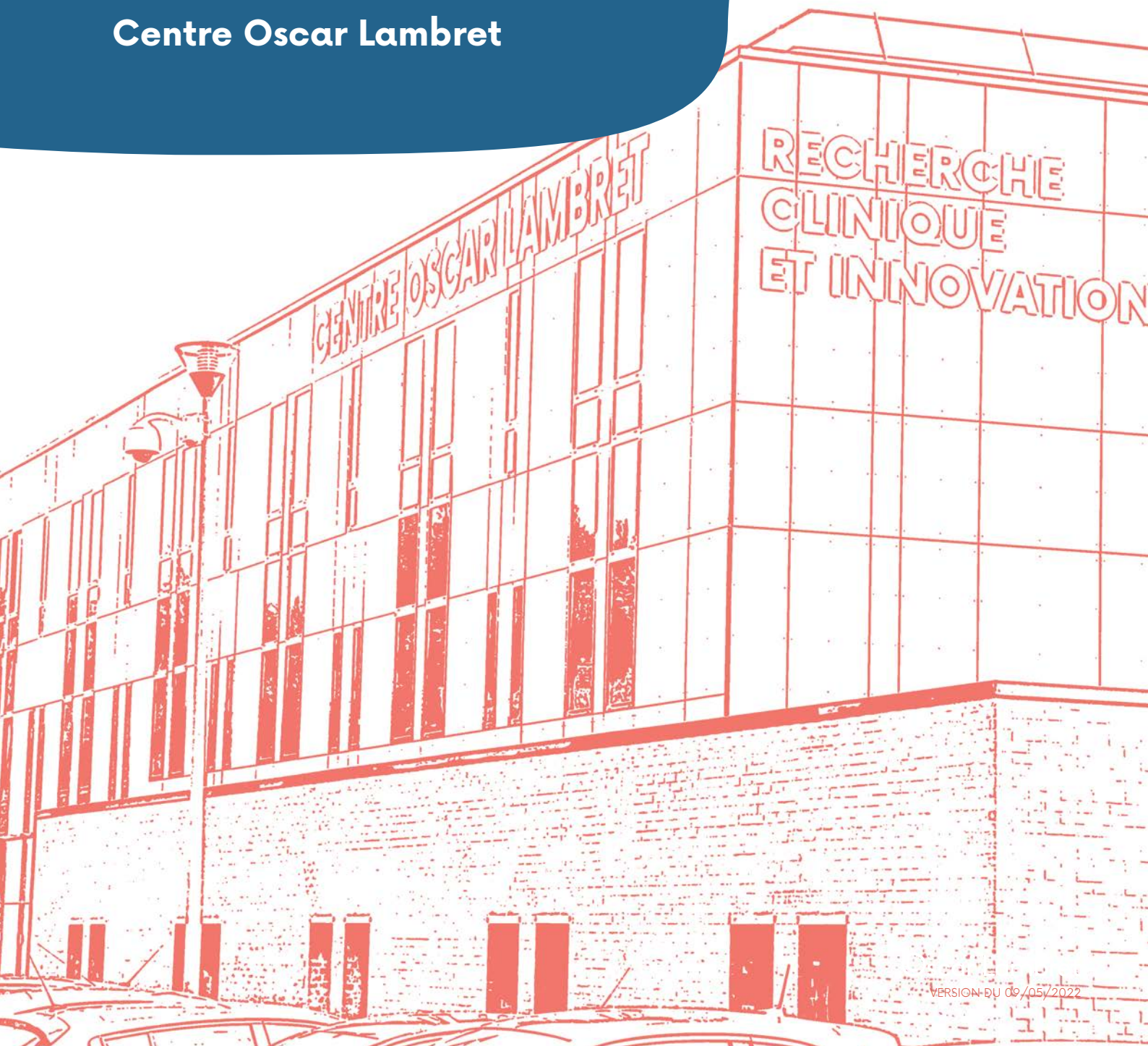


2021 ACTIVITY REPORT

DIRECTION OF
CLINICAL RESEARCH
AND INNOVATION

Centre Oscar Lambret





CENTRE OSCAR LAMBRET

RECHERCHE
CLINIQUE
ET INNOVATION

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CONTRIBUTOR TO SCIENTIFIC
RESEARCH 10**



A MESSAGE FROM THE DRCI DIRECTOR

First and foremost we should remember what the Direction of Clinical Research and Innovation (DRCI) is. ISO-9001 certified since February 2018, the DRCI, with the cross-disciplinary expertise of its 56 FTE, is responsible for all of the clinical research activities at the Oscar Lambret Center (OLC):

- Investigation activities: inclusion in all academic and industry trials, and caring for patients included in the DRCI's integrated care unit.
- Sponsorship activities: supporting OLC coordinators (or researchers from the northwest inter-region) from concept to publication.

As part of the collaboration between the OLC and Lille University Hospital (Cancer Alliance), the OLC coordinates the CLIP² (Certified Early Phase Center for adults and children) on the Lille site. It forges institutional partnerships with INSERM (PRISM team, CANTHER team), the CNRS (CRISTAL team), the Bordet Institute (and the European OncoDistinct network) and industrial partners (Bayer HealthCare, Roche). It helps to expand the international reach of the OLC's first-rate activities through European certifications:

- EURACAN certification for the management of rare gynecological cancers
- EURACAN certification for the management of sarcomas
- ESMO certification for Medical Oncology and Supportive



EURACAN



Care

- Certification from INCa's national network for preclinical radiotherapy research - Radio TransNet 2.0
- INSERM/CNRS certification (S Meignan's team, CANTHER)

The Center's research strategies revolve, on the one hand, around personalized medical and surgical treatments for women's cancers and sarcomas and, on the other hand, radiotherapy, imaging and radiomics.

The DRCI also provides education and training, and has 17 trainees and interns. Their actors actively contribute to clinical cancer research training.

This was another difficult year due to the COVID-19 epidemic, but thanks to everyone's efforts, our activities remained strong, with a record-breaking number of total inclusions (1,309) and a plethora of publications (178).

Congratulations to everyone!



INVESTIGATION ACTIVITIES

OVERALL INCLUSION FIGURES

The proportion of active patients (new patients each year) included in interventional trials exceeds INCa's 10% threshold.

Year	Active patients at the OLC	Number included Interventional trials*	% active patients
2019	6627	1166	17,6%
2020	6671	1248	18,7%
2021	7007	1309	18,6%

*HSR1 and HSR2 (Type 1 and 2 Human Subjects Research)

In 2021

41 new trials were opened out of a total of **177 active trials** (enrolling).

1309 patients were included in HSR1 and HSR2 trials

1055 received treatment or underwent a procedure as part of this trial

254 patients were unable to receive the trial treatment after inclusion: molecular screening, failed procedure

In addition, 88 patients gave their consent but could not be included.

TRIALS AND NUMBER OF INCLUSIONS ACCORDING TO SPONSOR

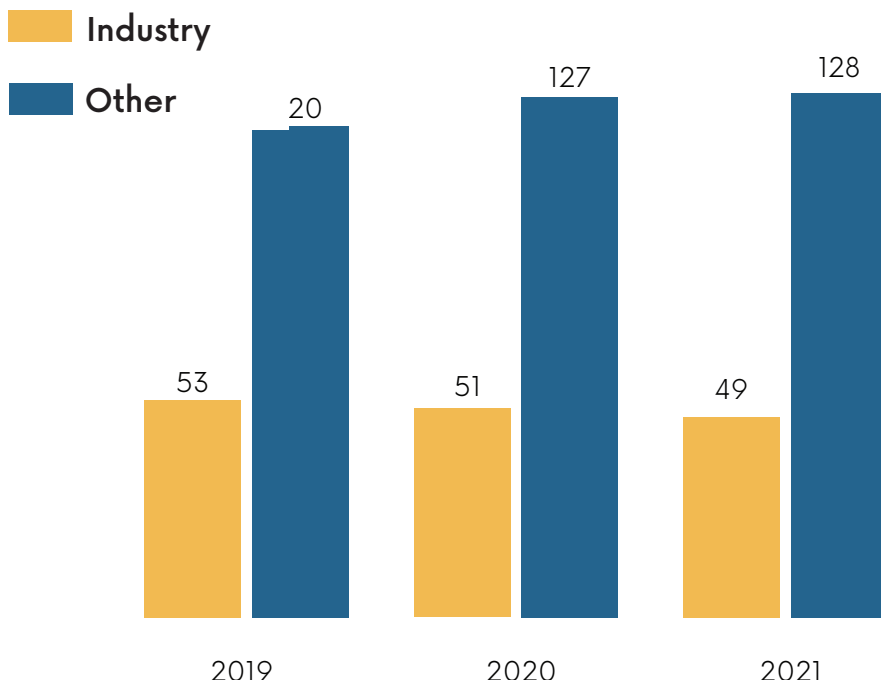
On average, 30% of interventional trials are industry-sponsored.

