

SCIENTIFIC REPORT

2021

ACTIONS FOR CANCER RESEARCH

The French National Cancer Institute is the health and science agency in charge of cancer control.

Working group

Scientific coordination

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2021

was a landmark year for the French National Cancer Institute. On February 4, INCa organised its institutional event at which the Ten-Year Cancer Control Strategy was launched by the French President.

THIS STRATEGY IS THE RESULT OF A BROAD CONSULTATION CONDUCTED IN 2020 WITH ALL STAKEHOLDERS IN THE FIGHT AGAINST CANCER:

researchers, carers, association leaders, public decision-makers, but also patients, their families and, more broadly, all citizens. The draft produced has thus been revised and improved, notably through the guidance of the International Scientific Advisory Board of the Institute.

AT A NATIONAL LEVEL, the Strategy marks the beginning of a new chapter in cancer-fighting history. A chapter in which innovation will be the keyword. A chapter that should lead to significant advances in all areas likely to reduce cancer and improve the quality of life of patients, during and after the disease.

IT IS ALSO WHY, AS SOON AS THE STRATEGY WAS ANNOUNCED, INCa and its partners promptly set out to define an initial five-year roadmap and to initiate the first actions using an operational and concrete approach. Based on this roadmap, by 2021, nearly one third of the 234 actions planned for the next decade had already been launched. Often quite new, they demonstrate our intention to innovate more and more for the benefit of the population and to step up our research efforts to achieve excellence. They also demonstrate our ambition to mobilise all stakeholders, and in particular regional actors, in order to take better account of the real needs of our fellow citizens.

THESE NEW ACTIONS ARE, OF COURSE, DESIGNED TO COMPLETE AND LINK WITH OUR CORE ACTIONS THAT HAVE ALSO BEEN STRENGTHENED THROUGH TO THE NEW RESEARCH PROGRAMMING LAW.

In addition, the timing is particularly favourable given the simultaneous launch of the European Cancer Plan and the work undertaken by the European Mission on Cancer. In this way, all this work creates suitable conditions to pave the way for a new era in cancer control and drive progress for all.

Professor Norbert Ifrah, MD

■ Chairman and CEO of the
French National Cancer Institute

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ACTIONS FOR CANCER RESEARCH



INSTITUT
NATIONAL
DU CANCER

SCIENTIFIC REPORT 2021

2021 total investments:

€54.28M in biology and basic sciences including

€4.28M dedicated to specific paediatric cancer research programmes

€3.03M

in clinical research, such as promoting access to innovative drugs

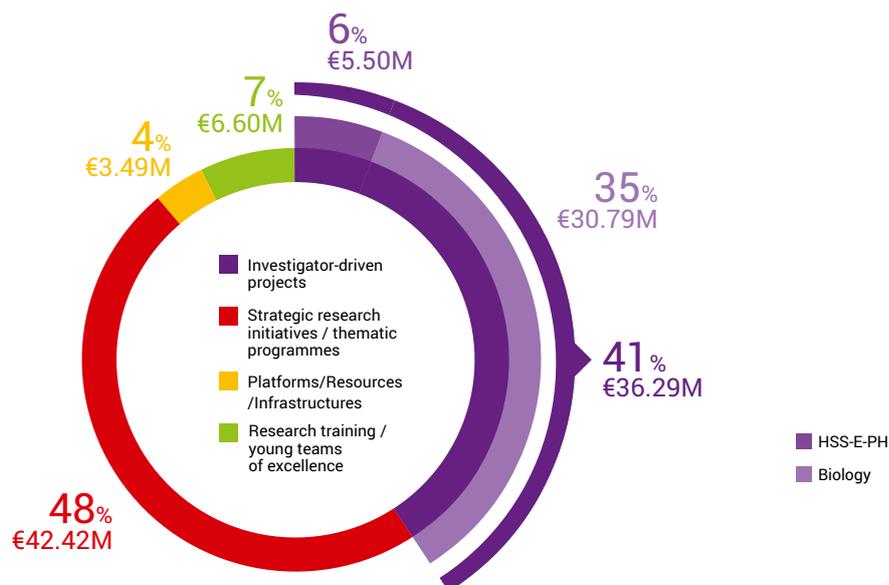
€17.91M

in research in human and social sciences, epidemiology and public health applied to cancer

€13.58M

in translational and integrated cancer research

2021 multi-year cancer research funding by programme type (INCa and ITMO Cancer-Aviesan): **€88.80M** invested



Total investments over the 2007-2021 period:

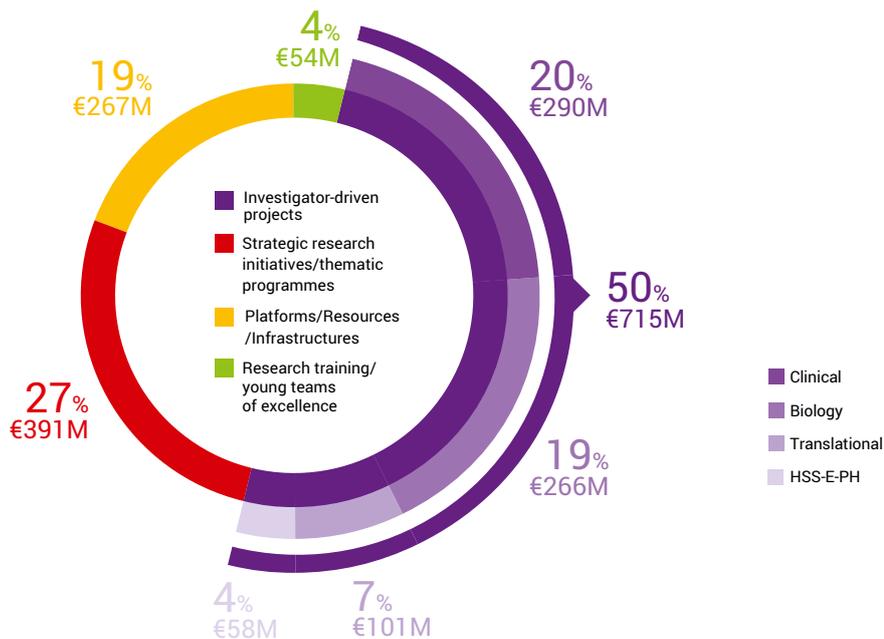
€584M
in biology and
basic sciences

€156M
in research
in human and
social sciences,
epidemiology
and public health

€310M
in translational
and integrated
cancer research

€377M
in clinical research

2007-2021 multi-year cancer research funding by programme type
(INCa, DGOS and ITMO Cancer-Aviesan): **€1.427Bn** invested





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The international scientific advisory board



This 16th report to INCa's international Scientific Advisory Board (SAB) reviews actions carried out both by INCa and Aviesan's Multi-Organisation Thematic Institute for Cancer (ITMO Cancer-Aviesan). This report is the key element for SAB members to review the actions undertaken and subsequently advise and guide the Institute during its structuring processes and its initiatives.

Composed of internationally renowned experts and appointed by the supervising Ministers, INCa's Scientific Advisory Board has been chaired by Prof. Catherine Lacombe since 2018.

Concerning the Institute's powers and missions, the Scientific Advisory Board:

- Ensures that INCa's scientific and medical policy is consistent;
- Reviews INCa's annual scientific report before it is presented to the Board of Directors;
- Makes recommendations and provides opinions on INCa's scientific strategies and their implementation.

The first part of this report is focused on the 2021 recommendations of INCa's SAB. The SAB's recommendations are central to the Institute establishing an action plan and proposing a strategy to handle cancer research challenges over the years.

THE INTERNATIONAL SCIENTIFIC ADVISORY BOARD MEMBERS

The members of the Scientific Advisory Board are:

- **Dr. Geneviève Almouzni**, PhD, Institut Curie, Paris, France
- **Mrs. Pascale Altier**, VBO Consulting, Saint-Rémy-Lès-Chevreuse, France
- **Prof. Cécile Badoual**, MD, PhD, Hôpital Européen Georges Pompidou, Paris, France
- **Dr. Jean-Pierre Bizzari**, MD, Celgene, Summit, USA
- **Prof. Cédric Blanpain**, MD, PhD, Université Libre de Bruxelles, Brussels, Belgium
- **Dr. Franck Bourdeaut**, MD, PhD, Institut Curie, Paris, France
- **Dr. Elizabeth A. Eisenhauer**, MD, Queen's University, Kingston, Canada
- **Prof. Yann Gauduel**, PhD, École Polytechnique – ENS Techniques Avancées, Palaiseau, France
- **Dr. Ivo G. Gut**, PhD, Centro nacional de analisis genomica (CNAG), Barcelona, Spain
- **Prof. Mette Kalager**, MD, PhD, Institute of Health and Society, University of Oslo, Oslo, Norway
- **Prof. Catherine Lacombe**, MD, PhD, Institut Cochin, Paris, France
- **Dr. Douglas R. Lowy**, MD, NCI Acting Director, Bethesda, USA
- **Prof. Marc-André Mahé**, MD, PhD, General Director, Centre François Baclesse, Caen, France
- **Prof. Dame Theresa Marteau**, PhD, University of Cambridge, Cambridge, United Kingdom
- **Dr. Patrick Mehlen**, PhD, Centre de recherche en cancérologie de Lyon, Lyon, France
- **Prof. Stefan Pfister**, MD, German Cancer Research Centre (DKFZ), Heidelberg, Germany
- **Prof. Louise Potvin**, PhD, Institut de recherche en santé publique de l'Université de Montréal, Université de Montréal, Montreal, Canada
- **Mrs. Fabienne Renaud**, Europa Donna France, Nantes, France
- **Prof. Gérard Socié**, MD, PhD, Hôpital Saint Louis, Paris, France
- **Dr. Naomi Taylor**, MD, PhD, National Cancer Institute, NIH, Bethesda, USA
- **Prof. Robert A. Weinberg**, PhD, Massachusetts Institute of Technology (MIT), Cambridge, USA
- **Prof. Laurence Zitvogel**, MD, PhD, Gustave Roussy, Villejuif, France

2021 RECOMMENDATIONS

- 1 Congratulations to INCa on already launching 78 actions and approval of the 10-year action plan
- 2 Clarity around some of the recommendations regarding screening programmes is needed – for example, there are harms from breast cancer screening which are not acknowledged in Les Eclairages.
- 3 An evaluation strategy for the impact of the 10-year plan will be important to develop
- 4 Specific recommendations regarding SIRIC:
The SAB acknowledges the importance of the SIRIC programme (i.e. centres of excellence) for translational cancer research in France and supports its renewal in an even stronger and better resourced format. The SAB encourages INCa to perform a benchmark analysis of what is offered in other countries such as Germany (through the German Cancer Consortium – <https://dtk.dkfz.de/en> for early translation and NCT network – <https://www.nct-heidelberg.de/en/the-nct/introduction/facts-and-figures/nct-network.html> for late translation) to increase the overall visibility and contributions of the SIRICs as core comprehensive cancer centres in France. To achieve these goals, the SAB has the following suggestions:
 - Increase the overall budget allocated to SIRICs;
 - Allocate a sizeable fraction of the SIRIC budget (at least 25%) to inter-SIRIC collaborations, which could decrease competition between SIRICs, increase their cooperation and strengthen cancer research interactions between centres with complementary and non-overlapping expertise in France;
 - Embed patient advocates in all SIRIC sites;
 - Given that many SIRICs have already benefited from 10 years of funding, infrastructure costs should be capped (for example, 10%);
 - Increase the duration of SIRICs but have each of them reviewed every 5 years by an international panel;
 - Consider periodic new calls for potential additional SIRIC centres, to reduce competition between cancer centres in France;
 - Approach regional/local decision-makers for potential co-funding of these important local/regional cancer research hubs.

5 It is critical that INCa continue to work together with ANSM to identify how to increase the speed of activation of clinical trials – a necessity for enhancing the competitiveness of France in clinical research and offering patients the opportunity to access novel therapeutics.

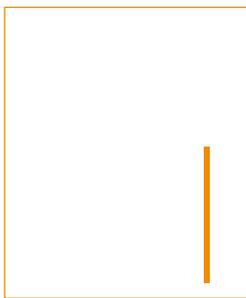
6 Some overarching comments on this session regarding the ITMO/INCa workshop:

- The themes presented today were very diffuse in their content;
- SAB recommends that each of the themes should have defined “big” questions which might focus calls for proposals and investment – more work is needed which will require bringing together relevant experts across fields to accomplish this. Goals, focus and priorities need better definition;
- Linkage to the 10-year action plan/strategy and its priorities should be clear. Detection, treatment and supportive care research.



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2021 Cancer Research Activity



In recent years, the research and health landscape in oncology has undergone a significant upheaval, giving France major opportunities to strengthen its innovative programmes while making it possible to initiate new ones. In the last few years, INCa has established a highly proactive policy, recognised by European and American colleagues, to expand collaboration in cancer research and to provide access to targeted therapies for patients identified as candidates through molecular tests.

INCa has a pre-eminent role in France with a national mandate encompassing all activity areas of value in the cancer control chain, from research to prevention and screening, to the organisation of cancer care and information for patients and their relatives.

Every year, INCa issues investigator-driven calls for proposals to the scientific community in the 4 main research areas: cancer biology, translational research, clinical research, and research in human and social sciences, epidemiology, and public health. The Institute completes its cancer research support through specific actions and allocations to support cancer research structuring and strategic research initiatives, such as fostering precision medicine, to promote access to innovation for all patients.

Moreover, ITMO Cancer-Aviesan completes cancer research support thanks to specific and thematic programmes aimed to support emerging fields, multidisciplinary projects, and basic and translational cancer research training.

The following section presents a detailed review of the research programmes conducted in 2021, and takes into account the actions undertaken since 2007.

BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH



Research focused on cancer biology helps to increase the basic knowledge on oncogenesis, development, and progression of cancer. The understanding of biological mechanisms opens up new prospects for advances in treatment, inhibition of resistance mechanisms, and the development of tools through the establishment of projects involving physics, mathematics, or information technology.

To promote and support this progress in the long term, INCa launches a recurrent call for proposals focused on cancer biology and basic sciences, completed by thematic calls for proposals programmed by ITMO Cancer-Aviesan in order to strengthen and support emerging and priority cancer research areas.

IN 2021, SUPPORT FOR BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH AMOUNTED TO:

€54.28M

€30.79M dedicated to support investigator-driven projects (PLBIO programme);

€18.36M to support thematic research programmes such as multidisciplinary projects and emerging topics;

€3.49M for cancer research equipment support

€1.64M to support young leaders and cancer research training.



The biology and basic sciences for cancer research programme (PLBIO)

Since 2005, INCa has issued an investigator-driven call for proposals to the French scientific community for the funding of original and promising projects in different areas and disciplines of basic research in oncology.

THE PROGRAMME IN 2021

In 2021, 55 projects were selected out of the 258 proposals submitted for a total amount of €30.8M (21.3% of the submitted applications were selected).

■ TABLE 1

FEATURES OF THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2021

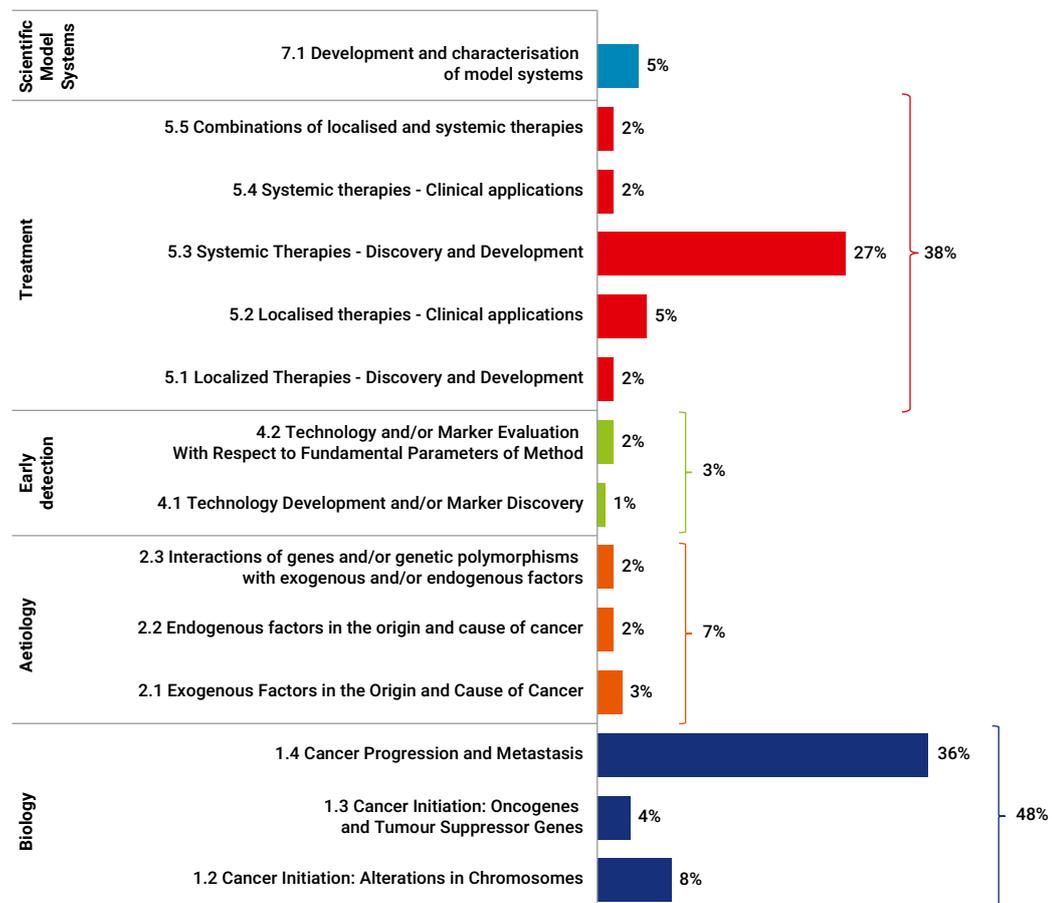
Objectives	To acquire new knowledge and develop new tools to create new therapeutic approaches. Open to all areas of basic research and to scientific disciplines involved in tumour biology research, this call was launched to: <ul style="list-style-type: none"> ● Enable the achievement of original projects; ● Strengthen multidisciplinary collaborations; ● Develop research in emerging areas.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€30.8M
Proposals submitted	258
Projects selected	55
Selection rate	21.3%

Figure 1 presents a detailed analysis of the funded projects:

- The aim of the majority of the funded projects (48%) is to study the biological mechanisms of cell transformation and disease progression, according to the international CSO classification¹ (CSO 1). Among these, 36% of the projects specifically concern the interaction between tumour cells and their microenvironment (cell mobility, tumour invasion, metastasis, cancer stem cells, immunological microenvironment, or angiogenesis, CSO 1.4). This category is well represented each year. This trend reflects the interest of these research fields in cancer biology;
- 6% relate to cancer aetiology (CSO 2);
- 3% concern the early detection, diagnosis, and prognosis of cancers (CSO 4);
- 38% of the funded projects study either molecular mechanisms of treatment response and resistance, or the identification of new therapeutic targets (CSO 5);
- 4.5% concern research and development of model systems (CSO 7).

1. The detailed description of the CSO classification is presented in Appendix 1.

FIGURE 1
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS
FOR THE BIOLOGY AND BASIC SCIENCES
FOR CANCER RESEARCH PROGRAMME IN 2021



2021:
55 projects
 selected for
 a total amount of
€30.8M

Figure 2 depicts a detailed analysis of the research topics of the selected projects:

- Immunology: 23% of the funded projects; with a huge focus on immune surveillance or mechanism of escape from immune surveillance;
- Microenvironment: 16% of the funded projects, with a majority of projects addressing the study of tumour infiltrating immune cells and the study of tumour–environment interaction;
- Cell signalling: 15% of the funded projects, with a particular emphasis on cellular metabolism and translation regulation;
- Genetics: 12% of the funded projects, mainly studying cell cycle regulation and/or senescence, transcription, DNA damage or replication/replicative stress.

FIGURE 2 ANALYSIS OF THE MAIN RESEARCH TOPICS STUDIED BY FUNDED PROJECTS IN 2020 AND THE DISTRIBUTION OF THE RESEARCH FIELDS INTO THESE MAIN TOPICS



**PLBIO:
the largest
research
programme
operated
and funded
by INCa**

THE PROGRAMME OVER THE 2007-2021 PERIOD

Since 2007, 531 projects have been selected out of 3,761 proposals submitted to the Biology and basic sciences for cancer research programme, for a total budget of €266.10M (Figure 3).

This programme is the Institute's most attractive programme considering the number of applications. As of this year, the PLBIO programme benefits from a substantial additional budget, thanks to the multi-year research programming law ("Loi de programmation de la recherche"), allowing a significant increase of the success rate. This increase was essential given the extremely high quality of the numerous applications submitted each year.

This highlights the importance of this call for support for research in cancer-related basic sciences, and identifies INCa as a major funding agency for basic sciences, alongside the French National Research Agency (ANR), which funds basic research outside the field of cancer.

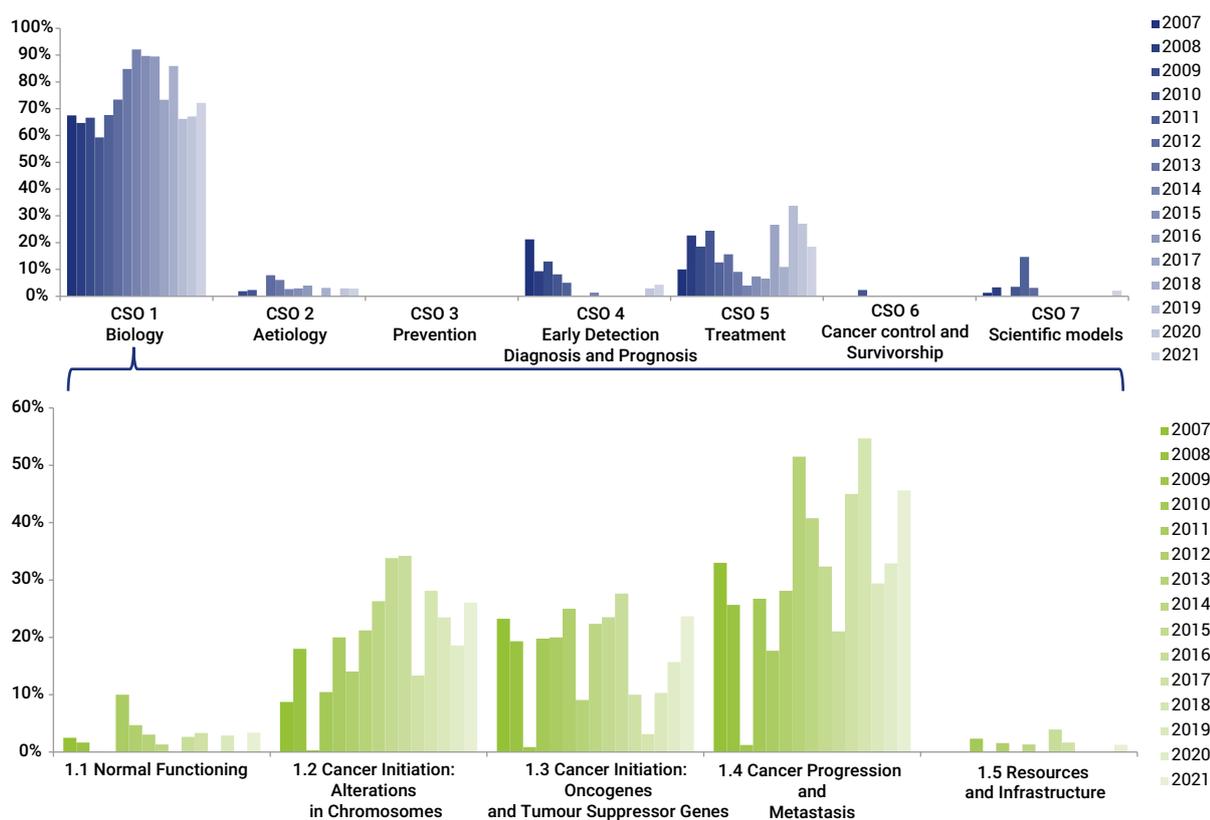
The analysis of the projects funded over the 2007-2021 period according to the CSO classification shows that the projects are mainly focused on the biological mechanisms of cell transformation and disease progression. This trend has been quite stable over the years (Figure 4).

■ FIGURE 3

TRENDS IN SELECTION AND FUNDING OF THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME OVER THE 2007-2021 PERIOD



FIGURE 4
DISTRIBUTION OF SELECTED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2021 PERIOD



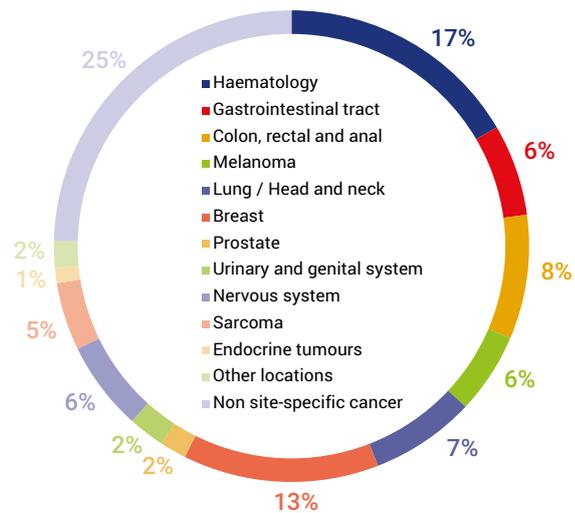
The majority of these projects study cancer progression and metastasis, especially the regulation of processes in tumour invasion, metastasis, angiogenesis, and immune microenvironment (Figure 4, bottom panel).

Around 25% of the projects are non-specific to a tumour type, highlighting that projects are more focused on general mechanisms of cancer initiation, development, and/or progression, together with research on molecular targets and therapies that could be applied to several pathologies. Projects studying haematological malignancies (17%), breast cancer (13%) and colorectal cancer (8%) are also well represented (Figure 5).

2007-2021:
531 projects
 selected for a total
 amount of
€266.1M

■ FIGURE 5

DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO CANCER SITES STUDIED FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME OVER THE 2007-2021 PERIOD



Setting up immuno-oncology webinar series sponsored by French National Cancer Institute and the National Cancer Center of Japan



The close collaboration between France and Japan on cancer has been further strengthened by a memorandum of understanding signed by INCa and the National Cancer Center of Japan. In this way, in December 2019, INCa and the NCC of Japan jointly organised a workshop on paediatric cancer.

To keep up the momentum of this collaboration, INCa and the NCC of Japan, together with the French Embassy have been discussing the opportunity of jointly organising another scientific event. The pandemic context even fuelled their desire to propose a more meaningful format.

The French National Cancer Institute and the National Cancer Center of Japan, with support from the Office for Science and Technology of the French Embassy to Japan, will thus organise a series of webinars focusing on immuno-oncology throughout 2022. These webinars will be also supported by the Kiyoko Goto and Paul Bourdarie Cancer Foundation.

These webinars will provide an opportunity for French and Japanese researchers to present their work. In fact, rather than establish a partnership between INCa and the NCC of Japan, both Institutes are keen to develop, build and further strengthen the close collaboration between the two nations in many areas of cancer research and clinical activities.

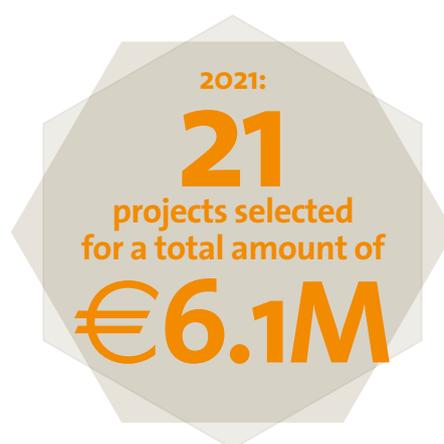
Thematic cancer research programmes by ITMO Cancer-Aviesan

INTERDISCIPLINARY APPROACHES TO ONCOGENIC PROCESSES AND THERAPEUTIC PERSPECTIVES: CONTRIBUTIONS TO ONCOLOGY OF THE PHYSICS, CHEMISTRY, AND ENGINEERING SCIENCES PROGRAMME (PCSI)

Initiated in 2019 following the redesign and split of the previous programme for research in physics, mathematics and engineering sciences related to cancer (PMSI), the PCSI programme aims to improve understanding of tumour diseases and improve cancer prognosis by funding projects based on concepts or tools from physics, chemistry or engineering sciences. It allows funding of both proof-of-concept (PoC) projects and full projects.

The programme in 2021

In 2021, out of 93 submitted proposals, 12 full projects and 9 “proof-of-concept” (PoC) projects were selected for funding, representing a total amount of €6.1M (Table 2 and Figure 6).



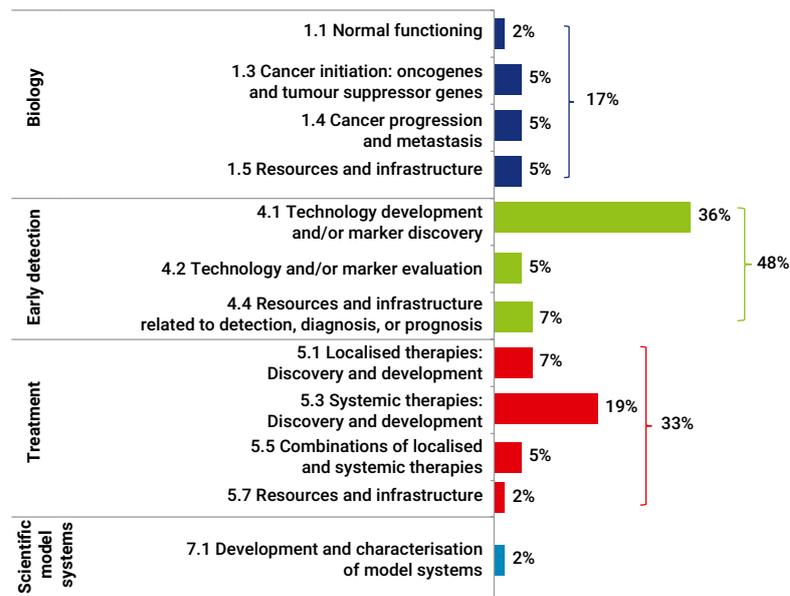
■ TABLE 2
FEATURES OF THE 3R PROGRAMME IN 2021

Objectives	To improve understanding of tumour diseases and improve the prognosis of patients thanks to concepts or tools from physics, chemistry or engineering sciences.
Programming institution	ITMO Cancer Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer Aviesan
Funding	€6.1M
Proposals submitted	93
Projects selected	21 (9 PoC & 12 Full)
Selection rate	23%

The funded projects focused on the development of systems or strategies based on cutting-edge physical or chemical technologies aimed at:

- Deciphering new mechanisms of carcinogenesis:
 - Optogenetic reprogramming of a single somatic cell to analyse cancer initiation in an in vivo model;
 - NMR ultra-high-resolution and high-resolution mass spectrometry to explore cancer cell metabolism and antimetabolic drug mechanisms in diffuse large B-cell lymphoma;
 - Spheroid models to visualise the mechanisms underlying positive effects of macrophages on tumour growth;

■ **FIGURE 6**
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PCSI PROGRAMME IN 2021 ACCORDING TO THE CSO CLASSIFICATION

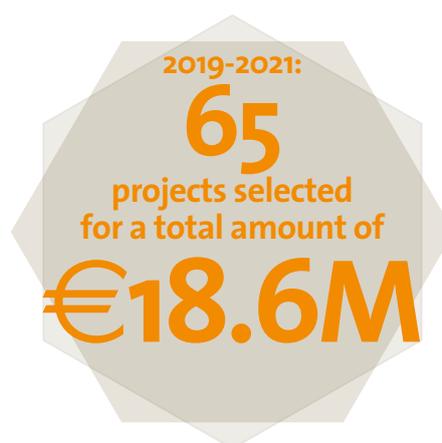


- Devices (e.g., in vivo compression apparatus) to explore the mechanisms and molecular determinants associated with cell sensitivity to compressive stress during tumour growth;
- Multimodal pipeline to characterise cell subtypes present in the tumour microenvironment matrix and correlate them with matrix organisation.
- Improving cancer detection and imaging:
 - Contrast agent for the detection/quantification of zinc in early phases of pancreatic cancers;
 - Time-gated Förster resonance energy transfer to detect femto- and attomolar concentrations of cell-free DNA or miRNA in liquid biopsies of colorectal cancer patients;
 - Sonogenetic bacteria for acoustic imaging of tumours and their microenvironment;

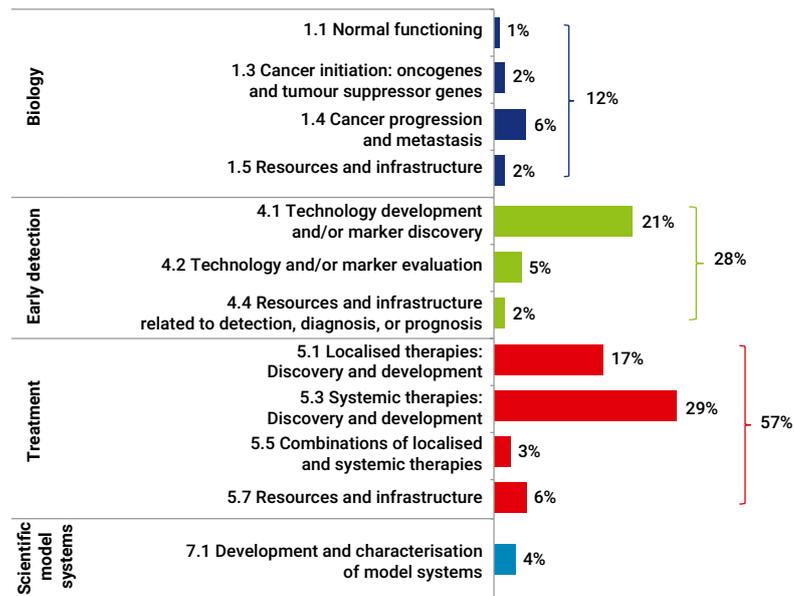
- Fourier-transform-infrared imaging technology to define spectroscopic signatures of triple-negative breast cancer subgroups and predict their radioresistance;
- Two-photon bioconjugated probes for in vivo cancer imaging;
- Ultrasensitive isothermal amplifying technology to detect multiple markers and identify tumour signatures (epithelial-to-mesenchymal transition in lung cancer or circulating markers of clear cell renal cell carcinoma).
- Developing new therapeutic strategies:
 - Theranostic tool based on the coupling of an aptamer targeting thrombospondin-1 with an antineoplastic agent in glioblastoma;
 - Chemicals triggering elimination of radioelements from radio-immunoconjugates to improve immune-PET quality for diagnosis and limit side effects of vectorised radiotherapy;
 - Inhibitor of sumoylation to combat therapeutic resistance in acute myeloid leukaemia;
 - Proteolysis-targeting chimaera-based peptides to inhibit the nuclear receptor PPAR γ (proliferator-activated receptor γ) involved in muscle-invasive bladder cancer progression;
 - Peptidomimetic and monoclonal antibody-based strategies to control the level of the protein s-CD95L involved in triple-negative breast cancer cell dissemination;
 - Single-drug resolution approaches to screen small nuclear inhibitors of non-homologous end-joining, a DNA repair mechanism;
 - Orthogonal conformational biosensors to develop allosteric inhibitors of the cyclin-dependent kinase CDK5 involved in several common cancers;
 - Nanohyperthermia system reversing mechanical tumour microenvironment property abnormalities to foster immune cells and anticancer drugs access in cholangiocarcinoma;
 - Nucleolipid nanoparticles to simultaneously deliver therapeutic radionuclides and TCTP (translationally controlled tumour protein) antisense oligonucleotide in highly aggressive prostate cancers;
 - Faster, more efficient, and more accurate system to calibrate proton beams before irradiation treatment.

The programme over the 2019-2021 period

In 3 editions, 65 projects were selected for a total funding amount of €18.6M. Technology development or marker discovery for cancer diagnosis (21%), and discovery and development of new therapies (46%), either localised or systemic, were at the core of the vast majority of the projects (Figure 7).



■ **FIGURE 7**
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PCSI PROGRAMME OVER THE 2019-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



ITMO Cancer-Aviesan programme “Epigenetics and cancer”- Report workshop

This programme (3 editions between 2013 and 2015) was aimed at establishing and strengthening multidisciplinary capabilities to explore cancer-associated epigenetic mechanisms. The restitution seminar was held in Paris on 20-21 October 2021, and successful applicants presented their findings achieved with the funding at 3 sessions: DNA modifications (9 projects), Other regulation mechanisms

(8 projects), and Histone modifications (12 projects). Round-table discussions were organised on 3 themes identified by the PIs themselves as key to progress in the field of epigenetics and cancer. Single-cell approaches, Chemical inhibitors of epigenetic regulators, and Functional impacts of epigenetic modifications. Working groups were set up under the patronage of ITMO Cancer-Aviesan to explore these subjects further.

INTERDISCIPLINARY APPROACHES IN ONCOGENIC PROCESSES AND THERAPEUTIC PERSPECTIVES: CONTRIBUTIONS TO ONCOLOGY OF MATHEMATICS AND COMPUTER SCIENCE PROGRAMME (MIC)

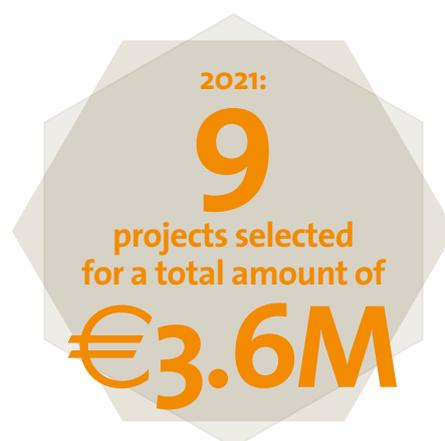
Initiated in 2019 following the redesign and split of the previous programme for research in physics, mathematics and engineering sciences related to cancer (PMSI), the MIC programme aims to improve understanding of tumour diseases and improve patients' prognosis thanks to the contribution of mathematics and computer science. Indeed, recent technological revolutions have progressively put these disciplines at the centre of large-scale studies, which have become crucial for oncology research. The programme is intended to unlock conceptual and methodological barriers at the frontier of mathematics, computer science and oncology.

The programme in 2021

In 2021, 9 projects were selected out of the 33 submitted for a total amount of €3.6M (Table 3 and Figure 8)

■ TABLE 3
FEATURES OF THE MIC PROGRAMME IN 2021

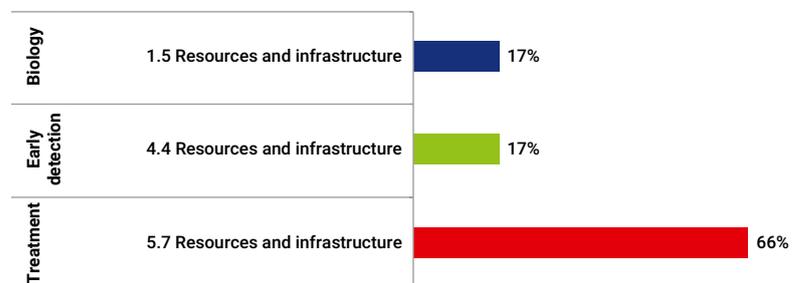
Objectives	To improve understanding of tumour diseases and improve patients' prognosis thanks to the contribution of mathematics and computer science
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€3.6M
Proposals submitted	33
Projects selected	9
Selection rate	27%



The funded projects focused on the development of logical, statistical, machine-learning-based models aimed at:

- Characterising new mechanisms and markers of cancer initiation and progression:
 - Bioinformatic methods/pipelines investigating ectopic gene activations in a variety of malignancies to understand tumour heterogeneity and identify biomarkers;
 - Artificial intelligence-based computational methods to develop integrative models of tumour heterogeneity and infer biological behaviour and associated clinical indicators;
 - Constraint-based modelling analysis using the resource balance analysis method to predict pathological phenotypes of cancer cell metabolism.
- Predicting response to treatment or investigating new therapies:
 - Deep generative model-based method to reveal invisible phenotypes and characterise the response of ovarian cancer to chemotherapy;
 - Computational model of transcriptional and epigenetic network to predict and overcome treatment resistance of acute promyelocytic leukaemia;
 - Model-based methods integrating multiscale and heterogeneous data to predict the long-term response to IFN α in myeloproliferative neoplasms;
 - Joint modelling of CA-125 (cancer antigen 125) dynamics to evaluate its predictive value as a biomarker of ovarian cancer progression and response to treatment;
 - Fine-grained multi-task deep learning models for virtual screening of more than 120,000 annotated drugs on 48 colorectal cancer cell lines;
 - Mathematical models of electroporation ablation combined with immunotherapy for liver and pancreas tumours.

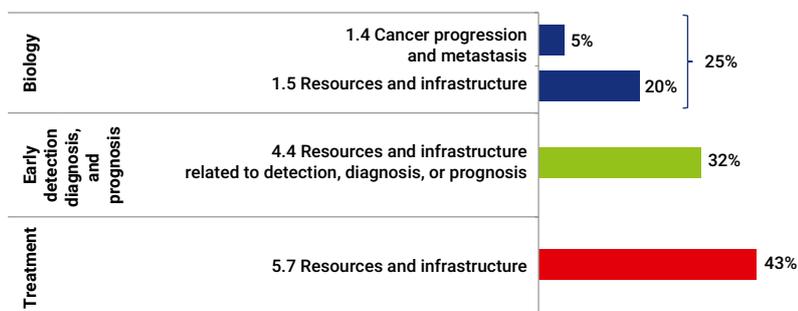
FIGURE 8
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE MIC PROGRAMME IN 2021 ACCORDING TO THE CSO CLASSIFICATION



The programme over the 2019-2021 period

In 3 editions, 22 projects were selected for a total funding amount of €9.7M. In line with the objectives of the programme, most of the projects belonged to the CSO Resources and infrastructures categories, whether they focused on cancer biology, detection, or treatment (Figure 9).

FIGURE 9
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE MIC PROGRAMME OVER THE 2019-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



CHARACTERISATION OF PRENEOPLASTIC LESIONS AND RISK STRATIFICATION (PNP)

Initiated in 2019 by ITMO Cancer-Aviesan and INCa, this call is aimed at characterising lesions with malignant potential, in space and time, and on a molecular, cellular, and tissue level. The objective is to contribute to a better understanding of the outcome of preneoplastic lesions (transition from premalignant to malignant, stabilisation, regression) by characterising the underlying mechanisms, the sequence of cancer formation, and the risk factors of lesion emergence and progression, to identify intervention targets and stratify lesions based on their risks.

A two-day retreat for the HTE (Tumour Heterogeneity and Ecosystem) programme

This virtual meeting took place on 17-18 March 2021. It provided partners with an opportunity to hear keynote presentations from international speakers and to present findings and perspectives from the different projects (crosstalk between tumours and their microenvironment, potential therapeutic targets, further multi-scale data integration). At this event, discussions took place with the French Institute of Bioinformatics (IFB) concerning the challenge set to set up and run an efficient data sharing infrastructure. The HTE consortium members had high praise for the intellectual stimulation generated by the programme's innovative format.

Joint seminar between ITMO Cancer-Aviesan (board and expert committee) & INCa Research and Innovation Division

- Conducting a critical review of former key strategic trends relating to cancer (2017, 2019, 2021-2030 Ten-Year Cancer Control Strategy), aiming to upgrade and boost topics that have not been sufficiently covered;
- Identifying and documenting recently emerging themes.

Four key points were identified:

- Tumour spatiotemporal dynamic analysis;
- Modelling, big data and artificial intelligence;
- New models and new technologies;
- Therapeutic innovation and access to innovation.

Working areas of these topics were submitted to the international scientific advisory board for further reflection. A collaborative document summarising the reflections from the joint seminar is in progress.

The programme in 2021

In 2021, 8 projects were selected for funding out of the 31 submitted for a total amount of €4.4M (Table 4 and Figure 10).

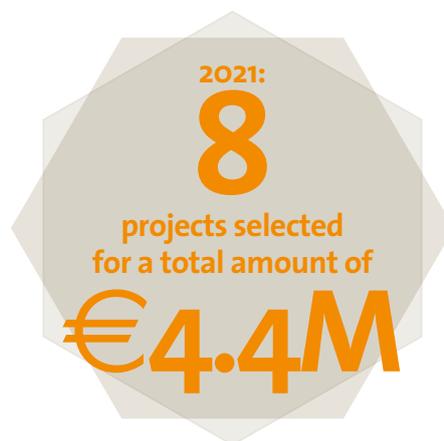
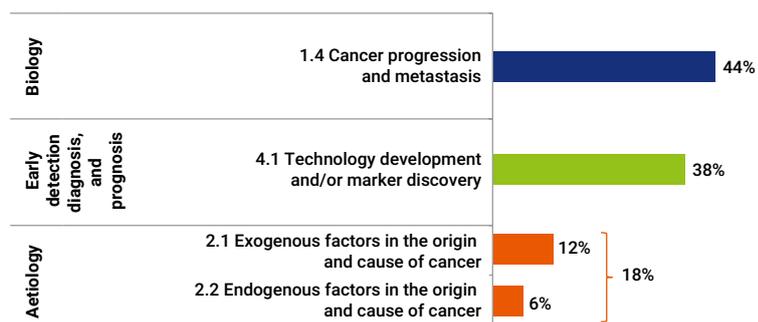
■ TABLE 4
FEATURES OF THE PNP PROGRAMME IN 2021

Objectives	To improve understanding of preneoplastic lesion outcomes so as to identify intervention targets and stratify lesions based on their risk of progression.
Programming institution	ITMO Cancer-Aviesan/INCa
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan and INCa
Funding	€4.4M
Proposals submitted	31
Projects selected	8
Selection rate	26%

The funded projects focused on high prevalence and low prognosis cancers (colorectal, breast and oropharyngeal tumours, hepatocarcinoma), and some rare cancers (Buschke Löwenstein tumour, malignant peripheral nerve sheath tumour). Multimodal approaches (genetics, epigenetics, anatomopathology, spatial imaging, bioinformatics, etc.) were used to analyse preneoplastic, tumoral or normal tissue at different scales (single cell, cell foci, and whole tissue). The projects were aimed at:

- identifying new mechanisms (genes, epigenetic alterations) involved in malignant transformation and evaluating their putative role as biomarkers or therapeutic targets;
- discriminating preneoplastic characteristics associated with low prognosis;
- analysing the role of preneoplastic microenvironment cell components (namely immune infiltrates) in malignant transformation.

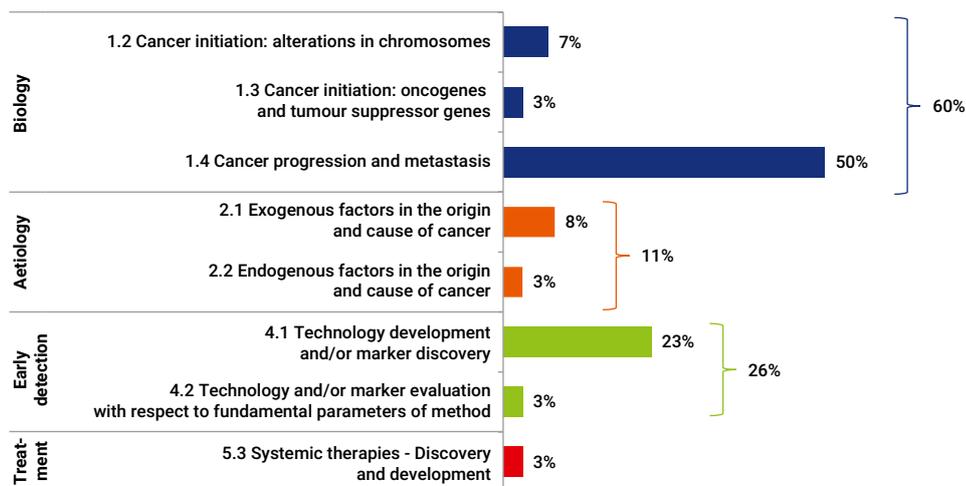
FIGURE 10
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PNP PROGRAMME IN 2021 ACCORDING TO THE CSO CLASSIFICATION



The programme over the 2019-2021 period

In 2 editions (2019 and 2021), 15 projects were selected for a total funding amount of €9.7M. In line with the programme’s objectives, projects belonged mainly to CSO categories including studies on the underlying mechanisms of cancer progression and metastasis, and seeking or evaluating new technologies or markers for early diagnosis.

