CLINICAL RESEARCH PLATFORM AT **Gustave Roussy** FRANCE

A comprehensive approach to innovative clinical research

One site, five skill levels, inclusive organisation, steady quality for early clinical phases

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.

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

Fabrice Barlesi

Director General

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

Through our transformation into a research foundation, we are gaining in agility, recognition and resources in the global oncology research ecosystem.

With PRISM, we are at the heart of true precision medicine that classifies tumours by biology, molecular and immune status, with nine university hospital research programmes underway at our site.

Being an integrated centre where research goes hand in hand with treatment procedures enables 40% of our patients to be recruited for clinical studies. To strengthen its clinical research capabilities, Gustave Roussy has set up an unprecedented organisation dedicated to clinical research.”

2024

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

- Phase I-II trials: Solid tumours and heme-related disorders
- Drugs, surgery, radiation therapy and nuclear medicine
- Immune Cell Enhancer and Cell Therapies Unit

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

Our multidisciplinary clinical research platform provides for

Better patient safety

Better quality

Better capacity

For innovative early clinical research

AN INTEGRATED PLATFORM OF CLINICAL AND TECHNICAL SKILLS

An all-inclusive formula

The integrated organisation increases capabilities for completing early clinical trial phases, while ensuring patient safety all in one place.

The integrated platform offers the same quality as early stage I, I/II, II procedures. It will be possible to include patients in phase III trials depending on the type of trial and the strategy tested.

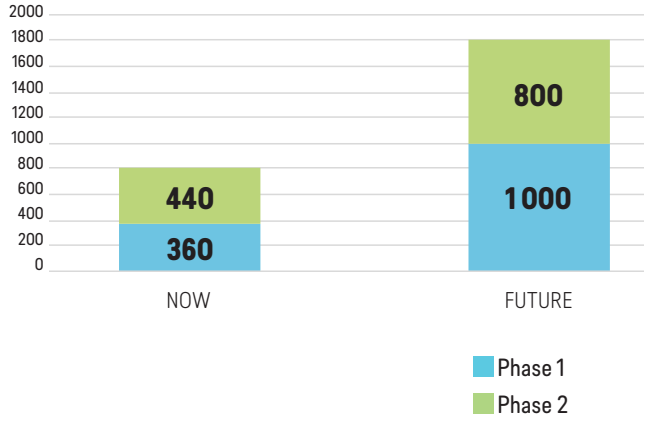
All phases I, I/II, II benefit from:
- → teams trained to the same high level of professional standards;
- → an optimised organisation, in particular bed occupancy rates;
- → the stability of the teams ensuring the good quality of the data collected at all phases of the trials.

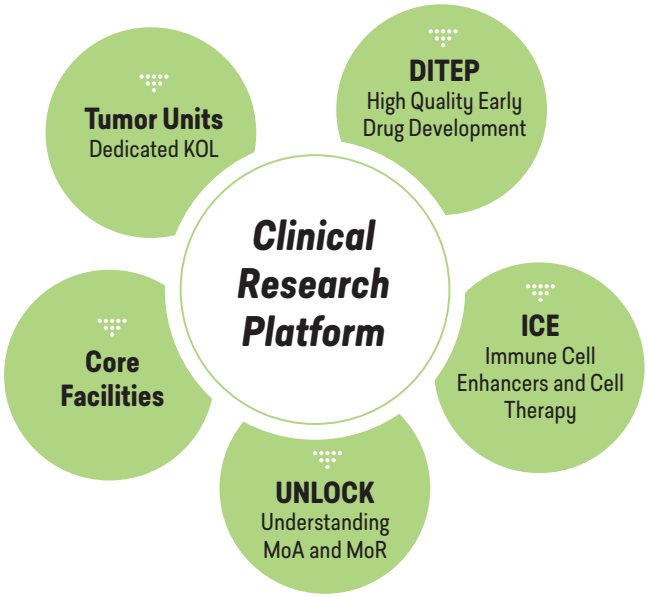
A realistic project of 1,000 patients included in phase I thanks to the international scope and doubling the number of patients included in phase II

All in one place, the clinical research platform brings together human resources of the same level of competence, technical resources and laboratories with the latest tools.

