trials to fast track access to innovation, especially for cancer with poor prognosis,
- **Study** of the benefit-risk ratio of new treatments,
- **Evaluation** and optimisation of treatment strategies and sequences,
- **Personalisation** of treatments according to the genetic and molecular profile of patients and tumours,
- **Prevention** and early detection of cancer especially through large cohort studies,
- **Improvement** of quality of life of patients by treatment de-escalation and long-term follow-up.

2 BE AT THE FOREFRONT OF KNOWLEDGE AND TECHNOLOGIES

Positioning ourselves at the front of oncology innovations requires combining scientific excellence, new paradigms and disruptive technology. Spearhead of innovation in oncology, as much in research as in care, Unicancer has taken a firm stance on:

- **Circulating DNA detection techniques** for improving early diagnosis, predicting treatment response, refining the prognosis and adapting supportive care,
- **Collection and exploitation of health data**, by launching or integrating large-scale data-base programmes and working on their interoperability,
- **Artificial intelligence** especially to support pathology.

3 MEET UNMET MEDICAL NEEDS AND MAJOR HEALTH ISSUES

Go where no one has gone before, to areas little covered by the pharmaceutical industry, looking at specific populations, especially the elderly, targeting rare cancers and cancer with poor prognosis: Unicancer dedicates a large part of its activity to rare diseases, because the medical and human challenges are significant in that area.
Beyond that, by investing in translational research and cross-analysis of data from clinical trials and real-life health data, Unicancer has been rolling out an innovative and to the purpose R&D strategy.
As a bonus, major publications hailed by the international community and changes in practices to benefit patients. Improving patient treatment and quality-of-life and answering to major health issues remains Unicancer's ambition in the years to come.

UNICANCER STRENGTHS & ASSETS

A network of 18 French Comprehensive Cancer Centers and 2 afiliates members, exclusive expertise in cancer, a culture of collaboration, integrated approach to the fight against cancer, Unicancer Research's strengths and assets can be covered in 3 points:

1 EXPERTISE AND INTEGRATION

- **French network** of dedicated cancer centres working on the three missions that are care, research and training.

- **A philosophy and organisation true to the spirit of Comprehensive Cancer Centers**, leading to integrated and multidimensional management and a cross-sectoral research approach, from fundamental research to real-life data, through clinical research, with a new Data Department especially.

- **Researchers** with groups per therapeutic area and cross-disciplinary groups for reinforced, but shared and collegial expertise.

2 AGILITY, LEADING-EDGE TECHNOLOGIES, PRAGMATISM

- **Unicancer, an expert, human-sized network** with tried-and-tested and efficient networking.

- **A combination of agility and pragmatism** so as not to spread resources thin and to use all sources and opportunities for innovation.

- **Leading-edge technical hubs** for conducting innovative and ambitious projects.

- **ISO 9001-certified** clinical research activity.

- **A biological resource** centre in Lyon, a data centre in Montpellier.

- **Certified and centralised** biobanks and data platforms.

3 NETWORK, PARTNERSHIP AND COLLABORATION

- **The coming together** of site research and a network within cancer centres and research through major programmes coordinated by Unicancer R&D Departments.

- **A tradition** within cancer centres raised to the rank of philosophy and strongly anchored in how Unicancer operates.

- **A historic leaning** which is seen in terms of multidisciplinarity, but also internationally and with all types of bodies, especially public-private (pharmaceutical companies and start-ups).

- **Two concrete examples:**
  - MATWIN (Maturation & accelerating translation with industry): innovation development centre in oncology and example of Unicancer's ambitious partner-based and translational dynamic.
  - EORTC (European Organization for Research and Treatment of Cancer) liaison office: a central role and recognition of Unicancer's excellence in cancer research.

PATIENT'S ROLE

PATIENTS AT THE HEART OF UNICANCER RESEARCH

The growing involvement of patients as active partners in the co-construction of research projects managed by UNICANCER R&D.

This marks a significant shift towards a more collaborative, patient-centred approach. Traditionally, clinical research has been conducted by researchers and healthcare professionals, with patients playing a generally passive role as study subjects. However, it is now recognized that patients have a unique expertise based on their experience of living with disease and treatment, which can greatly enrich clinical research.
By including patients right from the initial design phases of projects, we enable clinical studies to be co-constructed, taking into account patients' needs, preferences and priorities. Their active participation helps to define more relevant research objectives and to develop study protocols that better reflect patients' realities and expectations.

INVOLVING PATIENTS IN CLINICAL RESEARCH HAS SEVERAL ADVANTAGES :

- **It ensures that studies focus on issues that have a real impact on patients' lives.** By taking their perspectives and needs into account, we can steer research towards questions that have direct clinical significance and the potential to transform care.

- **Active patient participation promotes informed decision-making.** Their input into the development of protocols, selection criteria and judgement criteria provides valuable insights, taking into account both medical considerations and patient preferences. This collaborative approach leads to more balanced and relevant decisions.

- **Patient involvement strengthens adherence to treatments and study protocols.** By feeling involved and informed, patients are more likely to follow medical recommendations, actively participate in clinical trials and provide valuable data for treatment evaluation.

- **This better adaptation of protocols to what is acceptable to patients makes it possible to improve patient inclusion in trials.**

UNICANCER WANTS TO ACTIVELY INVOLVE PATIENTS IN CLINICAL RESEARCH

Their role in co-constructing projects is essential to ensure that clinical studies are relevant, patient-centered and likely to lead to significant medical advances.
As part of our commitment to promoting the active participation of patients in clinical research, without lengthening timeframes, we offer a series of initiatives aimed at integrating patients into various stages and processes of our projects. Here are just a few examples of these opportunities :

- **Consent/information leaflet** (in progress): We are working with the **Ligue contre le cancer** on this subject. The review of consents and information leaflets is fundamental to ensure that patients fully understand the implications of their participation in a clinical study. By giving patients the opportunity to review these documents, we show our respect for their autonomy and their right to make an informed decision about their participation. Clinical study documents can often contain complex medical jargon. The patient perspective helps to simplify language and makes information more accessible, improving overall understanding and minimizing the risk of misunderstanding.

- **CRP/Project feasibility committees** (coming soon): We invite referent patients to join project feasibility committees, where they will have the opportunity to better understand the challenges of clinical research and project implementation. Their active participation will also enable them to ask questions and give their opinion on the feasibility and acceptability of the studies, thus ensuring that projects meet patients' needs and expectations.

- **Document review:**

  - **Protocol Review Committees (PRC)** (coming soon): This involvement will enable patients to play a role in validating study methodology by participating in protocol review committees, and will have a significant added value.

  - **Proofreading of end-of-study reports for patients** (ongoing): Expertise as patients will provide a unique perspective on the clarity and accessibility of results for patients, ensuring that studies are tailored to their target audience.

- **(EU AAP) European calls for projects** (coming soon): Co-construction of European projects to contribute to the identification of relevant research themes and discussions on oncology research priorities. Patient involvement will help European research funds towards areas that have a direct impact on cancer patients.

- **Supportive care workgroups** (coming soon): We propose to integrate patients into the supportive care workgroups, enabling them to suggest relevant research topics to improve their quality of life during and after treatment. Their experience as patients will enrich discussions and ensure that supportive care truly meets patients' needs.

- **Inclusion of referent patients in our Unicancer scientific events with patient feedback** (ongoing):
We offer patients the opportunity to share their experience with the scientific community at our scientific events. Their testimonials will help raise 2 awareness among healthcare professionals of the issues and needs of patients, fostering better mutual understanding and closer collaboration.

- **Participation in in-house training courses** (coming soon) :
We offer in-house training courses to inform them about key aspects of clinical research, such as :
  - Studymethodology, o Researchethics,
  - Data protection.

These training courses will strengthen patients' ability to contribute in an informed and meaningful way to the various stages of clinical research.

- **Involvement of patients in the construction of regulatory dossiers (patient vision), e.g. for meta-analyses and data sharing - CNIL dossiers** (to come):
We invite patients to participate in the examination of regulatory dossiers, guaranteeing the quality and transparency of studies, but also to give their point of view as patients on data sharing and exploitation.

TO FURTHER STRENGTHEN PATIENT INVOLVEMENT IN CLINICAL RESEARCH, WE PROPOSE THE FOLLOWING MEASURES:

- **Referent patients by organ groups and transversal groups:** These referent patients will play a key role in representing patients' interests and facilitating their active participation in clinical research. They will help establish an essential link between patients and researchers.

- **Bi-annual feedback meetings where they can share their experience and ideas:** These meetings establish a constructive dialogue between patients, researchers and healthcare professionals, fostering better mutual understanding and fruitful collaboration.

- **Co-building national and international surveys on patient involvement in research, with the aim of sharing patients' experiences:** Their experience and point of view will enrich these surveys, enabling us to better understand patients' needs and expectations, and to share this experience with the international community.

By implementing these measures, we aim to strengthen patient involvement in clinical research, recognizing their unique expertise and positioning them as genuine partners in the co-construction of research projects.

This collaborative, patient-centered approach will help improve the relevance, the quality and the impact of clinical studies, while ensuring that patients' needs and expectations are fully taken into account.

EXPERTS GROUPS

Unicancer provides structural support to 10 internationally recognised and multidisciplinary expert groups dedicated to designing and steering innovative clinical studies. Their goals are to offer patients access to innovative treatments, to optimise therapeutic strategies and to contribute to scientific education and dissemination in their field, notably by developing collaborative networks.

TUMOR GROUPS

UCBG unicancer

French Breast Cancer Intergroup

President : Dr Thomas BACHELOT, Centre Léon Bérard, Lyon
Strategic priorities : Subtypes with poor prognosis, biology-driven strategies of therapeutic de-escalation, survivorship.

UCGI unicancer

Gastro-intestinal Group

President : Dr Christelle DE LA FOUCHARDIÈRE, Institut Paoli Calmettes, Marseille
Strategic priorities : Innovative phase II studies, new diagnostic approaches towards personalized treatment, translational research, large randomised phase II/III studies, rare cancers.

GETUG unicancer

Genitourinary Group

President : Pr Karim FIZAZI, Gustave Roussy, Villejuif
Strategic priorities : Therapeutic strategy studies, research programmes in rare tumours, development of biological research programmes in connection with clinical projects.

UCH&N unicancer

Head & Neck Group

President : Dr Caroline EVEN, Gustave Roussy, Villejuif
Strategic priorities : Early-phase studies, rare cancers, biology-driven medicine.

Sarcoma Group unicancer

Sarcoma / Rare cancers Group

President : Dr Nathalie GASPARD, Gustave Roussy, Villejuif (paediatrics) ; Pr Jean-Yves BLAY, Centre Léon Bérard, Lyon (adults)
Strategic priorities : Improvement of early management of sarcomas and other rare connective tissue tumours, translational research, biobankings.

CROSS-PATHOLOGY GROUPS

Immuno-Oncology Group unicancer

Immuno-oncology Group

President : Pr Frédérique PENAULT-LLORCA, Centre Jean Perrin, Clermont Ferrand
Strategic priorities : Cancer immunotherapy research, translational research, identification of predictors and biomarkers of extreme response or poor tolerance to immunotherapy.

GERICO unicancer

Oncology Geriatrics

President : Dr Capucine Baldini, Gustave Roussy, Villejuif
Strategic priorities : Innovative clinical research in oncogeriatry, methodological adaptation of the evaluation criteria to the geriatric population, diagnostic and therapeutic rationalisation. Expertise in the evaluation and description of geriatric populations, promote the use of G-CODE developed in the framework of DIALOG (Oncogeriatric intergroup associating SOFOG), specific questions for elderly subjects, innovative methodology & adaptive phase II, Evaluation of strategies in elderly patients.

Personalized Medicine Group unicancer

Personalised Medicine Group

President : Pr Christophe LE TOURNEAU, Institut Curie, Paris
Strategic priorities : Personalized biology-drivenmedicine, proof of concept studies, identification of predictors or biomarkers of treatment efficacy or resistance.

Supportive Care Group unicancer

Supportive Care Intergroup

President : Dr Didier MAYEUR, Centre Georges François Leclerc, Dijon
Strategic priorities : High standard clinical programmes for the evaluation of supportive cares, quality of life, cost-efficiency, humanities and social sciences. 4 strategic axes have been identified: The organization of the care pathway, Symptom management, Health Behaviour, Develop and strengthen patient trials.

UNITRAD unicancer

Translational Research and Development in Oncology Radiation

President : Dr Sophia RIVERA, Gustave Roussy, Villejuif
Strategic priorities : Changing practice clinical studies integrating translational research, Artificial Intelligence radiomic/Imaging, radiobiology (immunoradiotherapy/radiosensitivity/radiopotentialisation), radiotherapy quality assurance, PROMs and real-world data, new technologies and physics innovation.

MATWIN

MAturation and Accelerating Translation With INdustry

MATWIN is a French open-innovation platform, fully-owned subsidiary of Unicancer, dedicated to supporting innovation in oncology. For fifteen years, the platform has been offering various actions (expertise, accelerator programme, events, etc.) aiming at accelerating the development of innovative projects dedicated to the fight against cancer.

MATWIN manages 3 mains actions: the MATWIN accelerating program, a cancer-focused partnering event MEET2WIN, and the OncoSTART consortium which supports entrepreneurship in oncology.

www.matwin.fr

The program is based on a continuing partnership with major international companies keen to develop partnerships in the field.

Amgen, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Exact Sciences, GlaxoSmithKline, insitro, MSD, Pierre Fabre, Pfizer, Roche, Sanofi, Takeda

The MATWIN program is fully focused on supporting European scientists or entrepreneurs working on R&D innovative oncology projects, offering them access to expertise, coaching/mentoring and showcase opportunities to enhance their development potential during a 3 or 6 month-support.

In addition to this program, MATWIN is organizes also annually MEET2WIN, a European Partnering Convention entirely focused on oncology.
The event gathers nearly 300 European and international attendees (pharmaceutical companies, biotechs, startups, researchers, clinicians, investors, support structures, etc.) and generates +1,000 face-to-face meetings to optimize collaboration opportunities in the oncology area. This event has proved increasingly successful and is becoming a reference networking event to boost collaborative opportunities in the oncology field in Europe.

+300 SUPPORTED PROJECTS

50 STARTUPS CREATED POST MATWIN SUPPORT

+50 PROJECTS TRANSFERRED TO EXTERNAL PARTNERS

+20 CLINICAL TRIALS STARTED (2017-2023)

www.oncostart.fr

MATWIN is also in charge of the coordination of **OncoSTART**, a **French consortium** which brings together **14 key national organisations** dedicated to oncology research and innovation, pooling their specific ewxpertise, know-how and networks to boost entrepreneurship in the fight against cancer.

