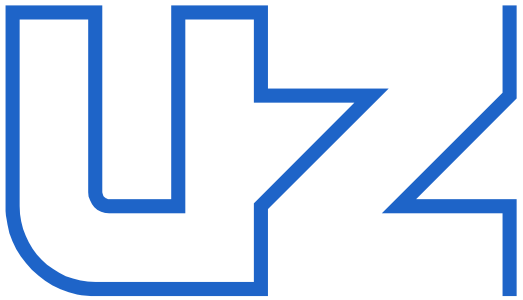

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Drug Research Unit Ghent (D.R.U.G.)

The Early Phase Clinical Drug Research Unit of the University Hospital Ghent

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Mission statement

To contribute to the **development** of new drugs by conducting clinical trials (majority of them **early phase**) in **healthy subjects** as well as in **adult patients**.

Since 2018 the Drug Research Unit Ghent contributes also to the development of new drugs by conducting clinical trials in **pediatric patients** in close collaboration with the pediatric department of the University Hospital Ghent.

In compliance with international legislation and quality standards.

Milestones

- 2001: Founded by Prof. dr. L. Van Bortel
- 2003: ISO 9001:2000 certified
- 2005: Contribution to development of drugs for developing countries
- 2006: Preferred partnership contract with global pharma industry
- 2009: ISO 9001:2008 certified

Milestones

- Part of Oncology care program initially
- NOV 2008: approval of the Phase I Unit Oncology by the medical board of the hospital; ISO 9001:2008 certified
- JAN 2009: approval of the Phase I Unit Oncology by the board and the CEO of the Ghent University Hospital
- From JAN 2011 on: 4 Key Activities supported by the hospital (Oncology, Clinical Immunology, Genetics & Neuroscience)

Milestones

- 2014: Close collaboration in between both units
- AUG 2015: New facilities on the campus
- OCT 2015: Official merging of D.R.U.G. and Phase I Oncology
- Until 2017: ISO 9001:2008
- 2018-2019: integration in hospital accreditation, NIAZ/Q-Mentum
- National accreditation Phase I pending
- 2018: start of pediatric clinical trials

Milestones

- Automatisation of procedures
- FAGG accreditation of phase I unit
- 2024: Move to Nobel I building

Expertise

Healthy subjects

- First in man, SD
- First in man, MD
- Phase-0 studies (eCTA) and proof of concept
- Biomarker/surrogate marker development
- Food/Drug interaction
- Bioequivalence
- Biologicals
- Special groups (hypertensives, elderly, postmenopausal women)
- Cardiovascular: telemetry, BP, arterial function & structure

Oncology

- First in man, dose escalation
- First in man, expansion cohorts
- Medical devices
- Interaction studies
- Biomarker studies
- QT studies
- Fresh biopsies
- Small molecules
- Immunotherapies
- CAR-T cell studies
- NGS based clinical trials

+ Patient studies for other hospital departments and other principal investigators