In 2021

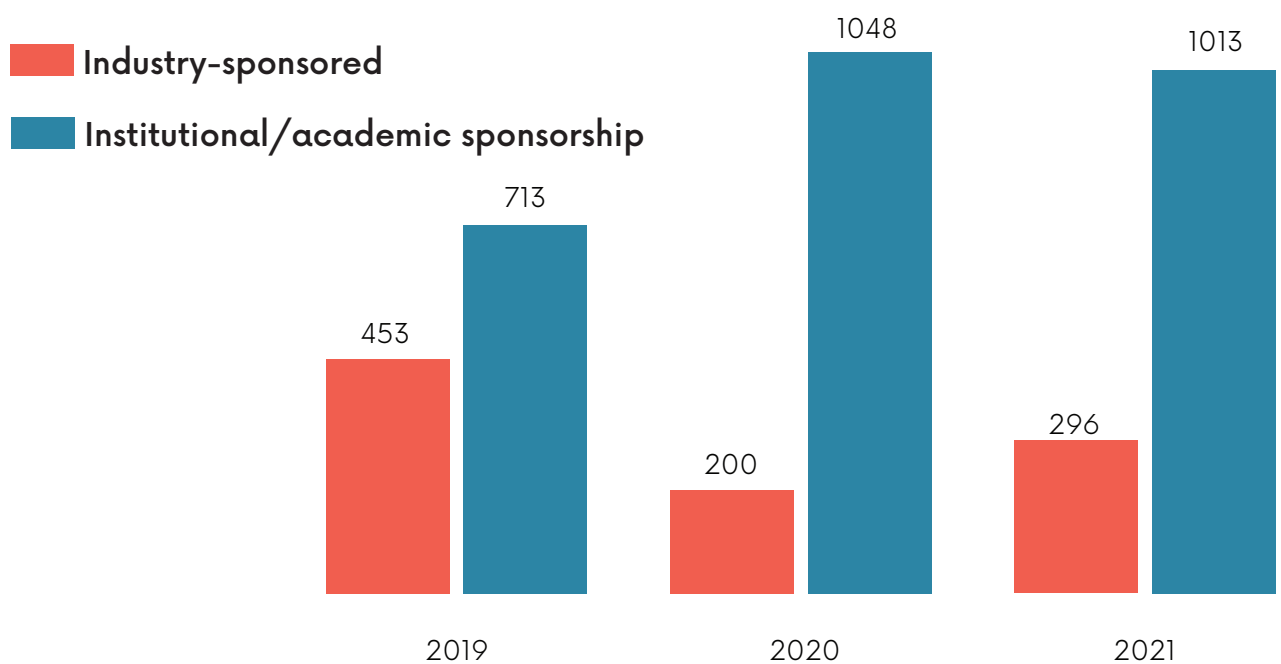
296 patients
were included in
industry-sponsored trials
and

1013 in academic trials, **264**
of whom were included in trials
sponsored by the OLC and **152**
were included in trials sponsored by
UNICANCER

Trials



Number of inclusions



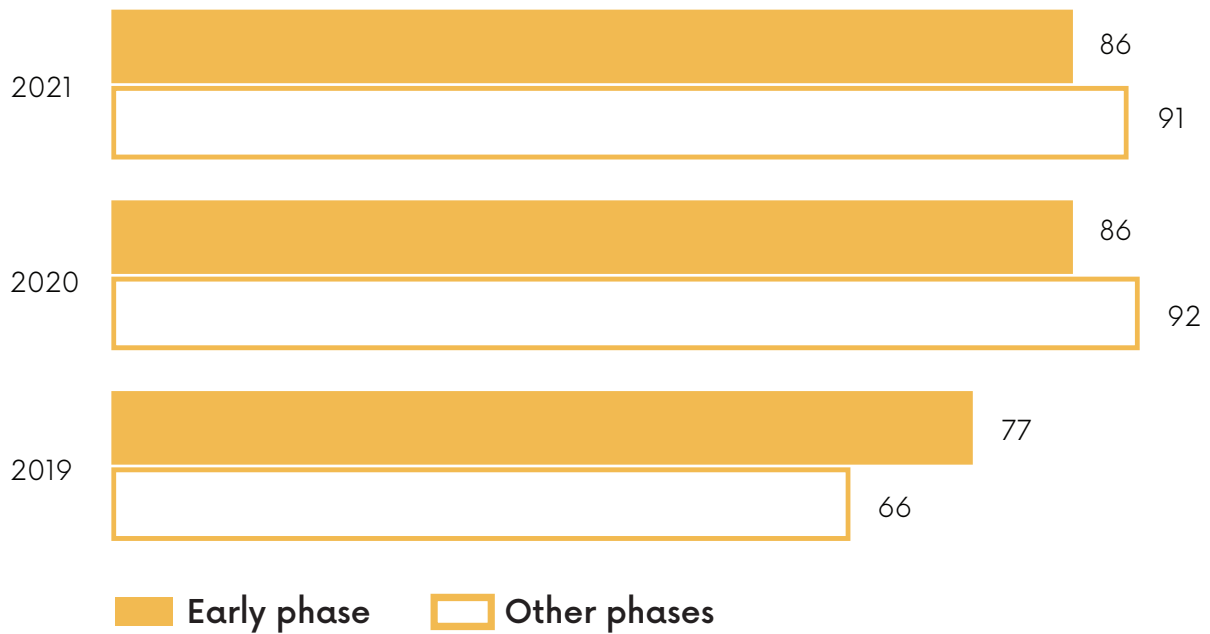
TRIALS AND INCLUSIONS ACCORDING TO PHASE

In 2021

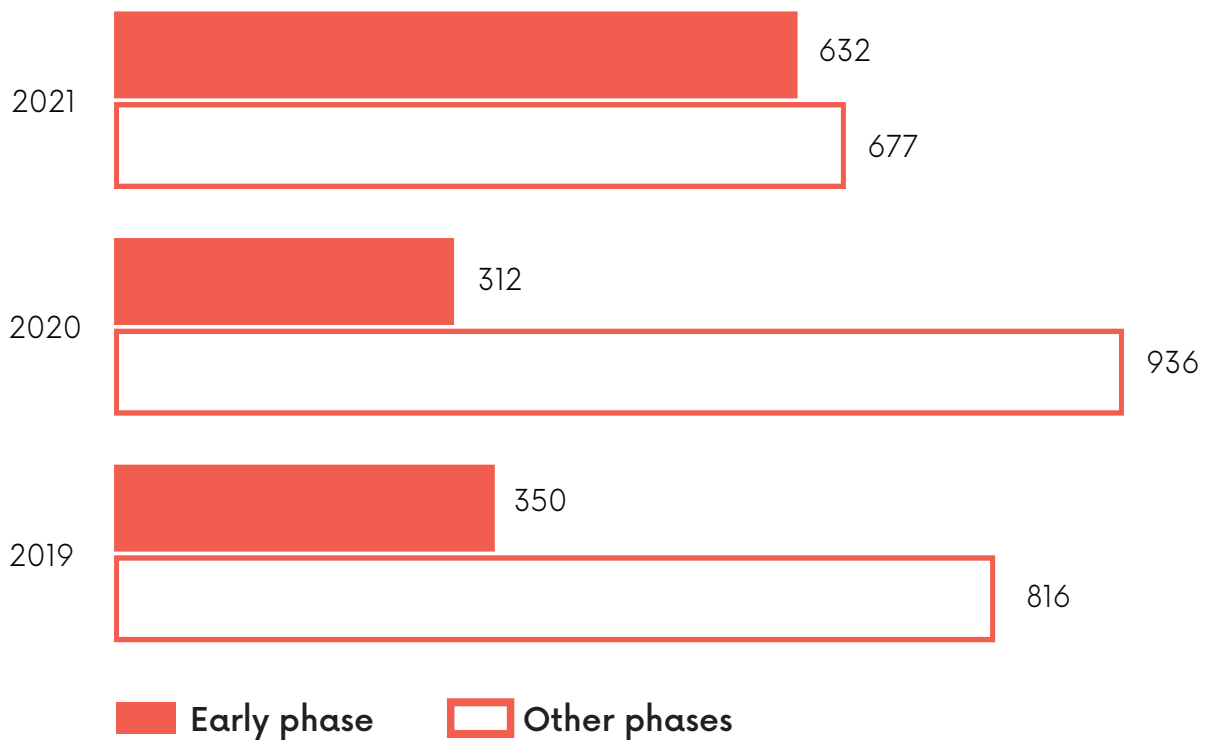
Early phase trials
accounted for **49%** of
all clinical trials.