MEET2WIN

Each year, MEET2WIN is combining conferences, workshops, projects elevator pitches and thousands of face to face meetings.

A large time is dedicated to networking, and a showcase is offered for startups looking forward to fundraising via a dedicated session called OUI (Oncology Upward Investment).

MEET 2WiN
Oncology Partnering Convention

www.meet2win.fr

This specific session allows selected companies to pitch their innovative solutions in front of a review panel of 15 major European investors able to support their growth, thus offering new opportunities of development support to leverage cutting edge innovation in oncology.

INTERNATIONAL COLLABORATIONS

Several major trials sponsored by Unicancer are conducted at an international level, thanks to key partnerships with other academic cancer research groups, or through an extended network of collaborating university hospitals and research teams, mainly in Europe but also overseas. **Unicancer**, as a major European academic sponsor in oncology, **seeks to gain worldwide visibility, with the ultimate goal of developing high-quality practice-changing clinical research and accelerating patients' access to innovation.**

Unicancer's international partners

NORTH AMERICA - AFT, ALLIANCE, CCTG, NCI, NCIC, NCCTG, MCCRC, SWOG

EUROPE - BIG, EADO, EORTC*, ESMO, GBG, GONO, ICR-CRUK, IBCSG, NCRI, NKI, SABO, SAKK, SOLTI

ISRAEL - ASSUTA

GLOSSARY

AFT - *Alliance Foundation Trials in oncology*
BIG - *Breast International Group*
CCTG - *Canadian Cancer Trials Group*
CRUK - *Cancer Research UK*
EADO - *European Association of Dermato Oncology*
EORTC - *European Organisation for Research and Treatment of Cancer*
FAGE - *Federación Argentina de Gastroenterología*
GBG - *German Breast Group*
ICR-CRUK - *Institute of Cancer Research - Cancer Research UK centre*
IBCSG - *International Breast Cancer Study Group*
GONO - *Gruppo Oncologico del Nord Ovest*
MCCRC - *Multiprofessional Critical Care Review Course*
NCCTG - *North Central Cancer Treatment Group*
NCI - *National Cancer Institute - USA*
NCIC - *National Cancer Institute of Canada*
NCRI - *National Cancer Research Institute - UK*
NKI - *Netherlands Cancer Institute*
SABO - *Swedish Association of Breast Oncologists*
SAKK - *Groupe Suisse de Recherche*

HIGHLIGHTS :

31 ACTIVE INTERNATIONAL TRIALS

7 ACTIVE COUNTRIES OUTSIDE OF FRANCE

110 RECRUITING SITES OUTSIDE OF FRANCE

(2016 - 2023 activity)

• CLINICAL RESEARCH

Optimizing diagnosis, exploring new therapeutic avenues, tailoring care to each patient, combining treatments to maximize response, and bringing together expertise at an international and particularly European level: these are the guiding principles of the trials conducted by the various Unicancer organ-specific or transversal groups.

In 2023, there is a particular focus on circulating tumor DNA, toxicity, therapeutic de-escalation, and multitherapies.

MAIN CLINICAL RESEARCH PROJECTS: PEACE

THE PEACE PROGRAM: ACHIEVEMENTS AND PERSPECTIVES IN PROSTATE CANCER PHASE 3 TRIALS

The European Consortium on Prostate Cancer (PEACE: Prostate Cancer Consortium in Europe) was established in 2013. It is a pan-European research group open to all prostate cancer specialists. With studies requiring increasing numbers of patients, genitourinary cancers experts from European organizations, including Unicancer via its GETUG expert group led by Prof Karim Fizazi, medical oncologist at Gustave Roussy, have come together to significantly contribute to research and best practices in prostate cancer treatment.

Since its creation, PEACE has facilitated the implementation of several phase III trials to address questions regarding the use of new therapeutic options for patients with prostate cancer:

STUDY NAME	BRIEF SUMMARY	STATUS EUROPEAN COUNTRIES	SPONSOR
PEACE 1 (GETUG-AFU 21)	A prospective phase III randomized study evaluating the combination of androgen deprivation therapy with docetaxel, with or without radiotherapy, with or without abiraterone and prednisone in patients with metastatic hormone-naïve prostate cancer (NCT01957436)	*Recruitment closed :* Germany, Belgium, France, Ireland, Italy, Romania, Spain, Switzerland	Unicancer
PEACE 2 (GETUG-AFU 23)	A randomised phase III factorial design, of cabazitaxel and radiotherapy targeted at pelvic lymph nodes in patients with localized prostate cancer presenting at least two high-risk relapse characteristics (NCT01952223)	*Recruitment closed :* Belgium, France, Italy, Spain	Unicancer
PEACE 3	A multicenter randomized phase III study comparing enzalutamide and the combination of Ra-223 and enzalutamide in patients with castration-resistant prostate cancer with asymptomatic or moderately symptomatic bone metastases (NCT02194842)	*Recruitment closed :* Belgium, Denmark, France, Ireland, Italy, Norway, Poland, Spain, Switzerland, United Kingdom	EORTC
PEACE 4	A phase III study evaluating the impact on survival of acetylsalicylic acid and atorvastatin in patients with castration-resistant prostate cancer (NCT03819101)	*The study is currently enrolling :* France, Switzerland	Gustave Roussy
PEACE 5 (STORM)	A randomised phase II trial addressing the question of salvage treatment for oligometastatic nodal relapse prostate cancer (NCT03569241)	*The study is currently enrolling :* Belgium	Ghent University

More recently, the Prostate Cancer Consortium has launched a program of multiple trials across 14 European countries. Under the PEACE 6 UMBRELLA PROGRAM, patients with metastatic prostate cancer will be assigned to a specific randomized comparative phase III trial of combination therapy vs standard of care (SoC) based on patient and disease characteristics.

TO THIS END, FOUR TRIALS HAVE BEEN SET:

- **PEACE 6 OLIGO PRESTO** is evaluating the role of local ablative treatment of metastases in hormone-sensitive oligometastatic prostate cancer patients (NCT04115007).

  SPONSOR: UNICANCER / STATUS: CURRENTLY ENROLLING

- **PEACE 6 VULNERABLE** is evaluating the efficacy of ADT ± darolutamide in de novo metastatic vulnerable prostate cancer patients with impaired functional capacity and ineligible for docetaxel or androgen receptor-targeted agents (NCT04916613).

  SPONSOR: UNICANCER / STATUS: CURRENTLY ENROLLING

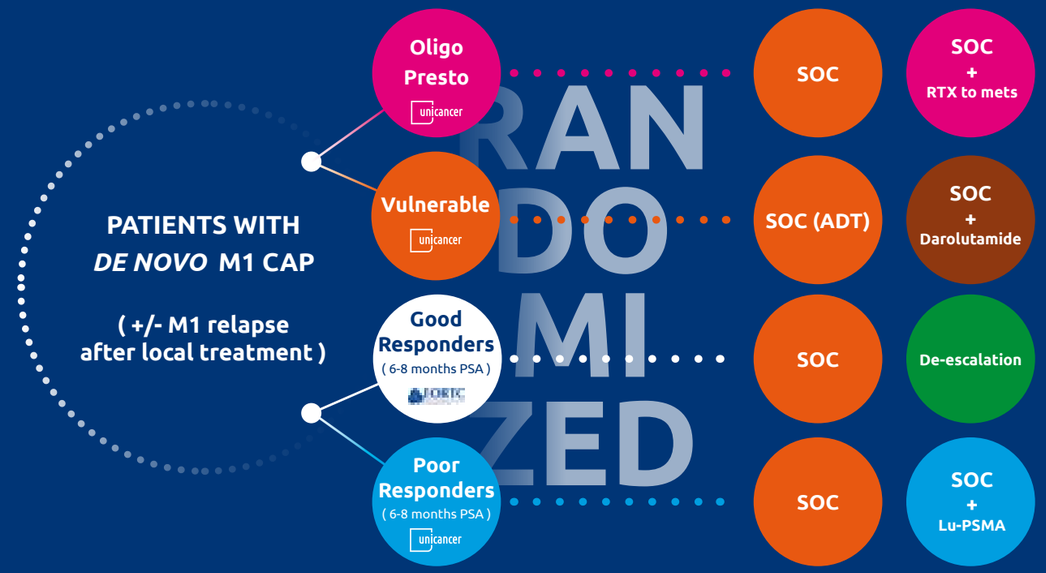
- **PEACE 6 GOOD RESPONDERS** is a pragmatic trial evaluating intermittent androgen deprivation therapy in the era of androgen receptor signaling pathway inhibitors (AR) (NCT05974774).

  SPONSOR: EORTC / STATUS: PATIENT ENROLLMENT IS EXPECTED TO START IN Q2 2024

- **PEACE 6 POOR RESPONDERS** is evaluating the efficacy of 177Lu-PSMA-617 combined with SoC versus SoC alone in patients with de novo metastatic hormone-sensitive prostate cancer with a serum PSA level ≥ 0.2 ng/ml (EudraCT 2022-502408-57-00).

  SPONSOR: UNICANCER / STATUS: PATIENT ENROLLMENT IS EXPECTED TO START IN Q2 2024

Additional trials may be added later, to cover any significant changes in the therapeutic landscape and the evolution of clinical guidelines.



In 2023, 2 new trials (PEACE 7 and PEACE 8) as part of the PEACE program were in preparation to evaluate the use of stereotactic radiotherapy in patients with localized or castration-resistant prostate cancer. Both trials are sponsored by Unicancer, with the aim of enrolling the first patient in 2024.

MAIN CLINICAL RESEARCH PROJECTS : MyPeBS

The MyPeBS (My Personal Breast Screening) project is a large-scale clinical trial to evaluate a new approach to breast cancer screening.

The study is being conducted in several European countries, randomized and multicentre with the purpose of evaluating the effectiveness of a personalised breast cancer screening.

MyPeBS seeks to develop a new fundamental approach to breast cancer screening that takes into account a given woman's individual risk factor for developing the disease compared to a standard screening.

Overall, we hope to recruit **56,435 women volunteers** (approximately 12,500 in France), living in Italy, France, the UK, Israel, Belgium, or Spain; aged between 40 and 70, and with no history of breast cancer. The personal experience of these women is crucial in this new procedure that this study is undertaking, as well as the associated psychosocial aspects that will be analyzed in MyPeBS and compared to the standard arm.

www.mypebs.eu

The ultimate goal of MyPeBS is to provide a more effective (better benefit/risk ratio) **breast cancer screening in Europe**, while demonstrating the acceptability, practical feasibility, and economic viability of such an approach. MyPeBS is a groundbreaking initiative that has the potential to transform breast cancer screenings and improve outcomes for women.

This 8 year project is coordinated by Dr Suzette Delaloge (Gustave Roussy, Villejuif) and managed by Unicancer.

MyPeBS
Personalising Breast Screening

CUMULATIVE INCLUSION OF PARTICIPANTS BY COUNTRY
IN THE MYPEBS STUDY AS OF DECEMBER 31, 2023

21 062 ITALY

10 656 FRANCE

9 964 ISRAEL

6 268 GREAT BRITAIN

3 001 SPAIN

2 192 BELGIUM

It involves 27 partners in 8 countries and is funded by the EU (H2020 - grant agreement number 755394) and the French NCI in France (PHRC 2017 research programs).
Sponsored by Unicancer, the MyPeBS clinical trial started in July 2019 and has included **53,143 participants as of December 31, 2023 (recruitment has been closed on July 31, 2023),** distributed as shown in the figure, while a total of 9,686 participants were recruited in 2023.

Results are expected on 2028 after the last follow-up of the participant.

INCLUSIONS BY EXPERT GROUPS

NUMBER OF PATIENTS INCLUDED IN 2023

PER GROUP AND PER INSTITUTION TYPE

	UCBG	UNITRAD	MED PERSO	UCGI	GETUG	IOG	SARCOMA	SDS	GERICO	UCH&N	UNICANCER SPECIFIC PROJECTS	TOTAL	%
Public hospitals of Paris (AP-HP)	615	36	1	87	87	49	12	4	4	23	0	918	7,5 %
Other public hospitals (excl AP-HP)	8319	0	0	19	19	0	0	0	0	0	0	8357	68,2 %
FCCCs	1417	147	5	80	275	61	14	16	10	35	0	2060	16,8 %
Other private non-profit hospitals	7	1	0	38	10	6	2	0	0	11	0	75	0,6 %
Private clinics	253	47	2	19	80	11	0	0	0	1	0	413	3,4 %
City medical practice	24	8	0	22	16	2	0	3	0	0	0	75	0,6 %
Foreign institutions	350	0	0	0	0	0	0	0	0	0	0	350	2,9 %
TOTAL	10985	239	8	265	487	129	28	23	14	70	0	12248	
POURCENTAGE	89,7 %	2,0 %	0,1 %	2,2 %	4,0 %	1,1 %	0,2 %	0,2 %	0,1 %	0,6 %	0,0 %		

FOCUS ON THE UNICANCER NETWORK

OF FRENCH COMPREHENSIVE CANCER CENTRES (FCCCS)

	UCBG	UNITRAD	MED PERSO	UCGI	GETUG	IOG	SARCOMA	SDS	GERICO	UCH&N	UNICANCER SPECIFIC PROJECTS	TOTAL	%
Léon Bérard center	165	3	0	1	5	0	8	0	2	1	0	186	9,0 %
Jean Perrin center	41	1	0	3	7	3	0	0	0	0	0	55	2,7 %
Curie Institute	83	7	0	0	2	1	0	0	0	0	0	90	4,4 %
Gustave Roussy	356	14	0	4	22	0	4	0	4	7	0	406	19,7 %
Oscar Lambret center	47	6	0	9	6	4	0	0	0	1	0	71	3,4 %
Francois Baclesse center	50	1	0	1	14	4	0	5	1	2	0	94	4,6 %
ICO	155	11	0	5	65	11	0	0	0	0	0	246	11,9 %
Bergonie Institute	34	3	0	1	39	0	2	0	2	0	0	82	4,0 %
Claudius Regaud Institute	72	5	1	3	23	4	0	0	1	14	0	125	6,1 %
Lorraine Institute of Oncology	17	2	0	0	3	0	0	0	0	0	0	22	1,1 %
Jean Godinot Institute	80	6	1	8	9	1	0	1	0	0	0	100	4,9 %
Paoli calmettes Institute	43	1	2	4	7	17	0	0	0	0	0	73	3,5 %
ICM - Val d'Aurelle	4	6	0	4	5	1	0	0	0	0	0	64	3,1 %
Antoine Lacassagne center	37	9	0	1	10	7	0	0	0	8	0	73	3,5 %
Georges-François Leclerc center	73	4	0	1	17	1	0	0	0	0	0	98	4,8 %
ICANS	7	5	0	22	15	4	0	0	0	0	0	53	2,6 %
Henri Becquerel center	51	6	0	0	0	0	0	0	0	1	0	55	2,7 %
Eugène Marquis center	68	9	1	12	18	1	0	10	0	0	0	119	5,8 %
Sainte-Catherine Institute	34	4	0	1	8	2	0	0	0	1	0	48	2,3 %
TOTAL	1417	103	5	80	275	61	14	16	10	35	0	2060	
POURCENTAGE	68,8 %	4,4%	0,2 %	3,9 %	13,3 %	3,0 %	0,7 %	0,8 %	0,5 %	1,7 %	0,0%		