■ **FIGURE 11**
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PNP PROGRAMME OVER THE 2019-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



New programme dedicated to the microenvironment of poor prognosis cancers

In accordance with a major objective of the French Ten-Year Cancer Control Strategy, ITMO Cancer-Aviesan prepared, with the assistance of an international task force, a call for proposals for 2022 aiming at financing interdisciplinary or multi-intra-disciplinary projects to enable functional characterisation of the microenvironment of cancers with standardised 5-year post-diagnosis net survival rates <33% (lung; stomach; liver; gallbladder and bile ducts; hypopharynx and oesophagus; pancreas). Four lines of research will be proposed:

- High-definition spatiotemporal characterisation of the microenvironment leading to a functional study;

- High-definition deciphering of cellular and local signalling networks;
- Reprogramming of the tumour microenvironment;
- Development of *in vitro* or *ex vivo* models reproducing the spatiotemporal evolution of the tumour/microenvironment pair.

A wide range of specialities will be involved: biochemistry, mechanobiology, cell biology, surgery, anatomopathology, infectiology, immunology, biology of the vascular and lymphatic systems, haematology, bioengineering, image analysis, profiling and spatial technologies, cancer biology, clinical, physics, biophysics, chemistry, mathematics. This new call for proposals is scheduled for January 2022.

SUPPORT FOR CANCER RESEARCH EQUIPMENT

The “Equipment” programme was launched in 2016, in line with the 3rd Cancer Control Plan and a recommendation from the INCa Scientific advisory board. It is aimed at supporting equipment acquisition to foster the development of ambitious research in the field of oncology, to encourage interactions between research teams, and to increase the attractiveness and the position of French teams on the international arena.

The programme in 2021

■ TABLE 5
FEATURES OF THE EQUIPMENT PROGRAMME IN 2021

Objectives	To foster the development of ambitious research in the field of oncology, to encourage interactions between research teams, and to increase the attractiveness and the position of French teams on the international arena.
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€3.5M
Proposals submitted	60
Projects selected	18
Selection rate	30%

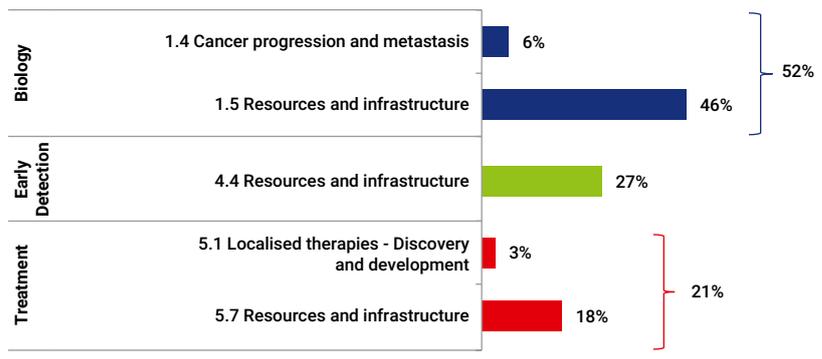


The funded equipment was mainly intended for imaging (44%), biochemistry/ proteomics (28%) and cellular characterisation/histology (22%) studies (Figure 12). These studies were aimed at:

- profiling tumours from a metabolic or proteomic point of view;
- deciphering tumour heterogeneity;
- exploring interplays between tumour and immune cells;
- implementing experimental models for oncogenesis, diagnosis and therapeutics screening imaging.

2016-2021:
105 projects selected
 for a total amount of
€17.2M

FIGURE 12
 DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE EQUIPMENT PROGRAMME IN 2021 ACCORDING TO THE CSO CLASSIFICATION



The programme over the 2016-2021 period

Over 5 editions, 105 equipment projects were funded for a total amount of €17.2M. Due to a shift inserted into the schedule of the Equipment call for proposals, 2020 was an off year.

Most of these grants were assigned to imaging (42%), cellular characterisation/histology (29%) or biochemistry/proteomics (15%) studies (Figure 13). Equipment was mostly requested for the purposes of basic research in biology (55%), and for early detection (26%), treatment (15%) and modelling studies (4%) (Figure 14).

FIGURE 13
 CATEGORIES OF FUNDED PROJECTS IN THE EQUIPMENT PROGRAMME OVER THE 2016-2021 PERIOD

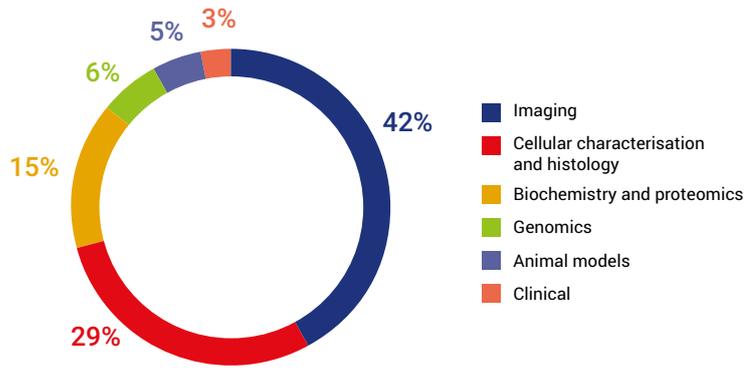
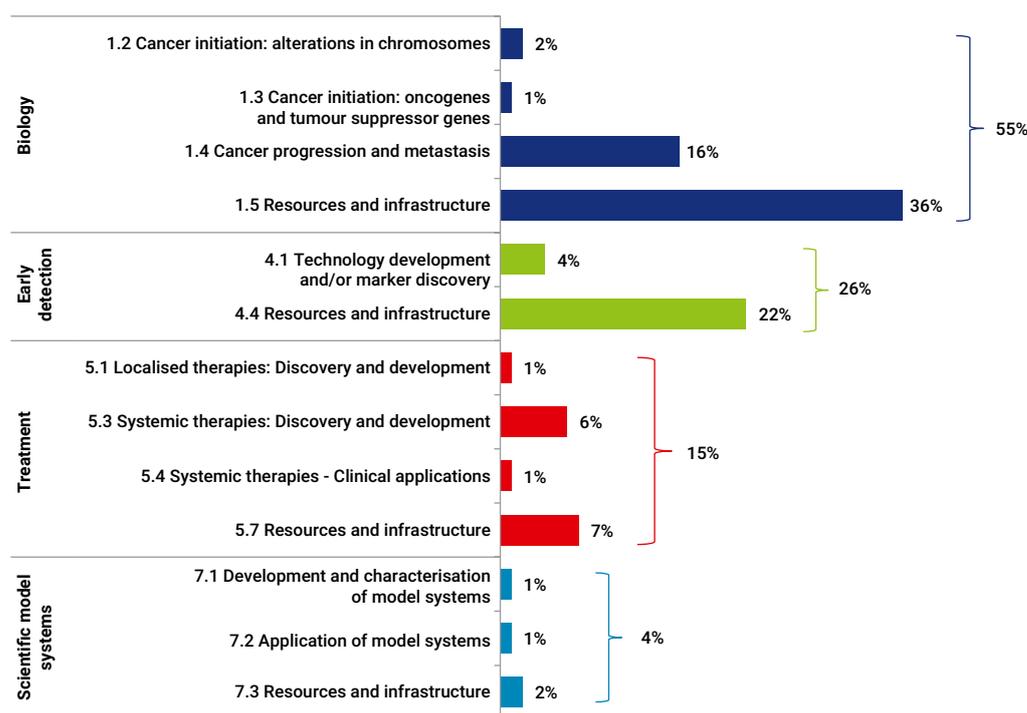


FIGURE 14

DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE EQUIPMENT PROGRAMME OVER THE 2016-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



Booklet to highlight materials funded by the ITMO Cancer-Aviesan Equipment programme

Over the 2016-2019 period, ITMO Cancer-Aviesan funded 87 items of equipment within its Equipment programme, for a total amount of €13.7M. The funded equipment mainly belonged to 3 categories: Imaging, Cell Characterisation and Histology, Biochemistry and Proteomics. Île-de-France and Occitanie, and to a lesser extent Auvergne-Rhône-Alpes and Provence-Alpes-Côte-d'Azur, were the regions with the highest number of funded equipment items.

A booklet gathering these materials was produced in 2021, which:

- Describes their characteristics, potential applications, and working environment;
- Presents some results achieved with the funded equipment;
- Provides contacts needed for collaboration, in keeping with one of the programme's main aims.

Support for paediatric cancer research

COORDINATING PAEDIATRIC CANCER RESEARCH ACTIONS – INTERNATIONAL SYMPOSIUM

Initially scheduled in 2020 and postponed, this virtual event targeted everyone (patients, parents, relatives, scientists from all backgrounds, researchers, and clinicians), this meeting aimed to generate new ideas and innovative strategies to improve knowledge of the causes and origins of these diseases, to try to prevent them, to diagnose them earlier, and to optimise their treatment while preserving the quality of life of these children and future adults.

In addition, this symposium was challenging since it needed to combine top scientific expertise with information accessible for everyone. Indeed, it is essential that families and researchers communicate and work together, to strengthen mutual understanding and to co-build the necessary actions.

Over 3 days, the programme included:

- 3 conferences illustrating how advances in basic research allow clinical advances, while highlighting the long period of research required before advances might be applied;
- 4 scientific sessions:
 - Developmental biology, stem cell and paediatric cancer
 - Paediatric cancer: from fundamental to modelling research
 - “Big data” and management of paediatric cancer
 - Immunology

2 round-table discussions, each co-moderated by a scientist and a patient representative;

- One round-table discussion that brought together young researchers who shared their experiences. They also engaged directly with associations in order to understand their expectations.
- Another round-table discussion focused on the organisation of research on childhood cancers and its application to the causes and origins of cancers.

PAEDIATRIC CANCER RESEARCH PROGRAMMES

In 2021, 2 calls for proposals were launched thanks to the renewal of a €5M allocation by the French Minister for Higher Education, Research, and Innovation.

Paediatric oncology research: contribution from interdisciplinary approaches

The aim of this call for proposals is to foster the emergence of ambitious interdisciplinary research projects. It allows the development of original approaches by pairing two teams with different scientific skills (and at least one of the two teams must not usually conduct cancer research).

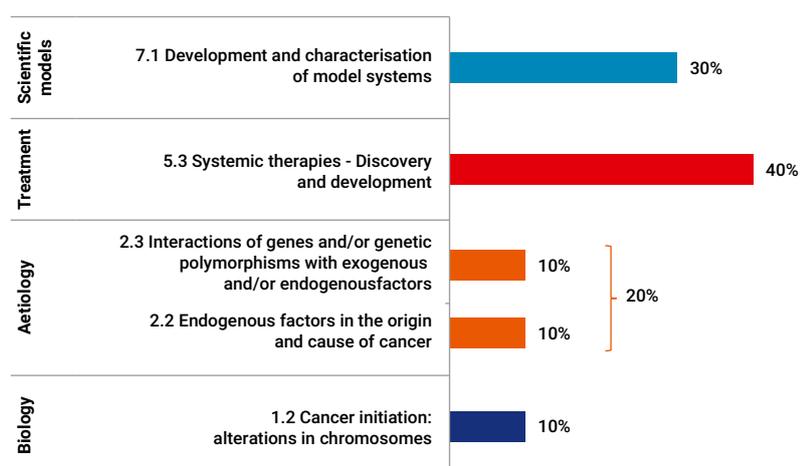
The proposed project should be built on contributions from the interdisciplinary approach(es) envisaged and must address one or more research questions in paediatric oncology.

In 2021, 5 applications out of a total of 8 were selected for funding, for an overall budget of €2.95M (Table 6 and Figure 15).

TABLE 6
FEATURES OF THE PROGRAMME FOR PAEDIATRIC ONCOLOGY RESEARCH:
CONTRIBUTION FROM INTERDISCIPLINARY APPROACHES IN 2021

Objectives	Development of interdisciplinary research projects in paediatric oncology.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€2.95M
Applications submitted	8
Applications selected	5
Selection rate	62.5%

FIGURE 15
DISTRIBUTION OF SELECTED APPLICATIONS ACCORDING TO CSO CLASSIFICATION



The selected and funded projects aim to:

- Use proteolysis-targeting chimaeras (PROTAC) compounds as a new therapeutic strategy for brain tumours;
- Reduce mitochondria-dependent metabolic flexibility for paediatric cancer therapy;
- Decipher the haematological phenotype of patients with *GATA2* mutation using new relevant models to better assess leukaemia risk and the time to bone marrow transplantation, and thus optimise the therapeutic strategy;
- Develop a paediatric glioma biochip model mimicking the microenvironment (biophysical and biochemical environment and interactions with the blood-brain barrier);
- Study the genetic factors influencing the risk of secondary cancers after childhood cancer in carriers and non-carriers of known predisposing-constitutional mutations to cancer.

“High-risk – high-gain” paediatric oncology research projects

This call for proposals aims to support highly innovative research projects that will open up new and original avenues and produce concrete advances in paediatric oncology.

The aim is to fund original and audacious research projects, conceptually new and risky, considered as “High-Risk – High-Gain”, which would be ineligible for funding in traditional calls for proposals.

These projects must be based on significant conceptual risk-taking, in order to propose a new or even disruptive approach. The potential impact of the proposed projects on paediatric oncology research could be of a high level.

● *The programme in 2021*

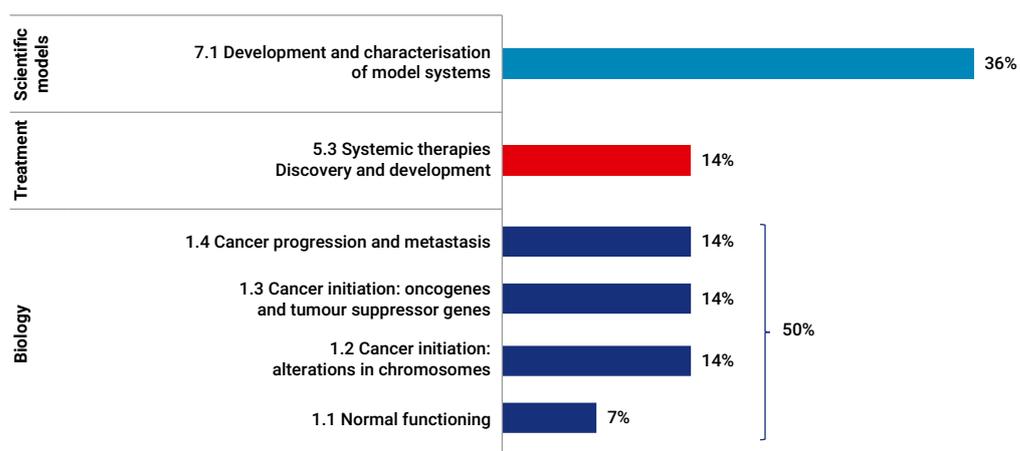
In 2021, 7 out of a total of 14 projects were selected for funding, for an overall budget of €1.33M (Table 7 and Figure 16).

■ **TABLE 7**

FEATURES OF THE “HIGH-RISK – HIGH-GAIN” PAEDIATRIC ONCOLOGY RESEARCH PROJECTS PROGRAMME IN 2021

Objectives	To enable the development of conceptually new and risky projects which would be ineligible for funding in traditional calls for proposals
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€1.33M
Proposals submitted	14
Projects selected	7
Selection rate	50%

FIGURE 16
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



The aims of the selected and funded projects are to:

- study osteosarcoma cell plasticity and microenvironment through drug sensitivity/resistance testing;
- develop brain immuno-organoid models to study cancer development and identify effective treatments in children and adolescents with high-grade gliomas;
- propose innovative Li-Fraumeni predisposition syndrome modelling in brain organoids;
- study the spliceosome and unconventional antigenic immune responses to develop a new pharmacological approach based on immunomodulators (IMiDs) in paediatric cancers;
- identify the link between the development of neural circuits, integration of different cell types in these circuits and the development of paediatric cancers and subsequently the impact of tyrosine kinases inhibitors on neural circuits;
- study embryonic brain tumours with *BCOR* gene alteration;
- study the oncogene concept *in vivo* in single-cell embryonic neural tumours.

The scientific evaluation committee and the representatives of the Paediatric Task Force highlighted the interest and the added value of this programme. Thus, in 2022, this call for proposals will be renewed, and project duration will be extended to 4 years (in comparison to 2 years in 2021).

● **The programme over the 2020-2021 period**

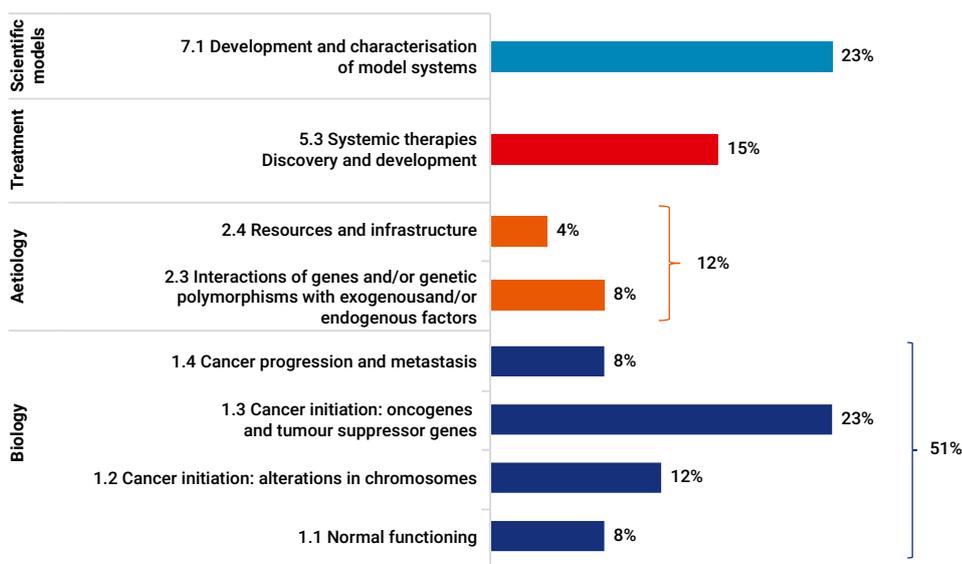
Since 2020, 32 proposals have been submitted to this call for applications, and 13 have been selected and funded (6 projects in 2020, and 7 projects in 2021) for a total amount of €2.23M. The overall selection rate for this call for proposals is 31% (Table 8).

■ **TABLE 8**
TRENDS IN SELECTION AND FUNDING OF THE “HIGH-RISK – HIGH-GAIN” PAEDIATRIC ONCOLOGY RESEARCH PROJECTS PROGRAMME OVER THE 2020-2021 PERIOD

Years	2020	2021	TOTAL
Funding (in €)	899,519	1,330,006	2,229,525
Proposals evaluated	28	14	42
Projects selected	6	7	13
Selection rate (%)	21.4%	50%	31%

The CSO typology of projects funded since 2020 shows that the projects mainly focus on basic research on cancer biology, model development, therapeutics, and also aetiology (Figure 17).

■ **FIGURE 17**
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2020-2021 PERIOD



Review of the programmes dedicated to paediatric cancer research over the 2019-2021 period

Since 2019, and in the context of the additional annual funding of €5M allocated, INCa has set up 7 research programmes in concert with the Paediatric Task Force:

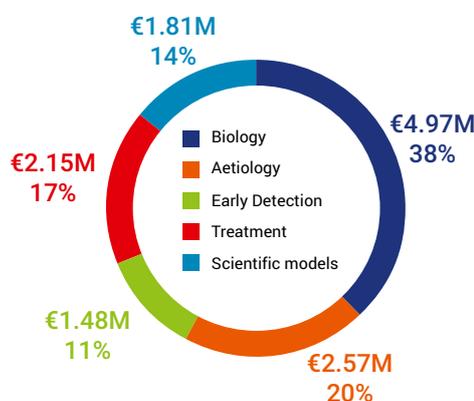
- 2 programmes in 2019: the programme for accelerating basic and translational research in paediatric oncology: help in pooling, structuring and sharing research data and the programme for research in paediatric oncology: post-doctoral fellowships and international mobility grants;
- 3 programmes in 2020: the programme for origins and causes of paediatric cancers, the programme for research in paediatric oncology: post-doctoral fellowships and international mobility grants, and the “high-risk – high-gain” paediatric oncology research project programme;
- 2 programmes in 2021: the programme for paediatric oncology research: contribution from interdisciplinary approaches, and the “high-risk – high-gain” paediatric oncology research project programme.

These programmes have made it possible to:

- bring teams together within a consortium and several federations;
- drive structuring and sharing of data on a national scale;
- fund a research programme dedicated to the study of the origin and causes of paediatric cancers;
- set up new collaborations;
- foster the development of international projects;
- define unexplored research questions;
- fund highly innovative and disruptive projects;
- fund interdisciplinary research projects;

In total, almost €13M has been specifically allocated to supporting paediatric cancer research (Figure 18).

FIGURE 18
DISTRIBUTION OF SUMS ALLOCATED FOR PAEDIATRIC CANCER PROJECTS OVER THE 2019-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



Contribution of ITMO Cancer-Aviesan to the INCa/ITMO Cancer-Aviesan joint action for oncopaediatics

ITMO Cancer-Aviesan was involved in 5 areas of the joint action in 2021:

- international meeting on Basic research in childhood cancer, held in Paris on 16-18 June 2021: participation in the scientific committee
- pediatrie.e-cancer.fr website: participation in the drafting of specifications;
- bibliometric analysis of French literature on oncopaediatics research over the 2015-2020 period: drafting of specifications with key-word determination, contact with the CNRS Institut de l'information scientifique et technique (INIST), initial analyses;
- recording of French teams and researchers involved in oncopaediatics: participation in the mapping process;
- recording the oncopaediatic projects funded within the scope of ITMO Cancer Aviesan programmes.

Support for professional careers in cancer research

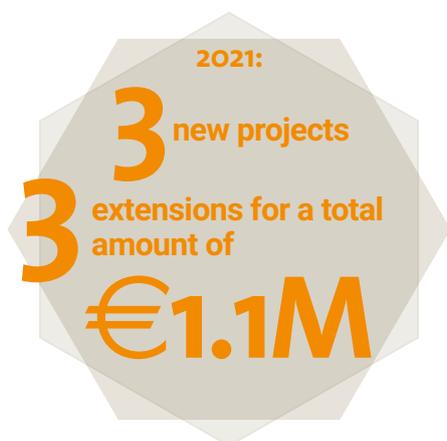
SUPPORT FOR THE ATIP-AVENIR PROGRAMME

Under a partnership between CNRS and Inserm, the ATIP-Avenir programme is aimed at enabling young scientists to create and lead their own research team within an established Inserm or CNRS laboratory in France. ITMO Cancer-Aviesan contributes to the funding of the awardees pursuing a cancer research project.

The programme in 2021

■ TABLE 9
FEATURES OF THE ATIP-AVENIR PROGRAMME IN CANCER RESEARCH IN 2021

Objectives	To promote the establishment of promising young PIs in cancer research by funding their starting team for 3 years and/or for a 2-year extension
Programming institution	CNRS and Inserm
Operating institution	CNRS and Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€1.1M
Projects funded	6 (3 new and 3 extensions)

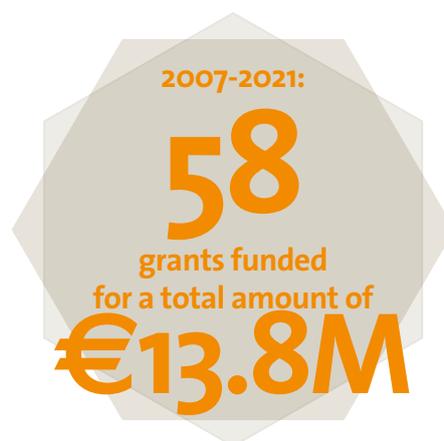
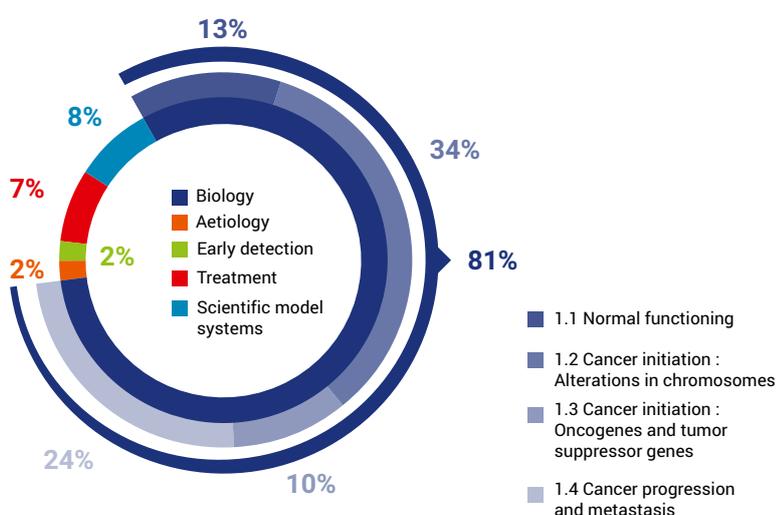


In 2021, 3 new projects were funded, focusing on: the development of a new anti-metastatic strategy based on the targeting of tumour vessel abnormalities; the identification of master transcriptional regulators to decipher high-grade glioma heterogeneity; the unravelling of biophysical properties of circulating tumour cell clusters. Three projects that were already receiving funding were funded for a 2-year extension.

The programme over the 2007-2021 period

Over the 2007-2021 period, 58 grants were funded by ITMO Cancer-Aviesan for a total amount of €13.8M. More than 80% of the projects were devoted to cancer biology research (Figure 19).

FIGURE 19
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS
FOR THE ATIP/AVENIR PROGRAMME OVER THE 2007-2021 PERIOD ACCORDING
TO THE CSO CLASSIFICATION



SUPPORT FOR THE ANR JCJC PROGRAMME

The JCJC (Jeunes chercheurs ou jeunes chercheuses) programme is one of the four funding instruments of the annual Generic Call for Proposals of the French National Research Agency (ANR). It is designed to give young researchers in various scientific fields access to co-funding in a large number of research themes, basic or applied, in addition to their allocated recurrent funding. In 2020, ITMO Cancer-Aviesan developed a partnership with ANR to fund JCJC projects related to cancer research.

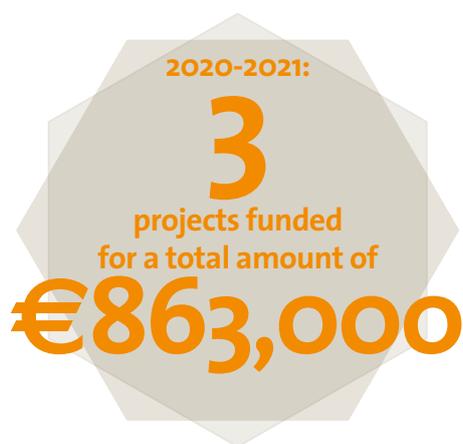


The programme in 2021

In 2021, 2 projects were selected and funded for a total amount of €580,000 (Table 10). These projects were aimed at deciphering the mechanisms of heme-regulated protein destruction in physiology and cancer pathogenesis, and exploring the characteristics of tumour-specific T cells in acute myeloid leukaemias.

■ TABLE 10
FEATURES OF THE JCJC PROGRAMME IN CANCER RESEARCH IN 2021

Objectives	To support established young researchers with additional funding of their project in the cancer field.
Programming institution	French National Research Agency (ANR)
Operating institution	French National Research Agency (ANR)
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€582,000
Projects funded	2

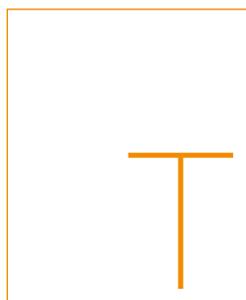


In 2020, 1 project was selected and funded for a total amount of €281,000. This project was aimed at exploring the potential and the cellular dynamics of immunotherapy-associated focused ultrasound strategy for glioblastoma treatment and developing tool(s) to predict its efficacy in clinical settings.

The programme over the 2020-2021 period

Over the 2020-2021 period, 3 grants were funded by ITMO Cancer-Aviesan for a total amount of €860,000. They focused on cancer treatment (50%), biology (33%) and early detection, diagnosis or prognosis (17%).

TRANSLATIONAL AND INTEGRATED CANCER RESEARCH



Translational research in oncology aims to bridge the gap between basic research and clinical research in order to translate scientific progress into products and procedures that benefit patients.

In line with the previous Cancer control plans, translational research receives significant support through dedicated calls for proposals, programmes to strengthen training in this research field and a policy of designated multidisciplinary integrated research sites.

In 2021, support for translational and integrated cancer research amounted to

€13.58M:

€12.36M dedicated to support strategic initiatives and thematic programmes;

€1.22M to support translational and multidisciplinary cancer research training.



National translational cancer research programme (PRT-K)

The objective of this call for proposals (PRT-K), launched for the first time in 2007 and recurrent since 2009 in partnership with the French Ministry of Health (DGOS), is to promote interdisciplinary projects, bringing together laboratory researchers and clinicians. Sharing of specific expertise, skills and knowledge should promote the translation of scientific and medical discoveries into clinical advances for cancer patients.

In 2021, the French Ministry of Health decided to defer the launch date of this call for proposals by 6 months. The final evaluation for project funding will be conducted in 2022.

Prevention research: Contributions of biology (basic and translational research)

The French National Cancer Institute (INCa) has made prevention the headline priority of its new Cancer Control Strategy (2021-2030). The Institute is determined to reinforce and supplement its existing actions and initiatives in order to meet the ambitious targets set by the government, particularly the goal of reducing the number of preventable cancer cases by 60,000 per year by 2040 (currently estimated at 153,000 annually).

In 2021, the Institute decided to devote an interdisciplinary research programme to matters of prevention. **This new three-year programme aims to improve prevention through a holistic approach ranging from basic biological research and translational research to the analysis of behavioural factors (human and social sciences, epidemiology, public health and intervention research). A series of calls for proposals will be organised with this goal in mind.** In order to invite proposals from all disciplinary fields, and to encourage interdisciplinary collaborations, the specific targets of these calls for proposals will evolve over the three-year period.

As such, the first call for proposals was devoted to biology and cancer sciences, aimed at generating new knowledge pertaining to cancer risk factors and protective factors (on a biological level: cells, micro-environment, etc.), and to the discovery and development of new, more effective, more targeted screening techniques and in more tumour sites.

The “Prevention Research: Contributions from Biology” call for proposals (PREV-BIO) was open to all fields of basic and translational research in biology, and all scientific disciplines involved in the fight against cancer.

For this call, 6 projects were selected for funding out of the 35 proposals submitted, for a total amount of €3.07M (Table 11).

■ TABLE 11
FEATURES OF THE PREVBIO PROGRAMME IN 2021

Objectives	To support innovative projects in the field of cancer prevention, focusing on the development of fundamental knowledge and/or new, more effective and more specific tools and strategies for cancer detection, early screening and the prevention of recurrence.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€3.07M
Proposals submitted	35
Projects selected	6
Selection rate	17%

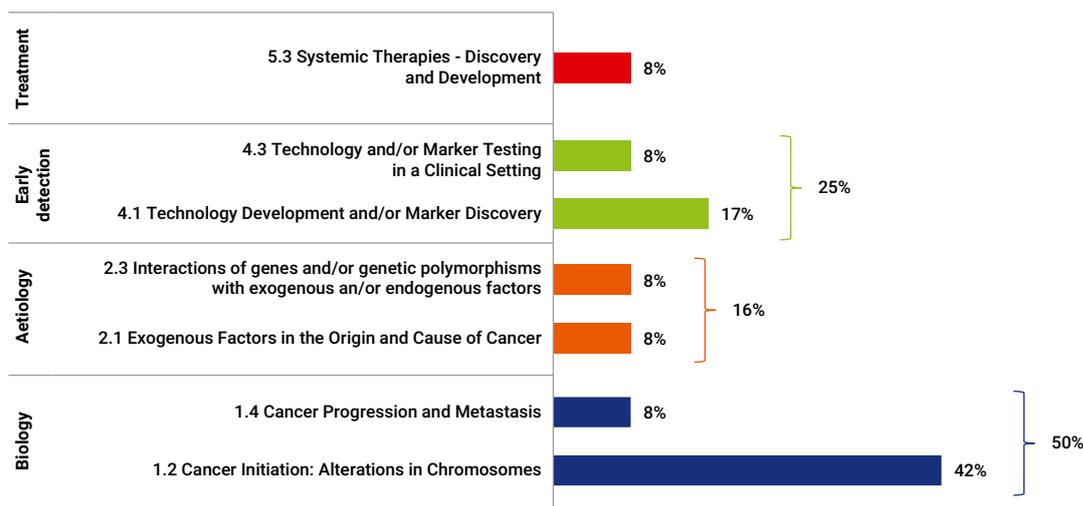
The aims of the projects selected for this call are to:

- detect circulating HPV DNA in blood or plasma samples for prognosis determination and post-treatment monitoring of oropharyngeal squamous cell carcinoma patients;
- provide better tools to evaluate oral squamous cell carcinoma progression risk and stratify patients (immune-based stratification and evolutionary biomarkers);
- identify the mechanisms involved in the establishment of genetic instability in tetraploid cells due to nuclear instability in ovarian cancers;
- study the regulation of RNP condensates upon ageing;
- study the synergistic impact of breast cancer risk factors on the epigenome;
- understand and prevent environment-driven transformation of pre-leukaemic myeloproliferative neoplasms, through large-scale translational approaches.



Half of the funded projects focus on the biological mechanisms of cancer initiation and disease progression (Figure 20). Other projects focus on identifying and testing cancer markers, while others aim to identify the causes or origins of cancer (genetic, environmental, lifestyle, and the interactions between these factors).

FIGURE 20
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



Launch of the first TRANSCAN-3 joint translational call

The TRANSCAN-3 network, preceded by TRANSCAN1 and TRANSCAN-2, is a cross-national cooperation, bringing together 31 funding organisations from 20 countries, with the common goal of supporting high-impact translational cancer research through joint transnational calls for proposals, and by an efficient investment of dedicated national/regional public funding, leveraged with foundation/charity-based resources and EU financial support.

In 2021, TRANSCAN-3 launched its first Joint Transnational Call for research proposals (JTC 2021) co-funded by the European Commission on “Next generation cancer immunotherapy: targeting the tumour microenvironment”. The projects will be selected in mid-2022 and should start by the end of 2022.

Reducing sequelae and improving quality of life

This programme was conducted within the framework of the 10-year cancer control strategy launched in February 2021. Part of the area aimed at decreasing sequelae and improving quality of life, the scope of this call was:

- to encourage projects aimed at enhancing knowledge and the means to reduce sequelae caused by the disease and cancer treatments;
- to promote interdisciplinarity, the proposals submitted should include at least 2 teams from 2 different research disciplines: fundamental research, translational research, clinical research, research in social and human sciences – epidemiology – public health.

Projects should address the following topics:

- supportive care (pain, physical fatigue, psychological issues);
- quality of life (as a whole);
- reconstructive surgery;
- fertility preservation and restoration.

For this first edition, 8 projects were selected for funding out of the 26 submitted, representing over €4M (Table 12).

■ **TABLE 12**
FEATURES OF THE PROGRAMME FOR MULTI-THEMATIC AND MULTI-DISCIPLINARY RESEARCH – REDUCING SEQUELAE AND IMPROVING QUALITY OF LIFE IN 2021

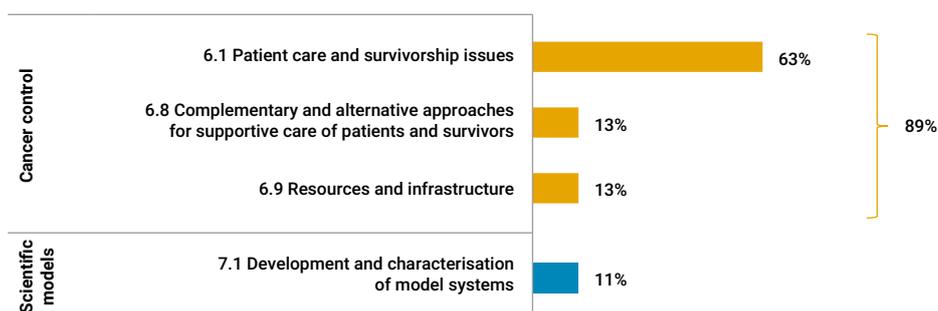
Objectives	Reducing sequelae and improving quality of life
Programming institution	INCA
Operating institution	INCA
Funding institution	INCA
Funding	€4.16M
Proposals submitted	26
Projects selected	8
Selection rate	31%

The topics covered by the selected projects were fertility (1), treatment toxicity (1), fatigue management (2), adapted physical activity (2) and quality of life (1)

The distribution according to the CSO classification shows that 63% of the selected projects (5 projects) deal with patient care and survivorship issues (Figure 21).



FIGURE 21
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PROGRAMME FOR MULTI-THEMATIC AND MULTI-DISCIPLINARY RESEARCH – REDUCING SEQUELAE AND IMPROVING QUALITY OF LIFE IN 2021



Integrated research action programme (PAIR)

Since 2007, the French National Cancer Institute has launched an Integrated Research Action Programme (PAIR) focusing on a specific type of cancer. This programme is aimed at promoting cooperation between all scientific disciplines (basic research, clinical research, epidemiology, public health and social and human sciences) around core projects. This transversal programme aims to accelerate patient access to progress in research. Since 2009, the PAIR programme has been run by INCa in partnership with the ARC Foundation for Cancer Research and the French Cancer League.

PAIR ON BRAIN TUMOURS

In 2019, the 3 partners decided to renew their partnership in order to support, develop and co-fund a new PAIR devoted to brain tumours.

A dedicated Steering Committee was set up, particularly to define the scientific research priorities. Chaired by Professor Khê Hoang Xuan (AP-HP Pitié-Salpêtrière, Paris), this committee is composed of renowned experts in neuro-oncology, neuropathology, basic research, radiotherapy and imaging, paediatrics, epidemiology, human and social sciences. In 2020, the Steering Committee was split into 4 sub-groups to work on the research priorities, aiming to help INCa draft the most relevant call for proposals. Patient representatives were also involved in the discussions, and their opinions and recommendations were taken into account. In October 2020, the brain tumour PAIR workshop was organised and attracted over 150 attendees.

Brain tumour
programme:
7
projects selected
for a total amount of
€5.13M

In 2021, the PAIR devoted to brain tumours was launched based on the research priorities identified by the Steering Committee. This call for proposals is aimed at increasing and enhancing dynamic research capabilities, promote scientific excellence and the emergence of innovative projects, and allow medical and scientific priorities to be defined.

This call for proposals, focused on brain tumours, concerns projects seeking to address issues arising from all disciplines by adopting a cross-disciplinary and integrative approach in order to improve the understanding and management of these cancers.

Projects are likely to address issues relating to all primary brain tumours, with brain metastases being excluded from the scope of this call for proposals. Issues addressed are divided into four areas:

- Area 1: Improve fundamental knowledge through an integrative approach
- Area 2: Improve diagnosis, measure response to treatment and monitoring
- Area 3: Develop innovative treatments
- Area 4: Consider quality of life and disability.

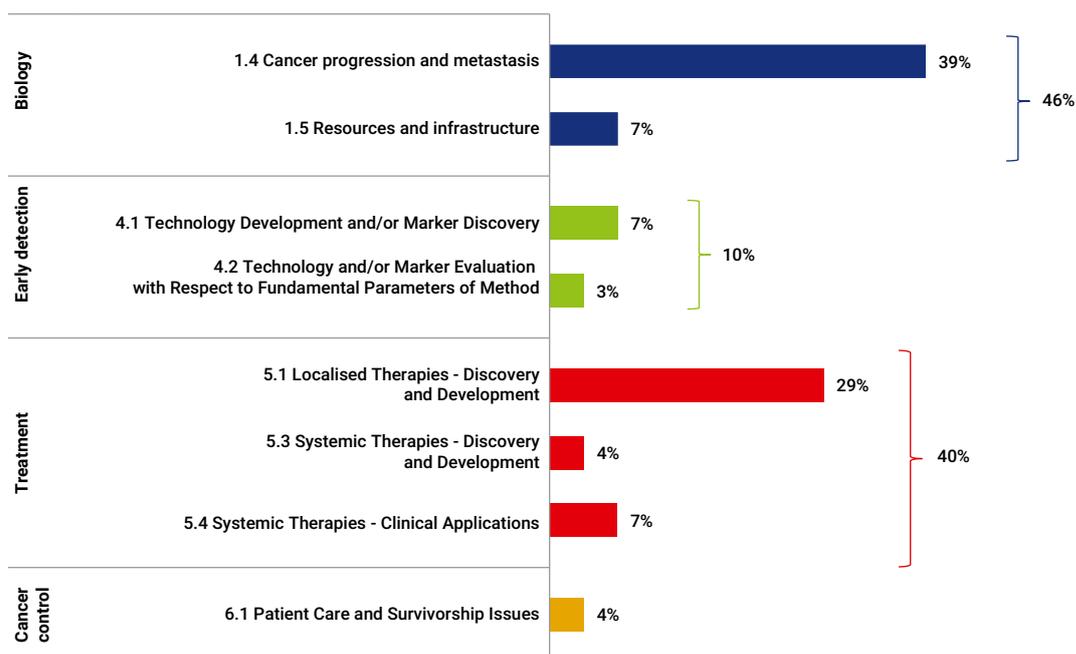
Seven projects were selected out of the 40 submitted for a total amount of €5.13M (Table 13). In total, the seven projects funded included 36 research teams.

■ **TABLE 13**
FEATURES OF THE BRAIN TUMOUR PAIR PROGRAMME IN 2021

Objectives	To address issues arising from all disciplines by adopting a cross-disciplinary and integrative approach in order to improve the understanding and management of brain tumours
Programming institution	INCA
Operating institution	INCA
Funding institution	INCA/ARC Foundation for cancer research/French Cancer League
Funding	€5.13M
Proposals submitted	40
Projects selected	7
Selection rate	17.5%

The distribution of the selected projects according to the CSO classification shows that most projects concern biology (46.4%) and treatment (39.3%) (Figure 22).

FIGURE 22
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



THE PAIR PROGRAMME OVER THE 2007-2021 PERIOD

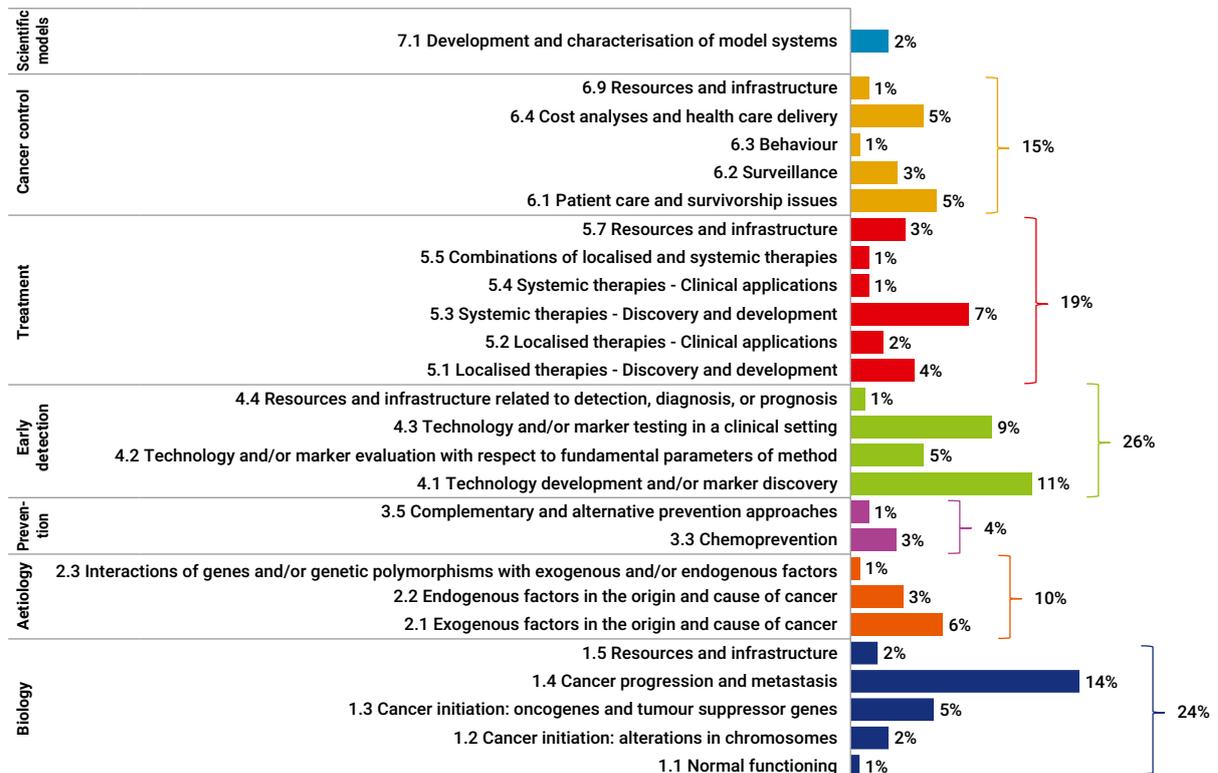
Since 2007, 11 PAIR programmes have been launched and funded, leading to the funding of 88 cancer research projects for a total amount of €51.43 M (table 14).

The analysis of the funded projects according to the CSO classification is consistent with the integrative aspects of the programme since all the cancer research fields are represented (Figure 23). The main categories are 25.7% for early detection, diagnosis and prognosis and 24.2% for biology and 19.1% for treatment.

TABLE 14
INTEGRATED RESEARCH ACTION PROGRAMME (PAIR) SELECTION TRENDS OVER THE 2007-2021 PERIOD

Years	Cancer sites	Funding institutions	Selected projects	Funding (€M)
2007	Early colorectal cancers	INCa/Roche/Amgen	14	4.34
2008	Lymphomas	INCa/Roche/Amgen	7	5.21
2009	Hepatocellular carcinomas	INCa/ARC Foundation/ANRS	12	5.95
2010	Prostate	INCa/ARC Foundation/French Cancer League	8	5.62
2011	Upper aerodigestive tract cancers	INCa/ARC Foundation/French Cancer League	7	4.13
2012	Gynaecological cancers	INCa/ARC Foundation/French Cancer League	6	3.41
2013	Melanomas	INCa/ARC Foundation/French Cancer League	9	5.12
2014	Early breast cancers	INCa/ARC Foundation/French Cancer League	8	3.76
2017	Paediatric cancers	INCa/ARC Foundation/French Cancer League	3	5.04
2018	Pancreatic adenocarcinomas cancers	INCa/ARC Foundation/French Cancer League	7	3.68
2021	Brain tumours	INCa/ARC Foundation/French Cancer League	7	5.13
Total			88	51.43

FIGURE 23
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2021 PERIOD



RadioTransNet: national radiotherapy preclinical research network

Established and designated by INCa in 2017 for 3 years, RadioTransNet is the national preclinical research network in radiotherapy coordinated by Philippe Maingon and Vincent Marchesi. RadioTransNet was granted €200,000 for the first two years, and received additional funding of €80,000 for 2021.

In 2021, the main activities of RadioTransNet were:

1. To define a roadmap based on the priorities highlighted and discussed during the 4 workshops organised in 2019 and 2020 (definition of target volumes; interactions of irradiations with healthy tissues; contribution of combined therapies; modern approaches to dose calculation);
2. To set up an observatory of research in preclinical radiotherapy through an online survey. Updated each year, this observatory would help track the progress of research activities in preclinical radiotherapy in France;
3. To strengthen links with European networks.

Structuring the field of pre-clinical research in radiotherapy remains a priority for the further development and success of oncological radiotherapy in France. The French National Cancer Institute is thus keen to pursue this action further. In June 2021, INCa launched a second call for applications in order to designate a national network for preclinical research in radiotherapy for the 2022-2025 period. The applications received should be evaluated in 2022. This new designation, for a 4-year period, should help meet the challenges arising from current knowledge and anticipated needs in the coming years, to achieve ever-increasing efficacy in the fight against cancer.

