



CONDUCTING — EARLY CLINICAL TRIALS WITH THE DITEP

**GUSTAVE/
ROUSSY** —
CANCER CAMPUS
GRAND PARIS

DITEP 
Drug Development Department

CONDUCTING — EARLY CLINICAL TRIALS WITH THE DITEP

4	About the Drug Development Department (DITEP) - Phase I Research Facility
5	Certification Label
5	DITEP Staff and Care Wards
5	Collaboration across Gustave Roussy Departments & External Partnerships
6	Regulatory Contract and Budget
6	Committee Review Process
6	Contract & Budget
7	Facilities and Equipment
7	About the Pharmacy
7	About the Local Laboratory
8	Digital Diagnostic Capabilities
8	Other Equipment
8	Storage Facilities
9	Capabilities & Specific Skills
9	Molecular Testing
9	Management of Immune-related Toxicities
9	Regarding Investigators
10	Study Procedure and Information
10	Informed Consent
10	Site Training
10	Complaint Management
10	Source Documentation/CRFs
10	Site Monitoring
10	Audit/inspection
11	DITEP CONTACTS

You will find in this leaflet the details about our organization and capacity to conduct early clinical trials. For specific requests you may have regarding your protocols, please feel free to contact us.

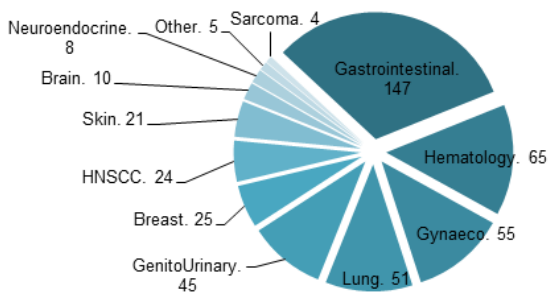
ABOUT THE DRUG DEVELOPMENT DEPARTMENT (DITEP) - PHASE I RESEARCH FACILITY

Gustave Roussy (private hospital) is a Cancer Centre, affiliated to the UNICANCER Federation. It is neither affiliated with a government agency nor part of a government funded health service. As part of our mission to offer access to innovative therapies for cancer patients, the Drug Development Department (DITEP) of Gustave Roussy is committed to early clinical trials, and conducts around 90 phase I/II studies yearly to test new drugs for the treatment of various cancers (adult patients). We have research experience with different types of sponsor: industry, academic, and investigator initiated.

Over the last 3 years (2015-2017), our site conducted 134 early clinical trials which have been enrolling adult patients with advanced solid tumors or hematologic malignancies, whose (one study may have enrolled different types of cancers):

- Ovarian / Fallopian / Peritoneal Cancer: 35 studies
- Breast Cancer: 27 studies
- Prostate Cancer: 21 studies
- Lung Cancer: 54 studies
- Gastric Cancer: 59 studies
- Urothelial Bladder: 16 studies
- Skin cancer : 14 studies
- Pancreatic Adenocarcinoma: 19 studies
- Hematologic malignancies: 27 studies

In 2017, 104 early clinical trials were opened at Gustave Roussy, and 460 adult patients with various types of cancers (see below) were treated in early clinical trials conducted by DITEP (including AcSé program):



Early clinical trials with immunotherapeutic agents represented 52 trials in 2017, with 246 patients treated, including trials with intratumoral injections. Moreover, 806 patients were enrolled in our precision medicine programs.

Certification | Label

The DITEP has a certification from the French Health Regional Agency (ARS) to conduct First-in-Human (FIH) trials. It is also certified as an early clinical trials center (CLIP2) by the French National Cancer Institute (INCa). Since November 2016, the DITEP has the ISO 9001:2015 certification (Quality Management System) for its activities of access to therapeutic innovations, management of early clinical trials, and science outreach.