Stipulations

High Quality

Quality control - Quality assurance

Quality management system - Document management

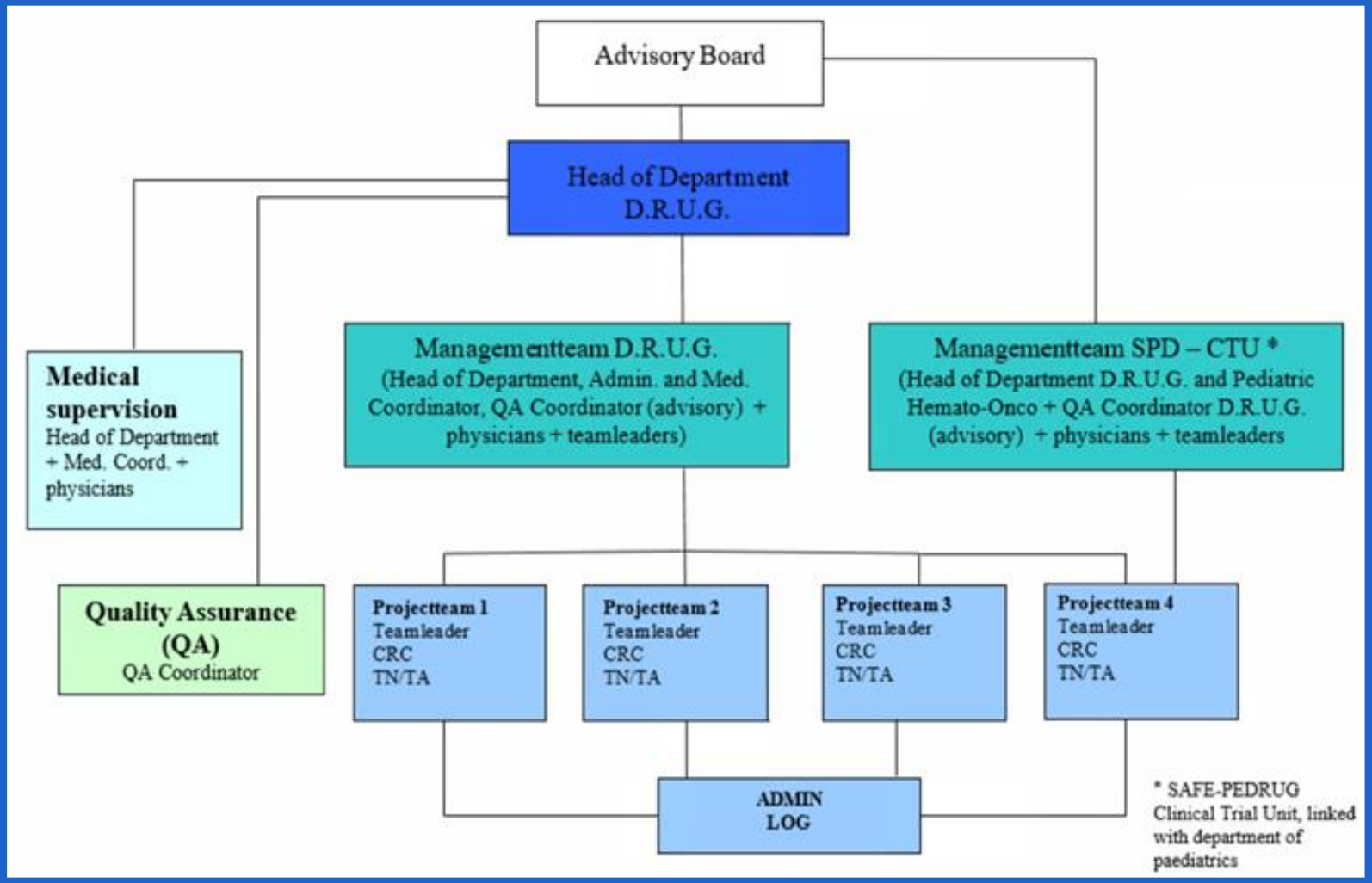
Training employees

Apparatus: temperature management and control – Calibrated devices

FDA - FAGG Inspections

Second party audits

Staff


Advisory Board
Head of Department
D.R.U.G.
Medical supervision
Head of Department + Med. Coord. + physicians
Managementteam D.R.U.G.
(Head of Department, Admin. and Med. Coordinator, QA Coordinator (advisory) + physicians + teamleaders)
Managementteam SPD – CTU *
(Head of Department D.R.U.G. and Pediatric Hemato-Onco + QA Coordinator D.R.U.G. (advisory) + physicians + teamleaders
Quality Assurance (QA)
QA Coordinator
Projectteam 1
Teamleader
CRC
TN/TA
Projectteam 2
Teamleader
CRC
TN/TA
Projectteam 3
Teamleader
CRC
TN/TA
Projectteam 4
Teamleader
CRC
TN/TA
ADMIN
LOG
* SAFE-PEDRUG Clinical Trial Unit, linked with department of paediatrics