48% of all inclusions were
inclusions in early phase trials

Trials



Number of inclusions



NUMBER OF INCLUSIONS PER COMMITTEE AND ACTIVITY

Interventional studies	Number of studies	Number of inclusions	Active patients
ANESTHESIOLOGY & ALGOLOGY	2	0	NA
GASTROINTESTINAL	23	71	896
GYNECOLOGY	19	93	1018
NEURO-ONCOLOGY	1	2	102
PEDIATRICS	32	52	212
PULMONOLOGY	7	8	725
SARCOMAS/RARE TUMORS	11	63	270
SENOLOGY	26	381	2148
UROLOGY	19	66	640
ALL TUMORS	22	540	NA
UAT (Upper Aero-digestive Tract)	15	33	776
Total	177	1309	

The DRCI also takes part in observational (non-interventional) trials:

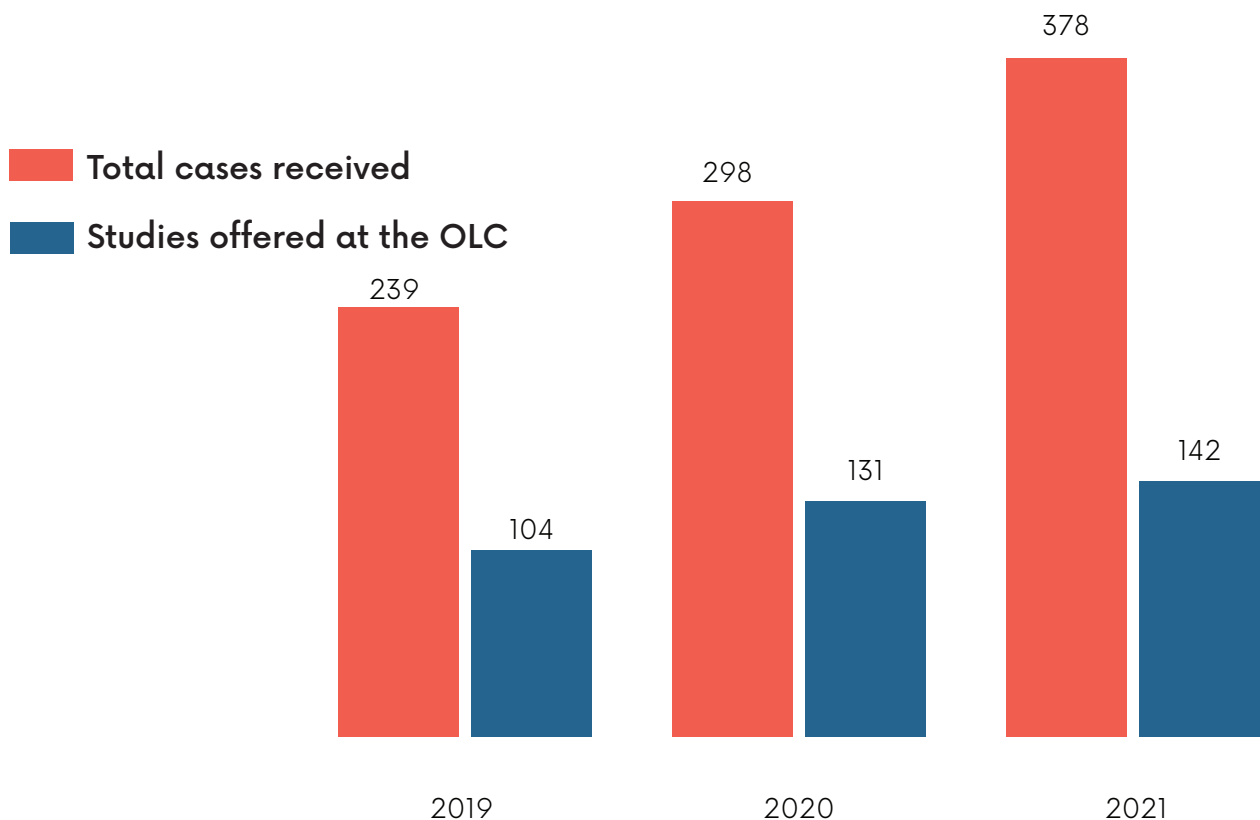
30% of all inclusions were inclusions in these observational trials (551).

A total of **1860** patients were included in interventional and observational trials.

EXTERNAL SCREENING:

In partnership with the Jules Bordet Institute in Brussels, the CLIP² in Normandy, the Curie CLIP² and the Gustave Roussy CLIP², the Lille CLIP² organizes a weekly inter-regional staff meeting centralizing and processing all inclusion requests from the OLC and external doctors (Haut de France and Normandy).

For every request made, we check with our 5 partner early phase centers whether it is possible to offer a clinical trial. This enabled 378 cases from external doctors to be handled by the DRCI in 2021. And for 142 of these cases, an open study at the OLC was offered.





AN EXAMPLE OF OUR EXPERTISE

In March 2020, the SYD1875 study was opened at the OLC, a first-in-human dose escalation and expansion study with the novel antibody-drug conjugate SYD1875.

The study drug contains a humanized IgG1 monoclonal antibody against the 5T4 oncofetal antigen.

This study is intended for patients with a metastatic or locally advanced solid tumor who have received all standard treatments and who have a positive 5T4 status.

For the 1st stage of the trial, the dose escalation phase, only 3 European centers have been opened (2 in France and 1 in Belgium). Thanks to its CLIP² certification and experience in conducting phase I trials, the OLC is one of these 2 centers selected by the trial's sponsor, pharmaceutical company BYONDIS.

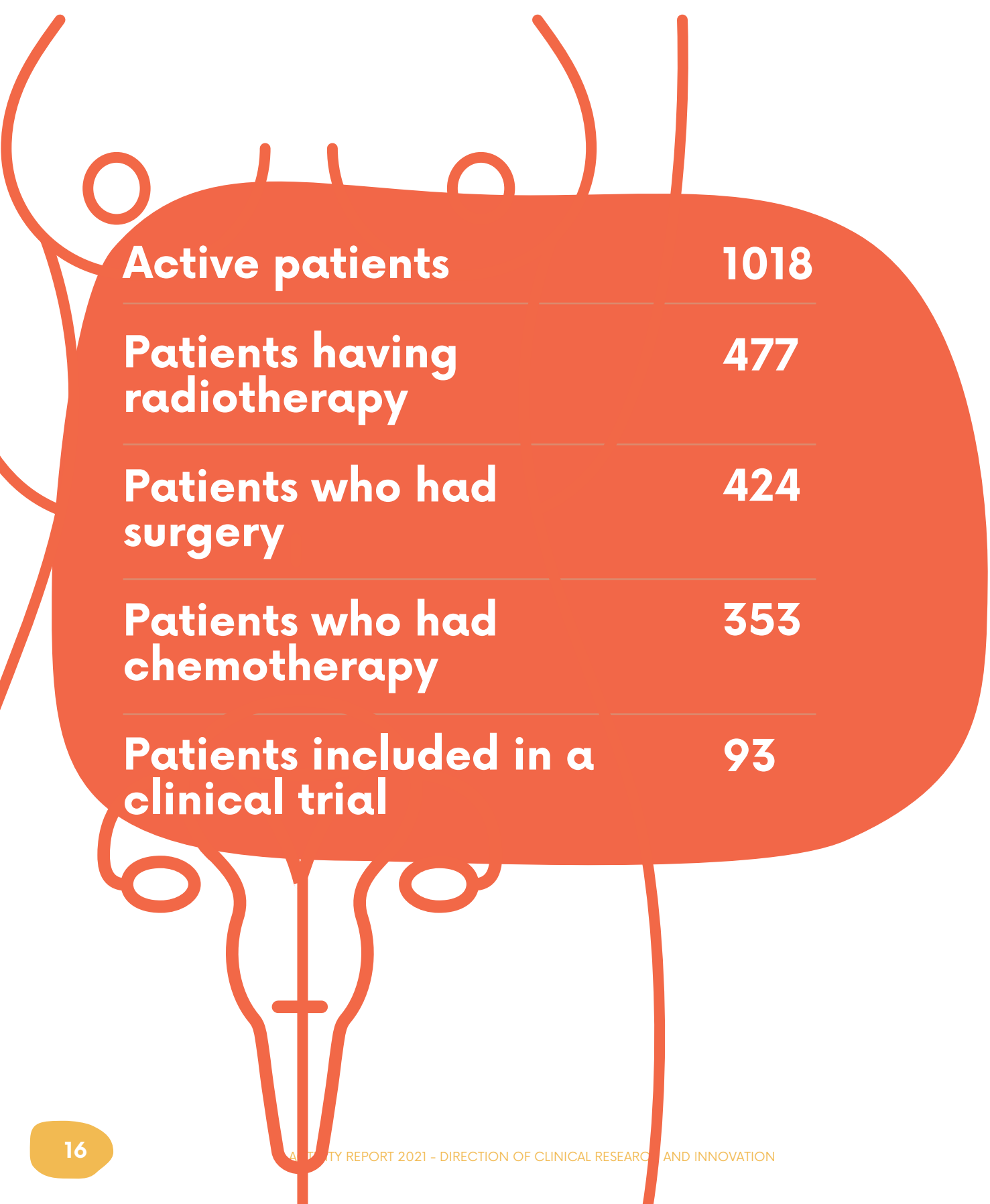
Between March 2020 et December 2021, the tumors of 135 patients at the OLC or the Haut de France Region were sent for testing at a centralized laboratory to determine the tissue expression of 5T4 on tumor tissue, thanks to a team of invested investigators and the efficient logistics that the CRAs and medical research assistants put in place.

In August 2020, the first patients meeting the study criteria (in particular expressing 5T4) were treated in the trial at the Oscar Lambret Center. They received care in the DRCI from a medical and nursing team trained in clinical research and the specificities of phase I trials at the first dose levels. We were able to observe a clinical benefit for some patients, including one patient with a rare tumor who had run out of treatment options. She was treated for 2 years with the experimental treatment which succeeded in blocking the progression of her disease.

This type of trial requires patients to be constantly monitored and adverse events to be recorded meticulously. The effects observed must be reported to the sponsor immediately and the medical team must be available to answer questions or requests for further information from the trial's medical managers with whom frequent exchanges are scheduled.