DITEP STAFF AND CARE WARDS

The DITEP counts:

- 13 principal investigators and sub-investigators with a double expertise in early clinical trials and pneumology, hematology, immunology, radiotherapy, urology, senology, digestive tract.
- 26 study coordinators, one being dedicated to a given study.
- 12 data managers, dedicated to the data entry and monitoring.
- A financial team, in charge of financial agreements, budget and invoicing.
- A quality assurance officer, in charge of all the quality documents.
- Nursing Staff: 25 dedicated days nurses and 7 night nurses for early clinical trials, trained for its specific activities and GCP, + 4 day care helpers. Under the responsibility of 2 Nurses Managers (day staff) and 2 nurses Managers (night staff).
- 13 single-patient beds within our inpatient unit. This unit receives patients who require full-time hospitalization as per protocol or for safety surveillance due to side effects over the week.
- 14 armchairs within our outpatient care unit (+ 2 armchairs dedicated to PK). This outpatient unit is operational every day from Monday to Friday from 7:00 am to 7:00 pm (including PK single sampling on Saturday mornings). This unit also receives patients who require nursing and related care.

COLLABORATION ACROSS GUSTAVE ROUSSY DEPARTMENTS & EXTERNAL PARTNERSHIPS

Thanks to our PI and sub-investigators' double expertise, the DITEP is in close interaction with different specialists to recruit patients for particular tumor types cohorts. All of DITEP experts are part of the early clinical trial multi-disciplinary tumor board (RCP-150). This weekly committee is in charge of all patients' referral validation in our phase I programs, for the review of all on-going trials and medical decisions regarding any complex situations of safety or treatment decisions.

The DITEP also interacts with several platforms in Gustave Roussy to conduct our trials:

- The radiologists' team, trained in all assessment criteria (RECIST 1.1; Cheson, IrRC; OMS...).
- The Interventional Radiology Team, having the ability to perform tissue biopsy and intratumoral injections.
- The Pathology Department.
- The Pharmacy Department.
- The Nuclear Medicine Department (PET Scan, MUGA...)
- Ophthalmological and cardiovascular exams have to be outsourced to another medical institution.
- The laboratory for biological analysis is accredited NF EN ISO 15189

Main contacts :

COPIL application: guylene.chartier@gustaveroussy.fr

CSET application: sandrine.lancereau@gustaveroussy.fr

Contract & budget: laurent.daley@gustaveroussy.fr and sylvie.leal@gustaveroussy.fr

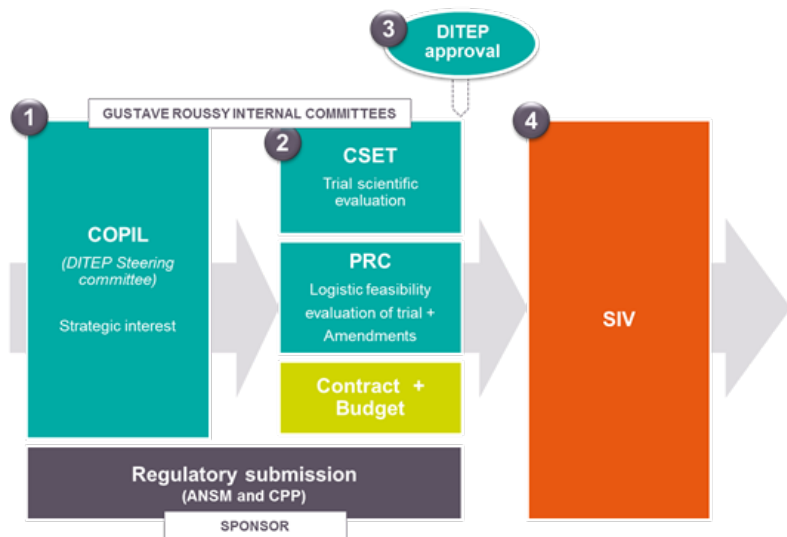
Committee Review Process

The initiation of a study requires 3 internal committees (IRB) approvals from:

- The COPIL, for strategic interest (internal DITEP)
- The CSET, for scientific interest (Gustave Roussy Institutional Committee)
- The PRC, for logistic feasibility, the CSET submission being in parallel.

The COPIL and CSET committees meet monthly, the PRC meets twice monthly.

The submission to our internal committees can be in parallel of the regulatory submission to the ANSM (French National Agency for Medicines and Health Products Safety) and to the CPP (French Ethics Committee).



