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INSTITUT NATIONAL DU CANCER

SCIENTIFIC REPORT

2019

ACTIONS FOR CANCER RESEARCH

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

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e-cancer.fr

INTRODUCTION

ACTIONS FOR CANCER RESEARCH

INSTITUT NATIONAL DU CANCER

SCIENTIFIC REPORT 2019

2019 will remain a singular year for the French National Cancer Institute. Indeed, it marks both the end of the third Cancer Control Plan and the aim of the public authorities to handle cancer control issues with the drafting of a ten-year strategy proposing a new model for mobilisation and action.

ON 4 FEBRUARY 2019, during the French National Cancer Institute's meeting, the main principles of a future ten-year cancer control strategy were set out: to focus the fight against cancer on its priority issues and to apply a longer time-scale tailored to the complexity of the projects to be carried out. Officially entrusted to the Institute by the law of 8 March 2019, the ten-year strategy project has been conducted with very broad consultation, involving our Scientific Advisory Board, our Board of Directors and all our partners. In addition, we consulted all the stakeholders, such as research organisations, hospital federations, institutional partners, representatives (healthcare professionals, patients, associations, citizens, and users), as well as regional health and research structures. This process of co-construction, on an unprecedented scale, has enabled us to build the outlines of an ambitious, innovative, and unifying strategy based on common and shared objectives. Three major challenges have thus emerged for the next decade: improving cancer prevention, limiting the side-effects of treatments, and improving the quality of life of those affected by the disease, and finally, addressing poor prognosis cancers in adults and children. At the time of writing, a finalised version is being written, taking into account a range of feedback from our partners. In this regard, INCa is extremely grateful to the SAB for its highly valuable contribution. In addition, within the framework of this law, and since 2019, the French Ministry of Research has allocated an additional €5M of funding per year to support paediatric cancer research to propose dedicated new actions in addition to recurrent funding of basic research in childhood cancers through INCa's regular programmes. Within this framework, four novel calls of proposals have been launched in 2019 and 2020.

2019 WAS ALSO A PIVOTAL YEAR in that it also marked the beginning of the work on the Institute's next objectives and performance contract with the State and, at a national level, the draft of the ambitious multi-year research programming law. These two projects will aim to reaffirm, improve, and strengthen our commitments in cancer research support, particularly in maintaining our main cancer research flagships, such as the investigator-driven calls for proposals, support for cancer research structuring, as well as promoting access to innovation.

AS IN PREVIOUS YEARS, 2019 saw the continuation, intensification and launch of major initiatives in all areas of cancer control. Amongst the major advances to highlight, mention can be made of the extension of the "right to be forgotten", the launch of the new organised screening programme for cervical cancer, and the adoption of a new reference best practice framework for announcing a cancer diagnosis and supporting patients in their care pathway. Furthermore, several actions have been carried out in the cancer research field, including the designation of 16 CLIP^2 centres, including 7 with paediatric activity, the development of innovative therapies with the roll-out of CAR-T cell therapies, and the new funding allocated to research on paediatric cancers. Progress for all, in the best conditions of quality and safety of care, continues to guide our action and that of all our partners.

THIS SCIENTIFIC REPORT PRESENTS a detailed review of the research programmes conducted in 2019, as well as main key figures of the 2014-2019 Cancer Control Plan, to the extent possible due to the Covid-19 pandemic context and the subsequent national lockdown that impacted our activity when drafting the document in 2020.

Professor Norbert Ifrah, MD
■ Chairman and CEO of the
French National Cancer Institute

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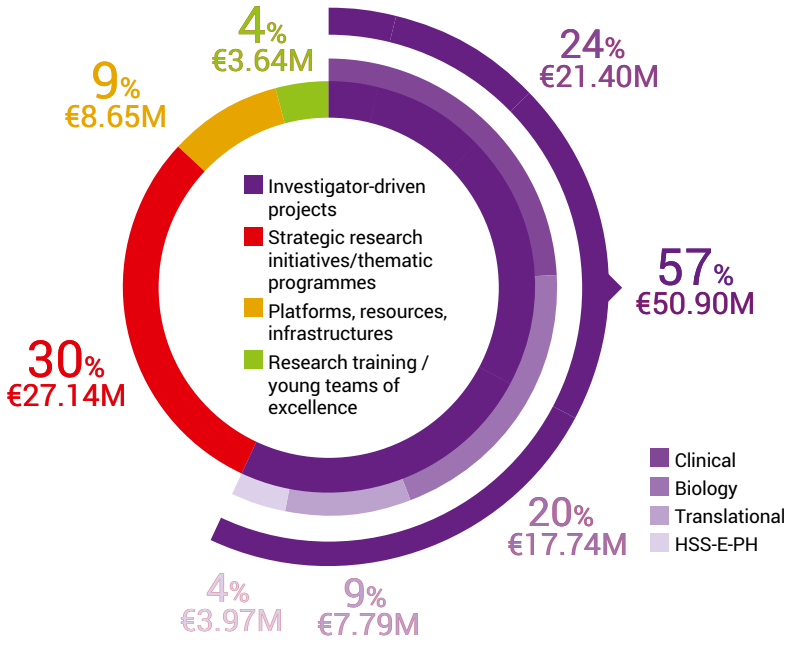
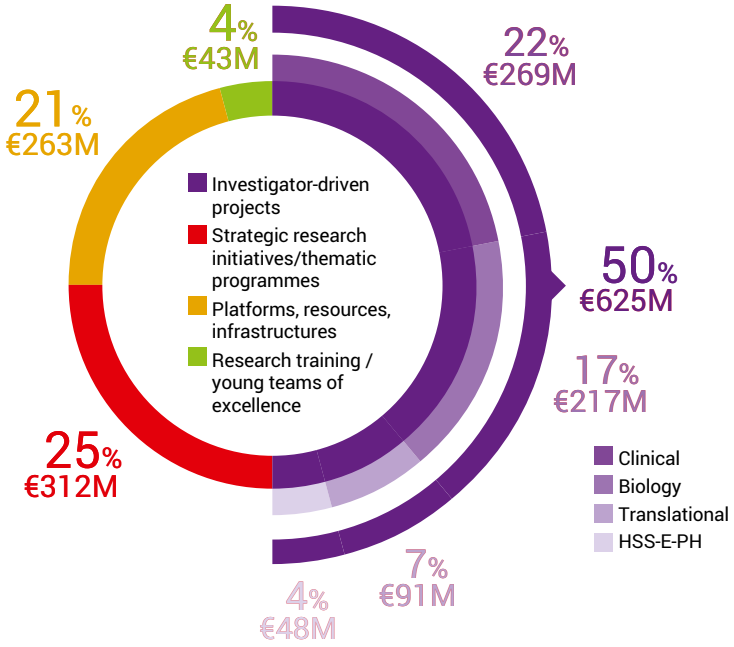
2019 multi-year cancer funding by programme type (INCa, DGOS and ITMO Cancer-Aviesan): €90.32M invested



2019: 2 new programmes launched to support paediatric cancer research for a total amount of €3.67M

- International mobility of young researchers in paediatric oncology: **2** grants awarded
- Accelerating basic and translational research in paediatric oncology: help in pooling, structuring, and sharing research data: **4** projects selected

2007-2019 multi-year cancer funding by programme type (INCa, DGOS and ITMO Cancer-Aviesan): €1.24Bn invested



Total investments over the 2007-2019 period:

€490M in biology and basic sciences

€136M in research in human and social sciences, epidemiology and public health

€270M in translational and integrated cancer research

€347M in clinical research

1

The international scientific advisory board

This 14th 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.

With regard to 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 2019 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
- **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
- **Ms. Dominique David**, Founder and Chairperson of the Association pour la recherche sur les tumeurs cérébrales, Aix-en-Provence, France
- **Prof. Johann de Bono**, MD, PhD, The Institute of Cancer Research and the Royal Marsden, London, United Kingdom
- **Prof. Olivier Delattre**, MD, PhD, Institut Curie, Paris, France
- **Prof. Anne Eichmann**, PhD, Yale School of medicine, New Haven, USA
- **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
- **Dr. Mette Kalager**, MD, PhD, Harvard T.H. Chan School of Public Health, Boston, USA
- **Prof. Catherine Lacombe**, MD, PhD, Institut Cochin, Paris, France
- **Ms. Estelle Lecointe-Artzner**, Founder and Chairperson of the Association Info Sarcomes, Rennes, France
- **Dr. Douglas R. Lowy**, MD, NCI Acting Director, Bethesda, USA
- **Prof. Marc-André Mahé**, MD, PhD, General Director, Centre François Baclesse, Caen, France
- **Dr. Bernard Malissen**, PhD, Centre d'Immunologie de Marseille-Luminy, Marseille, 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, Montréal, Canada,
- **Prof. Gérard Socié**, MD, PhD, Hôpital Saint-Louis, Paris, France
- **Dr. Naomi Taylor**, MD, PhD, Institut de Génétique Moléculaire de Montpellier, Montpellier, France
- **Prof. Robert A. Weinberg**, PhD, Massachusetts Institute of Technology (MIT), Cambridge, USA
- **Prof. Laurence Zitvogel**, MD, PhD, Gustave Roussy, Villejuif, France

2019 RECOMMENDATIONS

INCa

1 Congratulations on the scientific report and thanks to Professor Christine Chomienne for her exemplary leadership during the past years. We also congratulate the different team members for their work and important presentations.

2 SAB acknowledges its role in contributing to the scientific direction of INCa is now codified in March 2019 Health law.

3 The SAB spent the bulk of its time discussing the new Cancer Research Strategy development plan and content and offers the following.

Process for strategy development

1 The SAB agreed with the planned process.

2 The working groups and their outputs as well as the feedback from the consultations, and the SWOT analysis will be key in developing a strategy that will:

- **a.** Build on the research strengths of France, its networks and its research infrastructure. There are unique strengths that should be called out;
- **b.** Address gaps or weaknesses defined in the SWOT analysis;
- **c.** Allow France to grow its reputation as international leader in cancer research and its impact on positive health outcomes for all citizens (addressing inequities).

Content of the strategy

The SAB offers the following comments and recommendations:

1 The overarching key goal of research is ***to improve health for all*** in France – reducing incidence, morbidity and mortality of cancer. INCa deserves congratulations for the progress of the past decade and now it is time ***to expand*** and accelerate the impact on cancer outcomes.

2 The SAB noted the efforts that were made to focus as well as to be proactive by anticipating emerging important areas for research (e.g. immunebased therapies).

3 Consolidation of database resources:
- **a.** INCa should take a leadership role to create national resources for data sharing, support and research into new thematic initiatives (e.g. common databases and data elements);
- **b.** For older initiatives (e.g. SIRICs, data bases), INCa should be proactive in leveraging past investments to bring together projects and infrastructure addressing common questions to create economies of scale as well as enhance opportunities for research;
- **c.** As a steward of these precious resources, INCa must ensure they are harmonized to international standards and optimized for collaborative use, both nationally and internationally.

4 The excellent investigator-driven fundamental research program must continue.

5 The already excellent programs, underpinned by critically important support for infrastructure and clinical and translational research, as well as important new topics such as large data science and pediatric oncology should continue in the new strategy as planned.

6 Clear goals, timelines and metrics for success should be defined to make decisions about NEW strategic programs and future funding as well as to determine whether they are rolled into other core funding programs

7 **Three themes** – the SAB agrees improvements are needed in cancer prevention, in the quality of life of patients living with cancer and in the outcomes of some cancer types with the poorest survival rates:
- **a.** The working groups planned will provide insights into the SWOT analysis of current state in these areas as well as where the greatest impact of investment in research can be found;
- **b.** Achieving goals of improvement in these areas will require ***new investments*** in research in etiology, prevention (primary and secondary) research, biology, behavioural science, implementation science, clinical research as well as ***capacity building (human resources)***.

8 **A fourth theme** which would be cross-cutting over all aspects of cancer care should be considered for inclusion:
- Researching and reducing inequities in aspects of cancer prevention, treatment and outcomes.

Feasibility and funding

1 The SAB notes that Cancer remains a leading cause of morbidity and mortality in France – Investment in cancer research is a clear priority to lead to improvement in health outcomes.

2 The new INCa research strategy with its inclusion of a broader mandate will require substantial increased financial and human resources to realize the potential positive impact on cancer outcomes. The SAB thus feels strongly that a substantial increase in government investment in the INCa budget, commensurate to the ambitions of those goals, is required.

2

2019 cancer research activity report

In recent years, the research and health landscape in oncology has undergone a major 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. INCa has renewed the call for proposals for population health intervention research on reducing cancer-related inequalities and pursued its partnership with the French public health research institute (IReSP) to support research on tobacco control. The Cancer Control Plans focus on specific research priorities, in collaboration with institutional partners, which are mostly planned by ITMO Cancer-Aviesan through multiple calls for proposals. For instance, in 2019, INCa and ITMO cancer launched a new joint call dedicated to precancerous lesions, to improve early cancer detection and prevention.

In order to continue and bolster INCa's aim to promote access to innovation, a new early-phase clinical centres (CLIP^2) designation campaign has been launched and has led to the designation of 16 centres throughout France, including 7 with paediatric activity.

In March 2019, a new governmental health law commissioned INCa with the task of defining a ten-year cancer control strategy, with specific monitoring of funds allocated to research in paediatric oncology. Within the scope of this law and since 2019, the French Ministry of Research has allocated €5M extra funding per year to support paediatric cancer research, by launching novel actions and programmes in addition to recurrent funding for basic research in childhood cancers through INCa's regular programmes and calls. In 2019, two first novel calls for applications were launched to support human capabilities and data structuring and sharing.

As mentioned, 2019 has involved some intense brainstorming, mobilising INCa's teams and institutional partners to elaborate the next ten-year cancer control strategy. The first draft of this strategy has been submitted to INCa's International SAB, who made important and valuable comments that will be considered in the final version of the strategy currently under construction.

This following section presents a detailed review of the research programmes conducted in 2019, 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.

In order 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.

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

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

THE PROGRAMME IN 2019

In 2019, 34 projects were selected out of the 294 proposals submitted for a total amount of €17.74M (11.6% of the submitted applications were selected).

Figure 1 presents a detailed analysis of the funded projects according to the international CSO classification[1] (CSO1). The aim of the majority of the funded projects (66.2%) is to study the biological mechanisms of cell transformation and disease progression and 33.8% study either molecular mechanisms of response and resistance to treatments, or identification of new therapeutic targets (CSO 5). It is worth noting that the percentage of projects funded belonging to the latter has increased compared to 2018 (10.9% in 2018 compared to 33.8% in 2019).

2019:
34 projects
funded out of the 294 proposals submitted for a total budget of
€17.74M

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

TABLE 1
FEATURES OF THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2019

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: • Enable the achievement of original projects; • Strengthen multidisciplinary collaborations; • Develop research in emerging areas.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€17.74M**
Proposals submitted	**294**
Projects selected	**34**
Selection rate	**11.6%**

As highlighted in Figure 1, nearly 29.4% of the projects specifically concern the interaction between the tumour and its 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.

Projects studying the mechanisms of DNA repair and the regulation of gene expression (epigenetic regulation or transcription, CSO 1.2) or oncogenes, tumour suppressor genes and signalling pathways involved in cell proliferation and cell transformation (CSO 1.3) represented 33.8% of the funded projects.

Besides the CSO classification, figure 2 presents an analysis of the main research topics addressed by the selected projects. These topics are genetics (24%), cell signalling (18%), immunology (18%) and microenvironment (12%).

Amongst the projects studying genetics, the majority concern the analysis of DNA damage/DNA repair signalling (56%). As regards projects on cell signalling, 42% focus on cellular metabolism (42%), and for projects on immunology, the most represented scientific field is immune surveillance (67%). Finally, microenvironment projects mainly concerned the study of tumour-infiltrating immune cells (38%).

FIGURE 1
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2019

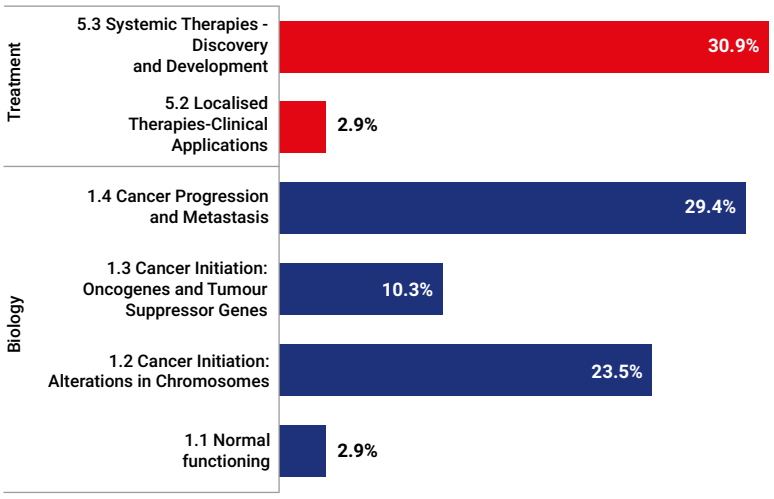


FIGURE 2
ANALYSIS OF THE MAIN RESEARCH TOPICS ADDRESSED BY FUNDED PROJECTS IN 2019 AND THE DISTRIBUTION OF THE RESEARCH FIELDS INTO THESE MAIN TOPICS

THE PROGRAMME OVER THE 2007-2019 PERIOD

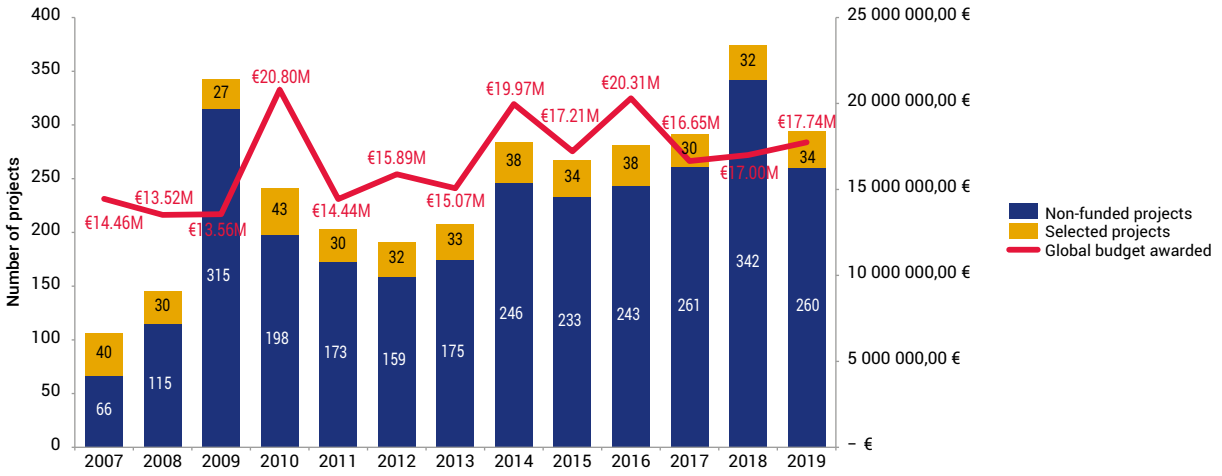
Since 2007, 441 projects have been selected out of 3,227 proposals submitted to the Biology and basic sciences for cancer research programme, for a total budget of €216.58M (Figure 3).

The number of letters of intent has been increasing steadily since 2011, reaching a peak of 374 applications submitted in 2018. In 2019, 294 letters of intent were submitted, which is a more usual number of applications.

This programme is the Institute's most attractive programme in terms of number of applications. This observation highlights the importance of PLBIO in supporting research in cancer-related basic sciences. Therefore, INCa is a major funding agency for basic sciences, alongside the French National Research Agency (ANR), which funds basic research outside the field of cancer.

FIGURE 3

TRENDS IN SELECTION AND FUNDING OF THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME OVER THE 2007-2019 PERIOD

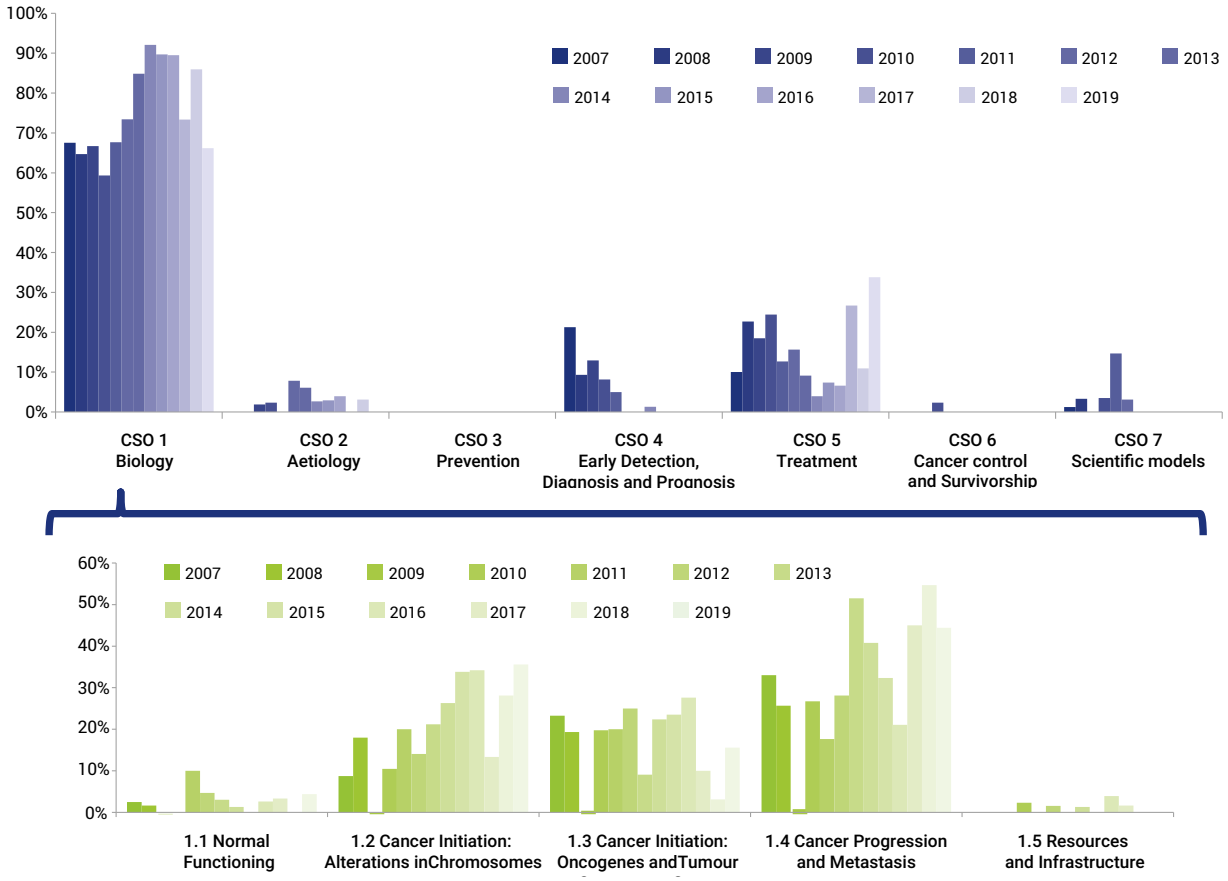


The analysis of the projects funded over the 2007-2019 period according to the CSO classification shows that the projects are mainly focused on the biological mechanisms of cell transformation and disease progression. This trend has been quite stable over the years (Figure 4).

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).

FIGURE 4

DISTRIBUTION OF SELECTED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2019 PERIOD



Nearly 30% of the projects are non-specific to a tumour type, highlighting the fact 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 (16%), breast cancer (13%) or colorectal cancer (9%) are also well represented (Figure 5).

PLBIO:
the largest research programme operated and funded by INCa

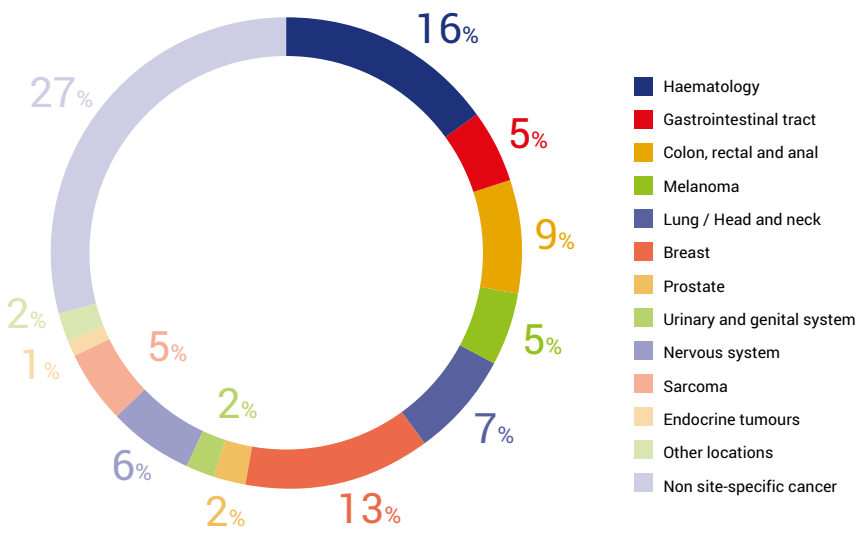
441 projects

funded for nearly

€217M

over the 2007 - 2019 period

FIGURE 5
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO CANCER SITES STUDIED FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME OVER THE 2007-2019 PERIOD



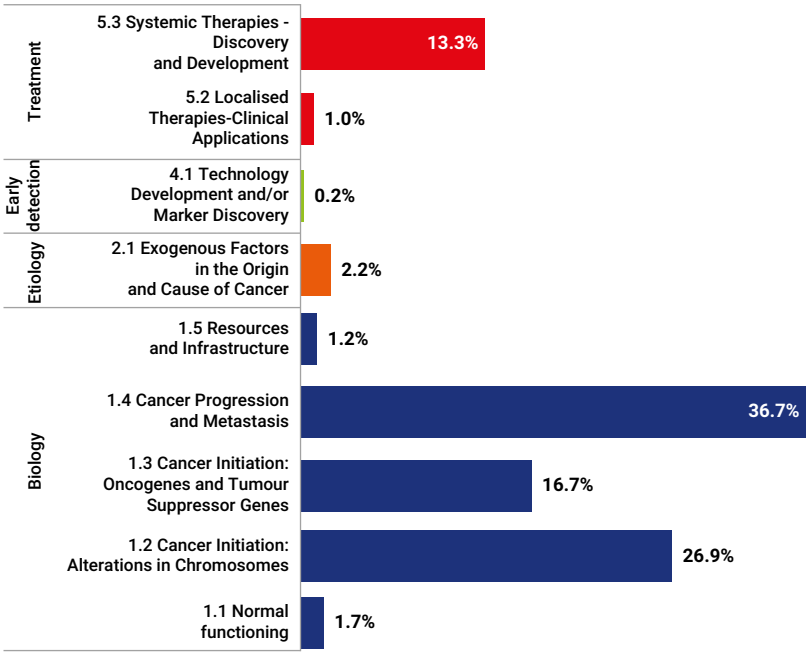
THE PROGRAMME OVER THE 2014-2019 CANCER CONTROL PLAN

Objective 13.1 of the 2014-2019 Cancer Plan (which aims to support basic cancer research) has helped fund 206 projects through the PLBIO call for proposals for a total amount of €108.9M.

Reflecting the main fields studied by the principal investigators of PLBIO applications, the aim of the majority of these funded projects (88.3%) is to study the biological mechanisms of cell transformation and disease progression, according to the international CSO classification (CSO1) (Figure 6).

FIGURE 6

DISTRIBUTION OF SELECTED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME ACCORDING TO THE CSO CLASSIFICATION OVER THE 2014-2019 PERIOD

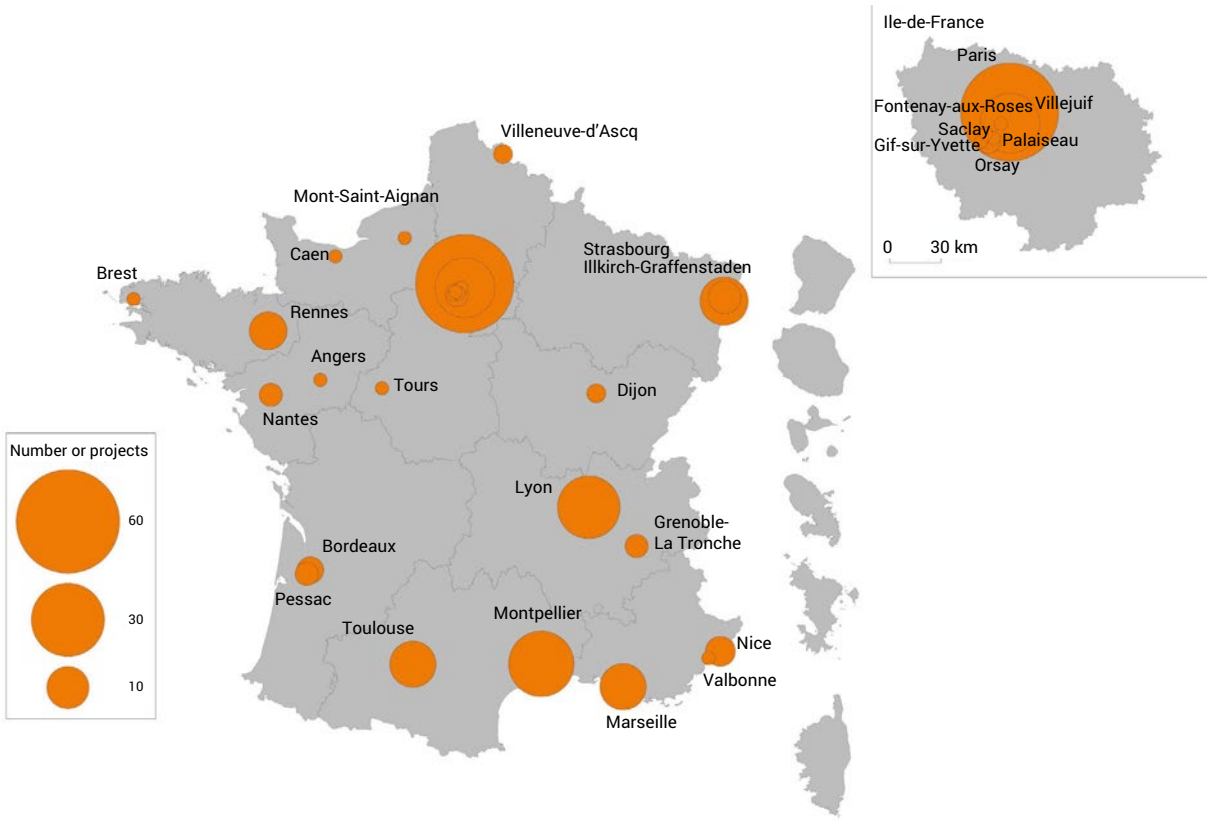


2014-2019:
206
projects funded
for a overall amount of
€108.9M

This Cancer Plan has provided significant funding for knowledge acquisition about cancer initiation (i.e. epigenetic regulation or transcription (CSO 1.2), oncogenes, tumour suppressor genes and signalling pathways involved in cell proliferation and cell transformation (CSO 1.3)) and cancer progression (i.e. cell mobility, tumour invasion, metastasis, cancer stem cells, immunological microenvironment, or angiogenesis (CSO 1.4)).

The labs involved in the funded projects are distributed throughout Metropolitan France, with 4 locations particularly represented: Paris and its surrounding areas, Montpellier, Lyon, and Strasbourg and surrounding areas (Figure 7). These locations are highly dynamic regions in terms of basic cancer research.

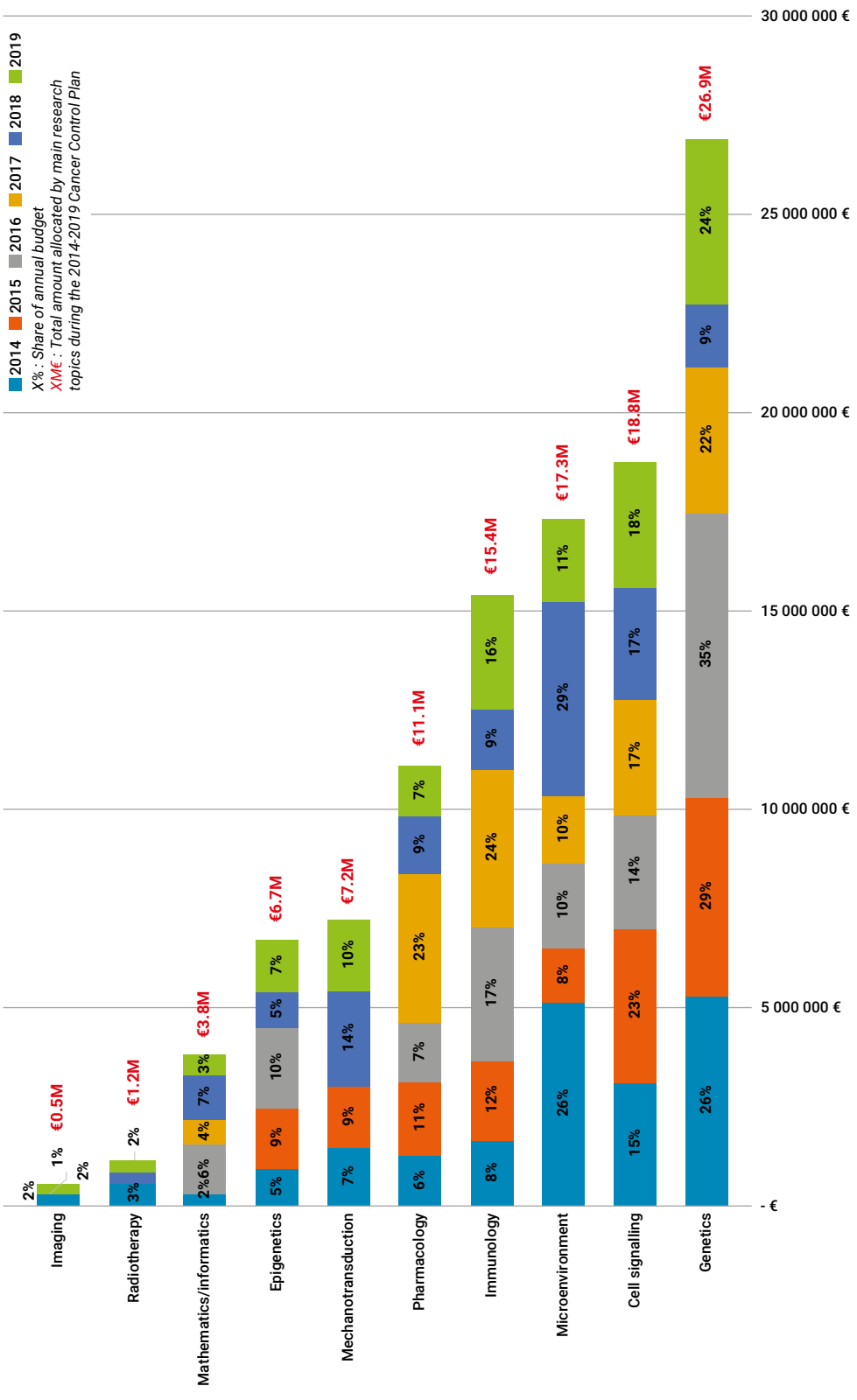
FIGURE 7
GEOGRAPHICAL DISTRIBUTION OF LABS INVOLVED IN FUNDED PROJECTS (IN TERMS OF PRINCIPAL INVESTIGATORS)



Concerning the funding of the main research topics studied in the projects selected during the 2014-2019 Cancer Control Plan, Figure 8 shows that the most funded research topic is genetics. Moreover, this topic has represented one of the highest allocated budgets per year (years 2014, 2015, 2016, and 2019).

The three other main research topics, which received a substantial share of Cancer Control Plan funding, are cell signalling, microenvironment, and immunology. The budget allocated to these three topics every year varied over the 2014-2019 Plan period.