In total, **11 out of the 27 patients included in Europe were able to be treated at the OLC during this first phase of the trial, which ended in December 2021.**

GYNECOLOGY



Active patients	1018
Patients having radiotherapy	477
Patients who had surgery	424
Patients who had chemotherapy	353
Patients included in a clinical trial	93

MAIN PUBLICATIONS

Long-term oncological safety of sentinel lymph node biopsy in early-stage cervical cancer: A post-hoc analysis of SENTICOL I and SENTICOL II cohorts. Balaya, V ; Guani, B ; Morice, P ; Querleu, D ; Fourchette, V ; Leblanc, E & al. *Gynecol Oncol* 2021

Regorafenib or Tamoxifen for platinum-sensitive recurrent ovarian cancer with rising CA125 and no evidence of clinical or RECIST progression: A GINECO randomized phase II trial (REGOVAR). Trédan, O ; Provansal, M ; Abdeddaim, C ; Lardy-Cleaud, A ; Hardy-Bessard, AC ; Kalbacher, E & al. *Gynecol Oncol* 2021

A New Paradigm in Managing Advanced Ovarian Cancer: Differentiating Patients Requiring Neoadjuvant Treatment from Primary Cytoreduction. Kraus, F ; El Hajj, H ; Le Deley, MC ; Aissaoui, O ; Gachon, B ; Chevalier, A & al. *Cancers (Basel)* 2021 ;13

Laparoscopic ureteral reimplantation applying the modified psoas hitch and Lich-Gregoir onlay technique: a 10-step surgical video. Hudry, D ; El Hajj, H ; Narducci, F ; Leblanc, E. *Int Urogynecol J* 2021

Rationale and study design of the CHIPPI-1808 trial: a phase III randomized clinical trial evaluating hyperthermic intraperitoneal chemotherapy (HIPEC) for stage III ovarian cancer patients treated with primary or interval cytoreductive surgery. El Hajj, H ; Vanseymortier, M ; Hudry, D ; Bogart, E ; Abdeddaim, C ; Leblanc, E & al. *ESMO Open* 2021 ;6 :100098

How to make a vaginal cuff before laparoscopic radical hysterectomy. Querleu, D ; Leblanc, E ; Dargent, D. *Int J Gynecol Cancer* 2021; 31:1610-1611

Care as Usual: An Acceptable Strategy to Apply During the COVID-19 Pandemic in a French Tertiary Gynecologic Oncology Department.. Blache, G ; El Hajj, H ; Jauffret, C ; Houvenaeghel, G ; Sabiani, L ; Barrou, J & al. *Front Oncol* 2021 ;11 :653009

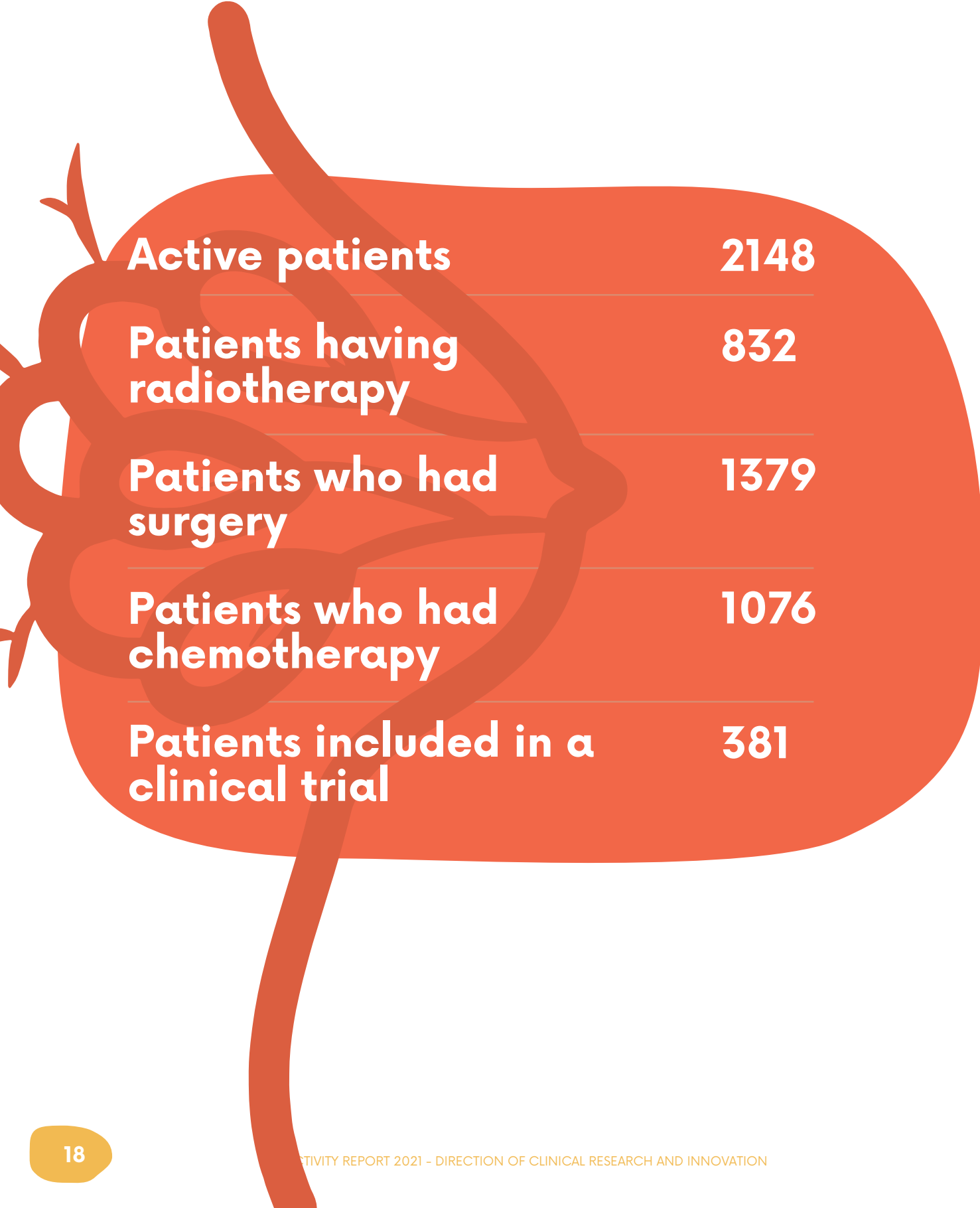
[How I do... to train obstetrics and gynaecology residents in robotic surgery: Implementation of a pedagogical training program in a department equipped with the surgical robot]. Koual, M ; Hudry, D ; Nguyen-Xuan, HT ; Bentivegna, E ; Bats, AS ; Azaïs, H. *Gynecol Obstet Fertil Senol* 2021 ;49 :557-560

Performance of Multiparametric Functional Imaging to Assess Peritoneal Tumor Burden in Ovarian Cancer. Mallet, E ; Angeles, MA ; Cabarrou, B ; Chardin, D ; Viau, P ; Frigenza, M & al. *Clin Nucl Med* 2021 ;46 :797-806

Guidelines for Clinical Practice of the French College of Obstetricians and Gynecologists 2021: Prophylactic procedures associated with gynecologic surgery. Touboul, C ; Legendre, G ; Agostini, A ; Akladios, C ; Bendifallah, S ; Bolze, PA & al. *Gynecol Obstet Fertil Senol* 2021; 49:805-815

Concordance between preoperative ESMO-ESGO-ESTRO risk classification and final histology in early-stage endometrial cancer. Daix, M ; Angeles, MA ; Migliorelli, F ; Kakkos, A ; Martinez Gomez, C ; Delbecq, K & al. *J Gynecol Oncol* 2021; 32: e48

SENOLOGY



Active patients	2148
Patients having radiotherapy	832
Patients who had surgery	1379
Patients who had chemotherapy	1076
Patients included in a clinical trial	381

MAIN PUBLICATIONS

De novo metastatic breast cancer in patients with a small locoregional tumour (T1-T2/N0): Characteristics and prognosis. Gaillard, T ; Carton, M ; Mailliez, A ; Desmoulins, I ; Mouret-Reynier, MA ; Petit, T & al. Eur J Cancer 2021; 158:181-188

A phase II randomised study of preoperative trastuzumab alone or combined with everolimus in patients with early HER2-positive breast cancer and predictive biomarkers (RADHER trial). Campone, M ; Bachelot, T ; Treilleux, I ; Pistilli, B ; Salleron, J ; Seegers, V & al. Eur J Cancer 2021 ;158 :169-180

Classification of 101 BRCA1 and BRCA2 variants of uncertain significance by cosegregation study: A powerful approach. Caputo, SM ; Golmard, L ; Léone, M ; Damiola, F ; Guillaud-Bataille, M ; Revillion, F & al. Am J Hum Genet 2021; 108:1907-1923

Multicenter evaluation of breast cancer patients' satisfaction and experience with oncology telemedicine visits during the COVID-19 pandemic. Bizot, A ; Karimi, M ; Rassy, E ; Heudel, PE ; Levy, C ; Vanlemmens, L & al. Br J Cancer 2021 ;125 :1486-1493

Palpable Nodules After Autologous Fat Grafting in Breast Cancer Patients: Incidence and Impact on Follow-up. Dile, P ; Hannebicque, K ; Renaudeau, C ; Bogart, É ; Ceugnart, L ; Regis, C & al. Aesthetic Plast Surg 2021 ; :

TUMOSPEC: A Nation-Wide Study of Hereditary Breast and Ovarian Cancer Families with a Predicted Pathogenic Variant Identified through Multigene Panel Testing. Lesueur, F ; Eon-Marchais, S ; Bonnet-Boissinot, S ; Beauvallet, J ; Dondon, MG ; Golmard, L & al Cancers (Basel) 2021; 13:

Lack of prognostic impact of sentinel node micro-metastases in endocrine receptor-positive early breast cancer: results from a large multicenter cohort. Houvenaeghel, G ; de Nonneville, A ; Cohen, M ; Chopin, N ; Coutant, C ; Reyat, F & al. ESMO Open 2021; 6:100151

Evolution of overall survival and receipt of new therapies by subtype among 20 446 metastatic breast cancer patients in the 2008-2017 ESME cohort. Grinda, T ; Antoine, A ; Jacot, W ; Blaye, C ; Cottu, PH ; Diéras, V & al. ESMO Open 2021; 6:100114

Prophylactic nipple-sparing mastectomy with immediate breast reconstruction: results of a French prospective trial. Houvenaeghel, G ; Cohen, M ; Dammacco, MA ; D'Halluin, F ; Regis, C ; Gutowski, M & al. Br J Surg 2021; 108:296-301

Unhealthy behaviors after breast cancer: Capitalizing on a teachable moment to promote lifestyle improvements. Di Meglio, A ; Gbenou, AS ; Martin, E ; Pistilli, B ; Ligibel, JA ; Crane, TE & al Cancer 2021; 127:2774-2787

Functional Cerebral MRI Evaluation of Integration of Breast Reconstruction into the Body Schema. Régis, C ; Le Deley, MC ; Bogart, E ; Leguillette, C ; Boulanger, L ; Chauvet, MP & al. Ann Surg Oncol 2021

FOCUS ON ACTIVITIES DURING 2021 IN

SARCOMAS/ RARE TUMORS

Active patients **270**

**Patients included in
a clinical trial** **63**



MAIN PUBLICATIONS

High Prevalence of 5T4/Trophoblast Glycoprotein in Soft Tissue Sarcomas. Groothuis, P ; Penel, N ; Italiano, A ; Kotecki, N ; Dijcks, F ; Dokter, W. *Cancers (Basel)* 2021; 13 :

Characterization of Macrophages and Osteoclasts in the Osteosarcoma Tumor Microenvironment at Diagnosis: New Perspective for Osteosarcoma Treatment? Gomez-Brouchet, A ; Gilhodes, J ; Acker, NV ; Brion, R ; Bouvier, C ; Assemat, P & al. *Cancers (Basel)* 2021 ;13 :

Characterization of Macrophages and Osteoclasts in the Osteosarcoma Tumor Microenvironment at Diagnosis: New Perspective for Osteosarcoma Treatment? Gomez-Brouchet, A ; Gilhodes, J ; Acker, NV ; Brion, R ; Bouvier, C ; Assemat, P & al. *Cancers (Basel)* 2021 ;13 :

A single-arm multicentre phase II trial of doxorubicin in combination with trabectedin in the first-line treatment for leiomyosarcoma with long-term follow-up and impact of cytoreductive surgery.

Pautier, P ; Floquet, A ; Chevreau, C ; Penel, N ; Guillemet, C ; Delcambre, C & al
ESMO Open 2021; 6:100209

Desmoid-type fibromatosis: toward a holistic management.

Penel, N ; Kasper, B ; van Der Graaf, WTA. *Curr Opin Oncol* 2021; 33:309-314

A randomized phase III trial comparing trabectedin to best supportive care in patients with pre-treated soft tissue sarcoma: T-SAR, a French Sarcoma Group trial. Le Cesne, A ; Blay, JY ; Cupissol, D ; Italiano, A ; Delcambre, C ; Penel, N & al. *Ann Oncol* 2021; 32:1034-1044

Efficacy and safety of regorafenib in patients with metastatic or locally advanced chondrosarcoma: Results of a non-comparative, randomised, double-blind, placebo controlled, multicentre phase II study. Duffaud, F ; Italiano, A ; Bompas, E ; Rios, M ; Penel, N ; Mir, O & al
Eur J Cancer 2021 ;150 :108-118

Systemic therapies in advanced epithelioid haemangiioendothelioma: A retrospective international case series from the World Sarcoma Network and a review of literature. Frezza, AM ; Ravi, V ; Lo Vullo, S ; Vincenzi, B ; Tolomeo, F ; Chen, TW & al. *Cancer Med* 2021; 10:2645-2659

Expression and prognostic significance of PDGF ligands and receptors across soft tissue sarcomas.

Brahmi, M ; Lesluyes, T ; Dufresne, A ; Toulmonde, M ; Italiano, A ; Mir, O & al.
ESMO Open 2021; 6:100037

Final analysis of the randomized trial on imatinib as an adjuvant in localized gastrointestinal stromal tumors (GIST) from the EORTC Soft Tissue and Bone Sarcoma Group (STBSG), the Australasian Gastro-Intestinal Trials Group (AGITG), UNICANCER, French Sa. Casali, PG ; Le Cesne, A ; Velasco, AP ; Kotasek, D ; Rutkowski, P ; Hohenberger, P & al. *Ann Oncol* 2021 ;32 :533-541

PEDIATRICS

Active patients

212

**Patients included in
a clinical trial**

52

MAIN PUBLICATIONS

Randomized Phase II Trial of Vincristine-Irinotecan With or Without Temozolomide, in Children and Adults With Relapsed or Refractory Rhabdomyosarcoma: A European Paediatric Soft Tissue Sarcoma Study Group and Innovative Therapies for Children With Cancer Defachelles, AS ; Bogart, E ; Casanova, M ; Merks, JHM ; Bisogno, G ; Calareso, G & al J Clin Oncol 2021 ;39 :2979-2990

Managing Adverse Events Associated with Dinutuximab Beta Treatment in Patients with High-Risk Neuroblastoma: Practical Guidance. Barone, G ; Barry, A ; Bautista, F ; Brichard, B ; Defachelles, AS ; Herd, F & al Paediatr Drugs 2021 ;23 :537-548

Unresectable thoracic neuroblastic tumors: Changes in image-defined risk factors after chemotherapy and impact on surgical management. Delforge, X ; De Cambourg, P ; Defachelles, AS ; Haffreingue, A ; Rod, J ; Kassite, I & al. Pediatr Blood Cancer 2021 ;68 :e29260

Phase I or II Study of Ribociclib in Combination With Topotecan-Temozolomide or Everolimus in Children With Advanced Malignancies: Arms A and B of the AcSé-ESMART Trial. Bautista, F ; Paoletti, X ; Rubino, J ; Brard, C ; Rezai, K ; Nebchi, S & al J Clin Oncol 2021 ;39 :3546-3560

Childhood ovarian nonseminomatous germ cell tumors: A highly curable disease with few long-term treatment-related toxicities-Results of the French TGM95 study. Pavone, R ; Pacquement, H ; Pasquet, M ; Sudour-Bonnange, H ; Hameury, F ; Sarnacki, S & al Int J Cancer 2021 ;149 :1705-1712

Successive Osteosarcoma Relapses after the First Line O2006/Sarcome-09 Trial: What Can We Learn for Further Phase-II Trials? Thebault, E ; Piperno-Neumann, S ; Tran, D ; Pacquement, H ; Marec-Berard, P ; Lervat, C & al. Cancers (Basel) 2021 ;13 :

Personalized Massive Open Online Course for Childhood Cancer Survivors: Behind the Scenes. Berger, C ; Casagrande, L ; Sudour-Bonnange, H ; Massoubre, C ; Dalle, JH ; Teinturier, C & al Appl Clin Inform 2021 ;12 :237-244

The art of war as applied to pediatric gliomas: Know your enemy]. Bailleul, Q ; Rakotomalala, A ; Ferry, I ; Leblond, P ; Meignan, S ; Furlan, A Med Sci (Paris) 2021 ;37 :159-166

Clinical characteristics and outcomes of children with WAGR syndrome and Wilms tumor and/or nephroblastomatosis: The 30-year SIOP-RTSG experience. Hol, JA ; Jongmans, MCJ ; Sudour-Bonnange, H ; Ramirez-Villar, GL ; Chowdhury, T ; Rechnitzer, C & al Cancer 2021 ;127 :628-638

Oncologic supportive care for a personalized support of all patients. Lervat, C ; Vanlemmens, L ; Bondil, P ; Jacquot, J ; Scotté, F ; Gofti-Laroche, L Bull Cancer 2021 ;108 :210-223

A Spontaneously Necrotic Wilms' Tumor Mimicking Renal Abscess: A Tricky Diagnosis not to Miss. Sevrin, F ; Rocourt, N ; Leroy, X ; Coulomb-L'Hermine, A ; Sudour-Bonnange, H J Pediatr Hematol Oncol 2021 ;43 :e173-e175

What does a non-response to induction chemotherapy imply in high-risk medulloblastomas? Adelon, J ; Dufour, C ; Foulon, S ; Masliah Planchon, J ; Meyronnet, D ; Bourdeaut, F, Palenzuela G, Fouyssac F, Raimbault S & al J Neurooncol 2021 ;153 :425-440

Lenvatinib with etoposide plus ifosfamide in patients with refractory or relapsed osteosarcoma (ITCC-050): a multicentre, open-label, multicohort, phase 1/2 study. Gaspar, N ; Venkatramani, R ; Hecker-Nolting, S ; Melcon, SG ; Locatelli, F ; Bautista, F & al Lancet Oncol 2021 ;22 :1312-1321

SPONSORSHIP ACTIVITIES

In 2021, the sponsorship activity had:

32

studies
monitoring
patients

2

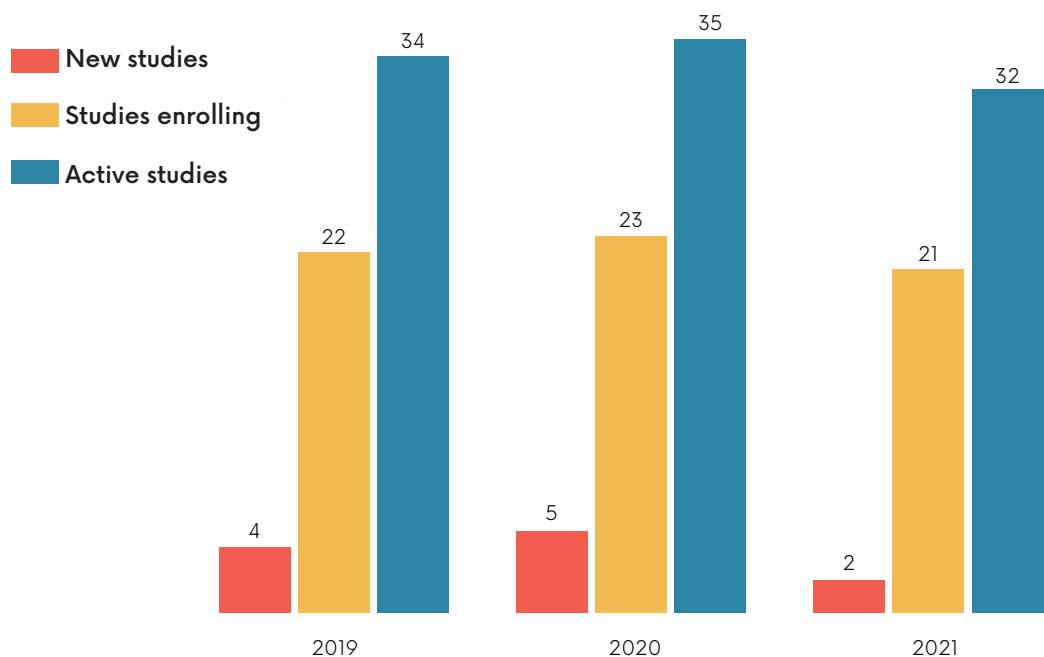
new studies set up

21

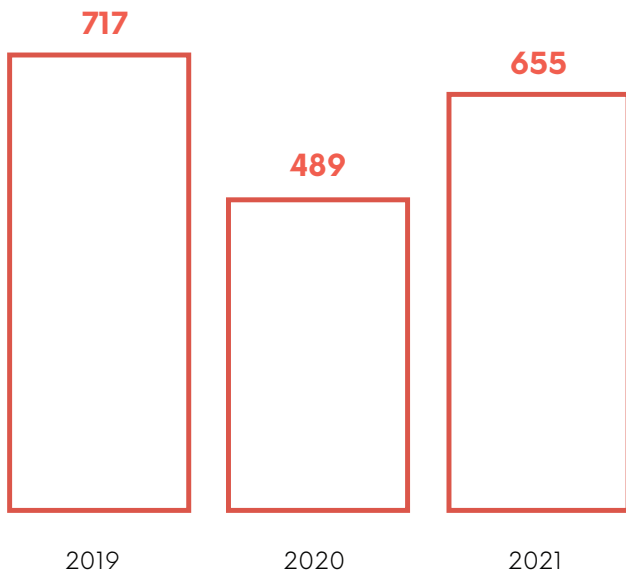
studies enrolling, one for
which we are one of the
sponsor's two national
representatives