INCLUSIONS BY TUMOUR LOCALISATION

NUMBER OF PATIENTS INCLUDED IN 2023

BY TUMOUR LOCALISATION AND INSTITUTION TYPE

	BREAST	BREAST-OF WHICH MYPEBS	DIGESTIVE	GENITO-URINARY	SARCOMA	LUNG	GYNEACOLOGICAL	HEAD & NECK	MULTIPLE LOCALISATIONS	TOTAL	%
Public hospitals of Paris (AP-HP)	126	495	87	87	16	34	0	23	50	918	7,5 %
Other public hospitals (excl AP-HP)	6	8313	19	19	0	0	0	0	0	8357	68,2 %
FCCCs	1177	324	80	275	24	56	0	35	89	2060	16,8 %
Other private non-profit hospitals	2	5	38	10	2	1	0	11	6	75	0,6 %
Private clinics	89	194	19	80	0	12	0	1	18	413	3,4 %
City medical practice	20	1	22	16	0	11	0	0	5	75	0,6 %
Foreign institutions	0	350	0	0	0	0	0	0	0	350	2,9 %
TOTAL	1420	9682	265	487	42	114	0	70	168	12248	
POURCENTAGE	11,6 %	79,0 %	2,2 %	4,0 %	0,3 %	0,9 %	0,0 %	0,6 %	1,4 %		

TUMOR GROUPS

French Breast Cancer Intergroup

GROUP OVERVIEW

Academic excellence and operational capacity are the recognized qualities of the French Breast Cancer Intergroup, formed through a partnership between the Breast Cancer Group (UCBG), established in 1994 within Unicancer, and the cooperative group ARCAGY-GINECO dedicated to clinical and translational research in women's cancers. This nationwide intergroup has been accredited by the French National Cancer Institute since 2013 and has a European presence.
With over 100 centers (university hospitals, general hospitals, cancer centers, private institutions) and 600 investigators across France, UCBG is recognized as a major player in breast cancer research. It serves as a key partner for pharmaceutical and biotechnological industries, as well as national and international academic stakeholders. UCBG is supported by a scientific board comprising prominent medical oncologists, surgeons, pathologists, methodologists, and oncology-radiotherapists, including two patient association representatives. The board, chaired by Dr Thomas Bachelot, Coordinator of the Department of Medical Oncology at the Centre Léon Bérard in Lyon and specialist in metastatic breast cancers, was renewed in May 2023.

The intergroup's strategy revolves around four main axes:
- Enhancing prevention through dedicated studies,
- Precision medicine to combat high-risk cancers,
- Rational therapeutic de-escalation to minimize long-term toxicities, and
- Long-term survival and quality of life improvements.

2023 achievements

INCLUSIONS, STUDY LAUNCHES, AND COMMUNICATION: MYPEBS IN CHICAGO AND CLOSER TO PATIENTS

2023 marked the completion of inclusions – 53,000 women across 6 countries – for the MyPeBS trial, a flagship project under **axis 1 "Developing prevention studies"**, funded by the European Horizon 2020 program. This international randomized trial aims to compare personalized and stratified breast cancer screening with systematic screening for women aged 40 to 70 years.
Under axis 2, the TRAKER study, investigating the potential benefits of molecular surveillance of relapses using circulating tumor DNA (ctDNA) in ER-positive, HER2-negative breast cancer patients receiving adjuvant endocrine therapy, was launched in 2023. This international study, a collaboration between the Royal Marsden Hospital in London and Unicancer, offers personalized ctDNA testing surveillance to patients at higher risk, aiming to determine its clinical utility in detecting relapses.
In terms of communication, the 2023 report includes 7 high-profile publications, including results from the **DAISY study** in Nature Medicine and the **PERNETTA study** in JAMA Oncology, along with multiple presentations at international conferences. UCBG notably presented at ECR on integrating SNPs in MyPeBS and at ASCO with an oral presentation on ESR1 mutations based on PADA-1 study data. Additionally, a partnership with Klineo platform was established to enhance visibility of ongoing UCBG clinical trials among patients and healthcare professionals.

Dr Thomas BACHELOT
President

UCBG
unicancer

OUTLOOK FOR 2024

2024

4 axes, 6 trials, and 1 congress

2024 will continue the group's focus on its four action axes, emphasizing therapeutic de-escalation challenges and aiming to launch at least 6 new clinical studies. International collaborations and organizing the scientific meeting of the FEM-NET network of excellence, in which UCBG participates, are also on the agenda.

TUMOR GROUPS

Gastro-intestinal Group

GROUP OVERVIEW

From the Program of Concerted Actions in Colorectal and Digestive Cancers (ACCORD) launched in 1991 to the Unicancer Group dedicated to Gastro-Intestinal Cancers (UCGI) created in 2011, there have been 20 years of research in digestive oncology, continued and amplified for over 10 more years. The cooperative UCGI group, which brings together oncologists, radiotherapists, surgeons, and other experts from various Cancer Centers, benefits from recognized expertise nationally and internationally. Over 30 years, the group has implemented numerous research projects, clinical trials, and translational studies that have led to changes in practice in the management of patients with digestive cancers. UCGI research projects are managed by Unicancer's R&D Directorate or led by the Comprehensive Cancer Centers (CLCC) and since 2023 have been accredited, ensuring scientific quality.

Today's ambitions are both scientific, medical, and strategic:

- Conduct innovative phase II studies to promote access to innovative treatments and treatment combinations,
- Implement large-scale studies aimed at changing practices or dedicated to rare situations, notably within the national PRODIGE intergroup but also internationally,
- Develop translational research programs linked to clinical projects,
- Promote the involvement of young physicians and contribute to the training of professionals in digestive oncology research.

2023 achievements

NEW PROJECTS, CONFERENCES, AND TRAINING: AN INTENSE YEAR FOR UCGI

Intense and dynamic on all fronts and all digestive cancers, 2023 was marked by several major projects and actions:

- Launch of new projects in esophageal (**LOGICAN, ATTENUATION, CIME, BEMAFLOT**) and hepatic cancers (**HESTIA, ALICE**) with the aim of improving patient care,
- Continued work in pancreatic cancer, particularly on biological collections (**GEMPAX, NEOPAN, PRODIGE24**) and ancillary studies of the PRODIGE24 trial that have defined predictive transcriptomic signatures for treatment sensitivity,
- In colorectal cancer, several major advances were made: creation of a clinical and biological database on BRAF mutated cancers (**COBRAF**), presentation of **PANIRINOX study** results at ESMO 2023 showing the utility of liquid biopsy for patient selection but no benefit in intensifying treatment in metastatic RAS/BRAF wild-type patients, completion of recruitment for the **IROCAS study** evaluating FOLFIRINOX treatment intensification, presentation at ASCO of long-term results from **PRODIGE-23** showing the benefit of neoadjuvant FOLFIRINOX-based treatment, publication on the management of elderly patients,
- Implementation of training sessions: ABCD days on digestive cancer biology, workshops for young practitioners, training days for clinical research associates, and other webinars available on demand.

Dr Christelle DE LA FOUCHARDIÈRE
President

UCGI
unicancer

OUTLOOK FOR 2024

ctDNA, personalized medicine, dose optimization: UCGI continues its efforts

Several large-scale projects will be continued or initiated in 2024:

- Start of the **CIRCULATE-3 project funded by PHRC-K 2023** in colorectal cancer, using circulating tumor DNA to guide adjuvant treatment decisions,
- Launch of a large personalized medicine program for biliary tract cancers (**SAFIR-ABC10**),
- Launch of studies aimed at optimizing treatments – a priority focus of the group – particularly in DPD-deficient patients (**TRIFLUOX-DP and FUDOSE**) or optimizing doses of targeted therapies (**TARGET-MONITO DIG project**),
- Structuring and provision of biological collections established within UCGI trials,
- Support for the emergence of new projects across all indications, facilitated by the dynamism of the UCGI group.

TUMOR GROUPS

Genitourinary Group

GROUP OVERVIEW

Translational research and clinical trials, particularly phase III trials, are the objectives of the Genito-urinary Group (GETUG) dedicated to uro-genital tumors. It brings together oncologists, radiotherapists, urologists, nuclear medicine physicians, pathologists, and statisticians.
Established in 1994, this cooperative group serves as a reference center nationally, with a network across various university hospitals, general hospitals, private clinics, and Comprehensive Cancer Centers (CLCC), as well as internationally.
Since 2010, GETUG has also integrated its efforts within the GETUG-ALLIANCE intergroup, formalizing collaborations with the French Association of Urology (AFU) and the Research Center on Prostatic and Urological Pathologies (CeRePP). This intergroup has been accredited by the National Cancer Institute since 2018.

2023 achievements

PEACE, ALBAN, AND CARLHA2: 6 ONGOING PHASE 3 TRIALS

GETUG is actively involved in the Prostate Cancer Consortium in Europe (PEACE), established in 2013. Several phase III trials have been initiated within this consortium to assess and optimize the use of new therapeutic options for prostate cancer patients.
In 2023, the **PEACE-6 program**, focusing on metastatic prostate cancer, expanded to 14 European countries. **PEACE-6** comprises four randomized phase III clinical trials, three of which are promoted by Unicancer and two launched in 2023.
PEACE-6 OLIGO-PRESTO evaluates the role of local ablative treatment of metastases in patients with oligometastatic hormone-sensitive prostate cancer.
PEACE-6 VULNERABLE assesses the efficacy of combined androgen deprivation therapy with darolutamide in patients with vulnerable de novo metastatic prostate cancer who have reduced functional capacity and are ineligible for docetaxel or androgen receptor-targeted agents.
PEACE-6 GOOD RESPONDERS is a pragmatic randomized phase III trial evaluating intermittent androgen deprivation therapy, while **PEACE-6 POOR RESPONDERS** investigates the effectiveness of Lu-PSMA-617 in patients with de novo metastatic hormone-sensitive prostate cancer.
In high-risk prostate cancer recurrence after prostatectomy, the phase III **CARLHA 2 trial** is currently enrolling participants to evaluate the efficacy of combining apalutamide with radiotherapy and an LHRH agonist.
For bladder cancer, 2023 marked the completion of enrollment in the **Alban trial.** This randomized trial is evaluating, across more than 500 patients, the combination of immunotherapy (atezolizumab) with intravesical BCG instillations in patients previously untreated with BCG and with high-risk non-muscle-invasive bladder cancer.

Pr Karim FIZAZI
President

GETUG
unicancer

OUTLOOK FOR 2024

Rare tumors, biological research, and outreach

For 2024 and beyond, GETUG has defined its development strategy around five major priorities:
- Establishment of highly competitive clinical trials with the ambition to change clinical practices and focusing on rare tumors,
- Valorization of previous clinical trials,
- Development of biological research programs within clinical trials, and finally
- Strengthening the group's visibility nationally by involving young researchers and addressing current issues surrounding patient care, and
- Enhancing international collaborations.

TUMOR GROUPS

Head & Neck Group

GROUP OVERVIEW

Initially a think tank of ENT specialists from Cancer Centers launched in 1991, the Head&Neck group was reactivated and restructured in 2009 with the ambition to conduct phase I/II studies in head and neck cancers. Integrated into a group certified by InCa since 2016, this multidisciplinary cooperative group includes around a hundred oncologists, surgeons, ENT specialists, radiotherapists, anatomical pathologists, and researchers from various cancer centers in France.

Group overview, 5 strategic priorities:

- Implementing innovative phase I-II clinical trials in head and neck cancers,
- Conducting research programs in rare ENT tumors in collaboration with health authorities, patient associations, and international academic stakeholders,
- Contributing to optimizing therapeutic pathways through targeted research programs, especially related to HPV-induced cancers, therapeutic de-escalation, or elderly patients,
- Promoting translational research and enhancing existing biological collections,
- Providing scientific and methodological support to project leaders affiliated with the group.

2023 achievements

PUBLICATIONS AND ENROLLMENTS IN RARE ENT CANCERS AND HPV-INDUCED CANCERS

Research on rare ENT cancers is a priority axis within the Unicancer Head&Neck group, involving clinical trials and ancillary studies aimed at testing new treatments and improving understanding of pathophysiological mechanisms or resistance.

In 2023, notable achievements included the publication of results from the NISCAHN study, evaluating the efficacy of nivolumab in advanced salivary gland cancers: while single-agent immunotherapy did not show significant benefits, the study paves the way for future combination treatment research.

Additionally, the group led French recruitment (the second largest recruiter) for the European EORTC 1206 study, evaluating androgen suppression therapy in salivary gland cancer patients expressing androgen receptors.

Oropharyngeal cancers caused by Papillomavirus, increasingly common, are another strong focus of the group's research, from screening and patient follow-up to therapeutic management. In 2023, the group actively participated in the biological collection program of the IMMUNEBOOST-HPV study, assessing the feasibility of neoadjuvant immunotherapy.

Dr Caroline EVEN
President

UCH&N

unicancer

OUTLOOK FOR 2024

Recruitment, results, webinars, and public campaigns

2024 promises to be dynamic with study launches, recruitment drives, and results publications.

Following 2023 enrollments, the first results are expected from the I**MMUNEBOOST-HPV and EORTC 1206 studies.** The 2024 publication of **ELAN-FIT study** results on elderly patients with carcinoma underscores the group's commitment within the broader ELAN program, evaluating treatment efficacy and tolerance in elderly ENT cancer patients, a particularly vulnerable population often excluded from clinical trials.

A new phase of the program focused on immunotherapy is under consideration.