Translational and multidisciplinary training programmes

BASIC AND TRANSLATIONAL RESEARCH TRAINING PROGRAMME (FRFT) BY ITMO CANCER-AVIESAN

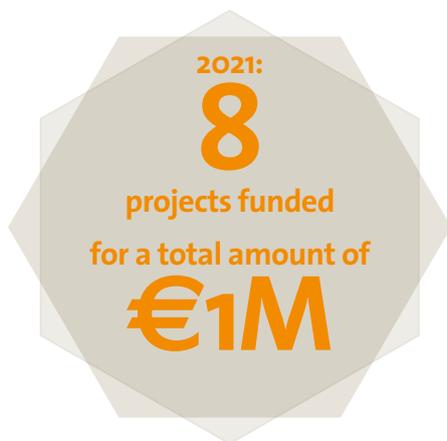
Launched in 2007, led by ITMO Cancer-Aviesan since 2011, the FRFT programme is aimed at supporting the complementary translational and basic research training of medicine, pharmacy, dentistry and veterinary science graduates through grants for Master's degrees, PhDs, and postdoctoral positions. In 2019, the programme was reviewed, with an emphasis on the career paths of M2 and PhD medical awardees: the review highlighted that only a few M2 degree awardees were continuing their research activities. Therefore, in 2021, the FRFT programme's scope was reassessed to focus on PhD thesis grants (FRFT-Doc).

PAEDIATRICS PAIR Follow-up

In 2016, INCa, the ARC Foundation and the French Cancer League launched a PAIR dedicated to childhood, adolescent and young adult cancers in order to increase and enhance dynamic research capabilities, and strengthen links between different disciplines in paediatric oncology. Three projects were selected, representing over €5M.

In November 2020, a second annual virtual meeting with the 3 principal investigators was held. They presented the good progress of their research projects based on the initial milestones. However, given the pandemic context, some endpoints were deferred, leading to a one-year extension for the 3 projects.

In 2021, the follow-up meeting was cancelled. The 3 projects will end in 2022 and the findings will be presented at a workshop scheduled in 2023.



The programme in 2021

■ TABLE 15

FEATURES OF THE DOCTORAL PROGRAMME ON BASIC AND TRANSLATIONAL RESEARCH TRAINING PROGRAMME (FRFT-DOC) IN 2021

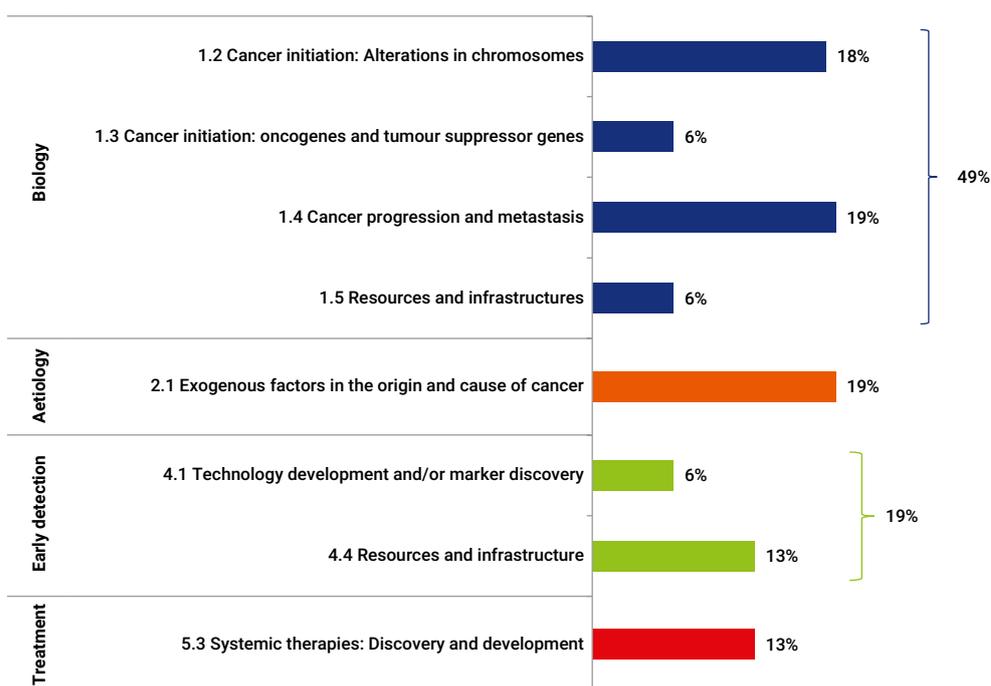
Objectives	To promote training of students or young medical, pharmacy and veterinary science graduates in translational research by funding doctoral theses on cancer.
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€1.0M
Proposals evaluated	37
Projects funded	8
Funding rate	22%

The funded projects aimed to decipher:

- the epigenetic mechanisms involved in phenotypic plasticity and treatment resistance in melanoma;
- the role of the neural microenvironment in the metastatic dissemination of neuroblastoma cells;
- the mechanisms whereby Epstein-Barr virus infects T/NK lymphocytes and triggers their malignant transformation;
- the role of the TCR/NF-κB pathway in HTLV-1-induced adult T-cell leukaemia or lymphoma.

They also focused on: the characteristics of LT CD8⁺ in 2 types of cancer where they have opposite prognostic values on tumour progression; underlying genetic predisposition mechanisms for rare malignant haemopathies; identification, in large cohorts, of surrogate markers of extranodal lymphoma response to treatment; the predictive role of a new identified glucocorticoid receptor polymorphism in order to personalise corticosteroid therapy in cancer.

FIGURE 24
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE FRFT-DOC PROGRAMME IN 2021 ACCORDING TO THE CSO CLASSIFICATION



The programme over the 2011-2020 period

Since 2011, 251 projects have been funded from 816 evaluated projects (funding rate of 31%), representing a total amount of €20.6M. Over this period, the FRFT programme funded 111 Masters, 123 PhD theses, and 17 post-doctorates (Table 16).

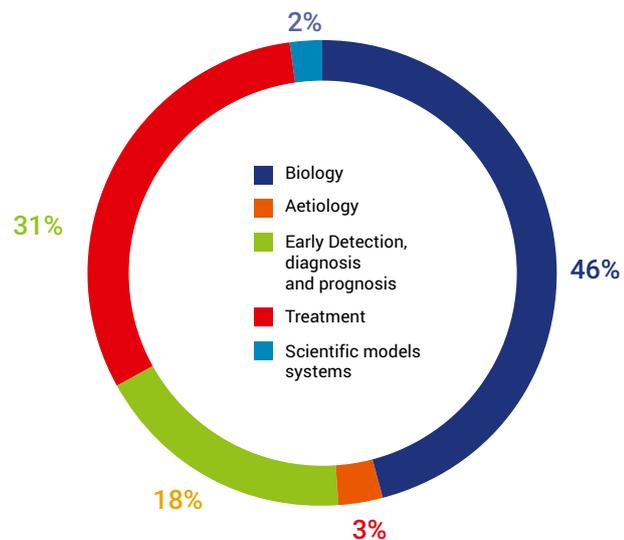
TABLE 16
TRENDS IN SELECTION AND FUNDING OF THE FRFT AND FRFT(-DOC) PROGRAMMES OVER THE 2011-2021 PERIOD

Year	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total
Funding (in €M)	1.50	2.12	1.36	2.35	2.11	2.01	1.98	2.44	1.72	1.97	1.0	20.6
Proposals evaluated	35	36	49	101	98	111	108	106	87	48	37	816
Projects funded	19	25	21	30	23	29	24	29	20	23	8	251
Selection rate	54%	69%	43%	30%	23%	26%	22%	27%	23%	48%	22%	31%



■ FIGURE 25

DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE FRFT AND FRFT(-DOC) PROGRAMMES OVER THE 2011-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



SUPPORT FOR THE INTERDISCIPLINARY RESEARCH PROGRAMME OF THE “FRONTIÈRES DE L’INNOVATION EN RECHERCHE ET ÉDUCATION (FIRE)” DOCTORAL SCHOOL BY ITMO CANCER-AVIESAN

The “Frontières de l’innovation en recherche et éducation” (FIRE) doctoral school is an international and interdisciplinary PhD programme, hosted by Université Paris-Cité and co-hosted by Université Paris Sciences et Lettres (PSL). It promotes original and ambitious research projects involving interactions between a wide range of academic disciplines. Research projects belong to one of two tracks: FdV (Frontières du vivant) and FAN (Frontières de l’apprendre et du numérique). Since 2010, ITMO Cancer-Aviesan has supported cancer projects within the framework of the FIRE programme in both the FdV and FAN tracks.

The programme in 2021

■ **TABLE 17**
FEATURES OF THE TRAINING IN INTERDISCIPLINARY RESEARCH – FRONTIÈRES DE L'INNOVATION EN RECHERCHE ET ÉDUCATION (FIRE) PARTNERSHIP IN 2021

Objectives	To promote ambitious cancer research projects using a broad range of academic disciplines.
Programming institution	FIRE graduate school
Operating institution	FIRE graduate school
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€105,000 (1 project)



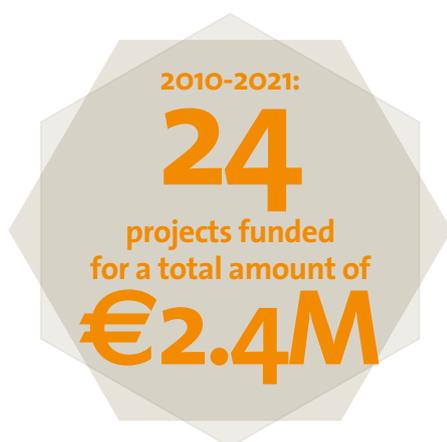
In 2021, 1 project was selected for an amount of €105,000. It belonged to the FAN track and was aimed at developing sonogenetic bacteria to probe tumour microenvironment by acoustic imaging.

The programme over the 2010-2021 period

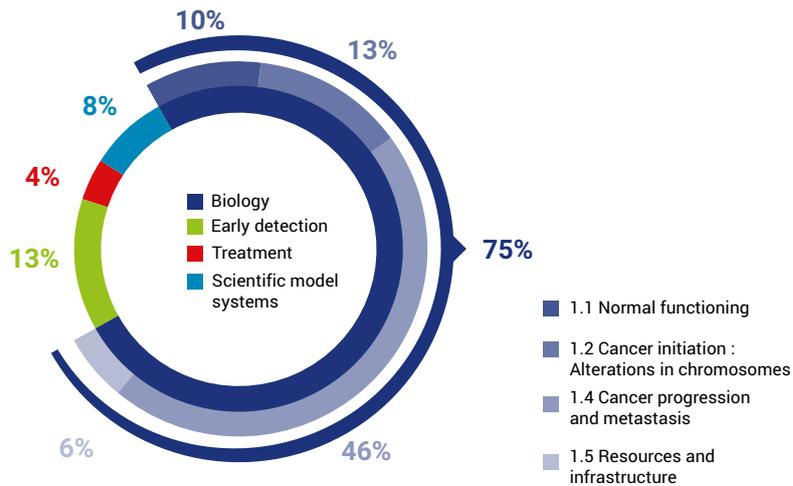
Over the 2010-2021 period, 24 grants were funded by ITMO Cancer-Aviesan for a total amount of €2.4M. Cancer biology research was at the core of 75% of the projects funded (Table 18 and Figure 26).

■ **TABLE 18**
TRENDS IN FUNDING OF CANCER-RELATED PROJECTS WITHIN THE FRAMEWORK OF THE FIRE (FDV OR FAN) PROGRAMME OVER THE 2010-2021 PERIOD

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total
Projects funded	2	2	2	2	2	3	4	2	2	2	2	1	24
Funding €M	0.2	0.2	0.2	0.2	0.2	0.3	0.2	0.2	0.2	0.2	0.2	0.1	2.4



■ **FIGURE 26**
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE FIRE PROGRAMME OVER THE 2010-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



SUPPORT FOR THE “DOCTORAL SCHOOL OF INFORMATION AND COMMUNICATION SCIENCES AND TECHNOLOGIES (STIC)” PROGRAMME BY ITMO CANCER-AVIESAN

The Doctoral School of Information and Communication Sciences and Technologies at Paris-Saclay University covers a unique thematic continuum in France in the field of digital technology and science. In 2018, ITMO Cancer-Aviesan launched a partnership with the STIC Doctoral School to finance some PhD theses related to oncology.

The programme in 2021

■ **TABLE 19**
FEATURES OF THE STIC DOCTORAL SCHOOL PARTNERSHIP IN 2021

Objectives	To promote dual training and foster innovative research by funding PhD theses at the interface of information technologies and oncology
Programming institution	Paris-Saclay University
Operating institution	Paris-Saclay University
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€95,000 (1 project)

2021:
1
 project funded
 for a total amount of
€95,000

In 2021, 1 project was funded for an amount of €95,000. It was aimed at developing deep learning algorithms for the identification, classification and prediction of the function of non-coding RNAs in bladder cancer.

The programme over the 2018-2021 period

In 3 editions (2018, 2020 and 2021), 4 projects were funded within the ITMO Cancer-Aviesan/STIC Doctoral School partnership, for a total amount of almost €385,000. Two projects belonged to the CSO “Scientific model systems” category, while the others belonged to the CSO “Biology” and “Treatment” categories.



CLINICAL CANCER RESEARCH AND ACCESS TO INNOVATION



Within the framework of the successive Cancer control plans, INCa has implemented several actions to support clinical research through calls for proposals, specific programmes to roll out targeted therapies and personalised medicine and the setting up of specific infrastructures. In addition, support for clinical research has been extended through international collaborations, the establishment of public-private partnerships, and support for access to innovation.

In 2021, support for clinical cancer research amounted to to support strategic cancer research initiatives, such as promoting access to innovative drugs

€3.03M

National clinical research on cancer

PROGRESS OF FUNDED PROJECTS FROM THE PHRC CANCER PROGRAMME

Since 2011, selected projects have been eligible to obtain one of the funding tranches subject to the justification of their progress status. This funding process makes it possible to monitor the projects selected for funding each year and to obtain a general overview of the clinical study flow of the PHRC cancer programme.

The funding is split into 5 funding tranches corresponding to the 5 key stages of the clinical trial implementation process:

- Tranche 1 is delivered once the project is selected;
- Tranche 2 is requested by the investigators when all necessary authorisations have been obtained and the study is recorded in an international clinical trial registry (Clinicaltrials.gov, Prospero or equivalent);
- Tranche 3 is requested when 50% of the planned inclusions or the data collections have been reached (if applicable);
- Tranche 4 can be requested when 100% of patients have been included and all patients have been monitored;
- Tranche 5 may be requested when a scientific article has been submitted to a peer-reviewed journal.

In 2021 for projects funded during the 2011-2020 period:

- 32% of projects requested tranche 2, corresponding to the approval stage.
- 25% of projects reached tranche 3, meaning they had reached the “50% inclusion” stage.
- 7% of projects had submitted an article or have published based on their preliminary results, corresponding to 30 projects selected over the 2011-2016 period.
- 22% of funded projects had not started the clinical study due to non-approval or another reason (lack of human resources, no longer having support from the pharmaceutical industry, etc.).

This analysis highlights several issues to address in order to facilitate clinical trial implementation and promote access to innovation. The first challenges could be:

- To reduce the delay for obtaining authorisations. This subject is ongoing, and ANSM has been working actively to achieve this improvement with fast-track procedures to be able to start inclusion;
- To develop ultra-multicentric studies to reduce the patient inclusion period;
- To contact project sponsors and/or investigators about the various issues faced in order to reinforce the steering of the clinical trials launched and thus achieve better feasibility assessment in the future.

A survey was conducted in 2021 to identify why projects were still blocked in tranche 4, at a stage of 100% patient inclusion and monitoring, for more than 2 years without any publication on the funded research findings.

Over the 2011 – 2016 period, 37 projects were concerned; more than two-thirds of studies had either already been published or were about to submit a publication.

Launch of PHRC cancer 2021 programme

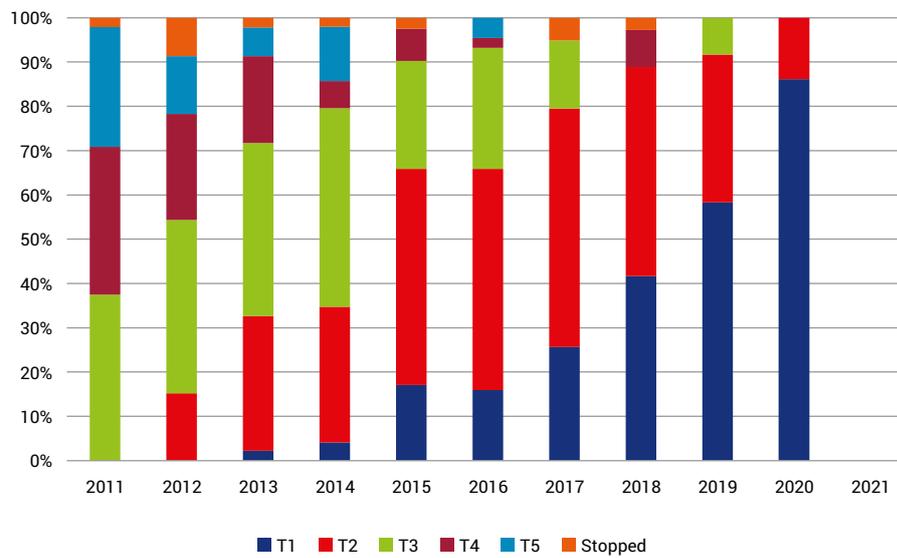
Due to the COVID-19 pandemic, all research programmes funded by the French Ministry of Health, including PHRC cancer, were deferred by 6 months.

In 2021, taking into account the priorities of the 10-year Cancer Control Strategy, a specific focus on therapeutic de-escalation trials was added with the following highlight: reducing the toxicity of treatments in the medium and long term as part of an approach to reduce sequelae and improve patients' quality of life. Therapeutic de-escalation trials concern drug-based treatments, but also surgery, interventional radiology and radiotherapy.

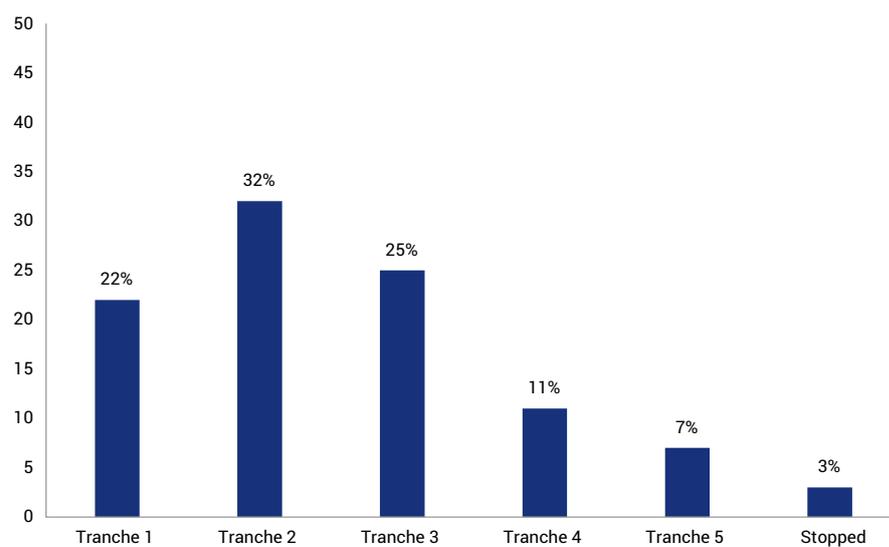
The findings are expected in 2022.

FIGURE 27
DISTRIBUTION OF FUNDED PROJECTS ACCORDING TO THEIR PROGRESS AND THE YEAR OF SELECTION (PANEL A)
AND PERCENTAGE OF TOTAL PROJECTS ACCORDING TO TRANCHE STATUS (PANEL B)

A



B



PHRC Cancer programme report workshop – Imaging in cancer prevention strategies

A focused annual report workshop is organised in order to evaluate and improve communication regarding the projects funded by the PHRC cancer programme. In October 2021, a joint session on Imaging in cancer prevention strategies with the French Society of Radiology was held during the “French-language radiology conference” (Journées francophones de radiologie). The findings of 4 projects were presented,

concerning two types of cancer: breast cancer (3), and prostate cancer (1). Of these projects, 1 is still ongoing (breast cancer), and 3 have been reached the publication stage.

Besides the findings presented, this workshop highlighted the contribution of imaging in the prevention strategy in oncology and allowed the PHRC-K project leaders to share their experience.

UTILISATION OF PROJECTS FUNDED OR SUPPORTED BY INCA'S PROGRAMMES

In 2021, INCa chose to commit to a policy of utilising findings or progress from projects funded or supported within the framework of INCa programmes such as PHRC-K or CLIP².

These are 2 examples of such utilisation in 2021 on INCa's website.

Findings of the PRODIGE 23 trial

PRODIGE 23 is a phase 3, open-label, multicentre, randomised trial which was funded by PHRC-K in 2012 and by the French Cancer League and Unicancer. The aim of PRODIGE 23 was to assess whether administering neoadjuvant chemotherapy before preoperative chemoradiotherapy could reduce the risk of distant recurrences in locally advanced rectal cancer.

A total of 461 patients were enrolled in 35 French health institutions between 2012 and 2017.

The findings of the PRODIGE 23 trial were that chemotherapy intensification using FOLFIRINOX before preoperative chemoradiotherapy improved outcomes significantly compared with preoperative chemoradiotherapy in patients with cT3 or cT4 Mo rectal cancer. Significantly improved disease-free survival in the neoadjuvant chemotherapy group and decreased neurotoxicity indicated that the perioperative approach is more effective and better tolerated than adjuvant chemotherapy.

Therefore, the findings of the PRODIGE 23 trial made it possible to establish a new gold-standard therapeutic regimen, improving patients' survival and quality of life.

The findings of the PRODIGE 23² trial were published in Lancet Oncology in April 2021. INCa has interviewed the PI of the trial, Prof. Thierry Conroy (Lorraine Institute of Oncology): <https://www.e-cancer.fr/Actualites-et-evenements/Actualites/Le-PHRC-K-source-d-avancees-therapeutiques-focus-sur-l-etude-PRODIGE-23-et-le-traitement-du-cancer-rectal-avance>

2. Thierry Conroy et al. Neoadjuvant chemotherapy with FOLFIRINOX and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23): a multicentre, randomised, open-label, phase 3 trial. Lancet Oncology. April 2021.

Findings of the VICTORIA study

VICTORIA is a multicentre, randomised, phase I/II study funded in 2015, as part of the specific call for proposals on innovative drugs, through a partnership with AstraZeneca. The Centre Léon Bérard Lyon conducted this clinical trial under its designation as an early-phase clinical trial centre (CLIP²). VICTORIA study aimed to assess the safety of AZD2014 + anastrozole versus anastrozole alone in patients with hormone receptor-positive endometrial adenocarcinoma in metastatic or advanced disease.

A total of 73 patients were enrolled in 12 French health institutions.

The study found that cancer had not progressed after two months in 70% of patients who received the combination. Progression-free survival was also longer for those who received the treatment combination. Also, complete responses were even observed: the metastases decreased in number and size. The findings of the VICTORIA study demonstrated the benefit of this combination.

The findings of the VICTORIA study were presented at the ASCO Conference in June 2021. In addition, INCa interviewed the PI of the study Prof. Pierre Heudel (Centre Léon Bérard), in July 2021 :

<https://www.e-cancer.fr/Actualites-et-evenements/Actualites/La-labellisation-en-tant-que-CLIP2-une-formidable-opportunite-de-recherche>

Importantly, the VICTORIA clinical trial illustrates the concrete progress enabled thanks to CLIP² support from INCa.

Cochrane Lung Cancer Group

Since 2013 and the transfer from Spain, INCa has supported the Cochrane Lung Cancer Group (CLCG). After this first action to fund this transfer, INCa funded the structuring of this group through funding allocated from 2017 to 2021. The Cochrane Group is an international organisation that produces and publishes systematic reviews and meta-analyses. The CLCG is the only France-based and French-speaking Cochrane Group.

The Lung Cancer Group Impact Factor rose from 3.333 in 2015 to 11.000 in 2020.

All its reviews are fully referenced in Wikipedia. Of these, 27 are used in medical practice guidelines in various countries, such as the United Kingdom, Germany, Canada, Australia, etc.

Most recent key publications:

- In early 2021, the group published the review “Single or combined immune checkpoint inhibitors compared to first-line chemotherapy with or without bevacizumab for people with advanced non-small cell lung cancer”. At the time the protocol was published, it was the first of its kind (“living review”) ever published in the Cochrane Library (a living review is a time-consuming new type of review in which the authors have to search for new publications on a monthly basis).
- In early 2022, the group published a review on “targeted therapy for advanced lymphoma kinase (ALK)-rearranged non-small cell lung cancer”.
- The group is currently about to publish the findings of the awaited high-priority review: “Impact of low-dose computed tomography (LDCT) screening on lung cancer-related mortality”, based on studies involving more than 94,000 people.

SUPPORT FOR CLINICAL RESEARCH IN FRENCH OVERSEAS DEPARTMENTS

One of the objectives of the 2014-2019 Cancer Control Plan was to boost clinical research in oncology mainly through mobile clinical research teams (EMRC) and the opening of investigation centres in French overseas departments (Action 5.2). As part of the implementation of the 2014-2019 Cancer Control Plan in French overseas departments, INCa has provided financial support to enable the development of clinical research in those territories, particularly the opening of investigation centres.

This action is now fully part of the 2021-2030 Cancer Control Strategy within the framework of Area 3, “Combatting cancers with poor prognosis”, and Action 5.2 (“Offer all patients the possibility of taking part in clinical trials, open up trials to more centres including those in overseas territories, while ensuring the quality of these centres for clinical research”).

For this purpose, INCa and the Interregional Group for Clinical Research and Innovation for Southwest and Overseas Hospitals (GIRCI SOHO) have identified projects suitable for opening investigation centres in French overseas departments. GIRCI SOHO includes the 3 overseas University Hospitals (CHU Martinique, CHU Guadeloupe, CHU La Reunion), as well as healthcare centres.

In 2019, seven projects were proposed for total funding of around €300,000 for 1, 3 or 4 years, which should enable 104 patients to be enrolled in clinical cancer trials in French overseas departments (colon cancer, head and neck cancer, cervical cancer, and leukaemia) (Table 20).

In November 2021, a total of 11 inclusions had been completed. Due to the 2020 pandemic, all 7 projects encountered set-up issues: delays in obtaining regulatory authorisations, signing agreements, and reported product supply issues. Altogether, this led to delays in starting the projects.

- Four projects have enrolled patients: LEANOX, OPEN, DEXAML-03, and ONCOGRAM (see Table 23). The first inclusions for the OPEN and ONCOGRAM projects were advertised on INCa’s website through a press release on 26 April 2021, which was relayed to the French Cancer League for distribution to their Overseas Committees.
- Two projects are planned to enrol patients: EMUTRAS (approval from the Committee for the Protection of Participants to open 2 overseas centres was received on 2 November 2021) and ONCOCOL (pending the signature of the centre’s approval to commence patient enrolment).
- The 7th SIMPA-01 project has not enrolled any patients; the sponsor decided to stop the inclusions on August 2021 for several reasons (excessive enrolment delay, product resupply issues, competing trials, etc).

Despite the low number of enrolments and issues encountered, the progress report on the 7 projects funded in 2019 is positive overall:

- patients from overseas departments have been able to access these trials;
- links have been established between medical investigators in the French overseas departments and in Mainland France, which has led to overseas centres being proposed and integrated into calls for proposals such as PHRC-K.

It was thus decided to make this action long-term to identify new projects in 2022, evaluated within the framework of previous calls for proposals such as PHRC-K.

■ **TABLE 20**

FEATURES OF THE CLINICAL RESEARCH PROJECTS SUPPORTED IN FRENCH OVERSEAS DEPARTMENTS AND ENROLMENT STATUS (NOVEMBER 2021)

Projects	Grant	Duration of the project	Investigation centres	Number of patients to be enrolled	Number of inclusions November 2021
LEANOX LEAn Body Mass Normalization of Oxaliplatin Based Chemotherapy for Stage III Colon Cancer Patients Treated in Adjuvant Setting: Impact on Oxaliplatin-induced Sensitive Neurotoxicity. A Multicentre Phase II Randomised Trial.	€25,915	36 months	CHU de Martinique	25	1
SIMPA-01 Efficacy of an Oral Immunomodulatory Nutrient on Survival During Postoperative Concomitant Chemoradiotherapy in Head and Neck Cancer.	€57,614	48 months	CHU Martinique CHU La Réunion Clinique S ^{te} Clotilde	12 15 12	stopped
EMUTRAS Detection of the Emergence of RAS Mutations in Circulating DNA in Patients With Metastatic Colorectal Cancer During Treatment With Anti-EGFR Therapy.	€10,248	36 months	CHU Martinique CHU La Réunion	10 3	Centres to be opened
OPEN Trismus Prevalence and Preventive Rehabilitation Associated With Therapeutic Education for Patients With Head and Neck Cancer Treated With Concomitant Radiochemotherapy.	€5,936	12 months	CHU La Réunion	5	2
ONCOCOL Phase III Study Comparing Neoadjuvant Chemotherapy with Carboplatin and Paclitaxel Followed by Standard Therapy, With Standard Therapy Alone in Women With Cervical Cancer and Para Aortic Positive Lymph Node.	€68,871	48 months	CHU Guadeloupe	6	Centre to be opened
DEXAML-03 Dexamethasone Plus Salvage Chemotherapy Versus Salvage Chemotherapy Alone in Patients with First Relapsed or Refractory Acute Myeloid Leukaemia: a Randomised, Controlled, Open-label, Multicentre, Phase III Study.	€29,000	48 months	CHU La Réunion	6	1
ONCOGRAM Study of the Therapeutic Response and Survival of Patients with Metastatic Colorectal Cancer (Stage IV) and Treated According to the Guidelines of a Chemosensitivity Test, Oncogramme®.	€94,455	36 months	CHU Martinique	10	7

Bibliographic report on social health inequalities and early-phase cancer clinical trials

Because of their personal vulnerability (disability, advanced age, language difficulties, etc.), their socio-professional category (CSP) or their particular circumstances (prison detention), some people find it difficult to access a high-quality healthcare pathway, including access to clinical trials. As part of the action IV.3 of France's Ten-Year Cancer-Control Strategy (2021-2030), which focuses on the fight against inequalities in access, measure IV.3.7 aims to include these vulnerable populations in clinical trials.

It is in this context that Sylvain Besle, sociologist with the SINCRO Group on

cancer care trajectories³ and holder of the INCa-supported HSS research chair⁴, was asked by the Institute to identify the obstacles and sources of leverage associated with these inequalities of access and to draw up a bibliographic summary on the place of these vulnerable populations in clinical trials, with initial recommendations and investigation avenues.

A prospective study aimed at evaluating the social health inequalities of patients included in early-phase clinical trials in CLIP² centres should be set up by 2022-2023.

STATUS REPORT OF CLINICAL CANCER RESEARCH

The 2021-2030 cancer Strategy reaffirms the objective of ensuring patients can access innovative therapies by facilitating their access to clinical trials. The COVID-19 pandemic of the past 2 years has raised the question of the resilience of clinical research in France in times of health crisis.

French clinical cancer research is recognised worldwide. However, the attractiveness of France in an environment of global competition raises the question of effectiveness in attracting clinical trials from pharmaceutical companies for patients' benefit. In this context, the Institute decided to launch a status report of French academic and industrial clinical research in oncology.

The first phase of this work began in the summer of 2021, with over fifty interviews with representatives of regulatory authorities, investigators, patient representatives, cancer associations, and pharmaceutical companies.

A benchmark was also prepared to compare France's clinical research activity with that of the following European countries: Germany, Spain, Italy, United Kingdom, and Belgium.

At the end of 2021, a status report was presented in 3 meetings, one for each of the following stakeholders: institutional representatives, academic researchers and representatives from the pharmaceutical industry.

3. Working group resulting from the collaboration of researchers from SESSTIM (Health Economic and Social Sciences and Medical Information Processing, Marseille) and Gustave Roussy (Villejuif).

4. <https://www.e-cancer.fr/Actualites-et-evenements/Actualites/Creation-d-une-chaire-de-recherche-en-SHS-appliquee-au-cancer>

The findings of this report highlighted 5 priorities for clinical cancer research:

- Refine the steering and funding strategy for academic research
- Reduce inequalities in access to clinical cancer research for patients
- Improve the patient experience throughout the clinical trial process
- Optimise administrative processes to reduce clinical trial launch times
- Anticipate and support impactful transformations in how clinical trials in cancer research are designed, carried out and evaluated.

Identifying of these priorities has provided a focus for working groups that will take place in 2022 to draft recommendations with clinical research stakeholders.

Public-private partnerships

Since 2011, INCa has promoted early access to innovative drugs for patients through cooperation with pharmaceutical laboratories (cooperation agreements) who supply and distribute innovative molecules to the CLIP² network. This access to drugs in development enables institutional investigators to propose academic clinical trials for indications or diseases not addressed by pharmaceutical laboratory development plans.

These trials, designed and proposed by CLIP²s, are aimed at promoting the early development of new therapeutic strategies, in indications that would probably not have been investigated by pharmaceutical firms, for the benefit of patients.

THE PROGRAMME IN 2021

In July 2020, INCa signed a new agreement with AstraZeneca to supply the 16 CLIP² centres with nine innovative drugs:

- AZD5153, BRD4 inhibitor
- AZD1390, ATM inhibitor
- Capivasertib (AZD5363), pan-AKT inhibitor
- AZD4635, A2aR inhibitor
- Ceralasertib (AZD6738), oral ATR inhibitor
- MEDI5752, anti-PD-L1/CTLA-4 bispecific antibody
- Monalizumab (IPH2201), anti-NKG2A antibody
- Savolitinib (AZD6094), cMET inhibitor
- Acalabrutinib, BTK inhibitor

This agreement made it possible to launch a call for proposals in September 2020. Among the 31 projects submitted by 16 CLIP² centres, 3 were funded for a total amount of €2.98M (Tables 21 and 22).



■ TABLE 21
FEATURES OF THE EARLY-PHASE CLINICAL TRIAL CALL

Objectives	The purpose of this call for proposals is to select, based on applications, early-phase clinical trial proposals aimed at assessing the drugs AZD5153, AZD1390, Capivasertib, AZD4635, Ceralasertib, MEDI5752, Monalizumab, Savolitinib, Acalabrutinib, administered in combination therapy
Programming and operating institution	INCa
Funding institution	INCa
Funding	INCa: €2.98M
Proposals submitted	31
Projects selected	3
Selection rate	9.6%

■ TABLE 22
CHARACTERISTICS OF THE SELECTED PROJECTS

Agents	Title	CLIP ² centre and PI
MEDI5752: anti-PD-L1/CTLA-4 bispecific antibody – AstraZeneca	TAYLOR: MEDI5752 in solid tumours with TertiArY LymphOid stRuctures	CLIP ² : Cancer Innovation Nouvelle Aquitaine Institut Bergonié, Bordeaux Prof. Antoine ITALIANO
MEDI5752: anti-PD-L1/CTLA-4 bispecific antibody – AstraZeneca Stereotactic radiotherapy	MEDISARC: Phase I study evaluating the safety of MEDI5752 in combination with stereotactic radiotherapy for the treatment of pulmonary metastases in patients with metastatic sarcoma	CLIP ² Institut Claudius Regaud Institut Claudius Regaud IUCT, Toulouse Dr. Thibaud VALENTIN
MEDI5752: anti-PD-L1/CTLA-4 bispecific antibody – AstraZeneca Monalizumab (IPH2201), anti-NKG2A antibody – AstraZeneca	MONAMI: Monalizumab and MEDI5752 in patients with MSI and/or dMMR metastatic cancer	CLIP ² Galilée AP-HP – Hôpital Saint-Antoine – PARIS Dr. Romain COHEN

Public and private partnerships – new call for proposals on innovative drugs

In 2021, the Institute and the pharmaceutical firm Merck signed a collaboration agreement to make innovative drugs available to the CLIP2. The four proposed drugs are:

- Pepsosertib (M3814): DNA-PK inhibitor
- Berzosertib (M6620): ATR inhibitor
- Tepotinib: MET inhibitor
- M1774: ATR oral inhibitor

Most of these innovative drugs from the Merck development pipeline are still in early development and thus have not yet received marketing approval.

Following the signing of this agreement, the Institute published a call for proposals for the 16 CLIP2 centres in June 2021. The selection and funding of projects will proceed in 2022.

THE PROGRAMME OVER THE 2010-2021 PERIOD

At the end of 2021, the Institute had launched 16 specific calls for proposals to propose 41 drugs under development, 32 projects were selected and 28 projects were funded for €17.85M to evaluate these drugs, 17 were co-funded by the ARC Foundation.

INCa Funding: €12.31 M

ARC Foundation funding: €5.54 M

By the end of 2021, 21 projects had started to enrol patients and the 6 other recently selected studies are scheduled to start in 2022 (Figure 28).

In this programme, the trials which have been able to commence have almost included 600 patients so far.

The distribution of the project funding highlights this programme’s specificity, with a large proportion of rare diseases. Trials addressing sarcoma, and soft tissue trials represent more than 20% of the funded projects compared to the PHRC-K programme, where they account for 8% and for which haematology represents a large proportion of the funding (Figure 29).

FIGURE 28
OUTCOMES OF SELECTED PROJECTS (NUMBER OF TRIALS)

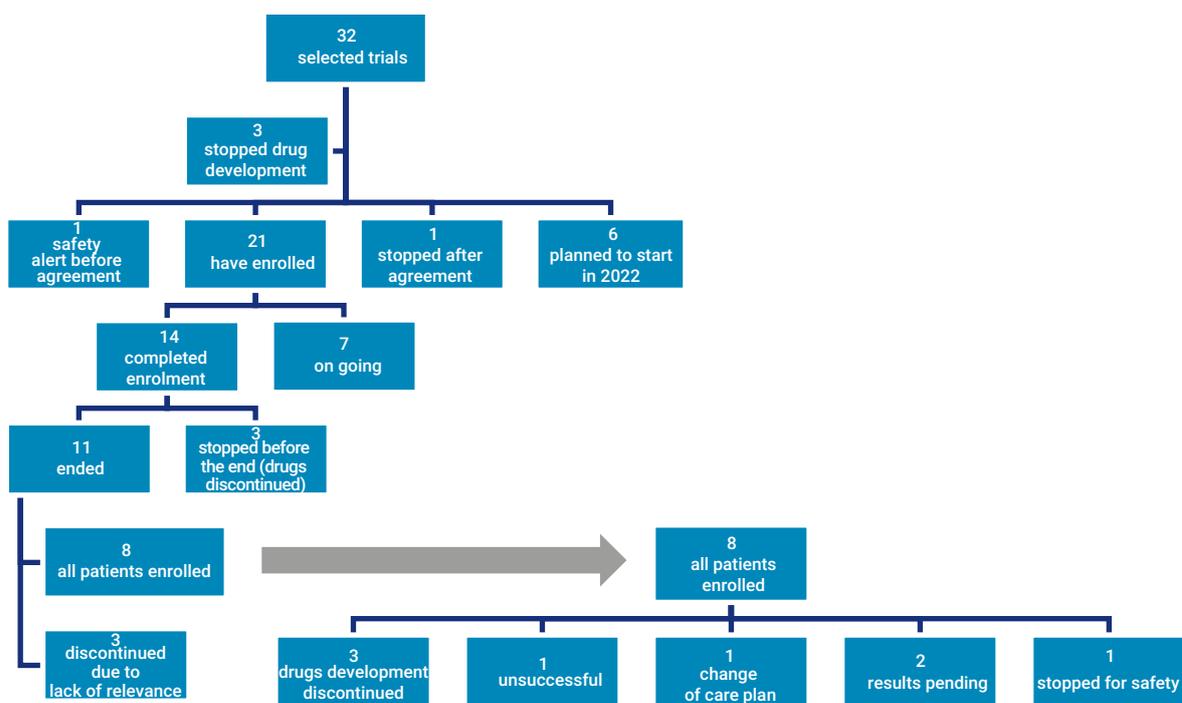
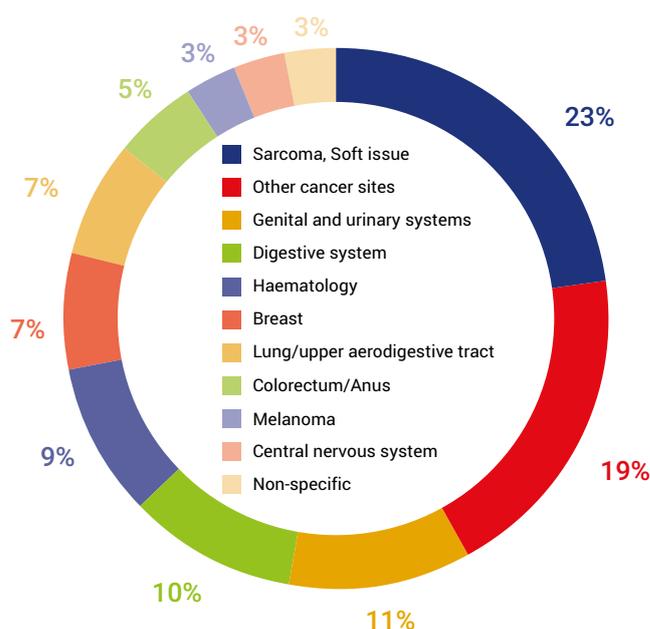


FIGURE 29
DISTRIBUTION OF SELECTED EARLY CLINICAL TRIALS ACCORDING TO CANCER SITES STUDIED OVER THE 2011-2021 PERIOD



INCa-LEEM cooperation - Measure III-5.1 Encourage the industrial sector to invest in the field of cancers with poor prognosis

Part of the Cancer Control Strategy 2021-2030, this action was initiated in 2021. In June 2021, a first meeting was organised between the Institute and representatives of LEEM's committees for cancer and France's attractiveness for clinical research (LEEM is a pharmaceutical industry federation). In this way, each was able to present their vision for improving industrial investment in cancers with poor prognosis.

This meeting helped highlight different points, such as the fact that cancer research investment is very dependent on the market access conditions and clarity for the drugs developed. For manufacturers,

this access needs to be clarified. However, experiments could be conducted to improve access.

The early access reform initiated in mid-2021 is an opportunity to improve this access. Therefore, we need to wait for the first feedback.

The Institute is committed to continuing to foster manufacturers to invest in the field of cancers with poor prognosis, within the framework of its recurrent actions, so that they make their drugs available:

- In trials selected by the PHRC-K
- In the calls for innovative drug projects, for collaboration with CLIP2
- In a renewed AcSé programme

Precision medicine initiatives

CAR T-CELLS

INCa is participating in T2EVOLVE “Accelerating development and improving access to CAR and TCR engineered T cell therapy”, a European Joint Undertaking driven by the Innovative Medicines Initiative (IMI). The IMI is an EU public-private partnership funding health and research innovation, which is currently transitioning to the Innovative Health Initiative.

Operationally launched in January 2021, T2EVOLVE is a 5-year project. Under the co-leadership and the coordination of Prof. Michael Hudecek, MD (Universitätsklinikum Würzburg, Germany) and Dr. Hélène Negre, PhD (Servier Iris and EPFIA project leader), T2EVOLVE is aimed at addressing several issues in accessing engineered T-cells across Europe: cost of manufacturing, lack of standardisation between clinical trials in this field, need for biomarkers to better predict the safety and efficacy of those therapies, equity of access across the different countries and healthcare systems in Europe.

INCa is task leader in two work packages:

- WP2, which specifically addresses the need for patient information, engagement and involvement in healthcare decisions in the field of engineered T-cells;
 - The ultimate objective of this WP is to deliver a white paper to the European Parliament summarising barriers to accessing engineered T-cells in Europe and suggesting sources of leverage to address them.
- WP5, which addresses needs for standardisation of analytical practices in this field, in the aim of improving prediction and comparison of safety and efficacy of the products.
 - The ultimate objective of this WP is to deliver guidelines for standardisation of analytical assays which will be widely distributed to key stakeholders in Europe.

Achieved milestones of the project and INCa-led tasks

● **WP2: Patient engagement**

INCa has contributed to the elaboration of a working group of patients and caregivers (WGPC). This group allows the consortium to orientate its work according to the patients’ perspective and feedback. Two meetings of the WGPC were held in 2021, aimed at collaborating on drafting a European survey on patient information and experience with CAR-T cells.

In this work package, INCa has also led the inventory of educational material for patients and healthcare professionals, as well as its review according to the PEMAT (Patient Education Materials Assessment Tool) standardised approach. References to these materials will be placed on the T2EVOLVE website as a “Hub” in 2022.

- **WP5: Standardisation of analytical practices**

Under the leadership of INCa, a Committee of European National Experts on engineered T-cells (CENET) has been created, including 15 experts from 14 different countries. Two meetings were held in 2021: they aimed at drafting a European survey on current analytical practices in the field of engineered T-cells.

In parallel with this survey, INCa is contributing to drafting the standardisation approach that WP5 members would like to apply to several analytical assays used to control engineered T-cell products. Standardisation guidelines are expected to be shared and distributed across Europe by the end of the project in 2025.

2022 INCa-led milestones and deliverables

In 2022, INCa will lead the launch and distribution of the WP5 European survey on analytical standards, the result of which are expected in the autumn.

Meanwhile, INCa will also lead the creation of explainer videos dedicated to patients and caregivers and addressing topics which would have been identified and agreed upon by the WGPC. At the end of December, INCa will also provide the T2EVOLVE Consortium with a first draft of the white paper on “Access to engineered T-cells in Europe”.

MOLECULAR GENETICS CENTRES: DEVELOPMENT OF SOMATIC GENETIC TESTING IN CANCER

Since 2006, INCa has supported structuring 28 molecular genetics centres (cancer genetics) all over France to ensure equal access to molecular diagnosis. Since 2013, to face the growing number of analyses required, the Institute has also supported the development of targeted high-throughput sequencing (NGS) for diagnostic purposes. DNaseq has now been rolled out to all the molecular genetics centres, and the rollout of RNAseq is in progress.

Activity of the 28 molecular genetics centres

The number of therapies requiring a biomarker to be prescribed is rising, and a variety of new biomarkers are currently in development. In this context, the Institute continues to propose and implement actions in order to support upgrades in molecular genetics.

2020 was an exceptional year due to the COVID pandemic. Indeed, it was the first time that the number of tests and patients tested decreased, probably mainly due to COVID lockdowns (Table 23). However, this decrease could also be partly explained by the shift in activity to private laboratories that are now developing genetic testing (activity not reported in this report).

■ **TABLE 23**
ACTIVITY OF THE 28 MOLECULAR GENETICS CENTRES

	2018	2019	2020
Number of patients benefiting from at least one test	136,000	143,000	142,000
Number of patients benefiting from at least one test for access to a targeted therapy	90,000	96,000	85,000
Number of NGS-tested patients	55,000	66,000	63,000
Number of tests	346,000	378,000	346,000
Number of tested predictive biomarkers determining access to a targeted therapy	185,000	202,000	196,000

In 2020, we observed a decrease in the number of tested patients with solid tumours, after a yearly increase in the number of patients benefiting from NGS testing. In the case of haematologic malignancies, the number of tested patients increased in 2020, although the rate of increase is lower compared to previous years (Table 24).

