CLINICAL RESEARCH PLATFORM AT **Gustave Roussy** FRANCE

A comprehensive approach to innovative clinical research

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

université PARIS-SACLAY
FACULTÉ DE MÉDECINE

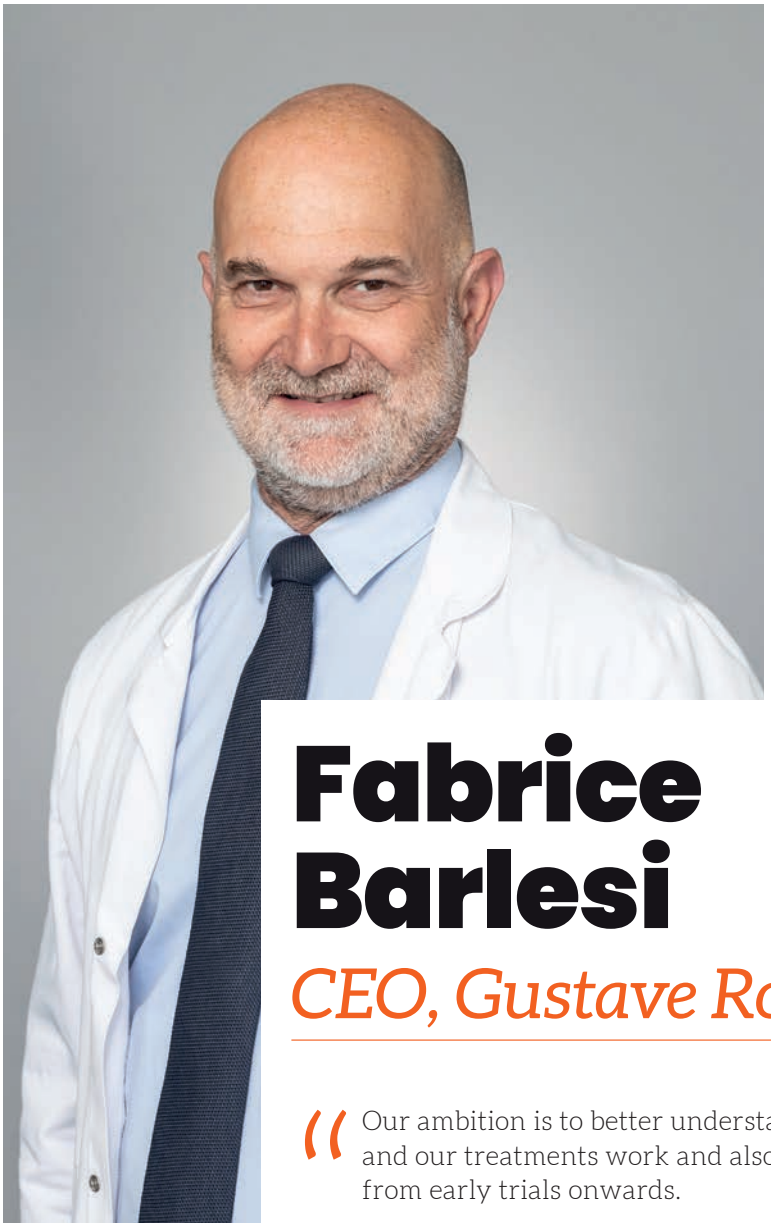
unicancer

Instituts thématiques Inserm
Institut national de la santé et de la recherche médicale

PRISM

DITEP
Drug Development Department

UNLOCK
BY GUSTAVE ROUSSY



Fabrice Barlesi

CEO, Gustave Roussy

> Our ambition is to better understand how medicines and our treatments work and also their resistance from early trials onwards.

Following the decade of genotyping and targeted therapies in 2000 and the decade of immuno-oncology in 2010, we are now entering the era of drug combination therapies and ultra-individualisation by offering our patients customised treatment pathways.

In one hand, with our PRISM and FRESH programs we want to offer to each patients at Gustave Roussy a true precision medicine that classifies tumours by biology, molecular and immune status. In the other hand, the UNLOCK program will allow us a better understanding of the mode of action of new drugs and our ambition is to better understand how medicines and our treatments work and also their resistance from early trials onward.

To strengthen its clinical research capabilities, Gustave Roussy has set up an unprecedented organisation dedicated to clinical research in early clinical trials in order to offer new hope and opportunity for patients.

2025

Integrating clinical research activities for studies requiring close monitoring and/or including complex protocol procedures within a single dedicated space

Gustave Roussy to double early testing capacity

Gustave Roussy is equipping itself with the resources to include 1,000 patients in phase I and more than 800 patients in phase II trials in a few years thanks to its platform, which allows for:

- → Vertical integration from phase I to II, and up to phase III when required by the clinical design;
- → Horizontal integration of haematological and solid tumours in early trials with the same technical and clinical quality.

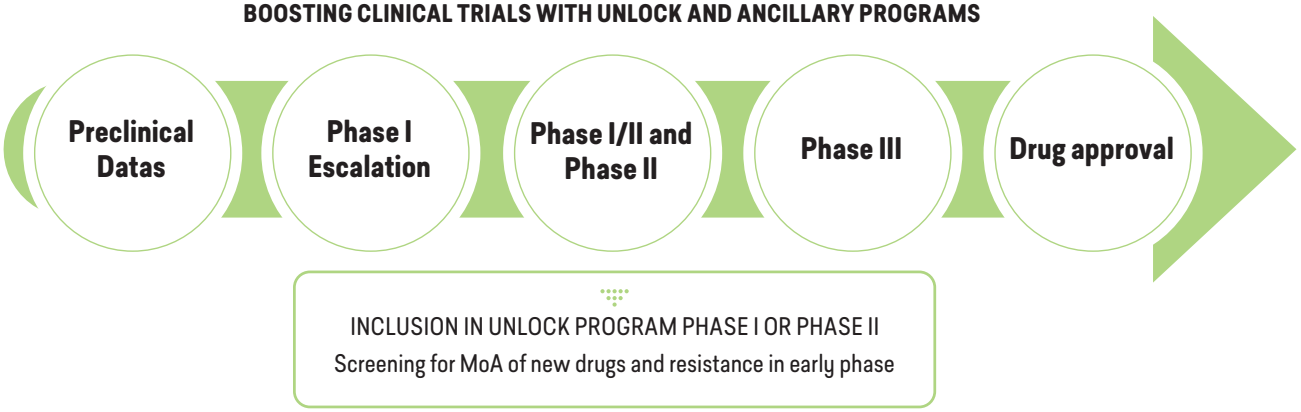
Unique physical location at Gustave Roussy main building