Facilities

- 20 beds for overnight stay
- Telemetry for 15 subjects
- 2 clinical laboratories (temperature controlled)
- 1 sample handling laboratory (temperature controlled)
- 1 drug storage room (temperature controlled/alarm)
- 3 freezers (-20°C) + 1 freezer (-70°C) (temperature controlled/alarm)
- 6 refrigerators
- Wifi network
- Canteen, recreation room, offices, reception, meeting room, monitor room, storage rooms and kitchen
- Biosafety level 1

For healthy subjects / patients

- **Overnights and measurements in separate rooms**
  (2 subjects/room for the night)

- **A group of 33 staff members**
  (except for the nights which are done by Assistant Trial Nurse)

- **5 investigators close on the spot**
  (24h/24h availability)

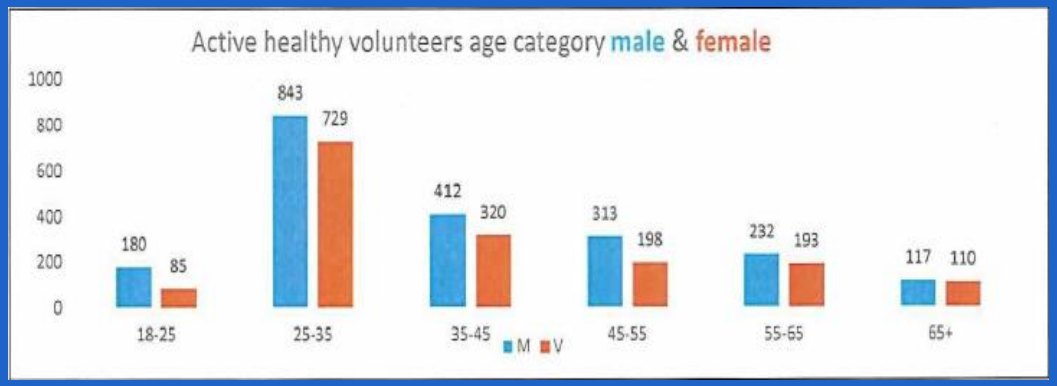
Sponsors

- Pharmaceutical industry (majority)
- University
- University hospital

Recruitment

Healthy subjects

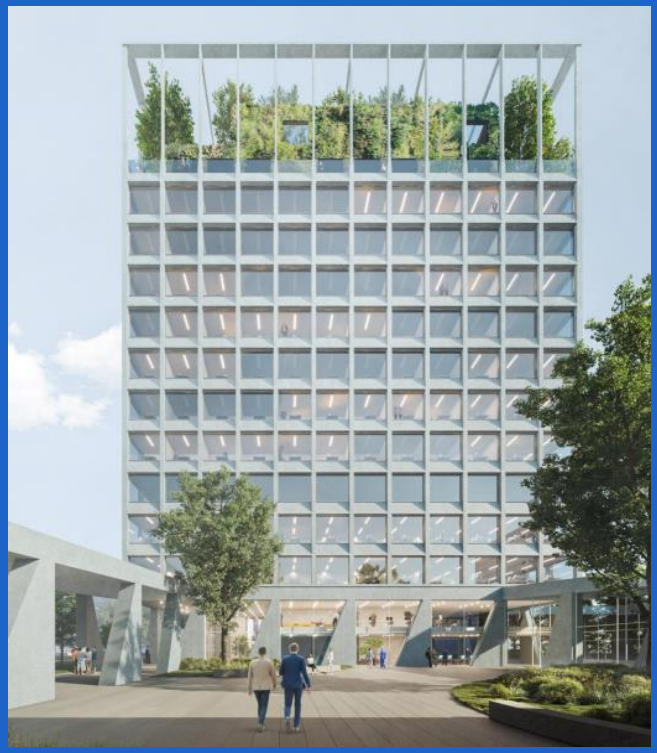
- Database with +/- 3800 active subjects (including patient-subjects)
- VCT (Verified Clinical Trials) prevents concurrent participation in multiple trials.
- Recruitment by e-mail and (online) advertisement