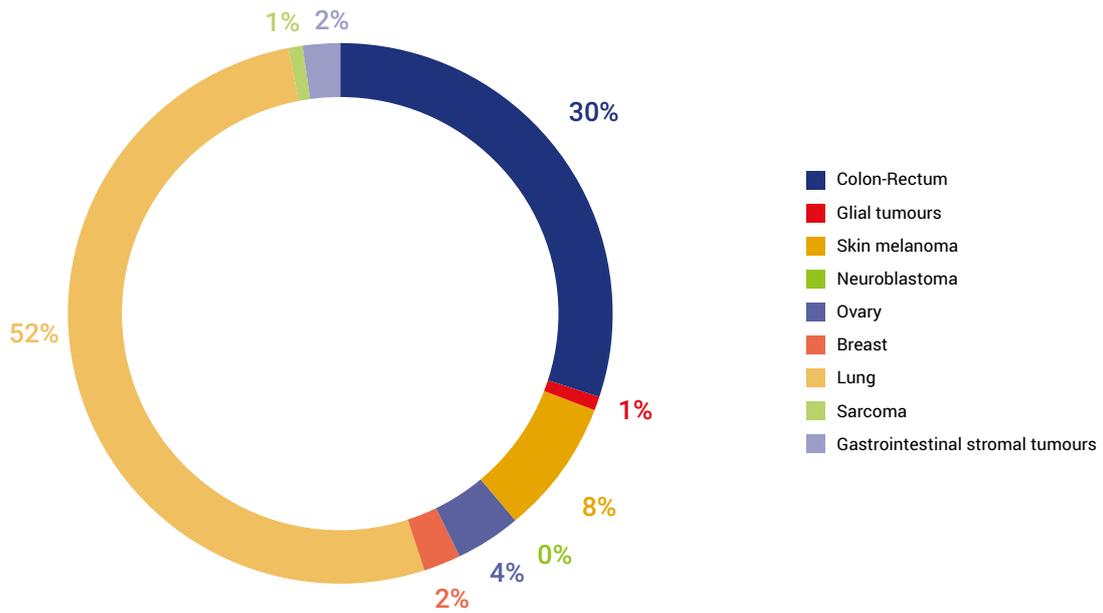
■ **TABLE 24**
NUMBER OF NGS-TESTED PATIENTS

	2018	2019	2020
Solid tumours	43,969	48,352	44,799
Haematologic malignancies	10,797	17,368	18,582
Total	54,766	65,720	63,381

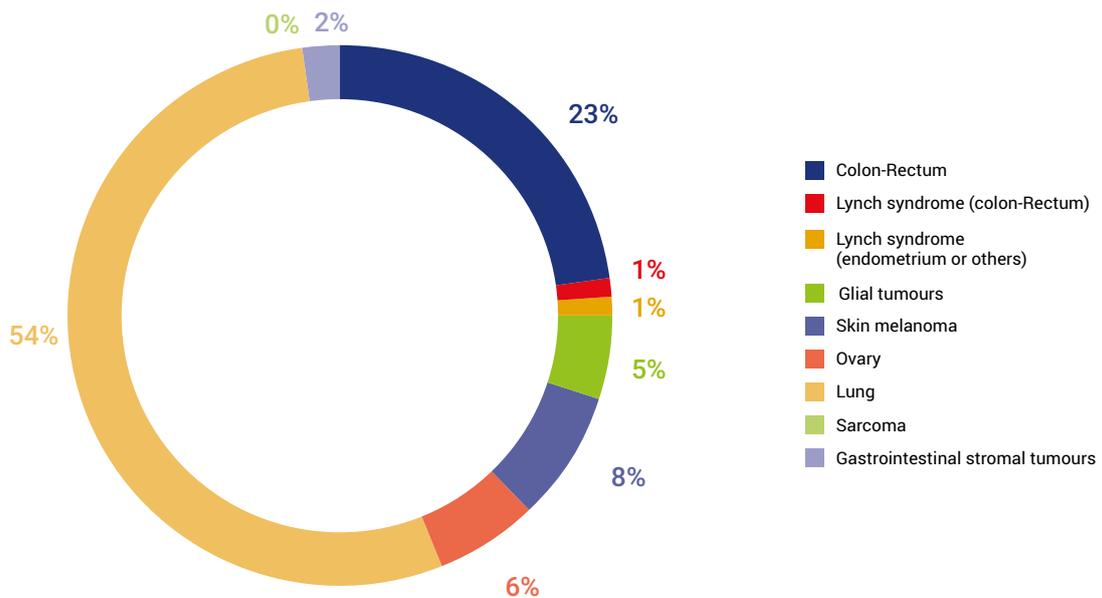
Figures 30 and 31 show the breakdown of the tumour sites of NGS-tested patients over the 2018-2020 period, respectively solid tumours and haematologic malignancies. No major trends seem to emerge and the breakdowns seem to be quite stable. Nevertheless, the number of NGS-tested patients with colorectal cancer has decreased over the years (30% in 2018 vs 20% in 2020).

FIGURE 30
BREAKDOWN OF SOLID TUMOUR CANCER SITES OF NGS-TESTED PATIENTS

2018



2019



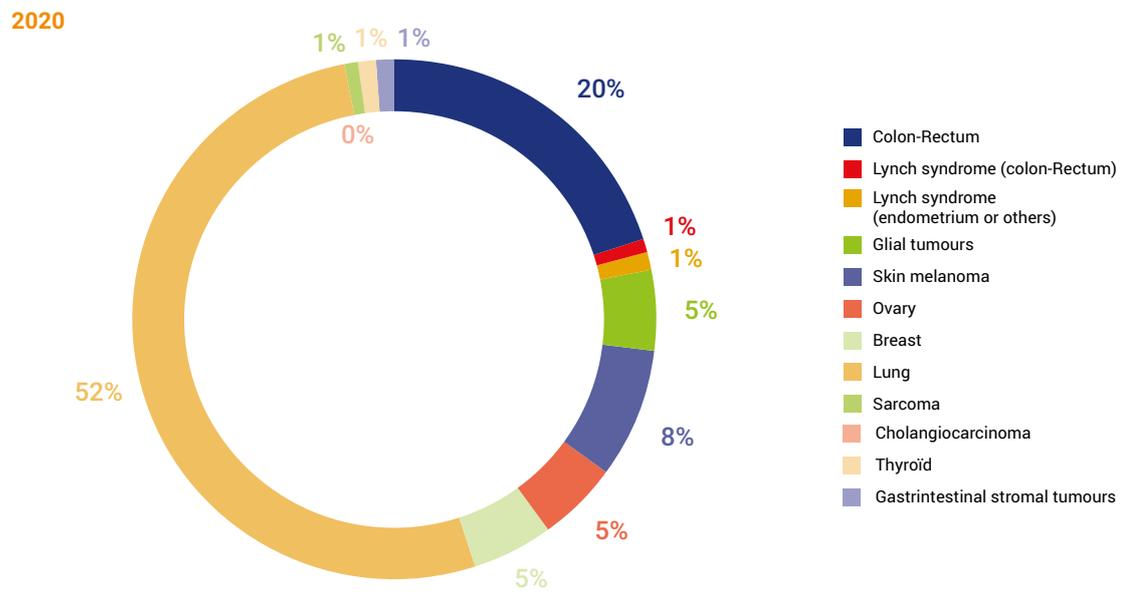
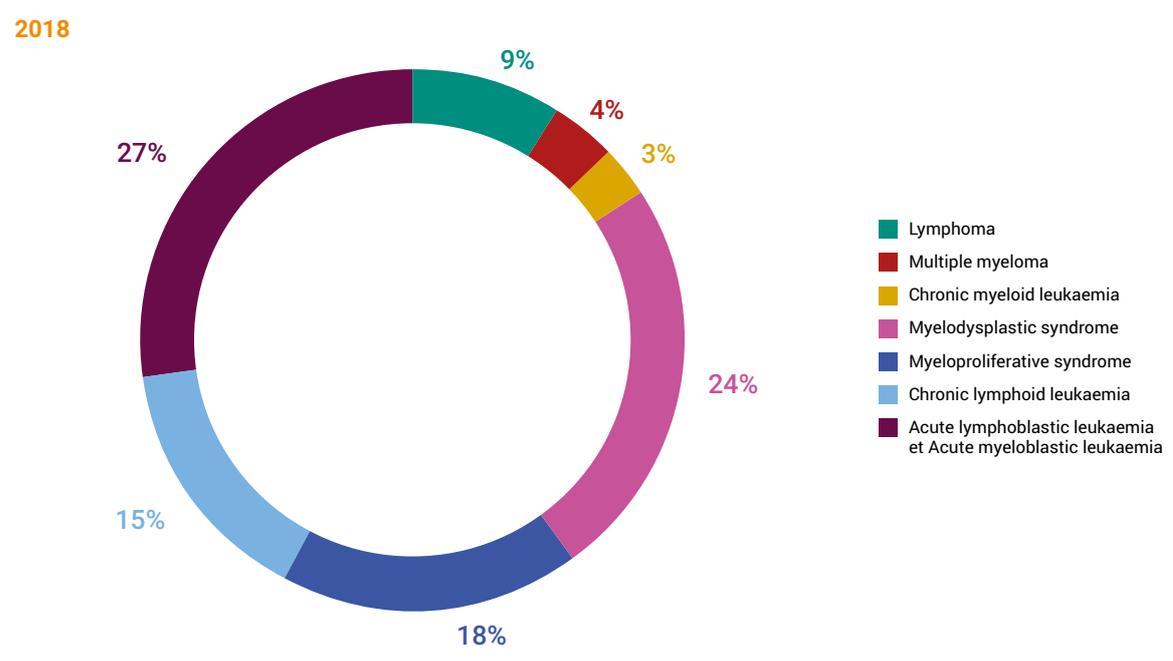
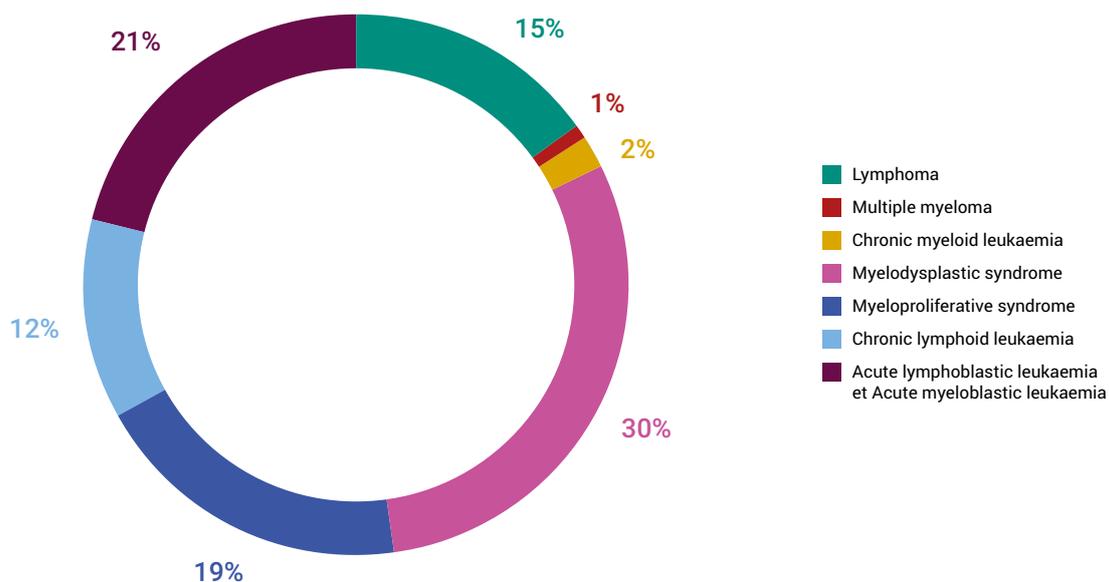


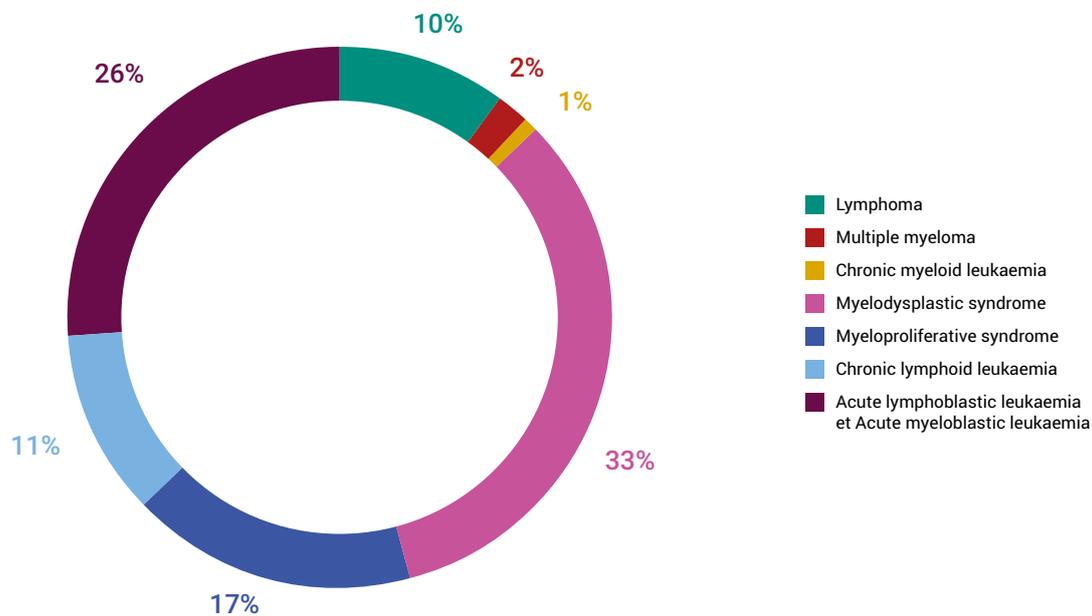
FIGURE 31
BREAKDOWN OF NGS-TESTED HAEMATOLOGIC MALIGNANCY PATIENTS



2019



2020



Issue of recommendations for somatic testing

The landscape of molecular somatic testing in cancer is becoming increasingly complex as more tests are required and the field is evolving at a rapid pace. Thus, issuing regular recommendations regarding these tests' prescriptions and/or procedures is necessary. This would be particularly helpful in guiding professionals in their practice, and ensure the best possible care. To this end, the Institute has been working with experts to issue several recommendations (pathologists, molecular geneticists and clinicians).

- **Recommendation for the prescription of somatic tests**

INCa has set up working groups to produce recommendations for the prescription of somatic tests in colon cancer, lung cancer and melanoma. These documents list all the different stages of the disease and recommend the tests to carry out according to the disease stage.

- **Evaluation of MMR tumoral status**

Initially, the testing of MMR deficiency was used to detect potential Lynch syndrome patients. Recently, it was also shown to be predictive of response to several immunotherapies in specific cancers, and a prognostic or diagnostic marker in others. The recommendations for MMR deficiency testing⁵ cover:

- The naming of the different tests and status;
- The samples to use ;
- The implementation
 - of the immunohistochemistry tests;
 - of the molecular biology tests;
- The test indications according to the tumour sites ;
- The patients to refer to a geneticist according to MMR status.

NGS test funding

Since 2015, genetic cancer test has not been reimbursed through the standard care system, but through a specific procedure dedicated to innovative tests (RIHN circuit, "Référentiel des actes Innovants Hors Nomenclature de biologie et d'anatomocytopathologie"). This system is subject to criticism because the number of tests reimbursed is increasing while the budget remains unchanged. In this way, the reimbursement rate for each test decreases yearly. In November 2021, the French Ministry of Health requested the French National Authority for Health to evaluate NGS cancer tests in order to integrate established ones into the standard care system and thus offload the RIHN scheme.

The 10-year Cancer Control Strategy presents a measure to "improve access to molecular biology by developing the funding model for innovative molecular biological tests, combining real-life follow-up and evaluation at three years" (action II-3.1). In this context, INCa will launch a study to identify the supply and needs for innovative testing in cancerology. This would help issue recommendations for updates to the RIHN scheme to guarantee access to innovation to all patients and the sustainability of the French healthcare system.

5. Évaluation du statut MMR tumoral/synthèse, Collection, Recommandations et référentiels, novembre 2021 INCa.

OncNGS: Development of commercial solutions for liquid biopsy diagnostics based on NGS-driven profiling

The oncNGS consortium groups 8 buyers in five European countries, supported by six entities. This consortium aims to challenge the market to develop novel affordable solutions to provide the most advanced NGS tests for all solid tumour and lymphomas patient within a pre-commercial procurement Horizon-2020 financed project. INCa is a supporting entity of the OncNGS consortium.

The mechanism of the pre-commercial procurement is to define and launch a call for tender to develop a solution for unmet market needs in a domain of public interest. The companies selected will need to develop the solution. The tender is run in such a way that at least two different solutions must reach the market.

EU countries aim to provide equal access to innovative medicines to all, through standard care or access to clinical trials, breaking down current unacceptable inequities due to the high costs of current diagnostic tests. The technological challenge consists in providing efficient molecular DNA/RNA profiling of tumour-derived material in liquid biopsies by means of a pan-cancer tumour marker analysis kit, including NGS analysis integrated with a decision support system, including analytical test interpretation and reporting.

In 2020 and 2021, the specifications of the required solutions were discussed to define the call for tender launched in late 2021.

NATIONAL ONCOGENETICS SYSTEM

Almost 5% of diagnosed cancers are related to hereditary cancer syndromes. These cancers are often discovered at an earlier age compared to that in the general population, with a risk of developing multiple tumours of the corresponding tumour spectrum throughout their lifetime. These hereditary forms of cancer are due to constitutional genetic anomalies affecting predisposing genes, transmissible to descendants. These inherited alterations are initially screened for in affected individuals (index patient) with personal and/or family medical history suggestive of a hereditary cancer condition.

In France, the diagnosis of these predispositions is implemented within the framework of the national oncogenetics system. In 2020, around 146 consultation sites were organised in 101 cities across the country (mainland France and overseas departments). It is also made up of 26 laboratories in charge of carrying out the genetic tests prescribed during consultations and of 17 specific monitoring centres for people at a very high risk of cancer. This system aims to identify people who have a hereditary predisposition to cancer (index or related patients) in order to offer them specific follow-up (appropriate monitoring and/or preventive surgery).

Since its creation, the Institute has been monitoring and coordinating the system, particularly, by organising the compilation of annual activity, in order to help develop the system and improve its access.

2020 activity: decrease in oncogenetic counselling and genetic testing, largely due to the COVID-19 health crisis

In 2020, 82,774 consultations were carried out throughout the territory (Table 25). Since 2003, this is the first time that a decrease has been observed in the annual number of consultations, i.e. a decrease in the total number of consultations of 5% compared to 2019 (+ 9% between 2018 and 2019).

When the result of genetic testing has a direct impact on the patient's care pathway (prescription of a PARP inhibitor, surgical procedure conditioned by the presence of a *BRCA* anomaly, inclusion of patients with therapeutic failure in a clinical trial, life-threatening condition, etc.), counselling teams have implemented accelerated procedures. In 2020, index patients receiving urgent counselling also decreased by 17% compared to 2019 (+ 26% between 2018 and 2019).

Moreover, we have also observed a decrease in the number of tests carried out by the 26 public laboratories known to the Institute (– 15% for index patients compared to 2019 and – 13% for relatives compared to 2019).

In 2020, the health crisis had a major impact on laboratory activity, particularly due to the first national lockdown, with the absence of more than 80% of the staff over two months and thus the total cessation of activity in some cases.

Securing new financial support to boost oncogenetic counselling in 2021

Until the beginning of 2020, the number of oncogenetics consultations rose continuously, on the one hand, because new families with hereditary forms of cancer were identified and on the other hand, because oncogenetic counselling now have a central role in the care pathway for patients.

However, several counselling network coordinators have warned of the system's limitations and lack of resources, particularly human resources (medical time, genetic counsellors) to meet growing demand, with the risk of increasing delays further.

Indeed, activity can only continue to increase with the development of precision medicine (future MA approvals of PARP inhibitors in new indications) and the implementation of "Plan France Médecine Génomique 2025" (French initiative for genomic medicine).

Since 2002, funding has been allocated by the DGOS (French Directorate General of Health Care Provision) to help set up new oncogenetic counselling services or reinforce already existing counselling services (annual envelope of €6.67M supplemented by an additional budget of €0.86M granted in 2015 and renewed in 2016, 2017, 2018, and 2019).

In order to address the expected increase in the number of consultations, the Institute requested further financial support from DGOS of €2M, which was granted in 2021 as part of the 2021-2030 National Cancer Control Strategy (*action 11.3.3 Make precision medicine accessible to all*).

The study on the inventory and assessment of the national oncogenetics system, which is in progress, will make it possible to propose, in addition to organisational improvements, an adjustment of the distribution model, or even possibly a new funding model for consultations.

■ **TABLE 25**
ACCESS TO CONSTITUTIONAL GENETIC TESTING IN ONCOGENETICS LABORATORIES

	2014	2015	2016	2017	2018	2019	2020
Total consultation number	56,897	63,618	71,821	77,478	79,892	87,367	82,774
Patient consultations (new families)	23,635	26,148	28,414	30,442	30,588	32,449	30,717
Relative consultations	9,223	9,971	11,512	11,317	12,131	12,628	30,717
Patients tested	20,845	24,706	28,304	29,404	30,051*	34,493	29,490
NGS tests	NS	17,912	23,453	27,120	28,120	34,032	28,982
NGS: % of total patients	NS	73%	83%	92%	95%	99%	98%
Patients with germline mutations	2,863	3,310	3,963	3,865	4,008*	4,056	3,804
Relatives tested	9,005	9,252	10,302	11,744	12,570*	13,866	12,041
Relatives with germline mutations	3,661	3,842	4,225	4,948	5,108*	5,393	5,191

* Results for 25 laboratories out of 26

ACSÉ PROGRAMME

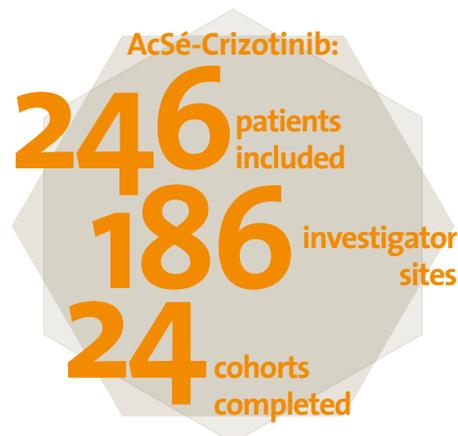
As part of the 2nd National Cancer Control Plan, the AcSé programme (Secured Access to innovative therapies) was launched by INCa in 2013, with the approval of the French Medicines Agency, to provide secured access to targeted therapies for patients in treatment failure situations, in non-authorised indications.

This programme addresses:

- safety issues, since it provides patients with controlled anti-cancer treatments based on their tumour profile and their potential molecular targets identified by one of the 28 molecular genetics centres designated by INCa, and assesses the potential efficacy and tolerance of these new therapies;
- equity of access to innovative treatments;
- the non-competition principle, since this programme is in addition to clinical trials already available and, thus, does not compete with research and development plans of pharmaceutical companies.

Since 2013, five trials have been set up:

- **AcSé-Crizotinib**, launched in 2013, to address the proof of concept and the feasibility of the programme by investigating the effect of the crizotinib agent, authorised for adult patients with lung cancer and presenting with *ALK* translocation. This clinical trial, closed to enrolment since 28 February 2018, has enabled



AcSé-Vemurafenib:

216 patients included
118 investigator sites
11 cohorts completed

AcSé-eSMART:

191 children included
10 investigator sites in France
16 study arms ongoing

AcSé-Nivolumab:

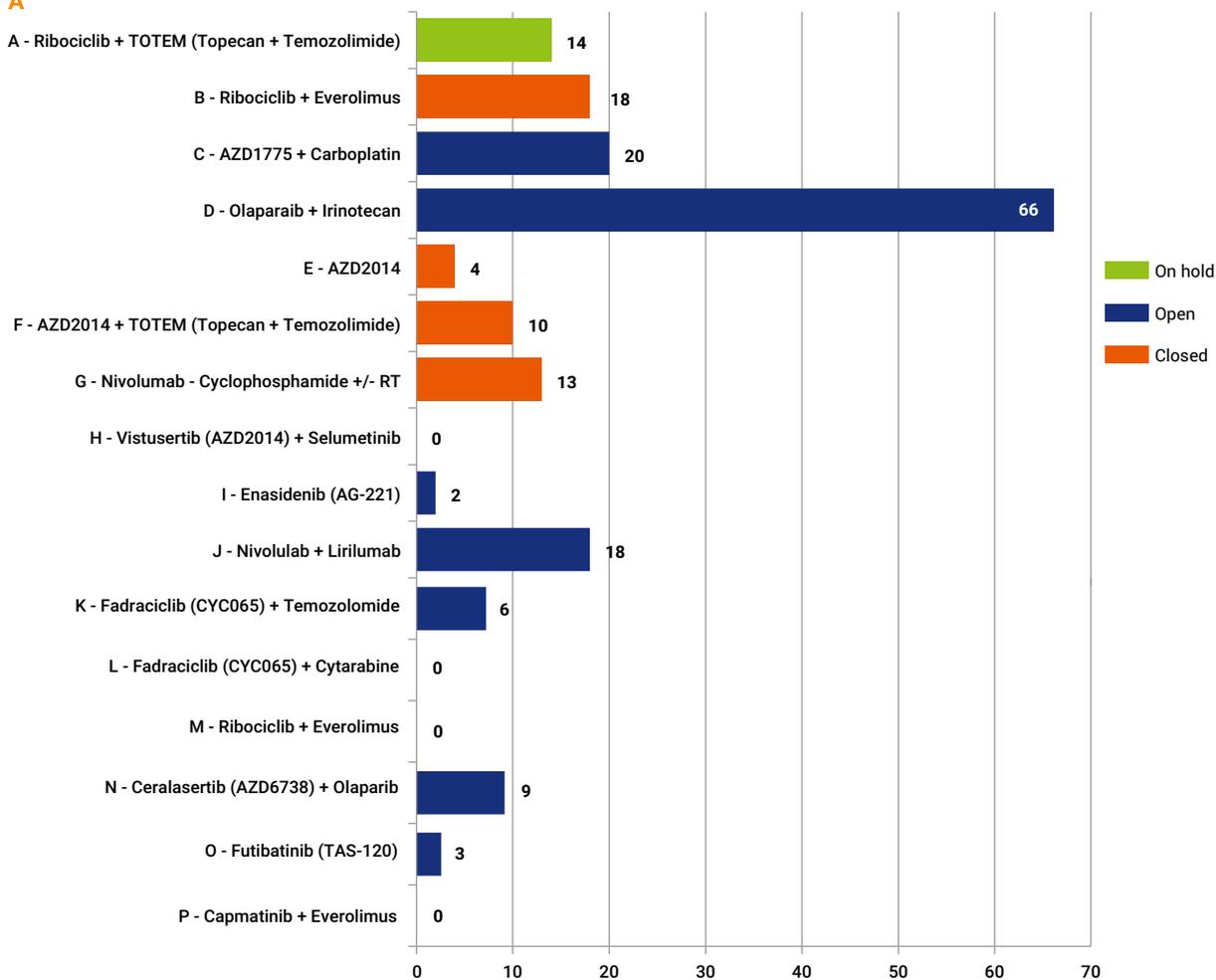
269 patients included
54 investigator sites
6 cohorts follow-up

the treatment of 246 patients carrying molecular alterations targeted by the drug (*ALK*, *MET* and *ROS1*) in more than 20 different cancer types. The first results have shown the efficacy of crizotinib for which the indication could be extended to different cancer types, such as anaplastic lymphomas (carrying an *ALK* translocation), oesogastric adenocarcinomas, stomach cancer, certain sarcomas, or lung cancer (carrying a *MET* mutation).

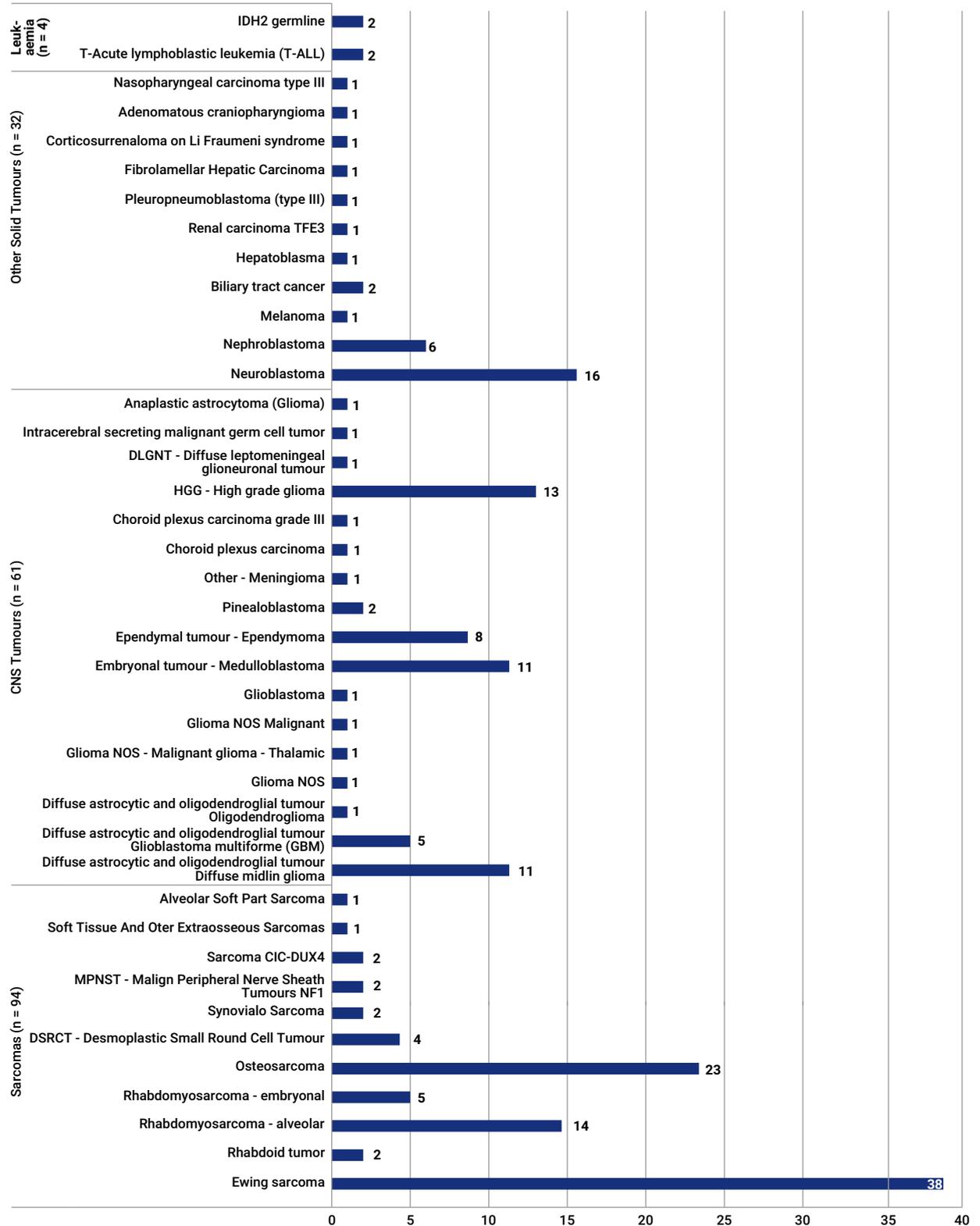
- **AcSé-Vemurafenib**, launched in 2014, to evaluate the efficacy of vemurafenib, indicated in the treatment of melanomas in patients with the *BRAF V600* mutation. This trial, initially planning 4 years of inclusion and the subject of 2 extensions of 12 months and 6 months, has been closed to enrolment since April 2019 and has enabled the treatment of 204 patients with a non-specific *BRAF* mutation in more than 10 different cancer types. The first findings have shown that vemurafenib provided a reasonable response rate and extended progression-free survival (PFS) in pre-treated non-small cell lung cancer (NSCLC) patients with *BRAF V600E* mutations, but was not effective in those with other *BRAF* mutations, emphasising the need to include *BRAF V600E* in routine biomarker screening.
- **AcSé-eSMART** (European Proof-of-concept Therapeutic Stratification Trial of Molecular Anomalies in Relapsed or Refractory Tumours in Children), launched in July 2016 and entirely dedicated to paediatric cancers. It simultaneously makes several targeted therapies available in the same clinical trial for children and adolescents with refractory or relapsed cancers, depending on the tumour molecular profile systematically screened within the framework of a specific PHRC-K project funded in 2014, the MAPPYACTS project. This innovative protocol, approved and opened in 5 countries (France, Spain, Italy, the Netherlands, and the UK), has led to the inclusion and treatment of 191 children (160 in France, 7 in Spain, 1 in Italy, 8 in the Netherlands, and 15 in the UK) within 16 study arms, representing more than 40 different histological types (Figure 32). In 2021, a new arm was opened: capmatinib + everolimus (funded through the innovative drug call for proposals, Novartis 2020).
- **AcSé-Nivolumab** and **AcSé-Pembrolizumab**, launched in May 2017, to evaluate two anti-PD-1 agents in the treatment of rare cancers, based on the organisation of rare cancer networks designated by the French National Cancer Institute. In this context, patients with rare cancer also benefit from secure access to innovation through anti-PD-1 immunotherapy, and scientific data on these new drugs will be collected in controlled clinical trials. In total, 13 types of rare cancers (cohorts) are involved in these two trials, which aim to include almost 550 patients subject to therapeutic failure over three years. 269 and 334 patients have been respectively enrolled in AcSé-Nivolumab and AcSé-Pembrolizumab, closed to enrolment since 31 December 2020 (Figures 33 and 34). Eight cohorts have reached their objective (inclusion and treatment of at least 50 patients), and for one of these – the sarcoma cohort – the number of inclusions has been increased due to the various histological subtypes included in this cohort.

FIGURE 32
**ACSÉ-ESMART: DESCRIPTION OF RECRUITMENT BY STUDY ARM (PANEL A), BY COHORT (PANEL B) AND STUDY CENTRES/
 COUNTRY (PANEL C) (DECEMBER 2021)**

A



B



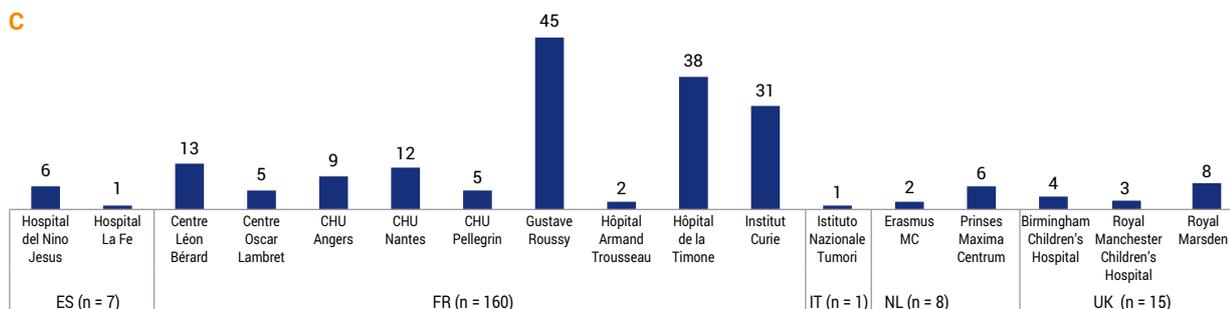


FIGURE 33
ACSÉ-NIVOLUMAB: DESCRIPTION OF RECRUITMENT BY COHORT (CLOSED IN DECEMBER 2020)

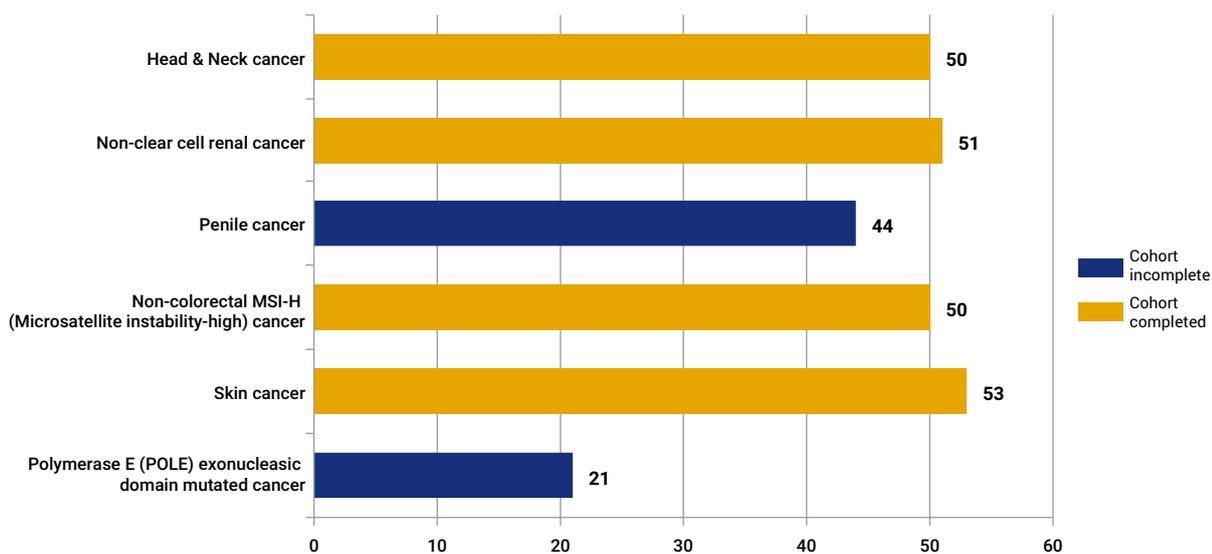
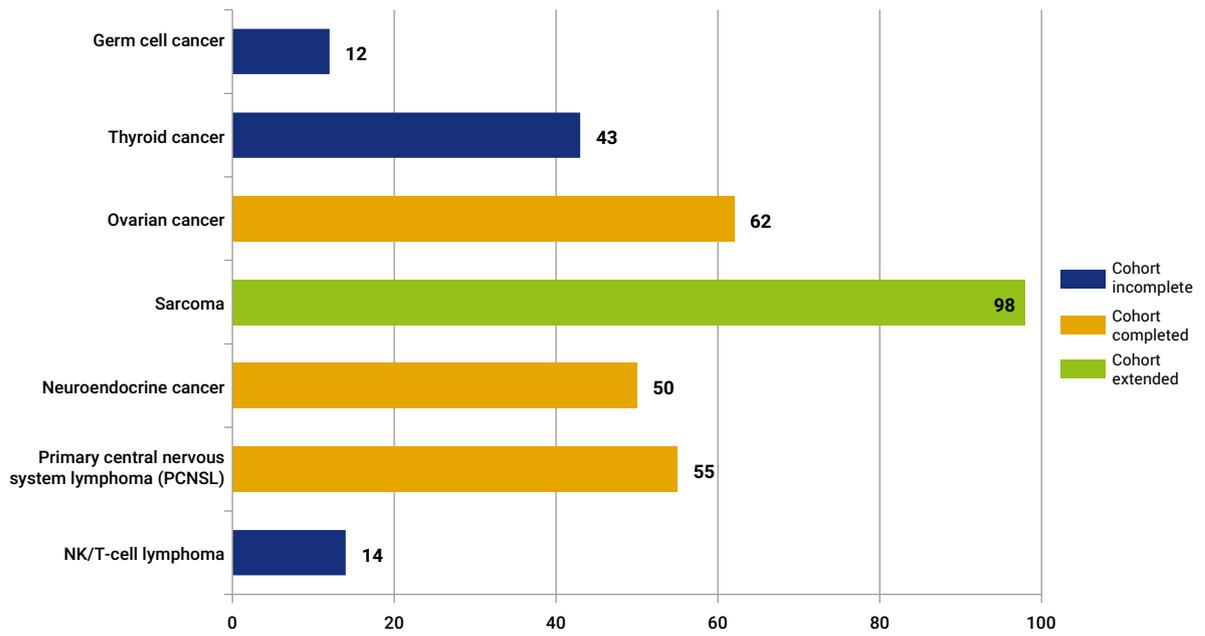


FIGURE 34
ACSÉ-PEMBROLIZUMAB: DESCRIPTION OF RECRUITMENT BY COHORT (CLOSED IN DECEMBER 2020)



INTERNATIONAL VISIBILITY OF ACSÉ PROGRAMME

Publications

- Aparicio T et al. (2021) The Activity of Crizotinib in Chemo-Refractory MET-Amplified Esophageal and Gastric Adenocarcinomas: Results from the AcSé-Crizotinib Program, *Target Oncol.* 2021 May;16(3):381-388. doi: 10.1007/s11523-021-00811-8. Epub 2021 Apr 13.
- Bautista F et al. (2021) 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, *J Clin Oncol.* 2021 Nov 10;39(32):3546-3560. doi: 10.1200/JCO.21.01152. Epub 2021 Aug 4.
- Morscher R J. et al (2021) First-in-child phase I/II study of the dual mTORC1/2 inhibitor vistusertib (AZD2014) as monotherapy and in combination with topotecan-temozolomide in children with advanced malignancies: arms E and F of the AcSé-ESMART trial, *Eur J Cancer.* 2021 Nov;157:268-277. doi: 10.1016/j.ejca.2021.08.010. Epub 2021 Sep 17.
- Pasqualini C. et al (2021) Phase II and biomarker study of programmed cell death protein 1 inhibitor nivolumab and metronomic cyclophosphamide in paediatric relapsed/refractory solid tumours: Arm G of AcSé-ESMART, a trial of the European Innovative Therapies for Children With Cancer Consortium, *Eur J Cancer.* 2021 Jun;150:53-62. doi: 10.1016/j.ejca.2021.03.032. Epub 2021 Apr 20.
- Ortiz-Cuaran S et al. (2020) Circulating Tumor DNA Genomics Reveal Potential Mechanisms of Resistance to BRAF-Targeted Therapies in Patients with BRAF-Mutant Metastatic Non-Small Cell Lung Cancer. *Clin Cancer Res* 2020 Dec 1;26(23):6242-6253. doi: 10.1158/1078-0432.CCR-20-1037. Epub 2020 Aug 28
- Mazières J et al. (2020) *Vemurafenib in non-small cell lung cancer patients with V600 BRAF mutations and non-V600 mutations.* *Ann Oncol.* 2020 Feb;31(2):289-294. doi: 10.1016/j.annonc.2019.10.022. Epub 2020 Jan 3.

Oral communications

- "High clinical activity of pembrolizumab in chordoma, alveolar soft part sarcoma (ASPS) and other rare sarcoma histotypes: the French AcSé Pembrolizumab study from Unicancer" *ASCO 2021 (AcSé Pembrolizumab) - Poster*

Discussion

- Blay J-Y, Penel N, Ray-Coquard I, Cousin S, Bertucci F, Bompas E, Eymard J-C, Saada Bouzid E, Soulie P, Boudou-Rouquette P, Dufresne A, Lequesne A, Mir A, Gambotti L, Legrand F, Simon C, Lamrani-Ghaouti A, Chevret S, Massard C.*
- "High activity of Nivolumab in patients with pathogenic exonucleasic domain *POLE* (ed*POLE*) mutated Mismatch Repair proficient (MMRp) advanced tumors" *ESMO 2020 (AcSé Nivolumab)*
Rousseau B, Bieche I, Pasmant E, Simmet V, Hamzaoui N, Masliah-Planchon J, Pouessel D, Bruyas A, Augereau P, Grob J-J, Rolland F, Saada-Bouzid E, Cohen R, Bouche O, Hoog-Labouret N, Legrand F, Simon C, Lamrani-Ghaouti A, Chevret S, Marabelle A.
 - "High clinical benefit rates of pembrolizumab in very sarcoma histotypes: First results of the AcSé Pembrolizumab study" *ESMO 2020 (AcSé Pembrolizumab)*
Blay J-Y, Ray-Coquard I, Penel N, Bertucci F, Bompas E, Saada-Bouzid E, Eymard J-C, Lotz P, Coquand E, Schott R, Soulie P, Linassier C, Lequesne A, Brahm M, Hoog-Labouret N, Legrand F, Simon C, Lamrani-Ghaouti A, Chevret S, Massard C.
 - "AcSé Nivolumab: résultats préliminaires pour le carcinome baso-cellulaire avancé" *JDP (Journées Dermatologiques de Paris) 2020 (AcSé Nivolumab)*
Veron M, Marabelle A, Grob J-J, Abi-Rached H, Chevret S, Simon C, Mortier L.
 - "AcSé Nivolumab: résultats préliminaires pour le carcinoma trichoblastique" *JDP 2020 (Journées Dermatologiques de Paris) (AcSé Nivolumab)*
Toulemonde E, Marabelle A, Fléchon A, Chevret S, Simon C, Beylot-Barry M, Mortier L.

Posters

- "Benefits of pembrolizumab in progressive radioactive iodine refractory thyroid cancer: Results of the AcSé Pembrolizumab study from Unicancer" *ASCO 2021 (AcSé Pembrolizumab)*
Leboulleux S, Godbert Y, Penel N, Hescot S, De La Fouchardière C, Blonski M, Lamartina L, Cousin S, Do Cao C, Hadoux J, Simon C, Hoog-Labouret N, Chevret S, Massard C.
- Nivolumab in pretreated metastatic penile squamous cell carcinoma: results of the penile cohort from the

*French AcSé prospective program**ASCO 2021 (AcSé Nivolumab)**Pouessel D, Beylot-Barry M, Saada Bouzid E, De Pontville M, Coquan E, Mahammed Hi, Gavoille C, Ghiringhelli F, Dereure O, Spano J-P, Tosi D, Fléchon A, Pannier D, Augereau P, Gambotti L, Legrand F, Simon C, Lamrani-Ghaouti A, Chevret S, Marabelle A.*

- *"Nivolumab in metastatic non-clear cell renal cell carcinoma: first results of the AcSe prospective study" ASCO GU (AcSé nivolumab)*

*Albiges L, Pouessel D, Beylot-Barry M, Bens G, Pannier D, Gavoille C, Oudard S, Chevret S, Hoog-**Labouret N, Legrand F, Simon C, Lamrani-Ghaouti A, Escudier B, Marabelle A, Flechon A*

- *"First results of the AcSé Pembrolizumab Phase II in the Primary CNS Lymphoma (PCNSL) cohort" ASH 2020 (AcSé Pembrolizumab)*

Hoang-Xuan K, Houot R, Soussain C, Blonski M, Schmitz A, Delwail V, Brachet P-E, Ghesquières H, Peyrade F, Tempescul A, Abraham J, Agape P, Ahle G, Baize N, Campello C, Gyan E, Jardin F, Oberic L, Rey P, Choquet S, Houillier C, Legrand F, Lamrani-Ghaouti A, Querel O, Hoog-Labouret N, Simon C, Chevret S, Massard C.

Based on the implementation of new types of clinical trials, the AcSé programme has clearly helped accelerate the emergence of innovation for the benefit of patients⁶.

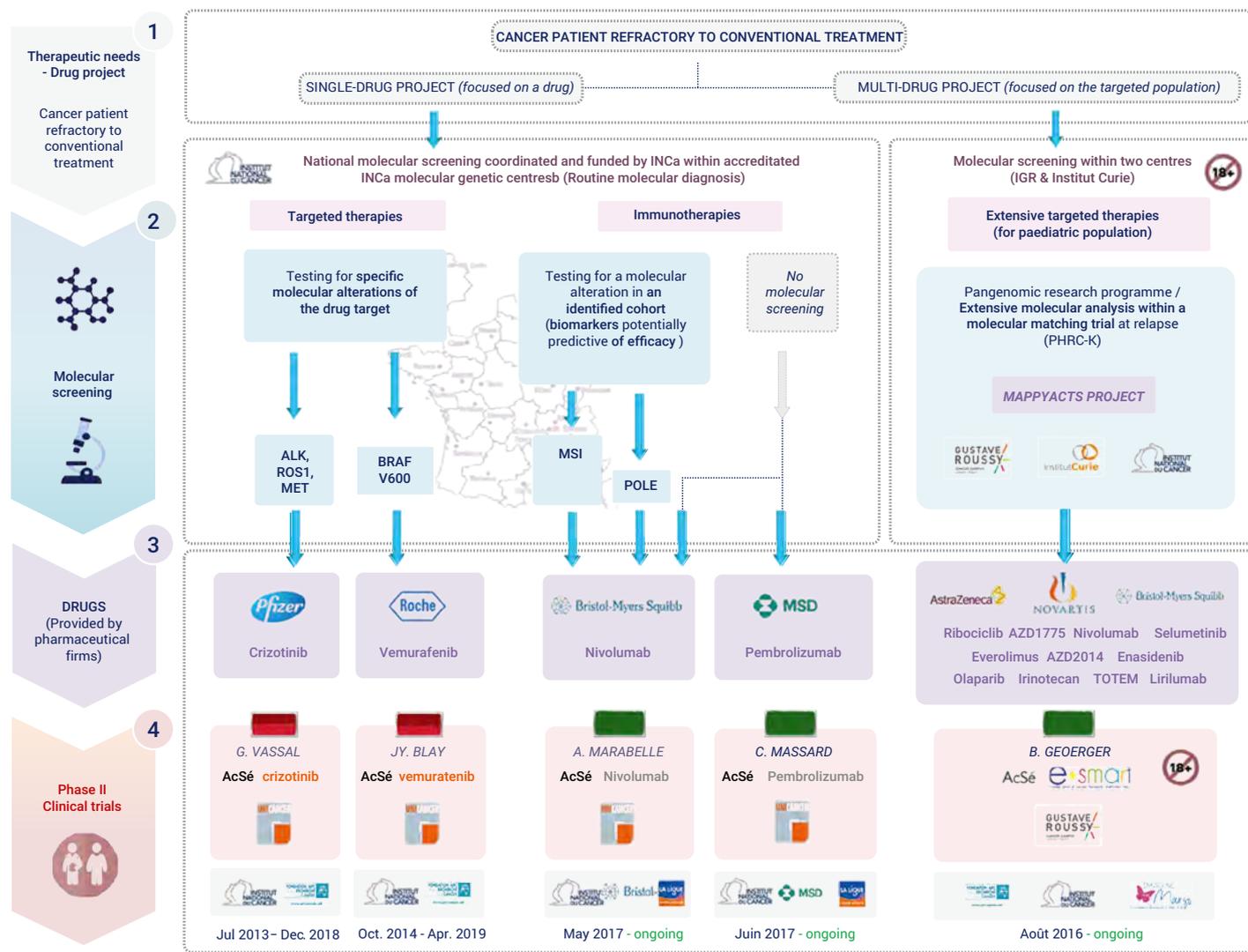
All of the key features, principles, and objectives of the programme have been observed and achieved:

- **Extensive molecular screening** has been carried out as part of the programme, and almost 17,000 patients have benefited from molecular screening within 3 of the 5 AcSé trials.
- Moreover, AcSé has met all expectations regarding **equity of access to treatment** throughout France. Indeed, nearly 200 centres have been opened in France with excellent territorial distribution. In addition, 8 European centres have also been opened since the implementation of the AcSé-eSMART trial.
- To date, 1,256 patients, including 212 children, have received innovative treatment within the AcSé trial framework.
- The **relevance and feasibility of this programme have been confirmed**: with the opening of more than 60 study arms spread over these 5 trials, the AcSé programme has clearly demonstrated its flexibility and adaptability.
- All of these trials have demonstrated a real momentum, both in adding new study arms and in removing ineffective ones. This feasibility, first demonstrated at a national level, is now confirmed at a European level with patients included in all 5 countries open to inclusion (France, Netherlands, Spain, Italy, UK).
- **AcSé has also helped include vulnerable populations**, as 212 children have been included as part of 2 of the 5 AcSé trials (AcSé-Crizotinib and AcSé-eSMART), and 9 patients over 81 years of age have also been included in AcSé-Vemurafenib.
- Finally, **AcSé has generated substantial data and disseminated it to the scientific community** through numerous scientific communications, with nearly 48 international communications, 3 press conferences, 1 patient guide, and 3 Temporary Use Recommendations (RTUs) filed.