- → Outpatient day care units
- → Hospitalisation units: Inpatient beds
- → Rooms for sampling and monitoring/follow-up
- → Medical consultation spaces
- → Paramedical & medical staff offices
- → Ultrasound-guided biopsies
- → Clinical operations staff

Operational sites

- → Pooling resources and sharing tools from all stakeholders
- → Harmonising processes to upgrade to the highest standards for all studies

BOOSTING CLINICAL TRIALS WITH UNLOCK AND ANCILLARY PROGRAMS



Our multidisciplinary clinical research platform provides for

> Better patient safety

> Better quality

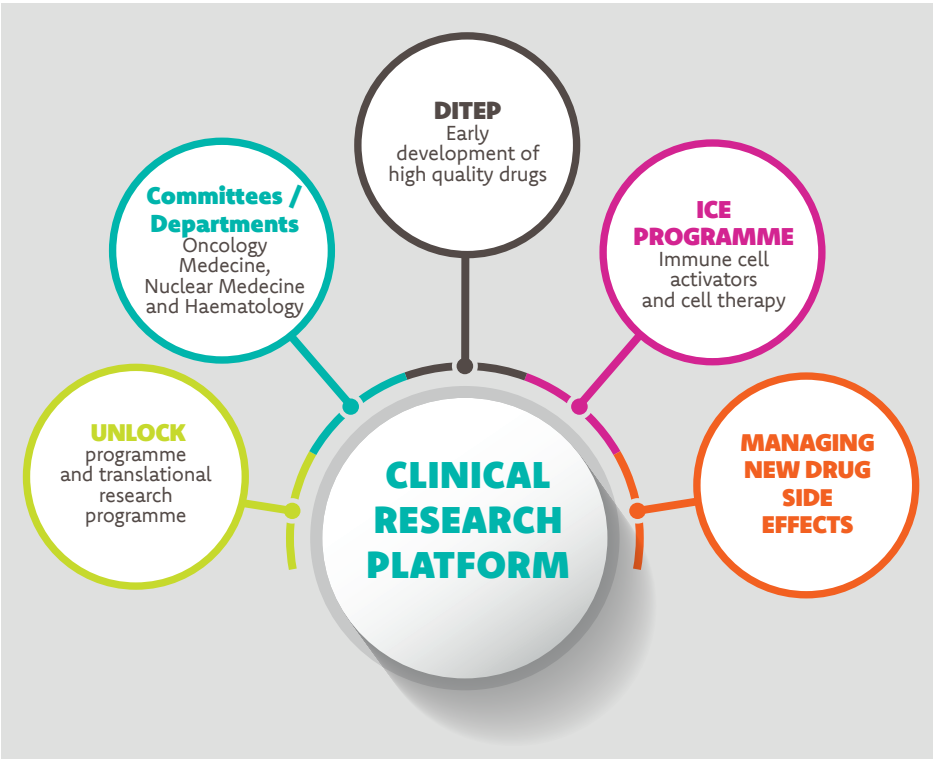
> For innovative early clinical research

2025 : A NOVEL CLINICAL RESEARCH PLATFORM / DITEP (4TH FLOOR)

A significant research activity in 2024

> More than 6000 patients enrolled
> 423 in Early Phases

In 2025, an innovative research platform



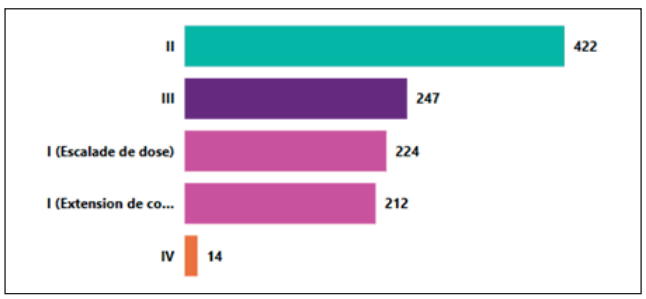
→ **Increased capacities for early phase I & II**

→ **Strong connection with translational research teams**

→ **Expertise**
- Inhibitors of different molecular targets, immune modulators, epigenetic and metabolic regulators.
- Expertise to develop new non-drug strategies, such as radiation therapy, nuclear medicine and new surgical techniques.

→ **Targets**
- Haematological cancers and all solidtumors in adults.