For the CSET submission, each PI will also provide a brief and simplified description of the trial that is intended to be released on Gustave Roussy website (French version only), in order to give visibility to the study: <https://www.gustaveroussy.fr/fr/essais-cliniques>

Contract & Budget

As per the Decree No. 2016-1538 of 16 November 2016 on the Unique Agreement for the implementation of commercial clinical trials involving human beings in health care institutions, 45 days are required to negotiate the contract and budget if Gustave Roussy is the site coordinator, 15 days if Gustave Roussy is an investigator site, starting from the reception of all documents required (a checklist will be provided by our institution).

FACILITIES AND EQUIPMENT

Our site has unrestricted access to the main facilities/equipment required by protocols during the conduct of a study within the pharmacy and our local laboratory.

About the Pharmacy

Our site is adequately staffed to perform both blinded and un-blinded roles, in case un-blinded drug monitoring is required. We do not have a satellite site for IP.

IP-storage and handling

The IP storage area is secured with controlled access. The temperature monitoring is available for the room temp (18°C-24°C), refrigerator (+2°C - +8°C), and freezers (-20°C and -80°C), and is alarmed in the event that there is an excursion. There is a backup plan in the event of a power outage or equipment failure, except for the room temp. Calibration certificates and temperatures recording files are available onsite upon request.

Our site has the capability to destroy IP on site/arranged directly via sub-contractor, and have a written SOP/policy/procedure for IP destruction.

Handling and preparation of drugs are done by qualified site personnel trained in aseptic manipulation in clean room. Remaining volumes from used vials are systematically destroyed after each preparation in order to avoid environmental contamination and for workers' protection purposes (occupational health and safety).

Controlled substances

Our site has the regulatory required licenses or registrations to receive, store, dispense and return controlled substances as required by local law. The storage facility for controlled substances is securely constructed with restricted access to prevent theft or diversion. Our site has the capability to destroy IP on site for controlled substances.

About the Local Laboratory

The laboratory, which counts 5 technicians and 1 manager, ensures the management and implementation of the pre-analytical technical procedures of the liquid biological resources of therapeutic trials that are intended to be sent to the sponsor. The unit is certified ISO and NF S96-900 since 2014.

The lab is equipped with:

- Non-frost free freezers at – 20 °C and -80 °C.
- 2-8°C refrigerator
- Centrifuge, refrigerated centrifuge (500 to 14000 RPM)
- Laminar flow hood

The calibration of equipment is done routinely. There is temperature monitoring for refrigerators and freezers. All records are maintained and available. There is a backup plan for a power outage of refrigerators and freezers. The system is alarmed if the equipment is out of range for refrigerators and freezers.

Digital Diagnostic Capabilities

- 12-lead ECG
- CT scanner
- MRI scan
- PET scan
- X-ray
- DXA scan
- Bone scintigraphy
- Bone marrow biopsy, aspiration
- MUGA
- Technetium-99m bone scan
- Biopsy (ultrasound-guided biopsy, CT-guided ...)

Other Equipment

- Resuscitation equipment (Fully Equipped Emergency Trolley, Oxygen, and Defibrillator; resuscitation team available 24h/24h)
- Adult Blood Pressure Cuff and Calibrated Manometer
- Height Measurement Device (Stadiometer)
- Weight measurement device
- Infusion volumetric Pumps
- Syringe pumps

All medical equipments have an annual maintenance check or more often (following the company's recommendation). This checkup is performed by the Biomedical Equipment's Department (contact person Mr. Alexandre Hyvert: alexandre.hyvert@gustaveroussy.fr).

Storage Facilities

Our archiving facilities are on site, except for closed studies (private company subcontracting): EVERIAL, 3 avenue Gustave EIFFEL, 28000 CHARTRES. Our onsite patient record storage is secured to protect patient privacy.

There is a storage area on site for study related materials, ex. Lab kits or other items.

Computer, Internet and Phone Line Capability



Our site has:

- Dedicated computers for the research studies
- Internal firewalls
- High speed internet access (browser IE, version 8)
- Wireless internet capabilities
- External phone lines
- International phone lines

CAPABILITIES & SPECIFIC SKILLS

- Intratumoral administration
- Tumoral biopsies in the outpatient care unit
- Intense blood samples collection (Pharmacokinetic, pharmacodynamic,...) at specified time points
- Shipment of baseline tissue samples (archived or fresh) to central lab even if tissue is stored on another site
- Preparation of PBMCs from peripheral blood
- Fixing tissues for shipment
- Urine collection

Molecular Testing

Our institution currently conducts molecular diagnostic testing in-house:

- IHC
- FISH
- NGS
- RNA-Seq for selected patients

The molecular testing results are reviewed during the Molecular Pluridisciplinary Committee (RCPM-150). It is dedicated to the weekly review of the molecular tumor profiles performed within our precision medicine programs, and aims at enrolling each phase I-eligible patient in the most proper clinical trial, based on actionable molecular abnormalities.