Regarding enrollments, recruitment is ongoing and expected to conclude in 2024 for the **PATHOS study**, which proposes de-escalation after surgery in HPV-associated ENT cancer patients, typically with favorable prognoses. Also in HPV-related cancers, the new **SURVEILLE-HPV study**, launched in 2023, began recruiting its first patients in early 2024, aiming to streamline and optimize follow-up for HPV-induced ENT cancer patients, including circulating DNA virus research for earlier detection of potential relapses.

These ongoing enrollments and recent successes highlight the group's expertise and ability to mobilize patients, especially in studies on rare cancers that are likely to be the focus of new future programs. Translational research will also be prominently featured in 2024, with ancillary studies in rare tumors and HPV-induced ENT cancers. This includes squamous cell carcinomas of the head and neck: while biological research results from the **ICING study** evaluating the efficacy of bintrafusp-alfa in resectable HNSCC were presented in early 2024 at the AACR conference, the first results from the ambitious ancillary program on biological collections from the **TOPNIVO and CHECK'UP studies** are also expected in 2024, aiming to better understand the mechanisms and resistance to immunotherapy.

Other key actions include a new series of webinars for professionals involved in ENT oncology research throughout the second half of 2024. ENT Oncology Training Days for clinical research associates are also scheduled (5th edition). Given the importance of raising awareness among the general public about ENT cancers, which are still too often misunderstood, the group is actively involved in "Rouge Gorge", the first national campaign for information and prevention of upper aerodigestive tract cancers, launched in April 2024.harmonisation of collection practices, emergence of a network of centres of excellence for specific analyses to serve the community).

TUMOR GROUPS

Sarcoma / Rare cancers Group

GROUP OVERVIEW

Launched in 1999, the Sarcoma Group relies on a longstanding partnership with the French Sarcoma Group (GSF-GETO), the Bone Tumor Study Group (Groupe d'Etude des Tumeurs Osseuses), and the French Society for the Fight against Cancers and Leukemias in Children and Adolescents (SFCE). It is a member of the cooperative intergroup INTERSARC, certified by Inca.

The Sarcoma Group boasts 13 studies and over 2000 enrolled patients, consistently integrating translational research to enhance understanding of biological mechanisms. The group focuses particularly on characterizing new predictive and prognostic biomarkers in pediatric sarcomas, where therapeutic advancements are rare and personalized treatment approaches are crucial.

2023 achievements

DATA AND CONSORTIUM

In 2023, the Sarcoma Group concentrated on data sharing and biobanks, critical for advancing research and discoveries in oncology, especially for rare diseases like sarcomas. The year saw the establishment of a national consortium equipped with working groups dedicated to pooling existing clinical and biological data on osteosarcomas. The Sarcoma Group plays an active and recognized role in this national initiative aimed at accelerating knowledge acquisition through the **BoostData initiative.**

Pr Jean-Yves BLAY
President (adults)

Dr Nathalie GASPARD
President (paediatrics)

Sarcoma Group

unicancer

OUTLOOK FOR 2024

Two significant studies

Announced in 2023, two major studies, **L-UTECIN for leiomyosarcoma and Inter-Erwing for Ewing sarcoma**, will be launched in 2024.

The L-UTECIN study will propose adjuvant chemotherapy for women operated on for leiomyosarcoma, a rare soft tissue cancer involving the uterus, with a high risk of relapse defined by the CINSARC genomic signature.

Developed in 2010, this biological test serves as a reliable prognostic factor not only in sarcomas but also in other cancers, identifying tumors at high risk of relapse versus those at low risk. In these aggressive diseases, preventing or delaying relapse is a major challenge.

INTER-EWING-1 is an international clinical research program coordinated by the University of Birmingham, involving 12 countries and 900 patients, including 225 recruited in France.

The aim is to improve survival among newly diagnosed Ewing sarcoma patients by evaluating multiple therapeutic modalities: innovative induction treatments, maintenance chemotherapy, radiotherapy, etc.

With a strong focus on this predominantly pediatric cancer, the Sarcoma Group contributes its expertise and experience to complex collaborative studies.

CROSS-PATHOLOGY GROUPS

Immuno-oncology Group

GROUP OVERVIEW

The Immuno-Oncology group (GIO), created in 2016, is a transverse, multi-disciplinary and pan-tumour group which proposes an ambitious oncology immunotherapy research programme around the following strategic areas: ● Search for predictors of response to immunotherapies to adapt treatments to the patient's profile and rationalize treatment combinations, ● Understanding of the mechanisms of immunotherapy resistance, whether innate or acquired, via a translational approach, ● Identification of the factors of occurrence of toxicities related to immunotherapies using large prospective cohorts, ● Development and evaluation of therapeutic strategies including immunotherapies, ● Development of innovative immunotherapy research programmes promoting patient access to novel therapies.

2023 achievements

CLINICAL TRIALS AND ANCILLARY RESEARCH: INCLUSIONS AND INITIAL RESULTS

The Group's dense and upbeat report for 2023 focuses on several flagship projects, including the following :

AcSé immunotherapy programme: the two trials in this programme, AcSé Nivolumab and AcSé pembrolizumab, raise questions about access to immune checkpoint inhibitors (anti-PD-1) in rare cancers: 269 and 334 patients were included respectively. The first results of the:

POLE (https://doi.org/10.1158/2159-8290.CD-21-0521) and Skin (basal cell carcinoma: https://doi.org/10.1016/j.ejca.2022.09.013) cohorts in the AcSé Nivolumab trial were published in 2022.

Sarcoma (https://doi.org/10.1016/S1470-2045(23)00282-6) and Skin (trichoblastic carcinomas (https://doi.org/10.1007/s00262-023-03449-9) cohorts in the AcSé Pembrolizumab trial were published in 2023. The two AcSé clinical trials have been ended in December 2023 (LPLV).

The ancillary research of this immunotherapy program, AcSé Cible, proposes a multi-parameter analysis of the clinical, biological, and radiological characteristics of patients treated with anti-PD-1 in the two AcSé trials, with the ultimate aim of identifying biomarkers with a good negative predictive value of cancer immunotherapy efficacy which could help clinicians to select for patients with real expected benefits from immunotherapy. The first results of the transcriptomic/genomic and radiomic analyses from this translational program are expected in 2024. During the year, GIO also entered into a new collaboration with Natera for ctDNA analysis of blood samples collected from AcSé Cible patients.

MOIO is a pragmatic and strategic study challenging the routine practice which compares for the first time in a non-inferiority randomized phase III study, the standard scheduling of a variety of immunotherapy regimens versus 3-monthly scheduling in adult patients with locally advanced or metastatic cancer in partial or complete response after 6 months of standard immunotherapy dosing (except melanoma in CR). Recruitment of patients (646 patients expected) is ongoing and involves the participation of 36 French participating sites. Ancillary studies of pharmacokinetics, immune-monitoring, tumour mutation burden and mutational status will be performed. Should the hypothesis of non-inferiority with an immunotherapy reduced dose intensity be validated, alternative scheduling could preserve efficacy while being cost-effective and allowing for a reduction of the toxicity with an increase in patient quality of life. An article on the methodology of this study has been published in 2023 in the journal BMC Cancer (https://doi.org/10.1186/s12885-023-10881-8)

Immuno-Oncology Group

Pr Frederique PENAULT-LLORCA
President

unicancer

OUTLOOK FOR 2024

2024

New projects and new ambitions

In line with the progress made on the projects in 2023, a number of publications are expected in 2024, including the final results of the AcSé Immunotherapy cohorts.

GIO will launch the **NEOREM & METAREM** clinical trials in 2024 as part of the **REMISSION programme**, a major RHU 2023 award-winning project that brings together a multidisciplinary consortium and aims to increase cancer treatment efficacy by providing patients with immunotherapies based on biology rather than histology. Thanks to baseline fresh tumor and blood samples, the molecular immune profile of patients will be determined. Depending on the results of this profile, patients will be rapidly oriented in dedicated therapeutic cohorts of the 2 Mater Protocols NEOREM (neo adjuvant therapy for localized tumors and METAREM (treatment of advanced cancers). This project will allow to: ● Provide new insights into the immune escape mechanisms of cancer cells, ● Identify new tumor specific or tumor agnostic therapeutic targets or pathways, ● Expand knowledge of cancer immunology, and foster interactions between academia and industry.

In 2024, the GIO's goal is to continue its momentum with a focus on 5 areas: ● Developing new clinical and translational projects,● Strengthening collaborations with new partners (learned societies, cooperative research groups, industrial companies, start-ups, etc.) to pool skills and set up innovative and strategic projects dedicated to immunotherapy, ● Improving its national and international visibility, ● Developing the activities of its Biological Task Force (valorisation of existing biological collections, harmonisation of collection practices, emergence of a network of centres of excellence for specific analyses to serve the community).

Pan-MSI-ACSE is the first project of the INCa's new AcSé programme, part of the 2021-2023 ten-year cancer control strategy. This new multi-arm, multi-target, multi-drug programme will help to answer the current clinical research questions posed by the latest approved targeted therapies and provide a larger number of patients with innovative treatments in an optimised and secure environment. Pan-MSI-ACSE is an open-label, randomised, multi-centre, comparative phase II trial evaluating the activity of an anti-PD1, dostarlimab, as a first-line treatment for unresectable metastatic or locally advanced non-colorectal and non-endometrial dMMR/MSI cancers, compared to standard chemotherapy. The first patient enrolled in this study is expected in June 2024.

CROSS-PATHOLOGY GROUPS

Oncology Geriatrics

GROUP OVERVIEW

Launched in 2002, GERICO is a multidisciplinary cooperative group dedicated to clinical research in oncogeriatrics at Unicancer. It comprises medical oncologists, radiation oncologists, surgeons, geriatricians, biostatisticians, health economics methodologists, and is chaired by Dr. Capucine Baldini. GERICO collaborates closely with other thematic groups within Unicancer. In 2014, a DIALOG intergroup was created with the French Society of Geriatric Oncology (SOFOG), and in 2022 with SOFOG and the national platform Elderly People and Cancer (PACAN), aiming to personalize oncogeriatric care.

Five main missions are at the heart of GERICO's priorities:

- Implementation of dedicated intra- and trans-tumor trials with a particular focus on therapeutic de-escalation strategies,
- Exploitation of databases,
- Development of translational studies integrating the biology of aging,
- Establishment of a Patients Committee,
- European and international outreach.

2023 achievements

PATIENT INVOLVEMENT, ONCOGERIATRICS DATA IN DATABASES, AND ASTER-T

Aligned with the group's strategic priorities, 2023 saw advancements in several programs. Patient involvement is a strong ambition within the group, and 2023 initiated the establishment, within the DIALOG intergroup, of a specific patient committee for oncogeriatric trials. This commitment to integrating patients and their experience now manifests from the trial planning stage: in 2023, patient advocates collaborated on a project to explore therapeutic de-escalation strategies.

The integration of an Oncogeriatrics component into existing databases is a long-term effort intensified by the group. Since 2023, collaboration with the team managing the ESME database has ensured systematic collection of items defined by GERICO for breast and lung cancers.

Following the notable ASCO 2022 publication of results from the ASTER-70 trial coordinated by Etienne Brain, demonstrating that the combination of chemotherapy and hormone therapy should not be routine for patients over 70, a translational study was launched.

ASTER-T aims to identify biomarkers associated with decreased quality of life in elderly subjects treated with adjuvant chemotherapy for localized breast cancer. Lastly, 2023 consolidated collaborations with the International Society of Geriatric Oncology (SIOG), the European Organisation for Research and Treatment of Cancer (EORTC), and the European Society for Medical Oncology (ESMO).

Dr Capucine BALDINI
President

GERICO

unicancer

OUTLOOK FOR 2024

Therapeutic prevention

Building on the 2023 initiatives, 2024 will focus on amplifying efforts in defined strategic areas, particularly around patient involvement and implementing geriatric components within databases. Access to innovation and new drugs with specific analysis and pharmacokinetic and pharmacodynamic modeling (PK driven), and the development of translational aspects of trials will also be pivotal. Medium-term goals include continuing intra- and trans-tumor dedicated trials, developing new methodological tools, utilizing real-world data, and expanding collaborations nationally, by organs, therapeutic axes, and within major clinical research programs.

CROSS-PATHOLOGY GROUPS

Personalised Medicine Group

GROUP OVERVIEW

Defined by ESMO as "an approach to care aimed primarily at identifying the most beneficial interventions adapted to the characteristics of the individual and their disease," personalized medicine became a strategic priority at Unicancer in 2013. With a highly stable governance (historically led by Prof. Fabrice André, Director of Research at Gustave Roussy, and currently chaired by Prof. Christophe Le Tourneau, oncologist at Institut Curie), and a quadrennial scientific program, the

MedPerso Group offers recognized multidisciplinary expertise focused on four priority areas:

- Early intervention in therapeutic decision-making to improve survival in difficult-to-treat or resistant cancers,
- Proposing clinical trials with innovative molecules at an early stage and integrating a translational research program to understand mechanisms of action and identify predictors,
- Intensifying clinical and translational research on epigenetic modulators and immunotherapies in cancers,
- Strengthening approaches based on mathematical modeling and artificial intelligence.

Always aiming for clinical application to benefit patients, the Personalized Medicine Group has launched around fifteen clinical trials and numerous translational research projects.

2023 achievements

FOCUS ON CTDNA IN TRAK-ER AND SAFIR03 STUDIES

The year 2023 saw the deployment of two studies: **TRAK-ER and SAFIR03.** These studies capitalize on the opportunities—and hopes—provided by circulating tumor DNA (ctDNA) analysis through liquid biopsy.
This type of analysis has quickly become a relevant tool to detect therapeutic failure or relapse as early as possible, enabling the proposal of alternative treatments in certain difficult cancers. In breast cancer, the TRACK-ER study aims to detect and treat relapses early through regular ctDNA analysis following adjuvant treatment. In metastatic breast cancer treated with hormone therapy, the SAFIR03 program uses ctDNA analysis to detect therapeutic resistances and promptly adjust treatment to prevent disease progression.

Pr Christophe LE TOURNEAU
President

Personalized Medicine Group

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OUTLOOK FOR 2024

Focus on cancers with poor prognoses and opening of a dedicated university hospital institute

In the realm of clinical trials, 2024 will see the launch of numerous projects focusing on different cancers (excluding breast cancer), with the ambition to improve outcomes for cancers with poor prognoses. On an institutional level, 2024 marks a change in the group's presidency and will be notably characterized by the inauguration of the **PRISM Hospitalo-University Institute** (National Precision Medicine Center in Oncology). Led by Gustave Roussy Institute and co-founded by Unicancer, INSERM, University Paris-Saclay, and Centrale Supelec, PRISM will be dedicated to precision medicine and aims to be a center of excellence offering a continuum of care, research, and education. The Unicancer Personalized Medicine Group will play a crucial role: within PRISM, the group will contribute scientific proposals, expertise in managing complex projects, and the capability to disseminate innovative technologies through its network of recognized cancer centers/institutions. The goal is to accelerate research in the field of precision medicine.