Patients

- **Internally:**
  Inclusion on a multidisciplinary basis, which is reflected by the composition of the Phase I working group of the hospital. Patients come from different departments: Medical oncology, GI oncology, pneumo-oncology, hematology…
- **Externally:**
  - Patients are referred on a regular basis from > 25 different hospitals
  - List of running clinical trials is sent on a regular basis to medical doctors involved in oncology in Flanders

Embedding in University Hospital Ghent



Phase I Oncology Working Group

- 4x/year meeting
- Discussion about trials (new and ongoing), listing side effects, recruitment issues, operation of the department,…
- Different oncology disciplines are represented next to the head of the department Prof. Dr. Rottey:
  - Cancer Centre UZ Ghent
  - Gastroenterology
  - Pneumology
  - Hematology
  - Medical Oncology
  - Radiation Oncology
  - Gynecology
  - Pathology
  - Pharmacy
  - Research physicians D.R.U.G. + 1 team leader of D.R.U.G.

Poli Medical Oncology

- 1st contact with patient interested in inclusion in Phase 1 trial
- Patient is informed about Phase I trials in general
- Patient is put on waiting list if no slot for trial is available

Day hospital and hospitalization Medical Oncology

- **Patient Care**
- **Day hospital**
  - **Blood transfusion**
- **Hospitalization:**
  - **Hypercalcemia**
  - **Neutropenic sepsis**
  - **Start up of parenteral nutrition**
  - **Optimization pain medication**
  - **Serious adverse events (SAE)**
  - **…**

HIRUZ

- HIRUZ is the Health, Innovation and Research Institute of the Hospital in collaboration with Ghent University
- HIRUZ facilitates the various individual aspects of translational biomedical research in an integrative manner

Intensive Care Unit and Emergency Department

- Interested in drug development existing in our unit
- Willing to take care of our patients if needed

Pharmacy

- A separate Clinical Trial Unit within the Pharmacy Department of the hospital
- Storage of study medication
- On site formulations
- Packaging of study medication
- Reconstitution of study medication
- Preparation of IV study medication
- Ordering and delivery of study medication
- Improvement of collaboration by performing audits by each other

For study related assessments/follow up study patients

- Laboratory (safety testing)
- Radiology (CT, MRI)
- Nuclear Medicine
  (PET-CT, bone scan, MUGA scan, …)
- Ophthalmology (ocular AE's)
- Dermatology (skin toxicities)
- Cardiology (echocardiography)
- Pathology (tumor tissue)
- Pneumology (lung function)
- Neurology (EEG)
- Anaesthesiology (high risk medication)
- Radiotherapy (antalgic radiotherapy)
- Interventional radiology
  (specific study drug administrations)
- Genetics (NGS sequencing)
- …

Collaboration – Oncology

Collaboration – Department of Medical Oncology

Collaboration – Ethics Committee & HIRUZ

Collaboration – ICU / Pharmacy

Collaboration – Other departments UZ Ghent 1

Collaboration – Other departments UZ Ghent 2

Biopsy samples (archived and fresh)

Fresh Biopsy Sampling

- Ultrasonography (liver biopsies)
- EUS-EBUS (thoracic/mediastinal biopsies)
- Plastic surgery (skin)
- Dermatology (skin)
- Head and Neck Department (biopsies head and neck region)
- Interventional radiology (Image guided biopsies)

Pathology Department

Handling of biopsy samples

- Preparing slides of archived tissue
- Handling of fresh biopsy samples following specific instructions:
- Diagnosis
- Paraffin embedding
- Preparing slides
- Freezing
- Genetic analysis
- ….