655

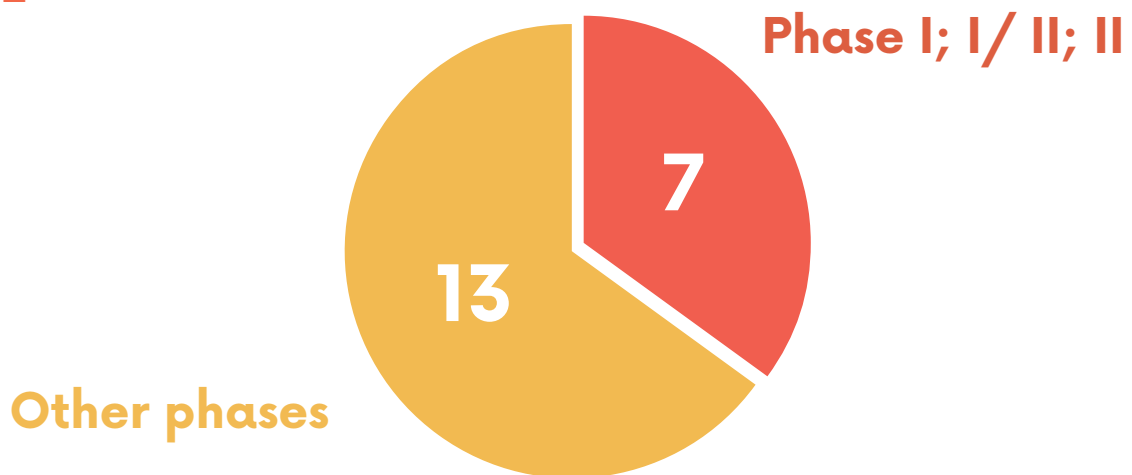
inclusions



NUMBER OF INCLUSIONS - 2019 TO 2021



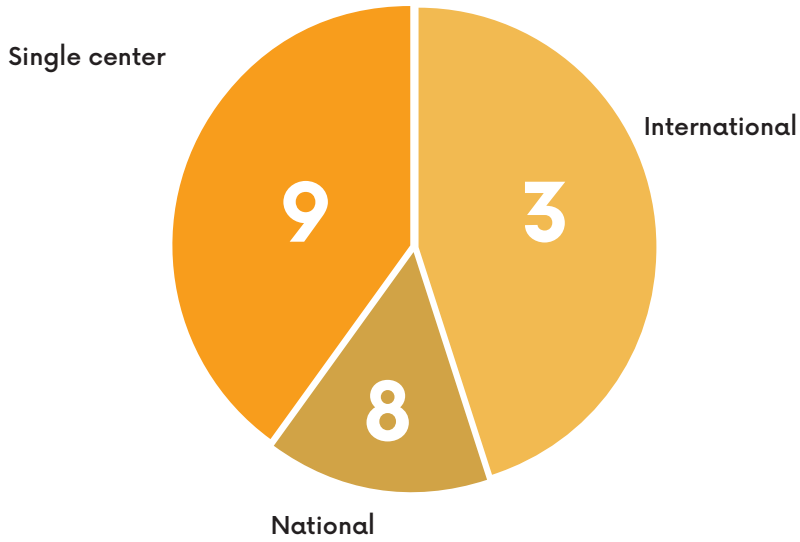
BREAKDOWN OF STUDIES ENROLLING ACCORDING TO PHASE



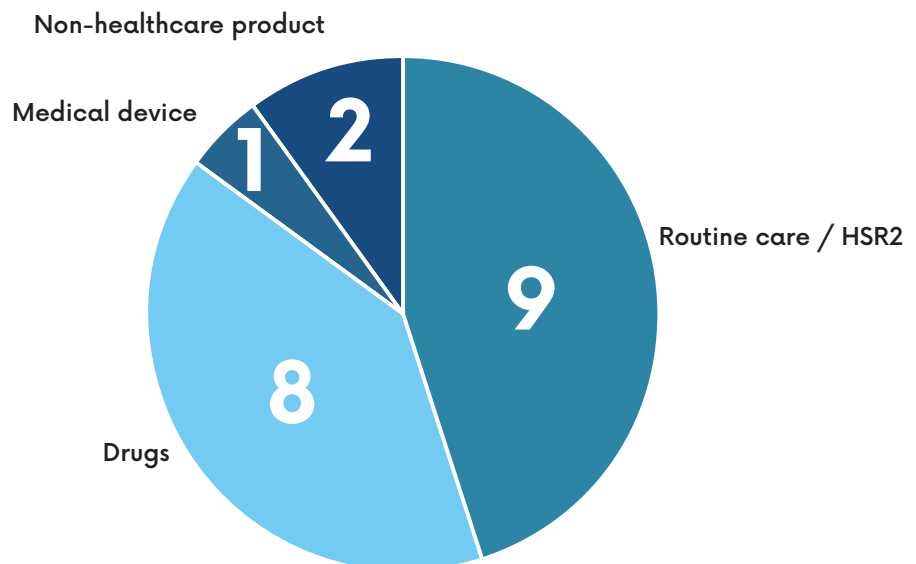
NUMBER OF INCLUSIONS IN PHASES I/II

Year	Inclusions in phases I/II
2019	75
2020	126
2021	169

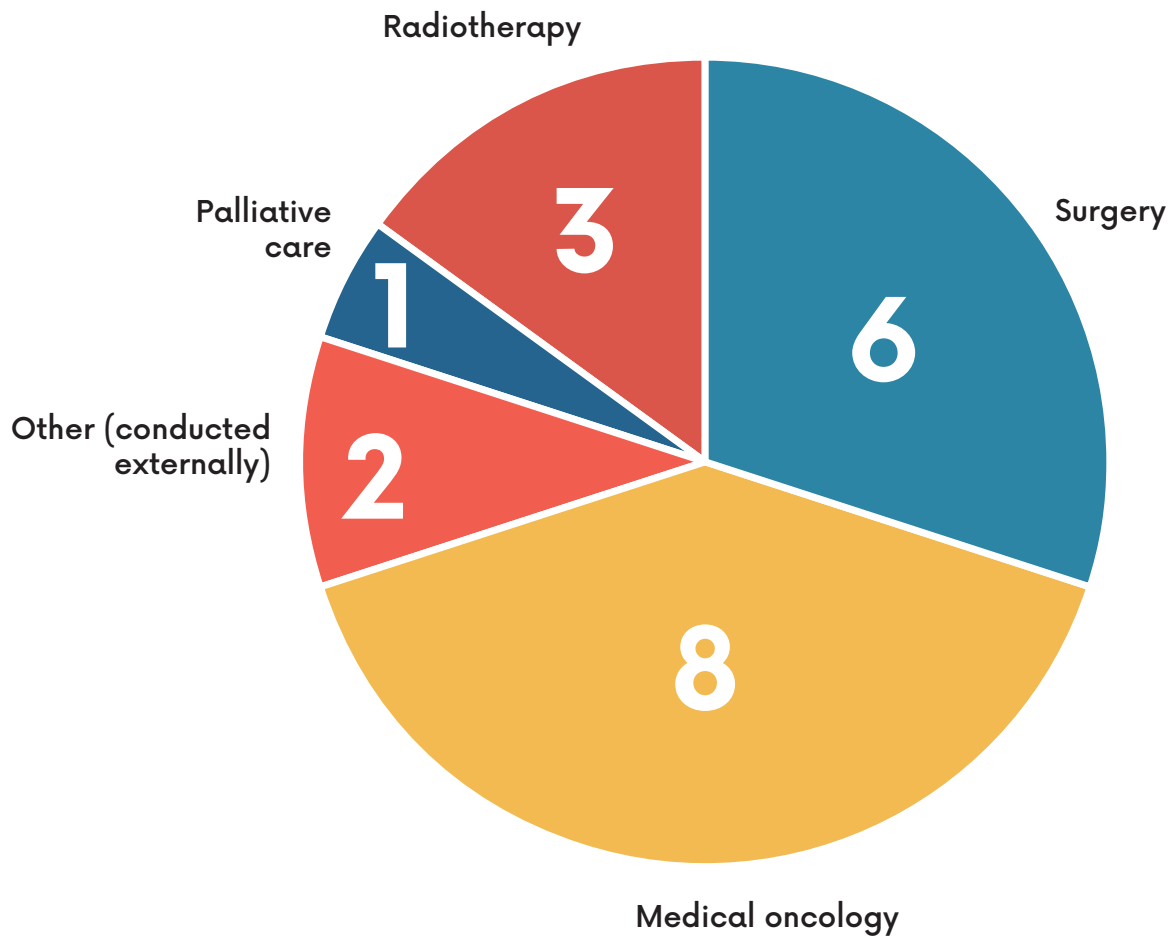
GEOGRAPHIC BREAKDOWN OF THE STUDIES



BREAKDOWN OF THE STUDIES BY TYPE



BREAKDOWN OF THE STUDIES BY DEPARTMENT



THE CLIP2 PEDIATRIC TRIALS

Through its CLIP² certification, the Oscar Lambret Center wishes to further its efforts in sponsoring pediatric trials.



PUBLICATION

ON THE VIT TRIAL IN THE JCO

One such trial, the VIT trial, was published in the Journal of Clinical Oncology in 2021. This international randomized phase 2 trial was sponsored by the Oscar Lambret Center, coordinated by Dr. Anne-Sophie Defachelles (a pediatrician at the OLC), and supported by the European Paediatric Soft tissue Sarcoma Study Group (EpSSG) and Innovative Therapies for Children with Cancer (ITCC).

This trial was funded by a Hospital Clinical Research Program and the French Society for Childhood Cancer and Leukemia (SFCE). It included 120 children and young adults (median age 11 years) treated for relapsed or refractory rhabdomyosarcoma in 37 centers in 5 European countries.

It demonstrated the clinical benefit of adding Temozolomide to the Vincristine-Irinotecan combination (VIT versus VI), with a significant improvement in overall survival, at the cost of what was deemed acceptable toxicity in these patients with rhabdomyosarcoma. The VIT combination is now included as a control arm in the follow-up European randomized trial conducted by EpSSG. It is a source of great pride for the oncopediatric team and the DRCI to have been able to conduct this international trial concerning a rare tumor, and to have it published so prestigiously.

Randomized Phase II Trial of Vincristine-Irinotecan With or Without Temozolomide, in Children and Adults With Relapsed or Refractory Rhabdomyosarcoma: A European Paediatric Soft Tissue Sarcoma Study Group and Innovative Therapies for Children With Cancer Trial. Defachelles AS, Bogart E, Casanova M, Merks JHM, Bisogno G, Calareso G, Gallego Melcon S, Gatz SA, Le Deley MC, McHugh K, Probst A, Rocourt N, van Rijn RR, Wheatley K, Minard-Colin V, Chisholm JC. J Clin Oncol. 2021 Sep 20;39(27):2979-2990. doi: 10.1200/JCO.21.00124. Epub 2021 Aug 3. PMID: 34343032

METROPD1 TRIAL

The Metro-PD1 trial (Randomized phase I/II study evaluating a PD-1 inhibitor (Nivolumab) in combination with metronomic chemotherapy in children and adolescents with a refractory or relapsed solid tumor), sponsored by the OLC, coordinated by Doctor Pierre Leblond (Léon Bérard Center in Lyon) and Professor Nicolas André (Marseille), is currently recruiting. In 2021 the 1st stage of the trial was completed after showing encouraging results, and the 2nd stage was opened.

The first stage of the trial (phase I) has now closed after recruiting 16 patients in 5 centers. It assessed the safety of three metronomic chemotherapy regimens (Cyclophosphamide + Vinblastine, or Capecitabine alone, or Cyclophosphamide + Vinblastine + Capecitabine) in combination with Nivolumab, in children and adolescents with a relapsed or refractory solid tumor. At the end of phase I, following the recommendations of the IDMC (Independent Data Monitoring Committee) which met on December 18, 2020, the Cyclophosphamide + Vinblastine + Capecitabine + Nivolumab combination was deemed safe enough to be evaluated in phase 2.

The second stage (randomized phase 2) now compares the efficacy of the metronomic combination Cyclophosphamide + Vinblastine + Capecitabine + Nivolumab against that of Cyclophosphamide + Vinblastine + Capecitabine without Nivolumab. It is now an international multicenter trial with 8 centers in France and 3 in Belgium. On 31 December 2021, 17 patients had been included in phase 2.

This project is supported and funded by BMS and the ACF foundation (Het Antikankerfonds, Brussels). Ancillary studies are underway to understand the role of the selective depletion of regulatory T cells, the modulation of myeloid-derived suppressor cells, or maturation of dendritic cells.

UPCOMING METROWILMS TRIAL

Lastly, the MetroWilms trial, a phase II study evaluating metronomic chemotherapy in patients with a refractory or relapsed Wilms tumor, coordinated by Doctor H el ene Sudour-Bonnange (Oscar Lambret Center) and Professor Arnauld Verschuur (Marseille), will start recruiting during the first half of 2022 (the ethics committee issued a favorable opinion in January 2022 and the ANSM authorization is pending). The OLC worked during 2021 to prepare this project, which is supported by the SFCE's Kidney Tumors Committee, and the project obtained partial funding from the Hauts de France Regional Council and various associations. The project was submitted to the Oncology Hospital Clinical Research Program PHRC-K 2021 and a letter of intent has been received. We are now awaiting a definitive answer.

The purpose of this phase 2, multicenter, non-randomized trial is to assess the efficacy of metronomic chemotherapy (combining vincristine, irinotecan, temozolomide, etoposide and retinoic acid) in patients who have a refractory or relapsing Wilms tumor. It expects to enroll 28 patients in 17 centers in France over 5 years.

Dr. Sudour talks about the importance and originality of this project

«This project is original in that currently there are no phase I/II clinical trials on nephroblastoma in France. Our regimen will allow continuous exposure by multiplying the mechanisms of action, which should increase the anti-tumor efficacy while only moderate toxicity is expected according to our current knowledge of this type of metronomic regimen. The use of retinoic acid in nephroblastoma, the relevance of which is based on solid preclinical data, is particularly novel in this regimen.