CROSS-PATHOLOGY GROUPS

Supportive Care Intergroup

GROUP OVERVIEW

Established in 2013 and affiliated with Unicancer in 2014, the Supportive Care Group was born within the Francophone Association for Supportive Care in Oncology (AFSOS).

The group's mission is to promote knowledge and implementation of supportive care disciplines in symptom management and patient support. Additionally, it aims to foster a participative approach within intra- and extra-hospital teams and to conduct clinical trials in the field of supportive care. Led by a board of oncologists, psychologists, and economists, and chaired by Dr. Didier Mayeur (CGFL-Dijon), the group is multidisciplinary, serving as a liaison with AFSOS, which gathers supportive care professionals, and with tumor groups. It boasts recognized expertise in social and human sciences, methodology, organization, and financing, making it a pivotal reference point for developing clinical trials. Aligned closely with the goals of the National Cancer Institute, the group has three main ambitions:

- Enhancing the management of symptoms related to disease or treatments by offering guidelines in supportive oncological care,
- Proposing an organization facilitating access to supportive care components, both in hospitals and at home,
- Introducing a team management model enabling comprehensive patient and caregiver support within services, while improving the quality of life for healthcare providers.

2023 achievements

ONCO-ADDICTION AND HEALTH ECONOMICS: MAJOR INITIATIVES OF THE YEAR

In 2023, the highly interdisciplinary Supportive Care Group undertook various actions to enrich its multifaceted expertise at national and European levels. Several projects were developed, particularly in onco-addiction and health economics. Special attention was also given to integrating patients into various working groups, aiming to enhance patient experience across all research levels and develop patient-related initiatives.

Dr Didier MAYEUR
President

Supportive Care Group

unicancer

OUTLOOK FOR 2024

Rigorous methodology and four strategic priorities

For 2024, the Supportive Care Group has defined four priority areas of action:

- Organizing care pathways by emphasizing the value of integrated oncology-supportive care, identifying needs and vulnerabilities, embedding supportive care approaches in best practices, actively involving patients, and addressing post-cancer care.
- Managing symptoms through both pharmacological and non-pharmacological treatments, optimizing treatments, and enhancing tolerance management.
- Health behaviors, focusing on nutrition, physical activity, and Non-Drug Interventions (NDIs).
- Patient involvement, aiming to develop and strengthen patient trials by involving users from study design to implementation and scientific valorization.

Across these strategic priorities, the Supportive Care Group aims to develop studies optimized by rigorous methodology: multicenter trials (involving at least 3 centers), of European or international scope, with evaluation methods adapted to complex interventions, multidisciplinarity, and systematic integration of quality of life and patient experience aspects, along with health economics considerations.

CROSS-PATHOLOGY GROUPS

Translational Research and Development in Oncology Radiation

GROUP OVERVIEW

Created in 2014, Unicancer Translational Research and Development Group in Oncological Radiotherapy (UNITRAD) aims to facilitate clinical research in radiotherapy, thereby accelerating progress in this field to bring benefit to as many cancer patients as possible.

UNITRAD organises its activity around five working groups: WG1: Artificial Intelligence, Radiomics/Imaging, WG2: Radiobiology Immuno-radiotherapy Radiosensitivity /Radiopotentialisation, WG3: New Technologies and Physics Development, WG4: Radiotherapy Quality Assurance / Safety, WG5: PROMs/ Real-world data. These five areas of research are fuelling the implementation of therapeutic trials and innovative clinical studies with a strong translational component, with the aim of standardising practices and facilitating access to innovation.

Since its creation, UNITRAD has been developing its portfolio of clinical and translational studies, with currently eight active clinical projects involving more than 1,600 patients, 65% of whom are in phase III. The Group is also involved in major real-life and cohort projects such as CANTO-RT and is developing collaborative networks in France and abroad for the development of innovative radiotherapy research programmes.

2023 achievements

COMMUNICATIONS

2023 was a year of communication! Starting with the oral presentation to the ESTRO plenary session of the first results of the HYPOG-01 phase III trial, comparing normofractionated radiotherapy versus moderate hypofractionated radiotherapy in 1,265 patients with breast cancer with an indication for regional lymph node irradiation in terms of lymphedema occurrence (ESTRO 2023-HYPOG01) (HYPOG-01 RESULTS). This could lead to real changes in radiotherapy practice.

European project: PRE-ACT

The flagship project for 2023 is the European project, PRE-ACT, funded as part of the Horizon Europe (https://preact-horizoneurope.eu/).

The PRE-ACT consortium, of which UNITRAD is a member, is made up of researchers from the UK, Greece, the Netherlands, France (UNITRAD), Italy and Switzerland, with combined expertise in computer science, AI, radiation oncology, medical physics, genetics, psychology, and health economics.

This project integrated data from three multi-centre patient cohorts/trials (REQUITE - University of Leicester, CANTO -Unicancer, HypoG-01 - Unicancer/UNITRAD) to design and implement an AI tool that predicts the risk of side effects, including arm lymphedema in breast cancer patients and provides an easily understood explanation to support shared decision-making between the patient and physician. The clinical impact of this tool will be studied in an international prospective randomised controlled phase III clinical trial, PRE-ACT01, sponsored by Unicancer and coordinated by UNITRAD. The PRE-ACT-01 clinical trial will launch in 2024.

Dr Sophia RIVERA
President

UNITRAD

unicancer

OUTLOOK FOR 2024

Lauch of the clinical trial **PRE-ACT-01**, as part of the European project PRE-ACT, which aims to test the impact of an arm lymphedema risk prediction communication, using explainable AI, together with targeted prophylactic strategy on the occurrence of this side effect and on the choice of radiotherapy modality and plan. This trial will adopt an innovative design in which the patients and medical team in the test arm will receive the risk prediction, but those in the control arm will not. A communication package built with a co-design methodology will ensure that AI outcomes are tailored to stakeholders effectively. The trial will evaluate whether using the AI platform together with targeted prophylactic strategy (compression arm sleeve prescription in patients with high risk of arm lymphedema) changed the arm lymphedema rate and impacted treatment decisions and quality-of-life. It is planned to recruit 783 patients in 2025 in 35 centres in France/The Netherlands/United Kingdom. In a longer term, the project can pave the way to future interventional strategic clinical trials assessing treatment personalization based on AI informed and shared decision making between patients and clinicians. This innovative approach could be practice- and game-changing in the clinic and would address an unmet need in AI explainability for healthcare decisions.

More generally, UNITRAD's objectives for 2024 are to:

- Develop new clinical and translational trials with a high clinical impact and international scope ;
- Enhance the value of clinical studies through biology/radiomics/IA/dosimetry/quality assurance ;
- Strengthen collaborations (learned societies/research cooperative groups/industrial companies /start-ups, etc.) in order to pool skills and set up innovative and strategic projects dedicated to radiotherapy ;
- Raise UNITRAD's national and international profile through congresses, publications and training courses.

The UNITRAD working groups are very active, implementing various programmes and initiatives of their own while developing inter-working group collaborations to optimise the quality of trials and the use of available data and materials. In 2022, various programmes will be launched: a project on the automatic and interoperable extraction of DICOM images for trials and real-life projects for WG1, and a series of webinars on the interoperability of data from radiotherapy care in order to accelerate research programmes for WG5 (Webinaires).

In 2023, UNITRAD and Unicancer Formation have joined forces to offer a varied and innovative training programme in the radiotherapy field. The training courses aim to improve the practices of health professionals and to promote the clinical research (Formation).

EORTC

EORTC TRIALS PORTFOLIO AND RECRUITMENT STATUS IN FRANCE IN 2023

Unicancer has been the local representative of EORTC in France since 2009.

This collaboration aims **to facilitate** the activation of EORTC-sponsored trials in France **and to stimulate the participation of the French investigational centres.**
The Unicancer EORTC liaison officer ensures all regulatory and operational tasks required for site initiation and monitoring in France and **is the preferred contact person of all French participating sites for all regulatory and operational questions.**

GLOSSARY

BTG - *BRAIN TUMOR GROUP (EORTC BTG)*
HNCG - *HEAD&NECK CANCER GROUP (EORTC HNCG)*
LCG - *LUNG CANCER GROUP (EORTC LCG)*
CLTF - *CUTANEOUS LYMPHOMA TASK FORCE (EORTC CLTF)*
GUCG - *GENITOURINARY CANCER GROUP (EORTC GUCG)*
ROG - *RADIATION ONCOLOGY GROUP (EORTC ROG)*
STBSG - *SOFT TISSUE AND BONE SARCOMA GROUP (EORTC STBSG)*

LIST OF EORTC
STUDIES APPROVED IN FRANCE IN 2023

EORTC RESEARCH GROUP(S)	EORTC STUDY NUMBER (ACRONYM)	STUDY TITLE	STUDY APPROVAL DATE IN FRANCE	NATIONAL COORDINATOR IN FRANCE	NUMBER OF EXPECTED PATIENTS (FRANCE/ALL COUNTRIES)
BCG	1984 (NOBLE)	Olaparib and durlavumab as neoadjuvant therapy for patients with BRCA-associated triple negative breast cancer	16/06/2023	Dr Etienne BRAIN (Institut Curie, Saint-Cloud)	ND/152
BTG	2013	Treatment and outcome of patients with primary brain tumors diagnosed according to cIMPACT-NOW recommandations and the 2021 WHO classification	17/01/2023	Dr François DUCRAY (Hôpital neurologique Pierre Wertheimer, Lyon)	ND/1550
HNCG	2120 (RAVINA)	Radiotherapy plus xevinapant or placebo in older patients with locally advanced head and neck squamous cell carcinoma: a randomized phase II study	27/07/2023	Dr Xavier LIEM (Centre Oscar Lambret, Lille)	ND/230
BCG	2129 (TREAT ctDNA)	Elacestrant for treating ER+/HER2- breast cancer patients with ctDNA relapse	15/11/2023	Dr Eleonora De Maio (Institut Claudius Regaud, Toulouse)	ND/1960

EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

HIGHLIGHTS:

IN **2023**

WE HAD **3 new** EORTC-SPONSORED TRIALS ACTIVATED

AND **10 studies** OPEN FOR RECRUITMENT IN FRANCE

LIST OF EORTC

STUDIES ACTIVE IN FRANCE IN 2023

EORTC RESEARCH GROUP(S)	EORTC STUDY NUMBER (ACRONYM)	STUDY TITLE	STUDY APPROVAL DATE IN FRANCE	NUMBER OF INCLUDED PATIENTS AS OF DEC 31, 2023 (FRANCE/ ALL COUNTRIES)
BTG	2013	Treatment and outcome of patients with primary brain tumors diagnosed according to cIMPACT-NOW recommandations and the 2021 WHO classification	17/01/2023	11/33
CLTF	1754 (REACH)	Study to determine the aetiology of chlormetine gel induced-skin drug reaction in early stage mycosis fungoides cutaleous T cell lymphoma (MF-CTCL)	28/10/2021	2/2
CLTF	1820 (MOGAT)	Open-Label, phase II, Multi-Center, study of Anti-CCR4 Monoclonal Antibody (mogamulizumab) Plus Total Skin Electron Beam therapy (TSEB) in patients with stage IB-IIB Cutaneous T-Cell Lymphoma	22/07/2021	2/10
GUCG-ROG	1414 (Pegasus)	Phase IIIb randomized trial comparing irradiation plus long-term adjuvant androgen deprivation with GnRH antagonist versus GnRH agonist plus flare protection in patients with very high risk localized or locally advanced prostate cancer. A joint study of the EORTC ROG and GUCG-Pegasus	09/08/2017	93/369
HNCG-ROG	1420 (Best Of)	Phase III study assessing the "best of" radiotherapy compared to the "best of" surgery (trans-oral surgery (TOS)) in patients with T1-T2, N0 oropharyngeal carcinoma	18/09/2017	1/79
HNCG	1559 (UPSTREAM)	A pilot study of personalized biomarker-based treatment strategy or immunotherapy in patients with recurrent/metastatic squamous cell carcinoma of the head and neck "UPSTREAM"	24/11/2017	143/250
HNCG	2120 (RAVINA)	Radiotherapy plus xevinapant or placebo in older patients with locally advanced head and neck squamous cell carcinoma: a randomized phase II study	27/07/2023	0/0
LCG	1525 (NivoThym)	Single-arm, multicenter, phase II study of nivolumab in patients with type B3 thynoma and thymic carcinoma previously treated with chemotherapy	03/06/2019	46/111
LCG-ROG	1702 (HALT)	Targeted therapy with or without dose intensified radiotherapy for oligo-progressive disease in oncogene-addicted lung tumors	07/01/2019	5/16
LCG	1825 (ALKALINE)	Activity of Lorlatinib based on ALK resistance mutations on blood in ALK positive NSCLC patients previously treated with 2nd generation ALK inhibitor	17/01/2021	13/68
STBSG	1809 (STRASS 2)	A randomized phase III study of neoadjuvant chemotherapy followed by surgery alone for patients with High Risk RetroPeritoneal Sarcoma	22/09/2020	4/78
All groups	1811 (E^2-RADIATE)	EORTC-ESTRO RADiotherapy InfrAstrucTure for Europe	11/06/2019	1/2357
All groups	1945 (OligoRARE)	Stereotactic body radiotherapy in addition to standard of care treatment in patients with rare oligometastic cancers (OligoRARE): a randomized, phase 3, open-label trial	05/03/2021	11/85
All groups	1553 (SPECTA*) RP-1759 (AYA/TYA)	Screening Cancer Patients for Efficient Clinical Trial Access Investigations on adolescent and young adults cohort within 1553-SPECTA	30/03/2017	16/114
All groups	1553 (SPECTA*) RP-1828 (IMMUcan)	Screening Cancer Patients for Efficient Clinical Trial Access Integrated IMMUnoprofiling of large adaptive CANcer patients cohorts	30/03/2017	506/1675
All groups	1553 (SPECTA*) RP-1843 (Arcagen)	Screening Cancer Patients for Efficient Clinical Trial Access Molecular characterization of rare cancer	30/03/2017	436/991
All groups	1553 (SPECTA*) RP-1920 (BioRadon)	Molecular characterization of NSCLC patients and exposure to indoor randon in Europe	31/01/2022	349/639

www.eortc.org/specta/

***** *SPECTA is a collaborative European platform that helps deliver high quality, molecular and pathological screening across tumor types to aid patient selection into clinical trials.*

PARAMEDICAL RESEARCH

A STRONG AXIS OF THE UNICANCER STRATEGIC PLAN

At the forefront of research, Unicancer's agile model allows and encourages the implementation of paramedical research on priority themes.