GUSTAVE ROUSSY CLINICAL RESEARCH ACTIVITY IN 2024



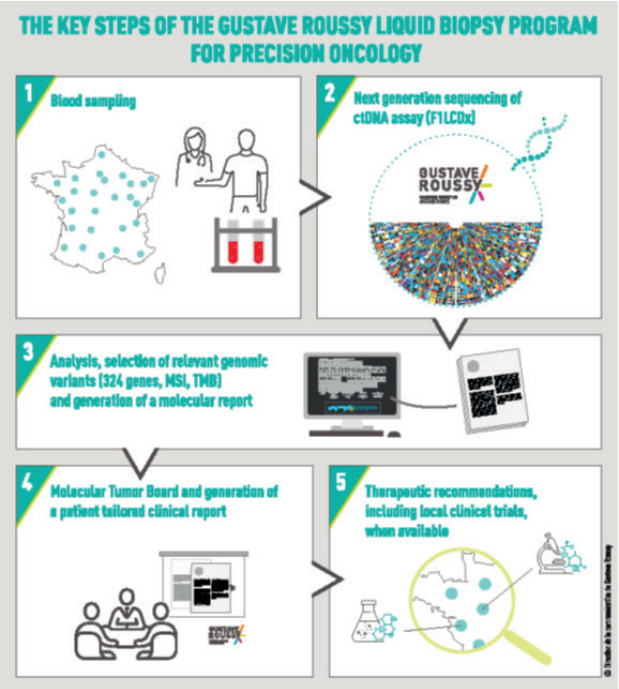
1119 patients

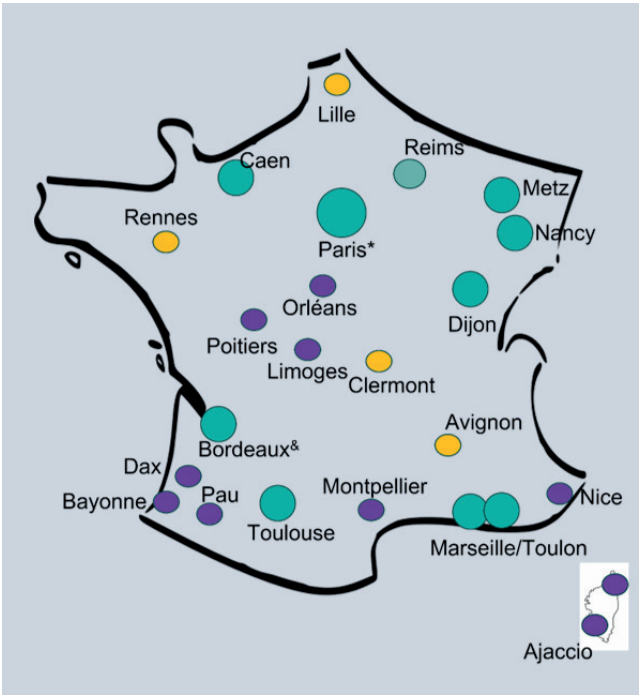
GENOMIC PROFILING BY LIQUID BIOPSY

A unique partnership with Roche and FMI

Roche

FOUNDATION MEDICINE®





- Experience of > 7,000 patients profiled since 2020 using F1LCDx
- Tech Transfer in a dedicated Gustave Roussy Lab open July 1st, 2024
- Exclusivity to operate F1LCDx in France
- Up to 8,000 samples/year expected by 2026

PRISM Portal Trial (Gustave Roussy Sponsored)
1,500 patients included in 2 years > 10,000 expected

PRISM

AMBITION

« give access to precision medicine to all patients at nation scale »

DITEP, MEDICAL DEPARTMENT DEDICATED TO EARLY PHASE CLINICAL TRIALS

Team

20 MD-PhD, MD, with dual expertise (pneumology, haematology, immunology, radiotherapy, urology, senology, industry partnership expert)

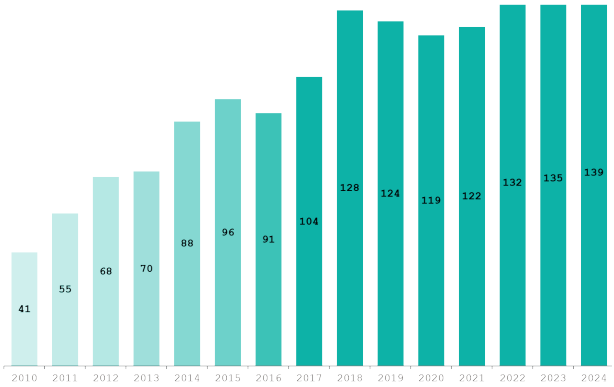
Facility

→ A week hospitalisation unit: 11 single patient beds
→ An outpatient day care unit: 17 armchairs
→ A dedicated clinical operations unit

Tumor Biopsies

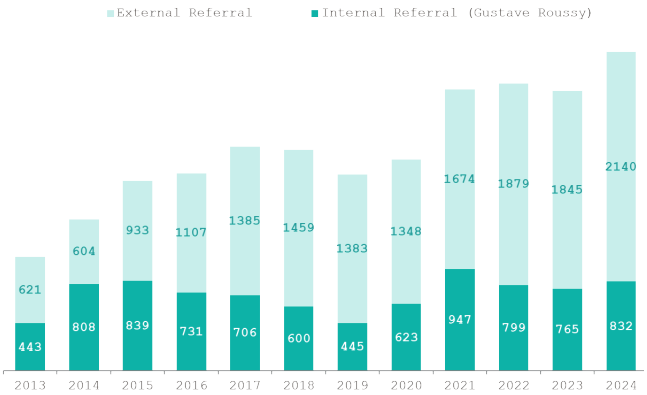
→ Capacities: 15 biopsies slot / week - 60 per month
→ More than 700 tumor biopsies in early phase trial patients in 2023
→ And over 1,000 at Gustave Roussy in phases II/III

YEARLY NUMBER OF ONGOING EARLY CLINICAL TRIALS

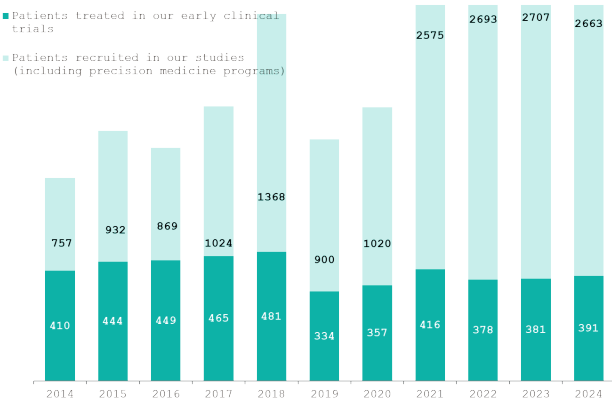


Largest phase I center in France, with national accreditations (ARS, CLIP2, INCa, ISO9001) and one of the larger centers in Europe