FIGURE 8
TOTAL AMOUNT ALLOCATED BY MAIN RESEARCH TOPICS DURING CANCER PLAN 2014-2019 AND SHARE OF ANNUAL BUDGET REPRESENTED BY EACH RESEARCH TOPIC



Thematic cancer research programmes (ITMO Cancer)

PROGRAMME ON PRE-NEOPLASIA

Through strategic discussions, INCa and ITMO Cancer-Aviesan raised the importance of early diagnosis to cure a greater number of patients and the increasing interest of preneoplasia as a model in studying cancer initiation and cancer prevention. Until recently, research aimed at understanding precancerous lesions has been relatively modest.

To define the possibilities of developing and fostering collaborative research in France on this topic, INCa and ITMO Cancer-Aviesan set up an interdisciplinary Task Force in March 2018, composed of researchers, clinicians and bioinformaticians. Following the task force's meetings, a seminar was held on November 2018. This provided an opportunity to define the relevant questions to be addressed, such as the definition of preneoplasia, the genesis of prelesions and their oncogenic mechanisms, as well as the different techniques for their study.

To foster research projects which focus on these questions, INCa and ITMO Cancer-Aviesan launched a call for proposals in January 2019. The objective of this call was the characterisation, in space and time, on a molecular, cellular, and tissue level, of lesions with malignant potential. The aim was to contribute to a better understanding of their outcome (transition from pre-malignant to malignant state, stabilisation, regression) by characterising the underlying mechanisms, the sequence of cancer formation and the factors involved in risk emergence and progression, so as to identify targets to intercept and prevent the development of cancer and stratify lesions based on the risk of progression.

For this call, 7 projects were selected for funding, out of the 24 proposals submitted, for a total amount of €4M (Table 2).

TABLE 2
FEATURES OF THE PRENEOPLASIA PROGRAMME IN 2019

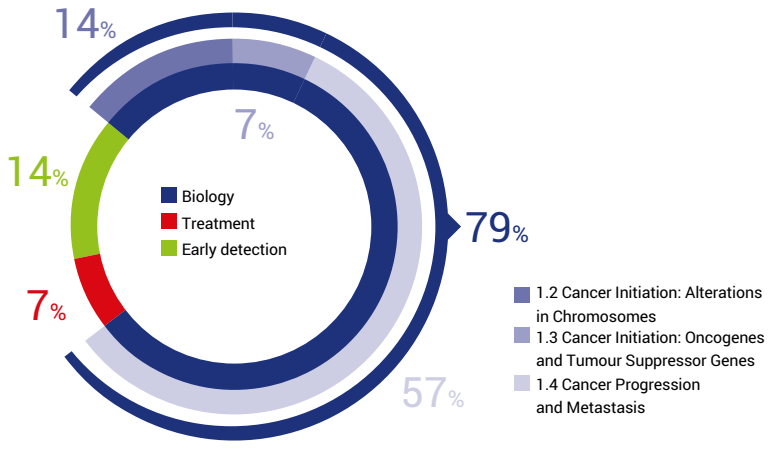
Objectives	To characterise, in space and time, on a molecular, cellular, and tissue level, lesions with malignant potential
Programming institution	ITMO Cancer Aviesan / INCa
Operating institution	INCa
Funding institution	Inserm for ITMO Cancer Aviesan
Funding	**€4M**
Proposals submitted	**24**
Projects selected	**7**
Selection rate	**29.2%**

The projects selected for this call aim to:

- Explore immune paracrine interactions in pre-neoplastic lesions in the pancreas;
- Investigate the mechanisms of anorectal pre-cancerous development in a model of intra-epithelial neoplasia;
- Model and target crosstalk between cancer precursor cells and their microenvironment in follicular lymphoma;
- Predict the value of immune and genomic alterations for the progression of pre-neoplastic bronchial lesions;
- Characterise cell populations in prostatic intra-epithelial neoplasia and their plasticity;
- Study the role of tissue-resident macrophages in malignant transition in ovarian cancer;
- Dissect the mechanisms of transformation of premalignant lesions in hepatocellular carcinoma and identify new biomarkers useful in clinical practice.

The majority of the funded projects focus on the biological mechanisms of cancer initiation and the early stages of disease progression, as more than two-thirds are classified in the CSO Biology category (Figure 9). Some of these projects also aim to identify and characterise different markers or to define signatures of cancer cells for early detection or staging (Early Detection, Diagnosis, and Prognosis category - 4.1). Finally, some of the objectives of one project consist of identifying novel drug targets.

FIGURE 9
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



DEVELOPMENT AND INTEGRATION OF NEW EXPERIMENTAL MODELS FOR CANCER RESEARCH: THE 3R RULE OPTIMISATION

Initiated in 2019, this programme aims to support the implementation of the 3R rule – reduce, refine, replace animal models - in the field of oncology. Its general objectives are to study the mechanisms of carcinogenesis, initiation, or metastatic dissemination, to identify biomarkers for prevention and early diagnosis, and to find new therapies by optimising the use of the 3R principles. Eligible projects should combine at least two entirely distinctive experimental models (*in vivo versus in vitro*, induced *versus* spontaneous, distinct animal species, etc.). These models should be designed and established to reduce the number of animals (based on statistical models), to refine experimental procedures and/or to replace induced animal models by alternate *in vitro* or spontaneous models.

In 2019, 52 proposals were evaluated and 6 projects were selected for a total amount of €2.4M (Table 3).

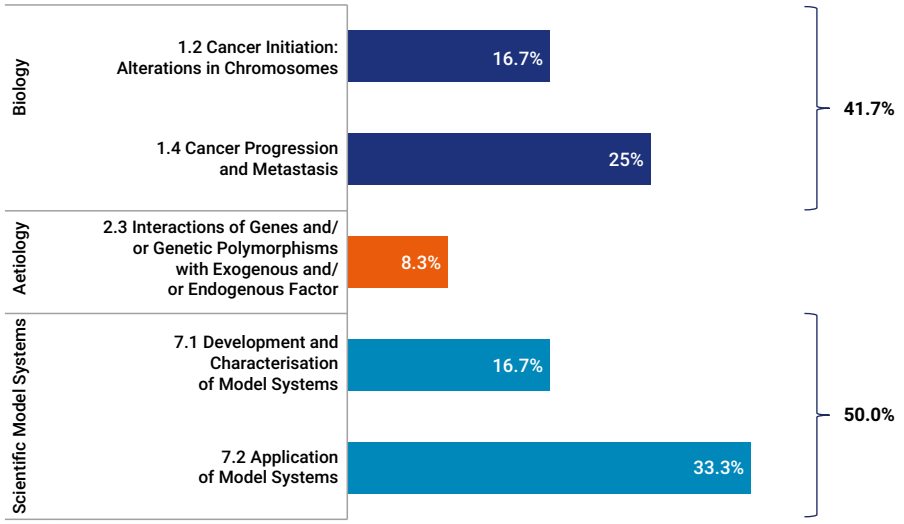
TABLE 3
FEATURES OF THE DEVELOPMENT AND INTEGRATION OF NEW EXPERIMENTAL MODELS FOR CANCER RESEARCH: 3R RULE OPTIMISATION PROGRAMME IN 2019

Objectives	To support the implementation of the 3R rule - reduce, refine, replace animal models - in the field of oncology
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€2.4M**
Proposals evaluated	**52**
Projects selected	**6**
Selection rate	**11.5%**

2019:
6
projects funded
for a total budget of
€2.4M

Selected projects focused on model development including: chicken embryos (to study candidate paediatric melanoma driver genes); 3D lung cancer cultures (to develop a new therapeutic index in FLASH radiotherapy); mini-pig spontaneous melanoma model (to compare with oncogenetic cascade in humans); 3D human proliferative hepatocyte model (for genotoxicity/mutagenesis studies); tumour ecosystems-on-chip (as novel platforms for preclinical studies of lung and breast cancers); combination of in vitro (microfluidics) and in vivo (zebrafish embryo) models (for pre-metastatic niche study).

FIGURE 10
DISTRIBUTION OF SELECTED PROJECTS IN 2019 ACCORDING TO THE CSO CLASSIFICATION



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

Between 2011 and 2018, oncology research was broadened to include physics, mathematics, computer science and engineering sciences within the scope of the PMSI (Physics, mathematics and engineering sciences related to cancer) programme. To give mathematicians even more opportunities to conduct research in the cancer field and to appraise the relevance of their models and hypotheses, a new call for proposals dedicated to mathematics and computer sciences was launched in 2019.

The Contributions to oncology of mathematics and computer science (MIC) programme aims to better understand tumour diseases and improve the prognosis of patients thanks to the contribution of mathematics and computer sciences. Indeed, recent technological revolutions have gradually put these disciplines at the centre of large-scale studies, which have become crucial for cancer research. The programme will unlock conceptual and methodological barriers at the frontier between mathematics, computer sciences and oncology.

In 2019, 44 proposals were evaluated and 5 projects were selected for a total amount of €2.26M (Table 4).

2019:
5
projects funded for a total budget of
€2.26M

FIGURE 11
DISTRIBUTION OF SELECTED PROJECTS IN 2019 ACCORDING TO THE CSO CLASSIFICATION

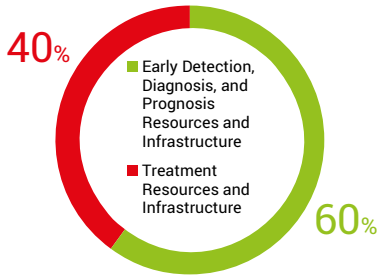


TABLE 4
FEATURES OF THE INTERDISCIPLINARY APPROACHES IN ONCOGENIC PROCESSES AND THERAPEUTIC PERSPECTIVES: CONTRIBUTIONS TO ONCOLOGY OF MATHEMATICS AND COMPUTER SCIENCE PROGRAMME IN 2019

Objectives	To better understand tumour diseases and improve the prognosis of patients 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	**€2.26M**
Proposals evaluated	**44**
Projects selected	**5**
Selection rate	**11.4%**

Selected projects focused on: multi-omic exploration of cancer-associated adipocytes as useful signatures in breast cancers; development of a mechanistic, dynamic model of response and resistance to immune checkpoint inhibitors in lung cancer; characterisation of the influence of initiating genetic alterations on the dynamics of development and treatment-resistance in breast cancer; development of an automatic, fast and accurate process for reporting the delivered radiotherapy dose in pelvic cancers; development of artificial intelligence tools trained on a large cohort of clinically annotated colon cancer patients to predict prognosis and genetic status of the tumour.

CONTRIBUTIONS TO ONCOLOGY OF PHYSICS, CHEMISTRY, AND ENGINEERING SCIENCES

Between 2011 and 2018, oncology research was broadened to include physics, chemistry, and engineering sciences within the scope of the PMSI (Physics, mathematics and engineering sciences related to cancer) programme.

To reinforce the role of chemistry and engineering sciences along with physics in cancer research, a new call for proposals was launched in 2019, jointly with ITMO Health Technologies-Aviesan.

The aim of the Contributions to oncology of physics, chemistry and engineering sciences (PCSI) programme is to better understand tumour diseases and improve the prognosis of cancer, by funding projects based on concepts or tools based on physics, chemistry or engineering sciences.

In 2019, 104 proposals were evaluated and 13 projects were funded for a total amount of €3.18M (Table 5).

TABLE 5
FEATURES OF THE INTERDISCIPLINARY APPROACHES TO ONCOGENIC PROCESSES AND THERAPEUTIC PERSPECTIVES: CONTRIBUTIONS TO ONCOLOGY OF PHYSICS, CHEMISTRY, AND ENGINEERING SCIENCES PROGRAMME

Objectives	To better understand tumour diseases and improve the prognosis of patients thanks to concepts or tools based on physics, chemistry, or engineering sciences
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€3.18M**
Proposals evaluated	**104**
Projects selected	**13**
Selection rate	**12.5%**

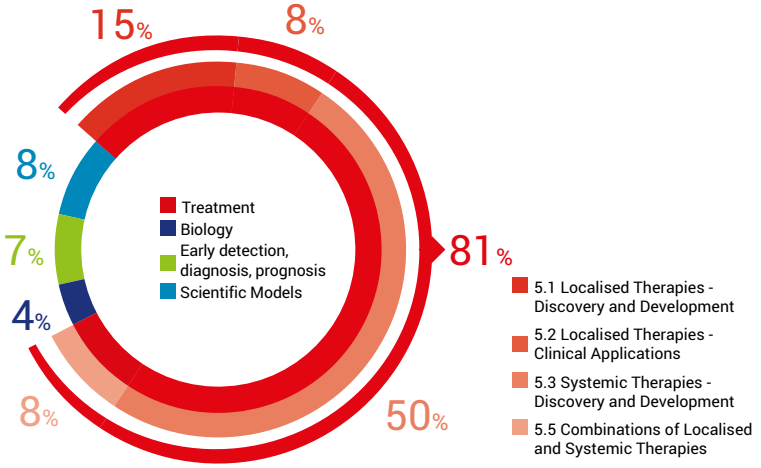
Selected projects mostly focused on new therapeutic strategies (80.8%):

- New drug synthesis and testing:
  - Inhibitors of an oncogenic pseudo-kinase in metastatic colorectal cancer,
  - Components manipulating the DNA damage response mechanisms or triggering DNA damages,
  - Proof of concept by click chemistry and preclinical trials of a drug repositioning to prevent breast and colon cancer relapse,
  - Antimitotic effects of a series of chemically modified compounds;
- New device development:
  - Nanoparticle helping increase cancer drug bio-availability and adjust biological activity,
  - Device optimising the cytosolic delivery of therapeutic molecules.

2019:
13
projects funded
for a total budget of
€3.18M

Other projects mainly focused on studying the underlying mechanisms of carcinogenesis (mechanical properties of tumour cell in vivo, pro-tumour effects of tumour-induced mechanical stress on stroma), response to treatment (cancer cell toxicity of a new class of sensitisers in photodynamic therapy, chemical bases underpinning sensitising effects of oxygen in FLASH radiotherapy, mechanisms of covalent targeted therapy using highly selective small nucleoside inhibitors, new instrumental and methodological approaches aimed at controlling the dose delivered during radioiodine thyroid therapy) or treatment resistance (chromatin dynamics involved in treatment resistance)

FIGURE 12
DISTRIBUTION OF SELECTED PROJECTS IN 2019 ACCORDING TO THE CSO CLASSIFICATION



SINGLE-CELL APPROACHES FOR THE STUDY OF ONCOGENIC PROCESSES

The Single-Cell Programme was launched in 2018 by ITMO Cancer-Aviesan to promote research in oncogenesis based on new approaches harnessing genetic, epigenetic, transcriptomic and proteomic information at the cellular level to identify or characterise factors that promote the emergence and progression of tumours, be it tumour clone population or microenvironment cells.

The programme in 2019

In 2019, 50 proposals were evaluated and 5 projects were selected for a total amount of €2.15M (Table 6).

Selected projects were mostly (70%) dedicated to basic research on cancer biology, with some focusing on treatment and modelling. They aimed at designing a molecular and cellular map of the interplay between immune cells and epithelial cells

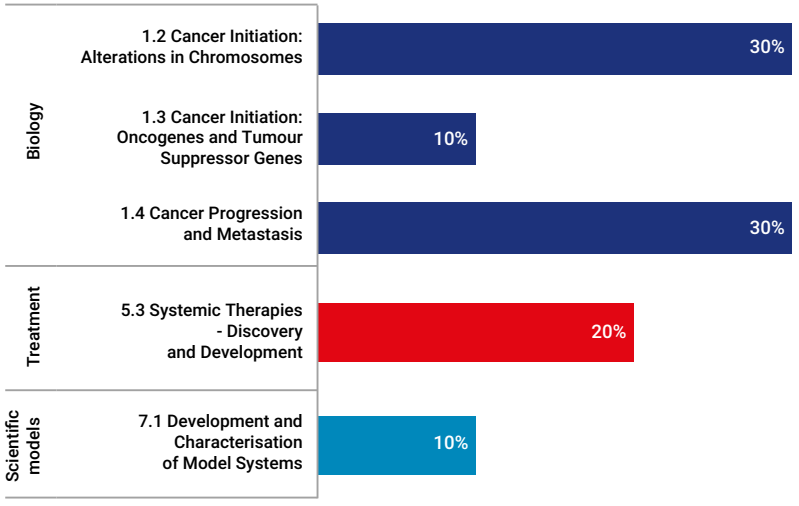
TABLE 6
FEATURES OF THE SINGLE-CELL APPROACHES FOR THE STUDY OF ONCOGENIC PROCESSES PROGRAMME

Objectives	To promote research in oncogenesis based on "Single-cell" approaches to identify and characterise factors that promote the emergence and progression of tumours
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€2.15M**
Proposals evaluated	**50**
Projects selected	**5**
Selection rate	**10%**

2019:
5
projects funded for a total budget of
€2.15M

throughout colorectal and anorectal cancer development; studying the dynamics and determinants of phenotypic diversity (by measuring cellular activities) during breast tumour progression and the emergence of resistance; modelling cellular heterogeneity in lymphomas to unravel dynamics operating in neoplastic B cells linked with their associated immune microenvironment; studying the influence of genetic heterogeneity among breast cancer cells on the 3D structure of the genome and subsequent gene regulation; modelling molecular circuitry in the different states (physiological, pre-tumour and tumour states) of thymocytes to understand tumour development in T-cell acute lymphoblastic leukaemia.

FIGURE 13
DISTRIBUTION OF SELECTED PROJECTS IN 2019 ACCORDING TO THE CSO CLASSIFICATION



2018-2019:
13
projects funded
for a total budget of
€6.12M

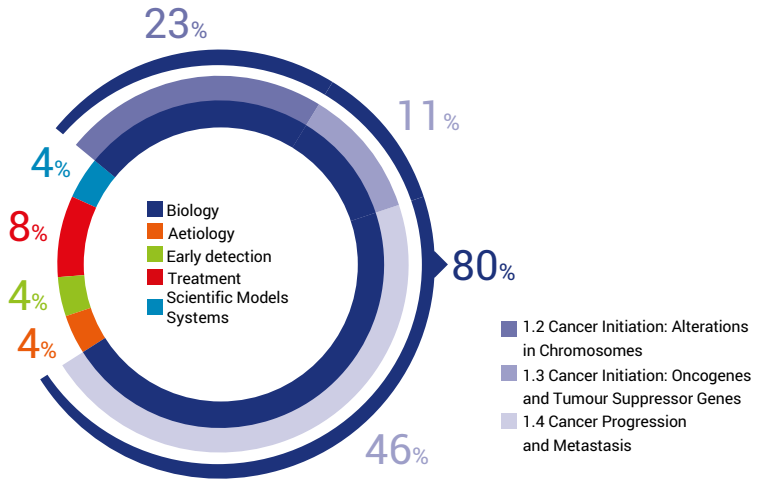
The programme over the 2018-2019 period

Since 2018, 13 projects have been funded within the framework of this multidisciplinary programme for a total amount of €6.12M (Table 7).

TABLE 7
TRENDS IN SELECTION AND FUNDING OF THE SINGLE-CELL APPROACHES FOR THE STUDY OF ONCOGENIC PROCESSES PROGRAMME OVER THE 2018-2019 PERIOD

Years	2018	2019	TOTAL
Funding (in €M)	3.97	2.15	**6.12**
Proposals evaluated	37	50	**87**
Projects selected	8	5	**13**
Selection rate (%)	21.6	10.0	**15.8**

FIGURE 14
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2018-2019 PERIOD

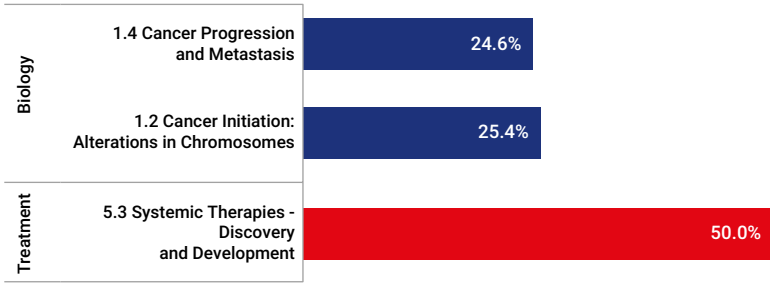


THE AVIESAN FEDERATIVE PROGRAMMES (PFA)

The major objectives of the Aviesan Federative Programmes (PFA) are to structure scientific communities in specific and priority areas by developing major national interdisciplinary consortia, and to create a momentum at the frontier between several fields to explore research niches that continue to be understudied by an interdisciplinary approach, developing complementary expertise.

This first edition of a PFA "Towards a new subcellular map of the cancer cell" was organised in 2019 by ITMOs Cancer-Molecular and Structural Bases of Life (BMSV)-Aviesan. It is aimed at federating expertise and skills between the cancer and the structural biology/biophysics/biochemistry communities, in order to unlock novel concepts in carcinogenesis requiring key interdisciplinary cooperation. The objectives are to contribute to the establishment of structural and functional mapping of the cancer cell and, in the longer term, to sustainably structure the dialogue between these two communities, to promote interdisciplinary national consortia and to develop unique expertise to respond to European and international issues in the field.

FIGURE 15
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION IN 2019



A total of 62 letters of intent were evaluated and 13 were selected by an international jury to form a consortium, with funding of €1.36M (Table 8). The consortium co-built the project *"NanoTumor: Toward the Tumor Cell Atlas"*, with two major objectives:

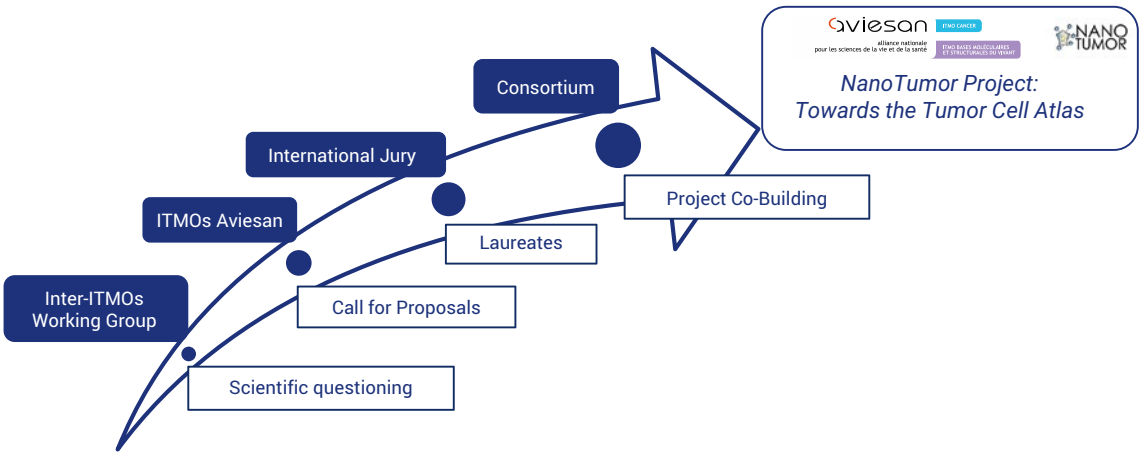
- To create and maintain synergistic action between the 13 teams with defined expertise spread over 7 sites, in order to consolidate the consortium, allow it to apply to national, European, and international programmes and foster further collaborations;

TABLE 8
FEATURES OF THE AVIESAN FEDERATIVE PROGRAMME

Objectives	To establish structural and functional mapping of the cancer cell by federating expertise and skills between the cancer and the structural biology/biophysics/biochemistry communities
Programming institution	Aviesan ITMOs Cancer- and BMSV-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€1.36M**
Letters of intent evaluated	62
Letters of intent selected	**13**
Selection rate	21%

- To launch experimental approaches and obtain key scientific results from the collaborative work between the teams throughout 4 work packages on the two major areas of the programme:
  - Identify, characterise, and determine the structure of multi-subunit macromolecular complexes involved in cancer onset or development,
  - Provide the first nanoscale map of cancer cells, at different steps of the metastasis cascade, from tumour initiation to metastasis formation.

Genesis of the 1st PFA Project: NanoTumor, Towards the Tumor Cell Atlas



SUPPORT FOR CANCER RESEARCH EQUIPMENT

In 2016, in compliance with the Cancer Control Plan and with 2015 recommendations of INCa's SAB, the board of ITMO Cancer-Aviesan decided to launch a call dedicated to equipment acquisition in order to enable 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 2019

In 2019, 59 proposals were evaluated and 16 projects were selected for a total amount of €2.17M (Table 9).

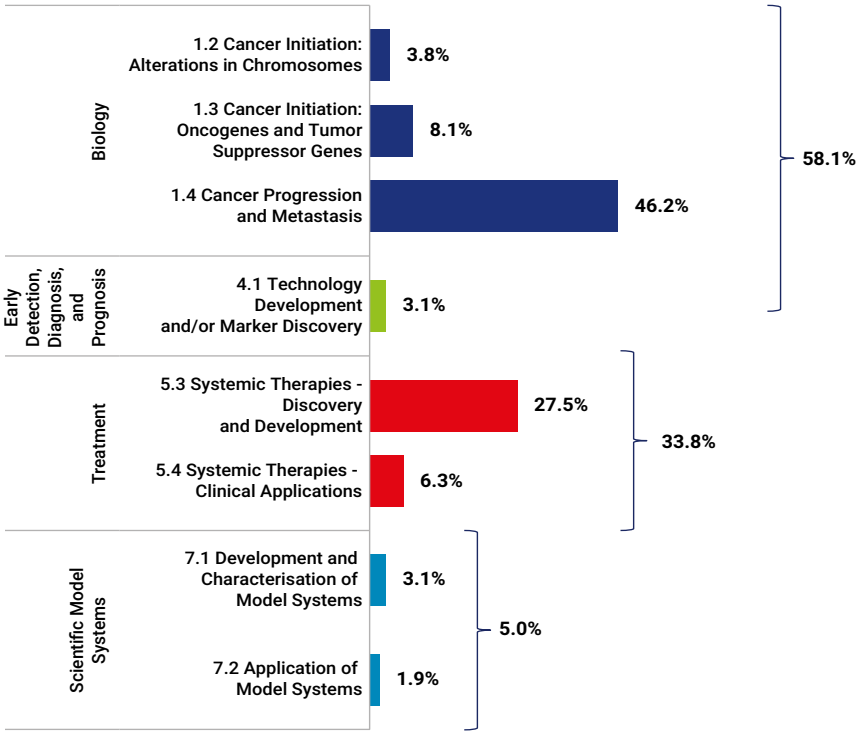
TABLE 9
FEATURES OF THE EQUIPMENT PROGRAMME

Objectives	To give laboratories the means in terms of equipment to lead an ambitious and innovative research policy. To encourage the acquisition of shared equipment, especially located on platforms.
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€2.17M**
Proposals evaluated	**59**
Projects selected	**16**
Selection rate	**27.1%**

The equipment requested in 2019 was mainly for imaging (e.g. confocal microscope for *in situ* 3D transcriptomic studies) and cellular characterisation (e.g. spectral flow cytometer for multiparametric analysis of cell populations). Equipment was mostly requested for the purpose of basic research in biology (58.1%) and treatment studies (33.8%), including clinical applications (6.3%). Equipment was mostly intended to be shared, particularly for:

- Analysis of the tumour micro-environment and the biology of cancerous cells and non-parenchymal cells in hepatocellular carcinoma;
- *In vivo* identification and sorting of rare cell (sub)populations (stem cells, circulating tumour cells, cancer cells, rare immune cells, etc.) or of subcellular particles (i.e. ribonucleic complexes) to shed light on the underlying molecular mechanisms of tumorigenesis, in different cancer types (melanoma, medulloblastoma, B-cell lymphoma) and stages (pretumoral, tumoral, metastatic);

FIGURE 16
DISTRIBUTION OF SELECTED PROJECTS IN 2019 ACCORDING TO THE CSO CLASSIFICATION



- Analysis of signalling pathways involved in the proliferation and migration of cancer cells and the role of T-lymphocytes in anti-tumour immunity;
- Analysis of whole cancer cell metabolism both in organoid and in single cells;
- Production of CAR-T cells as a treatment for resistant or relapsing acute lymphoblastic leukaemia;
- Molecular tagging for theranostics;
- Study of the impact of bacteria from host microbiota on chemotherapy efficacy;
- Patients stratification and treatment resistance analysis in a context of chronic lymphoid leukaemia and mantle cell lymphoma.

The programme over the 2016-2019 period

Since 2016, 87 grants for equipment have been awarded with an overall selection rate of 31% and for a total amount of €13.67M (Table 10). Most of these grants were for the Imaging (41%) and Cellular characterisation and histology (31%) equipment categories (Figure 17). As presented in Figure 18, the equipment was mostly requested for the purpose of basic research in biology (57.1%), and for early detection (26.3%), treatment (13.4%) and modelling studies (3.2%).

2016-2019:
87
equipment grants awarded for a total of
€13.67M

TABLE 10
TRENDS IN SELECTION AND FUNDING OF THE EQUIPMENT PROGRAMME OVER THE 2016-2019 PERIOD

Years	2016	2017	2018	2019	TOTAL
Funding (in €M)	4.93	3.18	3.39	2.17	**13.67**
Proposals evaluated	119	34	67	59	**279**
Projects selected	38	16	17	16	**87**
Selection rate (%)	32	47	25	27	**31**

FIGURE 17
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO EQUIPMENT CATEGORIES OVER THE 2016-2019 PERIOD

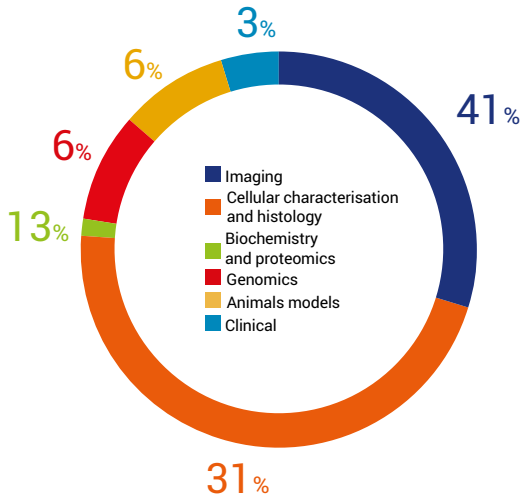
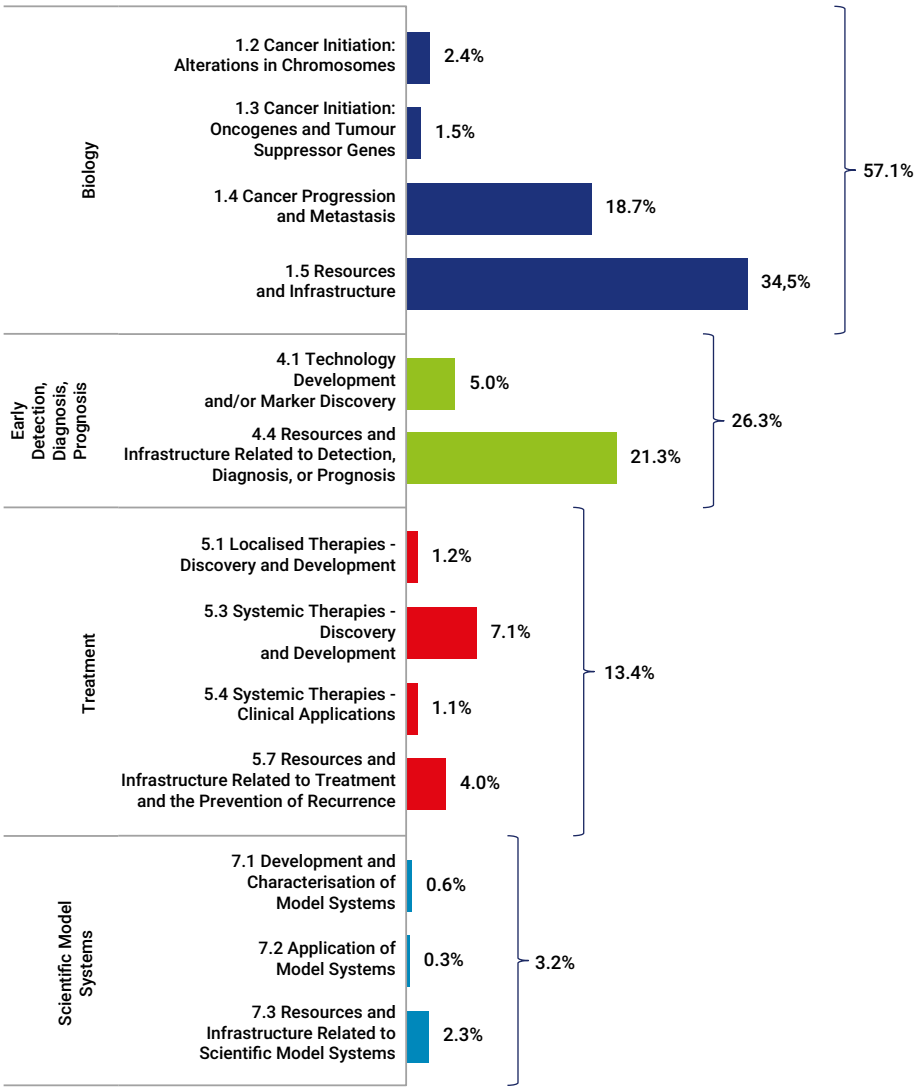


FIGURE 18

DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2016-2019 PERIOD

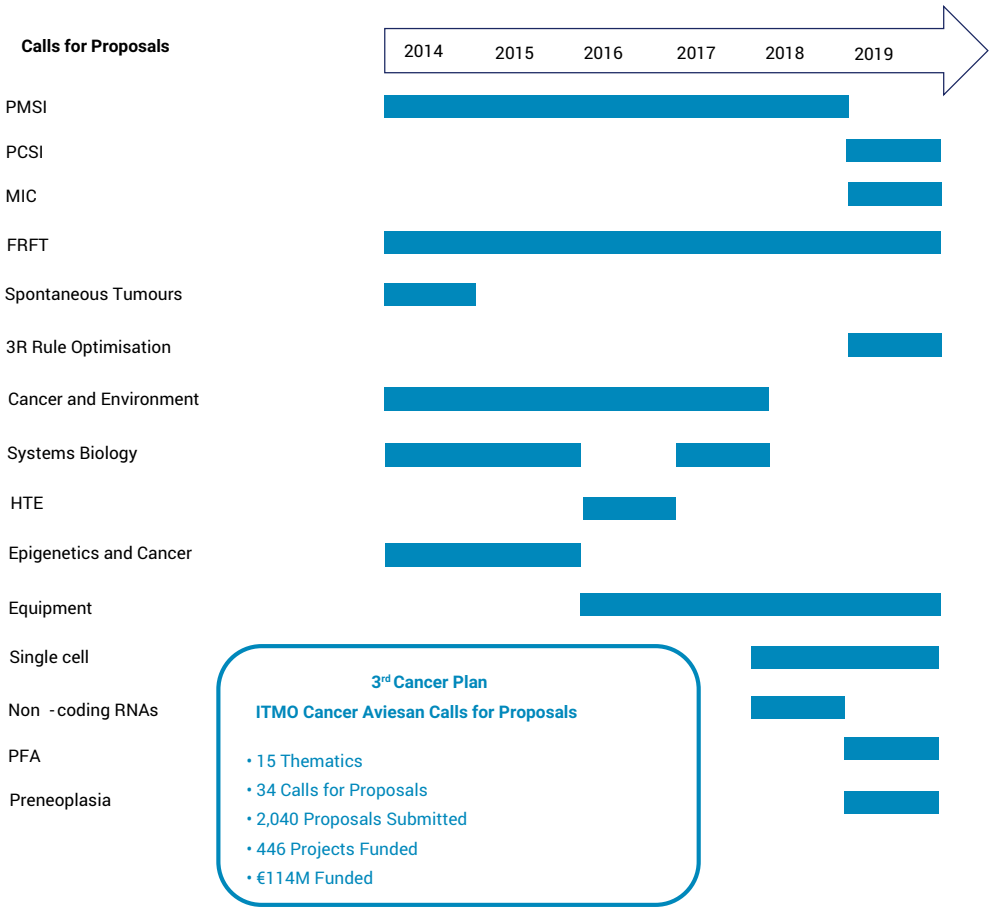


ITMO CANCER-AVIESAN CALLS FOR PROPOSALS WITHIN THE SCOPE OF THE 3RD FRENCH CANCER CONTROL PLAN

FIGURE 19

OVERVIEW AND KEY FIGURES OF THE DIFFERENT PROGRAMMES LAUNCHED AND FUNDED BY ITMO CANCER-AVIESAN DURING THE 2014-2019 CANCER CONTROL PLAN

[Bilan PK3 AAPs ITMO Cancer-Aviesan]



PMSI : Physics, Mathematics and Engineering Sciences Related to Cancer; PCSI: Physics, Chemistry and Engineering Sciences Related to Cancer; MIC: Mathematics and Computer Science Related to Cancer; FRFT: Basic and Translational Research Training; HTE: Tumour Heterogeneity and its Microenvironment; PFA: Aviesan Federative Programme

French paediatric oncology research study (2008-2018)

Launch of a public contract (selection of bid planned for summer 2020)

The aim of the study is to:

- Analyse our portfolio over a 10-year period;
- Describe the French scientific community implementing research projects in paediatric oncology (through CVs);
- Analyse France's contribution to this field on an international level.