48 international communications
3 press conferences
1 patient guide
3 Temporary Use Recommendations (RTUs) filed.

6. Buzyn A et al. (2020) *Equal Access to Innovative Therapies and Precision Cancer Care*. *Nat Rev Clin Oncol*. 2016 Jun;13(6):385-93. doi: 10.1038/nrclinonc.2016.31. Epub 2016 Mar 22.

■ FIGURE 35
KEY FEATURES OF THE ACSÉ PROGRAMME



New AcSé programme

The Ten-year Cancer Control Strategy aims to renew the AcSé programme, first initiated in 2013. Thus, measure 1.4, dedicated to new clinical trials, provides for implementing multi-arm, multi-target and multi-drug AcSé type clinical trials. In this context, discussions took place during 2021, in collaboration with experts from Unicancer and FHF Cancer.

These discussions with a group of experts from the two hospital federations have led to the proposal of a new, more agile AcSé programme:

This will make it possible to:

- Address current clinical research questions posed by the latest authorised targeted therapies thanks to a multi-arm, multi-target and multi-drug programme;
- Provide a larger number of patients, in an optimised and secure setting, with innovative treatments previously reserved for a limited number of patients.

The initial objective of the AcSé programme is thus maintained in a renewed approach for the patients' benefit.

The evaluation of drugs targeting a molecular anomaly in indications other than those with a marketing authorisation (MA) remains the general objective of the AcSé programme.

This new programme will be subject to change. It will rely on innovative methodologies, such as the use of composite primary endpoints, combining clinical and quality-of-life criteria.

The cohorts, targeting a biological question, may consist of several treatment arms. Combinations of treatments may also be considered.

Since the first AcSé trials, molecular screening programmes have developed considerably, with the generalisation of new generation sequencing (NGS), which is now available in the 28 hospital molecular genetics centres set up by the French National Cancer Institute, or in those of the France Genomic Medicine 2025 plan.

These screening tests can also be carried out in research programmes on patients undergoing first-line treatment. These initiatives will make it possible to identify patients eligible for this new trial and to give them access to a treatment corresponding to the anomalies identified, which is not always possible at present.

Finally, this new programme aims to provide more evidence of efficacy and comparison.

Four cohorts, built with the new outlines of the AcSé clinical research programme, are to be set up. They will be open to diseases not targeted by the MA:

1. Cohort targeting gene fusions for all cancers
2. Cohort targeting PARP inhibitor-sensitive abnormalities in solid tumours outside the MA.
3. Cohort targeting ErBb2 gene defects for solid or haematological cancers
4. Cohort targeting microsatellite instabilities outside colorectal and endometrial cancers

Clinical cancer research organisation: structures, infrastructures, and tools

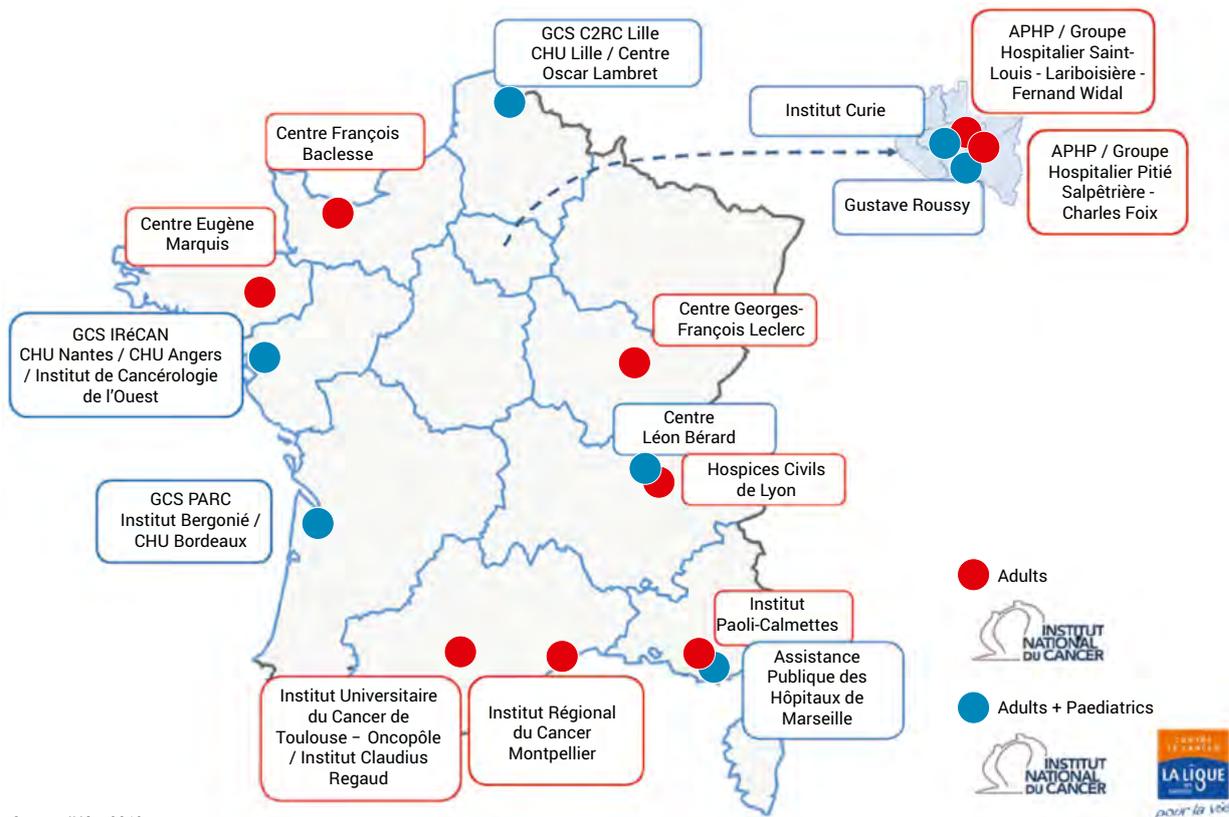
CLIP² – EARLY-PHASE CLINICAL TRIAL CENTRES

Sponsored by the 2009-2013 Cancer Control Plan, the initiative to structure clinical and translational research is supported by INCa through a specific designation: early-phase clinical trial centres (CLIP² centres). The second 2009-2013 Cancer Control Plan allowed the French National Cancer Institute to launch the set-up of specialised investigation centres in early-phase clinical trials. Thanks to the first designation initiated in 2010, the Institute has provided CLIP² centres with logistical and financial support to reach the highest international level in terms of quality, in carrying out early-phase clinical trials evaluating new drugs from pharmaceutical laboratories, biotechnology companies, or academic research.

This objective was continued in the 2014-2019 Cancer Control Plan by conducting, in partnership with the French Cancer League, a new designation of these structures in 2015, and identifying centres with paediatric activities. The third and latest designation has made it possible to renew and bolster its support for expert centres in early-phase clinical trials for adult and paediatric, adolescent and young adult cancers. Thus, among the 16 structures designated until 2024, 7 of these include paediatric oncology activities (Figure 36).

This programme has helped increase the visibility and attractiveness of these centres and also those of early-phase French clinical research (and should continue to do so), leading not only to an increase in the number of new trials launched, and the number of patients included every year within CLIP² centres, but also a growing interest among pharmaceutical companies in conducting early-phase clinical trials within these designated centres.

■ FIGURE 36
GEOGRAPHIC DISTRIBUTION OF CLIP² CENTRES (3RD DESIGNATION – 2019-2024)



2021 Activity report

Since 2010 (i.e. the first designation campaign), this initiative has contributed to the overall increase in the number of clinical trials initiated and the number of patients enrolled in CLIP² centres (Figure 37):

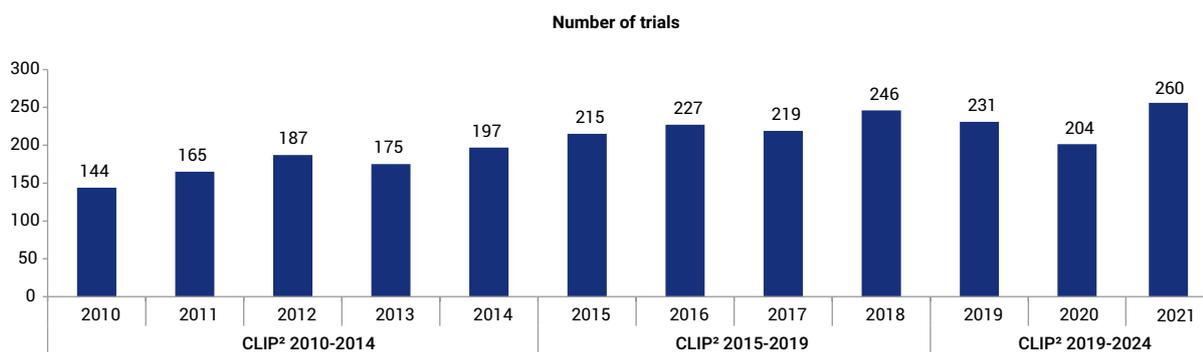
- + 80% increase in the total number of clinical trials launched, with 260 in 2021;
- + 242% increase in the total number of patients enrolled, with 6,325 patients enrolled and treated in 2021.

Since 2015 (i.e. the second designation), the total number of early-phase clinical trials has increased by about 20%, with the following distribution in 2021 (figure 38):

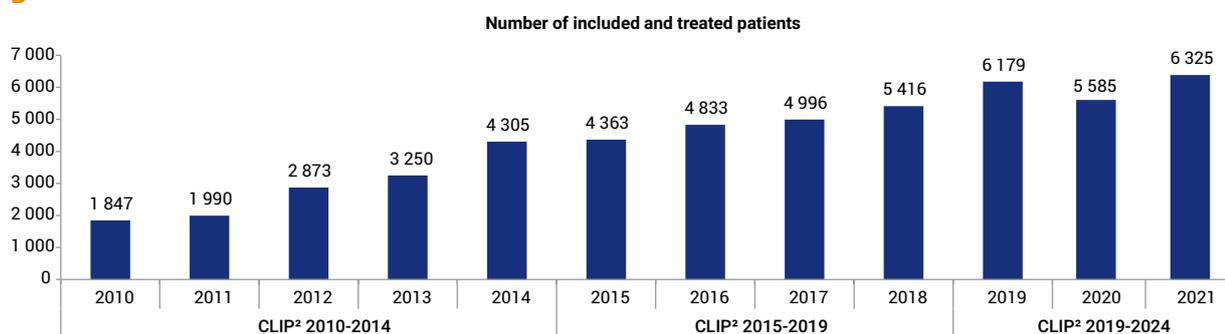
- 55% phase II trials;
- 22% phase I/II trials;
- 23% phase I trials.

FIGURE 37
TRENDS IN PROGRESSION OF THE NUMBER OF TRIALS INITIATED (PANEL A) AND PATIENTS ENROLLED (PANEL B)
OVER THE 2010-2021 PERIOD

A



B



Up to 2019, the distribution of academic and industrial trials was quite balanced (47% vs. 53% in 2019). In 2021, 68% of the trials were sponsored by industry and 32% were sponsored by academic institutions, including 17% by CLIP²-hosting institutions among which public-private partnership trials, developed and supported by INCa (Figure 39).

FIGURE 38
DISTRIBUTION OF NEW TRIALS LAUNCHED ACCORDING TO STUDY PHASE

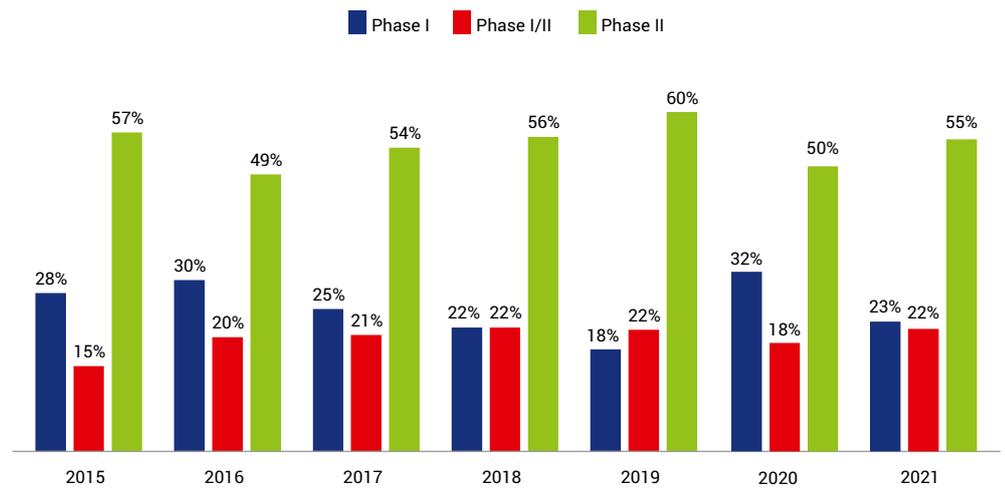
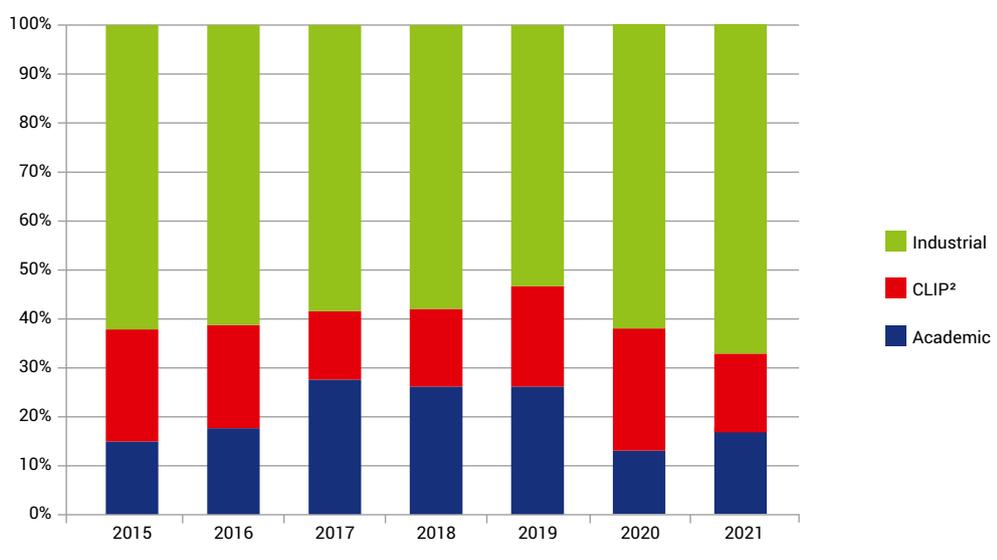


FIGURE 39
DISTRIBUTION OF NEW TRIALS LAUNCHED ACCORDING TO SPONSOR



The distribution by type of intervention evaluated has been quite stable since 2017, with 84% of study arms corresponding to “drug study arms”. The proportion of study arms evaluating monotherapies or drug combinations has tended to balance out since 2020, with in 2021 (Figure 40):

- 43% drug monotherapy experimental study arms;
- 41% drug combination experimental study arms;
- 8% drug and therapy combinations (i.e. evaluating at least one drug with one or more other therapies such as surgery or radiotherapy, etc.);

While the remaining 8% correspond to “non-drug study arms”, which may evaluate one or more non-drug interventions such as radiotherapy, surgery, device, biomarkers, imaging techniques, etc.

The distribution by therapy type evaluated has been fairly stable since 2017, with a predominance of immunotherapies over targeted therapies (+11%) and chemotherapies (+18%) since 2017, and a notable increase of approximately 20% in targeted therapies between 2020 and 2021. It should also be noted that nearly 20% of therapies assessed in the study arms are not clearly defined/identified (Figure 41).



Between 2010 and 2021:

- **+ 80% increase in the total number of clinical trials initiated, with 260 in 2021;**
- **+ 242% increase in the total number of patients enrolled, with 6,325 patients enrolled and treated in 2021.**

FIGURE 40
TRENDS IN DISTRIBUTION OF EXPERIMENTAL ARMS IN NEW TRIALS LAUNCHED ACCORDING TO TYPE OF INTERVENTION ASSESSED (PANEL A) AND THE DETAILED DESCRIPTION FOR THE "DRUG" ARM (PANEL B)

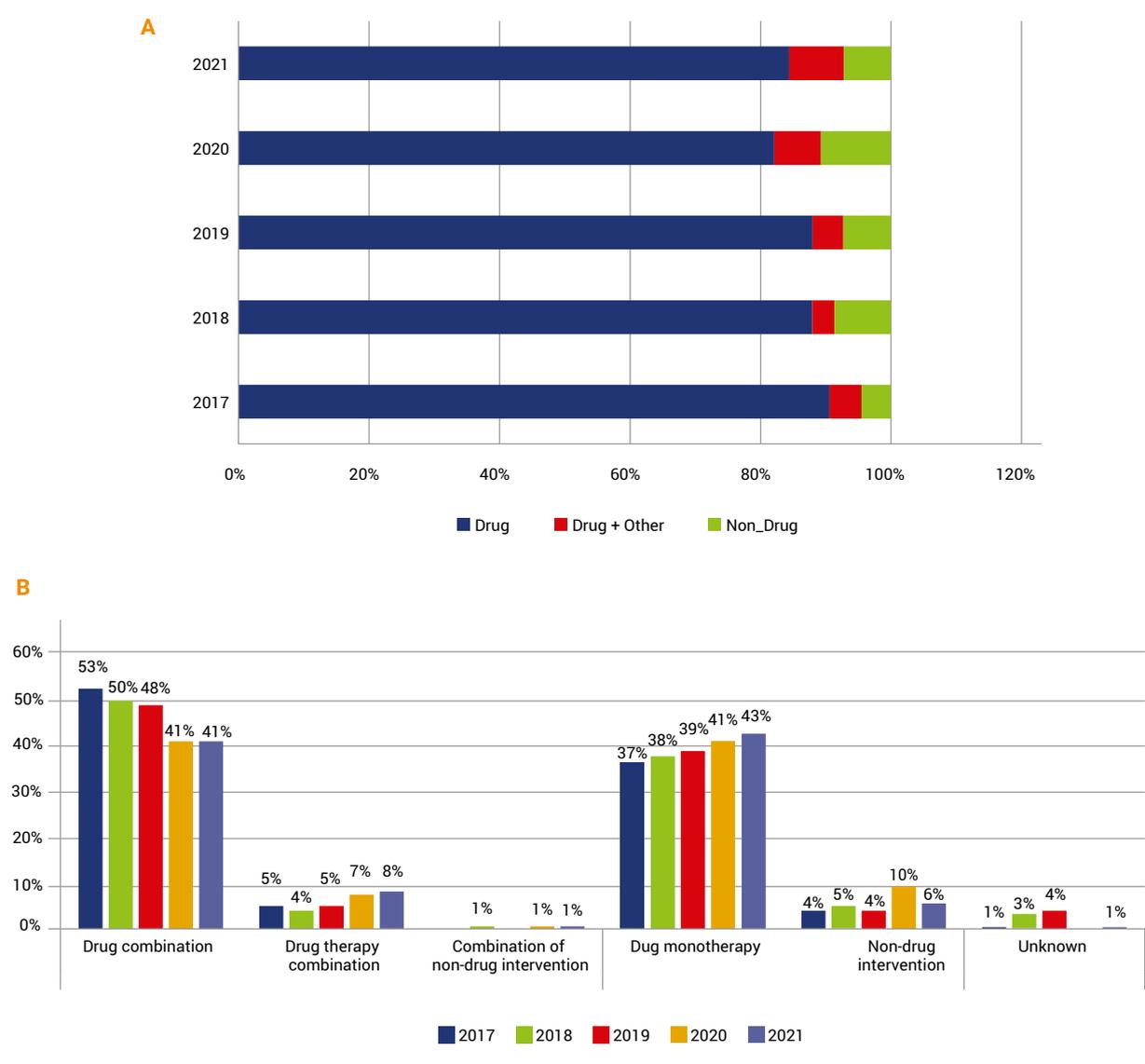
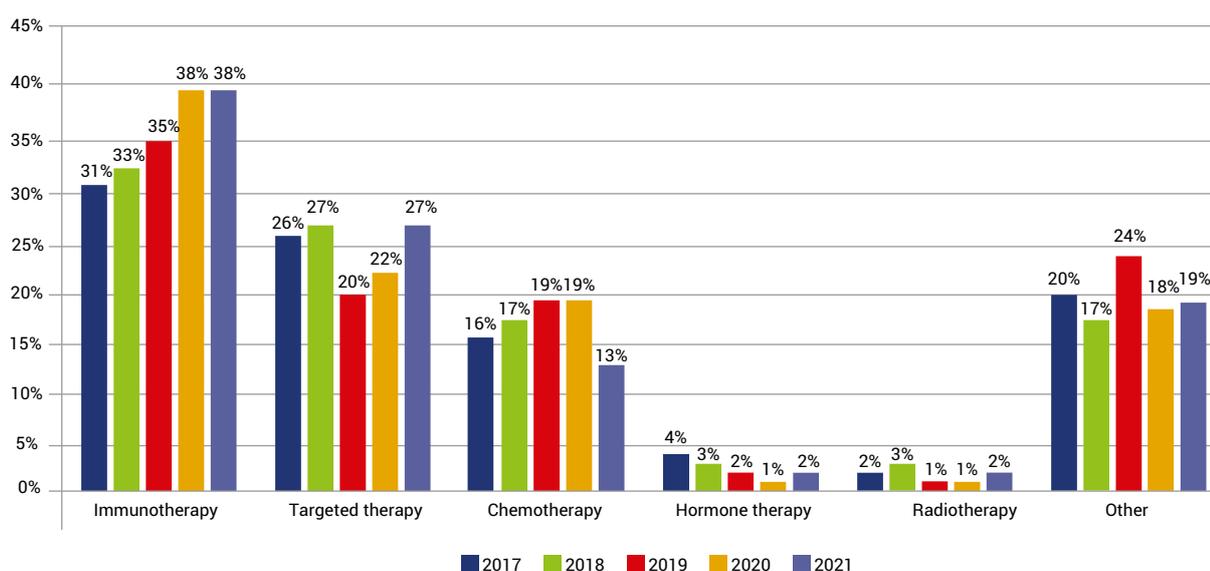


FIGURE 41
TRENDS IN DISTRIBUTION OF EXPERIMENTAL ARMS IN NEW TRIALS LAUNCHED ACCORDING TO TYPE OF THERAPY ASSESSED



Inter-CLIP² projects / working areas

- **Shared recommendations on interactions between CLIP² centres and sponsors or their representatives**

For years, clinical research actors have been reporting a common issue: the complexity of the implementation of clinical research, due in part to the over-interpretation of Good Clinical Practice (GCP).

In 2018, an inter-CLIP² working group launched an initiative with all of the CLIP² centres, to improve the operational implementation of clinical cancer research, by enhancing collaboration between investigator centres and industrial or academic sponsors, through shared recommendations.

These recommendations were issued after nearly two years of consultation; they aim to improve the conditions of interaction between the two parties and propose collaboration rules to be applied in reciprocal relations.

Firstly validated by all CLIP² centres and then favourably acknowledged by LEEM (“Les Entreprises du Médicament”), a pharmaceutical industry federation, these recommendations have now been agreed upon by both investigators and sponsors. They suggest an improvement in the quality of interactions and work between CLIP² centres and sponsors, and should help focus the activity of the investigator centres on the care of patients involved in clinical trials.

The implementation of the recommendations came into effect in the final quarter of 2021, after INCa and LEEM had disseminated them to the various stakeholders, through a dedicated communication campaign, relayed by the specialised press.

CT.gov activity and AI

Following the data visualisation project developed within the framework of the monitoring of early-phase activity conducted within CLIP² centres (“DATA-VIZ_CLIP”), several exploratory machine learning projects aimed at automatically typing clinical trials have been conducted.

This work, based on CNCR’s 2010-2019 cancer research report⁷ (CNCR: National Research Coordination Committee), was carried out thanks to a collaboration between INCa and CNCR’s bibliometric unit, and the availability of the list of clinical cancer trials reported on [clinicaltrials.gov](https://www.clinicaltrials.gov), with the associated diseases or sites standardised by medical oncologists.

The first results confirmed the feasibility of developing predictive algorithms which, after an initial learning phase, would automatically identify cancer-related trials and diseases or sites associated with a clinical trial.

These automatic typological predictions are in line with the logic objectified by the Institute for years, i.e., maximising the value of clinical cancer research data, while minimising the involvement of clinical research actors.

Study on screening-based trials

Since 2017, the Institute, in concert with the CLIP² coordinators, has set up a tool to identify clinical trials needing the presence of one or more specific biomarkers. This kind of information was not available until now, but it is now essential to guide patients into the most relevant clinical trials, given the new kind of drugs tested, the implementation of NGS in routine clinical practice in molecular genetics centres, as well as the multiplication of molecular screening programmes on large panels developed in many centres (Figure 42).

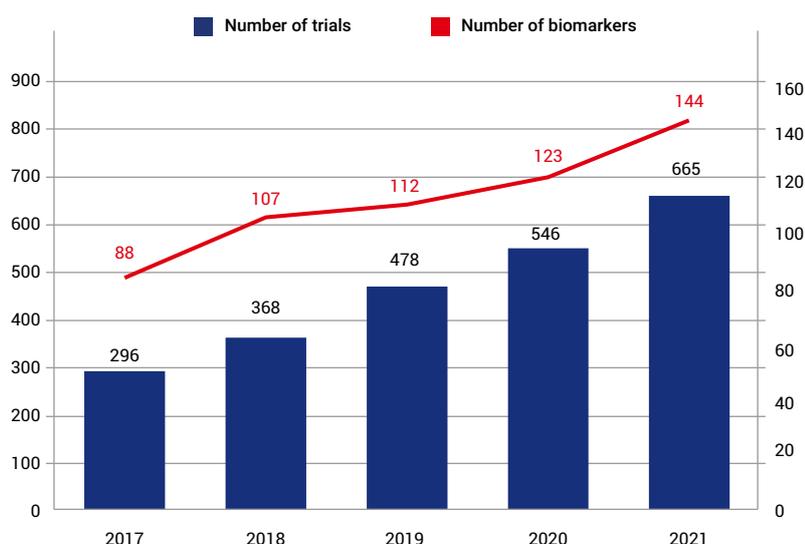
In this way, INCa has set up a list of clinical trials conducted within CLIP² centres. Initially focused on early-phase trials, this list has now been extended to all trial phases with molecular screening to ensure access for all patients.

In order to obtain an up-to-date list, a survey is carried out three times a year in CLIP² centres, in order to include the new trials launched and to remove the trials closed for inclusion. This list is shared by e-mail to investigators and members of Molecular Tumour Boards (approximately 350). It is also available on the Institute’s website: <https://www.e-cancer.fr/Professionnels-de-la-recherche/Recherche-clinique/Structuration-de-la-rechercheclinique/Les-CLIP2>

This list includes a search engine for biomarkers, as well as a list of minimum items of information such as trial title, pathology, age, type of genetic alteration (mutation, overexpression, translocation, fusion, copy number variation), and links to the [clinical.gov](https://www.clinicaltrials.gov) website.

7. https://www.cncr.fr/wp-content/uploads/2022/01/CNCR-FHF-LaRechercheEnCancerologie_rapport_vf.pdf

FIGURE 42
TREND IN THE NUMBER OF TRIALS AND BIOMARKERS LISTED



COOPERATIVE INTERGROUPS

Since 2020, a declarative survey on clinical cancer research activity has been specifically designed at the request of the cooperative intergroups and based on the national survey (see section 3.4.3.). This survey aims to quantitatively assess clinical cancer research activities in France in these cooperative intergroups every year.

As a reminder, cooperative intergroups can either be sponsors or involved in academic trials, and/or industrial trials: these 3 statuses have been addressed⁸.

Table 26 presents the main results of the survey conducted in 2021:

- In 2020, 100 cancer clinical trials were sponsored by 11 cooperative intergroups (or a group of the intergroup):
 - 10,272 inclusions were reported in 2,898 French centres (+ 43% increase compared to 2019).
 - These 11 cooperative intergroups, as sponsors, were active at an international level with 170 participating centres abroad;

⁸ Members of the cooperative intergroups participate in the design of the study methodology and/or the inclusion and follow-up of patients in the study.

Scientific facilitation on therapeutic de-escalation

In October 2021, the annual meeting of the cooperative intergroups was held on the theme of therapeutic de-escalation. The main approaches of the Ten-Year Cancer Control Strategy were presented. Each intergroup also presented its current or future actions regarding therapeutic de-escalation according to the different diseases and/or organs concerned.

- All the cooperative intergroups were involved in academic trials with 198 cancer clinical trials reported and 9,652 inclusions:
 - A 22% decrease in the number of inclusions in 2020 is reported compared to 2019;
 - We noticed that there were more clinical trials in 2020 but fewer inclusions compared to 2019 when the cooperative intergroups were involved in academic trials;
 - 6 cooperative intergroups were involved in industrial trials with 36 clinical cancer trials and approximately 500 inclusions reported;
- With a total of 20,346 inclusions in 2020, they represented 35% of national inclusions. The total number of inclusions in 2020 was stable compared to 2019 (20,375 inclusions reported in 2019).
- Strong clinical research activity in early phases (phase 1 and 1/2) and phase 3 was still observed in 2020:
 - 63% of inclusions were observed in phase 3 when the cooperative intergroups were sponsors,
 - 13% of inclusions were observed in early phases when the cooperative intergroups were involved in industrial trials.

Moreover, this survey analysed the staff involved in clinical cancer research activities: 206 members of clinical research staff (full-time equivalent) were assigned to clinical cancer research in cooperative intergroups in 2020.

■ **TABLE 26**
MAIN RESULTS OF 2020 CLINICAL CANCER RESEARCH ACTIVITY AMONG COOPERATIVE INTERGROUPS

Status of cooperative intergroup	Number of cooperative intergroups		Number of trials		Number of inclusions	
	2019	2020	2019	2020	2019	2020
Sponsors	9	11	86	100	7,192	10,272
Involvement in academic trials	13	13	162	198	12,469	9,652
Involvement in industrial trials	7	6	39	36	714	422

These results highlight the key role of intergroups in the clinical cancer research landscape, particularly in academic trials, both in terms of the design and conduct of clinical trials.

PATIENTS' ENROLMENT IN CLINICAL TRIALS

Initiated by the 2003-2007 Cancer Control Plan and boosted by the second and third Cancer Control Plans, INCa's annual declarative survey assesses clinical cancer research activities in France. Thanks to the data reported by University Hospitals, Cancer Care Centres, and Health Care Centres, this survey provides an estimation of the enrolment rate in cancer clinical trials every year in France.

This action is now part of the 2021-2030 Cancer Control Strategy, within the framework of area III.5 ("Ensuring access for patients to innovative therapies within the scope of clinical trials").

These data are presented annually to the French President.

In 2020, 58,198 patients were included in a clinical trial (Table 27):

- 28,275 patients in a therapeutic clinical trial;
- 78% were enrolled in academic trials;
- 52,292 patients in clinical trials addressing solid tumours;
- 5,906 in haematology.

Childhood and adolescent cancers were a priority of the third Cancer Control Plan and continue to be a priority of the 2021-2030 Cancer Control Strategy:

2,335 inclusions concerned children in 2020, with 94% included in academic trials;

1,929 inclusions concerned adolescents and young adults, with 88% enrolled in academic trials.

Another indicator closely monitored by the Cancer Control Strategy is the inclusion of elderly subjects. In 2020, 4,130 inclusions concerned patients over 75 years of age in total, 87% of these being included in academic trials.

■ **TABLE 27**
MAIN RESULTS OF CLINICAL CANCER RESEARCH ACTIVITY SURVEY IN 2020

	Academic	Industrial	TOTAL 2020
Number of inclusions	20,497	13,972	58,198
Number of inclusions in therapeutic clinical trials	20,497	7,778	28,275
Number of inclusions in clinical trials in solid tumours	39,630	12,662	52,292
Number of inclusions in clinical trials in haematology	4,596	1,310	5,906
Number of inclusions of children (0-18)	2,203	132	2,335
Number of adolescent and young adult inclusions (15-25)	1,704	225	1,929
Number of elderly adult (≥75 years old) inclusions	3,577	553	4,130

“PHARE” and “SIGNAL” national clinical breast cancer trials sponsored by INCa: availability of this collection and its associated data

INCa is the sponsor of PHARE and SIGNAL, two national clinical trials on breast cancer which have included 11,846 patients and collected approximately 80,000 biological samples.

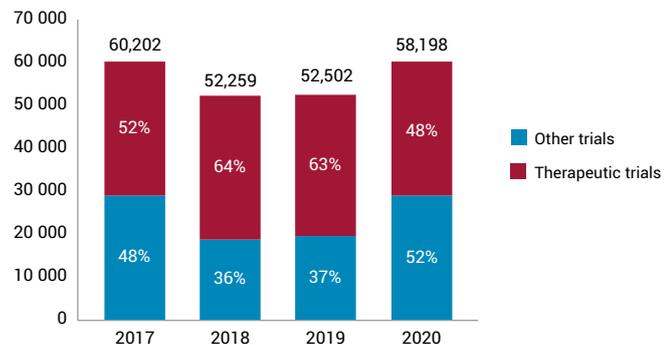
These clinical trials were closed in 2020 and INCa placed PHARE/SIGNAL collection on the CODECOH website of the French Ministry of Higher Education, Research and Innovation on 8 November 2021.

Since 2020, INCa has chosen to make this PHARE/SIGNAL collection and its associated data available to the scientific community to foster the development of breast cancer research projects. Any research project involving the use of PHARE/SIGNAL data and samples should be submitted to INCa after filling a request form, available on INCa’s website, and will be reviewed by the trial steering committee.

The results of INCa’s annual survey in 2020 show a steady increase in the number of patients enrolled in clinical trials for the last 11 years between 2009 and 2020:

- There is a 10.8% increase in the number of patients enrolled in 2020 compared to 2019, with 58,198 patients included in cancer clinical trials in 2020.
- The ratio of therapeutic trials grew significantly from 51.8% to 62.6% between 2017 and 2019 and decreased slightly by 14% in 2020 (Figure 43).

■ **FIGURE 43**
DISTRIBUTION OF CANCER CLINICAL TRIALS ACCORDING TO THERAPY
OVER THE 2017-2020 PERIOD



- Over the last 12 years (2009-2020), the number of patients enrolled in cancer clinical trials more than doubled, probably due to the Actions of the different Cancer Control Plans (Figure 44);
- The ratio of enrolment in academic versus industrial trials remained stable over the years, with a significant majority of inclusions in academic trials (76% versus 24%). However, between 2009 and 2020, greater growth was observed in academic trials (+ 107%) than in industrial trials (+ 55%) (Figure 44);
- The distribution among the different care providers is quite similar over the years: in 2020, 52% of the patients were enrolled in University Hospitals, 36% in Cancer Care Centres, and 12% in Health Care Centres (Figure 45).

FIGURE 44
GROWTH OF PATIENTS ENROLLED IN CANCER CLINICAL TRIALS (2009-2020)

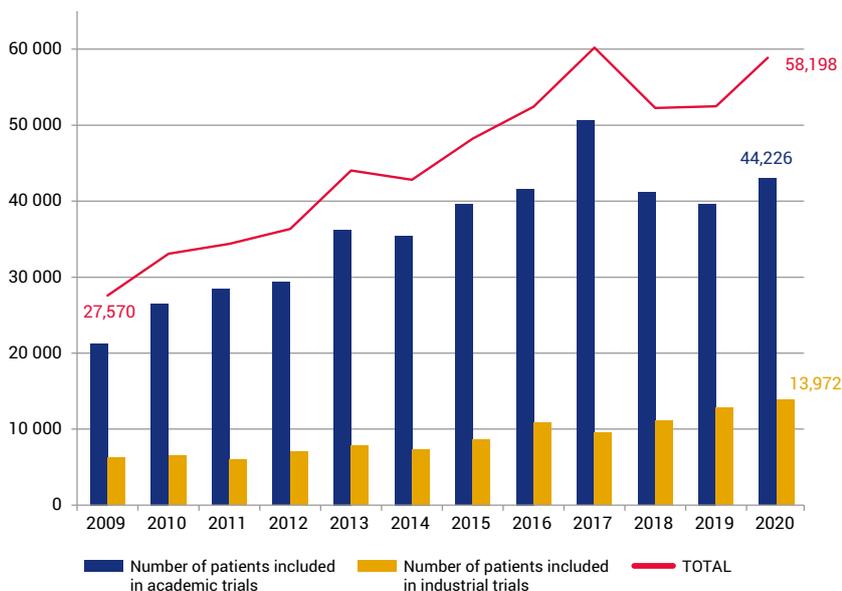
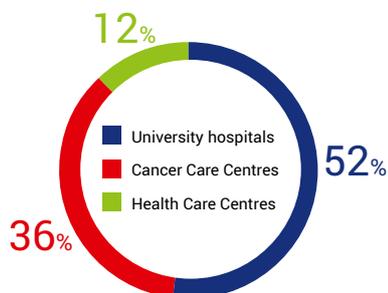


FIGURE 45
DISTRIBUTION OF PATIENTS ENROLLED IN CANCER CLINICAL TRIALS AMONG DIFFERENT CARE PROVIDERS IN 2020



2020: 58,198 patients recruited in cancer clinical trials, including 28,275 in therapeutic trials

- 52,292 patients in clinical trials in solid tumours and 5,906 trials in haematology
- 2,335 children enrolled
- 1,929 adolescents and young adults enrolled
- 4,130 patients are over 75 years
- 1,408 clinical research staff assigned to clinical cancer research.

Furthermore, this survey analysed the staff involved in clinical cancer research activities. The results show that 1,408 members of clinical research staff (full-time equivalent) were assigned to clinical cancer research in 2020 with 49% concentrated in University Hospitals.

Over the last 12 years (2009-2020), there was a constant increase in the number of clinical cancer research staff (+ 139% between 2009 and 2020).

INCA'S CANCER CLINICAL TRIAL REGISTRY

Since 2007, INCa's cancer clinical trials registry has allowed easy access to cancer clinical trials conducted in France. It is freely accessible on INCa's website, and provides high-quality and regularly updated information to patients, health professionals and the general public.

The INCa cancer clinical trials registry provides information accessible to the general public, and facilitates the search and selection of clinical trials. Visitors to the clinical trials registry can, with the help of a multicriteria search engine, accurately target their search using different selection criteria, such as the sponsor or target organ, and can also apply the geographic criterion using the geolocation module included in the registry.

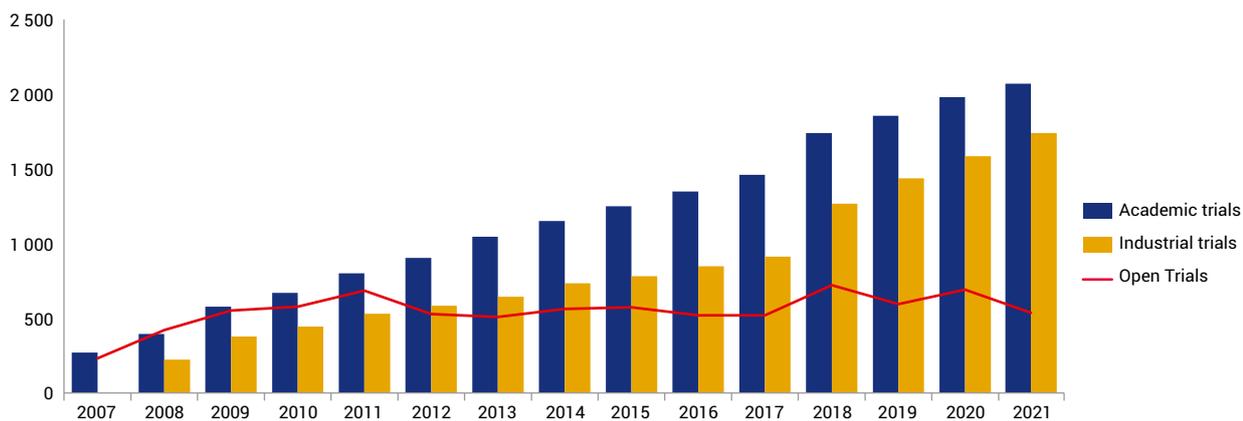
As part of a website redesign, the future pages of the registry need to evolve in order to improve browsing for users and it will offer the possibility of importing information about posted clinical trials in a workable format.

■ **TABLE 28**
INCA'S CANCER CLINICAL TRIALS REGISTRY

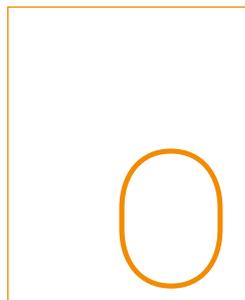
Objectives	Provide information on cancer clinical trials conducted in France.
Results	3,780 clinical trials advertised on INCa's website in December 2021, sponsored by more than 441 industrial and academic bodies. <ul style="list-style-type: none"> ● 596 ongoing recruiting trials. <ul style="list-style-type: none"> - 55% are sponsored by academic bodies. - 80% therapeutic trials.

INCa has developed a new database for the registration and administering clinical trials. This new portal will be accessible online for academic and industrial sponsors of cancer clinical trials to allow them to register their trials directly on the webpage of the new database.

FIGURE 46
NUMBER OF CLINICAL TRIALS IN THE REGISTRY PER YEAR (DECEMBER 2021)



RESEARCH IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY AND PUBLIC HEALTH



One of INCa's goals is to bring human and social sciences, epidemiology, and public health research on cancer in France up to the best international standards. Particular efforts are being devoted to increasing basic and health intervention research. Specific emphasis is placed on reducing social inequalities related to cancer, as well as increasing the impact of cancer prevention measures, participation rates in national screening programmes, and access to care.

In 2021, support for human and social sciences, epidemiology and public health applied to cancer research amounted to:

€17.91M

€5.50M

dedicated to support investigator-driven projects (PLSHS programme);

€8.67M

to support thematic research programmes such as population health intervention research and environmental cancer risks factors;

€3.74M

to support cancer research training.



Research programme for human and social sciences, epidemiology, and public health applied to cancer (PLSHS-E-SP)

The role of human and social sciences, epidemiology and public health (HSS-E-PH) in cancer research is reaffirmed in the 10-year cancer control strategy. The objectives of several measures of the strategy are based on advances that need to be made through HSS-E-PH research including prevention with a personalised approach as well as research into risk and protective factors for cancer. Indeed, although major medical progress has been achieved in cancer screening and treatment, questions remain on the social perceptions that populations have of cancer, screening barriers, environmental factors (e.g. exposome issue) and health risk behaviours, particularly persistence in smoking habits and heavy alcohol consumption, which are responsible for a large number of cancers.

Progress is also needed to improve the care pathway, through a better understanding of issues such as the sharing and appropriation of knowledge by caregivers and patients, better focused and adapted interventions, the quality of life of patients and relatives, treatment acceptability, health entitlements and ethics, etc. Finally, public health issues involve many research questions, so that the translation of knowledge into action can operate effectively, for the benefit of all, nationwide.

THE PROGRAMME IN 2021

In 2021, 19 projects were selected out of the 87 projects submitted, for a total funding of €5.5M (Table 29).

■ **TABLE 29**
FEATURES OF THE HSS-E-PH PROGRAMME IN 2021

Objectives	<ul style="list-style-type: none"> ● To enable the implementation of original research projects, in their endpoints and approaches, and scientific excellence in the different disciplines of HSS-E-PH applied to cancers; ● To stimulate research on emerging and innovative subjects, in order to open up new perspectives in our understanding of the challenges of cancer in the human and social sciences, epidemiology and public health; ● To develop and strengthen multidisciplinary scientific research by bringing together researchers from different disciplines around a precisely defined question or objective to provide more relevant answers.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€5.5M
Proposals submitted	87
Projects selected	19
Selection rate	21.8%

Scientific facilitation:

2021: In order to promote and disseminate innovative knowledge on specific current and/or emerging themes, the Institute organised several events, including:

- an annual Intercancéropôles/INCa HSS event which is being perpetuated in particular to facilitate reflection and the creation of working groups on emerging themes;
- an inter-SIRIC/INCa seminar which aimed to highlight and promote interdisciplinarity projects encouraged by the collaboration of actors from different backgrounds.

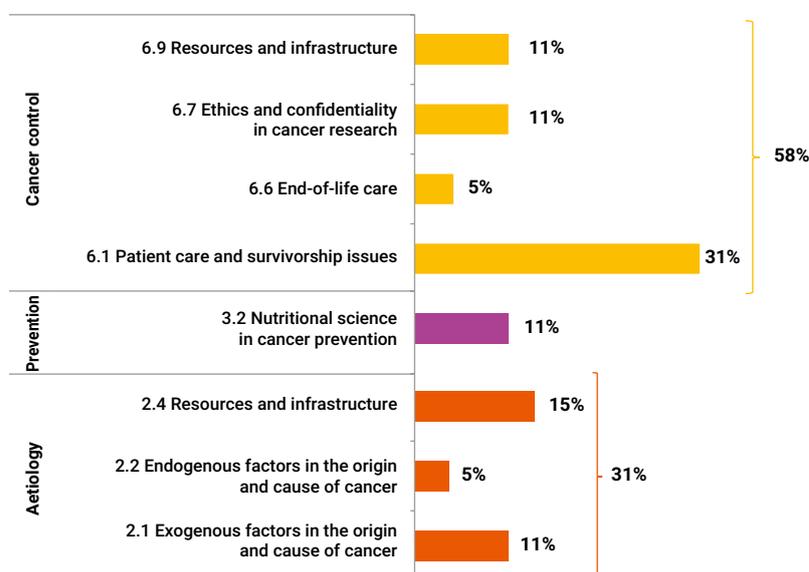
2021:
19
projects selected
for a total amount of
€5.5M

The topics of the 19 funded projects cover:

- risk factors for the development of cancer (6 projects);
- nutrition and Cancer (2 projects);
- patients and relatives' experience (3 projects);
- ethics (2 project);
- health system and public policy (1 project);
- palliative care and end-of-life care (1 project);
- inequities (4 projects).

Figure 47 shows the distribution of projects funded according to the CSO classification. The cancer control category is the largest (11 projects, representing 58%) with projects focusing on patient care (6 projects representing 58%), ethics and confidentiality (2 projects for 18%) and resources and infrastructure (2 projects for 18%). Aetiology represents 32% of funded projects with 6 projects, and prevention 10% with 2 projects.