Paramedical research is a decisive factor in improving treatment and organisation and is a genuine mission of the Cancer Centres (CLCC).

Thus, all the medical assistants in the CLCCs have the possibility of investing in research, benefiting from favourable conditions: adapted time, allocated means, inter-institutional synergies.

The Unicancer network supports emerging professions in healthcare research (IPA , IDEC , IDES, etc.).

The emulation and inspiration generated by such projects enhance the value of staff, build team loyalty and strengthen the attractiveness of our centres of excellence, by offering them stimulating and dynamic career prospects.
To date, more than **50 paramedical research projects have been carried out or initiated.**

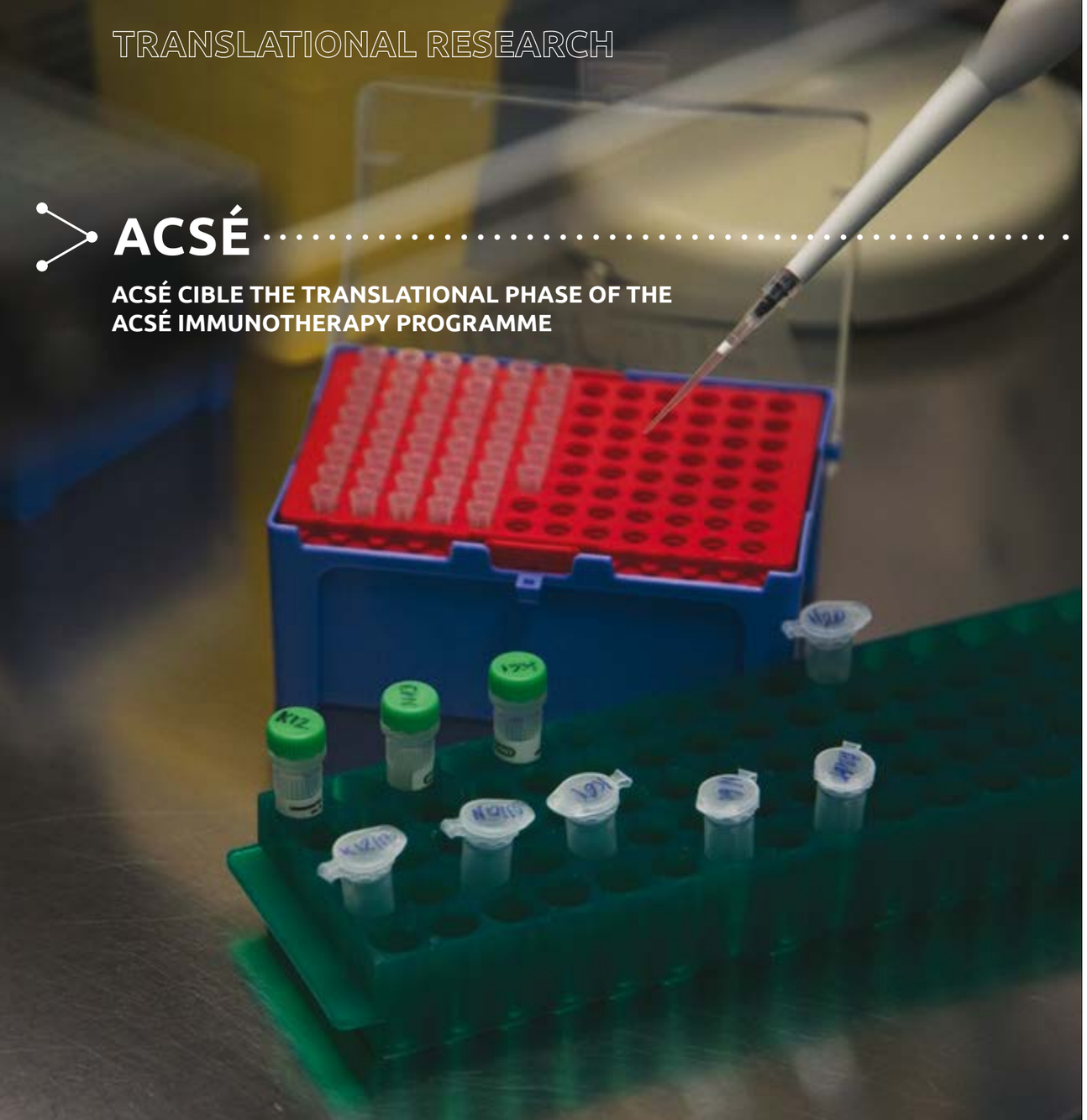
This figure illustrates the commitment of the teams, for whom constantly improving patient care is an absolute priority.

Research Annual Report 2023

• TRANSLATIONAL RESEARCH

Translational research, also known as transfer research, is increasingly emphasized at Unicancer, representing the forefront of our efforts in the twenty-first century.
This collaborative, multidisciplinary approach ensures that discoveries move swiftly from "bench to bedside," directly benefiting patients.

Studying the microbiota, defining the molecular signature of tumors, and developing tests to detect relapse based on circulating DNA are some of the areas currently being explored in these ambitious translational research programs.



ACSÉ

ACSÉ CIBLE THE TRANSLATIONAL PHASE OF THE ACSÉ IMMUNOTHERAPY PROGRAMME

The ancillary programme AcSé Cible which is part of the AcSé immunotherapy programme, proposes to take a more pragmatic approach on the question of biomarkers for immunotherapy.

This programme focus on factors that may contraindicate treatment with PD-1 antagonists, allowing clinicians to identify patients for whom treatment may have an absence of effect or even a deleterious effect (e.g. toxicity without efficacy, paradoxical hyper-progression, …).

AcSé

A multi-parametric analysis of the clinical, biological, and radiological characteristics of the AcSé patients treated by anti-PD-1 (nivolumab or pembrolizumab) is performed in order to identify combination of factors which strongly correlate with early failure of nivolumab or pembrolizumab therapy, as follows:

- Leverage the baseline tumour genomics & transcriptomics to identify mutations, pathways, or molecules associated to early treatments failure (WES + RNAseq on tumour samples at baseline).
- Determine the on-treatment disease kinetics for early preemptive treatment stratification upon anti-PD-1 Failure (ctDNA analysis).
- Identify features of the baseline immune tumour environment or circulating biomarkers (including anti-microbiota serum reactions) associated to an absence of clinical benefit to anti-PD1 therapy.

Two hundred patients from the two AcSé studies have been pooled and are being analysed together (“discovery cohort”), regardless of the tumour type, in order to develop a signature or a combination of markers predictive of treatment failure.

The reliability of the signature in predicting clinical outcome will be tested in the **300 additional patients** in the AcSé programme on top **of the first 200 patients** (“validation set”).

This ancillary project will provide practical clinical tools to select the prescription of these expensive treatments to patients with expected benefits while preventing patients without any hope of immunotherapy efficacy to be exposed to immune related adverse events.

Moreover, the results of this collaborative work will highlight new biological pathways responsible for primary resistance to anti-PD1 and identify potential novel therapeutic targets for cancer immunotherapy.

BIOLOGICAL RESOURCE CENTRE

The Unicancer biobank was set up in 2012 to meet the research strategy requirements by creating a collection of samples from the clinical research program. This collection was made available to all research teams to promote biological research and advances in cancer treatment.

The whole collection includes **89 077** samples, centralised at the Unicancer Biological Resource Center (BRC) located at Léon Bérard Centre in Lyon.
Samples were collected from **19 762** patients enrolled in a total of **77** studies. Historical collections are mostly focused on breast cancer. **8 848** new samples entered the collection in **2023**.

The BRC Steering Committee pursued the reflection initiated at the end of 2020 on a new global strategy to enhance the value of the existing collections and to rationalise the constitution of future collections.

mesdonnees.unicancer.fr

In **2023**, **5 422** samples were unarchived to feed **11** translational research projects, mainly based on advanced technics of molecular biology and deep learning medical imaging. Although our samples collections are available for all types of institutions, they have been mainly released for academic research teams in the CLCCs.
Samples can also be made available to industrial companies involved in research partnerships. Access to the collections is granted upon submission of a valid research project and subject to approval by the Unicancer's translational steering committee.
In order to increase the number of research projects received and to inform a broader community of research teams (universities other than CLCCs, industries, etc.), Unicancer has decided to improve its communication about the collections available. To this end, a new web portal will be made available through Unicancer website allowing the entire scientific community to access biological collection information (including the innate characteristics of the sample, the clinical parameters of the patient, and the genomic analyses already performed).

Through this website, patients treated within the network or people who have participated in a clinical trial can be informed about the re-use of their data and samples.
This dynamic website meets the requirements of the General Data Protection Regulation (GDPR).

HIGHLIGHTS

89 077
samples stored in total, representing approximately

215 000
aliquots*

8 848
new entries in 2023

5 422
outputs in 2023 used in

11 research projects

** Samples represent collection timepoints: several individual biological samples (called aliquots) can be collected at one given collection timepoint (e.g.baseline or Day 1 post treatment), therefore 1 sample actually represents 1 or more aliquots.*

SAMPLE DISTRIBUTION BY TUMOUR LOCALISATION

- Breast : **72 940**
- Basket trial : **15 773**
- Prostate : **5 226**
- Lung : **4 859**
- Head & Neck : **3 866**
- Pancreas : **1 784**
- Bone : **1 488**
- Colorectal : **1 451**
- Kidney : **936**
- Stomach : **743**
- Solid tumours : **12**

NUMBER OF SAMPLES BY SUBTYPE

- *Plasma : **32 496***
- *FFPE block : **16 332***
- *Slide : **14 531***
- *Whole blood : **11 328***
- *Serum : **10 107***
- *DNA : **7 550***
- *Frozen tumor : **5 735***
- *Tissue fragment : **3 704***
- *Peripheral Blood Mononuclear Cells : **3 695***
- *RNA : **1 923***
- *Buffy coat : **908***
- *Powder : **731***
- *Platelet-rich plasma : **342***
- *Dried blood spot : **246***
- *Protein : **217***
- *Dry tube sediment : **29***
- *Stool : **27***
- *Saliva : **7***

• HEALTH DATA RESEARCH

Onco Data Hub, WeShare, ESME, Consore, Canto, and the latest addition, OncoDS: Unicancer's health data projects are ambitious, unifying, and generate valuable advancements for better understanding the impact of cancer and its treatments.

As real-world data revolutionizes the approach to health research, these collections of information and data warehouses open up tremendous opportunities. Here is an overview of the major "Data" programs.

CANTO

STUDY OF CHRONIC TOXICITIES RELATED TO THE TREATMENT OF NON-METASTATIC CANCER

CANTO is a prospective cohort dedicated to research questions regarding survival after breast cancer.

The objective is to identify medium and long-term toxicities of anticancer treatments, evaluate their impact on patients and society, and predict them using molecular markers.

The cohort included 12 012 patients between 2012 and 2018.

In addition to regular medical follow-up, specific CANTO follow-up includes the response to **40 questionnaires** for each patient. It also involves the collection of 8 blood samples as well as fecal samples. It allows for the collection of primary tumor and data on radiotherapy, brain MRI, and HE/HES slide scanning, which aided in the cancer diagnosis. Since the end of 2020, a protocol amandment has allowed for the inclusion of patients under 45 years old at the initial diagnosis.

- **1250 young patients are expected to be included by the end of 2024.**
- **874 patients have been included so far (including 249 in 2023).**

This will enrich the cohort with young patients who have the highest prevalence of several post-treatment toxicities and deterioration of quality of life (QoL). To expand the cohort, it is also planned to include 3000 patients (1500 breast cancer patients and 1500 lung cancer patient in a new cohort) treated with innovative therapies to assess their impact on QoL. **Since January 2022, 481 breast patients have been included in this context (including 247 in 2023); in 2023, a new cohort has been opened for the recruitment of lung cancer patients (16 patients included in 2023).** The objective is to subsequently complete the program by focusing on other organs, and other cohorts will be considered (ovarian, digestive, head, and neck).

In 2023, discussions around the 6 strategic axes (1 Neurotoxicity; 2 Behavioral symptoms, inflammation, and aging, 3 Cognition; 4 Radiotherapy associated long term symptomatology, 5 Socio economic impact; 6 Novel technologies) identified for the valorization of the cohort have intensified. Currently, **105 research projects,** led by academic or industrial groups were approuved. **The research results in 2023 led to 8 publications (total of 42) and 13 new presentations (total of 65) at national and international conferences** (ESMO, ESTRO, SABCS, ASCO, ICCTF, EPICLIN, SFRO).

canto
CANcer TOxicities

2024

THE CHALLENGES FOR CANTO IN 2024 WILL BE TO:

www.canto.unicancer.fr

- **Maintain the existing cohort.** Data collection will continue to have data with a follow-up period of up to 10 years post-diagnosis.
- **Continue recruiting patients under 45 years old** (CANTO Young) to acquire more power for conducting analyses, particularly regarding the impact of the disease and its management on return to work.
- **Continue recruiting patients likely to be treated with innovative therapies** (CANTO Innov) - breast cancer-patients eligible to pembrolizumab, olaparib, TDM1, abemaciclib, ribociclid and lung cancer patients.
- **Consider the possibility of opening new cohorts** by diversying indications (ovarian, digestive, head, and neck).
- **Complete the infrastructure transformation** and develop data management procedures in a continuous quality development approach.
- **Promote the integration of new tools** enabling both the collection of data reported by patients and the massive collection of real-time data, while ensuring long-term follow-up of included patients (control of attrition).
- **Ensure effective matching with SNDS data** (operations in progress).
- **Maintain our business plan to become self-financed by 2025.**
- **Enrich the database** with biological data and specifically develop omics analyses from the collected samples (genomics, proteomics, metabolomics, etc.).