With these integrated capabilities, the platform is sized for ambitious projects aiming to include 1,000 patients in phase I in a few years' time.

PLATFORM: ESTIMATED NUMBER OF PATIENTS





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

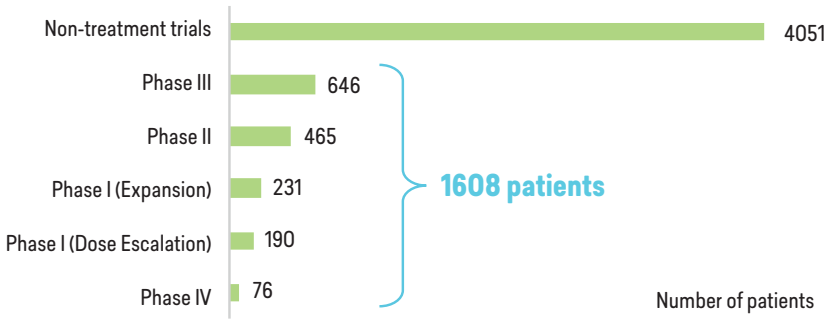
Haematological cancers and all solid tumours in adults.

Improvement on the way for...

- Providing access to innovative and precision medicine for more patients;
- Optimising efficiency of resources and tools (use of space, planning schedules, processes and patient journey);
- Upgrading medical and paramedical expertise;
- Understanding MoA/MoR to generate "omics" data and unravelling unknown mechanisms.

Management upgrading clinical trials to the highest quality standards, aiming for an easy transition from early to late clinical phases, based on dedicated teams throughout the development stages.

GUSTAVE ROUSSY CLINICAL RESEARCH ACTIVITY IN 2023



CANCER MEDICINE DEPARTMENT, A UNIQUE HIGH VOLUME MEDICAL ONCOLOGY EXPERTISE

KEY FIGURES

Over 70 medical oncologists (MD & MD-PhD)
Patients from all solid tumor types (breast, GU, GI, Lung, Gyne, Skin, Sarcoma...)
72 beds for in-patients hospitalisation
76 chairs for day care
90 new clinical trial activated per year
264 interventional clinical trials in 2022

Impact

- 2 Practice Changing Trials /y
- 400 publications /y
- 8 highly cited researchers (Clarivate / Web of science)
- Active role in international guidelines to disseminate new Standard of Care

From clinical expertise to Practice Changing Trials and Approval

With its high volume and expertise, Gustave Roussy's Cancer Medicine Department has a track record of transforming the Standard of care in Medical Oncology.
Across solid tumor types and from each organ oriented tumor board, has emerged experts involved in both academic and industry sponsored trials to transform innovation to standard practice. With a close interaction with the early phase clinical trials, Gustave Roussy's medical oncologists have boosted trials from phase I to phase III and defined new standards of care, transforming the prognosis of many advanced cancers as well as in earlier disease setting, such as in the adjuvant and neoadjuvant settings. Every year 2 Practice Changing Trials are led by Gustave Roussy's medical oncologists. The clinical expertise is recognized by the strong contribution of these medical oncologist as guidelines members and international meetings' faculty.

DITEP, MEDICAL DEPARTMENT DEDICATED TO EARLY PHASE CLINICAL TRIALS

Largest phase I centre in France, with national accreditations (AFNOR, ARS, INCa) and one of the larger centres in Europe

Team

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

Biopsies

- More than 700 tumour biopsies in early phase trial patients in 2023
- And over 1,000 at Gustave Roussy in phases II/III

KEY FIGURES

50% of total phase I activity of all French CLIP² centres (INCa designated early phase clinical trial centres)