Phase I Oncology Trials 2022

Patients	Mandator	Number of Trials	PI
Cancer patients	**Industry (21# sponsors)**	**39**	**S. Rottey**

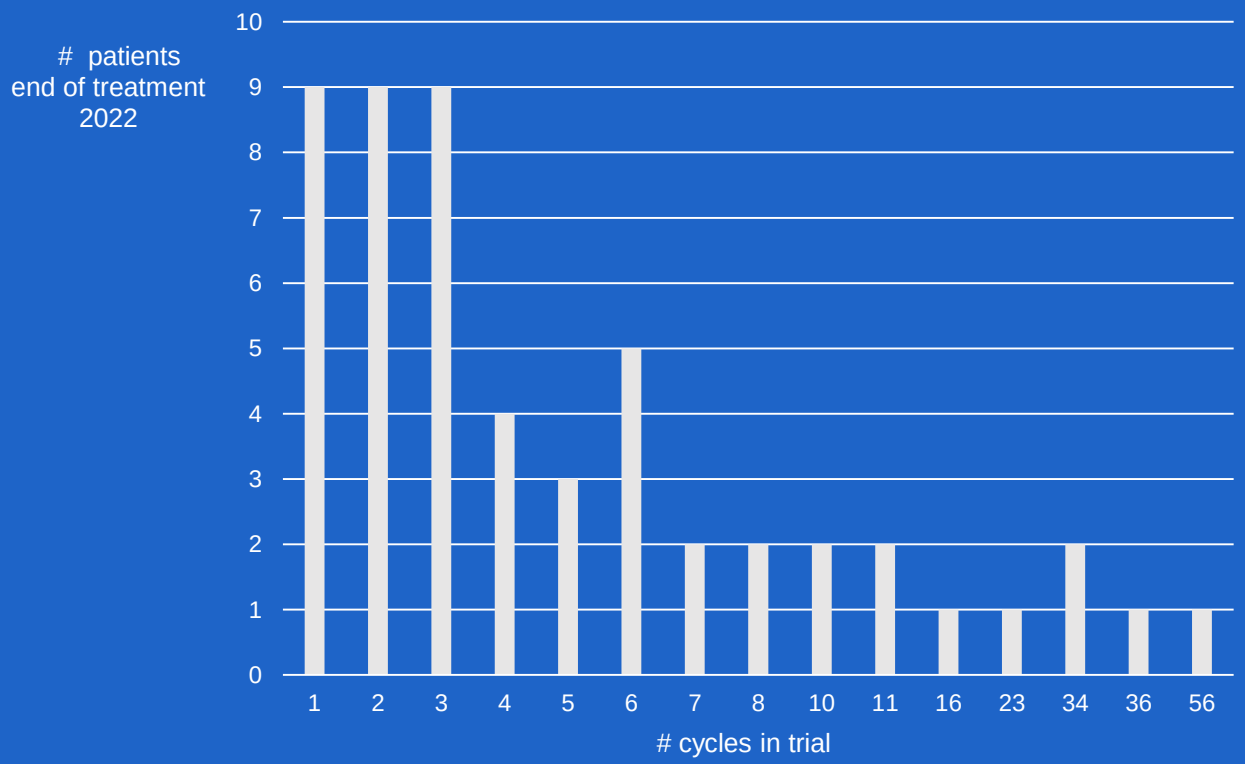
Subjects registered for Phase I Oncology trials in 2022: 156

Subjects in trial in 2022:

- Prescreenings:
  - 287 prescreening ICF's signed – modern trials !
  - 150 patients were prescreened in total, 124 patients were prescreened for multiple trials (2 or 3)
- 21 ongoing subjects from 2021 (excl. follow ups)
- 57 subjects signed main ICF in 2022
- Number of cycles in trial: 7,3 cycles in trial (4,6 cycles without outliers) - 1 cycle is mostly 3-4 weeks