REFERRAL OF PATIENTS TO DITEP FOR INCLUSION IN ECT

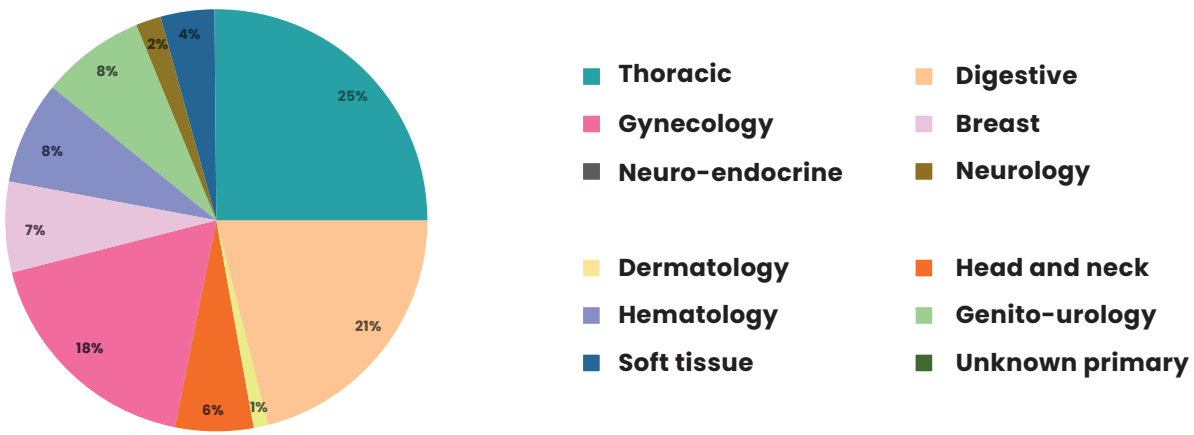


PATIENTS RECRUITED IN DITEP TRIALS



DITEP Phase 1 trials

436 patients with various types of cancer treated in early clinical trial in 2024



UNLOCK, DECIPHERING THE MECHANISMS OF ACTION AND RESISTANCE TO INNOVATIVE DRUG

Beyond the toxicity of treatments, the purpose of early phase trials is to better understand the mechanisms of action and resistance of our treatments in patients.
Future oncotheranostics from early phase clinical trials provide cellular and metabolic efficacy data and genetic and extragenetic resistance mechanisms.

Unlock's mission

To build a unique, multidisciplinary programme integrating medical and basic sciences to study mechanisms of MoA/MoR in highly innovative drugs during the early development phase.

Strategy

- Collect tumour samples at different points in time during treatment: before, during, after and when resistance occurs;
- Analyse samples using complex molecular techniques;
- Establish a clinical-genomic database with more than 1,000 patients, the premise to a complete atlas of tumour resistance.

From Moscato-Match-R to the Unlock programme

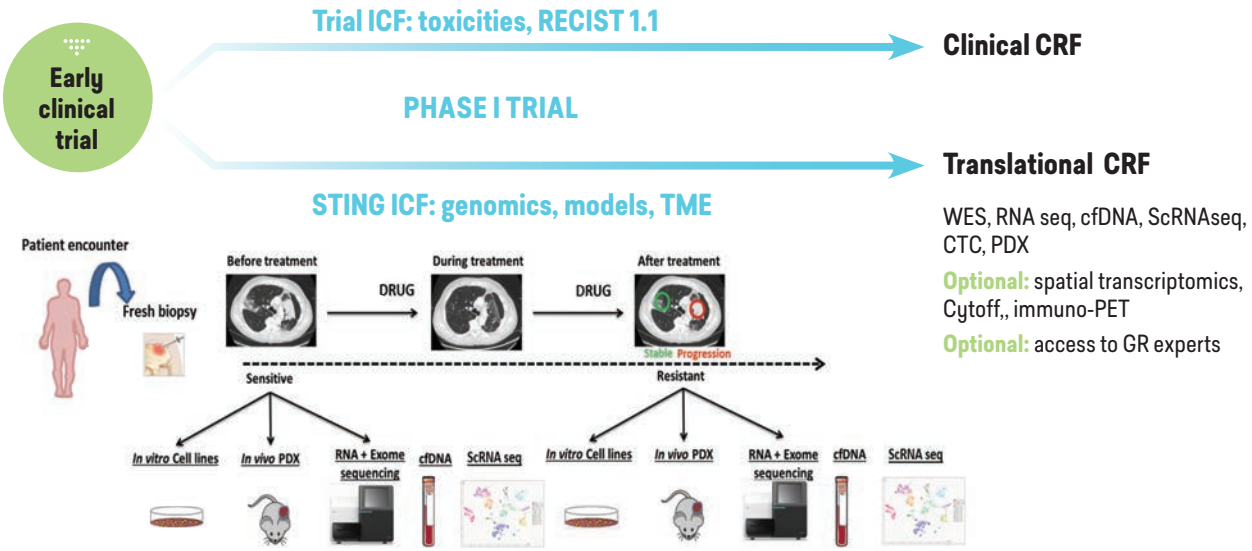
Unlock scientific problem

PHASE I TRIAL	PHASE II TRIAL
Very innovation drugs	Innovative drugs or recently approved drugs
Proof of concept (5-10 patients)	Larger sample size (50-80 patients)
Provide data to support phase 2 trial	Multicenter study

KEY FIGURES

more than 10 project ongoing

Large portfolio of drugs (ADC, new tragted therapies, radioligands, ADC, epigenetics drugs) novative molecule



Scientific assets

- Setting up prospective biobanks of samples from patients (n> 1,000 patients) treated with systemic drugs;
- Using high throughput molecular analysis, and integration into the clinical-genomic database;
- Developing relevant preclinical models of resistance.