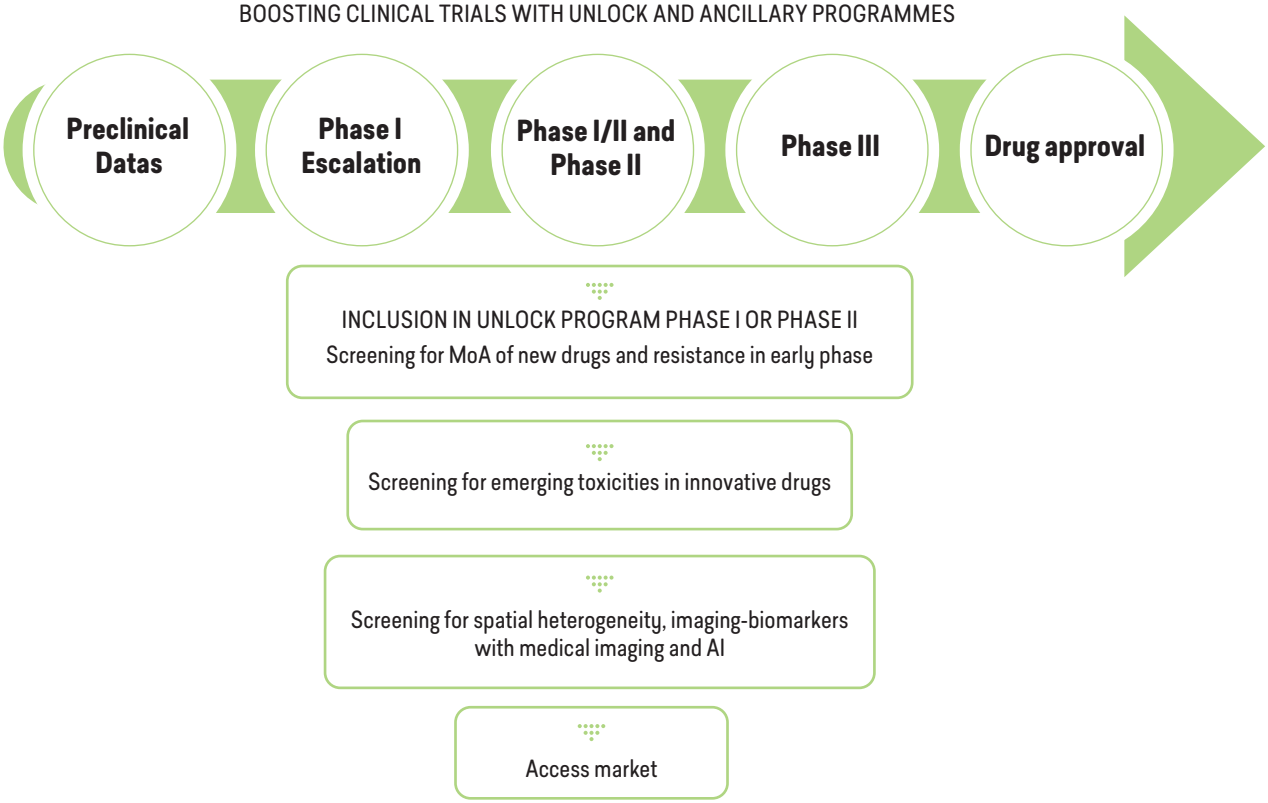
Unlock programme

- Screening for MoA of new drugs and resistance in early phase
- Screening for emerging toxicities in innovative drugs
- Screening for spatial heterogeneity, imaging biomarkers with medical imaging

Innovative drug toxicity under scrutiny

Gustave Roussy pioneered such toxicity monitoring with a unique organisation including a consultant specialists circuit, institutional guidelines, recurrent multidisciplinary team meetings (MDTM): a dedicated pharmacovigilance register for adverse outcomes and immunotolerance induced by immunotherapy.

BOOSTING CLINICAL TRIALS WITH UNLOCK AND ANCILLARY PROGRAMMES



More: In 2024, ToX New Drugs, a new multidisciplinary team meeting (MDTM) dedicated to innovative drug toxicities, is ongoing at Gustave Roussy.

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.