Support for paediatric cancer research

In November 2018, important political mobilisation driven by parents' associations led the French Minister for Higher Education, Research, and Innovation to provide an additional allocation of €5M, dedicated to fundamental research into paediatric cancers. It is through fundamental research that progress can be made in understanding the causes of childhood cancers, finding therapeutic approaches to paediatric cancers with a poor prognosis and, finally, limiting sequelae and improving quality of life for the children and for adults who were cured of cancer in their childhood.

This funding aims to support coordination and fundamental research projects of a new type. The French Ministry for Research has assigned the Institute the task of managing this new recurrent funding, the use of which is to be defined by a Task Force coordinated by the Institute and comprising three parents' groups: *Grandir Sans Cancer*, *Gravir* and *UNAPECLE*.

INCa also handles the links with its paediatric interfaces, including the dedicated action group of the International Scientific Advisory Board.

Moreover, the law of March 2019 specifies that INCa is in charge of setting out a ten-year cancer control strategy with specific monitoring of the funds allocated to research in paediatric oncology. This strategy must be defined in consultation with all the other public and private-sector players, healthcare professionals and stakeholders.

In this context, throughout 2019, the Task Force met at INCa monthly and the collaboration work with the collectives took shape starting with the launch of two specific programmes (see section 2.3.3. below).

Various actions have been implemented and were presented to the parents' and patients' associations during a seminar held at INCa in September 2019, in the presence of the French Minister for Research, Frédérique Vidal:

Based on the proposals of the three parents' groups, three research themes were selected for 2019 to have researchers from different domains work together and propose innovative actions for 2020 and 2021 in new research fields:

1. Data sharing;
2. Human development-environment-genetics-epigenetics;
3. Immunology mathematical models .

In order to identify research questions, determine the targets to reach and define new resources, preparatory work was carried out with all the stakeholders mentioned above. In November 2019, an interdisciplinary seminar was held to share, extend, and open up work processes and put forward proposals for actions and a work schedule in a collaborative and cross-disciplinary way between researchers and representatives of associations. This workshop led to the proposal of the launch of a call for consortia in 2020, as well as support for high-risk/high-gain projects (supporting a novel and audacious research idea without preliminary data).

ORGANISATION OF 3 INTERDISCIPLINARY WORKING GROUPS TO DEFINE INNOVATIVE CALLS FOR APPLICATIONS

Setting up new programmes on research issues identified by the Task Force and announced by the Minister in February requires preparation through working groups. The groups are run with the scientific community and the parents' associations involved in the Task Force collectives to prepare interdisciplinary workshops open to the entire scientific community. The lifetime of these working groups is dependent on the needs for progress in analyses and the set-up of corresponding programmes.

Objective of the working groups

The scientific community was invited to consider different research fields around a theme in order to propose innovative programmes for 2020 and 2021. The members of the Task Force will complete the researchers' discussion of the questions raised by parents; analyses conducted by associations will be forwarded.

Role of the working groups

- Precise definition of the research question;
- Objectives to be achieved;
- Definition of means to achieve these objectives and support measures (analyses, interdisciplinary seminars, network organisation, international links, calls for proposals, etc.).

Composition of the working groups

- Researchers and parent representatives selected by the Task Force collectives;
- Additional researchers proposed by bodies interfacing with INCa;
- Additional researchers proposed by INCa;
- Option to extend the membership in a second phase according to the actions to be developed.

Attractiveness to researchers from new fields, or start-ups was highlighted to help new ideas come to the fore.

Work methodology

Coordination by a two-person team made up of a representative of INCa and a representative of the three collective members of the Task Force. Each working group defines its own work method. As specified in the working group composition, representatives of the collectives can participate in all the groups.

The topics selected for 2019 are based on the themes proposed by the collectives.

- ***Bringing together researchers in human development (embryogenesis of various organs), researchers in environmental toxicity/chemistry, and researchers in genetic abnormalities in childhood cancers:***
  - Interaction among these disciplines should enhance the study and understanding of the origin of some paediatric cancers, particularly those occurring in early childhood, and include the study of environmental (pesticides, pollutants, etc.) and molecular (genetic and epigenetic) factors,
  - Interaction, for example, between groups of researchers from Inserm's cross-disciplinary programme "Human Embryonic Cell Atlas-HuDeCa", researchers in the "environment and cancer" field, and paediatric oncology researchers.
- ***Bringing together researchers in mathematics and computer sciences applied to modelling of cellular environment, particularly in terms of immunology, in relation to paediatric tumours:***
  - Interaction among these disciplines should enable, with the help of new paediatric cancer models (animal and cellular models) and data analytics expertise, the identification of new therapies through a better understanding of the tumour micro-environment, particularly in terms of immunology.
- ***Sharing of biological-clinical data:***
  - One of the requests from the collectives is for data pooling, and optimised data sharing of biological-clinical and public health data in relation to paediatric cancers, that present useful aspects for these rare diseases.

THINK TANK SEMINAR HELD ON NOVEMBER 2019

The general aim of this seminar was to share research conducted by the different working groups during 2019 and to propose a work schedule as part of a collaborative and cross-disciplinary process between researchers and representatives of associations.

In conclusion and based on general consensus, a programme to form a fundamental paediatric oncology research consortium will be proposed. Moreover, this seminar offered the opportunity to reaffirm that setting up CFPs, and particularly drafting, were the remit of INCa. This would be carried out within the framework and under the supervision of the Task Force and not the working groups meeting at this seminar for obvious reasons of conflict of interest.

Moreover, the future of the working groups was discussed. Indeed, the need to maintain one or more working groups on paediatric oncology research questions in order to continue rich and fruitful discussions among researchers and association collectives was highlighted. Nevertheless, the number, perimeters, and operating procedures of this/these working groups had yet to be defined and would be studied within the Task Force.

PAEDIATRIC CANCER RESEARCH PROGRAMMES

International mobility of young researchers in paediatric oncology

This new call for applications aims to support the international mobility of young researchers in paediatric cancer research. Its objectives are to increase the attractiveness of paediatric cancer research for young talents and to facilitate the career of young researchers in this field.

It is therefore aimed at young researchers who have obtained their PhD in France or abroad and are willing to complete a post-doctoral internship in science abroad or in France.

It is also aimed at supporting young researchers and students already remunerated in France for a research Master, a PhD, or a post-doctorate, and who wish to complete an internship abroad as part of their training.

TABLE 11
FEATURES OF THE INTERNATIONAL MOBILITY OF YOUNG RESEARCHERS IN PAEDIATRIC ONCOLOGY PROGRAMME IN 2019

Objectives	Boost the attractiveness of paediatric cancer research for young talent and facilitate the career of young researchers in paediatric cancer research
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€57,720**
Proposals submitted	**3**
Projects selected	**2**
Selection rate	**66.7%**

In 2019, 2 projects out of a total of 3 were selected for funding, with an overall budget of €57,720 (Table 11).

The two projects funded are international mobility grants.

The first funded project, relating to an international mobility grant, is part of a collaboration between a French laboratory and a laboratory located in Singapore. The aim of the project is to map the immune microenvironment of neonatal neuroblastoma and compare it to healthy tissue and advanced neuroblastoma in older children.

The second funded project, relating to an international mobility grant, is a collaboration between French and German laboratories. The aim of the project is to develop CAR-T cell therapies to treat solid paediatric cancers such as osteosarcoma.

The reviewers of the Scientific Evaluation Committee and the representative of the Committee for Health Democracy expressed their wish to see this call for applications renewed in 2020.

It was also proposed to split the call for applications into two parts. The first part should focus on international mobility grants for young researchers receiving a salary in France (Master's students, doctoral students, post-doctoral students), and the second part should focus on the financing of post-doctoral grants.

In addition, in order to define the changes to be made to this call for applications to better meet its objectives, an evaluation questionnaire was sent to all stakeholders involved in paediatric cancer research. The collectives, members of the Task force, as well as the Paediatric Action Group of INCa's International Scientific Advisory Board, responded to the questionnaire. On that basis, the following improvements will integrated in the 2020 edition:

- This call for applications will be divided into two distinct parts: the first part will focus on support for the international mobility of researchers receiving a salary in France (Master's students, doctoral students, post-doctoral students, doctors and researchers). The second will focus on the funding of post-doctoral fellowships. A single committee will evaluate the two parts of the call for applications;
- This call for applications will be open to basic research as well as research in Human and Social Sciences;
- The requirement for an already well-established collaboration between the two partner laboratories will be more flexible; it may be an initial collaboration;
- Support for international mobility, initially intended for students in Research Master 2, doctoral students, or post-doctoral fellows, will be open to physicians and researchers, with no age restriction;
- As part of the international mobility support, training internships may also last 3 months;
- The text of the call for applications will encourage the awarding of a double degree to doctoral students, by both universities;
- The text of the call for applications will also specify that parent's associations may be included in the research projects.

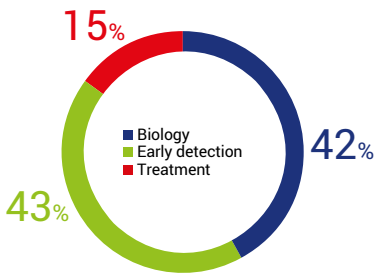
Accelerating basic and translational research in paediatric oncology: help in pooling, structuring, and sharing research data

The main objective of this new call for applications is to bring together researchers and paediatricians to form national federations around a pathology or group of pathologies of interest in paediatric oncology. These federations will need to share different types of data as well as tumour samples and images at different stages of the disease, in order to boost the research potential of each of the teams. The teams of the federations thus formed will have to rely on the pooling of locally available data, the sharing of these data requiring prior structuring work. These data should originate from many different sources (genetic data, omics, micro-environmental data, histology data, imaging data, clinical data at diagnosis and during patient follow-up, etc.).

TABLE 12
FEATURES OF ACCELERATING BASIC AND TRANSLATIONAL RESEARCH IN PAEDIATRIC ONCOLOGY: HELP IN POOLING, STRUCTURING, AND SHARING RESEARCH DATA PROGRAMME IN 2019

Objectives	Rapidly initiate a process for the implementation of data sharing in paediatric oncology, by mobilising and federating the different communities of researchers involved, as well as paediatricians.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€3.61**
Proposals submitted	**7**
Projects selected	**4**
Selection rate	**57.1%**

FIGURE 20
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO CSO CLASSIFICATION



In 2019, 4 out of a total of 7 projects were selected for funding, for an overall budget of €3M (Table 12):

- One project aims to set up a clinico-biologic-genomic and radiomic database of osteosarcoma;
- The second funded project aims to establish a clinical and biological database of paediatric acute myeloid leukaemia;
- The third funded project aims to set up a database of paediatric liver cancers;
- Finally, the fourth project aims to set up a multi-omics database relating to several paediatric cancers.

In 2020, a steering committee will be set up under the aegis of INCa and will meet at regular intervals to ensure the steering and monitoring of the research projects funded. It will pay particular attention to ensuring that the successful candidates:

- Establish governance for the pooling, structuring, sharing and use of data;
- Work in cohesion with INCa and the other groups supported under this call for applications, in order to allow interoperability of data from the different groups;
- Implement the sharing and use of data, biological resources, and images in research collaborations with other research teams;
- Follow INCa's future recommendations regarding the opening of the sharing of their data beyond their group, in order to aim towards national pooling of data in paediatric oncology;
- Follow INCa's future recommendations regarding compliance with the law on sharing of research data and the connection with the Health Data Hub.

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.

The 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.

THE PROGRAMME IN 2019

In 2019, 16 projects were selected for funding, out of the 119 submitted, representing an overall budget of €7.79M (€4.92M INCa + €2.87M DGOS) (Table 13).

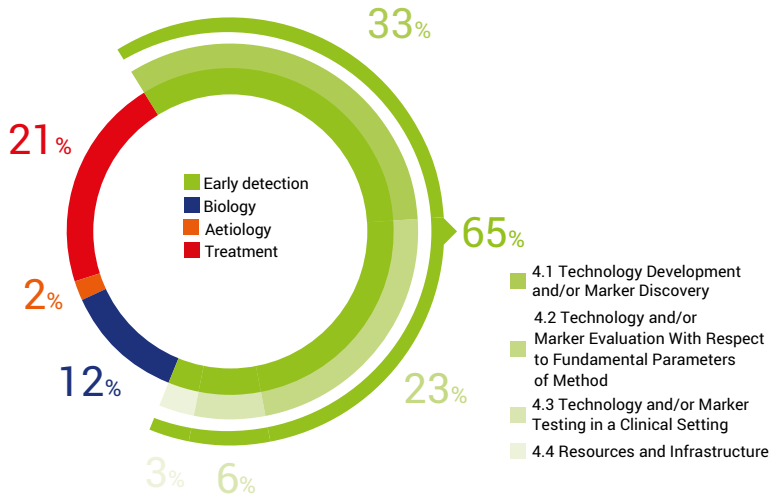
2019:
16
projects funded out of 119 proposals submitted, for a total budget of
€7.79M

TABLE 13
FEATURES OF THE PRT-K PROGRAMME IN 2018

Objectives	To hasten the transfer of knowledge with a view to its prompt application in clinical practice for the benefit of patients, by giving researchers an incentive to develop multidisciplinary projects in close collaboration with clinical players, in order to improve prevention, early detection, diagnosis, treatment and comprehensive care of cancer patients.
Programming institution	INCa/Ministry of Health (DGOS)
Operating institution	INCa
Funding institution	INCa/Ministry of Health (DGOS)
Funding	**€7.79M** **INCa: €4.91M** **DGOS: €2.87M**
Proposals submitted	119
Projects selected	**16**
Selection rate	13%

In compliance with the objectives of the programme, about two-third of the projects selected in 2019 are studying early detection, diagnosis, and prognosis (Figure 21). Over 20% of the studies are focusing on the development of treatments, especially discovery and development of systemic therapies.

FIGURE 21
DISTRIBUTION OF SELECTED PROJECTS IN 2019 ACCORDING TO THE CSO CLASSIFICATION

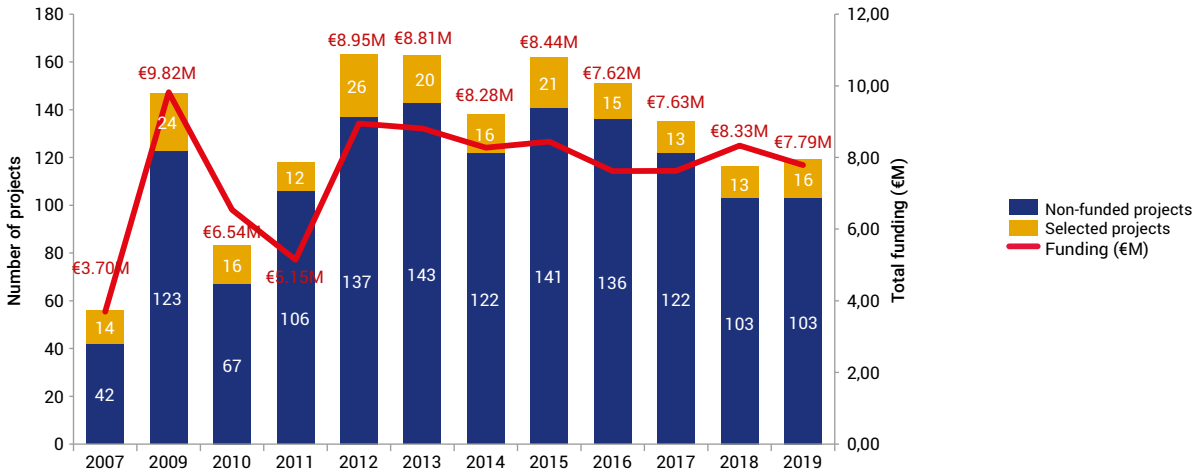


THE PROGRAMME OVER THE 2007-2019 PERIOD

Since 2007, 1,551 proposals have been submitted to this call for proposals, and 206 have been selected and funded for a total amount of €91.31M. The overall selection rate for this call for proposals is 13.3% (Figure 22).

FIGURE 22

TRENDS IN SELECTION AND FUNDING OF THE PRT-K PROGRAMME OVER THE 2007-2019 PERIOD

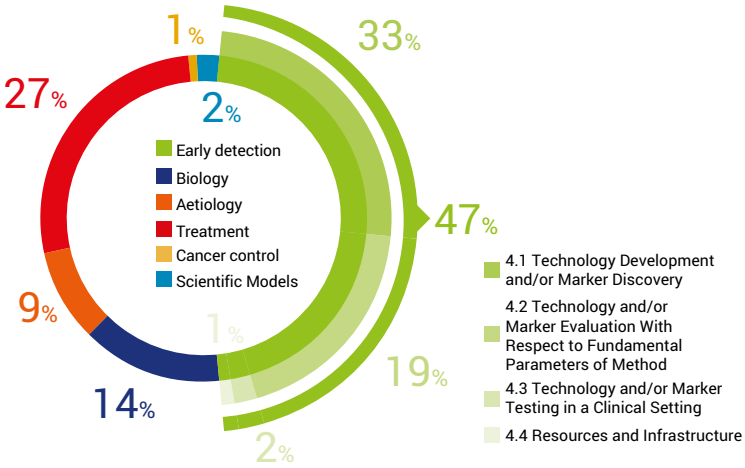


2007-2019:
206
projects funded for a total amount of
€91.31M

The CSO typology of the projects funded since 2007 corresponds to the characteristic profile for translational research (Figure 23), especially allocated to two main categories of research projects:

- Projects that involve the development of techniques for early detection, diagnosis, prognosis using biomarkers (genetic, biological, immunochemical, microbiological);
- Projects based on the improvement of patient care thanks to the development of new therapeutic strategies and to the understanding of mechanisms of treatment resistance.

FIGURE 23
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2019 PERIOD



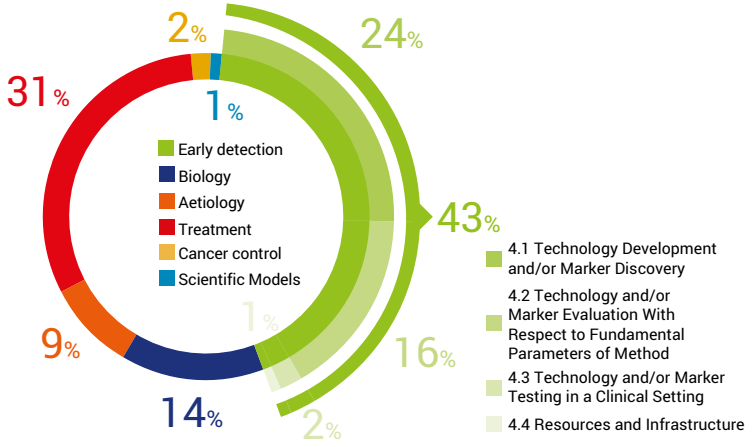
THE PROGRAMME OVER THE 2014-2019 CANCER CONTROL PLAN PERIOD

This programme is part of Action 5.1: Optimising the organisation of translational research by combining institutional funding.

94
projects funded for a total amount of
€48.22M
over the 2014-2019 Cancer Control Plan period

In accordance with action 5.1, INCa and DGOS have continued their joint effort to support translational cancer research. This call for proposals is well integrated within the scientific and medical community. It has made it possible in particular to finance projects aimed at improving systemic treatments (25%), and on technological developments and / or discovery of biomarkers for early detection, diagnosis, and prognosis (24%) (Figure 24).

FIGURE 24
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2014-2019 CANCER CONTROL PLAN PERIOD



Integrated cancer research programmes

THE RESEARCH AND ACTION PROGRAMME TO REDUCE SMOKING AND CHANGE CURRENT PREVALENCE OF TOBACCO-RELATED CANCERS

In France, daily smokers represent 26.9% of the general population. In 2015, for all adults aged 30 years and over, more than 68,000 cases of cancers were tobacco-related (54,000 for men and 12,500 for women), which represented respectively 28% and 8% of all new cancers nationwide.

In order to fund tobacco control actions, a specific fund was set up within the French National Health Insurance Fund for Employed Workers (CNAMTS): the tobacco control fund. The board of management of this fund is chaired by the director general of CNAMTS and made up of representatives from health insurance funds, ministers responsible for health and social security, the Interministerial drug and addictive behaviour prevention scheme (MILDECA), the French National Agency for Public Health (Santé publique France), INCa, as well as qualified leaders. This fund provides leverage enabling long-term action and making it possible to account for existing evaluation factors to propose the funding of new actions, particularly support for research.

The Tobacco Fund decided to allocate €14M to INCa and to the Institute of Research in Public Health (IReSP), €7M each, to:

- Support research in Tobacco with a call for research and intervention proposals to reduce and control tobacco consumption; and a call for doctoral grants with the same research areas;
- Support research coordination tools: exchange seminars, qualitative survey on the attractiveness of Tobacco.

The programme in 2019: the programme for research and intervention proposals to reduce and control tobacco consumption

The call for proposals covers all the aspects of research (fundamental, clinical or population depending on the sections) 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, social and human sciences, law, biology, epidemiology, etc.

It relates to all tobacco-related issues and diseases (cancer, cardiovascular diseases, addiction, etc.), as well as the composition of products, smoke and emissions resulting from their use. It is also intended to support and promote research on prevention and intervention research.

This call for research proposals targets researchers as well as professionals in the field seeking to apply a research approach. Therefore, the teams may include researchers, health care professionals, prevention and health promotion professionals and user associations, as well as decision-makers.

The call has been divided into 3 sections, with 2 or 3 areas in each:

- Section 1 INCa/IReSP: Tobacco in the general population
  - Area 1: Determinants & trajectories of smoking
  - Area 2: Public policies, strategies, and behaviours of stakeholders
  - Area 3: Electronic nicotine delivery systems (ENDS)
- Section 2 INCa: Tobacco & cancer
  - Area 1: Support for smoking cessation & cancer
  - Area 2: Screening for tobacco-related cancers
  - Area 3: Biology
- Section 3 IReSP: Diseases other than cancer
  - Area 1: Tobacco cessation in patients with conditions other than cancer
  - Area 2: Research on health services and systems other than oncology

2019:
23
projects selected for a total budget of
€6.89M

TABLE 14
FEATURES OF THE RESEARCH AND ACTION PROGRAMME FOR THE TOBACCO CALL FOR PROPOSALS AND CALL FOR DOCTORAL GRANTS IN 2019 (SECTION 1 & 2)

Objectives	To develop and put in place an integrated strategy to support research and actions related to tobacco and the cancers associated with it. To support young researchers.
Programming institution	INCa/ IReSP
Operating institution	INCa/ IReSP
Funding institution	INCa/ IReSP
Funding	**€6.89M** **INCa: €3.72M** **IReSP: €3.17M**
Proposals submitted	**39**
Projects selected	**23**
Selection rate	**59%**

TABLE 15
DISTRIBUTION OF THE SELECTED AND SUBMITTED PROJECTS RELATED TO THE TOTAL FUNDING FOR EACH SELECTION

Tobacco 2019 Call for Proposals	Section 1 INCa-IReSP*	Section 2 INCa	Section 3 IReSP	TOTAL
Proposals submitted	23	8	4	35
Proposals selected	11	5	4	20
Funding	€4.88M	€1.17M	€0.50M	€6.58M

*INCa: €2.44M; IReSP (Institute of Research in Public Health): €2.44M

As we need to reduce tobacco consumption in France, primary prevention and interventions in the general population are the first effective approaches to include in a new call for research and intervention proposals to reduce and control tobacco. As such, this area has represented the largest proportion of projects, including intervention research: mostly to delay the commencement of tobacco consumption in teenagers, or other specific populations: pregnant women, people with mental disorders, migrants.

In addition, the applicants had the possibility to submit an "emerging project", which is a new alternative to the full project compared to previous years. It allows researchers to submit a scaled-down project (12 or 18 months) and test its feasibility before submitting a full project (36 or 48 months). In 2019, these projects represent 38% of the projects funded in sections 1 and 2.

Concerning section 2 (tobacco & cancer), the 3 projects funded address research on early detection and lung and oral cancer screening (biomarkers, addictive process with e-cigarettes, etc.). The 2 other projects, which are emerging proposals, concerned smoking cessation programmes: on cancer patients, use of nicotine substitutes or cognitive behavioural therapy.

The call for doctoral grants has been divided into the same 3 sections as the call for proposals. It supports doctoral students with a 3-year grant. The implementation of this call has not been optimal: late communication, shortened response time, etc. In addition, out of the 4 projects submitted, 3 were funded, including one by INCa. The project focused on the influence of the social environment on smoking trajectories throughout life and their effects on health.

The other two projects were funded by IReSP. They focused on smoking cessation for smokers with cardiovascular diseases, and health-related quality of life and smoking among night shift hospital staff.

TABLE 16
DISTRIBUTION OF DOCTORAL GRANTS AWARDED IN 2019 ACCORDING TO THE FUNDER (3-YEAR FUNDING)

2019 Tobacco Call for doctoral grants	Funding INCa	Funding IReSP	TOTAL
Proposals selected	1	2	3
Funding	€103,000	€206,000	€309,000

The programme over the 2016-2019 period

Over the four years of calls for proposals on tobacco control, INCa has provided funding for 49 projects, for a total budget of €18.99M (table 17).

2016-2019:
66
projects selected for a total budget of over
€23M

TABLE 17
TRENDS IN SELECTION AND FUNDING OVER THE 2016-2019 PERIOD

Years	2016	2017	2018	2019	TOTAL
Funding (in €M)	3.52[1]	5.66[2]	7.21[3]	6.89[3]	**23.28**
Proposals submitted	21	22	55	39	**137**
Projects selected	7	11	25	23	**66**
Selection rate (%)	33	50	45	59	**48**

[1] Co-funding INCa/ARC Foundation/ French Cancer League
[2] Co-funding INCa/French Cancer League
[3] Co-funding INCa/IReSP

The call for proposals has clearly evolved over the last three years, particularly in the area of "Determinants & trajectories of smoking".

The recent change within the design of the call, the number of projects and the increasing mobilisation of the tobacco research field demonstrate the developments in the general research community for this international issue aiming to help people to quit smoking.

FIGURE 25
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE RESEARCH TOPICS OVER THE 2016-2019 PERIOD (SINCE 2018, PROJECTS SELECTED IN SECTION 1 & 2)

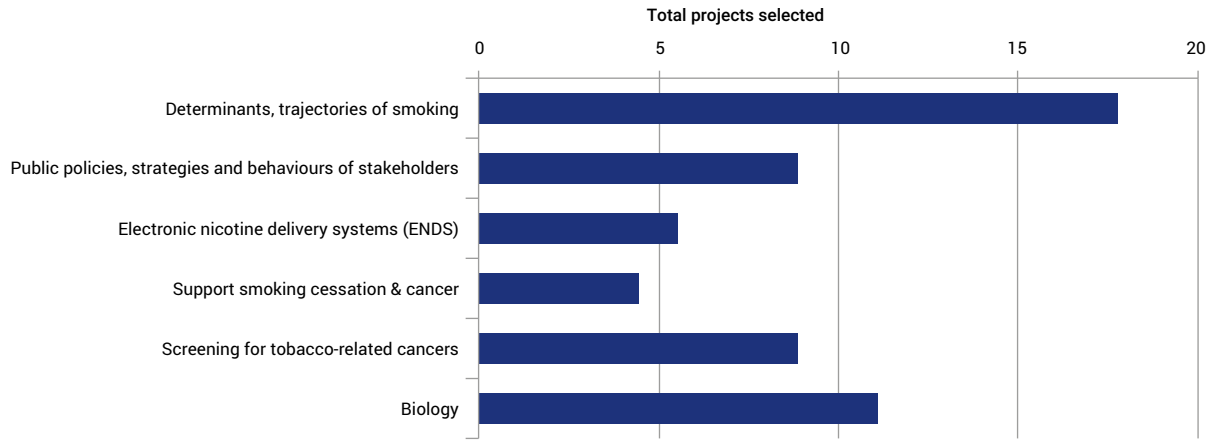
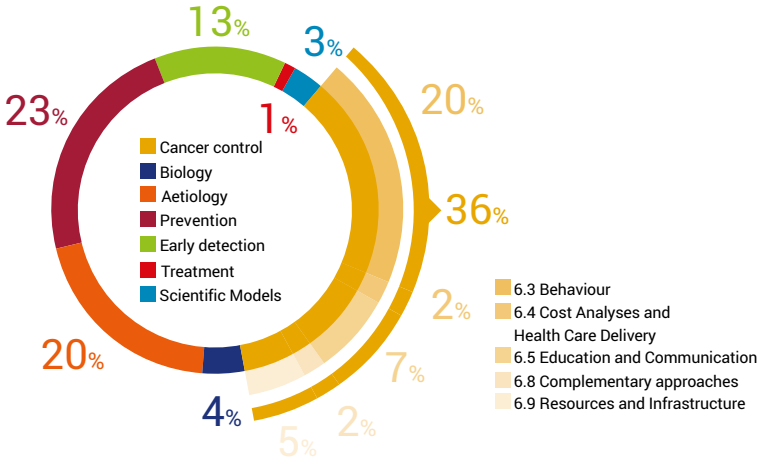


FIGURE 26
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2016-2019 PERIOD (SINCE 2018, PROJECTS SELECTED IN SECTION 1 & 2)



The programme over the 2014-2019 National Cancer Control Plan

Tobacco research is central to Cancer Plan 3. It comes under Objective 10 (National Tobacco Reduction Programme), then under Area 4 of the National Tobacco Control Programme (2018-2022): Monitoring, evaluating, researching, and disseminating knowledge about tobacco.

Over the 2014-2019 period, tobacco research was supported in different recurrent and specific calls for proposals launched by INCa:

- The investigator-driven programme in human and social sciences, epidemiology, and public health (HSS-E-PH);
- Population Health Intervention Research programme;
- The call for applications for doctoral grants in HSS-E-PH;
- The "DEPREV" call for proposals;
- The Research and intervention programme to reduce tobacco use and reduce the prevalence of tobacco-related cancers (Tobacco PRIORITE in 2015, 2016 and 2017) call for proposals, in partnership with the French Cancer League in 2016 and 2017;
- The call for proposals in partnership with IReSP (Fund Tobacco then Fund Addictions), since 2018.

In order to disseminate the knowledge produced and to mobilise the scientific community around these research issues, INCa has set up several exchange opportunities with scientists (researchers, field actors and decision-makers):

- From 2016 to 2019, Intervention Research symposiums (more than 200 attendees) where tobacco was addressed and discussed from a methodological point of view;
- In 2018 and 2019, seminars dedicated to "tobacco research" (40 people each): their objectives were to disseminate knowledge in the production process, to stimulate the production of innovative and transdisciplinary research questions. In 2019, the seminar focused on vaping research.

2018 -2019:

9 PAIR evaluated

74 cancer research projects evaluated

303 original publications in international journals

Impact on improving knowledge in the case of 90% of funded projects
Impact on clinical practice in the case of 60% of funded projects

THE INTEGRATED RESEARCH ACTION PROGRAMME (PAIR)

In 2007, INCa launched the Integrated Research Action Programme (PAIR) focusing on specific types of cancer. This programme was co-funded with Amgen and Roche in 2007 and with ARC Foundation and the ANRS in 2008. Since 2009, the PAIR programme has been launched and funded in partnership with ARC Foundation and the French Cancer League. The aim of this program is to promote cooperation between all scientific disciplines (fundamental research, clinical research, epidemiology, public health, and human and social sciences) around key structuring projects.

Since 2007, 80 cancer research projects have been funded for a total amount of €46.3M (Table 18).

TABLE 18
SELECTION TRENDS IN THE INTEGRATED RESEARCH ACTION PROGRAMME (PAIR) OVER THE 2007-2018 PERIOD

YEAR	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 League	8	5.62
2011	Upper aerodigestive tract cancers	INCa/ARC Foundation/French League	7	4.13
2012	Gynaecological cancers	INCa/ARC Foundation/French League	6	3.41
2013	Melanomas	INCa/ARC Foundation/French League	9	5.12
2014	Early breast cancers	INCa/ARC Foundation/French League	8	3.76
2017	Paediatric cancers	INCa/ARC Foundation/French League	3	5.04
2018	Pancreatic adenocarcinoma cancers	INCa/ARC Foundation/French League	7	3.68
Total			**81**	**46.30**

In 2018, INCa, ARC Foundation and Cancer League conducted a survey on the first 9 PAIRs conducted between 2007 and 2017 using self-reported surveys to describe the type of projects funded and assess the impact of the programme. The major findings of this survey obtained in 2019 were as follows:

- The average actual duration of funded projects was 42 months. The average allocated funding per project was €500,000. The average actual budget spent per project was €476,647;
- The CSO analysis showed that 39% of the funded projects concerned the field of early detection, diagnosis and prognosis (CSO 4); 19% biology (CSO 1); 16% aetiology (CSO 2), and 12% cancer control, survivorship and outcomes research (CSO 6);
- The analysis of established collaborations showed that 5 teams, on average, collaborated per project. More than two-thirds of the project leaders submitted their project in association with at least one team with whom they had never previously collaborated. New collaborations were initiated during the project duration in the case of two-thirds of these projects. The collaborations established during the project continued after the end of the project in the case of four-fifths of these projects.

At the time of this survey:

- The projects had an impact on improving knowledge in the case of 90% of these projects, and an impact on clinical practice in the case of 60%;
- In terms of concrete results, 303 publications in international journals were reported, two-thirds of the projects were the subject of international oral communications and 16% of the projects led to patents;
- Half of the funded projects enabled the development of new projects from the supported projects, having obtained other funding (leverage effect) for a total amount of €35M;

2020 PAIR on brain tumours

In 2019, INCa, ARC Foundation and the French Cancer League decided to propose a new PAIR devoted to brain tumours. The Steering Committee, consisting of renowned experts from neuro-oncology, neuropathology, basic research, radiotherapy and imaging, paediatrics, epidemiology, social sciences and humanities was set up, chaired by Professor Khê Hoang Xuan. The latter will be in charge of setting out the scientific research priorities in the aim of helping INCa draft the most relevant call for proposals that will be launched in 2020.

- The researchers funded by a PAIR programme displayed the following specificities: an integrative approach from fundamental to clinical, collaboration among researchers on the same disease, a strong drive on a focused research theme, partnership between the 3 major funders: INCa, ARC Foundation, Cancer League, and resulting funding.

In conclusion, the first 9 PAIRs have generated a real impact on improving knowledge and on clinical practice. The funded projects have led to numerous publications and international oral communications. The PAIRs have generated an important leverage effect for obtaining other funding. This programme has demonstrated its integrative capacity and its ability to federate the French research teams and the 3 major French cancer research funders around a targeted theme.