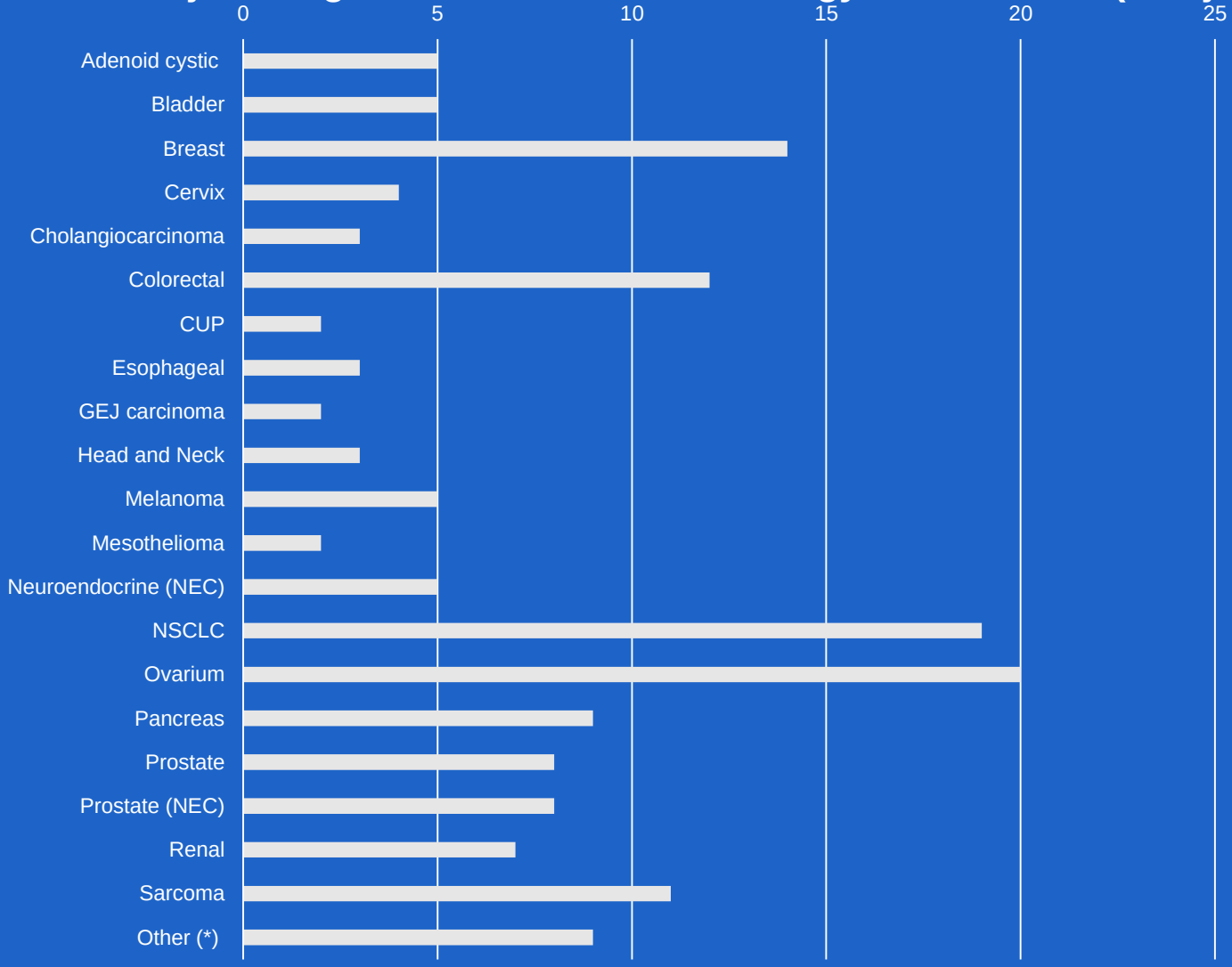
Phase I Oncology Trials 2022

Number of cycles per patient in trial (based on end of treatments 2022).