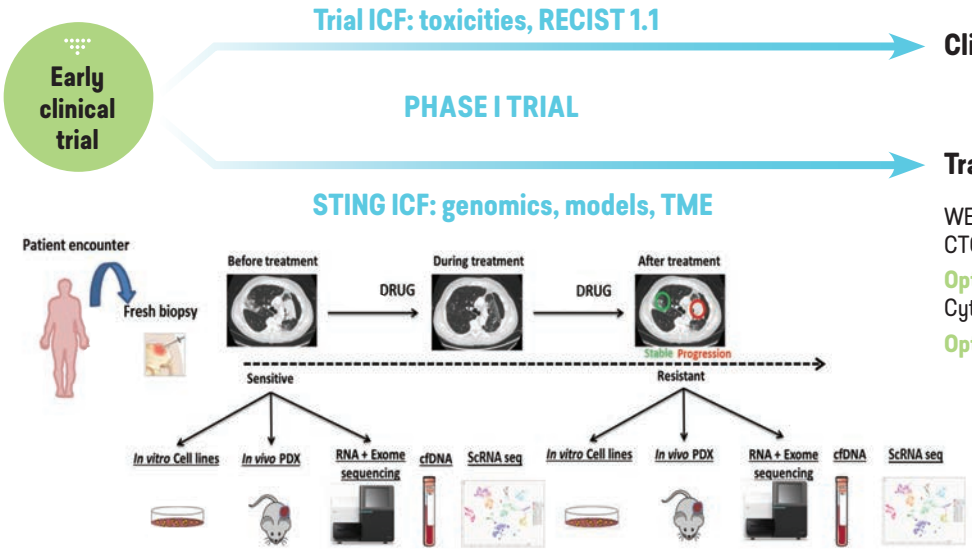
From Moscato-Match-R to the Unlock programme

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

175 patients included
164 biopsies performed
52 sequencing runs
17 resistance mutations identified on disease progression
Of which 15 by bypassing the target and 2 secondary mutations
41% of patients have been treated in an early phase clinical trial with an innovative 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

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.

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:

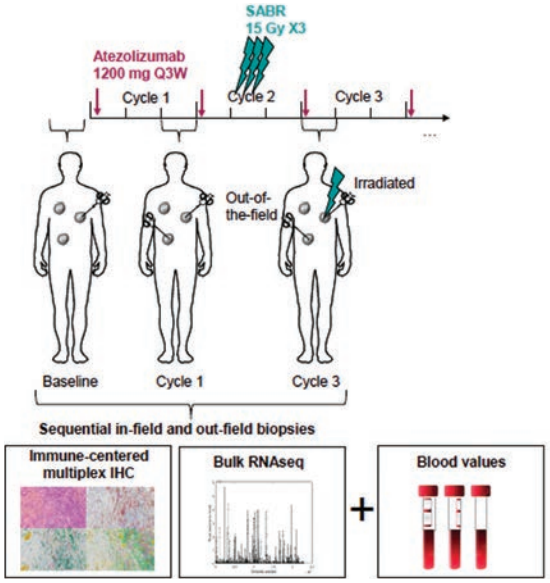
Advanced colorectal (N=60)

Advanced sarcoma (N=61)

Advanced NSCLC

Advanced RCC

Primary endpoint: 1-year PFS rate



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:

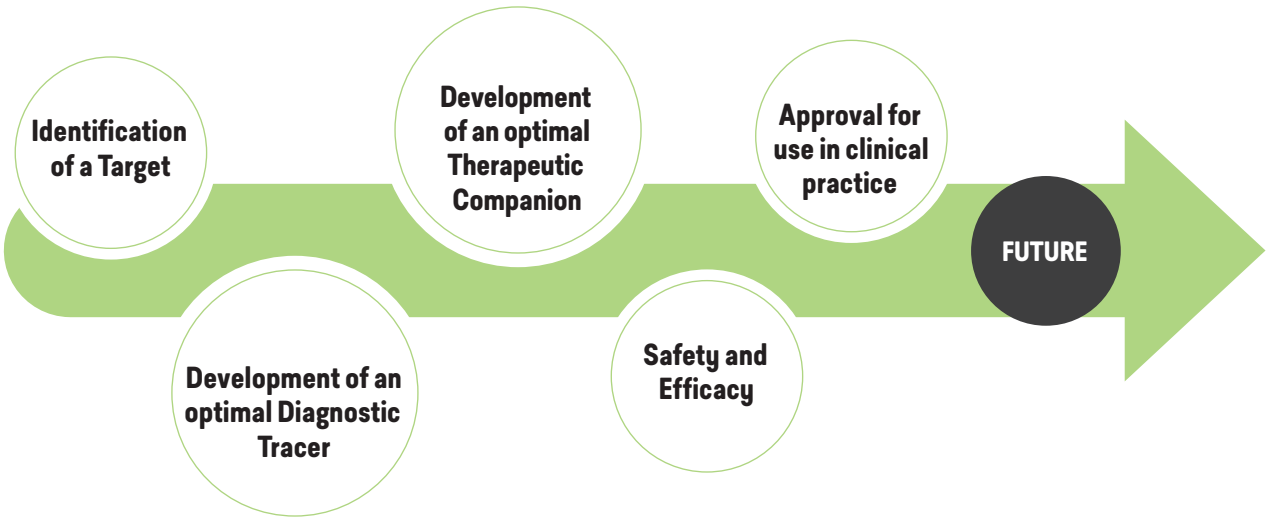
- Radiopharmacy facility
- Imaging facility

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



PRISM, THE PRESENT AND FUTURE OF PRECISION MEDICINE

Several adult and paediatric clinical research programmes have validated the feasibility of molecular profiling from fresh biopsies of solid tumours and blood malignancies to specify the exact cancer therapy to be used. Based on this experience, Gustave Roussy was certified as a university hospital complex (*institut hospitalo-universitaire* - IHU) and National Centre for Precision Medicine (PRISM) in 2023.

Upscaling thanks to the partnership with Foundation Medicine

A step forward, Roche, Foundation Medicine Inc. and Gustave Roussy have established a unique technical partnership with a high-throughput liquid biopsy analysis platform using Foundation One Liquid CDx technology, a comprehensive genomic profiling (CGP) test.

Essential clinical data support the tissue and liquid biopsy activity result. The objective is to increase analysis capacity to several thousand tests in order to better meet French demand, with the same level of information (analysis capacities currently stand at around 4,000 tests per year over the first year; can be expanded to 8,000 tests per year).

The results are regularly submitted as a biological analysis report to the Gustave Roussy/PRISM precision medicine database and to the weekly molecular multidisciplinary team meeting within the institution, which then refers patients to the dedicated early phase trials.

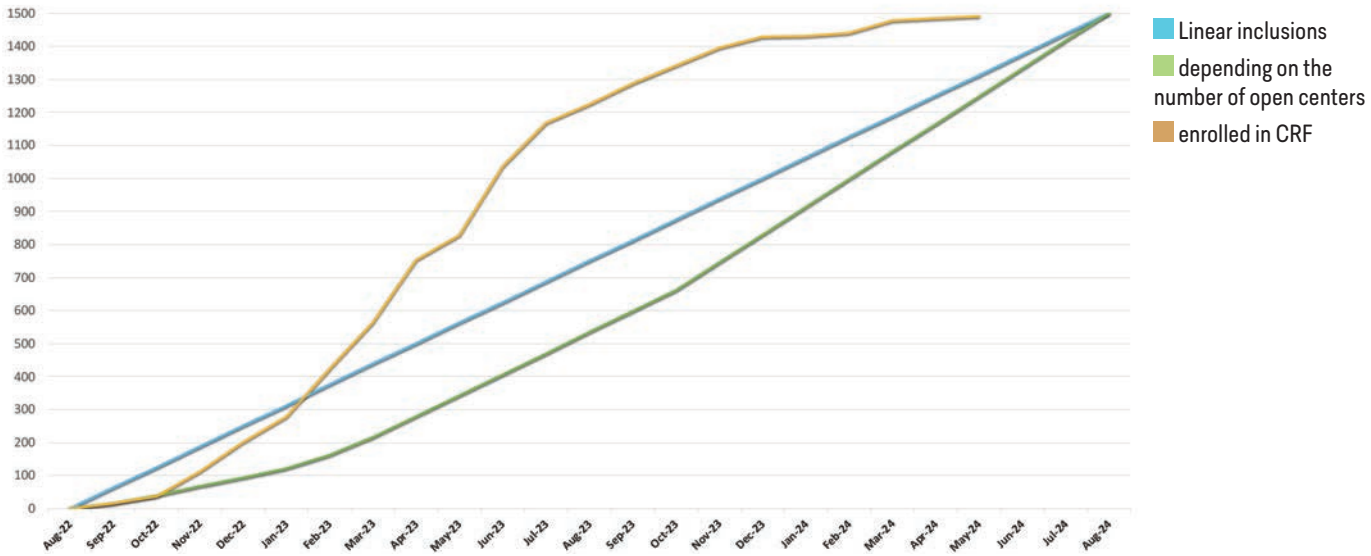
Dedicated lab and facility at Gustave Roussy