Examples of reported impact on clinical practice

- National colorectal cancer screening programme moves from Guaiac to Immunoassay Testing (screening – Early colorectal cancers PAIR)
- Establishment of specific signatures differentiating between ALK-negative systemic anaplastic lymphomas and CD30-positive peripheral T lymphomas without further specifications (prognostics – Lymphoma PAIR)
- Study included in the Dhumeaux report on the management of HCC in hepatitis C and in the recommendations of scientific societies (recommendation – Hepatocellular carcinomas PAIR)
- Definition of a signature predictive of viral infection in tumour tissues of the head and neck, with greater specificity than IHC p16, as a promising marker for the detection of high-risk HPV infection in the clinical setting (diagnosis- Upper aerodigestive tract cancers PAIR)
- Identification of predictive markers of response to chemotherapy (ERG), in a retrospective study, as a predictor of response to docetaxel in combination with hormone therapy from 2 phase III trials (predictive - Prostate PAIR)
- Quantitative evaluation of the performance of a new imaging technique: multi-spectral polarimetric Mueller imaging to improve early diagnosis of cervical cancer (diagnosis - Gynaecological cancers PAIR)
- Interest of exploring the anti-netrin-1 antibody (NP137) in a therapeutic indication of melanoma (Melanoma PAIR)

Paediatrics PAIR

In 2016, INCa, 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 bridges between different disciplines in paediatric oncology.

Three projects were selected for an amount of € 5.044 million and funding started in October 2017. An annual meeting with the 3 principal investigators was held at INCa in June 2019. All three presented the progress of their research projects according to the initial milestones. Discussion about the strengths and weaknesses was of a relevant interest in order to analyse the intrinsic and extrinsic difficulties, the obstacles they encounter and to tackle as well as the actions to be implemented.

The 3 projects are progressing correctly with regard to their respective initial calendar. Several points concerning the PAIR programme were raised during the discussion:

- What is the optimal size for PAIR projects and what is the relevance of these large collaborative projects?
- The question of the sustainability of the projects funded by the PAIR programme must be considered globally by the 3 partners;
- The issue of communication and dissemination of the tools produced to the patient community was addressed.

Support for integrated cancer research structuring

NATIONAL PRECLINICAL RADIOTHERAPY RESEARCH NETWORK: RADIOTRANSNET

In 2017, INCa launched a call for applications aiming to set up a national radiotherapy preclinical research network in order to structure and to integrate fundamental and translational radiotherapy research.

INCa's support is intended to:

- Promote multi- and interdisciplinary collaboration and improve partnerships between various players in radiotherapy research at a national level;
- Foster academic capabilities in terms of innovation, design, and management of preclinical projects;
- Enhance the international visibility and attractiveness of French radiotherapy research, and further develop European and international collaboration in this field.

RADIOTRANSNET, coordinated by Philippe Maingon and Vincent Marchesi, was designated in December 2018 by INCa and received a €200,000 funding for 3 years. A kick-off meeting was held on March 2019 bringing together INCa representatives and RADIOTRANSNET members.

In 2019, the project manager was recruited, the governance was set up and the Steering Committee met four times during the first year of RADIOTRANSNET's of launch: 27 March, 17 July, 9 October, and 12 December.

The 4 work packages were constructed with their set of detailed priorities and expected deliverables. For each work package, a coordinator was assigned, and a work methodology was defined.

WP1-Target Definition

The issues raised in WP1 are organised around:

- The definition of heterogeneity and biological volume of the tumour at the voxel: improved imaging methods for the characterisation of parameters such as hypoxia, vascularisation, immunogenicity, or microenvironment composition;
- Standardisation of the methods of delineation and software development around self-segmentation;
- Improving the definition of margins: modelling the probabilities of tumour control, movement management, "dose painting", etc.

WP2-Normal Tissue

The issues raised in WP2 are organised around:

- Modelling of undesired radiobiological effects;
- Evaluation of the individual response to irradiation and characterisation/identification of early biomarkers of this radio-sensitivity (radio-susceptibility);
- Mechanisms of secondary radio-induced effects, ways to diagnose them and to predict their severity and possible therapeutic actions against these side effects;
- Effects of fractionation, dose rate and particle type.

WP3-Combined Treatments

The issues raised in WP3 are organised around:

- The choice of strategies (validity of the hypothesis, innovative nature, clinical relevance, feasibility, etc.);
- The use of standardised methods;
- The development of protocols in preclinical models adapted for a correct evaluation of drug candidates.

WP4-Dose Modelling

The issues raised in WP4 are organised around:

- Minimising healthy tissue complications: reducing out-of-scope doses, use of hadrontherapy, improving treatment plans;
- Assessment of doses emitted during diagnostics and positioning: simulation and optimisation of protocols;
- Characterisation of beams and prediction of biological effects: micro- and nanodosimetry, radiobiological modelling;
- Creation of a decision support system: data standardisation and machine learning;
- Dose accumulation during treatment.

Three workshops were organised in July, September, and December 2019, devoted to WP1, WP4 and WP2, respectively.

Moreover, the RADIOTRANSNET website is now fully operational, with a newsletter published quarterly. The project development of RADIOTRANSNET during 2019 is in line with the estimated schedule.

CANCEROPOLES: SUPPORT FOR EMERGING PROJECTS

The mission of canceropoles is to promote the detection and emergence of new innovative research projects through regional or interregional calls for proposals, known as "Emergence". These calls are specifically intended to validate a proof of concept or to consolidate preliminary findings in order to increase their chances of success for national or international calls for proposal.

In 2019, INCa conducted a standardised survey aimed at all researchers who were funded from 2011 to 2018. This questionnaire was intended to collect information on the characteristics of emerging funded projects, on implementation conditions, project follow-up, the scientific and economic valuation of projects and the leverage effect created in order to assess the relevance and impact of this type of call for proposals.

Since the establishment of Emergence calls, 508 research projects have been funded for a total budget of €12.5M. The average budget allocated was €25k per project. The average selection rate for these calls for proposals varied from 16% to 32% depending on the canceropoles.

The overall response rate to the survey was 54.7% (278 responses/508 projects funded). Survey respondents to the survey to rate this call: 68% of researchers considered it very satisfactory, 29% satisfactory, and 4% moderately satisfactory.

Analysis of the responses to the questionnaire infers the following conclusions:

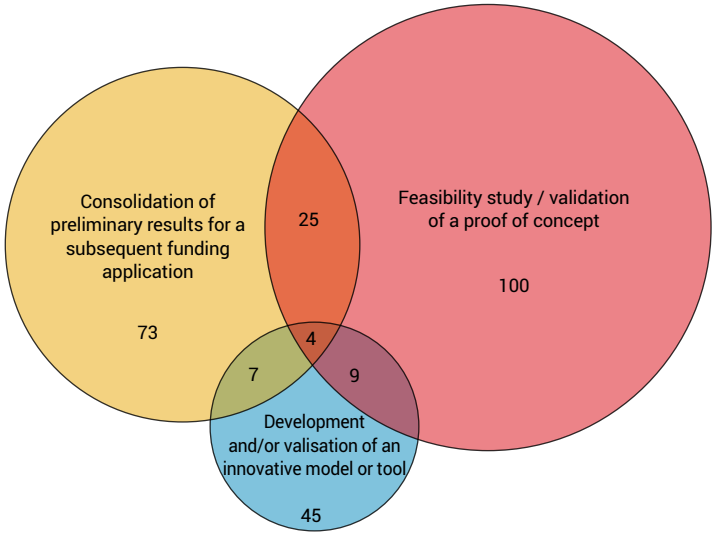
- 44% of the funded projects were intended to validate a proof of concept or a feasibility study, 34% to consolidate preliminary findings in order to apply for another call, finally 20% of the applications concerned the development or validation of an innovative model or tool (Figure 27);
- 64% of funded projects were basic research projects, 25% were translational research projects, and only 3% were clinical research projects; although human and social sciences, epidemiology and public health projects were encouraged, they represented only 8% of the responses obtained;
- 71% of the funded projects involved only one discipline, while 29% of the projects combined 2 or 3 disciplinary fields;
- 66% of emerging projects were carried out in collaboration with academic partners, and 3% with industrial partners;
- The partnerships set up during the project were continued after the end of funding in the case of 72% of the collaborative projects;
- 78% of respondents stated that the emerging project had been extended or that the results obtained allowed the launch of other subsequent projects;
- After funding from the canceropole, 74% of project leaders made subsequent funding applications; the success rate for these applications (ratio of accepted applications/submitted applications) was 59%, and the failure rate (ratio of unsuccessful applications/submitted applications) was 34% (7% of the results were still pending at the time of the survey);
- These calls have a significant leverage effect for obtaining additional funding: for each €1 invested by canceropoles, the researchers managed to raise between €2.5 and €8.1 from other funding sources;
- The findings from more than 68% of the emerging projects have been presented to the scientific community at national or international meetings;
- Although emerging projects are priming projects, 21% of the project leaders contacted a technology transfer office within the framework of their project. This development resulted in 41 patent filings, 2 licenses, and 10 industrial collaboration contracts.

Researchers were asked about the other potential impacts of this type of funding. In addition to the scientific impact, this type of funding had a positive impact on the establishment and strengthening of collaborations and on the training and recruitment

FIGURE 27

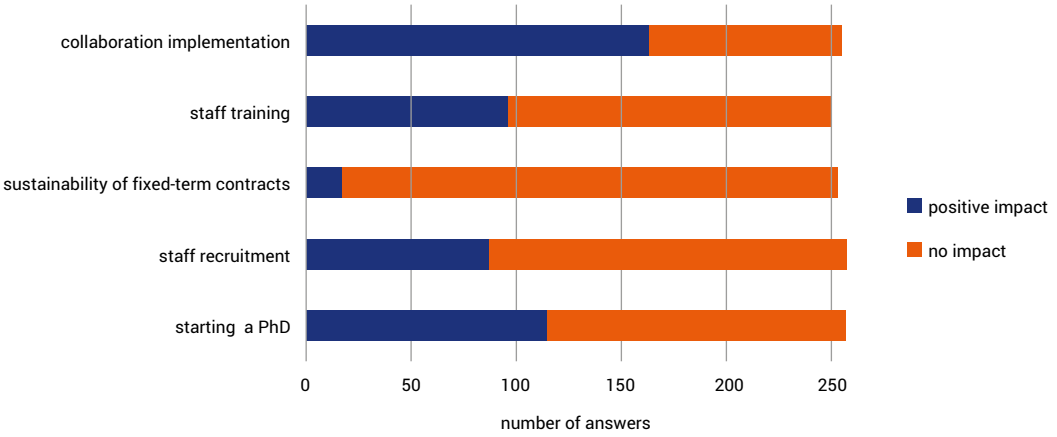
OBJECTIVES OF EMERGENCE CALL FUNDING APPLICATIONS (NUMBER OF RESPONSES FOR EACH OBJECTIVE)

The size of the circles is proportional to the number of projects. The diagram represents the number of projects according to the objective of the emerging project. The overlapping zones correspond to projects with 2 or 3 objectives.



of young researchers (Figure 28). The funded PIs also highlighted the positive effects on the development of technical skills, the development of new areas of research, especially for risky projects that could not have been funded otherwise.

FIGURE 28
OTHER POTENTIAL IMPACTS OF EMERGING PROJECT FUNDING



CANCEROPOLE ACTIVITIES DURING THE CANCER CONTROL PLAN

The multidisciplinary research structuring policy initiated in the first Cancer Plan resulted in 2003 in the establishment of 7 canceropoles (regional cancer research hubs) that work on a regional or inter-regional level for better coordination of cancer research between sectors and disciplines.

In 2014, a new call for applications was launched based on revised specifications and refocusing the missions of canceropoles on fields not covered by other organisations. In order to promote the development of innovative, collaborative, and competitive research in oncology, the actions developed by the canceropoles addressed the following priorities:

- To strengthen the competitiveness of research projects submitted to national and international calls for proposals, especially European ones;
- To strengthen scientific multidisciplinarity and expertise complementarity;
- To strengthen the detection of innovation and to enhance technology transfer;
- To strengthen support for young researchers;
- To support interactions with local authorities and regional structures in charge of research strategy and funding;
- To strengthen the links between research and care.

Actions, implementation strategies and associated monitoring indicators have been formally established in objective and performance contracts (COP 2015-2017),

defined in a concerted manner between INCa and each canceropole, and considering regional or inter-regional specificities. The results of 2015-2017 COP show that canceropoles have mobilised the scientific community with the organisation of 227 scientific events (symposia, seminars, annual days, etc.). The scientific events coordinated by the canceropoles have resulted in the creation of 79 working groups, bringing together the driving forces of research present in their areas. Links with regional coordination structures for clinical research (GIRCI, RRC, etc.) have been strengthened with the establishment of joint calls for proposals, funding for technological platforms, and the creation of clinical research networks.

One of the flagship actions led by canceropoles is the detection and funding of innovative emerging projects through the "Emergence" call for proposals. These calls, rolled out to all canceropoles since 2015, are intended to fund projects in order to consolidate preliminary findings necessary to obtain funding at a national level. This seed funding has shown a significant leverage effect for obtaining additional funding (see details in Emergence call survey report section).

Finally, the canceropoles have defined proactive research promotion policies, in partnership with regional players, for the detection and (co)-maturing of innovative projects. In this way, 301 projects have been identified by canceropoles and oriented towards technology transfer structures. Among these projects, 54 have resulted in patent applications, the creation of biotech companies, or the set-up of public-private partnerships.

In 2017, INCa reinforced the management of canceropoles and extended their designation for a new 5-year period (COP 2018-2022). Their missions have been refocused on fostering collaborations between researchers, support for new emerging projects, and the scientific and economic development of research findings.

INCa's financial support for canceropoles during the third Cancer Plan was €36M.

SIRIC DESIGNATION DURING THE CANCER CONTROL PLAN

The creation of 8 integrated cancer research sites (SIRIC) in 2011 and 2012 enabled the development of integrated research programmes of excellence, encompassing the entire continuum of basic, translational, clinical, and human and social science research. Fostering multidisciplinary interactions, SIRICs have facilitated the acceleration of the transfer of innovations for clinical applications in oncology. In 2015, a mid-term evaluation was organised to have the SIRICs assessed by a committee of international experts who provided an evaluation of the progress of integrated research programmes and of transversal structuring actions. In addition, recommendations were issued for the continuation of activities for the 8 SIRICs.

The importance and priority of this programme were supported in the third Cancer Control Plan which anticipated the launch of a second designation phase. This designation maintained the objectives set during the first designation:

- To carry out research of excellence which can be transferred for the benefit of those with cancer;

- To strengthen the level of creativity and international competitiveness of research on cancer prevention, diagnosis, and treatment.

In order to continue the momentum, INCa launched in 2017, in partnership with the French Ministry of Health (DGOS) and Inserm, a new call for SIRIC designation. The objective of this second designation was to take a leap forward in research organisation to better respond to the next challenges and to fight against cancer more effectively. This new campaign was open not only to previously designated structures, but also to new projects. Following an international scientific evaluation, 8 projects out of the 16 applications submitted were selected.

In compliance with the Cancer Control Plan, all the designated SIRICs signed partnership agreements with canceropoles with the objectives of defining a common strategy and pooling resources. Several joint actions between SIRIC and canceropoles have been carried out in order to consolidate research teams in a given area.

From 2015 to 2017, 34 joint scientific activities were organised (symposia, seminars, working groups, workshops, etc.) allowing the dissemination and promotion of research findings. Around 20 joint actions focusing on supporting the emergence of research projects through joint calls for proposals were conducted. They also agreed on pooling resources by developing technological platforms together. The establishment of an academic HSS research chair on the social challenges of precision medicine, associating INCa, the CLARA canceropole, the SIRIC from Lyon (LYriCAN) and other regional partners, is an emblematic example of collaboration between SIRICs and canceropoles enabling the development of ambitious research programmes and enhancing the attractiveness of an area.

Furthermore, SIRICs have worked together to build up a national collaborative initiative for the sharing and integration of biological and clinical data in oncology: the OSIRIS project. Initiated in 2015, the objective of this project was to promote the sharing of clinical, biological, and genomic data to improve their use for research purposes. This joint effort led to the definition of an "OSIRIS set" composed of 130 clinical and omic items for sharing clinical and biological data in oncology. This list is based on a conceptual and temporal model of the disease. This work received support from INCa (budget €300k) to lead a "proof of concept study" aiming to demonstrate data sharing feasibility and dataset interoperability from different personalised medicine molecular trials carried out in partner centres.

SIRIC funding receives joint support from INCa, the French Ministry of Health (DGOS), and Inserm. From 2014 to 2019, the budget allocated to this programme was €56M (of which €23.3M from INCa, €21.3M from DGOS, and €11.3M from Inserm for ITMO Cancer-Aviesan).

Translational and multidisciplinary research training programmes

THE BASIC AND TRANSLATIONAL RESEARCH TRAINING PROGRAMME

Support for basic and translational research is completed by an investment plan to promote training and career development for the next generation of investigators through grants for Master's degrees, PhDs, and postdoctoral positions. Launched in 2007, led by ITMO Cancer-Aviesan since 2011, the Basic and translational research training programme (FRFT) was amended in 2017 to include fundamental research. It aims to support complementary translational and fundamental research training of graduates of medicine, pharmacy, dentistry, and veterinary science.

2019:
20
grants awarded for total funding of
€1.72M

The programme in 2019

In 2019, a total of €1.72M was awarded for 20 grants for 8 Master's students, 11 PhD theses, and 1 postdoctoral fellowship (Table 19).

2011-2019:
220
grants awarded for total funding of almost
€17.6M

TABLE 19
FEATURES OF THE TRANSLATIONAL RESEARCH TRAINING PROGRAMME IN 2019

Objectives	To promote training of students or young medical, pharmacy and veterinary science graduates in translational research by funding master"s degrees, doctoral theses or post-doctoral research.
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€1.72M**
Proposals evaluated	**87**
Projects selected	**20**
Selection rate	**23%**

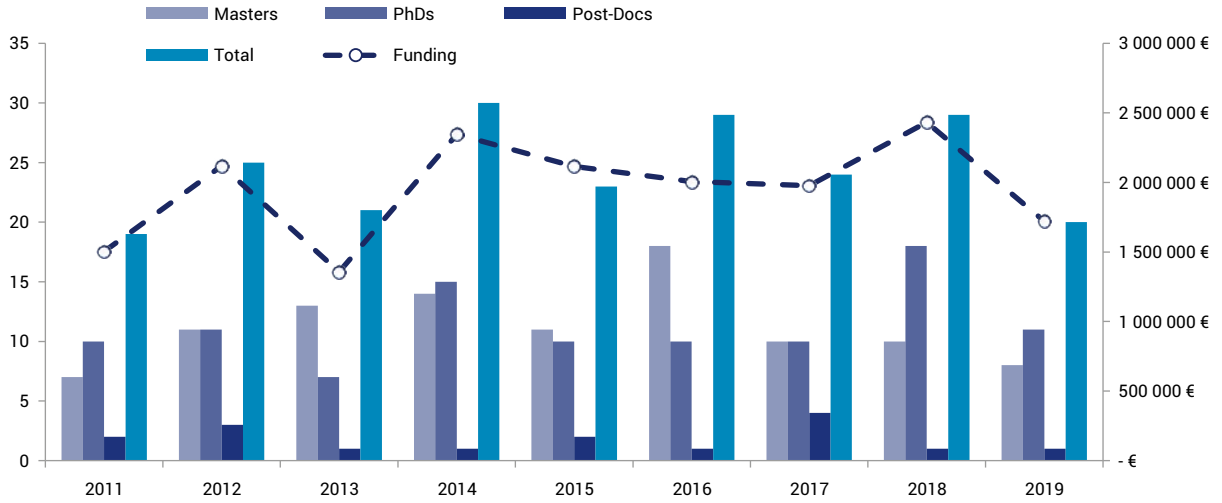
The programme over the 2011-2019 period

Since 2011, 220 training grants have been awarded to support training in translational cancer research for overall funding of €17.59M (Table 20).

TABLE 20
TRENDS IN SELECTION AND FUNDING OF THE BASIC AND TRANSLATIONAL RESEARCH TRAINING PROGRAMME OVER THE 2011-2019 PERIOD

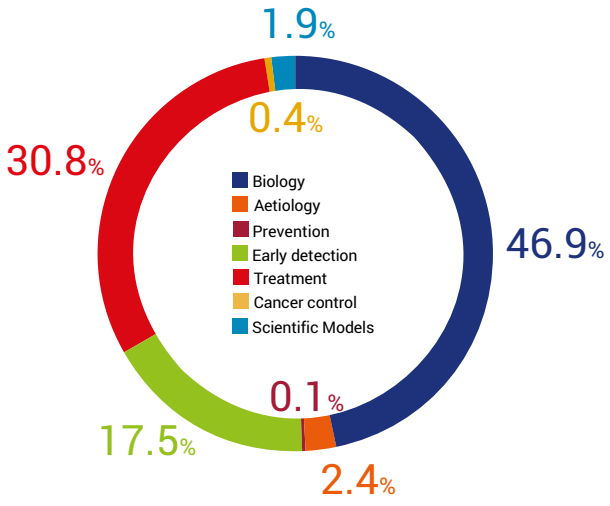
Year	2011	2012	2013	2014	2015	2016	2017	2018	2019	TOTAL
Funding (in €M)	1.50	2.12	1.36	2.35	2.11	2.01	1.98	2.44	1.72	**17.59**
Proposals evaluated	35	36	49	101	98	111	108	106	87	**731**
Projects financed	19	25	21	30	23	29	24	29	20	**220**
Financing rate	54%	69%	43%	30%	23%	26%	22%	27%	23%	**30.1%**

FIGURE 29
DISTRIBUTION OF SELECTED APPLICATIONS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2011-2019 PERIOD



Over the 9 years of the period, more than 45% of the grants were devoted to basic cancer research (understanding the general principles of cancer emergence or growth). Projects based on the development of therapeutic approaches accounted for just over 30% of the grants, while early detection and diagnostic approaches accounted for just over 17% of the grants (Figure 30).

FIGURE 30
DISTRIBUTION OF SELECTED APPLICATIONS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2011-2019 PERIOD



Ex post analysis of ITMO Cancer-Aviesan basic and translational research training programme

In 2019, ITMO Cancer-Aviesan conducted an ex-post evaluation of the Basic and translational research training programme over the 2011-17 period. A seminar with PhD school directors, experts and former awardees took place on May 2019 to discuss the programme itself and the question of research training for clinicians. Analysis showed that the majority of the PhD students funded pursued scientific research activities along their clinical activities after their thesis. Other outcomes identified include a better understanding of scientific research for master degree students, which is helpful even for clinicians not active in research. The research conducted has led to some clinical trials in addition to new knowledge.

Some changes in clinical practices regarding cancer diagnosis have been reported as impacts, pointing out the importance of keeping a strong interface between research and clinical care.

SUPPORT FOR TRAINING IN INTERDISCIPLINARY RESEARCH - FRONTIERS IN LIFE SCIENCES (FDV)

The FdV graduate school recruits students trained in various disciplines (e.g. biology, physics, mathematics, medicine, economy, linguistics, etc.) around the world in its PhD programme. This programme is hosted by Pôle de Recherche et d'Enseignement Supérieur (PRES) Sorbonne Paris Cité under the guidance of Paris-Descartes and Paris-Diderot Universities. The support for this programme is aimed at promoting multidisciplinary training to adapt and to meet the needs of cancer research.

The programme in 2019

In 2019, 2 projects were selected for a total amount of €210 000 (Table 21). They were aimed at developing modelling tools to evaluate mechanical forces involved during T-cell activation, including in cancer settings, and to explore cancer- and ageing-related molecular defects at the cellular level to reveal the protective role of cell senescence in carcinogenesis.

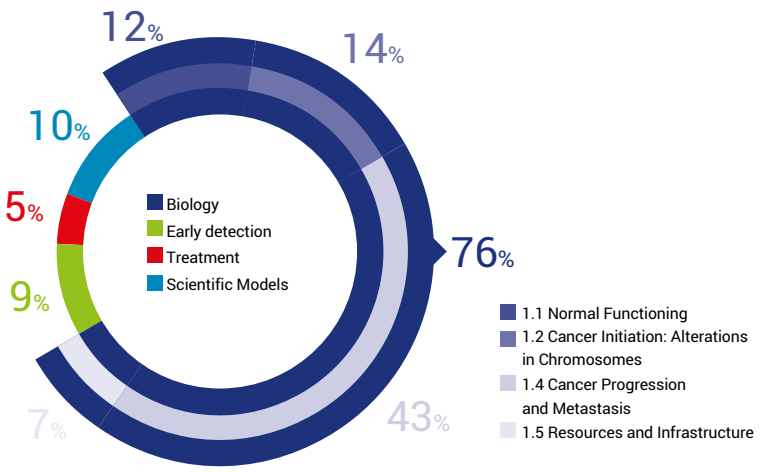
TABLE 21
FEATURES OF THE PHRC-K PROGRAMME IN 2018

Objectives	The PhD programme aims to promote ambitious research projects using a broad range of academic disciplines in order to understand living systems.
Programming institution	Frontiers in Life Sciences graduate school
Operating institution	Frontiers in Life Sciences graduate school
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€0.21M**
Proposals evaluated	**4**
Projects selected	2
Selection rate	**50%**

The programme over the 2010-2019 period

Over the 9 years of the partnership with this programme, 21 grants have been funded for €2.20M. More than 75% of projects were devoted to cancer biology research (Figure 31).

FIGURE 31
DISTRIBUTION OF SELECTED APPLICATIONS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2010-2019 PERIOD



SUPPORT TO ENABLE YOUNG SCIENTISTS TO CREATE AND LEAD A CANCER RESEARCH TEAM THROUGH THE ATIP-AVENIR PROGRAMME

Under a partnership between CNRS and Inserm, this call for proposals 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 awardees pursuing a cancer research project.

The programme in 2019

In 2019, 2 projects were selected, for a total amount of €600,000 (Table 22). They were aimed at exploring specific cancer-related mechanisms involved in chromatin compaction, epigenetic deregulation, macrophage activation in the tumour microenvironment and endothelial autophagy, in order to identify new cancer biomarkers or treatment targets. In addition, 2 projects previously selected were also extended for two additional years for €120,000.

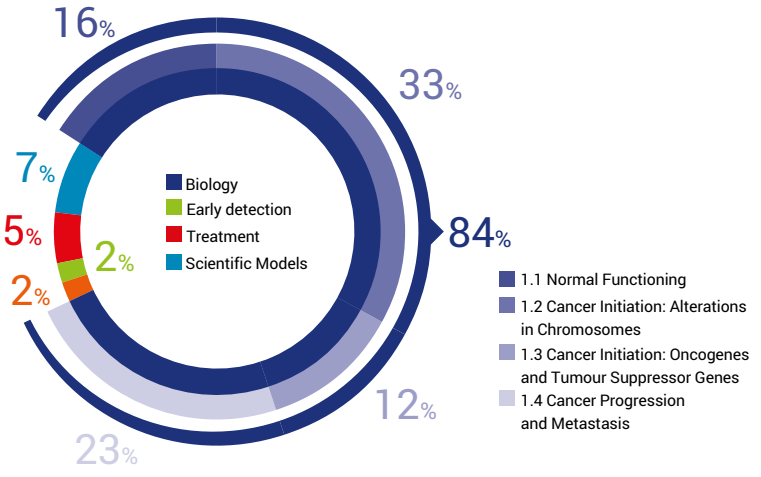
TABLE 22
FEATURES OF THE ATIP-AVENIR PROGRAMME IN CANCER RESEARCH IN 2019

Objectives	To promote the establishment of young promising PIs in cancer research by funding 3 years of their starting team
Programming institution	CNRS and Inserm
Operating institution	CNRS and Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€0.60M**
Proposals evaluated	**5**
Projects selected	2
Selection rate	**40%**

The programme over the 2007-2019 period

Over the 13 years of the programme, 51 grants were funded for a total amount of €12.68M. Almost 85% of projects were devoted to cancer biology research (Figure 32).

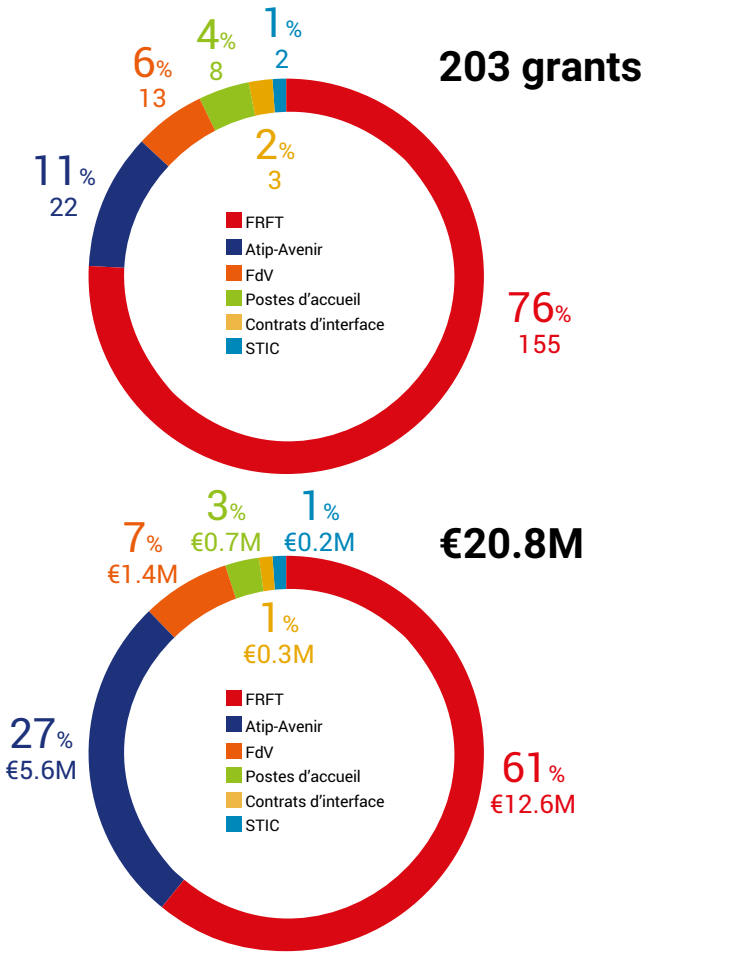
FIGURE 32
DISTRIBUTION OF SELECTED APPLICATIONS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2019 PERIOD



TRAINING PROGRAMMES WITHIN THE NATIONAL CANCER CONTROL PLAN

Over the period of implementation of the 3rd French Cancer Control Plan (2014-2019), ITMO Cancer-Aviesan funded more than 200 grants for a total amount of almost €21M (Figure 33). The vast majority of both grants (76%) and funding (61%) were devoted to the Basic and translational research training programme (FRFT), the rest being used to sustain research training partnerships (Atip-Avenir, FdV, Postes d'accueil, Contrats d'interface and STIC programmes).

FIGURE 33
DISTRIBUTION OF SUPPORTED GRANTS OVER THE 2014-2019 CANCER CONTROL PLAN (TOP PANEL: NUMBER OF GRANTS, BOTTOM PANEL: ALLOCATED AMOUNT)



CANCER CLINICAL 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.

The national programme for hospital clinical research on cancer (PHRC-K)

Nationwide funding of academic clinical research is organised through a specific call for research proposals operated by INCa, and funded by the French Ministry of Health (DGOS): national programme for hospital clinical research on cancer (PHRC-K).

PHRC-K funds cancer clinical research projects with the following objectives:

- Assessment of the efficacy of health technologies. To meet this objective, priority is given to funding research that, using controlled comparative methods, randomised or not, should help achieve recommendations with strong scientific evidence;
- Evaluation of the safety, tolerance, or feasibility of the use of health technologies in humans.

In accordance with the 2014-2019 Cancer Control Plan, the orientations of the PHRC-K programme particularly concern:

- Areas pertaining to advanced forms of tumour diseases, oncogeriatrics and paediatric oncology;
- Research projects addressing individual or collective behavioural modifications, or exploring drug-based approaches in the prevention of cancer risks;

2019:
36
clinical research projects funded out of the 174 submitted for a total budget of
€21.4M

- Projects that include assessment of patients' quality of life (during and/or after illness);
- Combination of several targeted drugs, or combinations of targeted drugs with chemotherapy or radiotherapy;
- Clinical validation of the efficacy of innovative health technologies for treatment or diagnosis;
- Reduction in the medium and long-term toxicity of treatments, and its assessment, especially for children and young adults, and patients with breast cancer;
- Increase of patients survival;
- Reduction in the medium and long-term toxicity of treatments, and its assessment, especially for children and young adults, and patients with breast cancer;
- Evaluation of treatment- or disease-related sequelae, and means for reducing them;
- Supportive care, palliative, and end-of-life care;
- Meta-analyses addressing controversial issues in treatment efficacy;
- As recommended by the 2014-2019 Cancer Plan, strong participation from major cooperative groups is expected, particularly with regard to proposing and conducting clinical trials aimed at addressing the major therapeutic questions of increasing survival and reducing the side-effects and delayed effects of treatments;
- Research in primary care and prevention (French national health strategy).

In addition, as recommended by the 2014-2019 Cancer Plan, strong involvement of cooperative intergroups is warranted, particularly with regard to proposing and conducting clinical trials aimed at responding to the major therapeutic questions: increasing survival, reducing the side-effects and delayed effects of treatments.

THE PROGRAMME IN 2019

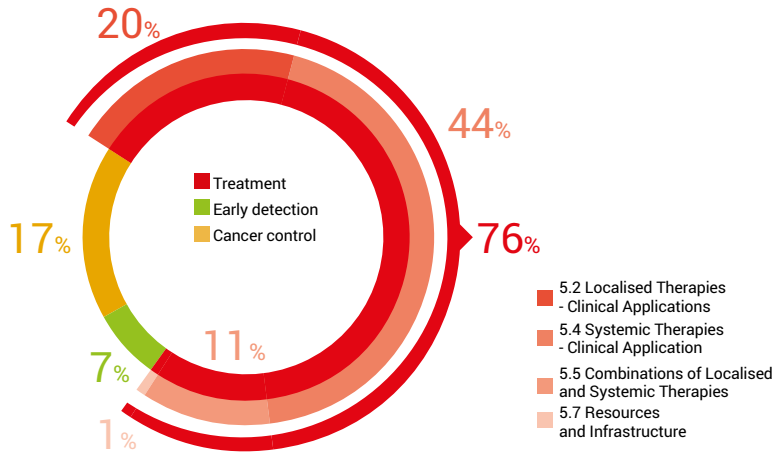
In 2019, 174 letters of intent were submitted to PHRC-K and 36 projects were selected for funding for a total amount of €21.4M (Table 23).

TABLE 23
FEATURES OF THE PHRC-K PROGRAMME IN 2019

Objectives	To assess the efficacy of health technologies; To evaluate safety, tolerance, or feasibility of the use of health technologies in humans.
Programming institution	INCa/Ministry of Health (DGOS)
Operating institution	INCa
Funding institution	Ministry of Health (DGOS)
Funding	**€21.4M**
Proposals submitted	174
Projects selected	36
Selection rate	21%

For 2019, the CSO analysis of funded projects shows that the majority of the funded projects belong to the treatment category (76.4%) and, particularly, to clinical applications of systemic and localised therapies (58.2% and 25.5%, respectively). The other topic studied is related to care and survival (16.7%) (Figure 34).