Management of Immune-related Toxicities

Our institution has implemented a program dedicated to the management of adverse effects occurring with immunotherapies (iTOX program), based on:

- The iTOX experts network
- The iTOX Gustave Roussy management guidelines (available also in mobile app)
- The iTOX monthly meetings
- The REISAMIC pharmacovigilance registry: Registry of Severe Adverse Effects of Immunomodulating Monoclonal Antibodies in Oncology: www.reisamic.fr

Regarding Investigators

- Investigator's participation in routine calls
- Participation at investigator meetings, national and international medical conference presentations
- Specific early clinical trials classes/courses presentation
- Training of young oncologists and fellows in early clinical trials and management of side effects

STUDY PROCEDURE AND INFORMATION

Main contact :

eve.netzer@gustaveroussy.fr

Informed Consent

Our site has a written SOP (policy/procedure) for Informed Consent. We require language translations for consents (French).

Site Training

Our site has a training program for the research staff, including GCP (eLearning). We do not use an external program to conduct research training. GCP training is validated by TransCelerate and renewed every 2 years. Our program has a provision for training staff when updates to protocols occur.

Complaint Management *StudyClaim*

A tool (StudyClaim) has been internally developed to centralize the major complaints posted by the sponsors, to ensure the setting-up and the follow-up of an action plan while assuring the traceability of the whole process (from the declaration to the closure of the complaint).

SOURCE DOCUMENTATION/CRF

Our source documents are both electronic and paper, electronic being for lab results and CT/MRI results. Confidentiality agreements need to be signed.

For the CRFs, our staff has used several electronic data systems such as Inform, Medidata Rave, Oracle, and more than 10 others. Our staff has performed more than 100 studies using EDC system.

SITE MONITORING

There is a PC located in an area that has adequate space for site staff and sponsors monitors to work and review source documents.

Monitors can have access to:

- Phone
- Fax
- Scanner
- Copy machines
- Internet access

AUDIT/INSPECTION

The DITEP has already been inspected by a Regulatory Authority: FDA, EMA.

DITEP CONTACTS



Head of SOPP: Guylène CHARTIER

GUYLENE.CHARTIER@gustaveroussy.fr

01 42 11 66 70



CRA managers: Moulay HOUSSAINI and Hadjer ZOUHRI

SOUFYAN.HOUSSAINI@gustaveroussy.fr

01 42 11 48 33

HADJER.ZOUHRI@gustaveroussy.fr

01 42 11 58 12



QA project manager: Eve NETZER

EVE.NETZER@gustaveroussy.fr

01 42 11 56 61



Operations coordinator: Sandrine LANCEREAU

SANDRINE.LANCEREAU@gustaveroussy.fr

01 42 11 62 61



Contracts: Laurent DALEY and Sylvie LEAL

LAURENT.DALEY@gustaveroussy.fr

01 42 11 56 51

SYLVIE.LEAL@gustaveroussy.fr

01 42 11 56 19



Invoicing: Pierre CRUCHET

PIERRE.CRUCHET@gustaveroussy.fr

01 42 11 49 34



Nurse Managers: Pascale DIELENSEGER and Sandrina RODRIGUES

Pascale.DIELENSEGER@gustaveroussy.fr

01 42 11 66 45

Sandrina.RODRIGUES@gustaveroussy.fr

01 42 11 56 23

WEBSITE



<https://www.gustaveroussy.fr/en/ditep>



<https://www.gustaveroussy.fr/fr/ditep>

/ DRUG DEVELOPMENT DEPARTMENT

114, rue Édouard-Vaillant
94805 Villejuif Cedex - France

Tél. : 01 42 11 42 11
Fax : 01 42 11 53 00

Suivez-nous sur



www.gustaveroussy.fr

DITEP 
Drug Development Department