GUSTAVE ROUSSY CANCER CAMPUS GRAND PARIS · CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD · CGFL CENTRE GEORGES FRANÇOIS LECLERC Ensemble, dépassons le cancer · Centre Baclesse unicancer NORMANDIE - CAEN

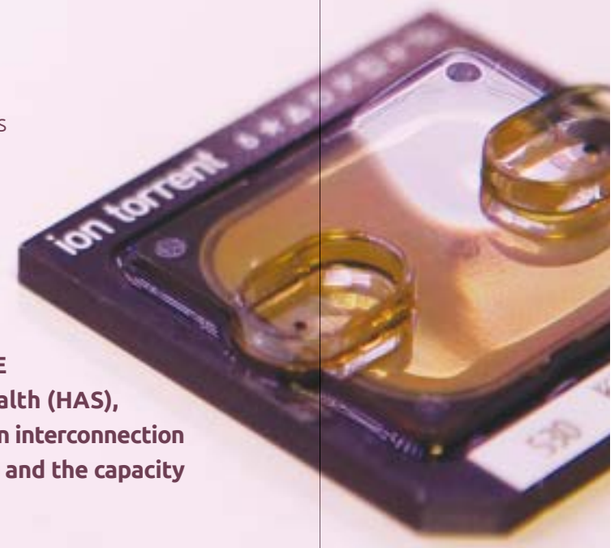
ESMÉ

THE ESME RESEARCH PROGRAM IS A FRENCH PLATFORM OF LONGITUDINAL RETROSPECTIVE REAL WORLD DATA ON CANCER MANAGEMENT IN ONCOLOGY.

It is a unique platform centralizing data from patient medical files describing the therapeutic decisions and care management in routine practice.

5 objectives :

- Provide data for epidemiological purpose
- Identify / describe specific subgroups of interest (age, biomarkers, etc.)
- Provide data to support the health economic models and requirements of the health technology assessment bodies:
  - Target population
  - Therapeutic sequences
  - Real-world efficacy
  - Health economic and outcome resources assessments
  - External control arm
  - Trial emulation
- Provide data to support development of predictive AI models and enable the development of simulation models for clinical research



2024

The prospects for 2024 are promising.
In addition to the accreditation in 2023 of the ESME databases by the French National Authority for Health (HAS), preparations are ongoing for the implementation of an interconnection with the French National Health Data System (SNDS) and the capacity to host a derived database from the SNDS.

Unicancer also setup partnerships with private and academic organization in the field of IA to enhance new approaches on the use of RWD.
Trial emulation and external control arm are growing subjects of interest with first publications using ESME data this year.

After ten years of existence, the ESME program now aims to expand internationally by working collaboratively with other European or American databases.

Research Annual Report 2023

ESMÉ

20

23

KEY

FI GU RES

32 598
CASES SELECTED
in Metastatic breast cancer database

51 067
CASES SELECTED
in Lung cancer database

13 331
CASES SELECTED
in Ovarian cancer database

+180
PROJECTS LAUNCHED
since the start of the ESMé research programme

24
NEW PUBLICATIONS
(communications in congress or publication in peer-review journals)

ODH

THE ONCOLOGY DRUG OBSERVATORY

The French RWD oncology drug centralized observatory to describe patient care in routine practice open to all actors accross the health system.

60 VARIABLES AUTOMATED DATA FLOW
from Electronic Medical Records in institutions

50 REPRESENTATIVE FRENCH HOSPITALS
by 2024 both non-profite and private

BREAST AND LUNG CANCERS
prior enlargement to other indications

OBJECTIVES

- Describe cancer management in France, and its evolution over the time (multi-annual updates).
- Provide data on innovative drug use (pre-MA and real-life setting) in medical institutions.
- Describe therapeutic trends (e.g. sequence of treatment strategies).
- Provide data to support the Health Economic Models of the Health Technology Assessment (HTA) bodiess.

Go further

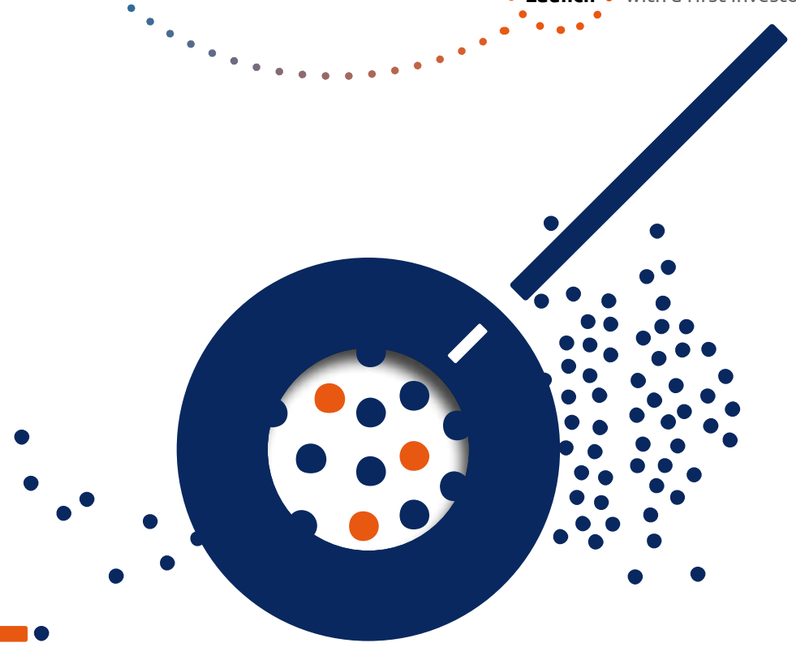
New cancers
New investors and partners
Linkage with other databases

2024
50 hospitals
65 000 patients
Linkage with SNDS (French Public Health Insurance database)

2023
30 hospitals
65 000 patients
First use for reimbursment price.

2022
25 hospitals
30 000 patients with processed and reliable data

2021
Launch with a first investor



ONCO*DS*

The OncoDS health data warehouse network is built upon the interconnection of 12 local warehouses within CLCC to provide data to stakeholders engaged in oncology research, innovation, and assessment.

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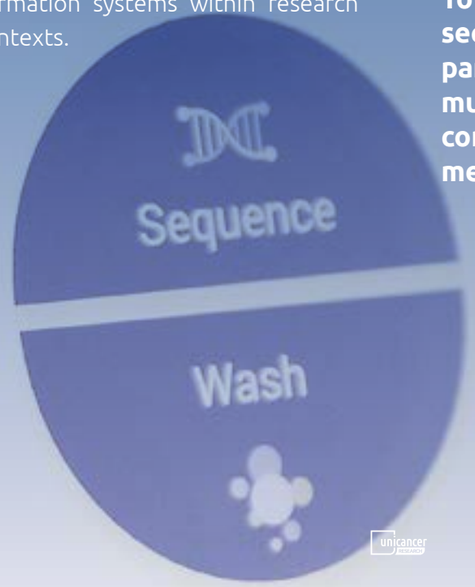
The OncoDS program (Onco Data Share), conducted within Unicancer's Data and Partnerships Department, **secured the HDH 2023 project bid aimed at facilitating and supporting the establishment of hospital-based health data warehouses.**

It revolves around upgrading each healthcare facility (ETS) with a "local EDS featuring a common data foundation." These local EDSs, which are queryable and interoperable, will be automatically supplied with care data from information systems within research project contexts.



The central OncoDS infrastructure (federated EDS) will exclusively house recent data in pseudonymized form, formatted in OSIRIS-RWD (OncoDS dataset), originating from research projects across various local EDSs and potentially from external sources.

The primary goal is to empower each establishment (ETS) to leverage its own data or engage in multi-establishment projects by sharing data, either within OncoDS or other research networks or EDSs.

Most ETSs predominantly rely on structured or restructured, standardized data, either via the CONSORE solution or other locally implemented solutions.

To enhance efficiency and facilitate secondary mutualization with other partnering ETSs, OncoDS opts for a multi-tool approach grounded in a common set of interoperable parameters among ETSs.

OncoDS

In addition to the internal objectives of each ETS, the program aims to facilitate a sustainable data-sharing approach by implementing the central OncoDS infrastructure, which includes consolidating initiatives by various stakeholders regarding data reuse.

Moreover, there's an increasing mastery in exploiting diverse data sources such as imaging, radiotherapy, and genomics. This enables the development of approaches utilizing AI models on both structured and unstructured massive data, particularly in collaboration with external partners.

Standardizing the establishments' EDSs is crucial to ensure the OncoDS program's interoperability, communicativeness, and standardization, thereby facilitating the scientific valorization of qualified oncology data at a high level. OncoDS paves the way for national and international collaborations, both public and private.

Open architecture is imperative for managing interoperability within "inter-warehouse" projects.

2024

In 2024, the realization of the OncoDS project is expected through the establishment of dedicated working groups to aid centers in structuring their local warehouses, developing the architecture for the central OncoDS infrastructure, and implementing associated project oversight committees.

CONSORE

The year 2023 is a pivotal year for the deployment of the data strategy of the network of the Centers and Unicancer with multiple projects including the ONCO*DS* data warehouse.

The CONSORE tool is at the heart of this strategy for the establishments and for the programs carried out by Unicancer.

THE OBJECTIVE OF CONSORE IS TO ENABLE THE CONSTRUCTION OF DATABASES WITH THE ABILITY TO GENERATE STRUCTURED DATA FROM 10 DATA SOURCES FROM ROUTINE CARE.

CONSORE
continuum soins recherche
unicancer

For the coming years, CONSORE's objectives revolve around 5 axes:

- **Governance** ensured by the Data and Partnerships Department of Unicancer with strong involvement from the Centers.

- The need to **bring the tool into compliance with the new standards set by the CNIL** (Commission Nationale de l'Informatique et des Libertés) in terms of security and confidentiality.

- **Analysis of data quality** with the implementation of a quality assurance plan allowing for objective measurement and corrective actions using new natural language processing techniques.

- **Progressive migration** of the model to ensure interoperability of data between Centers and with other hospitals.

- **New functionalities** including access to radiological images or incorporating radiotherapy as a new data source.

The CONSORE project, initiated in 2013, is reaching a pivotal period. The initial technologies used must be replaced based on the experience gained, with an opening of the tool to integrate all new techniques, for example in automatic language processing.

UNIBASE

The UNIBASE program was initiated in 2021 through a partnership between Unicancer and the Health Data Hub (HDH), with support from the Ligue Nationale Contre le Cancer in 2023.

UNIBASE finances multicenter studies to address scientific questions in the field of cancer. These projects rely on healthcare data to closely address real-life issues. In 2022, three projects were selected, paired with data from the National Health Data System to complement hospital data with "city" data to reconstruct a complete patient journey.

In 2023, five new projects were selected, three funded by the HDH, two by the Ligue Nationale Contre le Cancer :

2023 NEW PROJECTS

- The **UNI-AJA** project aims to establish a cohort of Adolescents and Young Adults (AJA) aged 15-29 with cancer in France.
- The **HORUS project** studies the morbidity and late mortality of children, adolescents, and young adults exposed to innovative drug therapies in oncology.
- The **HYPO-RT-prostate project** examines new hypofractionated radiotherapy schemes in localized prostate cancer for effectiveness and toxicity outcomes.
- The **CASEBA project** seeks to better define low-grade ovarian cancers for specific management and establish diagnostic recommendations.
- The **UNI-RIV project** studies predictive factors for response and the onset of toxicities in the treatment of prostate cancer metastases by vectorized internal radiotherapy (RIV) with 77Lu-PSMA.

UNIBASE

- The **DASTO project** aims to analyze the interactions between venous thromboembolic disease and cancer.
- The **REALIGIST project** seeks to identify why some patients with gastrointestinal stromal tumors (GIST) respond to targeted therapies while others do not.
- The **ISIS project** studies the risk of infertility after breast cancer in young women and the potential consequences of anti-cancer therapies on pregnancy, childbirth, and the child. These three projects are in the assembly phase in all aspects: medical, legal, and partnership. Initial results are expected by 2025.

These projects involve all the Comprehensive Cancer Centers and some University Hospitals, with 23 participating institutions and over 50 medical teams. The work carried out under UNIBASE relies on the pooling of human resources and the experience gained in each of the projects to benefit other current and future projects.

This positions Unicancer as a major player in the reuse of healthcare data for research by mobilizing large amounts of clinical data or images and using the latest advances in artificial intelligence.

These various projects aim to address questions that cannot be addressed by clinical research alone, complementing and introducing new methodologies.

WESHARE

WEB-BASED EXPLOITATION OF SOCIAL AND HUMAN SCIENCES TO ADVANCE CANCER RESEARCH

Unicancer, in association with a multidisciplinary consortium, is creating a new digital infrastructure: WeShare.

Coordinated scientifically by **Dr Ines VAZ LUIS** from Gustave Roussy, **it will enable the acceleration of a research in Human and Social Sciences and Quality of Life in cancer and post-cancer.**

3 AXES

3 main axes are identified and described in infrastructure below :

- **Implementation of a decentralized research via digital tools** (ePROs, eCosnent, Randomization, Biosensors …)
- **Creation of a Health Data Warehouse** that will allow the conduct of large-scale ancillary or secondary studies (using FAIR standards)
- **Creation of active communities of researchers** (transformative cancer research) **and patients, users and citizens** (patient-centred research)

The ultimate objective of the WeShare platform is **to identify new levers to act on the impact** of cancer and its treatment on patients' quality of life.

WeShare (ANR-21-ESRE-0017) **has been selected for the 2020 Equipex** call for projects by the ANR (French National Research Agency) under **the "Investissements d'avenir" programme and has been awarded €11M in funding.**

weshare.unicancer.com

Information on the platform and its modules is available on the WeShare website.

WeShare will last 8 years. In 2023, the third year of the implementation phase, the project has progressed primarily in the following areas:

- **Technical and scientific:** improvement of the graphical interface and ergonomics. The specifications for the Dashboards, eConsent, Randomisation, Biosensors and CRM modules have been drafted. The first 2 studies using the ePRO module have been launched;
- **Regulatory:** following the drafting of the Impact Assessment Plan (IAP), CNIL authorisation was obtained for the creation of the WeShare Health Data Warehouse;
- **Communication and dissemination:** launch of the WeShare website. WeShare has also been mentioned at 5 congress;
- **Valorisation:** WeShare's areas of differentiation have been identified, including the need to promote engagement tools, diverse and inclusive research as well as automatic data capture and interconnection with existing remote monitoring tools;
- **Partnerships:** the partnership with a European consortium coordinated by the VHIO (Spain) and including 6 countries as part of the PRAGMATIL study is continuing. Funding has been obtained for a second European consortium with IEO (Italy).

Other partnerships with European consortia are in progress.

PERSPECTIVES

In 2024, the ePRO module will also be available at the international level. The implementation of decentralised, remote research using digital tools associated with a community of researchers and patients, users and citizens can accelerate research in oncology and, in particular, in the fields of health and social services and quality of life. **The first 100% decentralised study will be conducted via WeShare in 2024.**

• RESEARCH IN THE FCCCs

Unicancer groups together 18 French Comprehensive Cancer Centres (FCCCs) spread across 20 hospital sites throughout France and one affiliate member. They are private, non-profit health establishments dedicated to cancer care, research and education.