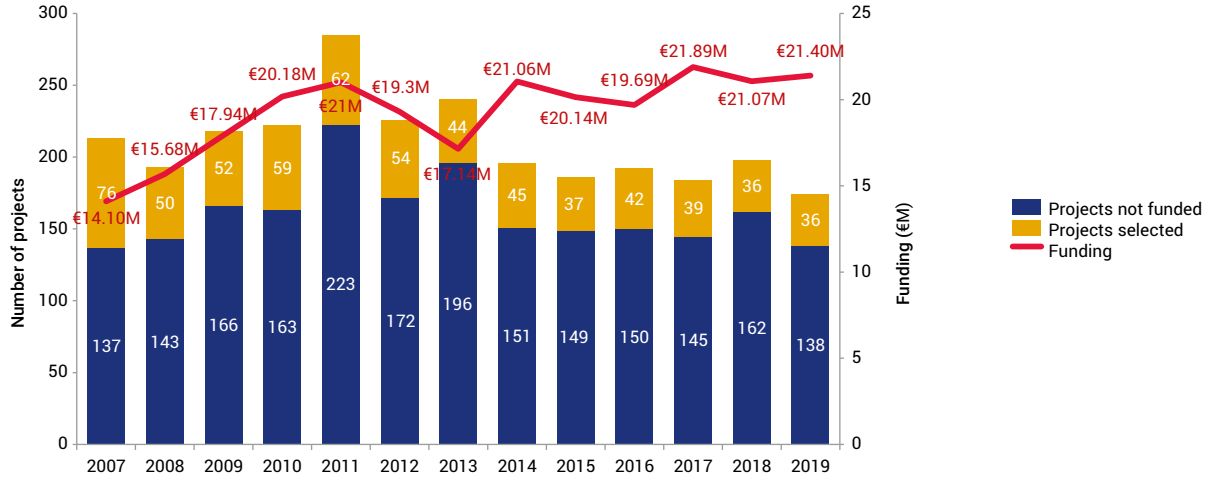
FIGURE 34
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION IN 2019



THE PROGRAMME OVER THE 2007-2019 PERIOD

Since 2007, 2,727 proposals have been submitted to the PHRC-K programme and 632 projects have been selected for an overall amount of over €250 (Figure 35).

FIGURE 35
TRENDS IN SELECTION AND FUNDING FOR THE PHRC-K PROGRAMME OVER THE 2007-2019 PERIOD



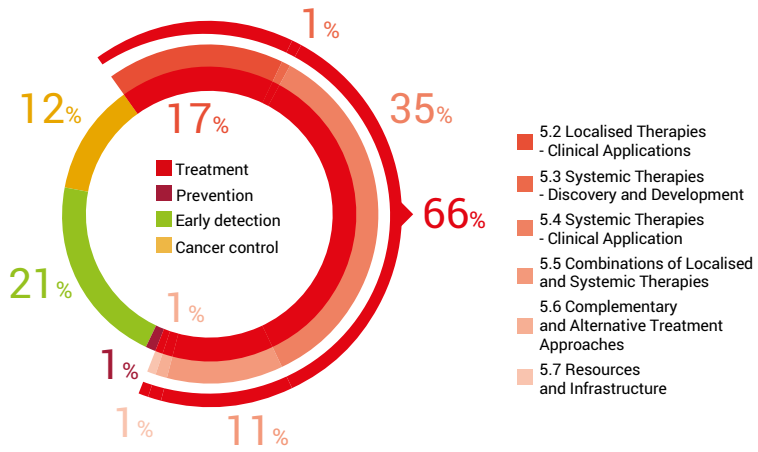
Over the 2007-2019 period, the CSO analysis of funded projects shows that the majority of the funded projects belong to the treatment category (65.4%) and,

2007-2019:
632
projects funded for a total amount of
€250M

Funded projects are mainly phase II (23-52%) and phase III (39-58%)

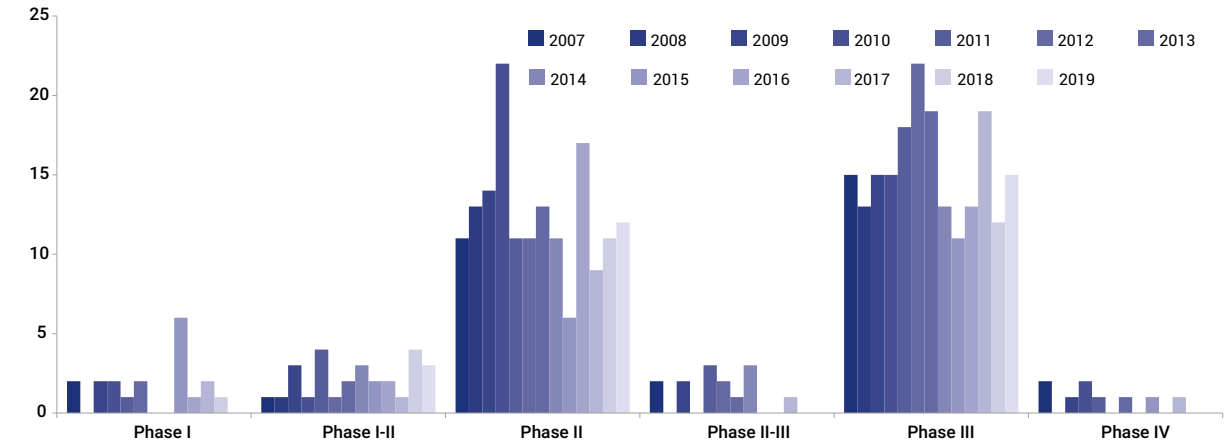
particularly, to clinical applications of systemic and localised therapies (52.9% and 25%, respectively). Moreover, the other topics studied relate to early diagnosis (20.4%) and care and survival (12.3%) (Figure 36).

FIGURE 36
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2019 PERIOD



Over the 2007-2019 period, the type of funded projects according to development phase were mainly phase II (from 23 to 52%), and phase III (from 39 to 58%) (Figure 37).

FIGURE 37
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO STUDY PHASE



THE PROGRAMME WITHIN THE NATIONAL CANCER CONTROL PLAN

Over the 2014-2019 period, 1,130 proposals were submitted to the PHRC-K programme and 235 projects were selected for an overall amount of over €125M. The overall selection rate for this period is 21%. This percentage is a little lower than for the whole period (2007-2019, overall selection rate of 23%). This is probably due to an increase in budgets for projects particularly those related to innovative technologies such as CAR-T cells.

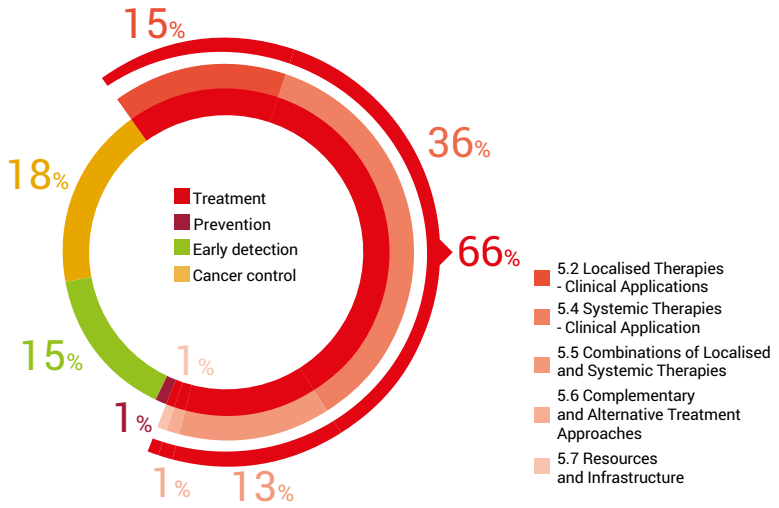
Figure 38 shows the distribution of the projects selected over the 2014-2019 period. The majority of the funded projects belong to the treatment category (66.5%) and, particularly, to clinical applications of systemic and localised therapies (54.7% and 22.9% respectively). Moreover, the other topics studied relate to early diagnosis (14.8%) and care and survival (17.8%).

The percentage of selected projects pertaining to the latter category is higher than for the entire 2007-2019 period: 12.3%. This is probably due to the orientation of the PHRC cancer programme in relation to the 2014-2019 Cancer Control Plan, with a focus on the following topics:

- Projects including assessment of quality of life (during and/or after illness);
- Reduction in the medium- and long-term toxicity of treatments, and its assessment, especially for children and young adults and patients with breast cancer;
- Evaluation of treatment- or disease-related sequelae, and means for reducing them;
- Supportive care, palliative, and end-of-life care.

Over the 2014-2019 period, an increase in projects related to care and survival is noted compared to the whole 2007-2019 period (17.8% vs 12.3%), supported by the Cancer Control Plan orientations

FIGURE 38
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2014-2019 PERIOD



Final PHARE trial findings

PHARE (Protocol for Herceptin® as Adjuvant therapy with Reduced Exposure) is a national randomised controlled trial in breast cancer, funded and sponsored by the French National Cancer Institute.

PHARE is an open-label, phase 3, non-inferiority randomised trial of patients with HER2-positive early breast cancer comparing 6 months versus 12 months of trastuzumab treatment concomitant with or following standard neoadjuvant or adjuvant chemotherapy. The study was undertaken in 156 centres in France. The primary objective was non-inferiority in the intention-to-treat population in the 6-month group in terms of disease-free survival with a prespecified hazard margin of 1.15.

3,384 patients were enrolled and randomly assigned to either 12 months or 6 months of adjuvant trastuzumab.

Published in The Lancet journal in June 2019[2], the results show that 704 events relevant to disease-free survival were observed (345 [20.4%] in the 12-month group and 359 [21.2%] in the 6-month group), and no difference in effects pertaining to trastuzumab duration were found in any of the subgroups (the non-inferiority margin was included in the 95% CI). The final analysis has concluded that this study did not show the non-inferiority of 6 months versus 12 months of adjuvant trastuzumab. The standard duration of adjuvant trastuzumab treatment should remain 12 months for patients with *HER2*-positive early breast cancer.

PROGRESS OF FUNDED PROJECTS OF PHRC CANCER PROGRAMME

Since 2011, selected projects have been able to obtain one of the funding tranches subject to justification of their progress status. This funding process makes it possible to monitor the projects selected for funding per 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 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.

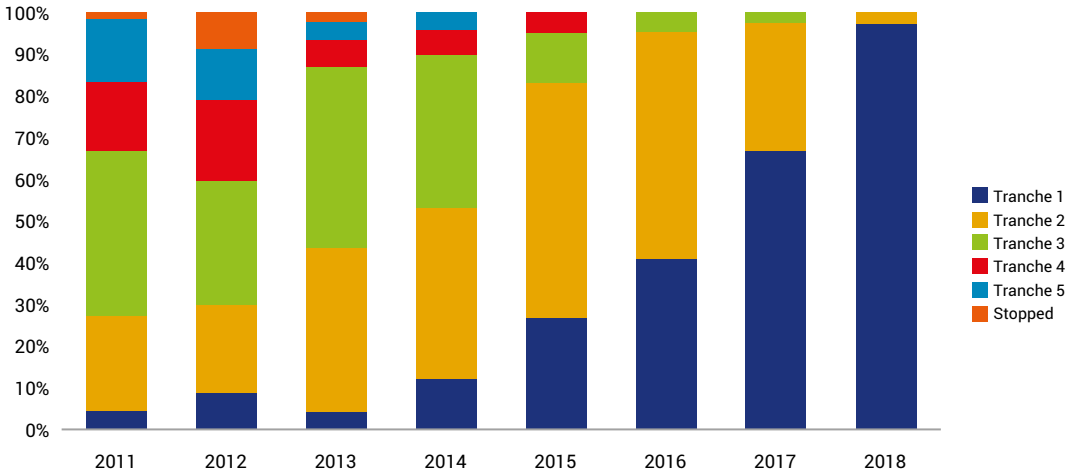
For the period of 2011 to 2018, 378 projects are concerned by monitoring according to funding tranches.

In 2019, for projects funded during the 2011-2018 period:

- 33% of projects requested tranche 2 which corresponds to the authorisation obtention stage;

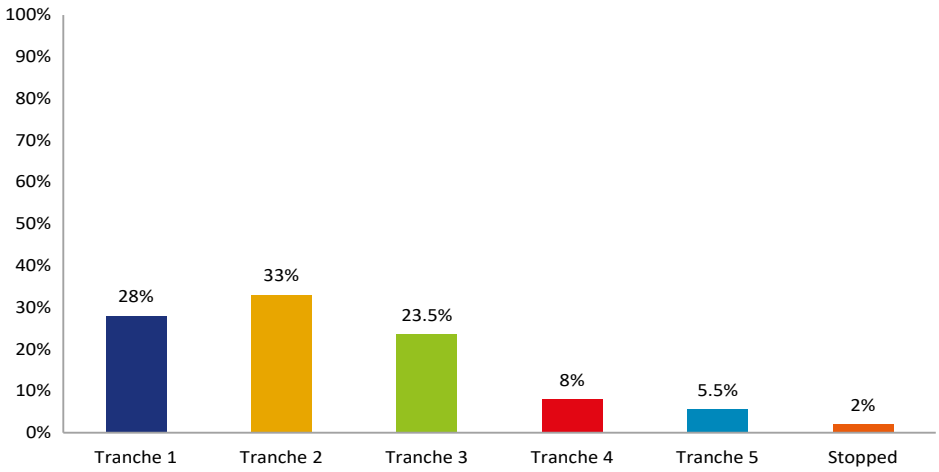
2. Xavier Pivot et al. (2019). *6 months versus 12 months of adjuvant trastuzumab in early breast cancer (PHARE): final analysis of a multicentre, open-label, phase 3 randomised trial.* Lancet 2019 Jun 29;393(10191):2591-2598. doi : 10.1016/S0140-6736(19)30653-1

FIGURE 39
DISTRIBUTION OF FUNDED PROJECTS ACCORDING TO THEIR PROGRESS AND THE YEAR OF SELECTION



- 23.5% of projects have reached tranche 3 which corresponds to the "50% inclusion" stage;
- 5.5% of projects have published on their primary endpoints, corresponding to 15 projects selected during the period from 2011 to 2014;
- 28% of funded projects did not commence the clinical study because they did not receive regulatory authorisation due to another obstacle (fewer human resources, no longer having support from the pharmaceutical industry, etc.).

FIGURE 40
PERCENTAGE OF TOTAL PROJECTS ACCORDING TRANCHE STATUS



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 develop ultra-multicentric studies to reduce the patient inclusion period;
- 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 solicit project sponsors and/or investigators to obtain information on the different difficulties faced while increasing the steering of the clinical trials launched for a better assessment of feasibility in the future.

Support for clinical research in French overseas departments

One of the objectives of the 2014-2019 Cancer Control Plan is 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 is providing financial support to enable the development of clinical research in those territories, particularly the opening of investigation centres.

GIRCI SOHO (Clinical Research and Innovation Organisation for Southwest and Overseas Hospitals) was created by a ministerial circular in 2005. It includes the 3 overseas University Hospitals (CHU Martinique, CHU Guadeloupe, CHU Reunion), as well as healthcare centres. GIRCI SOHO supports the latter in clinical research in the French overseas departments. INCa's Clinical Research Department worked in close collaboration with GIRCI SOHO in order to identify projects likely to be able to open investigation centres easily in French overseas departments.

Seven projects have been proposed to granting a total amount around €300,000 for 3 or 4 years, which should enable 104 patients to be enrolled in cancer clinical trials in French overseas departments (Martinique, Reunion, Guadeloupe) in the field of colon cancer, head and neck cancer, cervical cancer and leukaemia (Table 24).

TABLE 24
FEATURES OF THE CLINICAL RESEARCH PROJECTS SUPPORTED IN FRENCH OVERSEAS DEPARTMENTS

PROJECT	GRANT	DURATION OF THE PROJECT	INVESTIGATION CENTRES	PATIENTS TO BE ENROLLED
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 Multicenter Phase II Randomized Trial	€25,915	36 months	CHU Martinique	25 patients
SIMPA Efficacy of an Oral Immunomodulatory Nutrient on Survival During Postoperative Concomitant Chemoradiotherapy in Head and Neck Cancer	€57,614	48 months	CHU Martinique CHU Reunion Clinique Ste Clotilde	12 patients 15 patients 12 patients
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 Reunion	10 patients 3 patients
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 Reunion	5 patients
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 patients
DEXAML-03 Dexamethasone Plus Salvage Chemotherapy Versus Salvage Chemotherapy Alone in Patients with First Relapsed or Refractory Acute Myeloid Leukemia: a Randomized, Controlled, Open-label, Multicenter, Phase III Study	€29,000	48 months	CHU Réunion	6 patients
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 patients

International Rare Cancer Initiative (IRCI)

The International Rare Cancer Initiative (IRCI) is a strategic partnership between the National Cancer Institute) (NCI-USA), the National Institute for Health Research (NIHR-UK), Cancer Research United Kingdom (CRUK), the *European Organisation for Research and Treatment of Cancer* (EORTC-Europe), the French National Cancer Institute (INCa-France), the *Canadian Cancer* Trials Group (CCTG-Canada), the Clinical Oncology Society of *Australia* (COSA-Australia), and the *Japan Clinical Oncology Group* (JCOG-Japan). The driving mission of the IRCI is to make clinical trials in rare types of cancer practicable through international collaborations (see http://www.irci.info/).

Since 2018 and its second expression of interest (EOI), IRCI is supporting 10 working groups wishing to develop international trials on rare cancers. Among these, 3 projects designated by IRCI have a French leader or collaborator. However, as IRCI is not funding those trials, INCa has approved support to fund investigators to run IRCI trials in France (Table 25). The funding will provide salaries, technician support, travel, and regulatory costs to open centres.

TABLE 25
MAIN FEATURES OF THE IRCI CLINICAL TRIALS FUNDED

PROJECT	PRINCIPAL INVESTIGATOR	RARE CANCER	FUNDING BENEFICIARY	DURATION	FUNDING
SANTAL A Phase III Randomised Study of Chemo-radiotherapy Versus Radiotherapy Alone in the Adjuvant Treatment of Salivary Glands and Nasal Tumours (IMRT or Protontherapy)	Juliette Thariat	Salivary glands	GORTEC	36 months	€75,000
Evaluation of the efficacy of a 12-month adjuvant systemic immunotherapy (Tasquinimod) to prevent recurrence and progression after complete resection of non-muscle invasive upper urinary tract transitional carcinoma	Olivier Cussenot	Upper urinary tract transitional carcinoma	AP-HP	36 months	€57,000
Ampullome	Pierre Laurent-Puig	Ampullome	AP-HP	36 months	€75,000

Precision medicine initiatives

CAR T-CELLS

Since the beginning of 2019, the Clinical Research Department of the French National Cancer Institute has undertaken several actions on CAR T-cells in terms of management, coordination, development, and communication.

For research aspects, a working group dedicated to academic CAR T-cell research and bringing together major scientists and researchers working in the field was set up. A dedicated research kick-off meeting was organised in October 2018, and three sub-working groups were formed related to basic and translational research, prerequisites for products and platforms, and clinical research, to draw up specifications to help INCa support this academic research (September 2018-January 2019). Beyond national priority areas for academic research, the major issues that have been raised from these three academic research sub-working groups cover:

- Vectors and good manufacturing processes for basic research;
- Regulatory aspects and transfer to clinical research, funding of costly projects;
- Follow-up of patients (epidemiological as well as biological monitoring).

In April 2019, INCa organised a national workshop on CAR T-cells in Paris with national stakeholder speakers such as DGOS (Direction Générale de l'Offre de soins), ANSM (Agence Nationale de sécurité du Médicament et des produits de

santé), HAS (Haute Autorité de santé) and international academic researchers. This workshop was attended by more than 100 people to discuss key regulatory issues and academic research dedicated to CAR T- cells across Europe.

Regarding dissemination and institutional communication aspects, INCa has presented a poster "CAR T-cells challenge in France: a work developed by the French National Cancer Institute" at the first European CAR T-cell Congress co-organised by the European Haematology Association (EHA) and the European Society for Blood and Marrow Transplantation (EBMT). This congress took place in February 2019 in Paris.

Regarding medico-economic analysis aspects, , in March 2019, INCa drafted and published a position paper for the development of academic CAR T-cell production platforms following the request by CNAM (Caisse nationale d'assurance maladie, National Health Insurance Fund).

For international networking aspects, INCa has been actively involved in coordinating French academic researchers to enter into a European consortium project submitted to the IMI (Innovative Medicine Initiatives) Horizon 2020 Framework Programme on the subject of CAR-T cells: "Topic: Supporting the development of chimeric antigen receptor T cells".

The T²EVOLVE project, led by Michael Hudecek (professor of immunology at the University of Würzburg, Germany), was submitted to IMI in September 2019 and selected for the final evaluation planned in 2020 to accommodate the merger with the pre-defined industry consortium.

THE 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 the treatment of **246 patients** carrying molecular alterations targeted by the

"CAR T-cell regulatory framework"

28/03/2019: Ministerial Decree (NOR: SSAH1909328A) restricting the use of CAR T-cells to relevant health care centres.

18/02/2019 - ANSM Fast-track Programme: Medicinal drug trials with complex design and Advanced Therapy Medicinal Product (ATMP) such as CAR T-cells are eligible for the Fast Track programme conducted by ANSM.

30/04/2019 - Ministerial Decree (NOR: SSAS1908250A): Procedures for collecting, recording, and transmitting information related to Yescarta® (Gilead) and Kymriah® (Novartis).

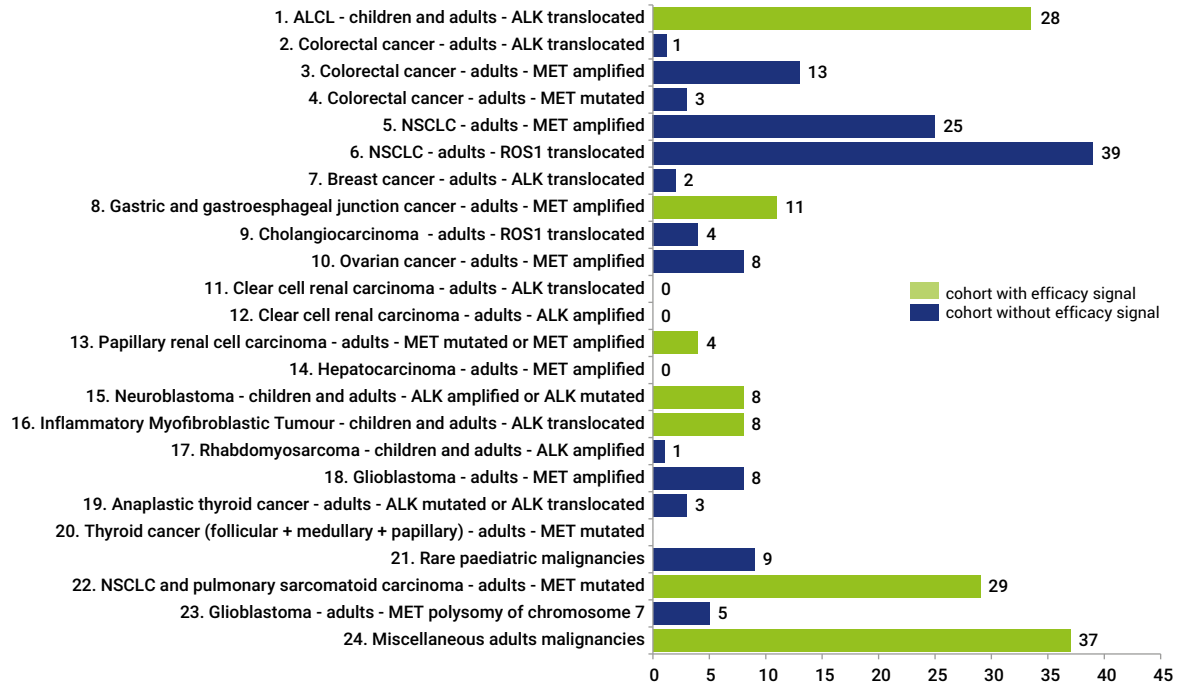
May 2019: The French Ministry of Health (DGOS) set up a working group to discuss the implementation of collecting procedures and real-time data transfer (with HAS, ANSM, INCa, ATIH, LYSA-LYSARC, haematologists).

AcSé-Crizotinib:
246 patients included
186 investigator sites
24 cohorts

drug (*ALK*, *MET* and *ROS1*) in more than 20 different cancer types (Figure 41). 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 planned 4 years of inclusion and the subject of 2 extensions

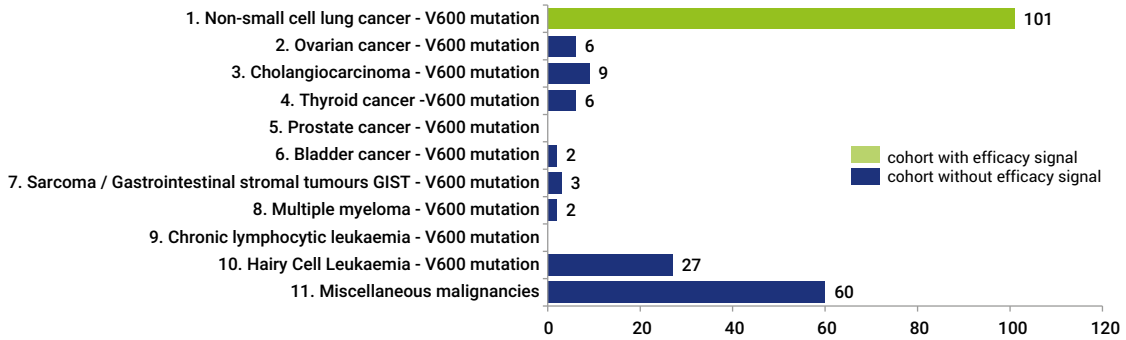
FIGURE 41
ACSÉ-CRIZOTINIB: DESCRIPTION OF RECRUITMENT BY COHORTS/STUDY ARMS (DECEMBER 2019)



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 (Figure 42). 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-Vemurafenib:
216 patients included
118 investigator sites
11 cohorts

FIGURE 42
ACSÉ-VEMURAFENIB: DESCRIPTION OF RECRUITMENT BY COHORT/STUDY ARM (DECEMBER 2019)

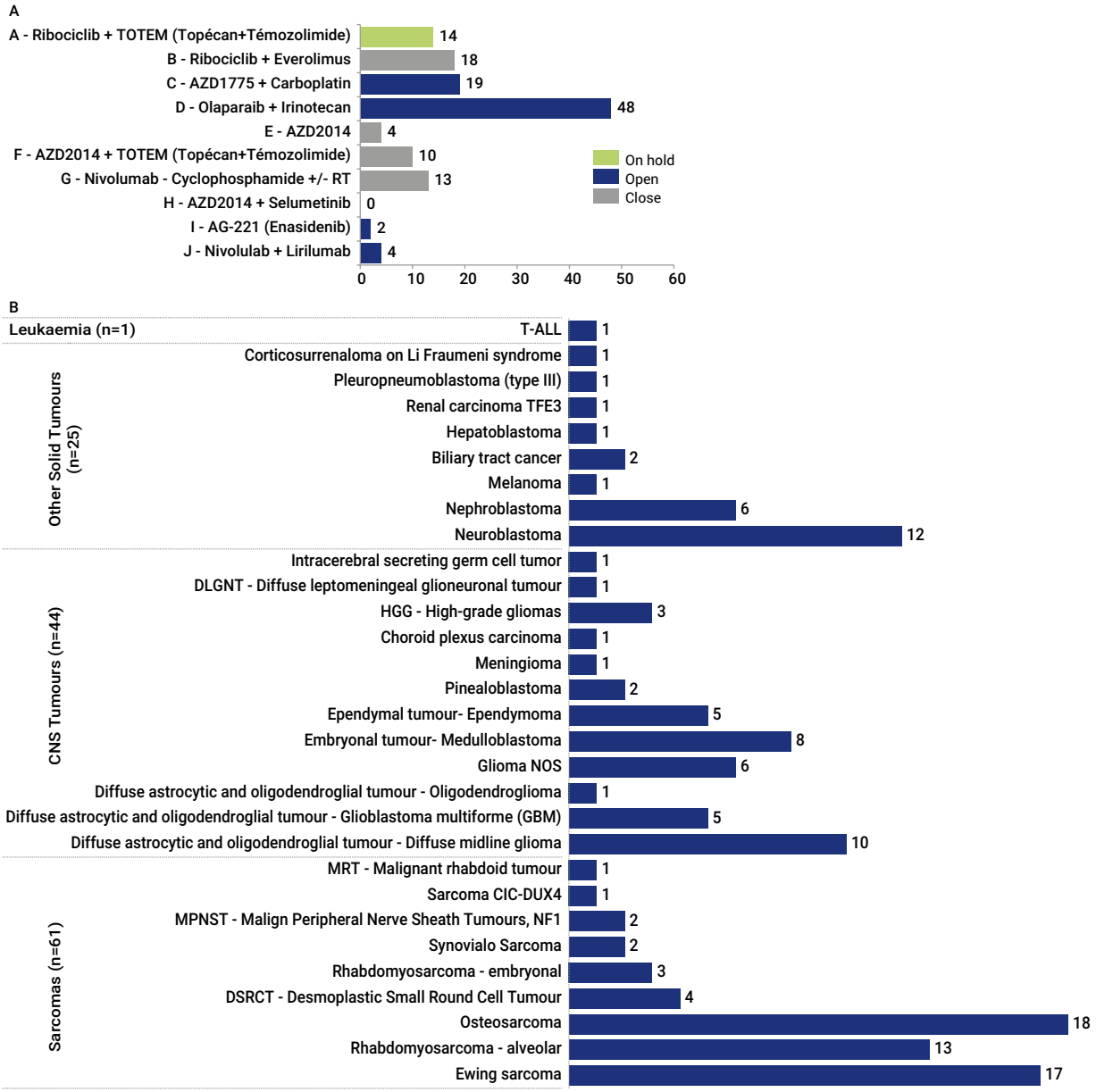


- **AcSé-eSMART (European Proof-of-concept Therapeutic Stratification Trial of Molecular Anomalies in Relapsed or Refractory Tumours in Children**), launched in July 2016 and entirely dedicated to paediatric cancers. It simultaneously makes several targeted therapies available in the same clinical trial 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, already approved and opened in 4 countries (France, Spain, Netherlands and UK), has led to the inclusion and treatment of 132 children (125 in France and 7 in the Netherlands) (Figure 43) within 10 study arms, representing almost 30 different histological types.

AcSé-eSMART:
132 children included
10 investigator sites in France
10 study arms

FIGURE 43

ACSÉ-ESMART: DESCRIPTION OF RECRUITMENT BY STUDY ARM (PANEL A) AND BY COHORT (PANEL B) (DECEMBER 2019)



The next step will be to further expand the European scope of this trial with inclusions in other participating countries: to date, 3 of the 6 participating countries (excluding France) have received regulatory approval from their competent authorities (CA / EC). The long-term objective would be to open 9 additional investigator sites within these new participating countries, which, added to the 16 centres already open, would bring the number of investigator sites to 25 phase 1 centres of the European ITCC network.

- **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.
  To date, **245 and 280 patients** have been respectively enrolled in AcSé-Nivolumab and AcSé-Pembrolizumab (Figures 44 and 45). Seven cohorts have already reached their objective to include and treat 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.

AcSé-Nivolumab:
245 patients included
54 investigator sites
6 cohorts

AcSé-Pembrolizumab:
280 patients included
48 investigator sites
7 cohorts

FIGURE 44
ACSÉ-NIVOLUMAB: DESCRIPTION OF RECRUITMENT BY COHORT (DECEMBER 2019)

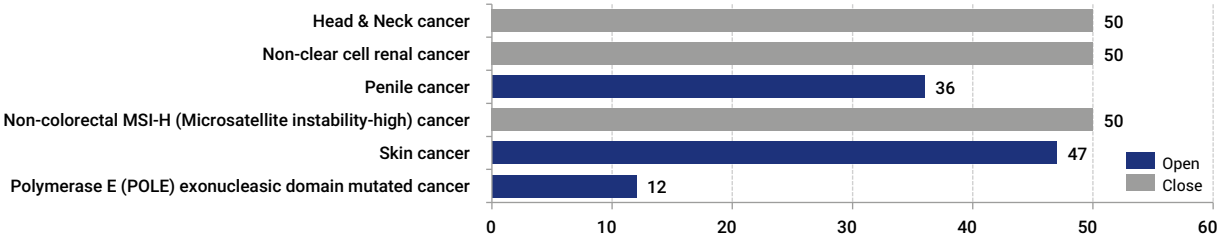
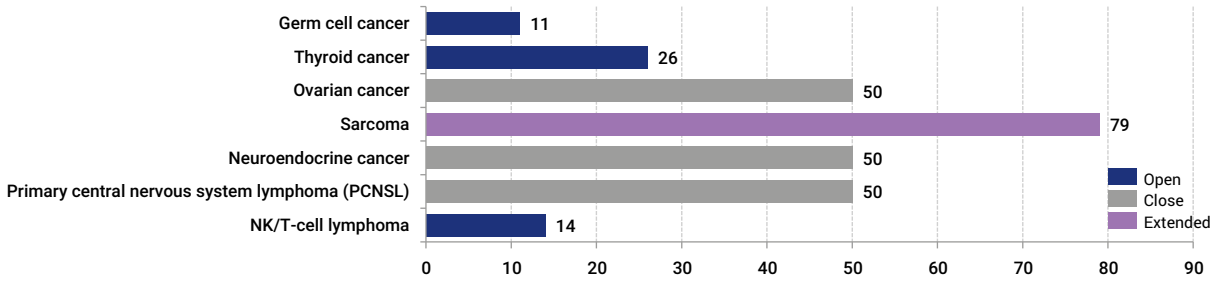


FIGURE 45
ACSÉ-PEMBROLIZUMAB: DESCRIPTION OF RECRUITMENT BY COHORT (DECEMBER 2019)



International visibility of AcSé programme

Publications

- Moro-Sibilot D et al. (2019) *Crizotinib in c-MET- or ROS1-positive NSCLC: results of the AcSé phase II trial*. Ann Oncol. 2019 Dec 1;30(12):1985-1991. doi: 10.1093/annonc/mdz407.
- 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.
- Broudic-Guibert M et al. (2019) *Persistent response to vemurafenib in metastatic ameloblastoma with BRAF mutation: a case report.* J Med Case Rep. 2019 Jul 25;13(1):245. doi: 10.1186/s13256-019-2140-6.