KEY FIGURES

165 PDX models already established from 20 tumour types and more than 30 therapies: TKI, ADC, PARPi, hormone therapies, etc.

Characterising PDX: IHC, WES, RNASseq and clinical annotation

EARLY CLINICAL TRIAL DITEP/RADIATION THERAPY

New irradiation technologies

- → Ultra-high-dose rate radiotherapy – Flash RT
- → Spatial fractionation
- → Mini-beams: ongoing clinical trials
- → Nanoagents: use of metallic nanoparticles (Pt, Gd, Au) which amplify the effect of nanometric scale radiation
- → Towards imaging biomarker-guided radiotherapy…

Imaging biomarker-guided radiotherapy… Towards ultra-precision radioimmunotherapy

SABR-PDL1 trial

Cohorts:

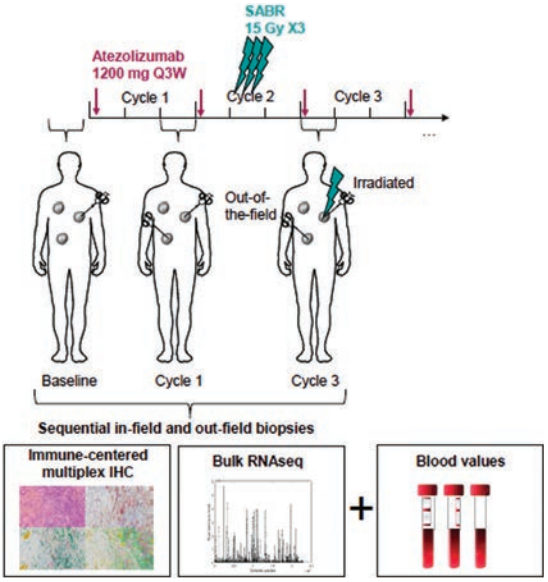
Advanced colorectal (N=60)

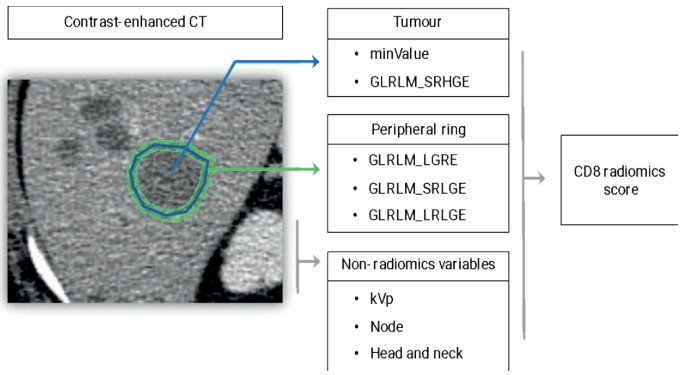
Advanced sarcoma (N=61)

Advanced NSCLC

Advanced RCC

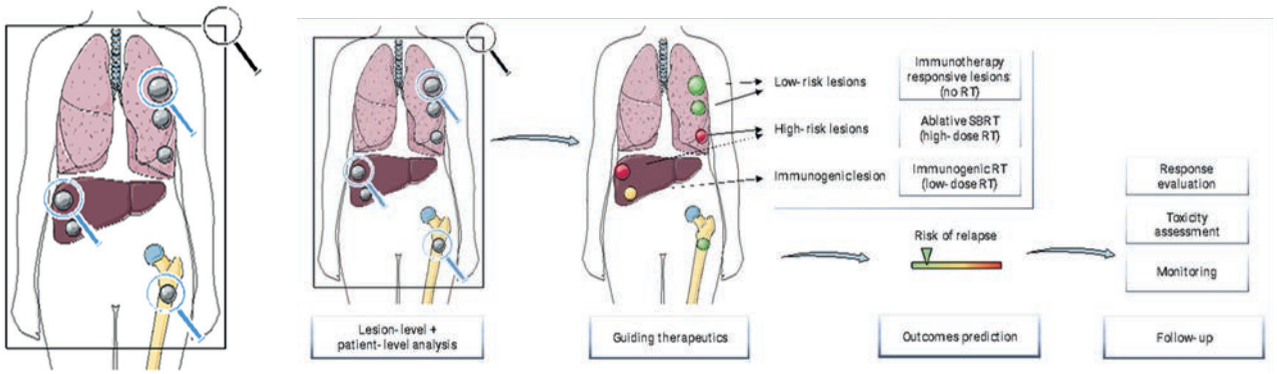
Primary endpoint: 1-year PFS rate





Pathology-driven imaging-biomarkers guided radiotherapy

- → Prediction of CD8 T cells using radiomics on contrast enhaned CTsc
- → Unique radiomic biomarker for IO validated by several studies and centers
- → Allowing assessment of spatial heterogeneity



Sun R et al JITC 2022

RADIOGLIANT THERAPIES

A joint early drug development authorisation (Nuclear Medicine Division within the Medical Imaging Department, Radiotherapy Department and DITEP) for better patient access to innovative radioligand or radiation-based therapies, including all quality standards for early drug development.