FIGURE 47
DISTRIBUTION OF SELECTED PROJECTS IN 2020 ACCORDING TO THE CSO CLASSIFICATION



THE PROGRAMME OVER THE 2007-2021 PERIOD

Over the 2007-2021 period, 260 projects were funded for a total amount of €58.32M. With the exception of the first year where all projects were funded and thanks to a regular increase in the funding budget over the last few years, the selection rate has been quite stable over the years (25%) (Figure 48).

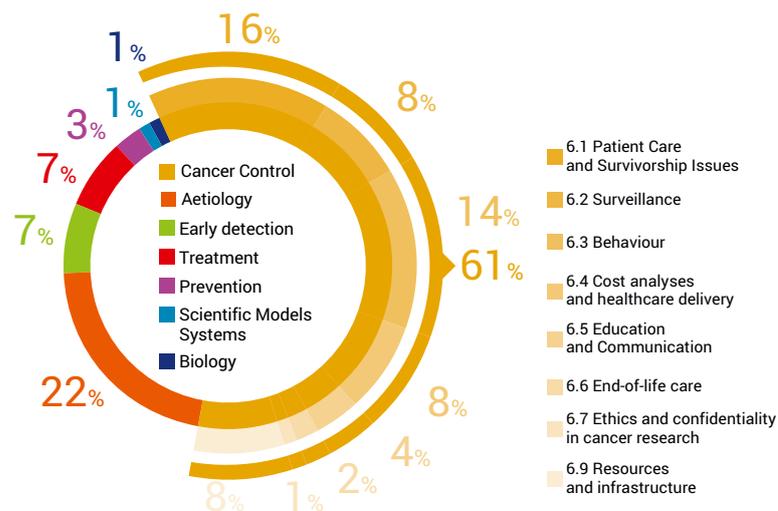
FIGURE 48
TRENDS IN SELECTION AND FUNDING OVER THE 2007-2021 PERIOD



Figure 49 presents the distribution of selected projects according to the CSO classification. In compliance with the objectives of this programme, the cancer control category represents 60% (patient care and survivorship issues and behavioural studies). Related to the epidemiology area of the programme, the aetiology category represents 22% of the selected projects.

In compliance with the objectives of the Ten-Year Cancer Control Strategy, projects addressing paediatrics, teenagers or young adults, as well as projects dealing with cancers with poor prognosis, supportive care or prevention are particularly welcomed.

■ **FIGURE 49**
THE DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



EVALUATION

In order to assess the added value of such a programme, INCa has launched a project to analyse the knowledge produced by the programme over the 2007-2020 period since its creation. In a few figures:

- 239 projects funded over the 2007-2020 period for a budget of €53M
- 156 completed projects will be analysed
- The analysis questions were co-constructed with an external service provider thanks to a €22K pilot project, accompanied by a scientific committee composed of 9 international experts
- 2 main areas of analysis have been determined, one descriptive and the other more qualitative

This project will be carried out in 2022 in partnership with another external service provider for a budget of €100k.

POPULATION HEALTH INTERVENTION RESEARCH PROGRAMME (PHIR) – STRENGTHENING THE SCIENTIFIC COMMUNITY

Since 2010, the French National Cancer Institute has been supporting population health intervention research (PHIR) with a dedicated call for proposals. This call selected 63 projects, including 19 emerging ones, for a total budget of €16.54M.

In order to support and strengthen the scientific community, INCa has organised several events:

PHIR Morning Webinar

In June 2021, a webinar was organised to boost the French PHIR scientific community and encourage interaction between researchers. The aim of this webinar was to promote the 10 projects selected in the 2020 edition which were presented by their respective PIs. Three thematic sessions were organised:

- Return to work and professional exposure;
- Pathways and accessibility to care;
- Interventions and impacts on the quality of life of patients and their entourage.

This event was attended by more than 100 participants: researchers, public actors and decision-makers, health professionals, students and other members of the PHIR community.

Participatory approaches: the place of beneficiaries

In June 2021, a webinar was organised in consultation with and for researchers in response to this community's needs. Indeed, the aim of this session was to address cross-cutting PHIR themes. Two round-table discussions were organised:

- The first one on the different points of view of PHIR actors regarding the challenges of participatory approaches:
 - Participatory and community approaches;
 - Collaboration between researchers and citizens; the partnership between researchers and operators.
- A second round-table discussion illustrated these remarks through 3 examples of prevention approaches (projects funded by INCa).

This event brought together more than 100 participants.

5th International French-speaking Conference on "Support systems for people affected by cancer and their entourage: contributions of PHIR"

Initially scheduled for March 2021, this conference was finally held on 29 and 30 November 2021 in Paris in a hybrid format. It brought together more than 200 participants over the two days with varied profiles: researchers, decision-makers, health professionals, field workers, patients, users, carers, expert patients, associations, etc.

This conference aimed to establish a picture of the knowledge produced on support and accompaniment systems for people affected by cancer and their relatives, and to identify new PHIR challenges in this area.

Over the two days, exchanges were organised in plenary sessions and workshops around 3 questions:

- What is the current picture of support systems?
- How is knowledge linked and partners managed?
- What are the prospects for PHIR to improve in the long term?

The plenary sessions are available on the event's website: (<https://colloque-risp-2021.fr/espace-numerique/>) and a special issue of a peer-reviewed scientific journal will be launched in 2022. This publication aims to continue the scientific reflection initiated over these two days. In this way, conference speakers and participants will have the opportunity to submit an abstract. This journal will be available at the end of 2023 and will be presented at the 6th International French-speaking Conference on PHIR.

Launch of the merged HSS-E-PH/PHIR programme

In 2021, a new design of this call for proposals was proposed (see PLSHS/RISP merger):

- Firstly, this call has been merged with a second historical call for proposals (investigator-driven HSS-E-PH projects)
- Secondly, it integrates 3 research priorities as defined by the Ten-Year Cancer Control Strategy:
 - Fighting against inequalities through a pragmatic approach adapted to different populations;
 - Mobilising to reduce cancers in children, adolescents and young adults;
 - Developing research on cancers with poor prognosis.

Launch of the call for applications to support two research networks in primary cancer prevention and health promotion

Improving cancer prevention is one of the priorities of INCa's Ten-Year Cancer Control Strategy. Primary prevention in France appears to be segmented, crossed by different approaches and insufficiently developed regarding its expected benefits for society. To address these challenges, in 2021, INCa launched a structuring call for applications to fund two research networks in primary cancer prevention and health promotion, for four years, with €1.6M each. These two structuring networks will make it possible:

- To increase the research skills in this field;

- To establish partnerships and to strengthen collaborations;
- To develop research questions and innovative scientific projects.

Supported by an international steering committee, this call for applications welcomes multidisciplinary research programmes building a continuum from aetiological research to interventional practice.

Submissions closed in October 2021 and the results will be announced in February 2022.

New research programme on Primary Prevention and Health Promotion

Strengthening primary cancer prevention research is necessary to help public health actors build their action plans. In line with this challenge, INCa's Ten-Year Cancer Control Strategy supports primary cancer prevention research and health promotion. In early 2022, a call for proposals for research in Human & Social Sciences, Epidemiology, Public Health and Interventional research addressing "Primary Prevention and Health Promotion" will be launched. Indeed, even though some cancer risk factors are now well-established and documented, innovative intervention models need to be developed to help populations adopt beneficial health behaviour. In the meantime, other factors are suspected of playing a role in cancer incidence,

and the data available are insufficient to understand the exposure of these factors and the ways to diminish them. Finally, long-term cancer prevention needs to set up favourable health environments and tackle determinants through a health promotion approach. Thus, in order to improve cancer prevention in France, this programme will aim to:

- Develop knowledge on risk factors and ways of reducing exposure ;
- Identify the determinants and environments favourable for health;
- Increase knowledge on interventions, their design, modes of intervention, evaluation, transferability, and implementation for the development of health-promoting environments and behaviours.

Supporting research addressing psychoactive substance abuse and addiction

Tobacco and alcohol are the leading causes of avoidable death in France. Tobacco consumption is responsible for 75,000 deaths per year, including 45,000 deaths from cancer (1 smoker out of 2 dies from the consequences of tobacco); alcohol is responsible for 41,000 deaths (15,000 of which are due to cancer); illicit drugs are responsible for 1,600 deaths each year⁹.

In order to fund tobacco control actions, a specific fund was set up in December 2016 within the National Health Insurance Fund (CNAM) and is notably financed by a tax on tobacco products. In 2019, the scope of intervention of this fund was extended to all psychoactive substances and became the Addiction Control Fund.

The governance of the fund is based on a Strategic Orientation Council (COS) chaired by the Director General of the National Health Insurance Fund and is composed of representatives of the National Health Insurance Fund associations involved in combatting addiction, public agencies or organisations in the field of health; administrations in the fields of health, research, education and justice.

This fund aims to perpetuate existing addiction control and prevention initiatives and is also an opportunity to propose funding of new initiatives, particularly in supporting research actions.

In 2021, the Addiction Control Fund allocated €14M to INCa and the Institute for Public Health Research (IReSP) to deploy research and intervention measures against addiction.

9. Observatoire français des drogues et des toxicomanies - <https://www.ofdt.fr/BDD/publications/docs/DCC2019.pdf>

Cancer Prevention Europe



Cancer Prevention Europe (CPE), a consortium of organisations across the whole of Europe, aims to reduce morbidity and mortality from cancer in European populations through prevention and earlier diagnosis of the disease.

This consortium aims to develop research at a European level and to disseminate knowledge and good practices. Coordinated by the IARC, the consortium is composed of 10 members (CRUCK, DCS, IEO, DKFZ, ICL, Karolinska Institute, Maastricht University, WCRFI and IARC).

This year, in the research area, the consortium worked on the management of several reviews of reviews, in particular on the use of connected objects in alcohol prevention, another on connected objects and prevention in the field of food as a protector against cancer. Other work has been initiated in this field and reflections on a position paper have been initiated.

PSYCHOACTIVE SUBSTANCES PROGRAMME

In the context of the Addiction Control Fund, INCa and IReSP are jointly in charge of a call for proposals to combat psychoactive substance use and addiction. This programme follows on from the “Tobacco INCa-IReSP” programme that was implemented in 2018 and 2019 and whose scope has been extended to all psychoactive substances.

This call for proposals aims to support research and to produce knowledge in the field of psychoactive substance use and the fight against addiction, in priority in relation to tobacco, alcohol and cannabis, identified as proven risk factors for cancer, but also in relation to other psychoactive substances as well as in relation to polyconsumption. It covers a wide range of disciplines, from intervention research, through human and social sciences, economic and political sciences, law, psychiatry, information and communication technologies, epidemiology, addictology and other public health disciplines.

This call for proposals is open to researchers as well as to health or other professionals who wish to engage in a research process. The teams can therefore be composed of researchers, health professionals, health prevention and health promotion professionals, user associations and decision-makers.

It is divided into 3 sections:

- Section 1 (INCa-IReSP): Psychoactive substances and general population;
- Section 2 (INCa): Psychoactive substances and cancer;
- Section 3 (IReSP): Psychoactive substances and diseases other than cancer.

Candidates can submit three types of proposals:

- “Full research proposals” (36 to 48 months – min. €100,000): projects that are advanced in their design and that are based on a controlled methodological approach and successful collaborations based, in particular, on data from pilot studies, emerging projects or feasibility assessments;
- “Pilot proposals” (18 to 24 months – max. €100,000): small-scale preliminary studies to determine the feasibility, time, cost and risks before conducting a similar project on a larger scale;
- “Emerging proposals” (12 to 18 months – max. €50,000): proposals aimed at developing research questions and intervention designs. This seed funding allows researchers and their partners to build a proposal that will be submitted (as a pilot proposal or a full proposal) to the next round of the call.

The programme in 2021

■ **TABLE 30**
FEATURES OF THE PSYCHOACTIVE SUBSTANCES PROGRAMME IN 2021
(SECTIONS 1 & 2)

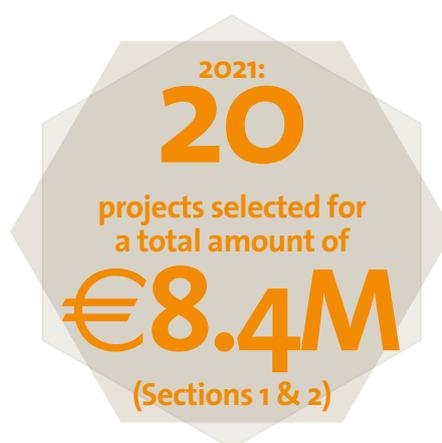
Objectives	To support research and to produce knowledge in the field of psychoactive substance use and the fight against addictions
Programming institution	INCa and IReSP
Operating institution	INCa and IReSP
Funding institution	INCa and IReSP
Funding	€8.4M INCa: €4.6M IReSP: €3.8M
Proposal submitted	42
Projects selected	20
Selection rate	48%

It is the first year the call was open to all psychoactive substances. More than half of the funded projects focus on tobacco (5 projects), alcohol (4 projects) or cannabis (2 projects), which are proven risk factors for cancer. The remaining funded projects focus on addiction mechanisms, polyconsumption and other substances.

Projects funded in Section 1 deal with diverse multidisciplinary research themes such as addiction mechanisms, treatment of substances use disorders, consumption pathways and risk factors for addiction.

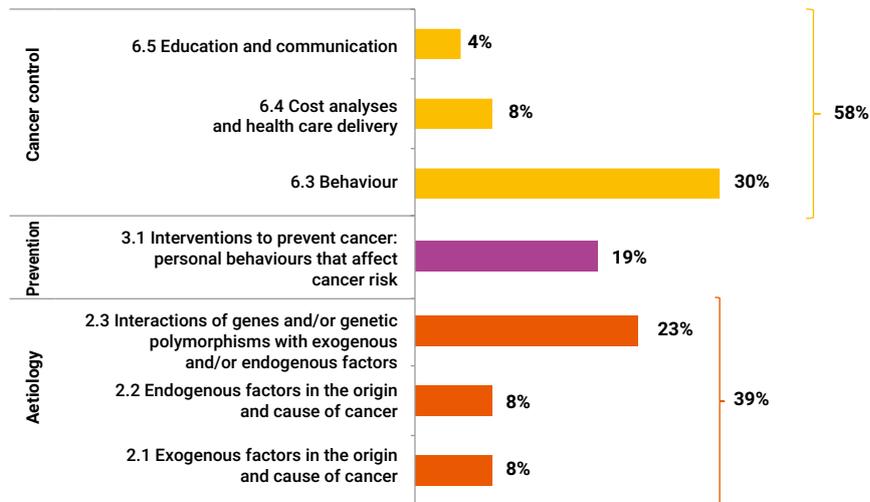
A total of 6 projects were funded in Section 2 (psychoactive substances and cancer), including 2 emerging projects and 3 pilot projects, underlying this field's dynamism. These projects address addiction in cancer patients, screening and care pathways for patients with addiction-related cancers and the link between substance use and cancer.

The programme over the 2016-2021 period



■ FIGURE 50

DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PSYCHOACTIVE SUBSTANCES PROGRAMME IN 2021 (SECTIONS 1 & 2)



2016-2021:
70
projects selected for
a total amount of
€29.5M

Over the past five years of calls for proposals in the fight against tobacco and psychoactive substances, INCa has co-financed 70 projects for a total budget of €29.5M, including 54 projects exclusively funded by INCa for a total budget of €21.1M).

■ TABLE 31

TRENDS IN SELECTION AND FUNDING OF TOBACCO AND PSYCHOACTIVE SUBSTANCES PROGRAMMES OVER THE 2016-2021 PERIOD

Year	2016	2017	2018	2019	2021	Total
Funding (in €M)	3,52 ¹	5,66 ²	5,86 ³	6,06 ³	8,37 ³	29,47
Proposals submitted	21	22	44	31	42	160
Projects selected	7	11	16	16	20	70
Selection rate	33%	50%	36%	52%	48%	44%

¹Co-funding INCa/ ARC Foundation /National Cancer League

²Co-funding INCa/ National Cancer League

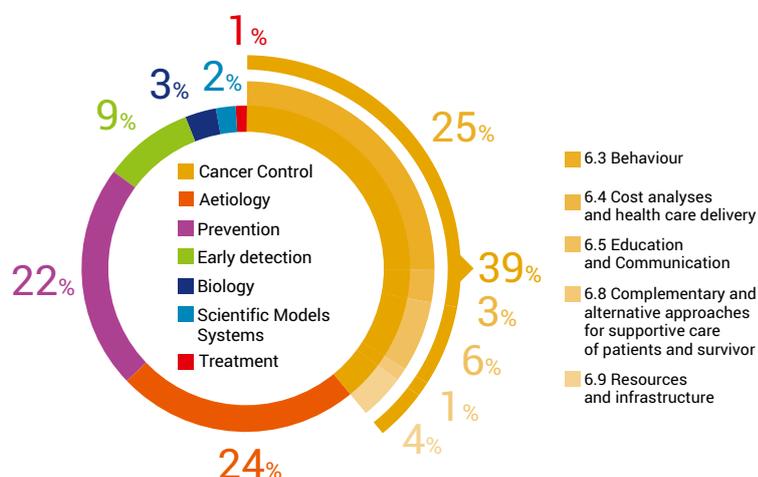
³Co-funding INCa/ IReSP

The programme has evolved significantly over the past 5 years. Initially focused on tobacco, the extension of its scope to all psychoactive substances in 2021 has led to the creation of a new call for proposals in line with the priorities of the Addiction Control Fund.

By supporting projects relating to all psychoactive substances, the programme has made it possible to structure research in the field of addiction (continuity of research teams, multidisciplinary projects and cross-cutting dimension of addiction) and address public health issues, such as polyconsumption or health inequalities.

The increase in the number of proposals submitted and the growing mobilisation of researchers on the theme of addiction underline the scientific community's commitment to this issue with international stakes.

FIGURE 51
DISTRIBUTION OF FUNDED PROJECTS OVER THE 2016-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



Call for applications for “Research Chair in Human and Social Sciences and Public Health on Tobacco and cancer prevention”

In 2021, the Institute launched a new call for applications dedicated to the creation of a Research Chair in Human and Social Sciences and Public Health on “Tobacco and cancer prevention”.

The objective of this chair is to support promising or emerging themes in tobacco research and to bring together researchers around the chairholder. The Chair programme may address cross-cutting issues (combating health inequalities, taking into account vulnerable and specific populations,

etc.) and/or be part of an intervention or community-based approach. Applicants are expected to propose both a scientific research programme and a teaching programme.

This call for applications was prepared in 2021 based on an analysis of the scientific literature and in co-construction with the members of the scientific evaluation committee. The Institute will support the funded application over 5 years for a total amount of €750,000.

PSYCHOACTIVE SUBSTANCES PHD PROGRAMME

INCa’s support for research addressing psychoactive substance use and addiction includes a dedicated call for PhD applications. Based on the same model as the call for proposals, the call for applications for PhD grants is jointly managed with the Institute for Public Health Research (IReSP) and is open to all psychoactive substances and is divided into three sections:

- Section 1 (INCa-IReSP): Psychoactive substances and general population;
- Section 2 (INCa): Psychoactive substances and cancer;
- Section 3 (IReSP): Psychoactive substances and diseases other than cancer.

The programme covers all aspects of research, as well as a broad array of disciplines, ranging from clinical research to public health, and including information and communication technologies, economic and political science, human and social sciences, law, biology, and epidemiology.

Aimed to support PhD students with a 3-year grant, this call for applications targets all students with a Master’s degree in human and social sciences, public health, epidemiology, or biology, enrolled in first or second year in a doctoral school.

The 2021 round of the call was a success with 32 applications submitted:

- 14 in human and social sciences;
- 12 in neurosciences;
- 5 in public health;
- 1 in biology.

The programme in 2021

■ **TABLE 32**
FEATURES OF THE PSYCHOACTIVE SUBSTANCES PHD PROGRAMME IN 2021

Objectives	To support PhD research and to produce knowledge in the field of psychoactive substance use and the fight against addiction
Programming institution	INCa and IReSP
Operating institution	INCa and IReSP
Funding institution	INCa and IReSP
Funding	€977,462
Proposal submitted	32
Projects selected	8
Selection rate	25%

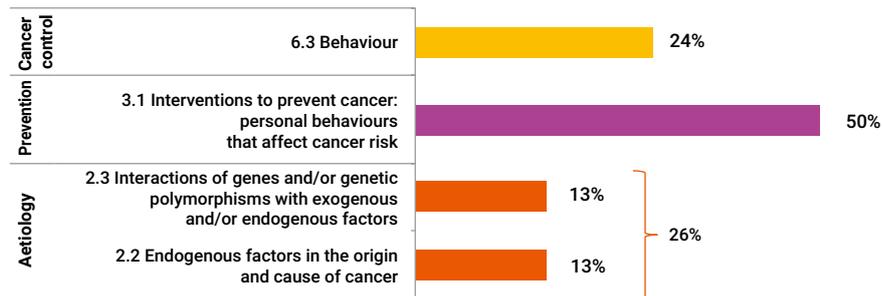
8 PhD students were selected and are funded by INCa (4 applicants) and IReSP (4 applicants). The 4 PhD thesis projects funded by INCa concern:

- Factors associated with first use of alcohol, tobacco, and cannabis in junior high school and persistence of use at one-year follow-up;
- Hypersensitivity: a vulnerability factor in addictive behaviours;
- Study on the effectiveness of virtual reality in the treatment of alcohol use disorder;
- Contribution of the amygdala-subthalamic pathway in emotional processes related to drug taking in a social context in rats.

All the funded PhD thesis projects fell under Section 1. It is the second year the call was open to all psychoactive substances. More than a third of the funded PhD projects focus on proven risk factors for cancer (2 projects on tobacco, alcohol and cannabis; 1 project on alcohol). The other funded PhD thesis projects focus on addiction mechanisms and on cocaine.



■ FIGURE 52

DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PSYCHOACTIVE SUBSTANCES PHD PROGRAMME IN 2021**The programme over the 2019-2021 period**

Over the past three years of calls for PhD applications in the fight against tobacco and psychoactive substances, INCa has financed 20 PhD thesis projects for a total budget of €2.3M.

■ TABLE 33

TRENDS IN SELECTION AND FUNDING OF THE TOBACCO AND PSYCHOACTIVE SUBSTANCES PHD PROGRAMMES OVER THE 2019-2021 PERIOD

Year	2019	2020	2021	Total
Funding (in €)	323,092 ¹	999,166 ¹	992,225 ¹	2,314,483
Proposals submitted	4	27	32	63
Projects selected	3	9	8	20
Selection rate	75%	33%	25%	44%

¹Co-funding INCa/IReSP

2019-2021:
20
PhD thesis projects selected for
a total amount of
€2.3M

The programme has evolved significantly over the past 3 years and now has a strong profile. Initially focused on tobacco, the extension of its scope to all psychoactive substances in 2020 has led to the creation of a new call for applications in line with the priorities of the Addiction Control Fund.

The increase in the number of PhD projects submitted and the growing mobilisation of PhD students in the area of addiction underline the commitment the junior scientific community to this issue.

PROGRAMME FOR JUNIOR RESEARCHERS IN TOBACCO AND/OR ALCOHOL

In 2020, INCa launched an innovative programme aimed at junior researchers who have obtained a PhD thesis over the past ten years and have an interest in tobacco and/or alcohol research, with an ambition to propose innovative ideas in the field of research in human and social sciences, public health and intervention research. This will help reduce the risks of cancers associated with these psychoactive substances.

Its objective is to identify the ways in which researchers working on subjects and fields of research other than tobacco and/or alcohol can take up these themes and, thus, participate in their progress by proposing new models, approaches, methodologies and scientific protocols.

It is aimed at supporting research related to tobacco and/or alcohol through a collaborative system of initiatives led by junior researchers, and developing a scientific community around these themes.

This call for applications is organised in three steps:

- pre-selection of candidates based on letters of intent;
- development of proposals including participation in a collaborative seminar;
- selection of candidates based on proposals and interviews.

The programme's first round in 2021 was a success, with 26 applications submitted and 13 applications pre-selected for the second stage of the call. Almost half of the pre-selected applications (6) were projects relating to population health intervention research, highlighting the fact that junior researchers are keen to devote themselves to this type of research that the Institute is seeking to foster.

The 13 pre-selected applicants participated in a collaborative webinar to help them finalise their proposals. During this webinar, the applicants presented their proposals and could exchange with other applicants and three guest experts.

8 junior researchers were selected for funding:

- video Intervention to Reduce Pregnancy Smoking Stigma (VI-PSS);
- focus on Cannabidiol (CBD) to reduce alcohol consumption: a qualitative approach;
- smoking in people with mental health problems: survey within dedicated healthcare and social support structures for adolescents living with mental health problems;
- motivating and implementing the reduction of alcohol consumption among different populations: an intervention that combines growth mindset and implementation intentions;

- Assessment of tobacco smoking and alcohol drinking and treatment outcomes among patients with lung or head and neck cancer;
- Determinants of tobacco and alcohol consumption and related social inequalities in Guadeloupe;
- Validation of the Cannabis Abuse Screening Test in General Practice;
- Promoting recovery from alcohol use disorder with a positive psychology intervention.

■ **TABLE 34**

FEATURES OF THE PROGRAMME FOR JUNIOR RESEARCHERS IN TOBACCO AND/OR ALCOHOL IN 2021

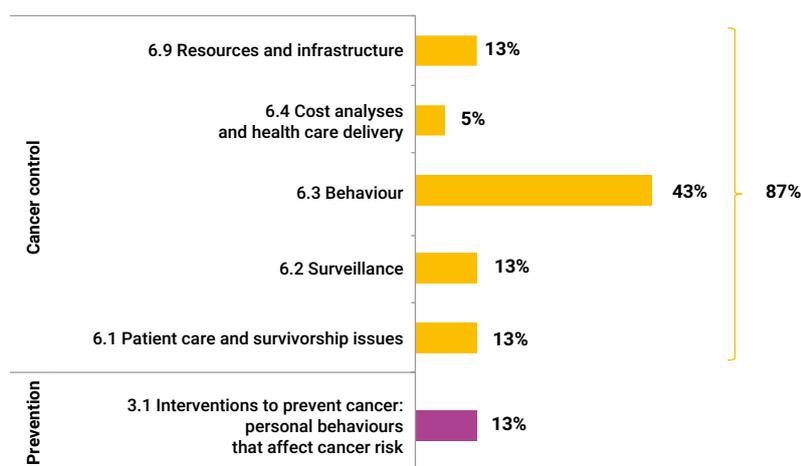
Objectives	<ul style="list-style-type: none"> ● To support research on tobacco and/or alcohol in Public Health and Human and Social sciences ● Develop the French scientific community around these topics
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€735,326
Proposal submitted	26
Projects selected	8
Selection rate	31%

For this first year of the programme, the distribution of funded projects by discipline is balanced, with half of the projects in Public Health and the other half in social sciences. The themes of these research projects are diverse in terms of substance studied:

- 5 of the funded projects study a single substance: 2 projects on tobacco, and 3 projects on alcohol;
- 3 projects study several substances: 2 projects on tobacco and alcohol, and 1 project on tobacco and cannabis.

Examples of research questions are: determinants of consumption, addiction management and quality of life, and 3 projects include population health intervention research.

■ **FIGURE 53**
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PROGRAMME FOR JUNIOR RESEARCHERS IN TOBACCO AND/OR ALCOHOL IN 2021



Webinar on E-cigarettes and new tobacco products: research prospects

The Ten-Year Cancer Control Strategy emphasises the need to continue and encourage support for research on e-cigarettes, vaping and ENDS, particularly in terms of measuring their effectiveness as tobacco cessation aids and their health impacts over the long term.

In December 2021, INCa organised a webinar on the theme “E-cigarettes and new tobacco products: research prospects”. It promoted the dissemination of knowledge on the topic of electronic cigarettes and new tobacco products, addressing various issues related to their use, including impacts on health and consumption pathways.

It addressed cross-cutting aspects related to the use of these products, included presentations of the first findings of research projects funded by the Institute on this topic, and helped a space for discussion and knowledge-sharing between researchers from various disciplines, stakeholders in the field, and policymakers interested in this theme. This day also provided an opportunity to mobilise the scientific

community around the topic with a view to organising an international conference on e-cigarettes to be held in December 2022 in Paris.

Investigators from INCa-funded projects were invited to present their first findings, methods and research prospects. In addition, three institutional interventions were organised:

- on French and European regulations on these products and their chemical composition
- on the recommendations of the French High Council of Public Health related to electronic cigarettes;
- on research in the United States on this topic, which provided an international perspective.

This webinar also provided an opportunity to present the first findings of a systematic literature review on the perception of e-cigarettes, comparing smokers and non-smokers of e-cigarettes. Conducted by the Institute, this study has been selected for a poster presentation at the SRNT conference in Baltimore (March 2022).

This event included 13 speakers and about 150 participants over one day.

Support for research on environmental risk factors

CHLORDECONE AND PROSTATE CANCER IN THE FRENCH ANTILLES

Chlordecone is an organochlorine insecticide used in the French Antilles (Guadeloupe and Martinique) from 1972 to 1993 to control the banana root borer. This highly stable persistent organic substance detected in soils is likely to contaminate certain vegetable or animal foodstuffs as well as aquatic environments. In addition, surveillance data show that the incidence rate of prostate cancer is higher in the French Antilles compared to Mainland France.

Therefore, the question has been raised whether exposure to chlordecone, both in banana plantation workers and in the general population through food, water, and air, could lead to an increased risk of prostate cancer development.

In this context, and following a request from the French Ministry of Health, INCa has set up a call for applications for an integrated and multidisciplinary cross-cutting research programme to better understand the link between chlordecone exposure and prostate cancer. This call for applications was built in collaboration with a scientific committee composed of national and international experts and with a support committee composed of French public bodies, national and local agencies and think tanks concerned by the issue.

In 2020, INCa launched the call for applications. It was organised into two phases:

1. Selection of researchers to set up a multidisciplinary research consortium (2020);
2. Co-building and submission of a finalised research programme, by the consortium (2021).

A scientific evaluation committee was set up in 2020, composed of ten multidisciplinary experts: the national and international experts from the committee, who were in charge of the initial recommendations, and additional experts from human and social sciences fields.

Ten applications among the eleven received were eligible and reviewed by the scientific evaluation committee. Four researchers were selected to be part of the consortium and their expertise covers the fields of epidemiology, biology and toxicology, human and social sciences, and knowledge of the French West Indies. The scientific evaluation committee recommended that the selected applicants consider adding the following expertise:

- Risk perception and risk communication;
- Assessment of current or past occupational, domestic or environmental exposure to pesticides or similar contaminants.

In response to this recommendation, the selected applicants submitted a proposal to include an additional expert in human and social sciences in the consortium, and to call for an adviser concerning exposure assessment.

The scientific committee approved this proposal, and thus the consortium was finalised in April 2021, made up of five multidisciplinary experts.

Once set up, the consortium members co-built the research programme. Five working seminars were organised for this purpose, including meetings with Santé publique France and Anses.

In September 2021, the consortium members submitted a preliminary research programme. The committee discussed the programme with the consortium and produced recommendations. Taking into account these recommendations, in October 2021, the consortium submitted a final version which was presented and discussed with the support committee.

With a budget of €3.45M, this research programme covers four work areas:

1. Study of pre-existing data (2010-2019) from the general cancer registries and from exposure assessment mapping;
2. Set-up of a new epidemiological case-control study in Martinique;
3. Study, in Martinique and Guadeloupe, of individual experiences, social mobilisations and institutional arrangements related to contamination by pesticides, including chlordecone;
4. Evaluation of the distribution of chlordecone in blood, fatty tissue and prostate tissue, as well as the effects of chlordecone exposure on markers of prostate cancer aggressiveness.

In November 2021, the Institute organised a kick-off seminar to present the consortium's research programme. This seminar also gave the floor to renowned environmental health experts from the international scientific committee. The conference ended with the consortium members discussing the issues related to this research. Over 120 participants attended this bilingual French-English seminar, one third of whom were from the French West Indies; attendees were evenly distributed between researchers, associations and administrative professionals.

Contribution to the chlordecone IV plan (2021-2027)

The research programme on chlordecone and prostate cancer led by the multidisciplinary consortium is part of the chlordecone IV plan, launched in 2021. It corresponds to the 12th measure of the research area of the plan.

Cancer conferences and environmental exposures

The French National Cancer Institute regularly presents its actions in support of environmental health research and communicates on the challenges of this field in the fight against cancer. In 2021, the Institute communicated in particular on the exposome concept and its challenges for cancer research, at the Fondation de l'Académie de Médecine and at the Cancéropôle Grand Ouest conference.

NATIONAL AND EUROPEAN WORKING GROUPS

With the new Ten-Year Cancer Control Strategy, the Institute has strengthened its involvement in structuring and promoting French research around environmental and occupational factors, and around incorporating the exposome concept. In this respect, several major actions have been undertaken since 2021.

INCa has expressed its support for a national and European programme on the exposome. This programme, entitled "France exposome" and headquartered in the Institute for Health, Environment and Work (IRSET, Rennes), is part of the 4th National Environmental Health Plan. It is a health biology infrastructure aimed at structuring and energising the scientific community, providing a scientific, methodological and technical service for research teams working in the environment-health field on the theme of the human chemical exposome, providing a basis for the Institute's research projects in particular. The Institute is represented on the strategic orientation and operating council of France Exposome.

The Institute has joined the French Hub of the European PARC partnership, coordinated by Anses, selected for funding by the European Union's "Horizon Europe" framework programme for 2021-2027. This follow-up will allow the expression of possible needs and ensure a link with the research financed by the Institute in this area. In addition, INCa is promoting the development of new, more holistic risk assessment approaches in its calls for proposals, such as exposure to substances and mixtures, combined factors, and the perception of these subjects by the population.

The Institute is participating in the national governance body for the research actions included in the chlordecone IV plan, launched in February 2021. This is the national scientific steering committee for chlordecone, composed of scientific experts, representatives of scientific alliances, ministries, and public health agencies.

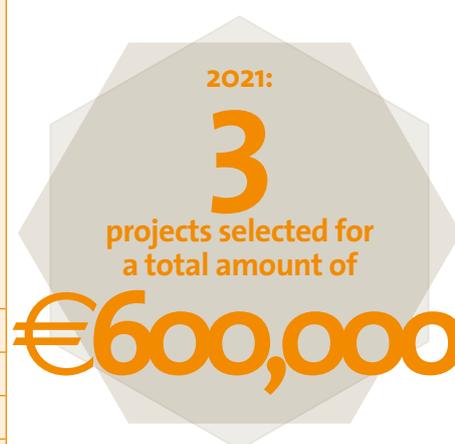
SUPPORT FOR THE NATIONAL ENVIRONMENTAL AND OCCUPATIONAL HEALTH RESEARCH PROGRAMME (PNR-EST) OF THE FRENCH NATIONAL AGENCY FOR FOOD, ENVIRONMENTAL AND OCCUPATIONAL HEALTH AND SAFETY (ANSES) BY ITMO CANCER-AVIESAN

This multi-agency programme addresses various public health issues related to the environment and workplace. ITMO Cancer-Aviesan has been funding cancer-related projects within this programme since 2011 (in 2010, INCa funded 8 PNR-EST projects in the first year of the partnership with Anses on cancer).

The programme in 2021

■ TABLE 35
FEATURES OF THE PNR-EST PROGRAMME IN THE CANCER FIELD IN 2021

Objectives	<ul style="list-style-type: none"> ● To evaluate the risk of cancer linked with exposure to potential carcinogens in the general population or at work. ● To analyse the effects of low-dose or cumulative exposure to CMRs on cancer risks. ● To identify environmental or occupational cancer risk factors. ● To analyse gene/environment/behaviour interactions in cancer risks. ● To develop cost/benefit assessment methods for cancer prevention or care. ● To identify and validate biomarkers allowing cancer risk estimation in occupational or environmental settings.
Programming institution	Anses
Operating institution	Anses
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€600,000
Projects funded	3



In 2021, 3 projects were selected for funding by ITMO Cancer-Aviesan for a total of €600,000. The projects focused on:

- evaluating exposures to endocrine disruptors and their link with several diseases including breast cancers;
- evaluating environmental ionising radiation exposures and their link with lung, breast, colon and prostate cancers;
- characterising the synergistic effects on breast tumorigenesis of endocrine disruptors with known (polycyclic aromatic hydrocarbons) or suspected (organophosphorus esters) carcinogenic effects.

The programme over the 2010-2021 period

Since 2011, 50 projects related to cancer have been funded by ITMO Cancer Aviesan within the framework of this programme for a total amount of €8.0M. In accordance with the objectives of the call, more than 80% of the funded projects addressed the aetiology of cancer, namely exogenous factors in the origin and cause of cancer, and interactions of genes or polymorphisms with exogenous or endogenous factors.

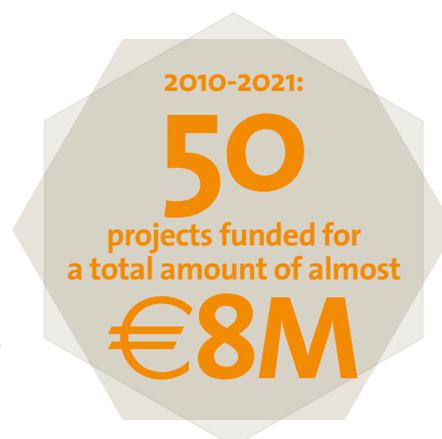
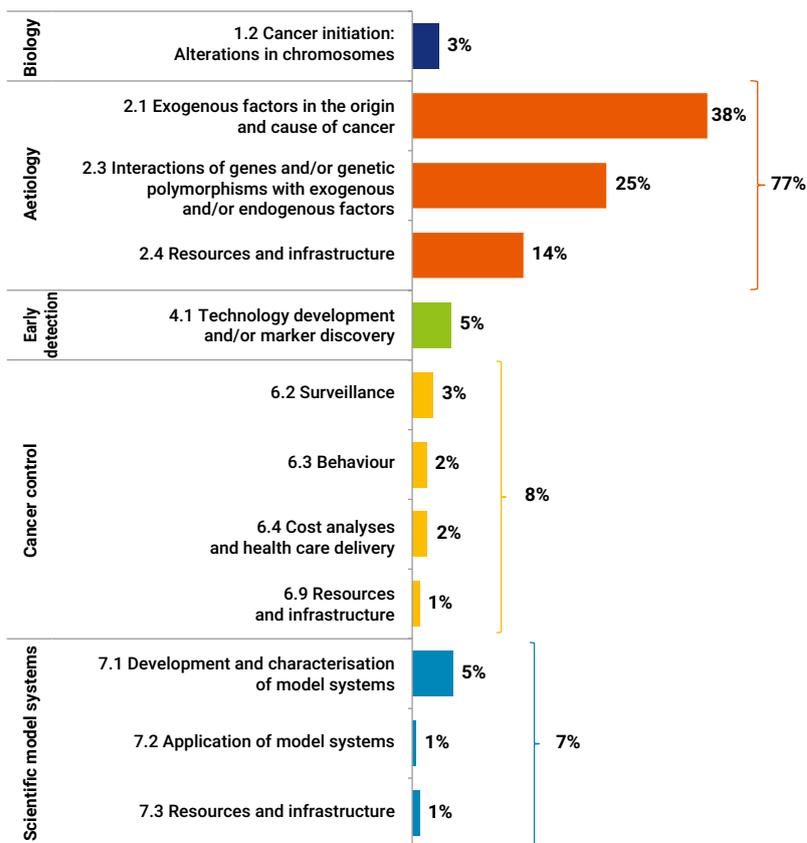


FIGURE 54
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PNR-EST PROGRAMME OVER THE 2010-2021 PERIOD ACCORDING TO THE CSO CLASSIFICATION



ITMO Cancer-Aviesan programme for “Environmental risk factors exposure and cancer” (K-Env) and support for the PNR-EST programme: promoting complementarity

Over the 2012-2017 period, ITMO Cancer-Aviesan funded research on cancers linked to environmental exposures via its K-Env programme (43 projects) and via the Anses PNR-EST programme (32 projects).

The comparison shows the complementarity between the two programmes, as well as their specific features:

- Only PNR-EST supported purely descriptive epidemiological studies or research in human and social sciences. The other fields were mainly shared between the two programmes;
- The communities were in mostly separate, as three-quarters of the PNR-EST awardees in the field of cancer did not submit any proposals to K-Env, and only 6% were successful candidates for K-Env;
- Fundamental research was more present in K-Env (77% vs 56%), whereas PNR-EST supported more epidemiological research (34% vs 23%) and projects in social sciences (10% of the projects);
- Chemical risk factor studies were predominant in both programmes (almost 60% of the projects),

but physical risks were studied to a greater extent in K-Env (12% vs 3%), while PNR-EST supported more projects on co-exposure to different types of factors (25% vs 19%);

- Both programmes led to new tools and knowledge in relation to mechanisms, but only PNR-EST resulted in the description of links between exposures and cancers and led to socio-economic insights;
- Given the multidisciplinary nature of the field, the findings were published in journals in a variety of domains for both programmes. There were differences, however, namely with five times more articles in multidisciplinary journals for K-Env (35% vs 7%), and three times more publications in public health journals for PNR-EST (23% vs 8%). The publication rate per project was similar (1.3 and 1.6 for K-Env and PNR-EST, respectively).

This comparative analysis showed the appropriateness of ITMO Cancer-Aviesan’s decision to continue supporting PNR-EST while programming its own call for proposals dedicated to the theme of “Cancer and environment”.

Support for professional careers and training

RESEARCH CHAIRS

Chair in health democracy / empowerment

In 2020, the Institute launched a call for applications for the creation of a new chair of excellence in human and social sciences entitled “Health democracy/ empowerment: involving citizens and people affected by cancer”, in partnership with Aix-Marseille University, the Paoli-Calmettes Institute, and the CANBIOS team (Cancers, Biomedicine and Society) at UMR1252 SESSTIM (Economic and Social Health Sciences and Information Processing). Based on the scientific evaluation committee recommendations, no proposals were selected, and the call for applications was renewed in 2021.

The overall objective of this research chair is to develop research in human and social sciences around health democracy and empowerment in of cancer care. This objective is aligned with the partners’ research priorities and aims to bridge a gap in research that has developed in this field, particularly in France.

The grant provided by the Institute for the chair is €750,000 for five years. The local partners will provide the necessary work infrastructure and will allocate €300,000 in salaries for post-doctoral researcher(s) and doctoral contract(s). Also, in order to ensure continuity of research and teaching on this theme after the five-year period of the chair, Aix-Marseille University will make every effort to maintain the Chairholder's position and that/those of the associated researcher(s).

Three applications were received and the chair was awarded in 2021.

Dedicated follow-up and support committees have been set up to support the work of the research chair.

Chair in psycho-oncology / intervention research

INCa, in partnership with the University of Lille, UMR 9193 SCALab, the Oscar Lambret Centre and the ONCOLille Institute, has launched the creation of a research chair in Human and Social Sciences (HSS) entitled: "Innovations in psycho-oncology and intervention research".

The general objective is to develop a research programme in human and social sciences aimed at increasing and disseminating knowledge about the adjustment processes of patients, their families and carers, and to design, use and measure the effectiveness of innovative intervention models with a view to optimising patient support, treatment and care.

The research chair was awarded on July 2021. The funding and duration are intended to structure the research and allow the University of Lille to maintain, insofar as possible, the position of the holder in order to ensure the continuity of research and teaching on this theme.

In total, nearly one million Euro (>€905K) have been committed to support this chair; this sum is broken down as follows:

- €750K allocated by INCa for the remuneration of the holder and the functioning of the chair;
- the SCALab laboratory, the Oscar Lambret Centre (COL) and the ONCOLille Institute will provide the necessary work infrastructure (offices, computer equipment, etc.) and the support of research staff for setting up projects (CRA time or study engineer);
- the University of Lille will support this programme through the funding of a dedicated doctoral contract (approximately €100K);
- the Oscar Lambret Centre will fund a 12-month post-doctoral contract (€55K).

This chair is accompanied by a support committee for at least the first two years, a monitoring committee for the entire duration of the chair (i.e. 5 years), and a scientific committee whose mission is to validate the scientific orientations of the projects and to evaluate the progress of the programme.

The research programme over the 2015-2021 period

Since 2015, a total of 5 research chairs have been allocated for a total amount of almost €2.1M:

- 2015: Cancer prevention;
- 2016: promoting and strengthening a culture of cancer-related basic and applied research in human and social sciences;
- 2019: developing research on the social challenges of personalised medicine and innovation in cancer care
- 2021:
 - Health democracy/empowerment: involving citizens and people affected by cancer
 - Innovations in psycho-oncology and intervention research

PHD PROGRAMME IN HSS-E-PH

For the 11th consecutive year, the French National Cancer Institute launched a call for applications to support four doctoral grants in order to promote research in HSS-E-PH applied to cancer control. A total of 22 projects were submitted, among which 2 were classified out of scope and one withdrew. The 19 reviewed projects are divided into 3 research categories. Table 36 presents the distribution of the applications reviewed. The distribution of projects according to discipline is substantially consistent between 2020 and 2021.

■ **TABLE 36**
DISTRIBUTION OF THE PROJECTS REVIEWED UNDER THE PHD PROGRAMME
IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY AND PUBLIC HEALTH

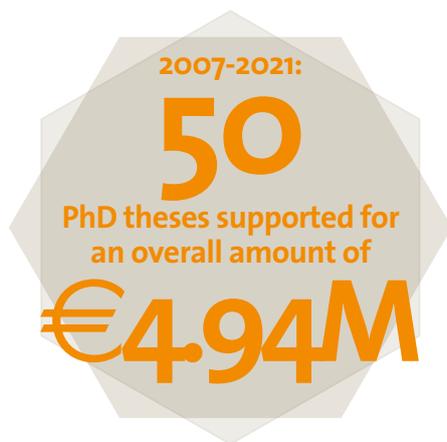
Research categories	Number of applications
Social sciences (sociology, anthropology, geography, management sciences, economics, political science, social marketing, etc.)	6
Epidemiology or biostatistics	7
Human sciences (psychology, cognition and learning, psychoanalytic studies, science of physical activity, etc.)	6

Following the review process, including interviews of applicants, four PhD theses were selected for funding (Table 37) for a total amount of €465,375.

Research café

In April 2021, a virtual event was organised in order to increase the visibility of the two chairs of excellence launched in 2021 by the Institute – the psycho-oncology chair in Lille and the empowerment chair in Marseille. The aim of this “research café” was to present the two research chairs, and answer any questions researchers may have. The partners of the two chairs were invited and had the opportunity to participate during the Q&A session. This research café was attended by about forty participants.





■ TABLE 37
DOCTORAL FELLOWSHIPS FUNDED IN 2021.

Title	Discipline
Changing the food supply: an effective policy tool to reduce cancer incidence?	Economics
Impact of new generation hormone therapies on cognitive function in elderly patients treated for metastatic prostate cancer.	Psychology
Modelling breast cancer screening and its impact on mortality reduction: Improvement with joint modelling and deep neural networks	Epidemiology
Physical activities under (tele)surveillance – The differentiated relationships of cancer patients with digital physical activity support devices	Sociology

Over the 2007-2021 period, 50 PhD theses were supported for a total amount of €4.94M.

PhD meeting

Since 2020, the Institute has set up a specific support and facilitation system for doctoral students funded by the Institute through the HSS-E-PH and SPA doc calls for applications.

These include annual meetings aimed at creating a space for exchanges between doctoral students by allowing them to

- Present their work;
- Meet other doctoral students, researchers and other stakeholders in the fight against cancer;
- Encourage a multidisciplinary research dynamic.

In addition, this organisation contributes to the Institute's influence and helps build a multidisciplinary community of researchers in the field of cancer control.

This mechanism therefore meets the objective of breaking down disciplinary barriers as set out in the Ten-Year Cancer Control Strategy and in the department's action plan.

In November 2021, 26 doctoral students met for a day and a half, on the Saint Just campus in the Oise region.