As part of this partnership, Gustave Roussy will increase its biopathology capabilities by creating an innovative genomic analysis laboratory that will be accessible to recognised experts, and to reference precision medicine centres and institutions in France. This new platform represents a step forward for cancer patients treated in France, with CGP being made available to as many people as possible. French doctors will have access to more accurate diagnosis for their patients in order to identify potential treatment options, promoting the development of new clinical trials that will support research and development, and contribute to the optimisation of treatment strategies and care pathways.

KEY FIGURES

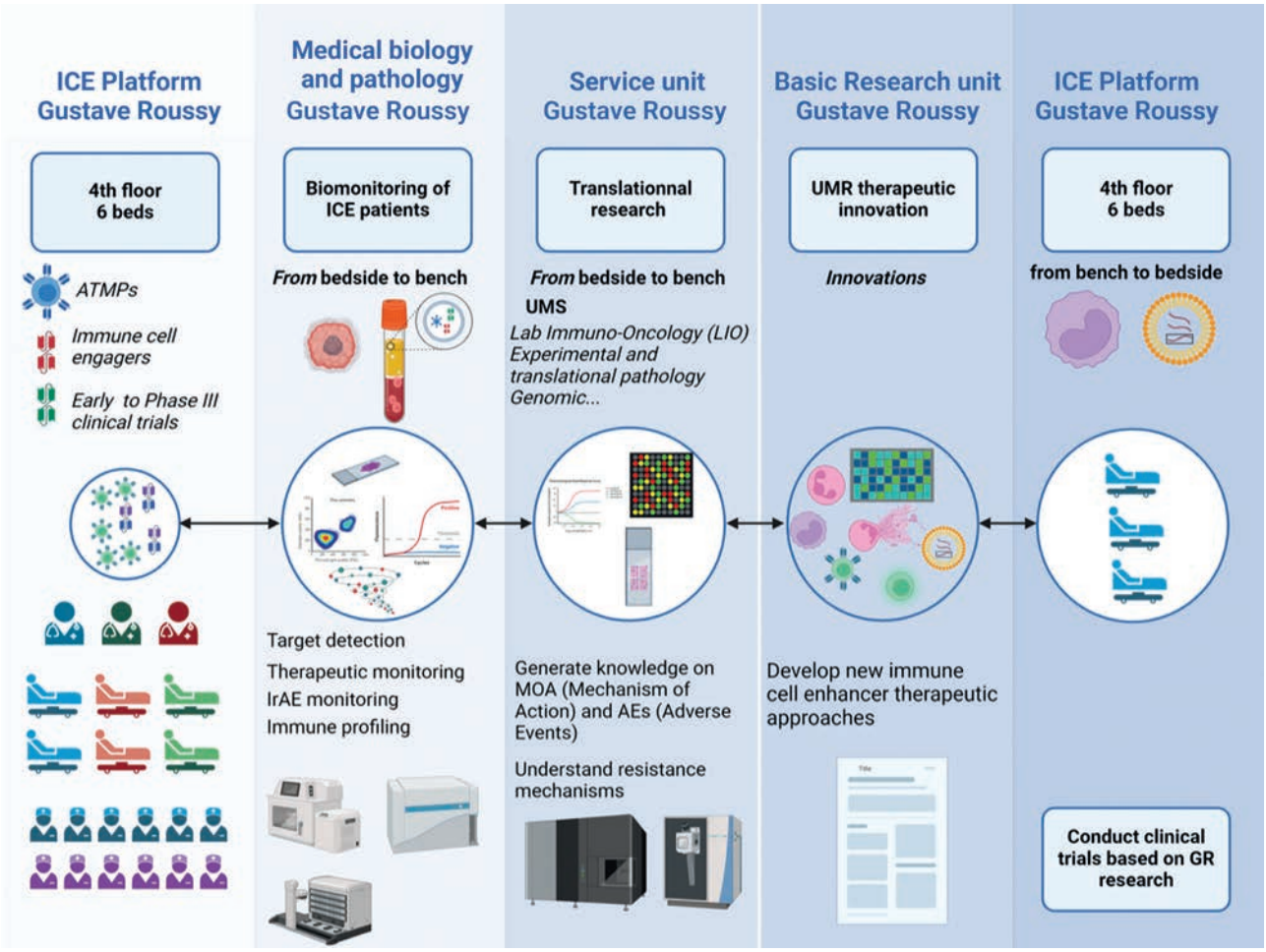
More than 2,000 patients/year already screened for molecular targets at our institution and more than 1,500 patients from other centres in France