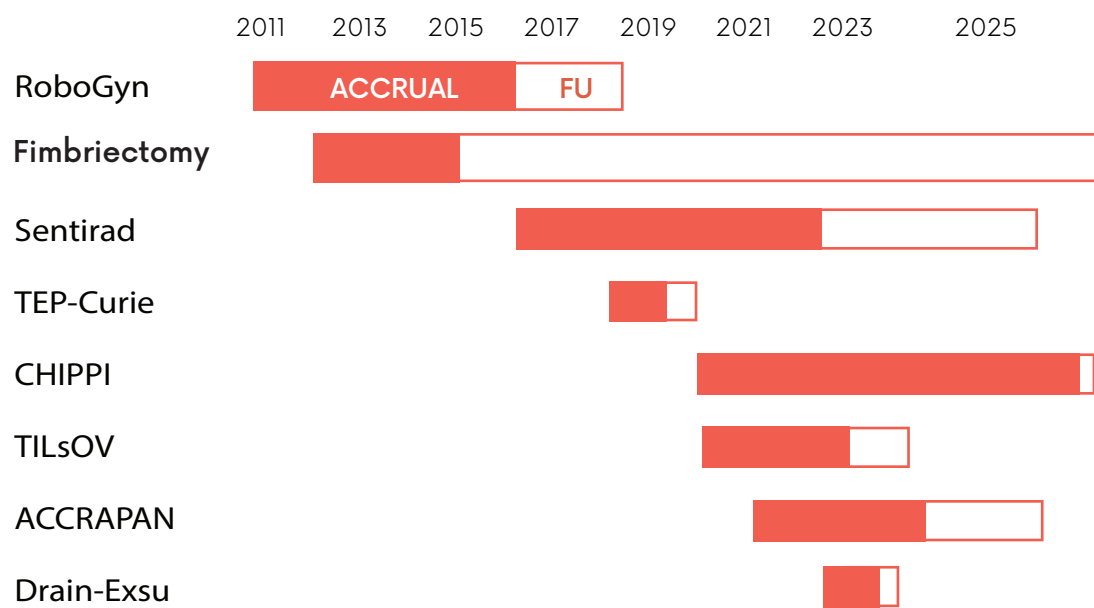
At the end of the study, we hope to demonstrate that the combination of these various drugs in a metronomic regimen is an effective therapeutic alternative to treat progressive Wilms tumors after at least 2 conventional lines of treatment, and well tolerated even in potentially heavily treated patients.”



GYNECOLOGICAL SURGERY AND RADIOTHERAPY STUDIES

Thanks to the momentum of the gynecology committee, and in particular the efforts of its surgical team led by Dr. Naducci, a long-term collaboration has been forged enabling projects sponsored by the OLC. These cancer surgery research projects focus on minimally invasive surgery (RoboGyn, Fimbriectomy, Sentirad, Drain-Exsu) or palliative surgery (HIPEC). There is no doubt that these projects will have practical clinical repercussions in the short term.

In addition, the team is setting up trials to personalize radiotherapy (TEP-Curie) and concomitant radiochemotherapy (ACCRAPAN). Lastly, the TILsOV project foreshadows the development of translational biology research within the Gynecology committee.



THE REGOSARC DOSSIER (OLC-BAYER PARTNERSHIP)

2021 saw further strong efforts by the Sponsorship/Methodology and Biostatistics Unit teams to prepare the submission of the application to extend the authorization for Regorafenib to soft tissue sarcomas.

In partnership with BAYER and in collaboration with the data management team at the Data Processing Center in Caen, it was necessary to prepare all the data for submission to the FDA/EMA in 2022 and the documentation relating to this data. It is a colossal effort for an academic sponsor to make all the data available so scrupulously.

This demanding experience helped improve the teams' quality approach and optimize processes. This work involved not only the DRCI but a variety of OLC teams, in particular the radiologists required to review all of the imaging. These efforts provided a final, pooled analysis clearly showing the benefit of Regorafenib in terms of progression-free survival in patients with soft tissue sarcomas (excluding liposarcomas).

This latest analysis will be presented at ASCO 2022 in Chicago in early June.

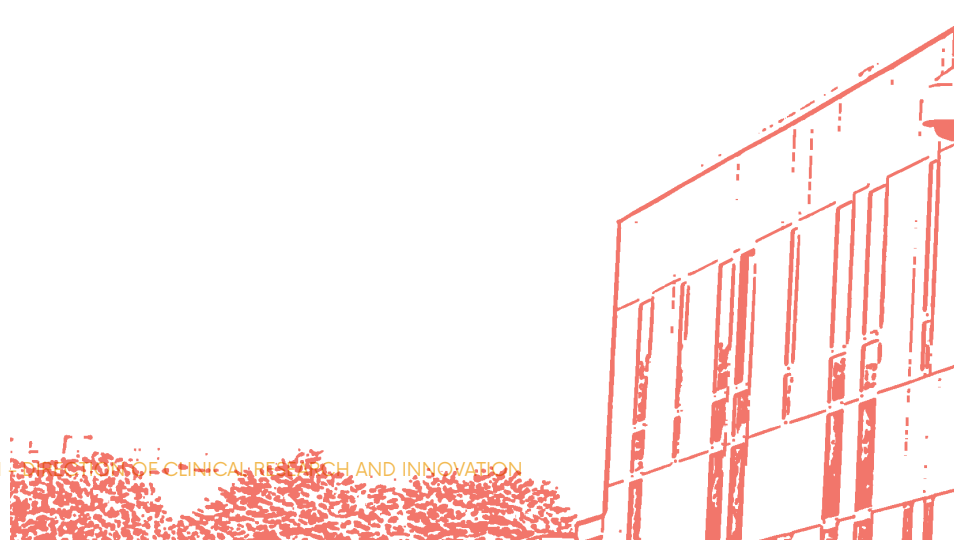


THE OSCAR LAMBRET CENTER, A MAJOR CONTRIBUTOR TO SCIENTIFIC RESEARCH

- **Find all of the Oscar Lambret Center teams' 2021 publications here:**

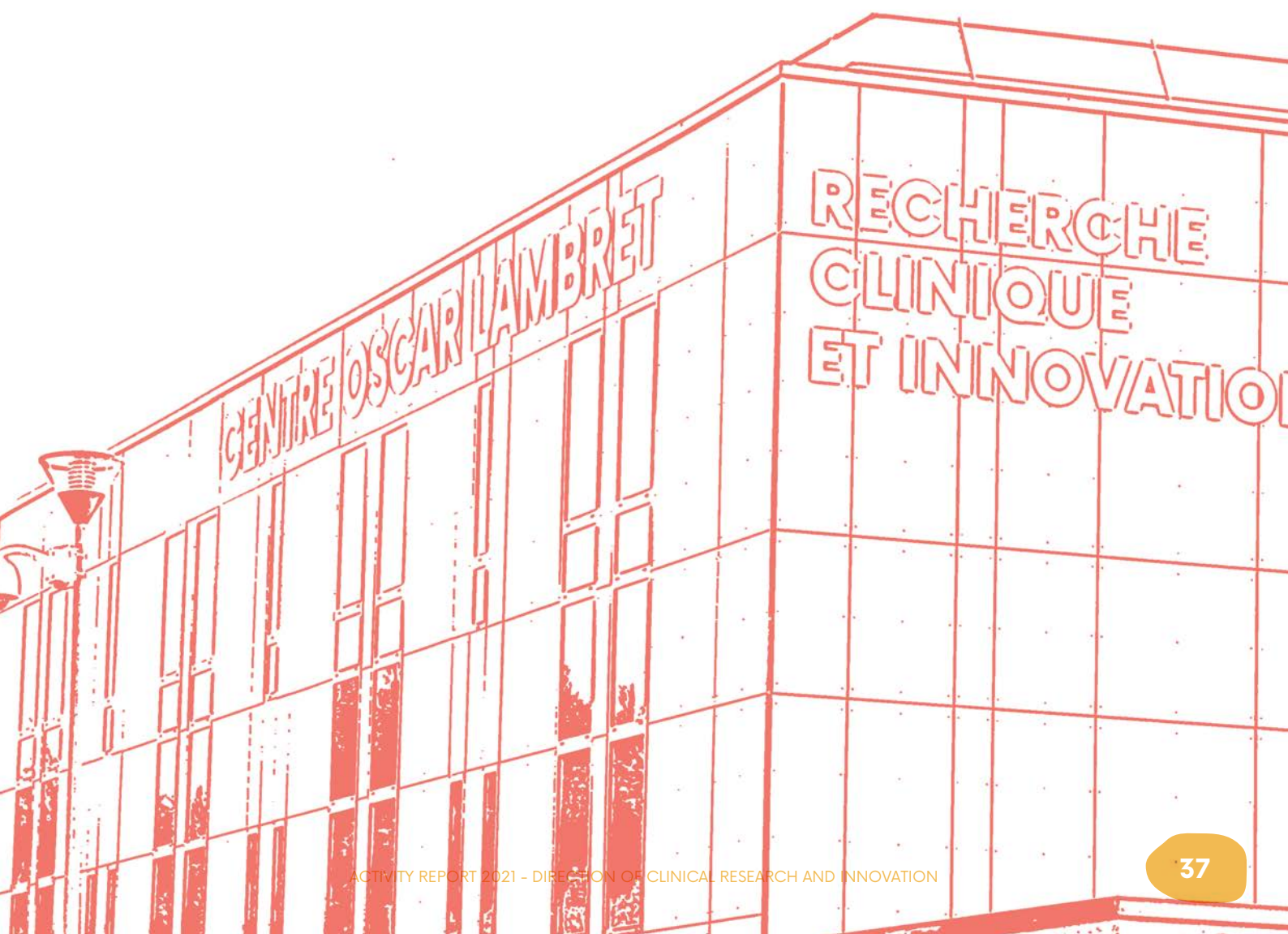


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Année	Total publications	Rang A	B	C	D	E	NC d'études	Score SIGAPS	Score fractionné
2019	136	31	27	29	12	31	6	1148	
2020	165	36	57	26	11	29	6	1569	123.29
2021*	178	32	64	42	12	24	4	1630	124.79
Total	479	99	148	97	35	84	16	4347	

*SIGAPS export dated January 24, 2022; score subject to change



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