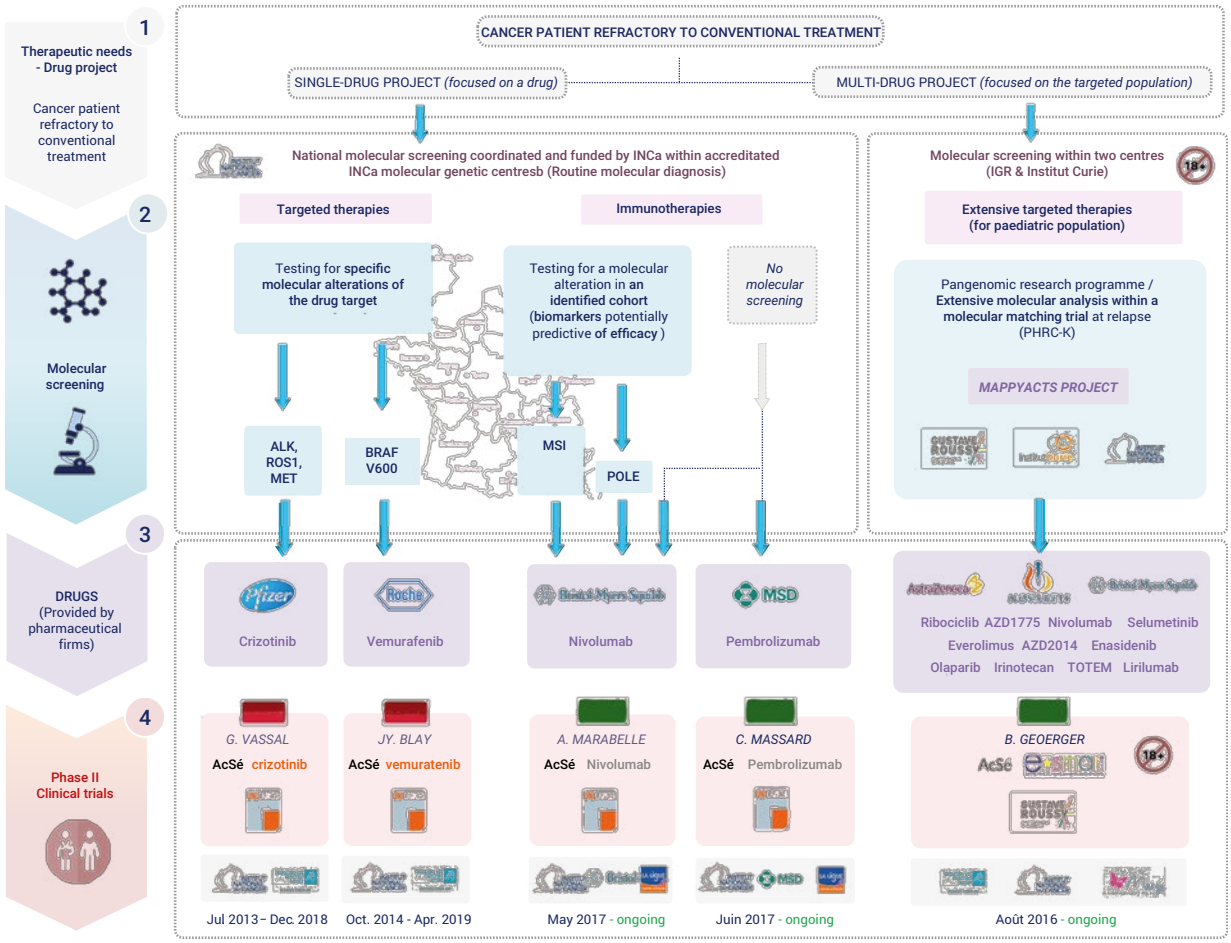
Oral communications

- *"Circulating tumor DNA analysis depicts potential mechanisms of resistance to BRAF-targeted therapies in BRAF-mutant non-small cell lung cancer"*
  WCLC 2019 (AcSé vemurafenib)
  Ortiz-Cuaran S, Mezquita L, Swalduz A, Aldea M, Mazières J, Jovelet C, Chumbi Flores W.R, Lacroix L, Loriot Y, Friboulet L, Westeel V, Ngocamus M, Pradines A, Tissot C, Raynaud C, Clement Duchene C, Quantin X, Gervais R, Brain E, Monnet I, Giroux Leprieur E, Avrillon V, Mahier-Aït Oukhatar C, Hoog-Labouret N, de Kievit F, Howarth K, Morris C, Green E, Pérol M, Besse B, Blay J.Y, Saintigny P, Planchard D.
- *"European Proof of Concept Therapeutic Stratification trial of Molecular Anomalies in Relapsed or Refractory Tumors in children and adolescents"*
  SIOP 2019 (AcSé-eSMART - "ARM D : Olaparib and Irinotecan")
  Gatz SA, Rubino J, Rossoni C, Andre N, Aerts I, Thebaud E, Nebchi S, Rondof W, Hübschmann D, Mortimer PG, Paoletti X, Vassal G, Geoerger B.
- *"Pediatric Cancer Precision Medicine: MAPPYACTS and ESMART"*
  SIOP 2019 (invited oral presentation in plenary session)
  Annual Meeting of the International Society of Pediatric Oncology SIOP 2019, Lyon France; Geoerger B.

Posters

- *"Circulating tumor DNA (ctDNA) analysis depicts mechanisms of resistance and tumor response to BRAF inhibitors in BRAF-mutant non-small cell lung cancer (NSCLC)"*
  ESMO 2019 (AcSé vemurafenib)
  Ortiz-Cuaran S, Mezquita L, Swalduz A, Aldea M, Mazières J, Jovelet C, Lacroix L, Pradines A, Avrillon V, Mahier-Aït Oukhatar C, Hoog-Labouret N, Howarth K, Guichou J.F, Morris C, Green E, Pérol M, Besse B, Blay J.Y, Saintigny P, Planchard D.
- *"High level of activity of Nivolumab anti-PD-1 immunotherapy and favorable outcome in metastatic/refractory MSI-H non-colorectal cancer: Results of the MSI cohort from the French AcSé program"*
  ESMO 2019 (AcSé nivolumab)
  Tournigand C, Flechon A, Oudard S, Saada-Bouzid E, Pouessel D, Le Tourneau C, Augereau P, Beylot-Barry M, Grob J.J, Chibaudel B, Soria J.-C, Simon C, Couch D, Hoog-Labouret N, Tiffon C, Chevret S, Andre T, Marabelle A.
- *"High clinical benefit rates of pembrolizumab in very rare sarcoma histotypes: first results of the AcSé Pembrolizumab study"*
  ESMO 2019 (AcSé pembrolizumab)
  Blay J.Y, Penel N, Ray-Coquard I, Schott R, Saada-Bouzid E, Bertucci F, Chevreau C, Bompas E, Coquan E, Cousin S, Soulié P, Le Cesne A, Mir O, Ryckewaert T, Brahmi M, Hoog-Labouret N, Couch D, Chevret S, Soria17 J.C, Massard C.
- *"Nivolumab in metastatic non-clear cell renal cell carcinoma: first results of the AcSe prospective study"*
  ASCO GU 2020 (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, GETUG
- *"European Proof of Concept Therapeutic Stratification trial of Molecular Anomalies in Relapsed or Refractory Tumors in children and adolescents"*
  ASCO 2019 (AcSé-eSMART - "ARM D : Olaparib and Irinotecan")
  Gatz SA, Rubino J, Rossoni C, Andre N, Aerts I, Thebaud E, Nebchi S, Rondof W, Hübschmann D, Mortimer PG, Paoletti X, Vassal G, Geoerger B.

FIGURE 46
KEY FEATURES OF THE ACSÉ PROGRAMME



The programme within the National Cancer Control Plan

The AcSé programme, launched in 2013 and based on the implementation of new types of clinical trials, has clearly helped accelerate the emergence of innovation for the benefit of patients, addressing the action 5.6 of the Cancer Control Plan* which aimed "to adapt clinical trials to the conceptual evolutions induced by the arrival of targeted therapies".[3]

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

- **Extensive molecular screening** was carried out as part of the programme, and approximately almost 17,000 patients have benefited from molecular screening within 3 of the 5 AcSé trials.

3. 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.

- Moreover, AcSé has met all expectations in terms of **equity of access to treatment** throughout France. Indeed, nearly 200 centres have been opened in France with an excellent territorial distribution. In addition, ten European centres have also been opened since the implementation of the AcSé-eSMART trial.
  To date, 1,119 patients, including 144 children, have received innovative treatment within the AcSé trial framework.
- The **relevance and feasibility of this programme have been confirmed**: with the opening of nearly 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 national level, is now confirmed at European level with patients included in all of the 4 countries open to inclusion (France, Netherlands, Spain, UK).
- **AcSé** has also helped **include vulnerable populations**, as 144 children have been included as part of 2 of the 5 AcSé trials (AcSé-Crizotinib and AcSé-eSMART), while 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 35 international communications, 3 press conferences, 1 patient guide, and 3 Temporary Use Recommendations (RTUs) filed.

MOLECULAR GENETICS CENTRES AND DEVELOPMENT OF SOMATIC TESTING

Since 2006, INCa has supported the structuring of 28 molecular genetics centres (cancer genetics) all over France in order 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. It has now been rolled out to all molecular genetics centres.

However, the number of cancer patients is increasing and the number of therapies requiring a biomarker prescription is rising. Moreover, a variety of new biomarkers are also in development. Thus, increasing the number of requisite and conducted tests, the number of available techniques, and improving test quality continue to represent challenges for the molecular genetics centres. In this context, INCa continues to propose and implement different actions in order to support improvements in molecular genetics.

Development of bioinformatic tools

- **Structured and interoperable NGS model report for solid tumours**

In 2016, a detailed model report for NGS somatic genetic testing for solid tumours was published. This document specifies the required information delivered to physicians. This report is integrated into the Cancer Communication File (DCC). To go a step further and, in collaboration with the Digital Health Agency (Agence du numérique en Santé), INCa integrated the model report in the field of interoperability in April of 2019. It defines the way each item contained in the report should be digitally recorded and describes an exchange

protocol, allowing quick and easy information sharing between genetics centres in the future. The software for this report will be updated in compliance with this new format. This will be a very important tool to facilitate multi-institution care, research projects, and clinical trials.

- **Variant of unknown significance database development**

NGS technology allows labs to identify known actionable molecular alterations and also unknown molecular alterations. In Silico bioinformatics tools enable labs to classify some of those unknown molecular alterations into groups depending on the probable consequence of this alteration: from benign to probably pathogenic or pathogenic. INCa is supporting a task force for the development of a database inventorying all the known and unknown molecular alterations identified in patients in France. A team of experts will collectively classify the unknown alterations in the different categories as they are identified or when new information is available. This will enable labs to be aware of other patients with the same alteration identified in other molecular genetics centres, how this alteration is described, and to facilitate contact between centres with similar patients to discuss therapeutic options if needed.

Biomarkers associated with immunotherapy development

Immunotherapy is still developing at a fast pace, with a large number of new treatments and associated biomarkers in development. Biomarkers such as PD-L1 status and Microsatellite Instability (MSI) are already used widely in care. Recommendations for performing MSI tests were published in 2016 in the context of the identification of Lynch syndrome patients. Since 2016, the use of MSI has evolved and although there is no marketing authorisation requiring MSI status to date in France, MSI has been shown to be a predictive marker for the response to some immunotherapies in a wide variety of solid tumours (in the US, pembrolizumab has been granted FDA approval for patients with unresectable or metastatic, microsatellite instability-high (MSI-H) solid tumours that have progressed following prior treatment and who have no satisfactory alternative treatment options). A working group with pathologists, molecular geneticists and clinicians has been set up in order to update the recommendations for test completion in the different cancer sites.

The Tumour Mutational Burden (TMB) is another predictive biomarker of the response to immuno-oncology therapy in development. However, some of the major clinical trials evaluating the use of this marker have been discontinued early with negative results regarding the predictivity of TMB for immunotherapy response. Other trials are still ongoing but for now the roll out of TMB is on hold until further results are published.

All these actions, linked with the molecular genetic centres' experience and improvement, have made it possible:

- To offer genetic testing to an increasing number of patients (table 26);
- To test an increasing number of genes

Indeed, in 2018, the tumours of 53,799 patients were tested with NGS out of 114,514 patients having at least one test in one of the 28 molecular genetics centres

(a change in genetic testing funding regulations in France now allows private sector laboratories to perform genetic testing in cancer. The figures below do not include the tests performed in private laboratories).

TABLE 26
ACCESS TO GENETIC TESTING IN MOLECULAR GENETICS CENTRES AND EXCLUDING PRIVATE LABORATORIES

		Access to at least one genetic testing procedure		Access to at least one genetic testing procedure in 2018
Cancer	**Biomarkers or technology**	**Starting year**	**Number of patients**	**Number of patients**
Lung	*EGFR*, *ALK* Translocation, *KRAS*, *BRAF*, *HER2*, *PI3KCA*, *ROS1* Translocation, NGS	2008	1,269	22,361
Colon - Rectum	*KRAS*, *BRAF*, *NRAS*, MSI, *MLH1* Methylation, NGS	2007	1,100	18,362
Breast	*HER2*, NGS	2008	5,416	8,966
Chronic myeloid leukaemia	*BCR-ABL*, Karyotype, FISH, NGS	2008	6,171	5,96
Melanoma	*BRAF*, *NRAS*, *KIT*, NGS, CGH	2010	651	6,142
Lymphoma	Karyotype, FISH, CGH, Cyclin D1, *BCL1/JH*, *BCL2/JH*	2009	2,180	6,863
Multiple myeloma	Karyotype, FISH, CGH, NGS	2008	2,557	4,427
Acute lymphoblastic or myeloblastic leukaemia	Karyotype, FISH, *FLT3*, *NPM*, *CEBPA*, *IDH1*, *IDH2*	2008	2,757	4,866
Sarcoma	Translocations, *MDM2/CDK4* Amplification, CGH, NGS	2008	1,360	3,169
Chronic lymphocytic leukaemia	Karyotype, FISH, IgVH, *TP53*, NGS	2008	1,799	4,045
Gastrointestinal stromal tumours	*KIT*, *PDGFRA*, NGS	2007	701	1,199

Recommendations for the prescription of somatic tests

Given the rapid development of treatment options for different cancer sites, it could be difficult for clinicians to stay up-to-date and decide which biomarkers they should prescribe for their patients. In order to ensure that each patient gets all the necessary tests for optimal care and optimise the number of tests performed in France yearly, INCa has set up working groups with pathologists, molecular geneticists and clinicians to produce recommendations for somatic testing in colon cancer, lung cancer and melanoma. The recommendations aim to list all the different stages of the disease and recommend which test should be carried out at which step to insure the best treatment for each patient.

Somatic testing during the Cancer Control Plan

One of the objectives of the National Cancer Control Plan is to consolidate France's leading position in personalised medicine. Regarding somatic genetic testing, the Cancer Control Plan aimed to support access to molecular genetic testing (action 6.2) and the implementation of Next Generation Sequencing, allowing NGS analyses of all cancers by the end of the plan (action 6.4).

Regarding action 6.2, standard cancer genetic tests are not yet reimbursed through the standard care system, but through a specific scheme devoted to innovative tests (RIHN circuit, 'Référentiel des actes Innovants Hors Nomenclature de biologie et d'anatomocytopathologie'). This system is subject to criticism since the number of tests conducted under this scheme is increasing, while the budget is fixed. Thus, the reimbursement rate for each test is decreasing yearly and reached less than 50% of the value of each test in 2019.

Regarding action 6.4, from 2015, targeted NGS has been rolled out to all molecular genetics centres. In 2018, 53,799 cancer patients benefited from NGS testing, close to the goal of 60,000 tests. However, not all molecular genetics centres analyse a hundred genes. Indeed, the number of genes tested using NGS techniques in some panels is closer to 20 or 30, highlighting room for improvement for this issue.

In addition, the set-up of whole genome analysis in France is being carried out under the Plan France Médecine Génomique 2025. Currently, two new genomics centres have been set up to perform whole genome sequencing; they are enrolling their first patients in 2020.

Tools and structuring actions have been developed to improve shared quality assurance approaches for the different steps of NGS testing:

- The development of the national project Gene&Tiss to organise external quality evaluation of molecular genetics tests on tumour tissue allows the centres to compare their results on the same tumour tissues;
- The development of a detailed, structured, and interoperable model of report for NGS somatic testing for solid tumours is a vector to improve the quality of the information received by clinicians;
- The set-up of a multidisciplinary molecular tumour board to guide the treatment decision and clinical trial opportunities based on the identified alterations;
- The creation of the Bioinfodiag network, federating the genetics centres' bioinformatics community enables experience sharing, the development of open source tools available to the community and promotes collaborations. Initiated by INCa, this network is now self-sufficient;
- The development of a database to share the molecular anomalies of unknown significance identified in patients allows the centres to have input from molecular experts and to potentially identify patients with the same anomaly in other centres and discuss treatment options with their physicians if needed.

France Genomic Medicine 2025 Plan: the MULTIPLI study over the 2018-2019 period

Assessing the feasibility of whole exome and RNA sequencing in the French cancer care system is the primary objective of the Multipli study, as one of the four pilot projects of the national France Genomic Medicine 2025 Plan. The Multipli study encompasses two innovative trials conducted on around 2,400 patients suffering from soft-tissue sarcoma (Multisarc) or metastatic colorectal carcinoma (Acompli).

Before launching the clinical study, the performance of the Multipli genomic workflow was evaluated through each stage, from sample collection to the molecular board report. Lessons learned from this evaluation provide guidelines for the Multipli study and for future clinical routine practice in France. ITMO Cancer-Aviesan funded the Multipli study with €0.69M in 2019 and with almost €1.5M over the 2018-2019 period.

NATIONAL ONCOGENETICS SYSTEM

Oncogenetics activity in 2018

Almost 5% of diagnosed cancers are related to hereditary cancer syndromes. These cancers are often discovered at an earlier age than 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 which are transmissible to offspring. These inherited alterations are initially screened for in affected individuals (index patient) whose personal and/or family medical history is suggestive of a hereditary cancer condition.

In France, the diagnosis of these predispositions is implemented within the framework of the national oncogenetics system. In 2018, it was organised around 149 consultation sites in 103 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 the consultations and of 17 specific monitoring centres for those at a very high risk of cancer. The purpose of this structure is to identify individuals who have a hereditary predisposition to cancer (index or related patients) in order to offer them specific follow-up (appropriate surveillance and / or preventive surgery).

From 2002, funding was allocated by the DGOS (the French General Directorate of Care Provision) to allow the creation of new oncogenetic consultations or the increase of already existing consultations (annual envelope of €6.67M supplemented by additional budget of €0.86M granted in 2015 and renewed in 2016, 2017 and 2018). Since its creation, INCa has been monitoring and coordinating the system, in particular by organising the reporting of annual activity, in order to participate in the development of the system and the improvement of its access.

The aims of INCa's Oncogenetics mission, supported by action 6.1 of 2014-2019 Cancer Plan, are to:

- Reinforce the system in the face of increasing demands to identify a maximum number of families with a hereditary predisposition to cancer in order to offer them appropriate long-term medical monitoring and adapted treatments;

- Develop activity in the least endowed regions and ensure access to oncogenetics consultations for the greatest number;
- Support the arrival of new targeted therapies, such as PARP inhibitors.

The number of oncogenetics consultations has steadily increased since the implementation of the system. The annual number of consultations increased by 1.4 between 2014 (launch of the 2014-2019 Cancer Plan) and 2018, increasing from 56,897 to 79,892 (+ 22,995 consultations), or approximately + 40% activity in 5 years (Table 27).

TABLE 27
ACCESS TO CONSTITUTIONAL GENETIC TESTING IN ONCOGENETICS LABORATORIES

	2014	2015	2016	2017	2018
Total number of consultations	56,897	63,618	71,821	77,478	79,892
Patient consultations (new families)	23,635	26,148	28,414	30,442	30,588
Relative consultations	9,223	9,971	11,512	11,317	12,131
Patients tested	20,845	24,706	28,304	29,404	30,051*
NGS tests	*Implementation in progress*	17,912	23,453	27,120	28,120
NGS: % of all patients	NS	73%	83%	92%	95%
Patients with germline mutations	2,863	3,310	3,963	3,865	4,008*
Relatives tested	9,005	9,252	10,302	11,744	12,570*
Relatives with germline mutations	3,661	3,842	4,225	4,948	5,108*

* Results for 25 laboratories out of 26

Since 2013, to face the growing number of analyses required, the Institute has supported the development of targeted high-throughput sequencing (NGS) for diagnostic purposes.

In 2018, 25 oncogenetics laboratories performed NGS (next generation sequencing) analyses for 28,120 patients (95% of all patients, versus 92% in 2017). NGS is now implemented in routine practice in all oncogenetics laboratories.

National oncogenetics system during the Cancer Control Plan

Objective 6.1 of the National Cancer Control Plan aims to develop an oncogenetics system and improve its access. The main results are described below.

- **Increase in oncogenetics consultations and genetic testing**

The total number of consultations was 56,897 in 2014 and 79,892 in 2018. Regular progress has been observed since 2014 (and since 2003), as for genetic testing (table 25). Despite the inflection of the curve since 2016, the number of consultations continues to increase (+ 3% between 2017 and 2018, + 8% between 2016 and 2017, + 13% between 2015 and 2016). This inflection could be explained by the saturation of the system, primarily due to human capacities rather than a decrease in demand.

PARP inhibitors and oncogenetics care pathways

Poly(ADP-ribose)polymerase (PARP) inhibitors are a targeted therapy for cancers with homologous repair deficiency (HRD). They were first approved by the FDA (US Food and Drug Administration) for the treatment of ovarian cancer and breast cancer. Patients with somatic and/or germline *BRCA1/2* mutations benefit more from these treatments than other patients.

In 2014, a first PARP inhibitor, olaparib, was approved by the European Medicines Agency (EMA) for the maintenance treatment of patients with recurrent ovarian cancer[4]. Its prescription is subject to the susceptibility of the tumour to platinum and the presence of a constitutional and/or tumour mutation within the *BRCA1* and *BRCA2* genes. In a context where prior information (appropriate genetic counselling) is crucial for patients and their blood relatives before any constitutional test after the somatic tests, in January 2017, the French National Cancer Institute published guidelines. This document proposes recommendations for the care pathway for patients with ovarian cancer who are potentially eligible for treatment with olaparib.

In 2018, olaparib was approved by the FDA for first-, second-, or third-line treatment of patients with HER2- metastatic breast cancer, carrying a deleterious or suspected deleterious genetic alteration, having received chemotherapy in a neoadjuvant, adjuvant or metastatic cancer treatment setting[5]. As result, the French National Cancer Institute updated the document published in 2017, adding recommendations for the cancer genetics pathway for breast cancer patients as described above[6].

With the increasing number of PARP inhibitor indications, genomic tumour testing could be offered at initial diagnosis, and rapid access to oncogenetic consultations is necessary. These recommendations are national guidelines to develop rapid-access genetic testing pathways to decrease the time to consultation for patients who require prompt treatment.

The purpose is to define, according to the type of mutation tested, the organisation allowing the necessary tests to be carried out within a time frame in compliance with patients' treatment, and to ensure that patients have all the necessary information about the potential personal and family implications of the outcome of these tests.

As result of future MA approvals of PARP inhibitors in new indications (prostate cancer[7], pancreatic cancer[8]), the Institute will be required to carry out regular updates.

- **Better regional access**

Regular regional structuring and an increase in access to the oncogenetics system should be emphasised (the regional average of the number of consultations per 100,000 inhabitants was 107 in 2018 (105 in 2017, 99 in 2016, and 84 in 2015)).

- **Reduction in the time to the first consultation**

The relative stability of the activity of consultations and oncogenetics laboratories since 2017 results in better control of deadlines. In 2018, the median time to obtain a first oncogenetic consultation appointment for an index patient was 11 weeks, while it was 13 weeks in 2014.

- **New procedures**

In addition, when the genetic testing result 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, etc.), consultation teams (and laboratories) have implemented accelerated procedures. In 2018, 4,103 index patients benefited from accelerated treatment with a reduction in the time taken to obtain the first appointment to 8 days.

4. Pujade-Lauraine E, Ledermann JA, Selle F, et al. *Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ ENGOT-Ov21): a double-blind, randomised, placebo-controlled*, phase 3 trial. Lancet Oncol 2017; 18: 1274–1284
5. Robson M, Im S-A, Senkus E, et al. *Olaparib for metastatic breast cancer in patients with a germline BRCA mutation*. N Engl J Med 2017; 377: 523–533
6. "PARP Inhibitors: Recommendations for a pathway in Oncology Genetics" INCa, October 2019 (Tools for Practice)
7. de Bono J, Mateo J, Fizazi K, Saad F, Shore N, Sandhu S, Chi KN1, Sartor O, Agarwal N, Olmos D, Thiery-Vuillemin A, Twardowski P, Mehra N, Goessl C, Kang J, Burgents J, Wu W, Kohlmann A, Adelman CA, Hussain M. *Olaparib for Metastatic Castration-Resistant Prostate Cancer*. N Engl J Med. 2020 Apr 28. doi: 10.1056/NEJMoa1911440. [Epub ahead of print]
8. Golan T, Hammel P, Reni M, et al. *Maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer*. N Engl J Med. 2019; 381(4): 317–327. doi: 10.1056/NEJMoa1903387

Clinical research organisation: structures, infrastructures, and tools

EARLY-PHASE CLINICAL TRIAL CENTRES CLIP²

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 Cancer Plan for 2009-2013 allowed the French National Cancer Institute to initiate the structuring of specialised investigation centres in early-phase trials. Thanks to the first designation initiated in 2010, the Institute provided the CLIP² centres with logistical and financial support in order 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 a second designation of these structures in 2015, and identifying the centres dedicated to children. Thus, among the 16 structures designated in 2015, 6 of these include paediatric oncology activities.

Designation in 2019

To continue this initiative started in 2010, the Institute launched in July 2018, in partnership with the French Cancer League, a new call for applications for the CLIP² designation in adult and paediatric oncology, for a period of 5 years, in order to renew and bolster its support for expert centres in early phase clinical trials for adult and paediatric, adolescent and young adult cancers (Table 28).

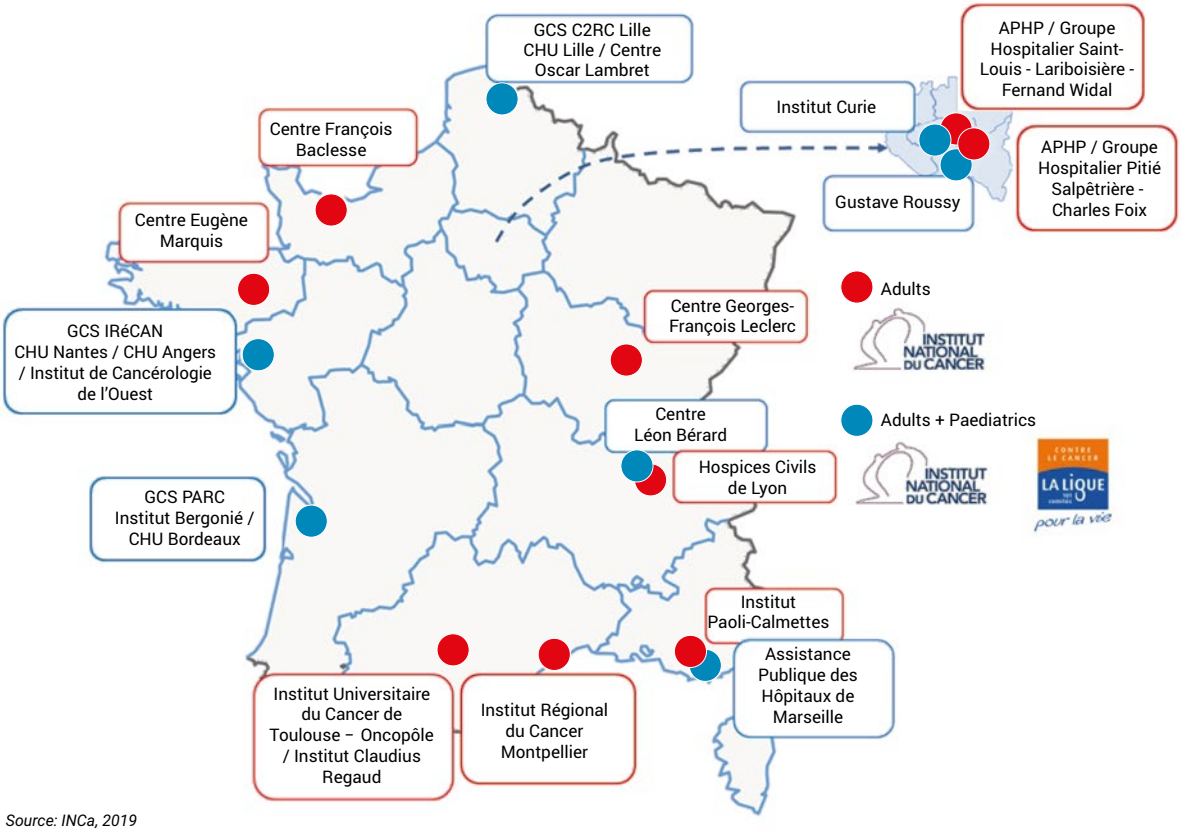
TABLE 28
FEATURES OF THE CLIP² PROGRAMME IN 2019

Objectives	• To provide wider availability for patients to new medications through an organised network that can offer access to early-phase clinical trials for all patients in France; • To increase the visibility and attractiveness of French clinical research throughout the pharmaceutical industry in France and abroad; • To improve the quality and increase the number of adult and paediatric early-phase trials in France; • To promote academic clinical research by assessing drugs for indications not addressed by pharmaceutical laboratory development plans; • Offer early-phase clinical trials to patients identified in molecular screening programmes.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa and French Cancer League
Funding	**€6.48M / 3 years** **INCa: €5.28M** **French Cancer League: €1.2M**
Proposals submitted	**20**
Projects selected	16
Selection rate	**80%**

This call for applications, open to previously designated centres, but also to new centres with sufficient early-phase clinical trial activity wishing to be designated, attracted 20 applications. These were evaluated by a scientific evaluation committee made up of international experts on the basis of evaluation criteria corresponding to the objectives and missions to be implemented by the CLIP².

The committee selected the same 16 CLIP² previously designated and renewed their accreditation for the 2019-2024 period (designation notified by INCa in April 2019), 7 of which have dual desig nation for their activity in adult and paediatric oncology (one more than in 2015), and will receive joint funding from the Institute and the French Cancer League.

FIGURE 47
GEOGRAPHIC DISTRIBUTION OF CLIP² CENTRES (3RD DESIGNATION – 2019-2024)



Source: INCa, 2019
Drafted y INCa's Research Division, 2020

This programme helped increase the visibility and attractiveness of these centres and also of early-phase French clinical research (and must continue to do so), leading to an increase in the number of new trials opened and the number of patients included every year within CLIP².

In parallel, pharmaceutical companies have also shown growing interest in the early-phase clinical trials conducted within these designated centres, as reported in the CLIP² activity reports.

Finally, this designation of early-phase clinical trial centres should enable innovative therapies to be available earlier in France and reinforce the expertise of French clinicians by giving them rapid access to these new molecules.

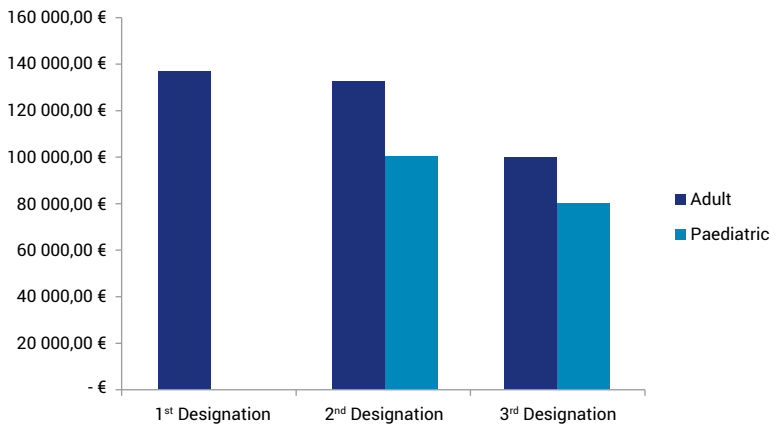
CLIP² are also able to apply to public-private partnership calls for proposals launched by the Institute.

Activity report over the 2010-2018 period

Over the 2010-2019 period, the Institute carried out three designation campaigns for early-phase clinical trial centres. Initiated in 2010, as part of the 2009-2013 Cancer Plan, in order to "Structure and stimulate research in the early phases of testing new anti-cancer drugs". The aim of this first designation was to identify and support a dedicated unit capable of conducting early-phase trials, within healthcare institutions. The second designation process, which is part of the 2014-2019 Cancer Control Plan, broadened the scope of these centres by assigning an important role to paediatrics and making it possible for CLIP² to be more than just a single site. Most CLIP² centres now include a set of services conducting early-phase trials under the coordination of a main site.

During the three designations, the total amount allocated was €26.1M, including €20.6M from INCa, €2.84M from the French Cancer League, €1.6M from the ARC Foundation and €1M from the Lilly Institute.

FIGURE 48
AVERAGE GRANT PER CLIP² PER YEAR



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

These public and private partnerships, initiated by the Institute in 2011, have led to the set-up of eighteen early phase clinical trials with 11 pharmaceutical companies, evaluating their innovative compounds in indications that are not part of their development plan.

In June 2019, the Institute and the pharmaceutical firm Novartis signed a collaboration agreement to make innovative drugs available to CLIP² in the context of a call for proposals. These innovative drugs from the Novartis development pipeline are all still in early development and had not yet received marketing approval.

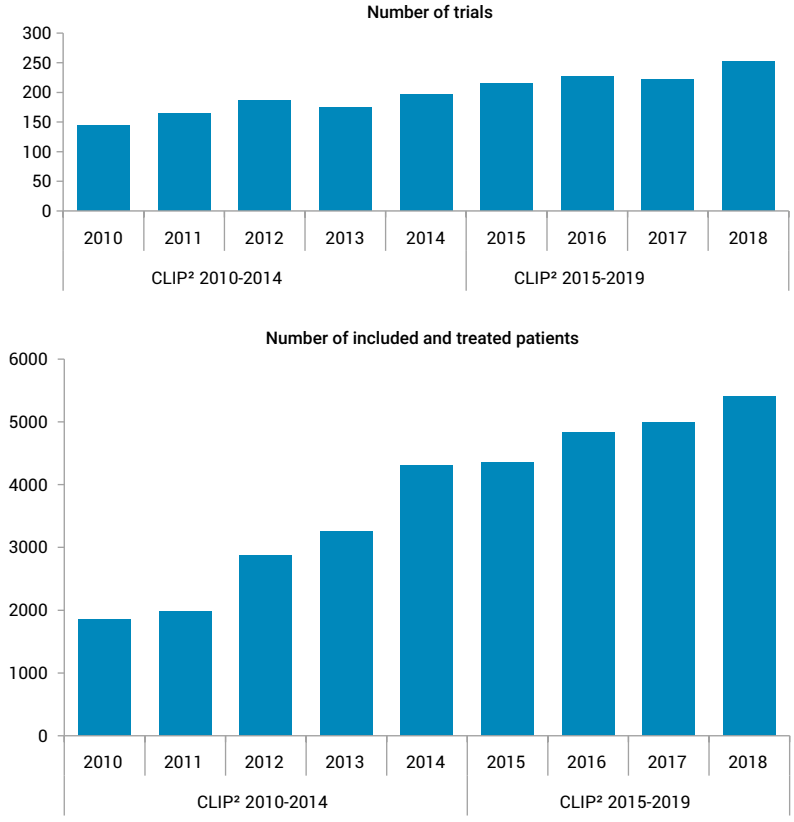
The four proposed drugs are:
- HDM201, an HDM2-P53 inhibitor;
- Spartalizumab (PDR001), anti-PD1;
- Capmatinib (INC280), c-Met inhibitor;
- LSZ102, oestrogen receptor inhibitor and modulator.

Following the signature of this agreement, the Institute published a call for proposals for the 16 CLIP² in July 2019. The projects will be selected and funded in 2020.

Between 2010 and 2018
- **+ 75% increase in the total number of clinical trials initiated, with 252 in 2018;**
- **+ 193% increase in the total number of patients enrolled, with 5,416 patients enrolled and treated in 2018.**

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 49):
- + 75% increase in the total number of clinical trials launched with 252 in 2018;
- + 193% increase in the total number of patients enrolled, with 5,416 patients enrolled and treated in 2018.

FIGURE 49
TRENDS IN PROGRESSION OF THE NUMBER OF TRIALS INITIATED AND PATIENTS ENROLLED OVER THE 2010-2018 PERIOD



Activity report for the Cancer Control Plan

Since 2015 (i.e. the second designation), the total number of early-phase clinical trials increased by about 17% in 2018 (figure 50):
- 56% phase II trials;
- 22% phase I trials;
- 22% phase I/II trials.

FIGURE 50
DISTRIBUTION OF THE NEW TRIALS LAUNCHED ACCORDING TO THE STUDY PHASE

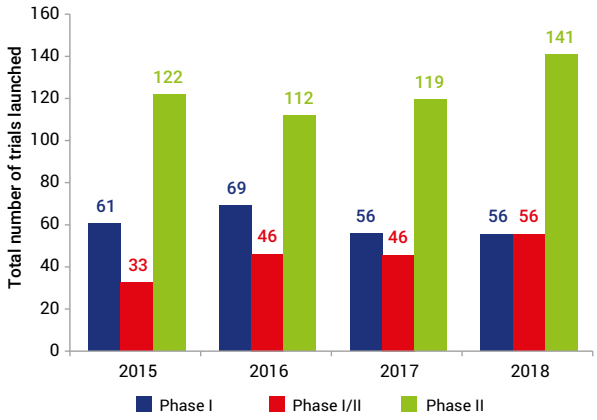
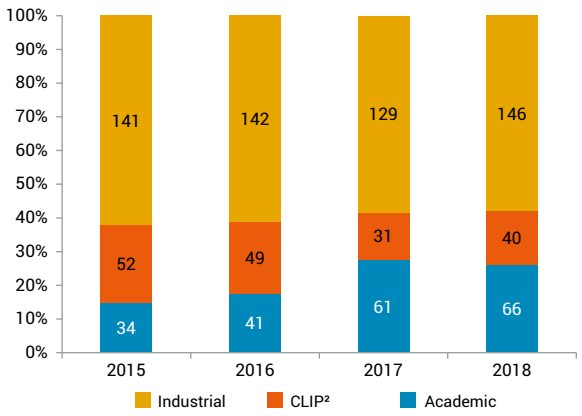


FIGURE 51
DISTRIBUTION OF THE NEW TRIALS LAUNCHED ACCORDING TO THE SPONSOR



The distribution of academically versus industrially-sponsored trials remained stable (40% vs. 60%) between 2015 and 2018, whereas among academic trials, just over a third are sponsored by the institution of the CLIP², including trials under public/private partnerships developed and supported by INCa.