Radioligand Therapy at Gustave Roussy

Nuclear Medicine Clinical trials scheduled in 2024–2025:
→ 13 in 1 year
→ Phases I, II and III

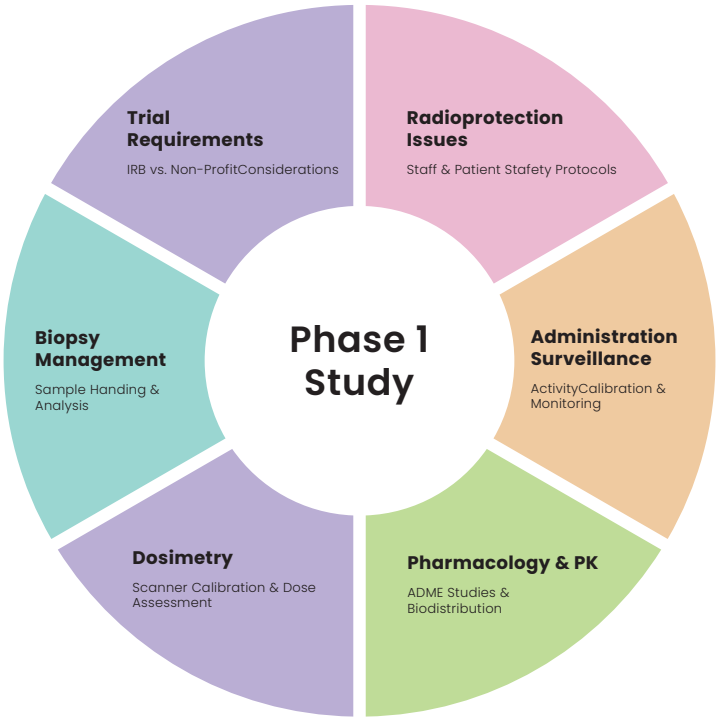
A dedicated platform with:
→ Radiopharmacy facility
→ Imaging facility

A historical reference centre for radioligand therapy with a dedicated theranostic unit (radiopharmacy, imaging facilities and radiation-protected rooms)

KEY FIGURES

More than 500 hundred treatments per year in different cancers

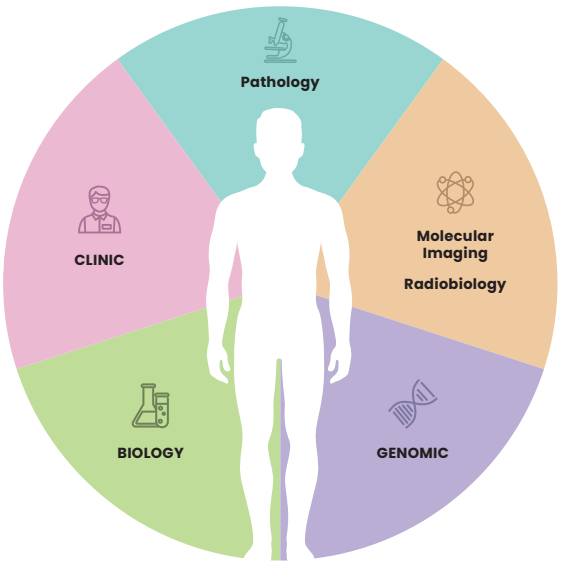
More than 10,000 PET examinations/ year using standard and innovative tracers



Conducting a Phase 1 Nuclear Medecine Study

Critical Components and Considerations

- Safety Focus
- Procedural Focus
- Scientific Focus
- Technical Focus
- Biological Focus



Research program

The target:
Specific for tumor
Stromal microenvironment
Immune microenvironment
Angiogenesis

Radioligand therapy

Radioresistance
Radiobiology

MIS (Molecular Imaging signature)
Advanced Imaging Analysis
Multiparametric
Radiomics
Dosimetry

Sting
Verasting
Unlock
FRESH

Paris-Saclay Multimodal Biomedical Imaging Lab

BioMaps
LABORATOIRE D'IMAGERIE BIOMÉDICALE

université PARIS-SACLAY · cea · cnrs · Inserm

ICE PROGRAMME – IMMUNE CELL ENHANCERS AND CELL THERAPIES

The ICE (Immune Cell Enhancer) platform aims to strengthen cellular therapy and T-cell engager activities by coordinating clinical research, translational research and basic research in solid oncology and haematology for adult patients. Innovative cellular and molecular therapy (T-cell engagers/enhancers) is a complex organisation requiring a dedicated unit.

Coordination

PRISM

UNLOCK BY GUSTAVE ROUSSY

CLINICAL

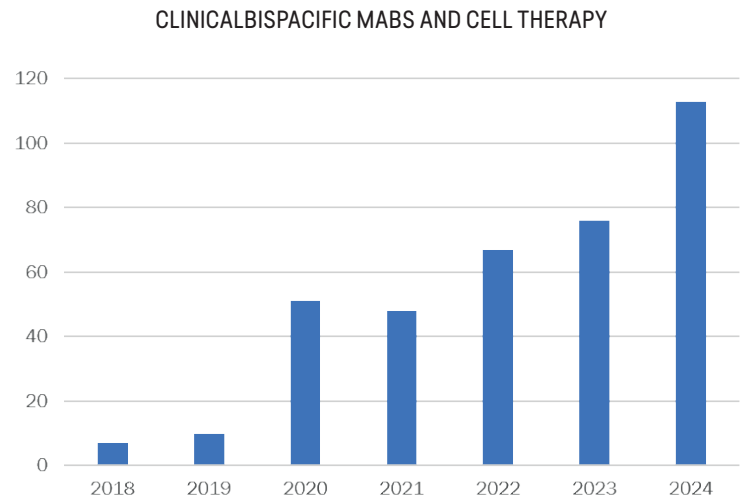
- → ICE drugs & Cell Therapy
- → Management of toxicities
- → Pan-tumour cohorts

TRANSLATIONAL

- → Mechanisms of action
- → Mechanisms of resistance
- → Biomarkers

DEVELOPMENT

- → Academic studies
  - Academic cell therapy
  - Adaptive clinical trials
- → Industry co-developments (drugs & technologies)