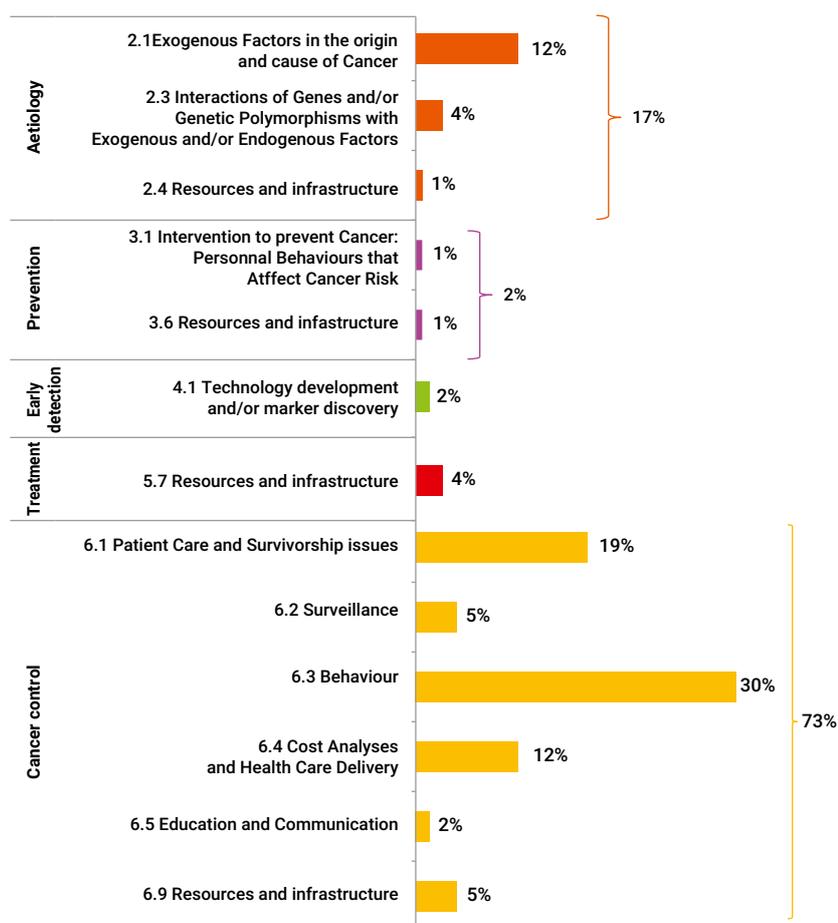
The programme of these meetings was co-constructed with the doctoral students, in order to meet their expectations and needs in an appropriate way.

The topic of these meetings was the impact of research on public health policies and practices.

The meetings were organised around presentations of the PhD students' thesis work, followed by time for discussion.

In addition, the deputy director of population health and chronic disease prevention at DGS, Ms Zinna Bessa, took part in the discussions with the doctoral students on the prospects for their work.

■ FIGURE 55
 DISTRIBUTION OF THE SELECTED GRANTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2021 PERIOD



REVIEW OF CANCER RESEARCH FUNDING AND EVALUATION

Review and trends in cancer research funding

CANCER RESEARCH FUNDING IN 2021

In 2021, 221 projects were selected and the total funding awarded to cancer research programmes amounted to over €88.80M, including:

- €67.78M from INCa;
- €21.03M from Inserm for ITMO Cancer-Aviesan.

Figure 56 shows the breakdown of multi-year funding for 2021 according to programme type:

- Investigator-driven calls concerning the 4 major research areas (biology, translational, clinical, human and social sciences, epidemiology, and public health).
- Strategic research initiatives and thematic programmes encompassing INCa's actions to support precision medicine, the intervention research programme operated and funded by INCa, the integrated programme addressing tobacco control in partnership with IReSP, and thematic research programmes managed by ITMO Cancer-Aviesan;
- Support for platforms, resources, and infrastructures;
- Research training and support for young teams of excellence, especially covering the PhD programme in human and social sciences, support for chairs, ATIP-Avenir, and translational research training programmes for MDs, pharmacists, and vets.

This figure shows that 41% of the allocated budget was devoted to competitive investigator-driven calls for proposals, managed by INCa. Importantly, due to a change in schedule, the clinical and translational research programmes were launched in late 2021. Those programmes represent the major financial contribution from DGOS.

Strategic research initiatives and thematic programmes represented 48% of total funding in 2021, and also include the thematic research programmes managed and funded by ITMO Cancer-Aviesan.

FIGURE 56
2021 MULTI-YEAR CANCER RESEARCH FUNDING BY PROGRAMME TYPE (INCA AND ITMO CANCER-AVIESAN):
€88.80M INVESTED

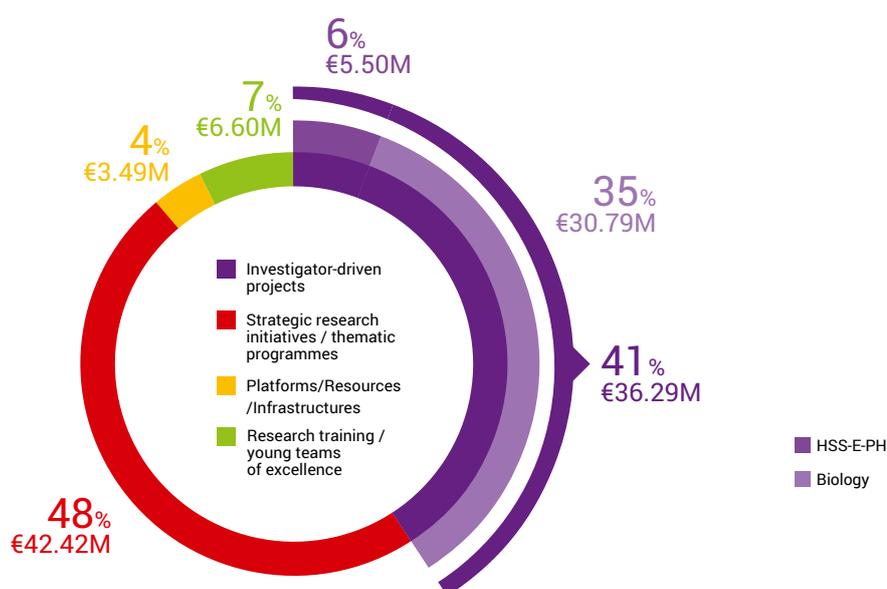
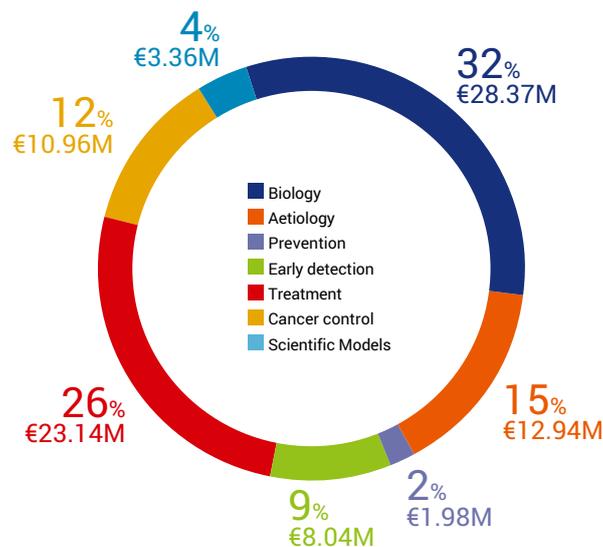


Figure 57 presents the funding allocation according to the CSO classification:

- The biology category represented the most significant investment in 2021 with €28.37M (32%);
- Treatment and early detection, diagnosis and prognosis amounted to €23.14M and €8.04M in 2021, respectively (26% and 9% of 2021 investments);
- Studies related to the aetiology category amounted to €12.94M in 2021 and represented 15%;
- Cancer control, survivorship, and outcomes research issues represented 12% of investments (€10.96M), while the prevention category represented 2% of investments in 2021 (€1.98M).

■ FIGURE 57

2021 MULTI-YEAR CANCER RESEARCH FUNDING ACCORDING TO THE CSO CLASSIFICATION (INCA AND ITMO CANCER-AVIESAN): €88.80M INVESTED



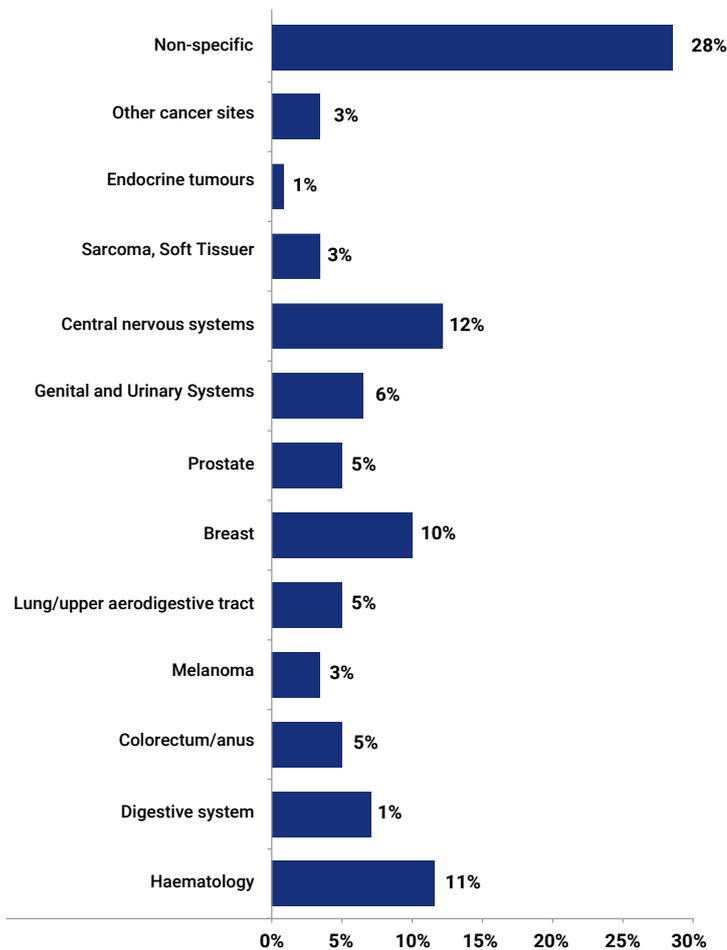
An overview of the ITMO Cancer-Aviesan funding over the 3rd Cancer Control Plan (2014-2019)

As a leader, or co-leader, of 17 research actions of the 3rd Cancer Control Plan, ITMO Cancer-Aviesan has allocated a portion of the Plan funds to actions mainly dedicated to basic research. To highlight key features of the supported institutions, ITMO Cancer-Aviesan performed an analysis of funding volumes allocated within its programmes and partnerships. For this study, 1,020 grants allocated to 383 research structures, for a total amount of slightly over €140M, were considered. An overview of the supported research structures was drawn up, which showed that:

- The highest-funded research centres were Institut Curie, Gustave-Roussy and the Cancer Research Centre in Lyon;
- The funded structures were spread throughout France, with a greater emphasis on 6 cities: Paris, Toulouse, Lyon, Marseille, Montpellier, and Grenoble;
- All the founding members and 8 associated members of Aviesan were funded. This diversity reflects the multidisciplinary nature of some ITMO Cancer-Aviesan programmes and, more broadly, the intrinsic cross-cutting nature of cancer research;
- Members of France Universités (formerly CPU), CNRS and Inserm were the highest-funded Aviesan members. However, 41 universities from France Universités were funded; CNRS and Inserm were thus the highest-funded single institutions;
- The vast majority of grants was allocated to joint research units, reflecting the diversity of the French research landscape. About half of the grants were allocated to 3 combinations of research supervision authorities: Inserm/France Universités, CNRS/Inserm/France Universités, and CNRS/France Universités;
- The awardees and their partners were mostly employed by CNRS, by a member of France Universités or by Inserm.

The breakdown of 2021 funding by cancer sites studied shows that 28% of the allocated budget was non-specific to a tumour type, over €24.95M (Figure 58). The main cancer sites studied were central nervous system, haematology, and breast.

FIGURE 58
2021 MULTI-YEAR CANCER RESEARCH FUNDING BY CANCER SITES STUDIED (INCA AND ITMO CANCER-AVIESAN):
€88.80M INVESTED



CANCER RESEARCH FUNDING OVER THE 2007-2021 PERIOD

Since 2007, a total of 3,790 projects have been funded through the different competitive calls for research proposals and grants for designation for over €1.427Bn.

Figure 59 shows the breakdown of 2007-2021 total funding by programme type:

- Investigator-driven calls for proposals of the four main research areas represented a total of 50% of 2007-2021 investments, or approximately €715M;
- Strategic research initiatives aimed at primarily supporting precision medicine initiatives and thematic programmes represented 27% of cancer research investments (€391M);
- Support for resources and infrastructures represented nearly 20% of total funding, approximately €267M, which highlights the drive to reinforce the organisational framework and the coordination of cancer research activities. Alongside support for investigator-driven projects, INCa has developed a proactive policy for fostering cancer research excellence through the designation of and support for dedicated infrastructures aiming to promote coordinated, integrative, and effective cancer research;
- Support for young teams and cancer research training represented a total of 4% of total investments (€54M).

FIGURE 59
2007-2021 MULTI-YEAR CANCER RESEARCH FUNDING BY PROGRAMME TYPE (INCA, DGOS AND ITMO CANCER-AVIESAN):
€1.427BN INVESTED

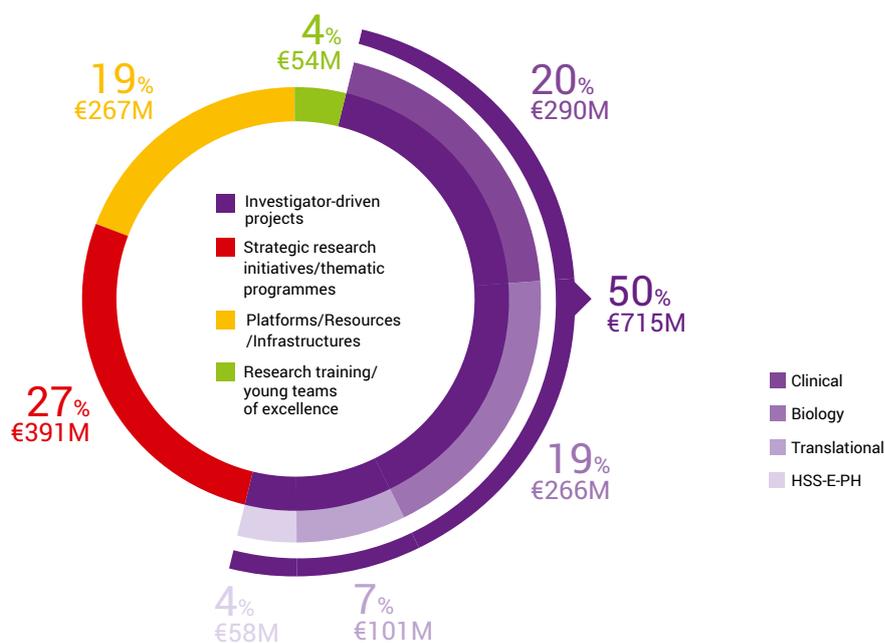
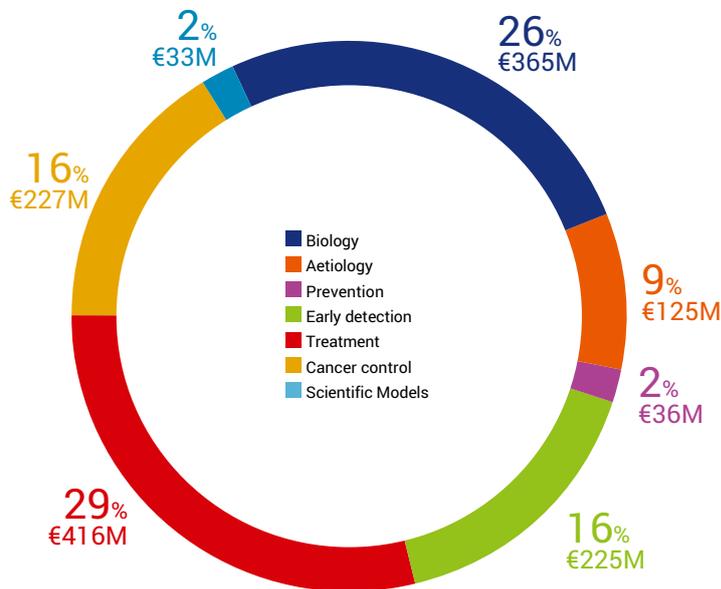


Figure 60 presents the distribution of total funding for 2007-2021 according to the CSO classification:

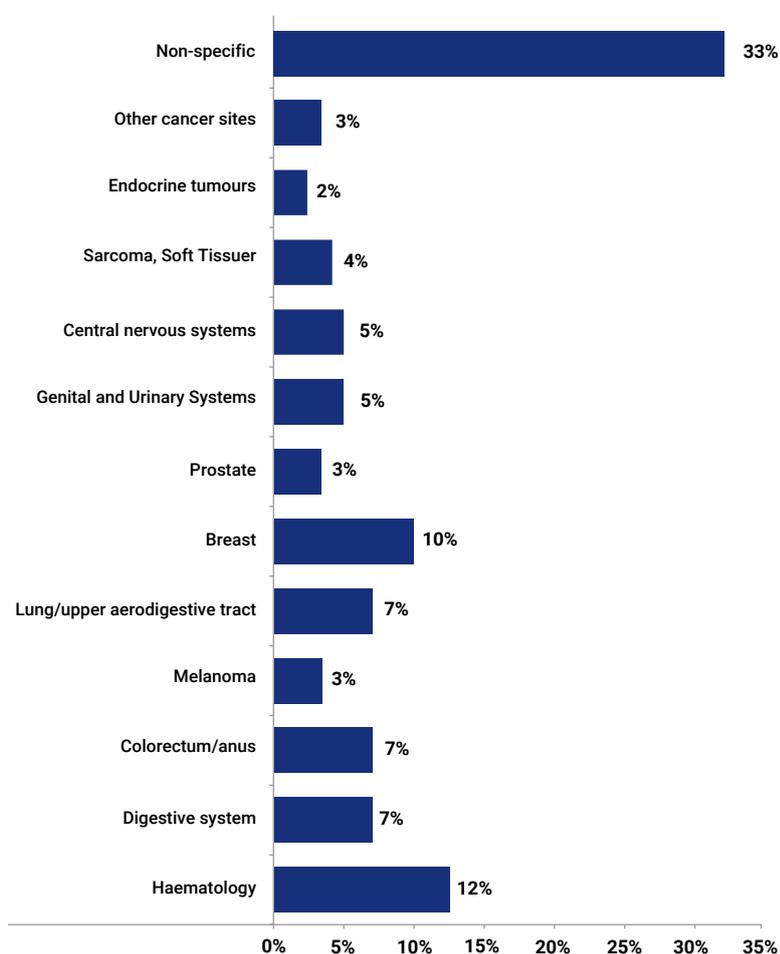
- Treatment and biology categories represented the most significant investment, with €416M and €365M, respectively;
- Cancer control, survivorship, and outcomes research issues represented 16% of total funding (€227M);
- The early detection, diagnosis and prognosis categories amounted to €225M;
- Research aimed at identifying the causes or origins of cancer – genetic, environmental, and lifestyle – and the interactions between these factors falls into the aetiology category, representing 9% of total funding with €125M;
- The prevention and scientific models categories amounted to €36M and €33M, respectively.

■ **FIGURE 60**
2007-2021 MULTI-YEAR CANCER FUNDING ACCORDING TO THE CSO CLASSIFICATION (INCA, DGOS AND ITMO CANCER-AVIESAN): €1.427BN INVESTED



Over the 2007-2021 period, 33% of the budget was allocated to non-specific cancer types (Figure 61). Haematological malignancies and breast cancer represented 12% and 10% of investments, respectively.

FIGURE 61
2007-2021 MULTI-YEAR CANCER FUNDING BY CANCER SITES STUDIED: €1.427BN INVESTED

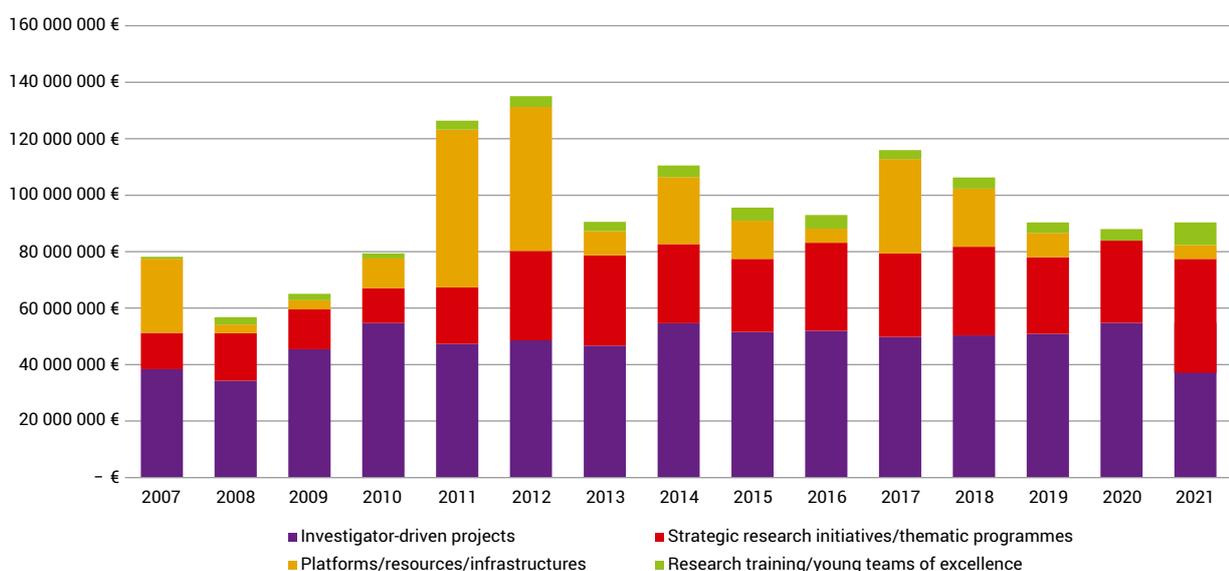


TRENDS IN CANCER RESEARCH INVESTMENTS

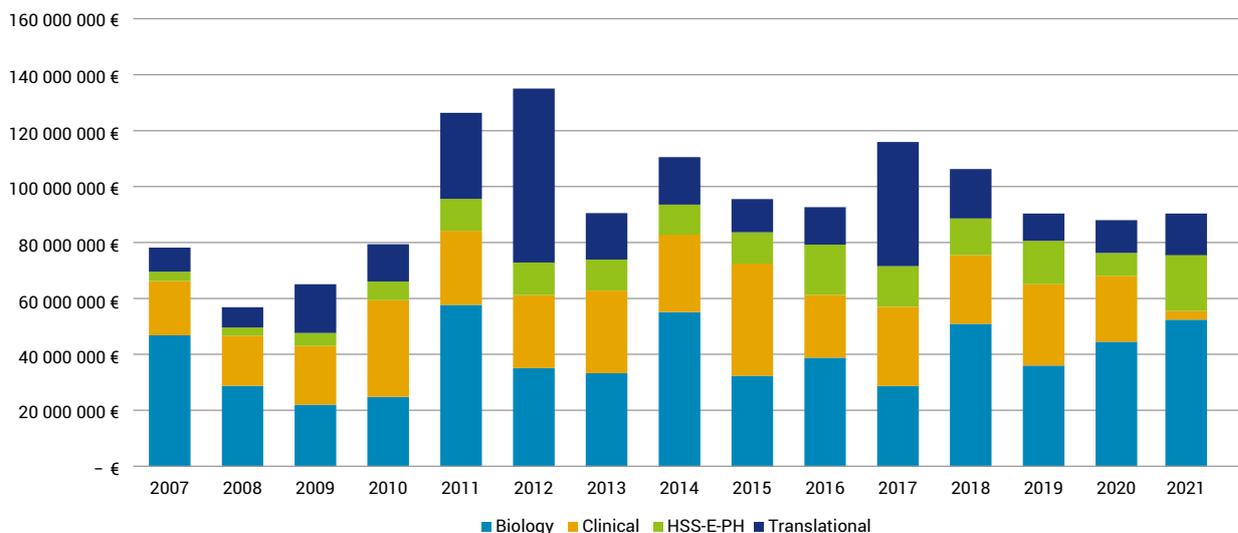
Figures 62 and 63 present the trends in total funding according to the programme type and cancer research fields over the 2007-2021 period, respectively.

The different structures supported in recent years have delivered significant multidisciplinary synergistic interactions for research funding and drug access to patients, and have provided a basis for the coordination of clinical, fundamental, and human and social science research at a regional level in France. Coordinating, maintaining, and reinforcing them to provide integrated and coordinated cancer research on a nationwide level is a key objective for the French National Cancer Institute.

FIGURE 62
TRENDS IN TOTAL FUNDING ACCORDING TO PROGRAMME TYPE OVER THE 2007-2021 PERIOD (INCA, DGOS, ITMO CANCER)



■ **FIGURE 63**
TRENDS IN TOTAL FUNDING ACCORDING TO CANCER RESEARCH FIELD OVER THE 2007-2021 PERIOD
(INCA, DGOS, ITMO CANCER)



National Plan for Open Science – first assessment and launch of a second plan

The first French National Plan for Open Science 2018-2021 has made major progress: France has adopted a coherent and dynamic policy in the field of open science, and the proportion of open-access French scientific publications has increased from 41% in 2017 to 61% in 2021.

In July 2021, the French Ministry of Higher Education, Research and Innovation strengthened its commitments by launching a second National Plan for Open Science which aims to generalise open science practices.

This plan continues the ambitious trajectory initiated by the law for a Digital Republic (2016) and confirmed by the Research programming law (2020), which includes open science in the missions of teaching/researchers and sets the national objective of 100% open-access publications in 2030.

The effort already initiated by the French National Cancer Institute and other French research funding agencies will be extended.

The aim is to increase the visibility of research findings in all disciplines, democratise knowledge access, and strengthen French research's international influence.

DORA French working group

In September 2021, following the publication of the UNESCO's recommendation on Open Science and the European Commission proposals to move towards a common understanding, the French Ministry of Higher Education, Research and Innovation set up a "DORA's working group". The French National Cancer Institute, together with institutions that have signed the San Francisco declaration on research evaluation,

wish to implement concretely the ambitions of open science in the various evaluation procedures, individual or collective, of projects or publications. Our objective is to develop reflection, propose and discuss concrete measures and to coordinate dedicated efforts and actions. The French working group also supports the preparation of the European Open Science Days, under the auspices of the French Presidency of the European Union, scheduled for February 2022 in Paris.

French research funder statement – Advances and perspectives of the French research funder working group on the evaluation of the impact of biomedical research projects.

In order to meet one of the objectives of the 2014-2019 Cancer Plan, the French National Cancer Institute has started a reflection to strengthen the monitoring and evaluation of funded projects. In 2017, a working group was set up to meet the ambitions of the Plan. This working group includes several institutional, associative and charitable partner institutions involved in the implementing of biomedical research projects in order to discuss the different methods and tools implemented to assess the impact of research actions.

Based on the 2019-2021 roadmap, several milestones have been achieved. It should be noted that for 2019-2021, a roadmap was defined by the

partners who were able to launch work (or who had already initiated it).

Deliverables in 2017-2021

- Standard models of follow-up reports requested from researchers during the project (intermediate reports) and at the end of the project (final report)
- An evaluation grid for internal use (end of project)
- Methodological guides (definitions and state of the art)
- Operational guides to facilitate the implementation of impact analyses
- A white paper

A short letter whose main objective is to publicise this collective work will be submitted to a peer-reviewed journal.

TEN-YEAR CANCER CONTROL STRATEGY-REVIEW OF CANCER RESEARCH FUNDING

2021 marks the launch of the Ten-Year Cancer Control Strategy, structured around 4 strategic challenges:

- Improving prevention;
- Limiting sequelae and improving patients' quality of life;
- Addressing cancers with poor prognosis;
- Ensuring that progress benefits all;

The Strategy is organised around 234 measures and the Institute has proposed a 2021-2025 roadmap.

In 2021, 78 actions were already launched, including cancer research actions.

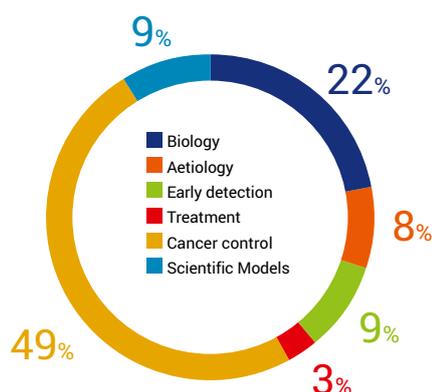
The first 2 calls for research proposals launched are:

- “Prevention Research: Contributions from Biology” to improve prevention through a holistic approach ranging from basic biological research and translational research to the analysis of behavioural factors
 - Open to all fields of basic and translational research in biology, and all scientific disciplines, this call aims to support innovative projects in the field of cancer prevention, focusing on the development of fundamental knowledge and/or new, more effective, and more specific tools and strategies for cancer detection, early screening and the prevention of recurrence
 - 6 projects selected for funding, out of the 35 proposals submitted, for a total amount of €3.07M
- “Reducing sequelae and improving quality of life” to encourage projects aimed at enhancing knowledge and the means to reduce sequelae caused by the disease and cancer treatments
 - By promoting interdisciplinarity, the proposals should address supportive care, quality of life, reconstructive surgery and fertility preservation and restoration;
 - 8 projects were selected for funding out of the 26 submitted for a total amount of €4.14M

In total, through these first two programmes, €7.22M have been specifically devoted to the Ten-Year Cancer Control Strategy (Figure 64)

In addition, several measures were also launched in 2021 and the results are expected for 2022.

FIGURE 64
DISTRIBUTION OF TEN-YEAR CANCER CONTROL STRATEGY RESEARCH PROGRAMMES ACCORDING TO THE CSO CLASSIFICATION



Bibliometrics on French paediatric cancer research (2008-2018)

In November 2018, additional funding of €5M per year for basic research on paediatric cancers was allocated. The Institute was commissioned to manage and coordinate the action plan under this additional funding.

The work being developed so far aims to:

- Provide qualitative information and ensure equal access to knowledge for all stakeholders;
- Disseminate research data from programmes funded by public funds;
- Improve the impact of research for the benefit of all patients.

A study was therefore conducted, by Technopolis and the Centre for Science and Technology Studies (CWTS – Leiden, Netherlands), to:

1. Analyse the portfolio of French paediatric oncology research projects funded by the Institute (and partners) over the 2008-2018 period, describing the topics funded and France's contribution to this topic;
2. Describe the French scientific community in paediatric oncology;
3. Compare national publications with international funding agency data.

Methodology: Scientometric analysis of international databases (via queries on titles, abstracts or keywords associated with articles, etc.), interviews, and a survey. Experts in the field were asked to assist with this work.

French research funder statement – Launching a new cycle for the 2022-2025 period

The joint review of the 2014-2019 Cancer Control Plan conducted by IGAS/IGESR of the 3rd cancer plan (July 2020) included our action in favour of impact evaluation and open science in the major advances.

All the partners are keen to continue this concerted approach. In addition to the different working groups, seminars involving all stakeholders will be organised and an international symposium in 2025 will be organised.

The composition of the working group will expand with new research funders and qualified personalities.

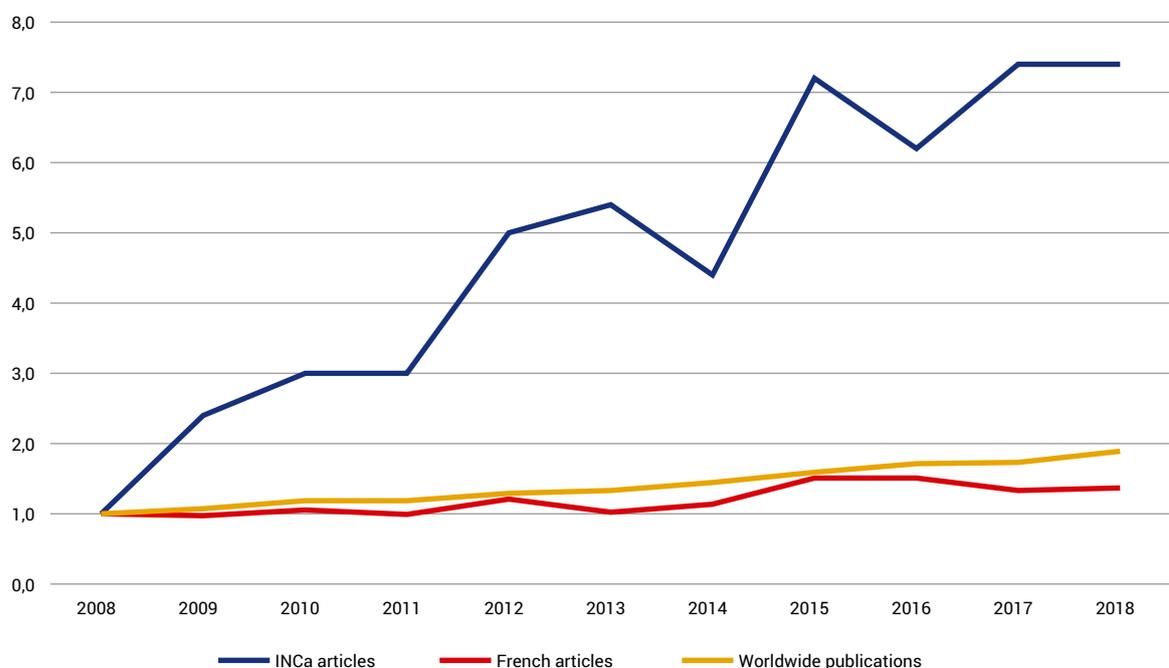
CONTRIBUTION OF PROJECTS SUPPORTED BY INCA

Between 2008 and 2018:

- 98,874 publications worldwide addressed paediatric oncology;
- 5,022 publications had at least one researcher located in France;
- French publications in paediatric oncology accounted for 5.3% of global publications (for comparison, the global share of publications from France was 2.6% in 2018);
- The 262 publications that mentioned INCa funding represented 5.0% of French publications, or 0.3% of global publications;
- Scientific production from projects funded by INCa increase 7-fold, while global production increased two-fold, and French production has increased by one third (Figure 65).

On a global scale, INCa's contribution (in volume) is modest, but the pace of progress in publications reflects a strong momentum in the projects supported by the Institute in the production of knowledge.

■ **FIGURE 65**
PUBLICATION RATE OVER THE 2008-2018 PERIOD (2008 = 1)



MAPPING PRODUCTION IN PAEDIATRIC ONCOLOGY

A thematic map of worldwide production in paediatric oncology (based on lexical analysis of the “title” and “abstract” fields of the publications) was produced. This work identified seven thematic clusters, four of which represent 74% of publications

- “Health risk & cancer risk” (25%)
- “Clinical studies & risk factors in rare paediatric cancers” (22%)
- “Paediatric leukaemia” (18%), and
- “Preclinical studies” (10%)

The other three clusters address “Hodgkin’s and non-Hodgkin’s lymphomas”, “Optimising radiotherapy”, and “Paediatric blood cancer”.

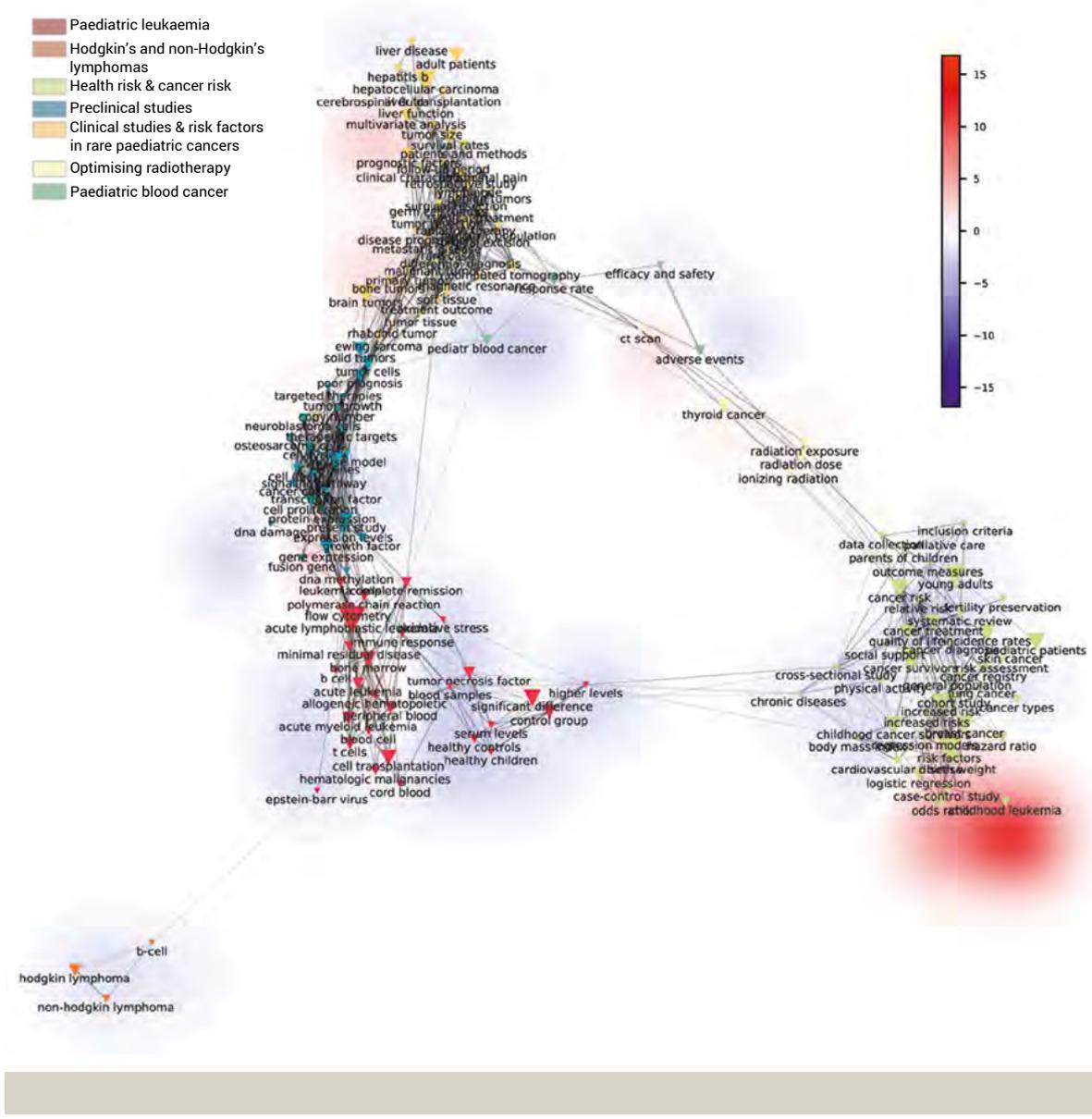
Figure 65 presents the projection of publications resulting from INCa funding and shows a particularly high specialisation (red intensity zone on the graph) for the “Health risk & cancer risk”/“Clinical studies & risk” clusters factors in rare paediatric cancers”/“Paediatric leukaemias”/Preclinical studies

The visibility of INCa-funded publications in the paediatric landscape (research landscape tools developed by CWTS) is remarkable since the proportion of INCa publications, which are in the 10% most cited publications, is very high (data not shown). To conclude, the publications arising from INCa-funded projects are in a limited number of clusters. This is in line with a specialisation profile, also reflected in the production of publications within these clusters, which are particularly visible at an international level in paediatric research.

POSITIONING AT A NATIONAL AND INTERNATIONAL LEVEL

The analysis of French paediatric cancer research funding shows that the Institute is the main French funder in paediatric oncology. The French Cancer League is another important funding source.

FIGURE 66
THEMATIC MAP OF FRENCH NATIONAL CANCER INSTITUTE FUNDING



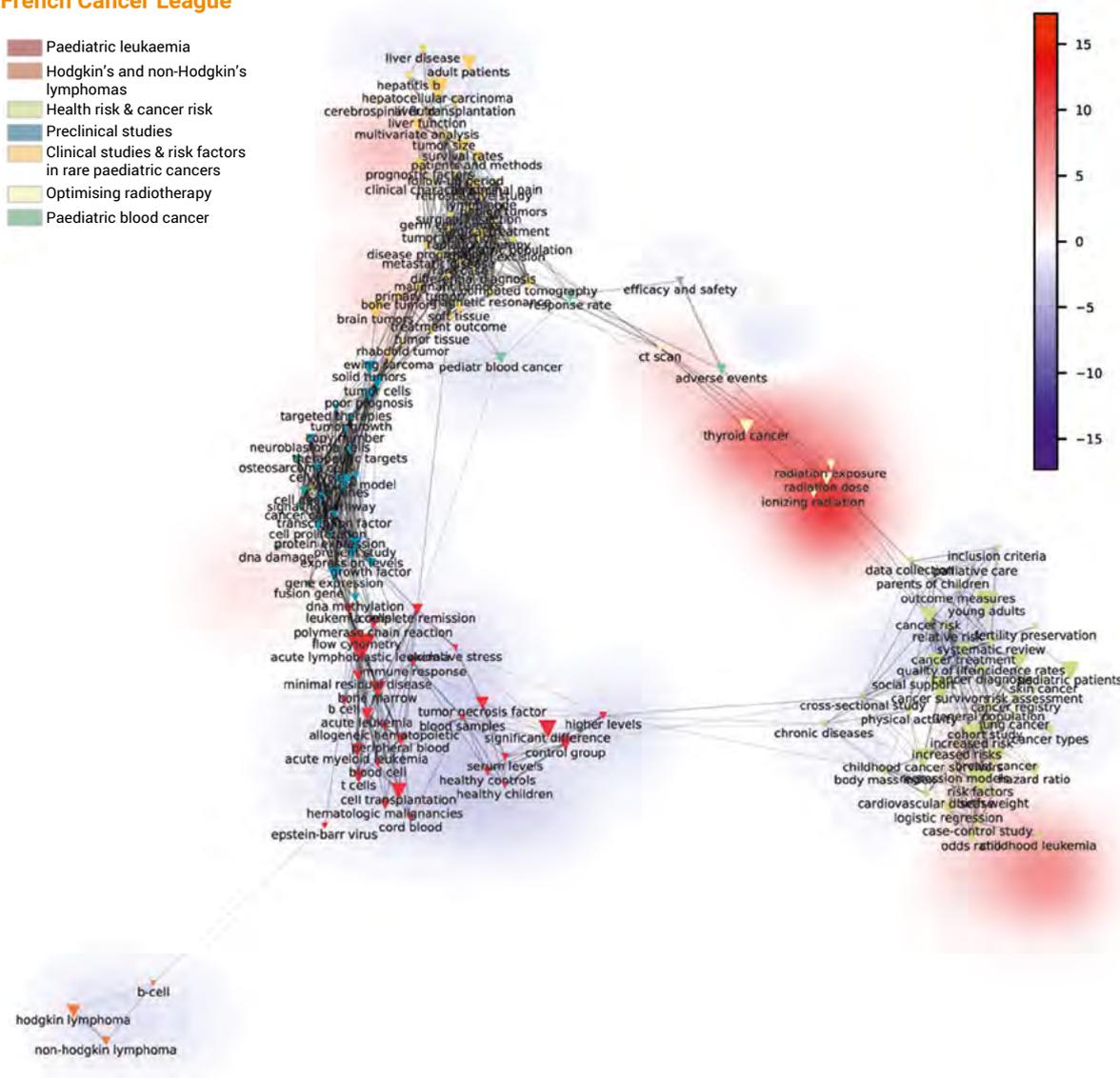
The United States is the largest funder of paediatric cancer research worldwide. Canada and USA account for more than half of the funding allocated to paediatric oncology research worldwide.

The projection of publications resulting from national or international funding (Figure 67) shows the level of specialisation (red intensity zone in the graph).

FIGURE 67
NATIONAL AND INTERNATIONAL POSITIONING (VS FRENCH NATIONAL CANCER INSTITUTE) – 2008-2018

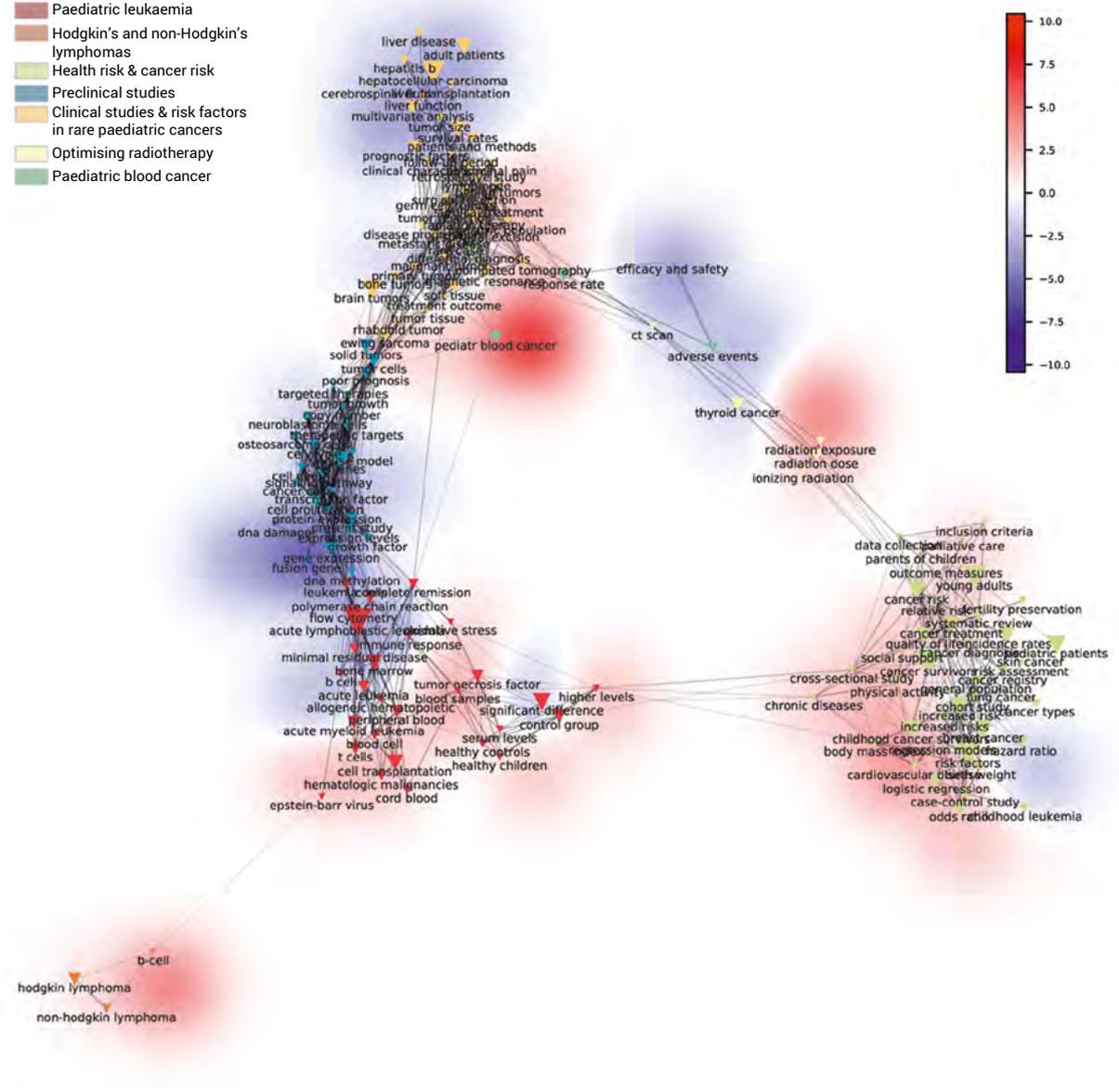
French Cancer League

- Paediatric leukaemia
- Hodgkin's and non-Hodgkin's lymphomas
- Health risk & cancer risk
- Preclinical studies
- Clinical studies & risk factors in rare paediatric cancers
- Optimising radiotherapy
- Paediatric blood cancer



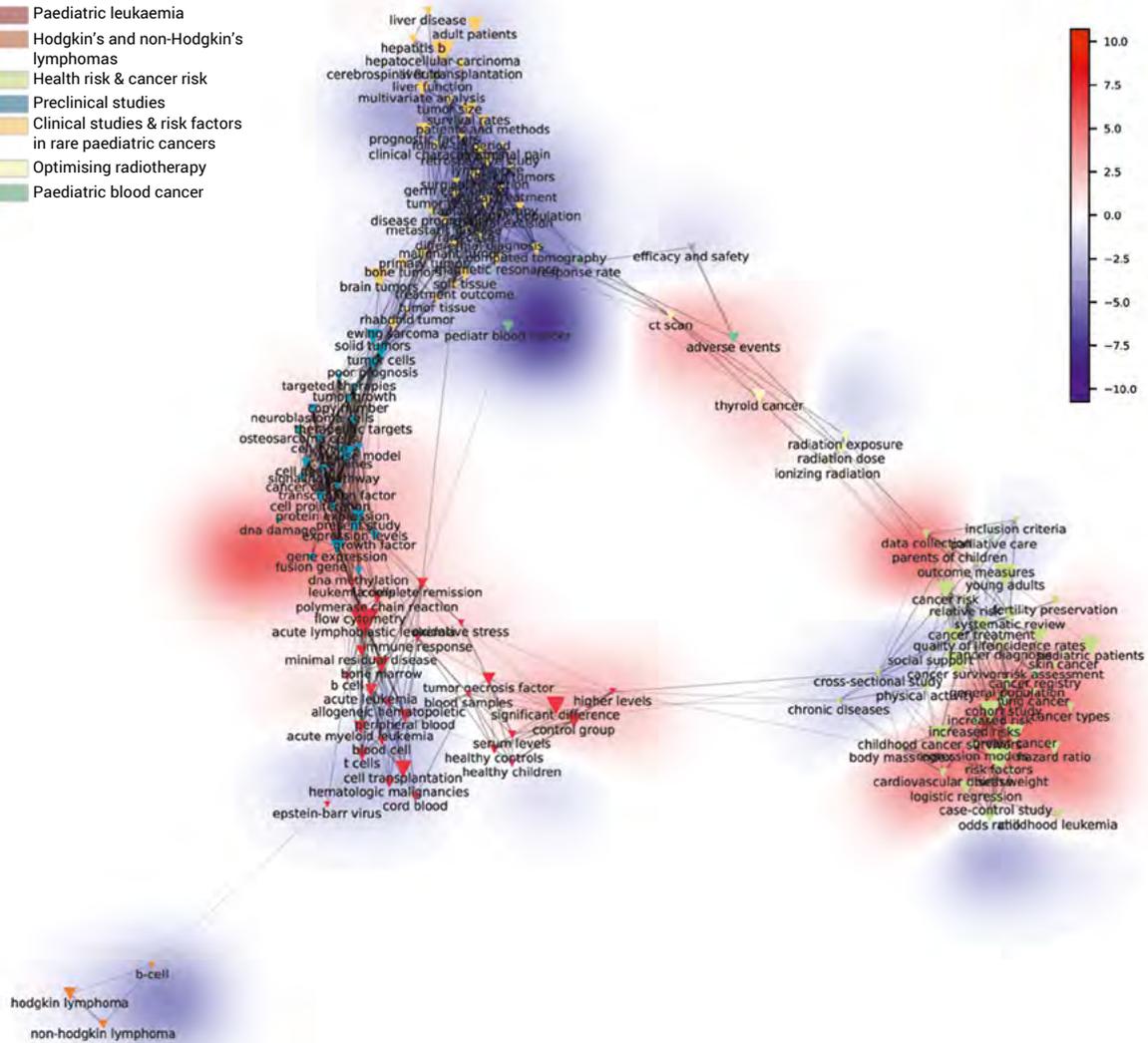
NIH

- Paediatric leukaemia
- Hodgkin's and non-Hodgkin's lymphomas
- Health risk & cancer risk
- Preclinical studies
- Clinical studies & risk factors in rare paediatric cancers
- Optimising radiotherapy
- Paediatric blood cancer



European Commission

- Paediatric leukaemia
- Hodgkin's and non-Hodgkin's lymphomas
- Health risk & cancer risk
- Preclinical studies
- Clinical studies & risk factors in rare paediatric cancers
- Optimising radiotherapy
- Paediatric blood cancer



DESCRIPTION OF THE FRENCH SCIENTIFIC COMMUNITY

The French paediatric oncology community represents almost 4,000 researchers. The mapping of French paediatric oncology research shows the presence of major French research centres and Cancer care centres. These organisations include 18 universities, two major research organisations CNRS and Inserm, six hospitals, and four Cancer Care Centres. Figure 68 shows the network of national and international collaborations. It has a strong national dimension, but it has a significant international (not only European) component (German Cancer Research Centre – DKFZ, Institute of Cancer Research – UK, St Jude Children’s Research Hospital – US, Karolinska Institute – Sweden, etc.)