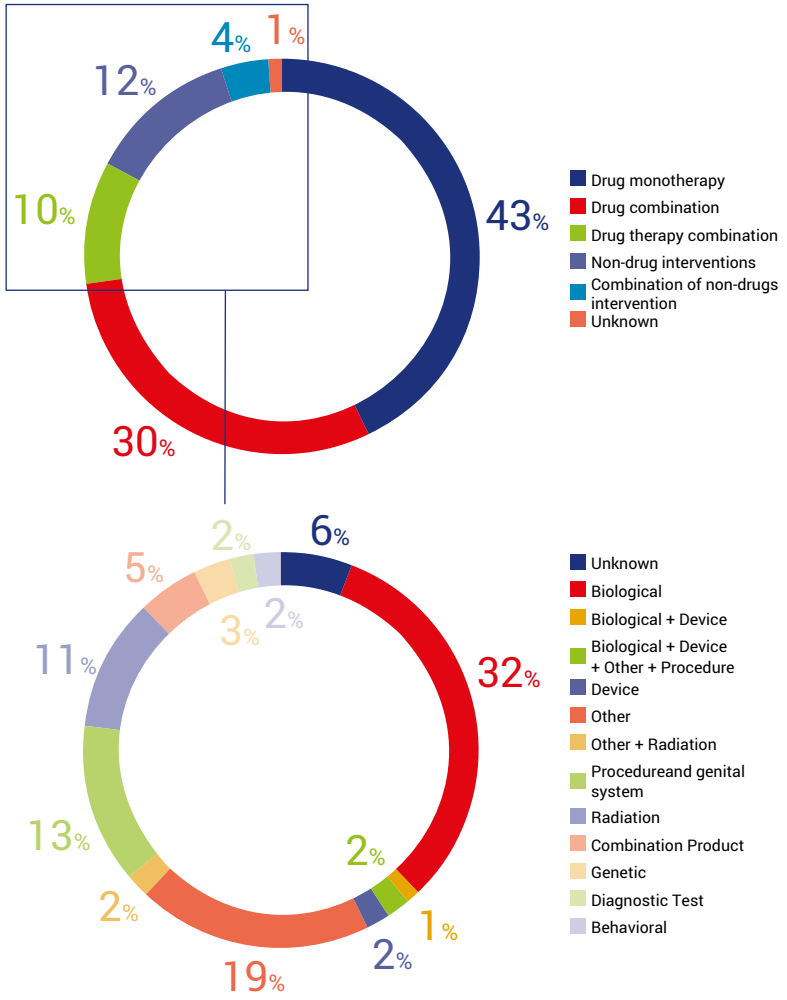
Regarding the distribution by type of therapy evaluated in 2018, 83% of the trials correspond to "drug trials" with a balanced proportion of drug monotherapy and combination drug trials (Figure 52):

- 43% drug monotherapy trials;
- 30% drug combination trials and 10% drug and therapy combination (i.e. evaluating at least one drug with one or more another therapies such as surgery or radiotherapy, etc.).

The remaining 16% correspond to "non-drug trials", which may evaluate one or more non-drug intervention such as radiotherapy, surgery, device, biomarkers, imaging techniques, etc.

FIGURE 52

DISTRIBUTION OF THE NEW TRIALS LAUNCHED ACCORDING TO THE TYPE OF THERAPY EVALUATED



ENROLMENT OF PATIENTS IN CLINICAL TRIALS

Initiated under the 2003-2007 Cancer Control Plan and strengthened by the 2009-2013 Cancer Control Plan, INCa's annual survey assesses clinical research activities in oncology in France. This survey provides an estimation of the enrolment rate in cancer clinical trials each year in France. These data are presented annually to the French President. Data for 2018 were reported by University Hospitals, Cancer Care Centres, and Health Care Centres.

The actions promoted by the second Cancer Control Plan have led to an increase of more than 70% of patients enrolled in cancer clinical trials thanks to the structuring of clinical research sites, and an incentive policy, particularly via the INCa clinical trial registry. In 2013, nearly 25,000 patients were included in therapeutic clinical trials. The objective of action 5.2 of the third Cancer Control Plan is to enrol 50,000 patients per year in therapeutic clinical trials by 2019.

The results show a steady increase in the number of patients enrolled in clinical trials for the last 10 years between 2009 and 2018:

- There is a 13.2% decrease in the number of patients enrolled in 2018 compared to 2017, with 52,259 patients included in cancer clinical trials for 2018 (Figure 53), 33,476 of these were enrolled in a therapeutic clinical trial. Therapeutic clinical trials increased between 2016 and 2018 from 28,222 to 33,476. The ratio of therapeutic trials has grown significantly from 51.8% to 64% between 2017 and 2018 (Figure 54);

FIGURE 53
PROGRESSION OF PATIENTS ENROLLED IN CANCER CLINICAL TRIALS (2009-2018)

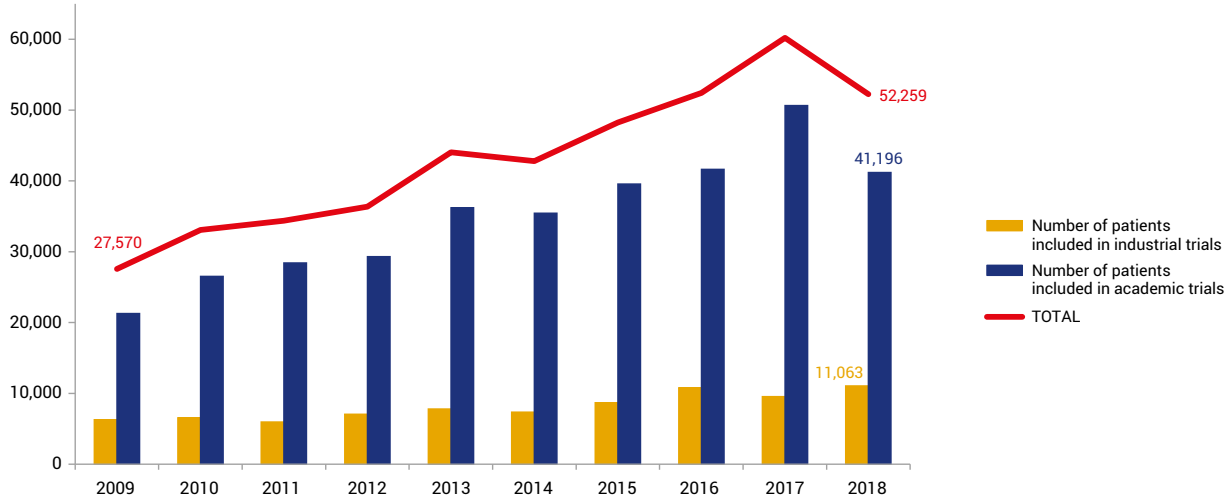


FIGURE 54
DISTRIBUTION OF CANCER CLINICAL TRIALS 2016-2018 ACCORDING TO THERAPY

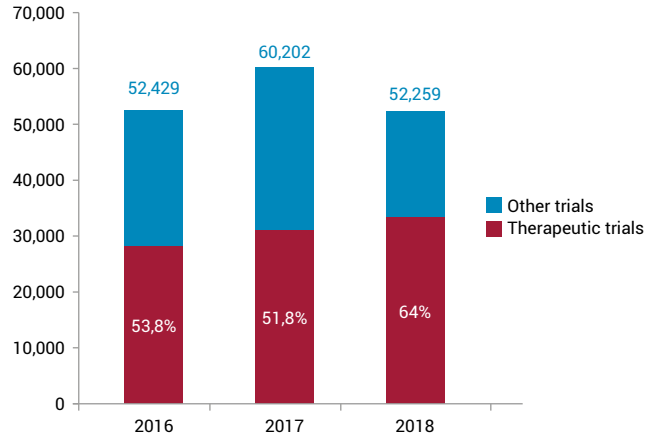
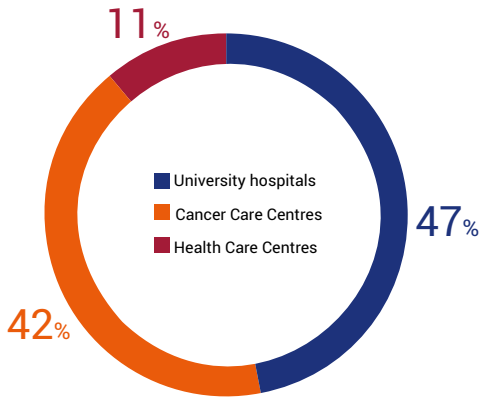


FIGURE 55
DISTRIBUTION OF PATIENTS ENROLLED IN CANCER CLINICAL TRIALS AMONG THE DIFFERENT CARE PROVIDERS IN 2018



- Over the last 10 years (2009-2018), the number of patients enrolled in cancer clinical trials has doubled, probably due to the Actions of the different Cancer Control Plans (Figure 53);
- The ratio of enrolment in academic *vs.* industrial trials has remained stable over the years, with a significant predominance of inclusions in academic trials (79% *vs.* 21%). However, between 2009 and 2018, greater progression was observed in academic trials (+ 93%) than in industrial trials (+ 43%) (Figure 53);
- The distribution among the different care providers has been quite similar over the years: In 2018, 47% of the patients were enrolled in University Hospitals, 42% in Cancer Care Centres, and 11% in Health Care Centres (Figure 55).

Annual meeting of the cooperative intergroups

In November 2019, the annual meeting for the cooperative intergroups was held at INCa's offices. INCa's 13 designated cooperative intergroups were represented.

The representative of each intergroup presented the communications made in reference international congresses (ASCO, ESMO, ASH, etc.) and/or potentially practice-changing publications.

The presentations highlighted the quality of the clinical research conducted by cooperative intergroups, particularly regarding:

- The definition of new standard treatments in prostate cancer, head and neck cancers, pancreatic cancer, and paediatric acute lymphoblastic leukaemia;
- Therapeutic de-escalation in lung cancer, prostate cancer, colorectal cancer, and Hodgkin lymphoma;
- Adverse effects of treatments in breast cancer and primary CNS lymphoma;
- Geriatrics and frail people in acute myeloid leukaemia, ovarian cancer, and head and neck cancers;
- Improvement of patient follow-up in lung cancer;
- Patient molecular characterisation in breast cancer;
- Registration studies in ovarian cancer, multiple myeloma, and acute myeloblastic leukaemia.

INCa's 10-year cancer control strategy was also presented. The ensuing discussion was extremely fruitful, with a real willingness from all the intergroups represented to be involved in this strategy in partnership with INCa.

INCA'S CANCER RESEARCH CLINICAL TRIAL REGISTRY

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

The INCa cancer clinical trial registry provides information accessible to the general public, and facilitates the search and selection of clinical trials. Visitors to the clinical trial 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.

TABLE 29
THE INCA'S CANCER CLINICAL TRIAL REGISTRY

Objectives	Provide information on cancer clinical trials conducted in France.
Results	3,293 clinical trials advertised on INCa's website in December 2019, sponsored by more than 371 industrial and academic bodies. • 595 ongoing recruiting trials. – 57% sponsored by academic bodies. – 80% treatment trials.

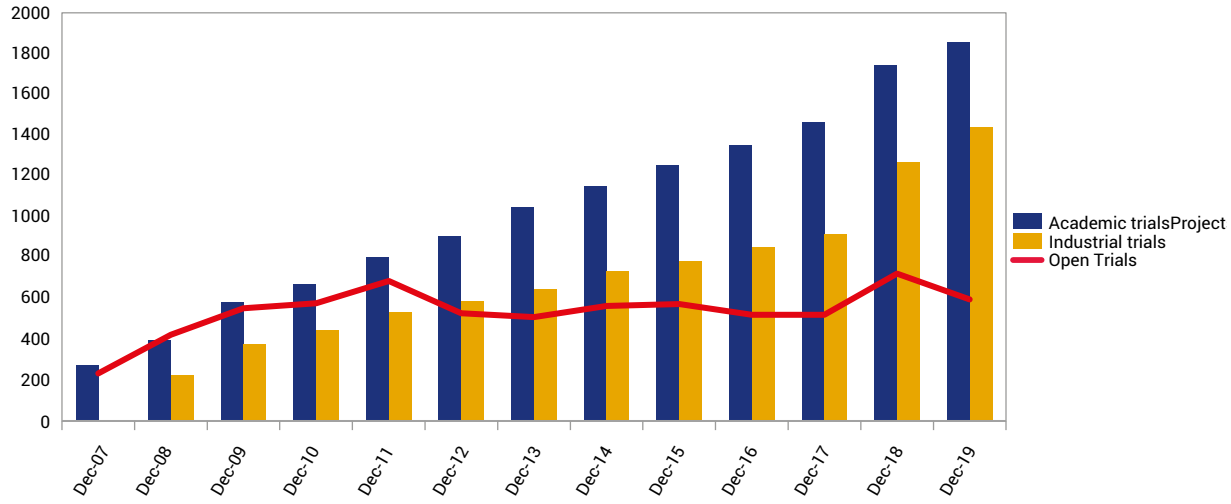
Launch of a new clinical trial database

Since November 2019, INCa has been working on the development of a new database for the registration and the administration of clinical trials. This new portal will be accessible via the Internet.

Academic and industrial sponsors of clinical trials in oncology will have the opportunity to register their trials directly in the webpage of the new database.

This clinical trial registration portal will be available in the last quarter of 2020.

FIGURE 56
TOTAL NUMBER OF CLINICAL TRIALS RECORDED IN THE REGISTRY PER YEAR (DECEMBER 2019)



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. In line with the 2014-2019 Cancer Control Plan, particular efforts are being devoted to increase 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, the participation rates in national screening programmes, and access to care.

The research programme for human and social sciences, epidemiology, and public health (HSS-E-PH programme)

The role of human and social sciences, epidemiology, and public health (HSS-E-PH) in cancer research was confirmed by the 2014-2019 Cancer Control Plan. The objectives of several strategic measures of the Plan are based on advances that need to be made through HSS-E-PH research. Indeed, although major medical progress has been achieved in cancer screening and treatment, questions remain on the social perceptions that populations have of cancer, on obstacles to screening, on health risk behaviours, in particular persistence in smoking habits and heavy alcohol consumption, which are responsible for a large number of cancers. Research in social and human sciences should also help to better understand the impact of the disease in the lives of people affected by cancer and their families. The research should also help to improve the care pathway, through a better understanding of issues such as the sharing and appropriation of knowledge by caregivers and patients, 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. In this context, the SIRIC and Canceropole designation process also addresses these research issues.

THE PROGRAMME IN 2019

In 2019, 15 projects were selected for funding, out of the 92 proposals submitted, for a total amount of €3.97M (Table 30).

TABLE 30
FEATURES OF THE HSS-E-PH PROGRAMME IN 2019

Objectives	• To enable the implementation of original research projects, in terms of their endpoints and approaches, and scientific excellence in the different disciplines of HSS-E-SP 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 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 in order to provide more relevant answers.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€3.97M**
Proposals submitted	**92**
Projects selected	15
Selection rate	**16.3%**

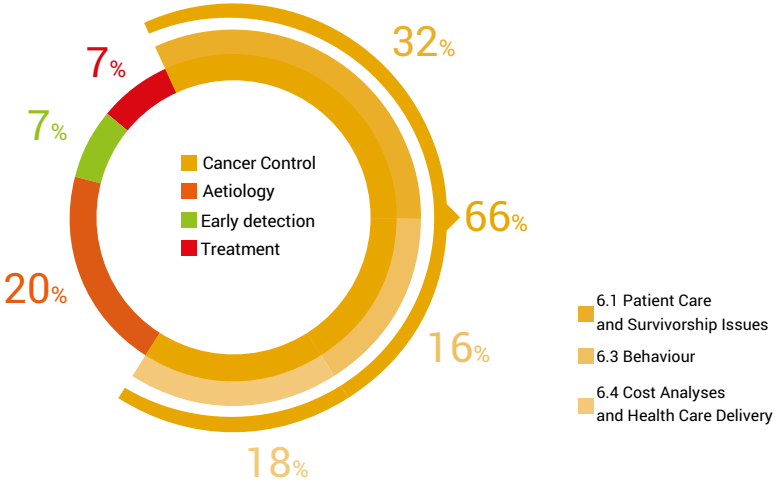
Among the 85 eligible projects, the three fields of research supported by the call for projects are represented:
- 5 epidemiology projects were funded out of the 37 submitted;
- 3 in public health out of the 14 submitted;
- 7 in human and social sciences out of the 34 submitted.

The subjects of study of the 15 funded projects concern:
- Risk factors for the development of cancer (6 projects);
- Health economics (2 projects);
- Nutrition and Cancer (2 projects);
- Health System and Public Policy (4 projects);
- Overseas territories facing cancer (1 project).

2019:
15
projects selected in the HSS-E-PH programme for a total amount of
€3.97M

Figure 57 shows the distribution of projects funded by CSO classification and highlights that cancer control is the largest category of research (66%) with projects focusing on patient care and survivorship, behaviours, surveillance, life care, ethics and confidentiality research, and cancer awareness and communication. This is followed by aetiology projects (20%) that focus on exogenous and/or endogenous factors related to the origin of cancers and risk factors.

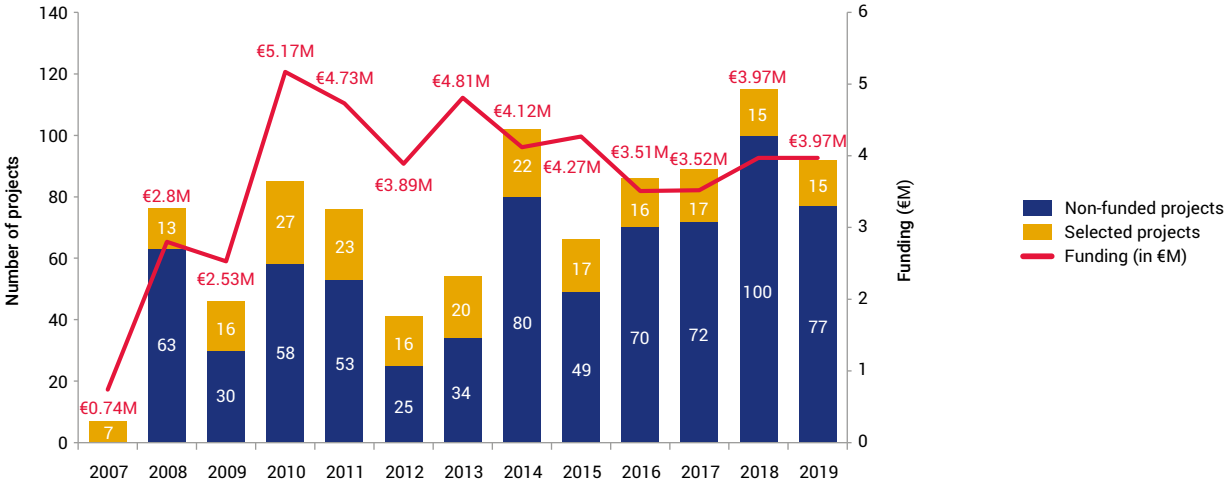
FIGURE 57
DISTRIBUTION OF SELECTED PROJECTS IN 2019 ACCORDING TO THE CSO CLASSIFICATION



THE PROGRAMME OVER THE 2007-2019 PERIOD

Since 2007, INCa has funded 224 projects out of the 935 submitted in human and social sciences, epidemiology, and public health for a total amount of over €48M (Figure 58).

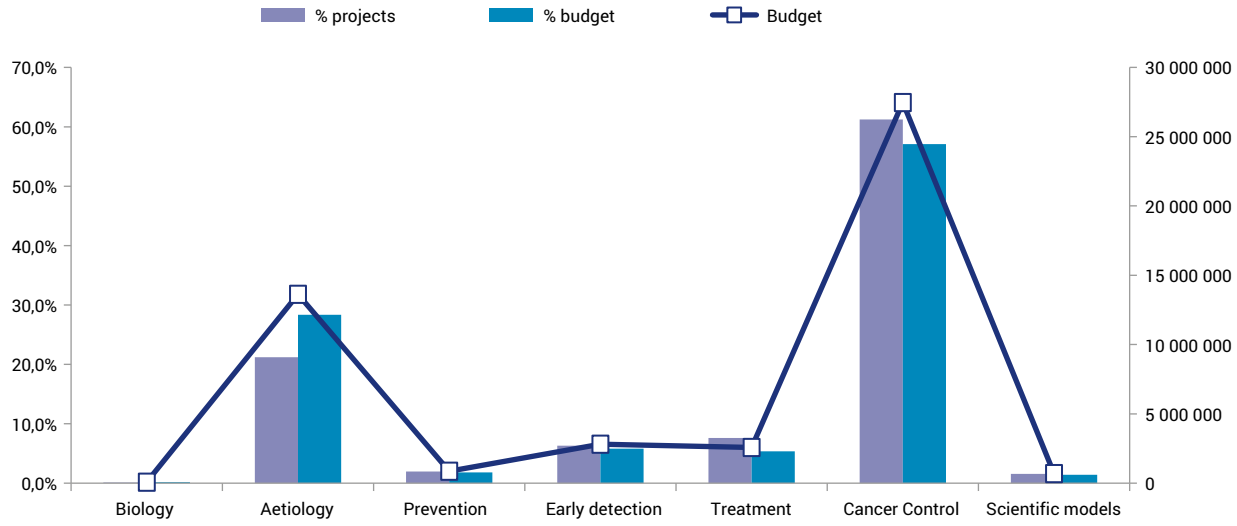
FIGURE 58
TRENDS IN SELECTION AND FUNDING OVER THE 2007-2019 PERIOD



Over the 2007-2019 period, an average of 18 projects are selected for funding out of 72 proposals submitted each year, excluding 2007 data. With the exception of the first year, the selection rate is relatively stable at around 25%, but a decrease has been observed in recent years as competitiveness increases. Over the last 10 years, the programme has stabilised and financed projects at an average of €4.2M per year for HSS-E-PH projects.

The programme promotes numerous research areas such as projects on cancer risk factors, palliative care and end-of-life care, cost modelling/analyses or comorbidities. Project proposals in the field of paediatrics and projects concerning cancer sites with poor prognosis or combating health inequalities are also particularly welcomed.

FIGURE 59
DISTRIBUTION OF PROJECTS AND TOTAL ALLOCATED BUDGET ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2019 PERIOD



Over the 2007-2019 period, nearly two out of every three HSS-E-PH research projects were devoted to cancer control, survivorship, and outcome research, for a total amount of more than €27M. Aetiology research accounts for more than one in five projects. Research projects on screening, early detection, and treatment account for a cumulative total of nearly 14% of the selected projects. Research on biology, prevention and scientific models represents a mere 4%, in compliance with the objective of the programme.

THE PROGRAMME AND THE 2014-2019 NATIONAL CANCER CONTROL PLAN

Among the 17 objectives of the Cancer 3 Plan from 2014 to 2019, several strategic measures are based on advances that need to be made through HSS-E-PH research such as guaranteeing the quality and safety of care, France's lead in personalised medicine and reducing the impact of cancer on patients' personal lives.

Over the narrower period from 2014 to 2019 relating to the Cancer 3 plan, INCa devoted more than €23M to HSS-E-PH research, by funding 102 research projects. As shown in Figure 60 and in compliance with the objectives of the programme, 62% of the selected projects address cancer control research issues (patient care and survivorship, behaviour, cost analyses, and surveillance). Moreover, the Aetiology section represents 26% of the selected projects, while research questions on treatment represent 10%.

Cancer Control Plan:

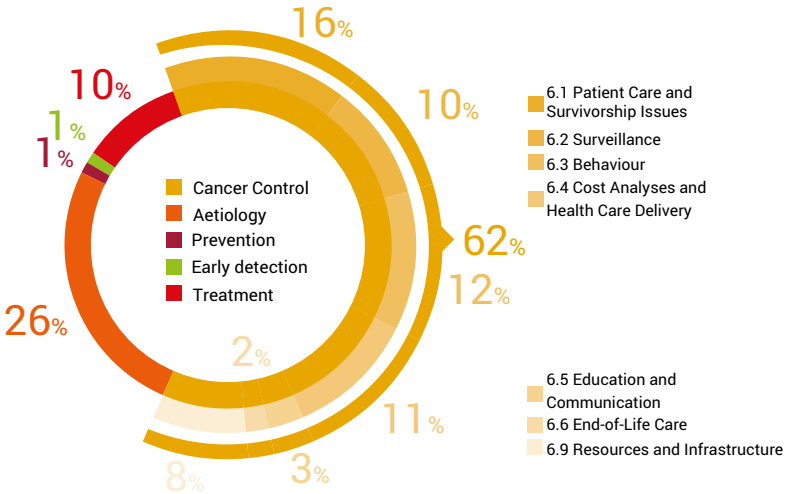
102

projects funded for a total amount of

€23.44M

FIGURE 60

DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION DURING THE 2014-2019 CANCER CONTROL PLAN PERIOD



Population health intervention research (PHIR)

In 2010, support for human and social science research was strengthened and completed by a dedicated call for proposals in Population Health Intervention Research (PHIR) to support programmes aiming to reduce health inequalities. In 2011, the Scientific Advisory Board recommended the set-up of a specific strategy for preventive research that should include behavioural and social sciences, public health, etc. Based on these recommendations and on the 2012 strategic report on cancer prevention research, the scope of the programme was extended in 2013 to health promotion interventions, including those aiming to change behaviours.

Since 2015, the scope of the call for proposals has included all aspects of cancer control: ranging from primary prevention, to secondary prevention, tertiary prevention, healthcare organisation, day-to-day life with the disease and its treatment and survivorship and rehabilitation issues. This call for proposals also encourages research in methodological issues. Furthermore, emphasis is placed on public health research transferability.

Through the PHIR programme, researchers are expected to establish strong partnerships between field practitioners and decision-makers.

Two types of proposals are expected:
- Full research projects presenting advanced research protocols, with a strong methodological approach and established partnerships, for 36 to 48 months of funding;
- Emerging research projects to encourage the development of intervention research on a topic relevant to the 2014-2019 Cancer Control Plan, to be funded for 12 or 18 months for a maximum of €30,000. This funding should enable researchers, in particular young researchers, interested in intervention research to build and to submit a proposal for the next edition of the call for proposals.

THE PROGRAMME IN 2019

In 2019, six projects were selected for funding, including one emerging project, for a total budget of €2.2M (Table 31). Out of 20 submitted projects, three consisted of emerging projects and two were full projects stemming from previously funded emerging projects, highlighting the interest of this funding track. However, none of the selected full projects stemmed from previously funded emerging projects.

TABLE 31
FEATURES OF THE POPULATION HEALTH INTERVENTION RESEARCH PROGRAMME IN 2019

Objectives	• To promote the emergence of projects in intervention research applied to cancers, that are original and of scientific excellence, and likely to produce knowledge that is scientifically valid and socially useful; • To encourage original partnerships between research teams in different disciplines (human and social sciences, public health, epidemiology, biostatistics, etc.), practitioners in the field and users, in order to facilitate the implementation and transferability of the findings in different contexts, and also the exchange of knowledge and skills between the world of research and that of intervention or decision makers.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€2.2M**
Proposals submitted	**20**
Projects selected	6
Selection rate	**30%**

THE PROGRAMME OVER THE 2010-2019 PERIOD

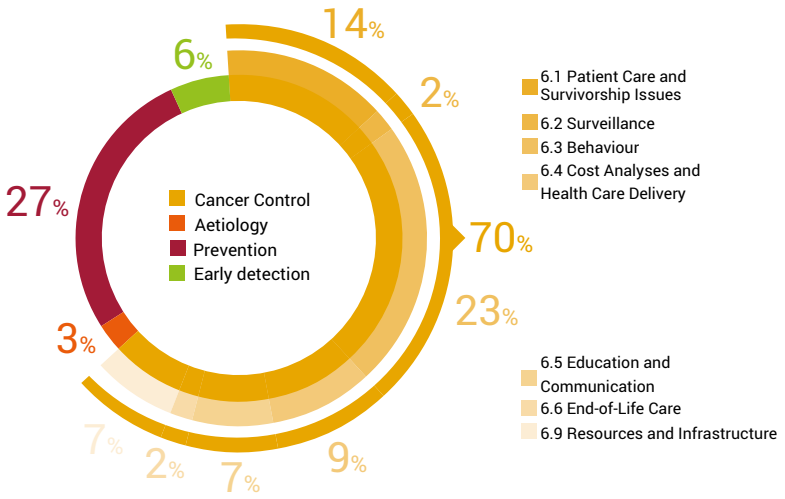
Since 2010, out of 279 projects submitted, 53 projects have been funded (including 15 emerging research projects) for a total amount of €14.34M (Table 32).

On average, 28 projects are submitted each year with a 19% selection rate. Although the "emerging research projects" funding track is recent, since its creation, this kind of project accounts for 40% of selected and funded projects. Based on the experience of emerging projects converted to full proposals, INCa is expecting an increased number of high-quality full projects in the coming years.

TABLE 32
TRENDS IN SELECTION AND FUNDING OF THE POPULATION HEALTH INTERVENTION RESEARCH PROGRAMME OVER THE 2010-2017 PERIOD

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Funding (in €M)	0.61	1.51	2.18	0.71	1.15	1.08	1.11	1.79	2	2.20	**14.34**
Proposals submitted	8	37	20	10	60	29	22	39	34	20	**279**
Projects selected	2	3	5	3	4	7	6	8	9	6	**53**
Selection rate	25%	8%	25%	30%	7%	24%	27%	21%	26%	30%	**19%**

FIGURE 61
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2010-2019 PERIOD



International symposium on Population Health Intervention Research

The fourth edition of the symposium on PHIR was held in Paris on 10 and 11 January 2019. Organised by the Institute in partnership with IReSP and INSERM, this international event was an opportunity to reflect on the contribution of PHIR to the reduction of inequalities. In total, 24 communications were presented, covering a wide array of themes and focusing on various populations. Two prizes were awarded – a "research" prize and an "intervention" prize – to promote and encourage the emergence of new players in PHIR.

The event succeeded in fostering exchanges between researchers, public decision-makers and intervention stakeholders, with more than 300 participants from all fields gathered together.

The two-day symposium ended with the intervention of two witnesses who offered some perspectives for PHIR and the reduction of health inequalities, and with conclusions by the chair and co-chair of the event.

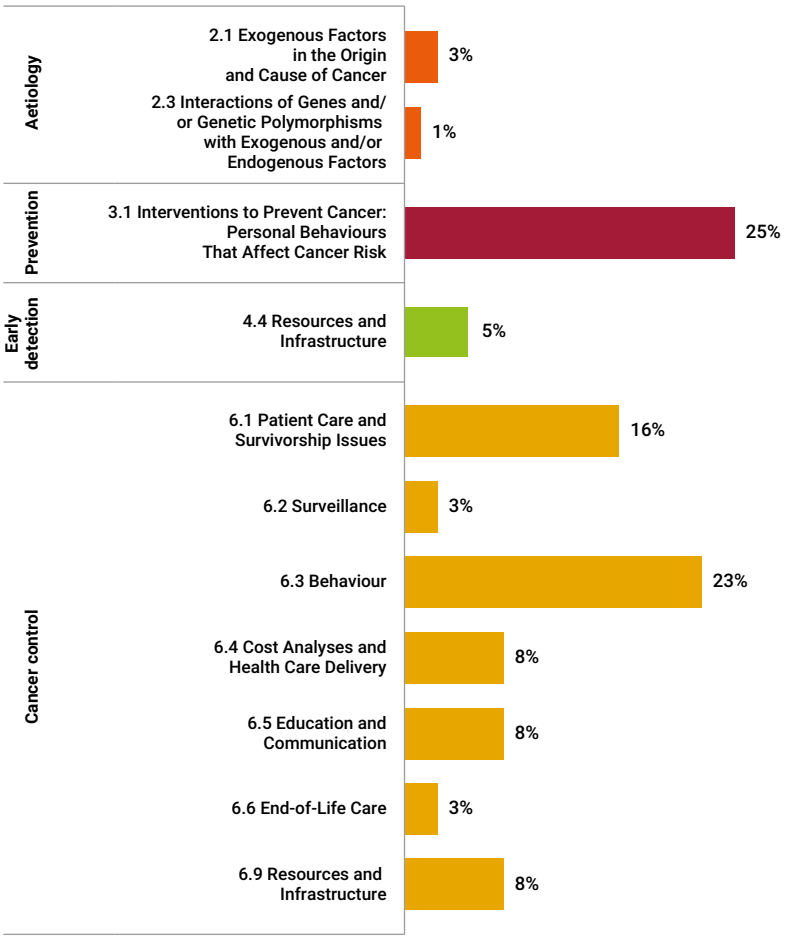
THE PROGRAMME AND THE 2014-2019 NATIONAL CANCER CONTROL PLAN

Over the Cancer Control period, INCa devoted more than €9.3M to PHIR by funding 40 research projects.

In order to support this research field, this programme includes a specific funding scheme to fund emerging projects intended to mature into full projects in upcoming years and then to propose specific interventions. Figure 62 presents the breakdown of the funded projects according to the CSO classification and highlights that research interventions on personal behaviours (CSO 3.1 and CSO 6.3 categories) represent nearly half of the funded projects (48%).

FIGURE 62

DISTRIBUTION OF THE SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2014-2019 CANCER CONTROL PLAN PERIOD



2019:
2
projects funded for
€0.41M

2010-2019:
54
cancer-related projects funded for
€8.2M

Programme of the French National Agency for Food, Environmental and Occupational Health and Safety (Anses) to support research on environmental risks

This multi-agency programme addresses various public health issues related to the environment and workplace. ITMO Cancer-Aviesan funded cancer-related projects for the 2011-2018 period.

THE PROGRAMME IN 2019

In 2019, 2 projects were selected for funding by ITMO Cancer-Aviesan for a total amount of €0.41M (Table 33).