	2024	projection 2025
C1D1	113	~150 pts
Dont phase 1	*70*	*~110*
Dont phase avancée	*43*	*~40*
Essais	30	~ 25
Dont phase 1	*21*	*~ 18*
Dont phase avancée	*9*	*~ 7*

Based on Q1-Q2 CTMS registered trials and Q3-Q4 extrapolation

TRANSLATIONAL PROGRAMME PROPOSAL

Coordination

Y. Loriot &
COPIL UNLOCK
Bispécific Ab
R. Flippot
N. Chaput

FX Danlos
Cell Therapy
C. Bigenwald
(PIONEER)

FIC
EARLY DRUG
DEVELOPMENT

QUESTIONS:
MOA
MOR

Immune landscape and determinants of outcomes

IMMUNE DYNAMICS	
Circulating lymphocyte subtypes, clonality & functionality	[flow cytometry, TCRseq, activation assays]
Cytokine profile & inflammatory markers	[high throughput cytokine assays, NETs]
MYELOID CONTEXTURE & IMMUNE TOLERANCE	
Circulating myeloid cell contexture	[single-cell RNA-seq]
Phenotypes of myeloid immune infiltration and resident macrophages	[MERScope]
EPIGENETIC DETERMINANTS OF RESPONSE	
Chromatin remodeling, T cell functionality and phenotypes	[scATAC/RNAseq]

Immune and tumor cell interactome

EX-VIVO TUMOR EXPLANTS	
Activation, migration and cytotoxicity upon treatment exposure	[Functional tests]
TARGET EXPRESSION	
Tissue and circulating target expression	[spatial proteomics, EVs]
IMMUNE AND TUMOR CELL MODELS	
Live imaging of PDOs & immune cells coculture	[Biomimetic complex organoids]
ICE drugs testing and immune engagement	[Drug assays]

Novel digital tools

DATA INTEGRATION
Multilayered predictors and digital twin
RADIOMICS-BASED PREDICTORS
PATHOMICS-BASED PREDICTORS

Ancillary research
Germline
features
Microbiome

Samples
Tissue
Plasma & PBMC

Technology partnerships
Novel biomarkers

ARTIFICIAL INTELLIGENCE (AI) AND CLINICAL RESEARCH

Artificial intelligence (AI) is revolutionizing both cancer research and patient care. From faster and more precise diagnosis, improving stratification efforts and prognosis to tailoring ultra precision therapies, AI is reshaping the landscape of precision cancer medicine

mosaic an owkin initiative

lifen

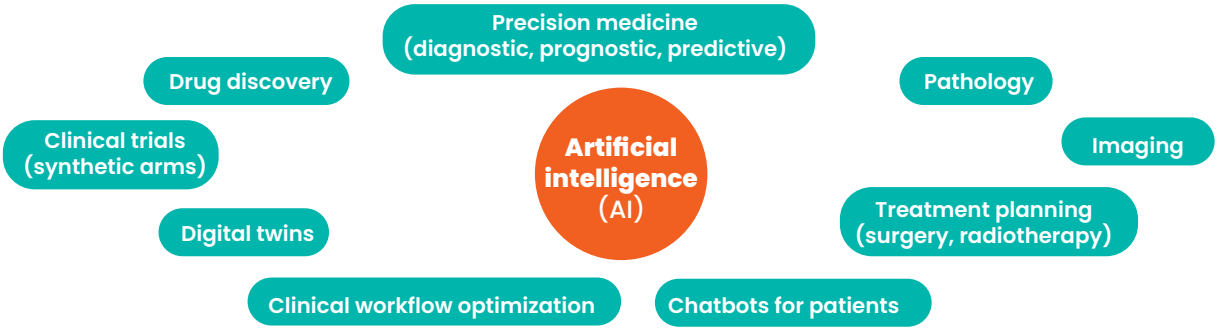
DS MEDITWIN

PartrAIt

A global strategy

- DataBase 400 k patients
- Four research Teams & one core facility
- Partnership with U Paris Saclay
- Institut Hospitalo Universitaire

- Pathomics & Radiomics
- Digital Twins
- Natural language processing for data capture
- Computational science
- Data integration



Workflow optimization

> Data extraction
> Database management
> Optimization of data entry
> Summarization of clinical notes
> Automatic matching to clinical trials...

→ Development of a LLM for Gustave Roussy (Marc Deloger and team)

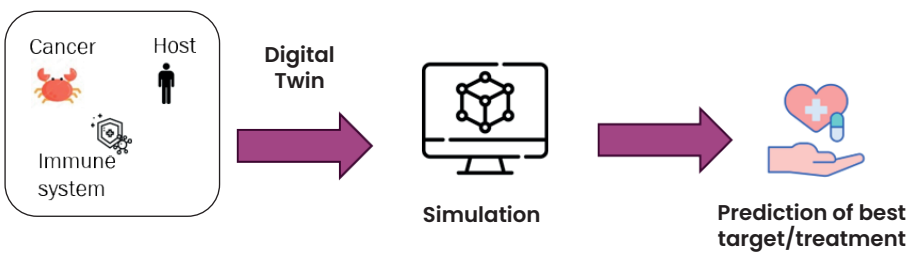
Meditwin program

MEDITWIN: large-scale academic-industrial consortium (including 7 IHU) for creation of digital twins in oncology, cardiology, neurology...