Researchers involved in INCa-funded projects represent 84.2% of the top 1% of researchers publishing in French paediatric oncology.

The interviews and the survey confirm that INCa funding is considered by the coordinators as a “quality label” for the evaluation of their research activity. The survey respondents highlight that this “quality label-like funding” is also welcomed by their scientific partners in France and other funders. Nevertheless, INCa funding seems to be considered less powerful for obtaining funding abroad.

This is the first study conducted based on our paediatric portfolio, and these findings are a primary insight before the €5M allocation. Although modest in terms of volume, the research funded by INCa is specialised and visible. This work will be updated every 5 years in order to measure/capture the effects of additional Institute funding to support paediatric cancer research.

3

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Strategic orientations for advancing cancer research

2021

represents a keystone for French Cancer Research institutional planning, marking the launch of two important events: on the one hand, the Ten-Year Cancer Control Strategy (TYCCS) taking over from the third Cancer Control Plan and, on the other, the

Multi-year research programming law (MYRPL) of the French Ministry of Research. For the first time for more than a decade, this allows a further boost in all areas of French cancer research thanks to a significant and unprecedented financial commitment from the French government.

At the same time, the year was also marked by the continuation of the pandemic, albeit at more tolerable levels for institutions and laboratories. INCa managed to run all its calls for research proposals in due time, and provided continuous financial support for research projects based on transparent methods, international evaluation and participation of patient advocates in all the scientific evaluation committees for INCa calls for proposals, in every field of cancer research. Naturally, this required a high level of adaptability among teams and a reorganisation and renewal of processes which, in some instances, will be used further in the future.

With respect to the recurrent core actions of the research division, we have reviewed structuring programmes such as Canceropoles and SIRIC for the years 2021-2022, with the help of external committees, in order to propose a new designation campaign in 2023, taking not only the new landscape and recent developments of French cancer research into consideration, but also the priorities of the TYCCS. The calls for applications will be launched in 2022, with changes intended to account for recommendations from both the scientific evaluation committees and the SAB.

We also worked on the design and simplification of some of our recurrent calls for proposals, for example, by merging them to provide a better visibility, thereby meeting the SAB recommendations. In the meantime, in 2021, an increase in success rates was observed for all investigator-driven programmes (PLBIO, PRT-K, PHRC-K and PLSHS) as a result of a significant contribution from the government. A striking example of this is the PLBIO programme (biology and basic sciences for cancer research programme), which has seen its success rate increase from 12.5% in 2020 to 21.3% in 2021. This effort should further increase in 2022 and 2023, to make French cancer research more competitive internationally.

Among the highlights of 2021 in terms of new actions implemented and described in detail in the previous sections, mention should be made, among others, of the selection of highly competitive projects within the framework of the brain tumour PAIR (in partnership with ARC Foundation and the French Cancer League), the launch of novel and original programmes in Paediatrics aimed at funding both interdisciplinary and High-Risk/High-Gain projects, and the launch of the second edition of the ITMO Cancer-Aviesan/INCa joint call on preneoplastic lesions.

However, 2021 was above all marked by the launch of new research actions across the four areas of the TYCCS: improving cancer prevention; limiting the side-effects of treatments and improving the quality of life of those affected by the disease; addressing cancers with poor prognosis in adults and children, and ensuring that progress benefits everyone. In the coming years, these TYCCS actions will be further emphasised and complemented, by taking advantage of both internal brainstorming sessions and meetings with our partners to establish a roadmap and a blueprint for new programmes.

In the following sections, we provide examples of actions that will be launched by 2022 and beyond, across the four areas of the TYCCS. These include new calls for proposals of research projects and calls for expressions of interest to set up research consortia or networks.

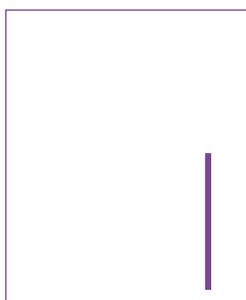
Within the Prevention and Quality of Life areas, cross-cutting multithematic and multidisciplinary calls for proposals will encompass human and social science approaches, intervention research, personalising prevention, supportive care, surgical reconstruction, preservation of fertility and its restoration, etc.

In line with the first High-Risk/High-Gain calls for proposals in paediatric cancers launched this year, we will extend the concept to cancers with poor prognosis in 2022. In addition, in order to take a quantum leap in the poor prognosis cancer research area, there is a clear need to strengthen interdisciplinary research, which has been one of the main priorities of the ITMO Cancer-Aviesan, notably through its calls “Contributions to oncology of physics, chemistry and engineering sciences” and “Contributions to oncology of mathematics and computer science”, that will be renewed. To complete these actions, ITMO Cancer-Aviesan is launching a new call in 2022 dedicated to the functional exploration of the microenvironment in cancers with poor prognosis.

A strong commitment will also be made to clinical research across several directions. Thus, increasing the funds allocated to the PHRCK programme will make it possible to support research projects focusing on de-escalating therapies. Likewise, we will pay particular attention to research in radiotherapy, by supporting the French national research network RADIOTRANSNET and through the launch of new calls for proposals on this topic. Last but not least, a new AcSé-like trial protocol is in preparation with a “basket of basket” design (different cohorts, different drugs) for patients lacking therapeutic options.

All these actions will also be considered in the international context, and the structuring actions should prove useful in preparing French cancer research for worldwide development and cooperation. Indeed, the French Ten-Year Cancer Control Strategy coincides not only with the new Europe’s Beating Cancer Plan, but also with the European Mission on Cancer, displaying many overlapping and converging features, both in health and research areas, with a strong emphasis on prevention and equal access to innovation and personalised treatments.

SUPPORT FOR BIOLOGY, TRANSLATIONAL AND INTEGRATED CANCER RESEARCH



In view of our missions and actions, several challenges will need to be met for 2022:

- Maintaining a high selection rate for calls for proposals. To do this, the Institute is committed to continuing the budgetary efforts already made this year.
- Continuing actions as defined in the Ten-Year Cancer Control Strategy, particularly to fight cancers with poor prognosis. Thus, the following will be set up:
 - A “High-Risk/High-Gain” call for proposals for poor prognosis cancer research (action III.1.3). In order to encourage novel approaches and support proposals liable to generate disruptive innovations, the French National Cancer Institute has set up a new “High-Risk/High-Gain” (HR/HG) call for proposals type. This call will aim to accelerate the discovery of new scientific knowledge through greater risk-taking in research, leading to revolutionary innovations which will help meet challenges (in terms of early screening or diagnosis, improving knowledge on the mechanisms of the onset of these cancers or of treatment escape, developing new treatments, etc.) raised by these cancers with poor prognosis.
 - Design of the best strategy for network designation dedicated to research on poor prognosis cancers (action III.1.1), with respect to the territorial distribution of the various research and care teams, the expected objectives and current scientific and medical knowledge. The purpose of these networks will be to improve knowledge through research, by encouraging the federation of the best teams to design and conduct integrated research programmes on poor prognosis cancers and to find innovative solutions for the treatment and management of these cancers. To consolidate this designation, the Institute plans to provide structuring support for the six Clinical and Biological Databases (BCB) dedicated to

these cancers in order to prepare them to support “networks of excellence”. The objectives of this action will be to facilitate access to quality data and biological resources for research teams working on these cancers, in particular those in the “networks of excellence”, and to improve the use and sharing of data on these cancers.

In this context, an evaluation of these six BCBs will be conducted in order to define an Objectives and Performance Contract for each.

- Launch of a reflection to define the research areas of the next Integrated Research Action Programme (PAIR) that will focus on the links between obesity and cancers (action I.1.4)
- Reflection to optimise the identification and follow-up of people with a hereditary predisposition to cancer (action II.3.3). A study will be carried out to assess the national oncogenetics system in order to measure its effectiveness, and to propose an organisation and funding system better suited to recent and expected developments in oncogenetics care.
- Mobilisation of expert groups for drafting and validating documents for the correct prescription of treatments in order to improve patient care (action II.3.5). The publication of indications for molecular tests for cancer patients with a view to prescribing targeted therapies will be made for colorectal adenocarcinoma and non-small cell bronchial cancer.
- Actions to develop and support the extension of multi-omics tests carried out by molecular biology platforms (action II.3.2) with the organisation of a national consultation with the heads of molecular genetics platforms and oncogenetics laboratories to define a roadmap to fund the development of new tests.

For the recurrent core actions and in terms of structuring, 2022 will be devoted to the renewal of various structures:

- Evaluation of Canceropoles (“regional cancer hubs” in charge of promoting research coordination and scientific facilitation at a regional level) to renew the signature of an Objectives and Performance Contract (COP) for 2023-2027, defined in a concerted manner between INCa and each Canceropole, and considering regional or inter-regional specificities, actions, implementation strategies, and associated monitoring indicators.
- Launch of call for proposals to select 8 new SIRICs (an initiative to develop and conduct integrated cancer research programmes of excellence within integrated cancer research sites).

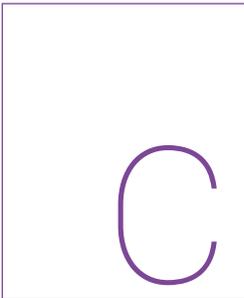
In line with the objectives defined for the use of the €5M envelope in paediatric cancer, new calls for proposals for paediatric cancer research will be launched with:

- A new edition of the “High Risk/High Gain” call for proposals (unlimited funding request per project);
- A call for proposals dedicated to innovative models in paediatric oncology. It is therefore proposed within the framework of this call for proposals, using pre-existing models (i.e. models used in adult oncology or not related to oncology) or from the development of new models, to provide new knowledge, notably on the causes of paediatric cancers, the cellular mechanisms of tumour progression or the microenvironment, and immune system escape in paediatric cancers.

And finally, on a European level, and in the context of the European TRANSCAN network (aiming to promote a transnational collaborative approach between scientific teams in demanding areas of translational research, to produce significant results of higher quality and impact, and to share data and infrastructures), the first Joint Transnational Call for Proposals 2021 (JTC 2021) focused on “Next generation cancer immunotherapy: targeting the tumour microenvironment” will be continued to select the best projects.

In addition to the numerous actions that will be carried out to fund research projects or to continue structuring actions, the coming years will include numerous consultations with professionals to define the best responses to their needs.

CLINICAL CANCER RESEARCH



linical cancer research represents an essential pillar of the Ten-Year Cancer Control Strategy. In addition to strengthening the recurrent core actions, the French National Cancer Institute has started to launch new specific actions.

In order to address the global action **Developing research to reduce sequelae and improve patients' quality of life**, a new call for proposals will be launched for thematic projects on **radiotherapy** in the continuity of the designation of the national network on pre-clinical research in radiotherapy. The prioritisation of this action is in line with our global strategy for fostering radiotherapy research. In order to promote multidisciplinary, applications should be submitted by 2 teams from 2 different disciplines from the fields of fundamental, clinical research or in human and social sciences-epidemiology-public health, with the aim of this programme enabling the emergence of research projects of excellence in topics that may be under-represented in our usual calls for proposals.

As early as 2022, we also expect to be able to foster new projects specifically addressing therapeutic de-escalation issues, through the PHRC-K call, thanks to additional funds (€5M) secured from the French Ministry of Health, and in line with SAB recommendations.

Regarding the “poor prognosis cancers” area, several actions will be continued to serve the global action **Ensuring patient access to innovative therapies in the context of clinical trials**:

- **Offer all patients the opportunity to participate in trials, open to more centres, including overseas**

It is imperative to be able to offer each patient affected by a cancer with poor prognosis the opportunity to take part in a clinical trial. This perspective must be systematically studied in a multidisciplinary review meeting (RCP). It must be considered early, without waiting for the emergence of new mutations or the onset of resistance.

- **Improve clarity of the clinical trial offering (thanks to an updated and accessible portal)**

Clarity of the clinical trial offering will be ensured thanks to the cancer clinical trials registry. A comprehensive database updated in real time will compile all the information specifying establishments offering trials, including overseas, enabling more and quicker patient inclusions (see Part II, section 3.4.4).

To serve the action **Ensuring that vulnerable populations are included in the conduct of clinical trials**, a study will be funded to identify the socio-economic barriers and source of leverage in respect of inclusion in early-phase clinical trials.

Finally, within the framework of the cross-cutting area and the global action **Combating loss of chance by paying specific attention to the continuity of actions to fight cancer in times of crisis**, themed workshops including all stakeholders will be organised to propose recommendations so that France remains a European leader in academic and industrial clinical research. These recommendations will help us in identifying new actions the Institute can implement.

From a more global and medium-term perspective, we are currently building with all stakeholders, including the national *Plan France Médecine Génomique 2025*, a new AcSé programme, considering 4 cohorts with different molecular abnormalities, which should start at the end of 2023.

Regarding our recurrent core actions, we will launch a new designation period for cooperative intergroups and a new period of designation for a national network on pre-clinical research in radiotherapy.

As raised by the SAB, a review of the impact of our funding is necessary, and we will carry out a quantitative analysis of all the results and publications of the projects funded by the PHRC-K over the 2005-2016 period.

STRATEGIC OUTLOOK IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY AND PUBLIC HEALTH



Prevention represents a key area of the Ten-Year Cancer Control Strategy. In this respect, research in the field of Human and Social Sciences (HSS), Public Health, and Population Health Intervention Research will contribute extensively in this area. In the coming years, as a continuation of the work previously undertaken, INCa will mainly use three tools to develop research in this field: funding research; promoting and disseminating knowledge; setting up and facilitating researcher networks; evaluating funding schemes, and producing HSS data on cancer.

Regarding research funding, the Institute will continue its work supporting the training of future researchers (students and PhD candidates) in the field, with the renewal of the call for applications for HSS-E-PH PhD grants and for Psychoactive Substances and Addiction. The first round of the research programme for junior researchers in the field of tobacco and alcohol¹⁰ trialled in 2020 was a resounding success and the scheme will be offered again this year.

2022 will see the launch of the first round of the merged call for proposals in HSS-E-PH and Population Health Intervention Research (PHIR) with unrestricted sections and thematic sections. This call for proposals will, on the one hand, unify two of the Institute's historic and emblematic calls.¹¹ On the other, it will incorporate 3 actions of the Ten-Year Cancer Control Strategy in specific sections: 1-action IV.3.6 (HSS and intervention research on determinants and innovative patient support); 2- action IV.2.2 (HSS & PHIR research on care and support for children and AYAs); 3- action III.1.5 (tertiary prevention research for poor prognosis cancers). This call for proposals has been set up following a recommendation from INCa's SAB: provide better visibility for the scientific community of calls for proposals, in order to respond to the national policy promoted in the field nationwide.

10. The missing link between the INCa-IReSP call for proposals and call for PhD applications, the aim of this call is to encourage innovative initiatives in the fields of HSS and PHIR, with a view to developing the scientific community in relation to tobacco and alcohol. This innovative scheme includes a pre-selection phase based on letters of intent, a discussion seminar involving international experts, and interviews to select 10 candidates.

11. These are 1- the free call for proposals in Human and Social Sciences, Epidemiology and Public Health; 2- call for proposals in the field of PHIR.

Action I.1.1. of the Ten-Year Cancer Control Strategy, aimed at bolstering and structuring primary cancer prevention research and health promotion, has helped fund two research networks: Concept and Sorisp. Following on from this action, action I-1.6 targets a range of areas: developing knowledge about known and probable cancer risk factors, identifying health-promoting determinants and settings, as well as increasing knowledge about interventions, their design, intervention methods, evaluation, transferability, and implementation. To meet these challenges, a call for proposals will be launched to help fund world-class, impactful research for cancer-related primary prevention and health promotion in France. A launch seminar will be organised in January 2022.

Research chairs offer a valuable framework for innovation for developing HSS and PH research on cancer prevention. This scheme above all makes it possible to put research teams in place to focus on relatively unexplored or emerging themes, and develop collaborations to sustain them over time. In addition, in its new format, this scheme will benefit over a 5-year period from support from INCa, financial contributions from partners, and an agreement in principle between the partner academic structures to create a position in this area after the 5 years have elapsed. In 2022, a tobacco research chair will be set up; it will particularly address primary prevention issues and combat inequalities in the addiction field.

Developing discussions between researchers and providing spaces for disseminating knowledge are key forms of leverage for structuring research in Human and Social Sciences, Epidemiology, and Public Health. Regarding PHIR development, as is the case every year, a seminar will be organised in the first half of the year. Developed for and with researchers, this seminar will include 2 phases. The first phase will relate to projects supported by INCa in 2022, and the second will deal with methodological issues.

In the field of tobacco, INCa and the US NCI will facilitate a workshop on “tobacco cessation interventions and tobacco use prevention”. This project, initially scheduled to take place in 2021, has been rescheduled to November 2022. The primary focus of this international workshop is to review the current state of knowledge on tobacco use and tobacco cessation interventions at a population level, and to identify existing gaps and priority research questions to reduce tobacco use, particularly among priority populations.

In February 2022, the European Cancer Meeting of the French National Cancer Institute will particularly focus on the Cancer and Employment theme. Following on from this meeting, an international conference on the theme of “Cancer, Work & Employment” will be held in Paris in November. Prepared with an international scientific committee, it will be aimed at bringing the scientific community together to focus on cancer:

- Work & Employment: Overview of the situation;
- Employment & legislation;
- Return and access to work, job retention and impact of cancer at work;
- Work & Employment and Health Disparities: an array of career paths.

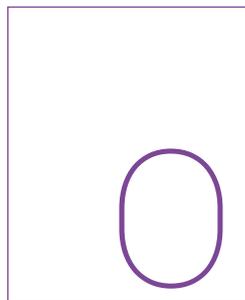
Finally, in partnership with CRUK, DKFZ and Anses, opportunities will be provided to discuss the organisation of the international conference on electronic nicotine delivery systems (E-Cigarettes). The objective of this conference, organised with an international scientific committee, will be to review the status of ongoing research on the pathways of users of these products and the impact of these products on health.

Moreover, in order to stimulate a drive for research into Human and Social Sciences and Public Health in the “inter-Canceropole” working groups, an annual event will once again be organised. In conjunction with the Canceropoles, a new format will be continued to provide a space for discussion between researchers and the HSS-E-PH-IR team on support schemes: Research Cafés. Lasting 90 minutes, the purpose of these virtual events is to present both existing and new support schemes, with an opportunity for discussion.

Regarding the evaluation of schemes supporting research, following on the preparatory work conducted in 2020 and 2021, a review of the projects funded in the call for Human and Social Science research proposals will be launched. This work will enlist an international scientific committee to monitor the review work, particularly on identifying the knowledge produced through this call for proposals.

Finally, in 2022, we will complete our analysis of the data from the 4th edition of the Cancer Barometer. This population-based survey carried out every five years is one of the few national studies conducted to investigate the French population’s perceptions of cancer risk factors. The department steered the scientific drafting of the questionnaire in consultation with Santé Publique France, researchers, stakeholders from the field, and user representatives.

INCA'S COMMITMENT TO OPEN RESEARCH – CHALLENGES FOR THE FUTURE



Open science represents an approach that is collaborative, transparent and accessible. Open science is now the norm, and all funding bodies, institutions and researchers recognise the benefit of open science and embed best open science practice into their processes.

Funding organisations play a key role in ensuring that open science practices are well embedded into the future research culture.

Funders have the opportunity and the responsibility to shift the incentives inherent in grant application processes and improve the way research is evaluated. In fact, the main role of funders in the context of developing alternative methods of evaluation (DORA, Leiden Manifesto, Plan S etc.) is to set clear policy expectations and provide the funding required to support the research community in adopting open science practices and develop and sustain key infrastructures and resources while ensuring discoverability, accessibility, interoperability, and reusability of findings.

We wish to ensure research outputs (papers, data, code and materials) can be accessed and used in ways that maximise health and societal benefits.

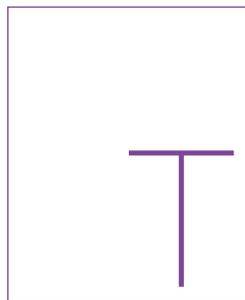
To address these challenges, we need to

- Reform reward and assessment structures: this implies explicitly recognising a broad range of research outputs (for example: valuing open practices as part of a researcher's track record, rewarding data sharing and data re-use, assessing the impact of a given contribution);
- Use responsible, transparent and open metrics;
- Develop and sustain national infrastructures;
- Enable and support the re-use of data and other outputs;
- Develop collaborative ways to use tools and mechanisms that allow a more efficient way to design, analyse, report, share and disseminate data ;
- Work to strengthen the implementation of policy and monitor compliance.

Collaboration and concerted efforts of all key players involved in research are necessary to ensure a future where research benefits from optimal reuse of research outputs, and a real impact on society can be achieved. It would be interesting for funders to take the opportunity to embrace current and developing digital technologies to improve their processes.

The French National Cancer Institute will continue to ensure the implementation of an action plan dedicated to open science in line with the national policy, and pursue our involvement in the national and European reflections; we will strengthen our actions promoting citizen science in the coming years.

STRENGTHENING AND SUPPORTING CANCER RESEARCH ACTIONS THROUGH EUROPEAN AND INTERNATIONAL COMMITMENTS



The French National Cancer Institute has a pre-eminent role in France with a national mandate encompassing all activity areas of value in the cancer control chain, from research to prevention and screening, to the organisation of cancer care and information for patients and their relatives. Fighting cancer requires a global endeavour and it is in the furtherance of INCa's mission to promote partnerships with institutions worldwide to support high-quality cancer control initiatives. INCa's favoured routes for implementing global cancer control are collaborative projects, transnational in design, that have proven to be of equal benefit to all participating members.

European actions

EUROPE'S BEATING CANCER PLAN: A NEW EU APPROACH TO PREVENTION, TREATMENT AND CARE



In February 2021, the European Commission presented “Europe's Beating Cancer Plan”, a main priority in the area of health of the von der Leyen Commission and a key pillar of a strong European Health Union. With new technologies, research and innovation as the starting point, the Cancer Plan sets out a new EU approach to

cancer prevention, treatment and care. It will tackle the entire disease pathway, from prevention to quality of life of cancer patients and survivors, focusing on actions where the EU can add the most value.

Europe's Beating Cancer Plan aims to tackle the entire disease pathway. It is structured around four key action areas with 10 flagship initiatives and multiple supporting actions:

- Prevention;
- Early detection;
- Diagnosis and treatment;
- Quality of life of cancer patients and survivors.

It will be implemented using the whole range of Commission funding instruments, with a total of €4Bn being earmarked for actions addressing cancer, including from the EU4Health programme, Horizon Europe and the Digital Europe programme.

Until now, INCa has actively contributed to the actions initiated by the European Commission. The launch of Europe's Cancer Beating Plan is an opportunity to be further involved in an integrated way to support cancer research-led innovation for the benefit of all.

By the end of 2021, the Institute was already involved in several actions:

- Joint action Network of Comprehensive Cancer Centres (CRANE);
- Joint Action Networks of Expertise (JANE).
- Coordination and Support Action to generate a blueprint for European Initiative to Understand Cancer (CSA UNCAN.eu).

Joint Action Network of Comprehensive Cancer Centres (JA CRANE)

The joint action is organised around 8 work packages, including 4 core work packages:

- WP5: The EU Network of comprehensive cancer centres: composition, governance, joining process, and functioning aiming to design the EU CCCs Network by defining the composition, coordination, and activities;
- WP6: Organisation of comprehensive high quality cancer care in the CCCs Network sets out to further develop the access and availability of the comprehensive high quality of care in CCCNs to all European member states (MS). It is a continuation of the theoretical framework of Comprehensive Cancer Care Networks (CCCNs) developed during the Joint Action CanCon and its translation into practice which was successfully achieved in JA iPAAC WP 10, "Governance of integrated and comprehensive cancer care";
- WP7: Framework to enable CCCs to develop a consensus of Comprehensive cancer centres, both standalone centres, and centres which are part of University or General Hospitals. It should be based on scientific evidence and experience from the Member States;
- WP8: Integrated Care Governance and Networks to propose a working definition of Comprehensive Care Networks in European health systems, based on the selection and analysis of empirical evidence and the perspectives of developments of this organisational approach in fields such as research translation into clinical practice, care coordination for highly-complex procedures and evaluation systems of network performance.

Flagship 5

The Commission will establish, by 2025, an EU Network linking recognised **National Comprehensive Cancer Centres in every Member State**. It will facilitate the uptake of quality-assured diagnosis and treatment, including training, research and clinical trials across the EU. This cross-border collaboration will improve patients' access to high-quality diagnostics and care and the latest innovative treatments. It can also help with patient mobility to ensure adequate treatment for patients with complex conditions. A new "EU Cancer Treatment Capacity and Capability Mapping" project will help map and share the different capabilities and expertise available across the EU.

This action will help deliver higher-quality care and reduce inequalities across the EU, while enabling patients to benefit from diagnosis and treatment close to home. The Cancer Plan aims to ensure that 90% of eligible patients have access to such centres by 2030.

The challenges for the project partners will be to define the conditions for setting up the CCCs, their functioning and their governance, at the end of the 24 months of the joint action.

The French National Cancer Institute co-leads WP7 (“Set of standards for research, including education, and set of governance standards of CCC”).

Initial work has helped identify guiding principles for the next steps:

- A common approach to identify key features and objectives that will drive future CCCs to excellence;
- An inclusive approach with broad coverage to ensure to reach the objective that 90% of eligible patients have access to such centres by 2030;
- A principle of continuous quality improvement in order to take into account the reality of the heterogeneous centres already existing in Europe;
- A principle of EU-wide solidarity, closely linked to the notions of cooperation and networking.

Joint Action Networks of Expertise (JA JANE)

The overall aim of this joint action is to set up 6 new networks of expertise (NoE) in the following areas

- WP 4 Sustainability to ensure that the established NoEs assemble the best knowledge, skills and facilities available in Europe;
- WP 5 Complex & poor-prognosis cancer to increase the efficacy of treatments and quality of care, reduce inequality across the EU, boost basic/preclinical research and the use of innovative technologies, promote education, clinical practice guidelines and multidisciplinary care development, as well as epidemiological surveillance;
- WP 6 Palliative care to support the integration of evidence-based palliative care into routine cancer care and to ensure equitable access to palliative care across EU MSs;
- WP 7 Survivorship to support the integration of evidence-based approaches to cancer survivorship into routine care and to ensure equitable access across EU MSs, also driving the identification of all relevant issues pertaining to the increased survival of cancer patients and possible solutions;
- WP 8 Personalised primary prevention to promote the implementation of personalised primary prevention at a community level;
- WP 10 Hi-tech medical resources which focus on the development of a NoE fostering the integration of omic technologies into the EU healthcare systems (HCSs) to improve cancer prevention, diagnosis and treatment. Indeed, cancer is to be considered as a disease that should be prevented, diagnosed early/in a timely fashion and treated appropriately within a continuum (the PDT cycle).

The establishment of these networks will also need to be accompanied by a critical evaluation of existing and future EU networking models, in order to optimise the functioning of the new networks of expertise. Each future network is the subject of a WP, the final deliverable of which will be the launch of a call for expressions of interest.

JA JANE is complementary to JA CRANE. The networking of experts should help to ensure high quality of care, and thus benefit future CCCs.

One of the challenges of the French position is to ensure good representation and recognition of French expertise. The affiliated entities (UNICANCER and FHF Cancer) have already identified experts by theme. The Institute, in conjunction with UNICANCER, leads WP10, dedicated to the network of experts on advanced medical resources.

Coordination and Support Action to Understand Cancer UNCAN.eu

The coordination and support action aims to generate a strategic agenda to launch the UNCAN.eu virtual institute, a European initiative to understand cancer proposed by the Mission Board and Europe's Beating Cancer Plan.

This blueprint will be organised as a research roadmap, focusing on a limited number of challenges that need to be addressed urgently at the supranational level by research groups in Europe and beyond. These challenges will be tackled mostly by large-scale research programmes identified through a competitive selection process. If and when necessary, targeted smaller-scale interventions addressing a very specific issue will also be initiated by UNCAN.eu. Challenges and programmes will be selected in close interaction with cancer patient advocacy groups to integrate European citizens' and cancer patients' and families' expectations in the proposed agenda. Patient and citizen empowerment will be strengthened to guarantee optimal implementation of the UNCAN.eu initiative. To address research challenges, existing data, samples and expertise will be located and shared to provide the first bricks to the research and innovation approaches of the UNCAN.eu platform.

The project was submitted in October 2021 and is structured around 6 WPs:

- WP1: Coordination and management;
- WP2: Next European challenges in cancer research;
- WP3: European infrastructures for cancer research & federated cancer research hubs;
- WP4: European patients and citizens in cancer research information and dissemination;
- WP5: Governance, organisation, logistics, finances and sustainability ;
- WP6: Inequalities in cancer research, improved science outreach.

Flagship 7

Alongside the "Genomics for Public Health" project, the **European Initiative to Understand Cancer (UNCAN.eu)**, planned to be launched under the foreseen Mission on Cancer to increase the understanding of how cancers develop, will also help identify individuals at high risk from common cancers using the polygenic risk score technique. This should facilitate personalised approaches to cancer prevention and care, allowing for actions to be taken to decrease risk or to detect cancer as early as possible.

France has been coordinating the CSA and one project.

INCa is more specifically involved in WP3, dedicated to the mapping of research infrastructures and European initiatives to establish the roadmap for a federated European cancer research data centre. The purpose of this European centre is to ensure data interoperability and reuse. This is undoubtedly one of the greatest challenges, since despite the mass of data collected, its use for research purposes is largely under-exploited.

The Institute will also participate in WP5, the objective of which is to establish the framework for the operation of the UNCAN.eu platform. More specifically, INCa will participate in the task on the link between the governance and logistic support of UNCAN.eu and the cancer plans of the Member States and other European initiatives.

The results are expected for 2022 and will drive the implementation of this flagship initiative of Europe's Beating Cancer Plan. If successful, the CSA will enable the launch of a dedicated call for proposals by 2023.

FRENCH EUROPEAN UNION PRESIDENCY PFUE



On the occasion of the French Presidency of the Council of the European Union, the first European Conference of the French National Cancer Institute will be held on 3 and 4 February 2022.

One year after the launch of France's Ten-Year Cancer-Control Strategy and Europe's Beating Cancer Plan, and on the occasion of World Cancer Day, this Conference seeks to step up cooperation and enhance synergy to help Europe advance in this fight, for the benefit of citizens from the 27 Member States.

This event aims to be a forum for discussion and co-construction of solutions for fighting cancer will allow key European institutional stakeholders and experts to share their views and make proposals regarding the five key themes on fighting cancer:

- Childhood cancers;
- Cancers with poor prognosis;
- Cancer prevention;

- Cancer and Employment;
- International cooperation in the fight against cancer.

The Conference will also provide greater visibility for key players in the fight against cancer and certain initiatives that they will present at masterclasses.

Recommendations and roadmaps will be issued after this event and will fuel the launch of different supranational initiatives that will also be a common thread for the following presidencies (Czech Republic and Sweden). The concrete actions expected to ensue aim to be in alignment with the different national initiatives and further strengthen the rollout of Europe's Beating Cancer Plan.

Global actions

Recent developments in research and innovation have improved our understanding of cancer. They are based on national and international cooperation between key players in cancer control. This cooperation can make a difference by creating new opportunities for research and innovation and by mobilising the international community in the fight against cancer, without forgetting the need to help the least developed countries.

NATIONAL CANCER CENTER OF JAPAN (NCC)

In 2016, the close collaboration between France and Japan on cancer was further strengthened by a memorandum of understanding signed by INCa and the National Cancer Center of Japan. Thus, in December 2019, INCa and the NCC of Japan jointly organised a workshop on paediatric cancer.

To keep up the momentum of this collaboration, INCa and the NCC of Japan, together with the French Embassy have been discussing the opportunity of jointly organising another scientific event. The pandemic context even fuelled their desire to propose a more meaningful format.

Throughout 2022, INCa and the NCC of Japan will thus propose a series of webinars on immuno-oncology. Rather than a partnership between INCa and the NCC of Japan, these webinars provide an opportunity for French and Japanese researchers to present their work. It is also an opportunity to develop, build and further strengthen the close collaboration between the two nations in many areas in cancer research and clinical activities.

The webinars will also act as teasers for the joint workshop scheduled in early 2023, in Japan.

In addition to talks of high scientific quality, this workshop will enable INCa and the NCC of Japan to share their research strategies in immuno-oncology as well as to renew their MoU that may cover the following common objectives:

- To share the French model of immuno-oncology research and care through the presentation of programmes and platforms for networking with Japanese counterparts whose cancer technology is at the forefront;

- To establish a comprehensive picture of immuno-oncology research in Japan through the intervention of institutional actors as well as other relevant partners in this field, such as patient or research organisations;
- To identify Franco-Japanese research topics for projects, to advance research and thus improve genomic cancer research;
- To identify options for cooperation.

More broadly, this close collaboration will also help build new partnerships, particularly with Japanese funding agencies in order to propose common programmes and initiatives and, thus, new funding opportunities.

EXPLORING GLOBAL INITIATIVES TO STRENGTHEN CANCER RESEARCH

In 2018, a €5M additional allocation dedicated to support paediatric cancer research enabled the French National Cancer Institute to extend and develop its scientific programming with new funding opportunities.

Indeed, the main new programme launched was the “High-risk/High-gain” call for proposals. This initiative aimed to support original and bold research projects, conceptually new and risky, which could not be funded in the context of traditionally existing calls for proposals. These projects must be based on significant conceptual risk-taking, in order to propose a new or even disruptive approach. The potential impact of the proposed projects on paediatric oncology research could be of a high level and would open up new and original avenues and produce concrete advances in paediatric oncology.

Building on the success of the programme and the challenges raised by the Ten-Year Cancer Control Strategy, in 2022, a specific edition will be launched to address poor-prognosis cancers.

While rather new in France, this kind of programme is already proposed by different international funding agencies and research institutes (CRUK, NCI, Weizmann Institute, etc.).

Nevertheless, the programmes mentioned above may not be considered as ambitious as expected in relation to current cancer research challenges and needs because of the time and the amount allocated. Despite some success, this kind of programme should be stepped up to a higher level. Indeed, addressing cancer’s toughest challenges requires tenacity, creativity and global collaboration. No single researcher, institution, country or scientific discipline can solve these problems alone. This has been recently observed and confirmed with the global

Covid-19 pandemics, further highlighting the crucial need for international scientific collaboration in both the public and private sectors to develop diagnostics, vaccines and treatments in order to tackle health emergencies.

Addressing the cancer burden at a global level is thus necessary to spread out efforts and benefit everyone. As such, it is worth reviewing and exploring international opportunities in line with the French National Cancer Institute's strategy and objectives.

The Cancer Grand Challenges initiative is the main international programme meeting these objectives.

Launched by CR-UK in 2015 and involving the US NCI since 2020, the aim of Cancer Grand Challenges is to support innovative, bold, multidisciplinary and international projects around the major challenges of basic cancer research in order to achieve major progress through global collaborations and very large-scale funding. Successful projects are funded up to £20M over 5 years (i.e. \$25M, which is approximately €23M)

Cancer Grand Challenges were devised to promote the emergence of innovative ideas to overcome obstacles, which are all the more important as they are shared by the whole community, to steer research in a strategic direction while reinforcing the creative energy of multidisciplinary teams in order to accelerate progress. In this way, collaboration, innovation and creativity represent the core features of the programme.

This programme is a new way of funding, supporting and accompanying research that should ultimately transform cancer research.

The French National Cancer Institute is exploring the possibility of participating in Cancer Grand Challenges and, particularly, identifying the most relevant terms of participation.

Beyond the scientific interest of this large-scale programme, being involved in such a programme would provide different opportunities for the Institute:

- Accelerating research to complement the various national initiatives already proposed;
- Challenging and restructuring French research, in particular to move upmarket scientifically (thinking differently, multi- and interdisciplinary partnerships, international openness, etc.);
- Impact and drive to meet the objectives of the Ten-Year Cancer Control Strategy.

4

Appendices

- Common scientific outline **177**
- INCa's calls for proposals: scientific and operational management **179**

COMMON SCIENTIFIC OUTLINE



Established in 2000, the International Cancer Research Partnership (ICRP) is a unique alliance of cancer organisations, working together to enhance global collaboration and strategic coordination of cancer research. It includes 150 worldwide organisations from Australia, Canada, France, Japan, the Netherlands, United Kingdom, and the United States. INCa joined this partnership in 2009.



This consortium aims to improve access to information about cancer research being conducted, explore opportunities for cooperation between funding agencies, and enable our members to maximise the impact of their independent efforts.

ICRP organisations share funding information in a common format (known as the Common Scientific Outline or CSO) to facilitate pooling data and evaluating data across organisations.

The Common Scientific Outline, or CSO, is a classification system organised around seven broad areas of scientific interest in cancer research. The development of the CSO is laying a framework to improve coordination among research organisations, making it possible to compare and contrast the research portfolios of public, non-profit, and governmental research agencies. This classification is subdivided in 7 categories:

- Biology
- Aetiology (causes of cancer)
- Prevention
- Early Detection, Diagnosis, and Prognosis
- Treatment
- Cancer Control, Survivorship, and Outcomes Research
- Scientific Model Systems

As a member of the ICRP consortium, INCa and its partners use this classification. The types of research projects funded by INCa, the French Ministry of Health (DGOS) and Inserm for ITMO Cancer-Aviesan that are presented in this report are based on this CSO classification.

THE DIFFERENT CSO CATEGORIES INCLUDE:

● CSO 1 Biology

- 1.1 Normal functioning
- 1.2 Cancer initiation: alterations in chromosomes
- 1.3 Cancer initiation: oncogenes and tumour suppressor genes
- 1.4 Cancer progression and metastasis
- 1.5 Resources and infrastructure

● CSO 2 Aetiology

- 2.1 Exogenous factors in the origin and cause of cancer
- 2.2 Endogenous factors in the origin and cause of cancer
- 2.3 Interactions of genes and/or genetic polymorphisms with exogenous and/or endogenous factors
- 2.4 Resources and infrastructure related to aetiology

● CSO 3 Prevention

- 3.1 Interventions to prevent cancer: personal behaviours that affect cancer risk
- 3.2 Nutritional science in cancer prevention
- 3.3 Chemoprevention
- 3.4 Vaccines
- 3.5 Complementary and alternative prevention approaches
- 3.6 Resources and infrastructure related to prevention

● CSO 4 Early Detection, Diagnosis, and Prognosis

- 4.1 Technology development and/or marker discovery
- 4.2 Technology and/or marker evaluation with respect to fundamental parameters of method
- 4.3 Technology and/or marker testing in a clinical setting
- 4.4 Resources and infrastructure related to detection, diagnosis, or prognosis

● CSO 5 Treatment

- 5.1 Localised therapies – Discovery and development
- 5.2 Localised therapies – Clinical applications
- 5.3 Systemic therapies – Discovery and development
- 5.4 Systemic therapies – Clinical applications
- 5.5 Combinations of localised and systemic therapies
- 5.6 Complementary and alternative treatment approaches
- 5.7 Resources and infrastructure related to treatment

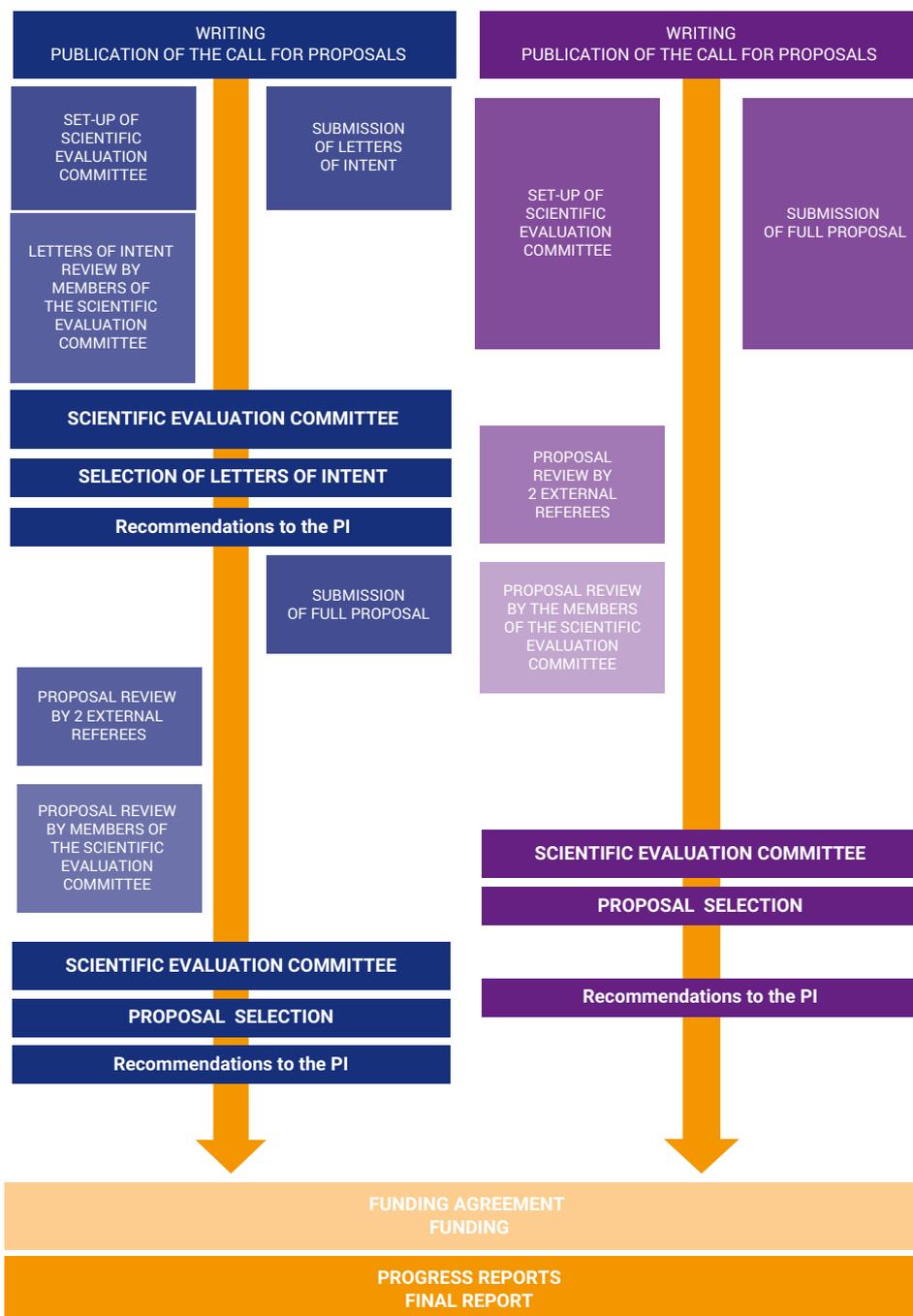
● CSO 6 Cancer Control, Survivorship, and Outcomes Research

- 6.1 Patient care and survivorship issues
- 6.2 Surveillance
- 6.3 Behaviour
- 6.4 Cost analyses and health care delivery
- 6.5 Education and communication
- 6.6 End-of-life care
- 6.7 Ethics and confidentiality in cancer research
- 6.8 Complementary and alternative approaches for supportive care of patients and survivors
- 6.9 Resources and Infrastructure related to cancer control, survivorship, and outcomes research

● CSO 7 Scientific Model Systems

- 7.1 Development and characterisation of model systems
- 7.2 Application of model systems
- 7.3 Resources and Infrastructure related to scientific model systems

INCA'S CALLS FOR PROPOSALS: SCIENTIFIC AND OPERATIONAL MANAGEMENT



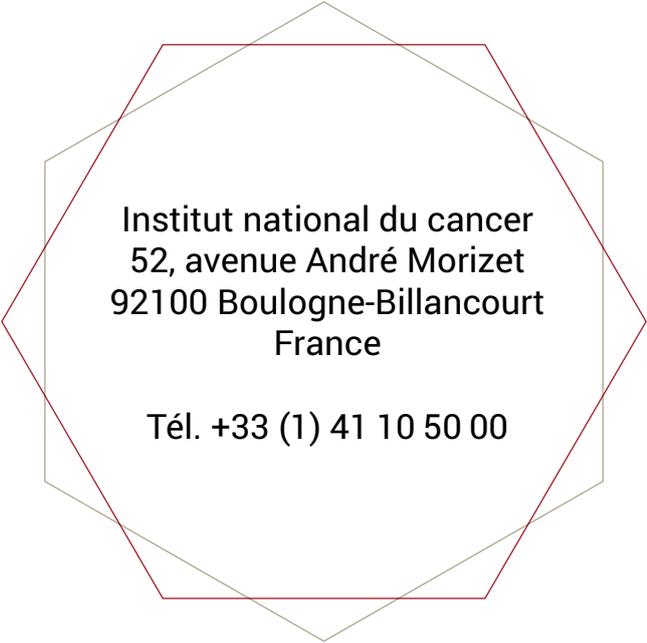


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