INCLUSIONS IN PRISM-PORTAL STUDY



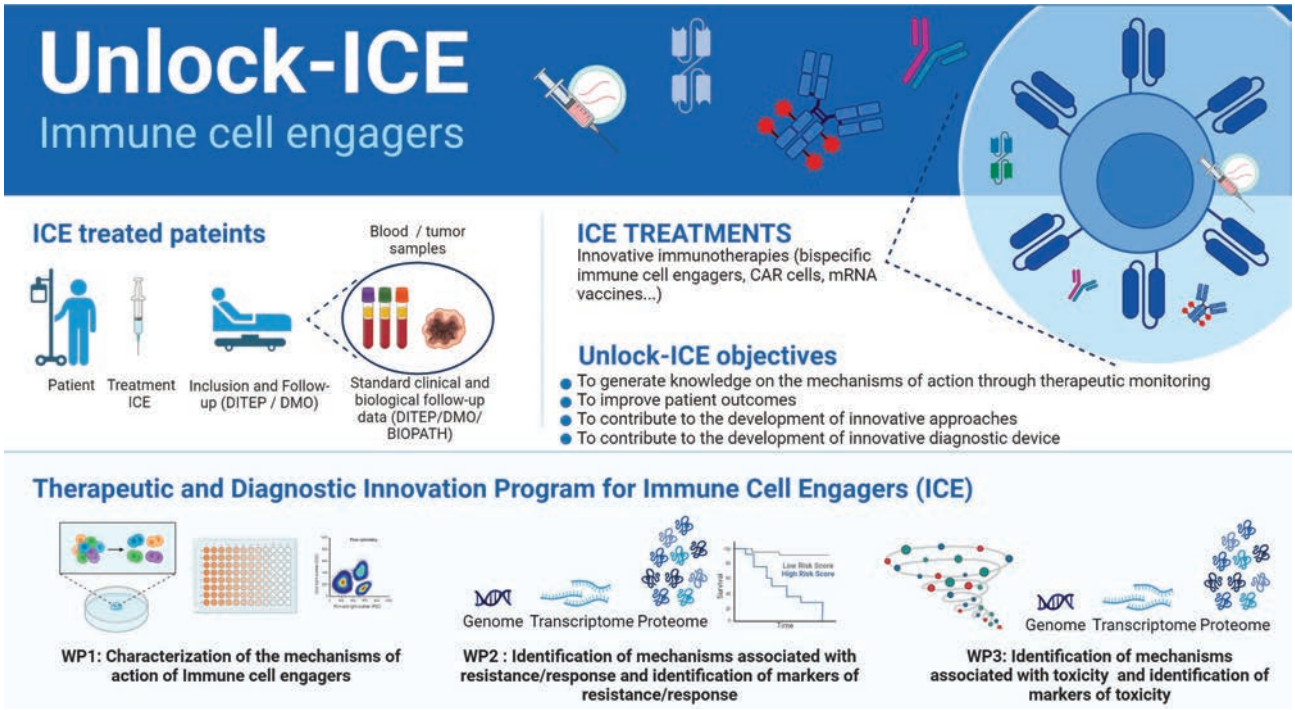
ICE PROGRAMME – IMMUNE CELL ENHANCERS AND CELL THERAPIES

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.



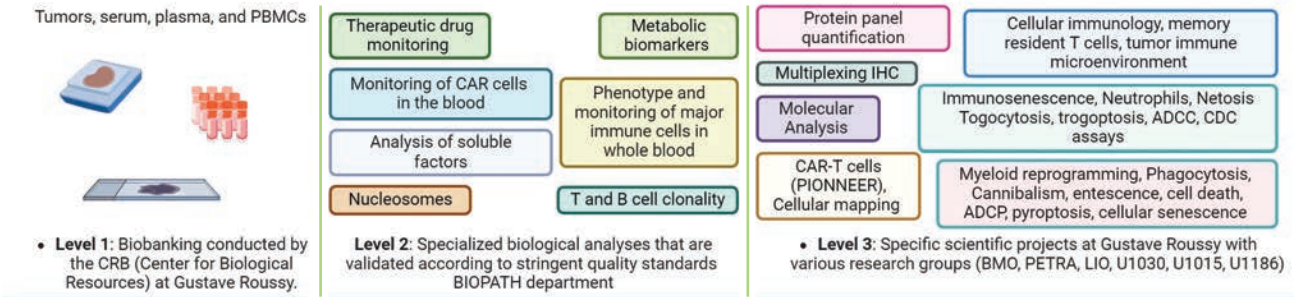
The clinical ICE unit will offer dedicated clinical research from early phase to phase III. This single site organisation will ensure effective coordination of these activities with a dedicated translational research programme (Unlock ICE programme).

This headlining multidisciplinary platform will bring together all the expertise required to manage these treatments, from administration to management of complications. A future accomplishment will be an interdepartmental team with expertise in cellular therapy from haematology, early drug development and medical oncology departments.



Unlock-ICE – alongside the biological profile for patients treated with Immune Cell Engagers (ICE)

Our objective: to dive further into the mechanisms of action of immune cell engagers, identifying predictive markers of response and toxicity, optimising the efficacy and safety of such therapeutic approaches.
Identifying factors that modulate the immune response, such as the tumor microenvironment and suppressive cells, will clarify synergistic therapeutic combinations or novel treatment modalities.



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.

As a leading and internationally renowned comprehensive Cancer Centre, Gustave Roussy has multiple assets in clinical, translational and basic research, based on the institutional R&D programmes set for the next five years. Our scientific strategy aims to structure an internal process for the emergence, selection and prioritisation of flagship programmes (10 currently identified) with the ambition to improve patients' living conditions and societal impact.

Through industry partnerships, our priority is to provide access to the most innovative and potentially effective agents, devices, or IT tools for our patients early in their development. Our teams are able to offer ancillary projects to optimise the development of new molecules, establish the mechanism of their action or define predictive biomarkers of their effectiveness or resistance along all clinical development pathways, from early to late phase trials.

Our large biological collections across all solid tumours as well as haematological malignancies and clinically annotated molecular databases also provide the opportunity for preclinical and translational collaborations, including radiomics/pathomics and data science, by bringing academic and industrial researchers and clinicians together.

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