Most of the research platforms accredited by the French National Cancer Institute (INCa) are hosted in our FCCCs, thus demonstrating the excellence and innovativeness of our research in the field of precision medicine.

2023 FCCCs KEY FIGURES

15%

OF THE PATIENTS

TREATED IN THE FCCCS ARE INCLUDED IN A CLINICAL TRIAL

versus

8.5%

of cancer patients in average in France

787

ACTIVE CLINICAL TRIALS

SPONSORED BY THE UNICANCER NETWORK

unicancer RESEARCH

Unicancer is ISO 9001 certified for its clinical research activity

UNICANCER, A UNIQUE NETWORK OF EXPERT CENTRES IN FRANCE

1 - 2 **INSTITUT DE CANCÉROLOGIE DE L'OUEST**
Unicancer Pays de la Loire

3 **INSTITUT BERGONIÉ**
Unicancer Nouvelle-Aquitaine

4 **CENTRE JEAN PERRIN**
Unicancer Clermont Auvergne Métropole

5 **CENTRE FRANÇOIS BACLESSE**
Unicancer Normandie-Caen

6 **CENTRE GEORGES-FRANÇOIS LECLERC**
Unicancer Bourgogne Franche-Comté

7 **CENTRE OSCAR LAMBRET**
Unicancer Hauts-de-France

8 **CENTRE LÉON BÉRARD**
Unicancer Lyon, Auvergne-Rhône-Alpes

9 **INSTITUT PAOLI-CALMETTES**
Unicancer Marseille

10 **INSTITUT DU CANCER DE MONTPELLIER**
Montpellier

11 **INSTITUT DE CANCÉROLOGIE DE LORRAINE**

12 **CENTRE ANTOINE LACASSAGNE**
Unicancer Nice

13 - 14 **INSTITUT CURIE**
Unicancer Paris – Saint-Cloud – Orsay

15 **INSTITUT GODINOT**
Unicancer Reims en Champagne

16 **CENTRE EUGÈNE MARQUIS**

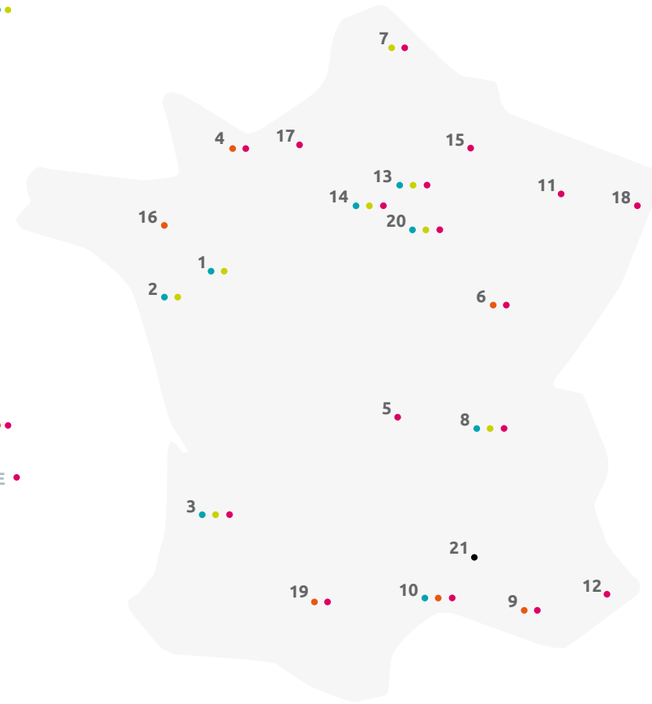
17 **CENTRE HENRI BECQUEREL**
Unicancer Normandie-Rouen

18 **ICANS**
Unicancer Strasbourg

19 **IUCT ONCOPOLE – INSTITUT CLAUDIUS REGAUD**

20 **GUSTAVE ROUSSY**

21 **ICAP - Sainte Catherine**
Avignon-Provence



- *SIRIC*
- *CLIP² - adult*
- *CLIP² - adult and paediatric*
- *Molecular genetics platform*

SIRIC HOSTED IN A FCCC OR INTEGRATING A FCCC:

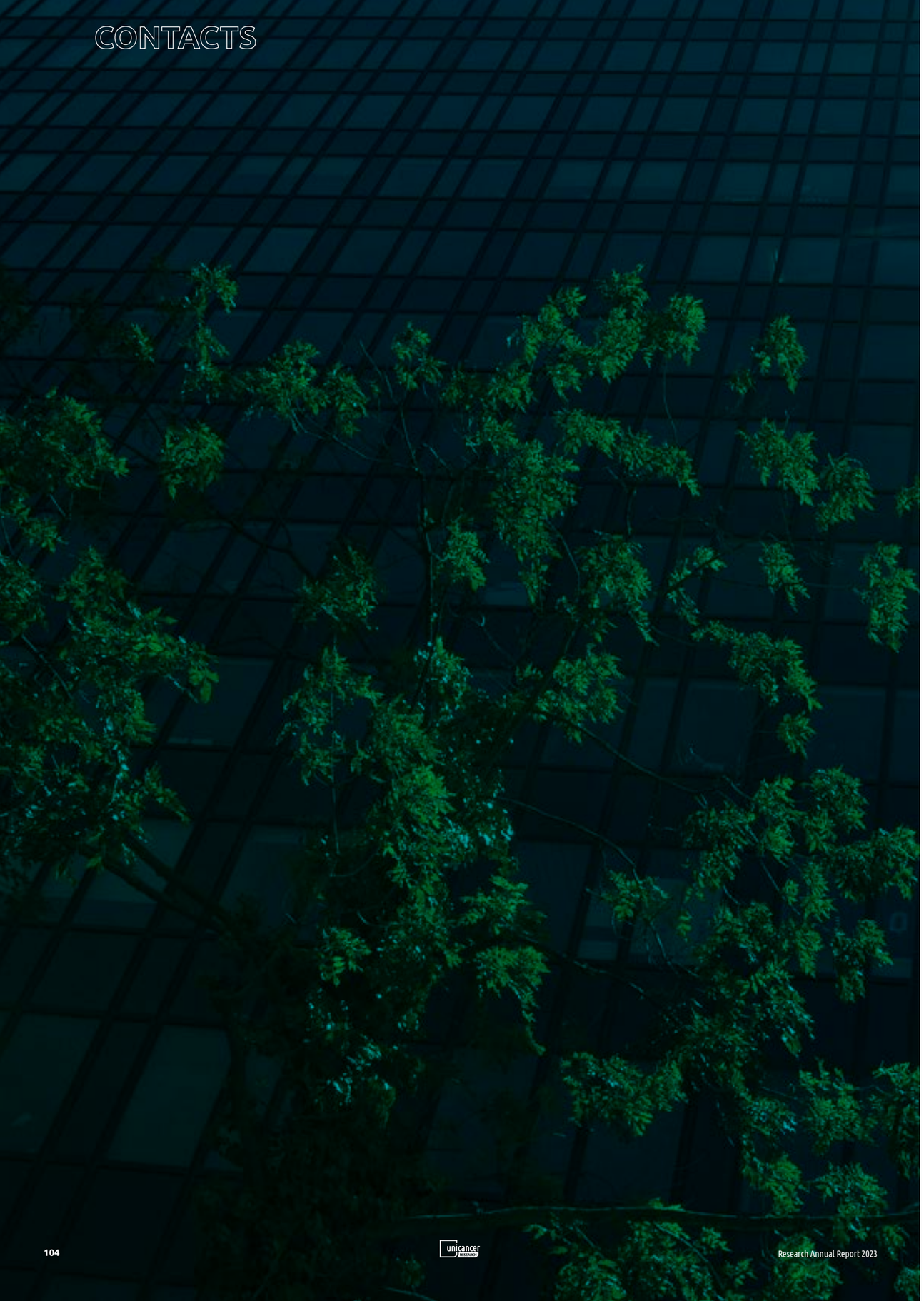
BRIO / Bordeaux Recherche Intégrée Oncologie (Institut Bergonié, Bordeaux)
LYriCAN / Manipulating cell plasticity for innovative cancer treatment (Centre Léon Bérard, Lyon)
SIRIC ILIAD / Imaging and Longitudinal Investigations to Ameliorate Decision Making (Institut de cancérologie de l'Ouest, Angers/Nantes)
SOCRATE 2.0 / Stratified Oncology Cell DNA Repair and Tumor Elimination 2.0 (Gustave Roussy, Villejuif)
SIRIC Montpellier Cancer (Institut du Cancer de Montpellier, Montpellier)
SIRIC Curie (Institut Curie, Paris)

CLINICAL TRIALS INCLUSIONS IN THE FCCCs

FRENCH COMPREHENSITE CANCER CENTRE (FCCCs)	CITY	ACTIVE PATIENT FILE	PATIENTS INCLUDED IN A CLINICAL TRIAL	TOTAL ACTIVE TRIALS	AVERAGE NUMBER OF PATIENTS INCLUDED PER CLINICAL TRIAL	% OF PATIENTS SIGNING AN INFORMED CONSENT *	% OF THE ACTIVE PATIENT FILE INCLUDED IN A CLINICAL TRIAL	ACADEMIC SPONSOR			INDUSTRIAL SPONSOR	
								NUMBER OF PATIENTS INCLUDED	NUMBER OF ACTIVE TRIALS	% OF PATIENTS INCLUDED IN AN INSTITUTIONAL CLINICAL TRIAL	NUMBER OF PATIENTS INCLUDED	NUMBER OF ACTIVE TRIALS
Bergonie Institute	Bordeaux	8 209	2 141	380	5,6	29 %	26 %	1878	168	88 %	263	212
Francois Baclesse Centre	Caen	8 054	623	155	4,0	8 %	8 %	562	100	90 %	61	55
Jean Perrin Centre	Clermont	6 644	468	133	3,5	7 %	7 %	394	96	84 %	74	37
Georges-François Leclerc centre	Dijon	5 511	702	283	2,5	23 %	13 %	505	159	72 %	197	124
Oscar Lambret Centre	Lille	7 645	948	174	5,4	13 %	12 %	766	127	81 %	182	47
Léon Bérard Centre	Lyon	11 167	1 639	414	4,0	16 %	15 %	1204	221	73 %	435	193
Paoli calmettes Institute	Marseille	10 580	1 180	262	4,5	13 %	11 %	947	152	80 %	233	110
Montpellier Cancer Institute - Val d'Aurelle	Montpellier	7 892	1 552	174	8,9	21 %	20 %	1430	110	92 %	122	64
Lorraine Institute of Oncology	Nancy	6 259	471	119	4,0	8 %	8 %	386	82	82 %	85	37
Institute of Cancer research in Western France	Nantes / Angers	12 966	1 391	261	5,3	14 %	11 %	1103	162	79 %	288	99
Antoine Lacassagne Centre	Nice	5 630	421	180	2,3	8 %	7 %	323	118	77 %	98	62
Curie Institute	Paris Saint Cloud	15 403	2 004	200	10,0	13 %	13 %	1694	121	85 %	310	79
Jean Godinot Institute	Reims	4 820	292	70	4,2	6 %	6 %	258	55	88 %	34	15
Eugène Marquis centre	Rennes	5 346	967	129	7,5	21 %	18 %	873	72	90 %	94	57
Henri Becquerel centre	Rouen	6 346	316	119	2,7	5 %	5 %	265	86	84 %	51	33
Paul Strauss Centre	Strasbourg	7 141	1 005	156	6,4	15 %	14 %	858	71	85 %	147	85
Claudius Regaud Institute	Toulouse	7 910	979	247	4,0	13 %	12 %	770	124	79 %	209	123
Gustave Roussy	Villejuif	13 591	4 885	517	9,4	38 %	36 %	4029	201	82 %	856	316
Total		151 114	21 984			16 %	50 %	18 245		83 %	3 739	
Mean		8 395	1 221	221	5	15 %	13 %	1 014	124	83 %	208	97
+/- SD		3088	1072	117	2	9 %	8 %	892	46	6 %	194	76
median		7 769	973	177	4	13 %	12 %	814	120	83 %	165	72
min		4 820	292	70	2	5 %	5 %	258	55	72 %	34	15
max		15 403	4 885	517	10	38 %	36 %	4 029	221	92 %	856	316

FRENCH COMPREHENSITE CANCER CENTRE (FCCCs)	TOTAL ACCEPTED INCLUSION (INCLUDED PATIENT SCREENED AND NOT INCLUDED)	% OF THE ACTIVE PATIENT FILE ACCEPTING A CLINICAL TRIAL	% OF PATIENT ACCEPTING A CT BUT NOT INCLUDED AFTER SCREENING	% OF PATIENT INCLUDED AFTER SCREENING
Bergonie Institute	2 366	29 %	13 %	87 %
Francois Baclesse Centre	665	8 %	70 %	30 %
Jean Perrin Centre	480	7 %	43 %	57 %
Georges-François Leclerc centre	1 270	23 %	86 %	14 %
Oscar Lambret Centre	1 032	13 %	30 %	70 %
Léon Bérard Centre	1 816	16 %	35 %	65 %
Paoli calmettes Institute	1 344	13 %	58 %	42 %
Montpellier Cancer Institute - Val d'Aurelle	1 696	21 %	63 %	37 %
Lorraine Institute of Oncology	499	8 %	51 %	49 %
Institute of Cancer research in Western France	1 839	14 %	66 %	34 %
Antoine Lacassagne Centre	465	8 %	40 %	60 %
Curie Institute	2 072	13 %	36 %	64 %
Jean Godinot Institute	296	6 %	15 %	85 %
Eugène Marquis centre	1 096	21 %	21 %	79 %
Henri Becquerel centre	319	5 %	75 %	25 %
Paul Strauss Centre	1 073	15 %	60 %	40 %
Claudius Regaud Institute	1 056	13 %	34 %	66 %
Gustave Roussy	5 130	38 %	57 %	43 %
Total	24 514	16 %	41 %	59 %
Mean	1 362	15 %	48 %	52 %
+/- SD	1129	9 %	21 %	21 %
median	1 085	13 %	47 %	53 %
min	296	5 %	13 %	14 %
max	5 130	38 %	86 %	87 %

** With the development of personalised medicine, an increasing number of clinical trials include a molecular screening as eligibility criteria. Patients who have accepted and signed an informed consent can be denied in a second step due to the negative result of the molecular screening (on average, 67% of patients are not included in the trial after the molecular screening). Such trials represent an average 40% of industrially sponsered trials and 13% of the academically sponsored trials proposed in our centres.*



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