WP3: Precision Medicine for Oncology (PRISM, Dassault Systèmes)

Create digital twins for cancer patients
- Multi-scale
- Evolving in time
- Integrating Cancer/Host/Immunity

Allow simulation and prediction of best personalized treatment/best target



DS MEDITWIN
DASSAULT SYSTEMES
Inria
iHU FRANCE
ICAN
Institut du Cerveau
ihu STRASBOURG
imagine INSTITUT DES MALADIES GÉNÉTIQUES
FOReSIGHT
PRISM

THE LARGEST CANCER CAMPUS IN EUROPE

The Gustave Roussy Campus is a unique ecosystem in France and Europe dedicated to the fight against cancer, bringing together healthcare, research and industrial innovation in a single location. Its healthcare campus offers patients excellent care, combining medical expertise with personalised support.
The research campus brings together internationally renowned teams engaged in cutting-edge research to better understand, diagnose and treat cancer. Finally, the industrial innovation campus facilitates partnerships with companies and start-ups, accelerating the development of new therapies and technologies.
This integrated model fosters synergies between researchers, clinicians and industry, with a common goal: to accelerate innovation and improve patient care.

"The highest level of care, research, innovation and value creation."

→ **Launch of the Paris Saclay Cancer Cluster**
- Co-founded with Sanofi, Inserm, the Institut Polytechnique de Paris and the Université Paris-Saclay
- A high-potential ecosystem bringing together the best scientific, human and technological expertise to cure more patients

→ **Directly connected to Paris, airports and train stations**

→ **A massive €480 million investment plan over 5 years to build a HUB 3.0 with:**

> A campus dedicated to care

> A campus dedicated to research and teaching

> An economic development campus

TO THE SOUTH, A CAMPUS DEDICATED TO CARE

→ **Central building**
- Renovation of facades under way

→ **Interception building**
- Targeted prevention for people at risk of cancer
- City-hospital collaboration
- Development of new screening methods

→ **A new building dedicated to prevention, diagnosis, outpatient and international activities**
- Improvement of patient intake and care pathway
- Scheduled to open in 2029

"On a single site, all disciplines and activities are brought together for greater efficiency in patient care and interactions between doctors, researchers and industrial partners."

TO THE NORTH, A CAMPUS DEDICATED TO RESEARCH AND TEACHING

→ **Existing buildings:**
- Research pavilion 1 and 2
- Molecular medicine building

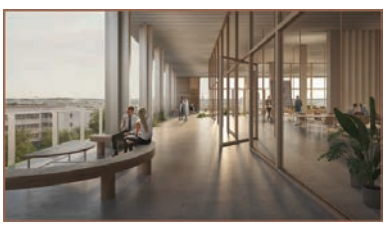
→ **New research building**
- Start of work: 2025 | Delivery: early 2028
- 33,000 m² - €160 million
- Objectives: 40 to 60 research teams

→ **New tertiary building**
- Start of work: 2025 | Delivery: 2027
- A new car park, offices and a new amphitheatre with 200 spaces and 3 modular rooms that can accommodate up to 240 students

"The construction of a new research building will, in particular, double our workforce. Furthermore, the tertiary building is an essential project for optimising functional spaces and developing Gustave Roussy's educational activities."

THE FUTURE GUSTAVE ROUSSY RESEARCH CENTRE

> A new 33,000 m² research building (+ 30 %)
> **€160 million**
> **May 2025:** start of work
> **Early 2028:** official opening



100,000 M² DEDICATED TO INNOVATION AND ECONOMIC DEVELOPMENT

→ Biocluster I (Amundi, Kadans, Perelis buildings)
- Lab 116 by Perelis: available since October 2024
- Byos by Amundi: available since February 2025
- The Hive by Kadans: delivered in November 2025

→ Biocluster II (Fort de la Redoute)

→ Metro line openings
- Line 14: since 18 January 2025
- Line 15: June 2026

« The creation of a real neighbourhood that will host companies, healthcare and research players, in particular to enable the transformation of research products to improve the care offer for our patients but also to strengthen our international attractiveness. »

PARTNERSHIPS AND CONTACTS

WORKING IN A NATIONAL AND EUROPEAN PROFESSIONAL NETWORK

Gustave Roussy certified CLIP2 by the French Cancer Institute (INCa)

CLIP2 are research centres specialised, within healthcare organisations (university hospital center, cancer centre), in early phase trials on new medicines from pharmaceutical companies and academic laboratories, and biotechnology companies. They receive logistics and financial support from the Institute to achieve the highest international level of quality in early phase clinical trials.
Special partnership with two cancer centres within the united French league Unicancer: Institut Bergonié (Bordeaux) and Centre Léon-Bérard (Lyon).

Cancer Core Europe - an on-going wide-scale collaboration including regulatory bodies

Gustave Roussy is engaged in close dialogue with:
- The French drug safety agency (ANSM);
- Patient safety committees supervising clinical trials (CPP);
- The French health innovation agency (AIS), providing support for development resources in health innovations.

CONTACTS

Prof. Benjamin Besse, MD, PhD
Director of Clinical Research
benjamin.besse@gustaveroussy.fr

Prof. Christophe Massard, MD, PhD
Head of the Department of Therapeutic Innovation and Early Stage Trials (DITEP)
christophe.massard@gustaveroussy.fr

Prof. Laurence Albiges, MD, PhD
Head of the Department of medical Oncology
laurence.albiges@gustaveroussy.fr

Dr. Édouard Dupis, PharmD
Industrial Partnerships Project Manager
edouard.dupis@gustaveroussy.fr

CONTACTS

Prof. Eric Deutsch, MD, PhD
Head of the Radiotherapy Department
Eric.deutsch@gustaveroussy.fr

Prof. Desiree Deandreis MD, PhD
Head of the Nuclear Medicine Unit
Desiree.deandreis@gustaveroussy.fr

Prof. Yohann Loriot MD, PhD
Deputy Head of the DITEP, PI of UNLOCK
Yohann.loriot@gustaveroussy.fr

Dr. Ronan Flippot, MD
Head of the ICE unit
Ronan.flippot@gustaveroussy.fr

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CANCER CAMPUS GRAND PARIS

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