Phase I Oncology Trials 2022

Diagnoses subjects registered for Phase I Oncology trials in 2022 (subjects)



Other includes rare tumor types or which presented only once:

- Rare (chordoma, germ cell type endometrial carcinoma, penile carcinoma, sinonasal carcinoma, uterine carcinosarcoma, atypical carcinoid lung)
- Only once: endometrium, stomach, meningioma

Referral of patients for Phase I Oncology Trials : analysis of 33 patients in MAY 2023 in our Phase I unit treated

UZGent Medonc	7
UZGent Longziekten	2
UZLeuven Medonc	1
Nijmegen Nederland	1
MMiddelares Gent Gastro	1
St Lucas Brugge Longziekten en Gastro	2
AZ Sint Nikolaas Medonc	1
St Jozef Izegem Medonc	1
UZGent DIO	1
AZ St Lucas Gent	3
AZ Zeno gastro	1
AZ Groeninge Kortrijk	4
AZ St Jan Brugge Medonc	6
AZ West Veurne Longziekten	1
ASZ Aalst Medonc	1

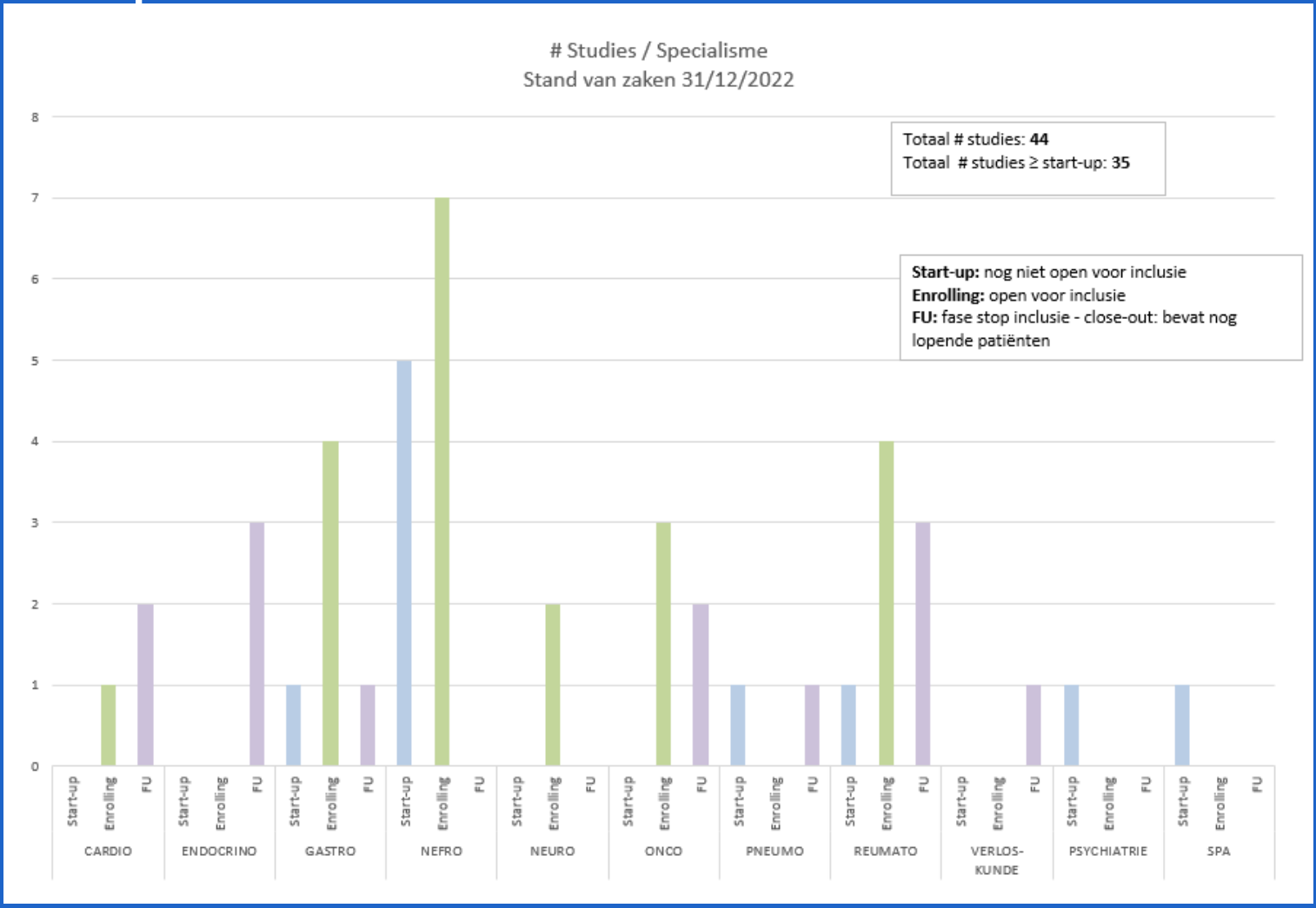
Some patients entered the unit via second opinion in UZGent at another department.

Phase I Trials in Healthy Subjects 2022

Type	Mandator	Number of Trials	Number of Randomized Healthy Subjects	PI
First in Humans	Industry	2	96	S. Rottey
Other studies	Industry	2	103	S. Rottey

Paediatric Trials – SPD-CTU

Snapshot of trials in DEC/2022



Summary

Centre of Excellence:

- Qualified staff
- Approval system – double control
- External audits
- Accreditation phase I unit pending

Short timelines

Takes advantage of University Knowledge Centre / embedding in a University Hospital environment

Clinical Research Centers on UZ Campus

Center for Vaccinology (CEVAC)

- Mission: Contribute to the development of new vaccines and the improvement of existing vaccines for the prevention or treatment of infectious diseases
- Conduct of Clinical Vaccine Trials (Phase I, II, III) in dedicated Clinical Unit and Immuno-Monitoring Lab (CEVAC CORE lab)
  (University Hospital Ghent and University Ghent)
- Founded in 1986 and gained experience since then in over 200 clinical vaccine trials.
- Experienced, GC(L)P trained team of MD's (4), coordinators (2), project managers (2), study nurses (5), lab technicians (15) and a QUA-team (2)
- Large database of > 11000 healthy volunteers (adolescents, adults, elderly)

CANCER RESEARCH INSTITUTE GHENT (CRIG)

CRIG's mission is to unite, stimulate and enhance the impact of cancer research at Ghent University, Ghent University Hospital and VIB-UGent. Hereby, CRIG have six different objectives:

- Stimulating top research
- Collaborating and sharing knowledge and technology, across different expertise domains
- Interaction between the lab and the clinic
- Communicating and interacting with the outside world
- Education and networking for young researchers
- Valorization of research

VLAAMS INSTITUUT voor BIOTECHNOLOGIE (VIB)

Scientists at VIB conduct pioneering research across a wide spectrum of disciplines ranging from cancer, inflammation and neuroscience to plant biology. Their scientists are world leaders in their fields, and this is one of their greatest strengths.

- Center for Cancer Biology
- Center for Inflammation Research
- Center for Plant Systems Biology
- Center for Medical Biotechnology
- Center for Brain & Disease Research
- Center for Microbiology
- Center for Structural Biology
- Center for Molecular Neurology
- NeuroElectronics Flanders (NERF)

Memberships investigator

Prof. Rottey is Past President of BSMO
Board Member of Haelixia
Board member of BMUC

Prof. Dr. Sylvie Rottey – Head of the Department
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