TABLE 33
FEATURES OF THE 2019 NATIONAL RESEARCH PROGRAMME ON ENVIRONMENTAL AND OCCUPATIONAL HEALTH IN THE FIELD OF CANCER

Objectives	• To evaluate and analyse environmental risks for human health in the general population or at work. • To address emerging and known risks, which can generate complex scientific debates, and for which a single approach can include concepts, methods, and tools from different disciplines.
Programming institution	Anses
Operating institution	Anses
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€0.41M**
Letters of intent evaluated	**44**
Full proposals evaluated	23
Projects selected	**2**
Selection rate	**4.5%**

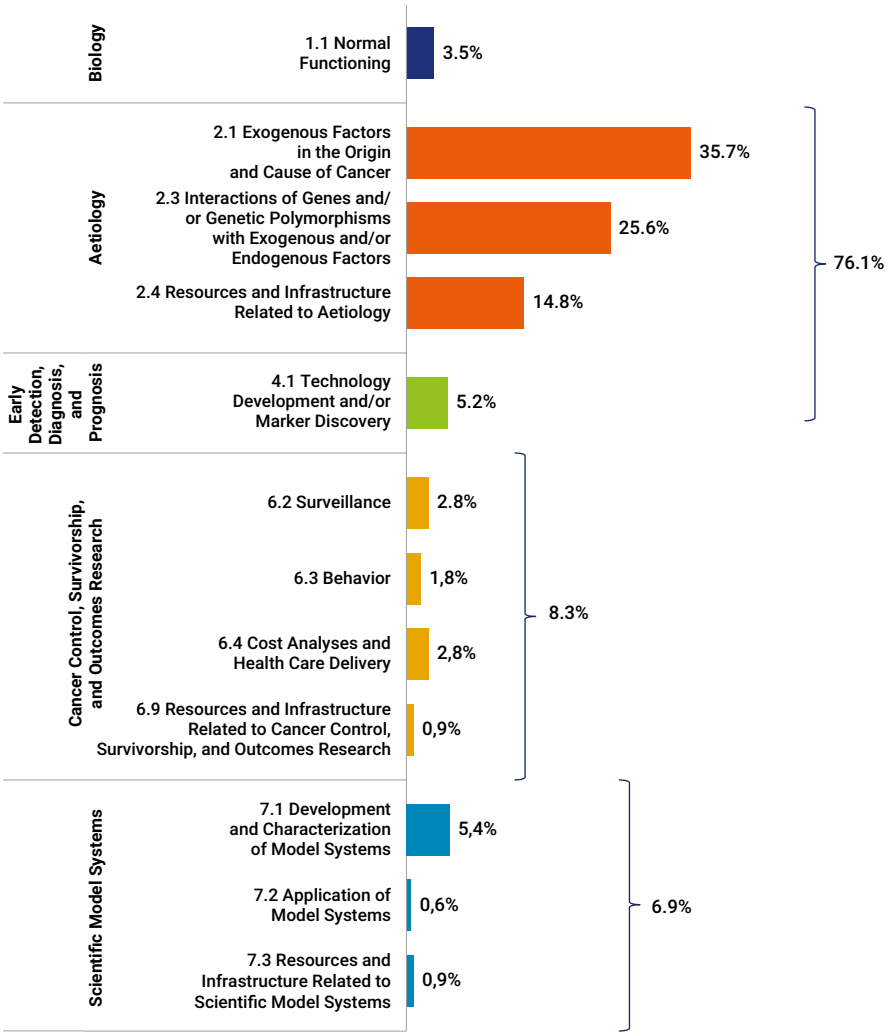
Projects focused on the association between long-term exposure to prevalent pollutants in drinking water and highly incident cancers (breast and colorectal) in a large cohort, and on the evaluation of maize aflatoxin emergence related to climate change in France and ways to control it.

THE PROGRAMME OVER THE 2010-2019 PERIOD

Since 2010, 54 projects have been funded within the framework of this programme for a total amount of €8.2M. Funded projects have primarily addressed the aetiology of cancer in accordance with the objectives of the call (76.1%).

These projects have largely aimed to assess the role of exogenous factors alone or in interaction with endogenous factors in the onset of cancer. The remaining projects have dealt with biology (normal functioning), early detection (mainly marker discovery), cancer control and model system development and characterisation (Figure 63).

FIGURE 63
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2010-2019 PERIOD



Chlordecone and prostate cancer in the French Antilles

Chlordecone is an organochlorine insecticide that was used in the French Antilles (Guadeloupe and Martinique) between 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 France.

The question therefore arose that 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 Ministry of Health, the 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 elaborated in collaboration with a scientific committee composed of national and international experts and with a support committee composed of French public bodies and national and local agencies and think tanks concerned by the issue. These groups were commissioned to propose recommendations on the additional research work to be carried out likely to enhance knowledge on the subject.

The integrated and multidisciplinary cross-cutting research programme will aim to federate knowledge and skills through the cooperation of teams from different research fields such as environmental epidemiology, toxicology, public health, oncology, genomics, human and social sciences, or computer science. The teams will be working as a consortium implementing several work packages. This collaborative programme would help optimise the production of knowledge in these different research areas and would promote its dissemination for a better understanding of the link between exposure to chlordecone and prostate cancer risk in the context of the French Antilles.

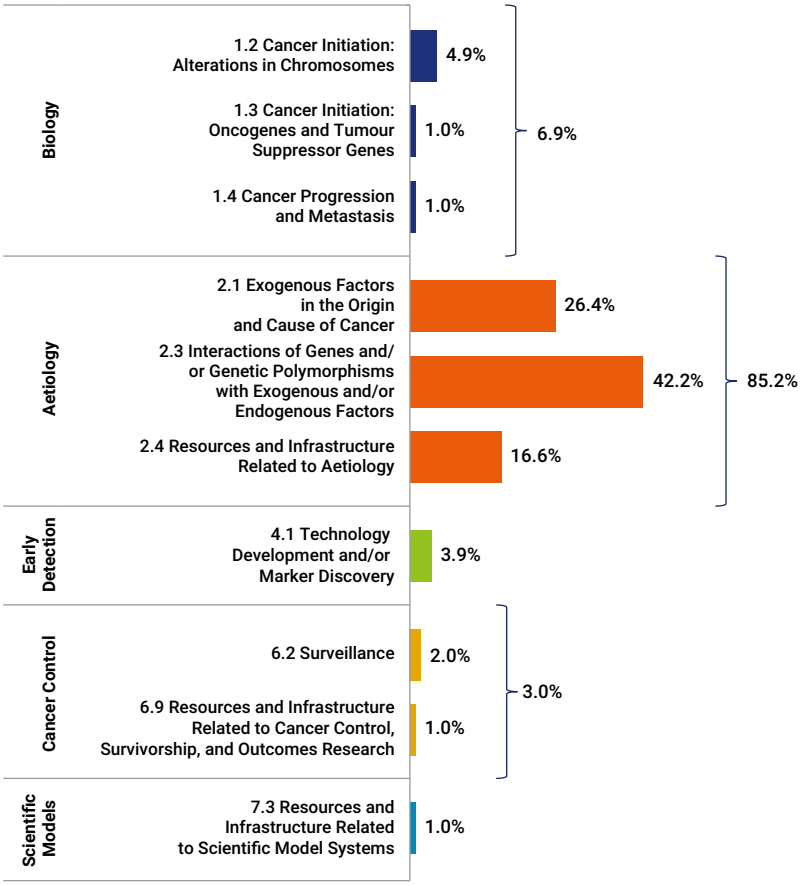
In late 2019, INCa published a press release advertising the launch of the call for applications in 2020.

ENVIRONMENTAL CANCER RELATED PROGRAMMES AND THE 2014-2019 NATIONAL CANCER CONTROL PLAN

Including both its own programme on the exposure effects of environmental risk factors on cancer (4 editions over the 2014-2019 period) and its partnership with Anses on the National Research Programme on Environmental and Occupational Health (6 editions over the 2014-2019 period), ITMO Cancer-Aviesan has funded 51 projects in the field of environment for a total of €16.8M. In accordance with the objectives of the calls, the funded projects mostly (85.2%) concerned cancer aetiology (Figure 64).

FIGURE 64

DISTRIBUTION OF THE SELECTED PROJECTS AIMING TO ADDRESS CANCER-RELATED ENVIRONMENTAL RISKS FACTORS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2014-2019 PERIOD



HPV vaccination acceptability among school-age girls

A Call for Expression of Interest on HPV vaccination acceptability among school-age girls was launched in 2018 by ITMO Public Health-Aviesan and the French Institute for Public Health Research (IReSP) within the framework of the 3rd Cancer Plan. A total of 7 expressions of interest were selected and included the Prev'PHV project, which was aimed at co-constructing, implementing, delivering, and assessing a multi-component intervention intended for all stakeholders, in order to increase HPV vaccination uptake while taking social and local inequalities into account.

TABLE 34
FEATURES OF THE PREV'HPV PROGRAMME IN 2019

Objectives	To study the acceptability of HPV vaccination among school-age girls
Programming institution	IreSP and ITMO Public Health-Aviesan
Operating institution	IReSP
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€1.93M**
Proposals evaluated	11
Projects selected	7
Selection rate	63.6%

Preparation of a new research chair in "Health democracy/ empowerment: Involving citizens and people affected by cancer"

2019 saw the preparation of the creation of a new excellence chair programme for human and social sciences 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).

The overall objective of this Chair is to develop research in social and human sciences on health democracy and empowerment in the field of oncology.

Support for HSS-E-PH training

THE EXCELLENCE CHAIR PROGRAMME IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY, AND PUBLIC HEALTH

The Institute supports the creation of research excellence chairs since 2015 and has allocated a total budget of €1.5M to this end. Already 3 research chairs have been supported and brought to the national level with the support of numerous partners:

- In 2015, a research chair dedicated to **cancer prevention** was launched in partnership with the Institute for Public Health Research (IReSP) and the School of Public Health (EHESP) with a total funding of €450,000. This chair is intended to strengthen the interaction between research, decision-making and practice, and also to develop a curriculum for students, professionals, field workers and decision-makers;
- In 2016, a research chair was launched in partnership with the University of Lille 3 and the ONCOLille Integrated Cancer Research Site (SIRIC) with a total funding of €450,000. This chair aims **to promote and strengthen a culture of cancer-related basic and applied research in human and social sciences**, by supporting the acquisition of scientific and clinical skills by researchers and professionals, and by improving the French scientific training curriculum;
- In 2019, the research chair was launched in partnership with the LYriCAN Integrated Cancer Research Site (Lyon SIRIC), the Lyon Auvergne Rhône Alpes Canceropole (CLARA), University of Lyon (UDL) and the multidisciplinary University Claude Bernard Lyon 1 with a total funding of €600,000. This research chair aims **to develop research on social challenges of personalised medicine and innovation in oncology**.

SUPPORT FOR HSS-E-PH TRAINING: PHD PROGRAMME

For the 9th consecutive year, the French National Cancer Institute, in partnership with the School for Advanced Studies in Social Sciences (EHESS) and the Doctoral

Network in Public Health at the EHESP School of Public Health (EHESP), launched a call for applications to offer four doctoral grants in order to promote research in HSS-E-PH applied to cancer control. A total of 25 applications were submitted to INCa, slightly down on 2018 (36 applications). Out of these submitted projects, 1 was classified outside the scope of the call for applications. The 25 projects reviewed are divided into 3 research categories. Table 35 presents the distribution of the applications reviewed. The distribution of projects according to discipline is substantially consistent between 2018 and 2019.

TABLE 35
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.)	9
Epidemiology or biostatistics	11
Human sciences (psychology, cognition and learning, psychoanalytic studies, science of physical activity, etc.)	5

In 2019,
4
PhD students were awarded: psychology, sociology, and biostatistics.

Following the review process, including interviews of applicants, four PhD theses were selected for funding (Table 36).

TABLE 36
DOCTORAL FELLOWSHIPS FUNDED IN 2019.

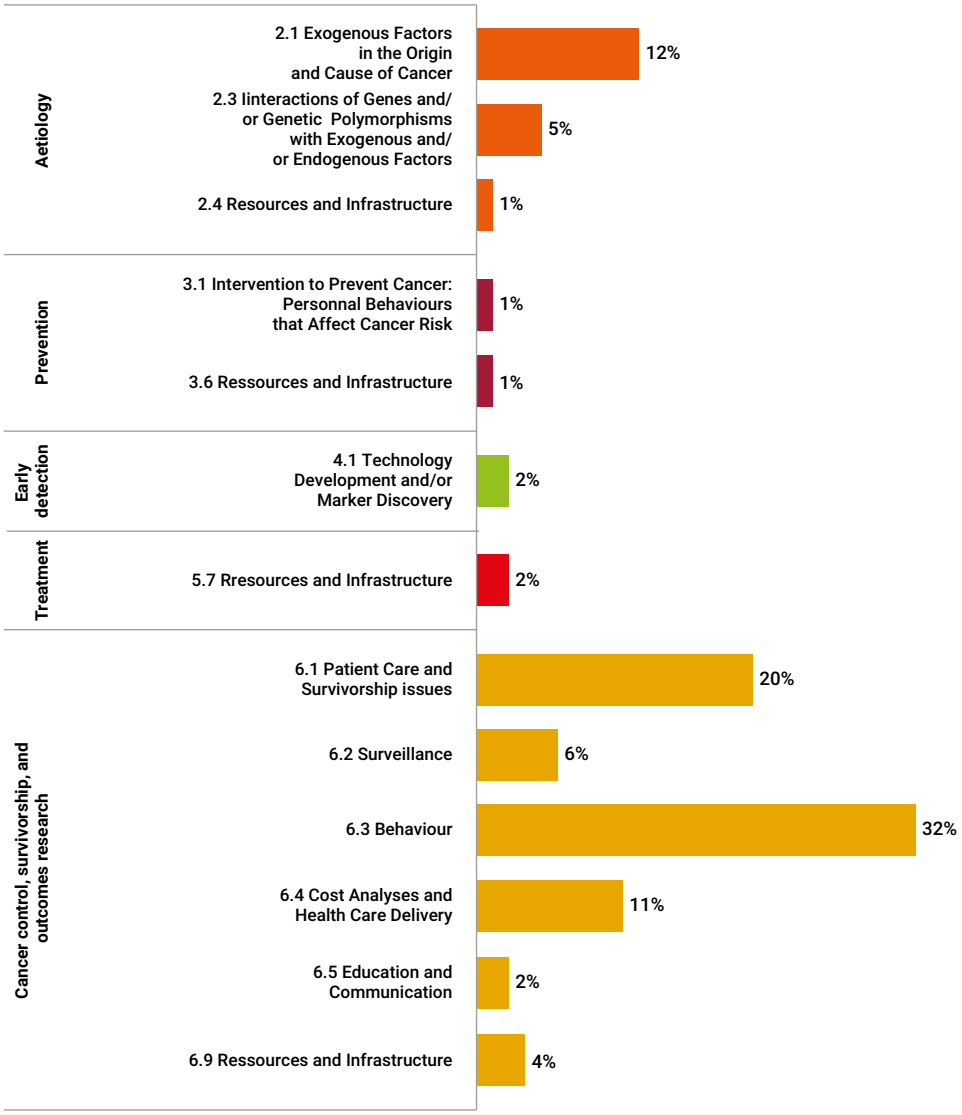
Title	Discipline
Cervical Cancer Screening (CCS) with women in precarious situations - Psychosocial analysis and elaboration of a training programme dedicated to professionals.	Humanities
Epidemiological approach of relationships between sugar intake, sugary food and beverage consumption, usual exposure to artificial sweeteners	Epidemiology
Exploration of the challenges of home hospitalisation (HAD) based on a large population survey of oncology patients, with an analysis of their experience from the perspective of disparities and social pathways, inequalities and access to care in oncology, and more generally in terms of equity of care	Social sciences
Occupational exposure to endocrine disrupting chemicals and risk of hormone-sensitive cancers	Epidemiology

2007-2019:
42
PhD theses supported for an overall amount of
€4.06M

Over the 2007-2019 period, 42 PhD theses were supported for a total amount of €4.06M.

FIGURE 65

DISTRIBUTION OF SELECTED GRANTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2019 PERIOD



INTERNATIONAL COMMITMENTS

INCa guarantees France's international commitments in cancer control with the aim of playing a role accelerating progress on a European and global level and, with the ambition of universal access to information, prevention, screening, and care for patients affected by cancer.

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, by mobilising the international community in the fight against cancer, without forgetting the imperative of helping the least developed countries.

INCa's international action contributes fully to the achievement of the 2014-2019 Cancer Control Plan and France's global health strategy by:

- Implementing partnerships and strategic initiatives to encourage cutting-edge research and innovation;
- Strengthening European actions in cancer control and research;
- Developing governance, international mechanisms, and instruments for cancer control (WHO, IARC, UICC, etc.).

In its activities, INCa promotes an integrated vision of cancer control including all fields of intervention related to cancerous diseases at the service of patients, their relatives, users of the health system, the population health professionals, researchers, and policy-makers.

FIGURE 66
INCA'S GLOBAL PORTFOLIO

INCa's participation in European actions

In 2018, 1.9 million people died from cancer in Europe[9], representing one out of five cancer-related deaths worldwide. Although health remains under national jurisdiction, the European Union has implemented numerous actions in cancer control, complementing the efforts of the Member States and improving coordination at a European level. This commitment will be reiterated in the next multi-annual financial framework (2021-2027), through new and continued initiatives: the EU Cancer Beating Plan and the Cancer Mission.

In 2019, INCa actively contributed to the actions initiated by the European Commission (DG Health, DG Research and Innovation and DG Connect). In the course of the year, the Institute was involved in 6 joint or transnational actions in the areas of translational research (TRANSCAN-2, 2015-2020), rare cancers (JARC, 2016-2019), innovation (iPAAC, 2018-2021), and social and economic impacts of the disease (CHRODIS+, 2017-2020).

9. GLOBOCAN 2018, Estimated number of deaths in 2018, all cancers, both sexes, all ages

FIGURE 67
KEY ELEMENTS OF THE NEW EU RESEARCH AND INNOVATION PROGRAMME, HORIZON EUROPE

Horizon Europe is the new EU Research and Innovation Programme	
PREVIOUS PROGRAMME	Horizon 2020
PERIOD	7 years (2021-2027)
BUDGET	€100billion
OBJECTIVES	- To strengthen the EU's scientific and technological bases - To boost Europe's innovation capacity, competitiveness and jobs - To deliver on citizens' priorities and sustain our socioeconomic model and values
STRUCTURE	Three pillars: 1. Open Science 2. Global Challenges and Industrial Competitiveness 3. Open Innovation
KEY NOVELTIES	- Creation of the European Innovation Council - New R&I Missions - Extended association possibilities - Open science policy - New approach to Partnerships

INNOVATIVE PARTNERSHIP FOR ACTION AGAINST CANCER (IPAAC)

The Innovative Partnership for Action Against Cancer (iPAAC) Joint Action (JA) brings together 44 partners from 24 European countries. It aims to build upon the outcomes of the previous EPAAC (European Partnership for Action Against Cancer) and CanCon (Cancer Control) Joint Actions.

The general objective of the iPAAC JA is to develop innovative approaches to improve cancer control. The innovation that will be covered within the JA consists of further development of cancer prevention, comprehensive approaches to the use of genomics in cancer control, cancer information and registries, improvements and challenges in cancer care, mapping of innovative cancer treatments and governance of integrated cancer control, including a new analysis of National Cancer Control Plans. The key objective is to develop a European roadmap aimed to provide recommendations on how to better implement national cancer control policies.

INCa is involved in 4 of 10 iPAAC's work packages (WP), which focus on cancer prevention (WP5), on genomics in cancer control and care (WP6), on innovative therapies in cancer (WP9) and on the implementation of iPAAC outputs in national policies and of their sustainability (WP4).

WP on innovative therapies in cancer

The work-package highlighted the main challenges, linked with the integration of innovative medicines into best practice guidelines. It also looked at access to innovative medicine, pointing to examples of early-access schemes already in place and the main factors responsible for non-reimbursement.

Until the end of the project, the teams will work on optimising the so-called Horizon Scanning schemes and real-time monitoring of innovative anticancer drugs.

WP on cancer prevention

Screening

Experience-shared by INCa in the field of screening within the framework of WP5:

- Role of technical and operational facilitator of the scheme;
- Generalisation of a cervical cancer screening programme, roll-out of a programme organised at a national level based on regional monitoring centres;
- Integration of immunological testing for the detection of cancers of the colon and rectum, and deployment of a programme organised at a national level based on local structures (departmental, then regional): organisation, methods of migration, monitoring and quality assurance, experience on migration from one programme to another;
- Experience in terms of democracy or participatory approaches (citizen and scientific consultation followed by a renovation plan, analysis of preferences in terms of benefit-risk balance for women);
- Vision of an integrated approach to risk levels: Support for the implementation of a study on the effectiveness of a screening strategy stratified according to risk levels;
- Reflection on different themes related to screening (screening for prostate cancer, lung cancer, HPV test, reduction of inequalities, decision support tools, etc.).

Prevention

INCa participated in the development, definition of the work plan in the field of prevention, follow-up to be given in respect of the European code against cancer, innovative initiatives to develop and relay prevention actions on both sides in Europe.

The question of identifying and sharing persuasive prevention actions at European level, in particular those that have an impact on the reduction of social inequalities in health, is a crucial issue that WP5 of the IPAAC project aims to address.

WP on Care organisation

INCa contributed to the definition of “neglected cancer” or cancer with a poor prognosis, and to the identification of public policy measures to promote in the treatment of pancreatic cancer.

For further information, please consult the website: https://www.ipaac.eu/

ERA-NET: ALIGNING NATIONAL/REGIONAL TRANSLATIONAL CANCER RESEARCH PROGRAMMES AND ACTIVITIES (TRANSCAN-2)

The TRANSCAN-2 ERA-Net is a unique European network of 28 research funding agencies and ministries from 15 Member States, 3 Associated Countries, and Taiwan. The overarching aim of TRANSCAN-2 is to achieve sustained coordination in the area of translational cancer research beyond national boundaries. TRANSCAN-2 members coordinate their funding strategy through joint calls for research proposals.

In addition, INCa coordinates the work package dedicated to the network strategy and scientific research priorities. In 2018, most of the work package missions were completed.

To improve European coordination of national efforts via ERA-Net and to continue advancing translational cancer research, TRANSCAN-3 has been confirmed and should be implemented as early as 2021.

For further information, please consult the website: https://www.transcanfp7.eu/

JOINT ACTION ON RARE CANCERS (JARC)

The new Joint Action on Rare Cancers funded by the European Commission is responding to the many challenges of rare cancers, including the implementation of the Directive 2011/24/EU of the European Parliament and the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare. This Directive is meant to grant EU patients the right to access safe and high-quality healthcare across European borders, and foresees the designation of European Reference Networks (ERNs) for rare and complex diseases, including rare cancers. ERNs will link up health care providers and centres of expertise of highly specialised healthcare, for patients with conditions requiring a particular concentration of resources or expertise regardless of where they are in Europe.

The JARC will help shape ERNs, but also contribute to improving health outcomes for patients with rare cancers in the EU. Its objectives are:

- To prioritise rare cancers in the agenda of the EU and Member States with a view to promoting quality and harmonisation of clinical practices, as well as innovation through clinical and translational research;
- To develop shared solutions, to be mainly implemented through the ERNs, for quality care, research & education, prevention & diagnosis of rare cancers.

INCa's participation in JARC is grounded on the organisational scheme developed since 2009 by INCa and the Ministry of Health for rare cancers in adults. In this framework, INCa contributes to the development of recommendations to improve the quality of registration of rare cancers and to strengthen their epidemiological monitoring. Sharing its experience of setting up 18 national networks in France, the Institute also assists in designing a framework of quality standards applicable to all networks and centres for rare cancers. Within the JA, careful consideration is given to childhood cancers: INCa is involved in the production of guidelines on models of healthcare to assure adequate follow-up of children, adolescents and young adults surviving cancer.

After three years of work with 34 Associated Partners and 18 Member States, JARC has ended with a final meeting held on 11 September 2019 at the European Parliament, where the final JARC recommendations (Rare Cancer Agenda 2030) were presented and an assessment of the state of the art and future with ERNs was analysed.

For further information, please consult the website: http://jointactionrarecancers.eu/

JOINT ACTION ON IMPLEMENTING GOOD PRACTICES FOR CHRONIC DISEASES (CHRODIS+)

CHRODIS+
IMPLEMENTING GOOD PRACTICES FOR CHRONIC DISEASES

A joint action dedicated to chronic diseases was launched in 2017. Its goal is to support Member States through cross-national initiatives to reduce the burden of chronic diseases, while assuring health system sustainability and responsiveness. The development and sharing of tested policies and projects across EU countries is the core idea behind this action. INCa has been designated by the French Health Authorities to participate in CHRODIS+ and has actively contributed to the preparation of the Joint Action. INCa is involved in a work package dedicated to "employment and back-to-work issues for people with chronic conditions". The aim of this WP is to improve work access and participation for patients with chronic diseases.

Two evidence-based, practice-oriented guides for the employment sector are under development:

- A Training Tool to help employers understand the operational benefits of the inclusion, integration and reintegration of people suffering from chronic disease;
- A Toolkit for the Adaptation of the Workplace.

In 2018, INCa drafted one of the three literature reviews developed under the work package during the year. The report which focuses on "Cancer and employment" provides knowledge and valuable inputs for the development of the Training Tool and the Toolkit. It will be published in 2019 and some of its insights will be presented through scientific papers.

The work package on "employment and back-to-work issues for people with chronic conditions" aims also to base recommendations, targeting policy-makers, to ensure that legislative frameworks provide better accessibility to existing employment support for those with chronic diseases.

The CHRODIS PLUS Budapest Conference on May 2019 was one of the key events in this project where over 180 chronic disease experts from 26 countries participated to discuss and provide feedback on the real-life experiences project partners have gained during the initiative's first 20 months. This conference demonstrated the impact that CHRODIS PLUS has on public health systems across EU Member States with a special emphasis on proving that the good practices, models, and tools that the project implements can be tailored to various national and local settings across Europe.

For further information, please consult the website: http://chrodis.eu/

EC PRE-COMMERCIAL PROCUREMENT PROJECT ON NEXT GENERATION SEQUENCING FOR ONCOLOGY (ONCNGS)

The OncNGS consortium challenges the market to research and develop novel affordable solutions to provide the best NGS tests, for all solid tumour/lymphoma patients. The challenge will consist in providing: (1) effective molecular DNA/RNA profiling of tumour-derived material in liquid biopsies by means of (2) a pan-cancer tumour marker analysis kit including NGS analysis integrated with (3) an ICT decision support system including analytical test interpretation and reporting.

Using the solutions provided, the oncNGS consortium will be able to address their common identified unmet medical needs:

- Establishment of valuable common tumour profiling strategy helping provide equal access to innovative medicines to all;
- Outcome research analysis after treatments with targeted therapies as diverse testing leads to a reduction in the pooling capacity of results obtained, needed to obtain sufficient sample numbers to perform statistical analyses;
- Application of such essential testing to all patients, breaking down current unacceptable inequities due to the high costs of current diagnostics tests.

OncNGS is a strong consortium composed of eight buyers from five member states. The OncNGS consortium will challenge the market by launching a pre-commercial procurement procedure, a competitive process enabling the buyers to compare the developments carried out by the contracted suppliers through three phases: solution design, prototyping and clinical validation of a limited set of R&D supplies.

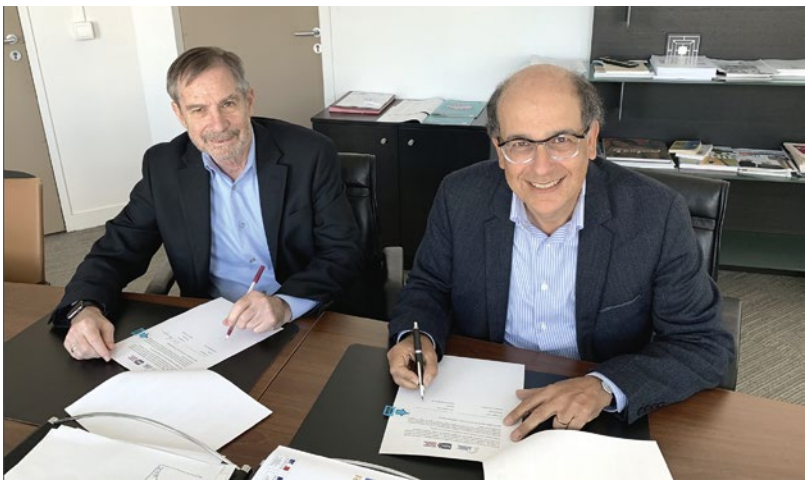
INCa's global commitments

NATIONAL CANCER INSTITUTE – USA

The INCa-NCI partnership has developed over the years. New areas of collaboration were identified during the executives' meeting in June 2018 on the margins of ASCO in Chicago. INCa's and NCI's executives are committed to finding concrete deliverables within the framework of our cooperation.

Recognising that international cooperation provides an opportunity to combine expertise and share experiences, INCa and the NCI signed a Letter of Intent in September 2019 to develop collaborations in the area of pre-cancer research with the following objectives:

- To promote cooperation between investigators and within the research community;
- To encourage the conduct and organisation of research;
- To ensure the dissemination and communication of the Participants' respective work.



To ensure a close collaboration, NCI and INCa expect to communicate about the progress and/or issues of the projects. The Participants may select their own centres and teams to engage in various consultations, workshops, and data sharing.

In line with this process, two visits to the NCI were organised, in April 2019 and November 2019, in partnership with ITMO cancer Aviesan. These meetings and workshops allowed progress to be made on 2 cooperation projects: paediatric cancers, precancer and research on cancer prevention, in particular on tobacco prevention.

JAPAN

In 2017, a Memorandum of Understanding was signed between the National Cancer Center of Japan (NCC) and INCa for a period of three years. To reinforce this collaboration, the NCC and INCa, with the help of the French Embassy in Tokyo, organised a seminar on paediatric cancers in December 2019. This workshop had the following objectives:

- To share the French model of research in paediatric cancers through the presentation of programmes and platforms for networking and clinical trials with our Japanese counterparts whose cancer technology is at the forefront but whose research remains relatively scattered;
- To establish a comprehensive portrait of paediatric cancer research in Japan through the intervention of institutional actors as well as other relevant partners in this field such as patient or research organisations;
- Identify Franco-Japanese research topics for projects to advance research and thus improve the healing of children and adolescents with cancer;
- Identify options for creating a global initiative for paediatric cancers.

To continue collaboration in this area, the French Embassy in Japan will finance high-level scientific grants in 2020.

GERMANY

In January 2019, a delegation from INCa met with German representatives from the Ministry of Research (BMBF), Ministry of Health (BMG) and the Helmotz Association. The objective was to find new ways to best align the French and German agenda for cancer research and care in the context of the new German Cancer Plan (Nationale Dekade Gegen Krebs) and the French ten-year cancer control strategy elaboration.

A quick overview showed that three common interests can be identified: prevention research, phase IV clinical studies and long-term survivorship. In order to move forward, French, and German experts should meet by 2020 in the context of the German Presidency of the EU in order to come together with relevant research items on which to collaborate.

In September 2019, on the sidelines of the international scientific council and the canceropôle meeting, INCa welcomed Professor Mickael Baumann, director of the DKFZ and co-president of the German Decade Against Cancer, in order to consider the cooperation opportunities of France and Germany in the priority areas identified by the development of the French and German ten-year strategies, including a European axis.

Global partnerships

UNION FOR INTERNATIONAL CANCER CONTROL (UICC)

With the support and participation of INCa, UICC organised a workshop on 13 and 14 June 2019 in Dakar, bringing together 45 representatives of the Ministries of Health from 10 countries in French-speaking Africa, technical partners, donors and civil society represented by UICC members developing activities in the region, with a view to eliminating cervical cancer and combatting female cancers.

This event was part of the current context of the WHO call for action for the elimination of cervical cancer, in particular in connection with the regional consultations of the WHO AFRO region during which UICC organised an interactive session dedicated to partnership approaches in May 2019, and the Cofac-col network meeting in March 2017 in Abidjan organised by WHO and INCa.

This workshop enabled participants from the 10 countries represented, as well as the technical partners and regional offices of multilateral agencies to:

- Map the state of the fight against cancer in the countries represented, both from the perspective of public authorities and civil society;
- Inform on the highlights from international actions in this area, especially concerning the first feedback on the draft Global Strategy for the elimination of cervical cancer as a public health problem;
- Report on the activities and perspectives of the main regional and international stakeholders in this field, including technical partners and multilateral agencies;
- Confirm the interest of the main stakeholders in collaborating in the framework of a partnership to increase joint efforts and activities in the fight against female cancers, in particular cervical cancer;
- Explore existing models of public health partnerships in the sub-region by drawing on the experience of other areas of global health, such as reproductive and maternal health, in the implementation of partnership models and integrated approaches to increase access to all essential services across the cancer care continuum. Discuss the main strengths of this partnership on a technical level (how it would address the shortcomings of the different stages along the continuum) and governance aspects.

The workshop resulted in the collective definition of recommendations and next steps towards such a partnership. It will be followed by collaboration and networking activities, in particular through the funding of exchange grants between representatives of the participating countries.

WORLD HEALTH ORGANIZATION (WHO) – SESSION TOWARDS A PARTNERSHIP FOR WOMEN'S CANCER IN AFRICA

In January 2019, at its 144th Session, the Executive Board requested the Director-General to develop, in consultation with Member States and other relevant stakeholders, a draft global strategy to accelerate cervical cancer elimination, with clear goals and targets for the 2020–2030 period, for consideration by the Seventy-third World Health Assembly, through the Executive Board at its 146th session.

The strategy proposes an approach that will enable countries to reach 2030 global targets for key interventions that, in turn, will lead to elimination of cervical cancer as a public health problem (hereafter referred to as "elimination"). The proposed targets for 2030 are:

- 90% of girls fully vaccinated with the human papilloma virus ("HPV") vaccine by 15 years of age;
- 70% of women screened with a high-precision test at 35 and 45 years of age;
- 90% of women identified with cervical disease receive treatment and care.

With the support of INCa, this session was aimed at stimulating reflection on how sound and effective partnerships could facilitate the attainment of the targets proposed above. Participants were thus invited to align their partnership thinking with the emerging regional perspectives on implementation of the global strategy.

To inform this session, the results of a short survey on partnerships within the Africa region and three (3) examples of partnerships were presented to the participants.

Group work discussions resulted in concrete recommendations that will inform the regional consultation on partnerships' issues. They will also inform the Dakar Workshop that will include 12 countries in West Africa, key stakeholders, including leads of existing partnerships.

INTERNATIONAL CONSORTIUM: "SUCCESS"

Cervical cancer is one of the world's deadliest – but most easily preventable – forms of cancer for women, responsible for more than 270,000 deaths annually, 85% of which occur in developing countries. Early screening and treatment of precancerous lesions are essential to avert invasive cervical cancer, but high cost, slow integration into national guidelines and new national programmes, along

with a lack of robust evidence for effective management of HPV, especially among women living with HIV, hinder the scale-up of preventive solutions.

The three-year SUCCESS project introduces and promotes the best available screen-and-treat tools to prevent cancer in women most at risk, especially those living with HIV.

Led by Expertise France and in collaboration with Jhpiego, an international non-profit health organisation affiliated with Johns Hopkins University, and the Union for International Cancer Control (UICC), SUCCESS will be implemented in Côte d'Ivoire, Burkina Faso, Guatemala, and the Philippines.

SUCCESS will implement a cervical cancer control approach based on:
- High-performance screening;
- HPV testing and thermal ablation of precancerous lesions;
- Increased awareness and information for communities.

The programme also relies on technical support from national cancer institutes: the French National Cancer Institute (INCa), the US National Cancer Institute (NCI), the National Cancer Center (NCC) - Japan, and the National Cancer Institute (INCA) - Brazil.

COOPERATION WITH IARC: CESTA PROJECT

In 2014, WHO updated the cervical cancer screening and treatment guidelines and included primary screening options with VIA and HPV testing. Although the guidelines were evidence-based, the available data that was used to draft the recommendations was scanty, principally in low-resource settings. A research gap was identified for clinically relevant studies for the screening algorithms of interest.

The "Cervical Cancer Screening and Treatment Algorithms Study Using HPV testing in Africa" (CESTA) aims to compare the performance of cervical cancer screening and treatment algorithms using primary HPV testing included in the WHO guidelines, but also including novel ways of screening and treating pre-cancerous lesions. Funded by the French National Cancer Institute, the project expects to estimate the sensitivity of VIA (visual inspection with acetic acid) to detect histological high-grade squamous intraepithelial lesions or worse (HSIL+) when used as triage of HPV positive women within a screen-and-treat algorithm, stratified by HIV serostatus, to model the cost-effectiveness of the $HPV^{+}VIA^{+}$treat and HPV^{+}treat strategies, stratified by HIV serostatus and to estimate the safety and side-effects of cryotherapy and thermal ablation, stratified by HIV serostatus.

It will help inform international guidelines for cervical cancer screening and treatment including in populations with high HIV prevalence for LMIC. Using CESTA recommendations, the project will advocate for the adaptation of international and country-level guidelines, by working through coalitions and our local operating partners.

MINISTRY OF SCIENCE AND TECHNOLOGIES OF TAIWAN

The long-term relationship and exchanges with representatives of Taiwan's Ministry of Science and Technologies in France led to the signature of a MoU in 2017. The emphasis is placed on collaborative cancer research. The signature of this MoU has helped foster French-Taiwanese partnerships with the aim of co-funding joint cancer research projects within the scope of INCa's call for proposals on cancer biology, the Biology and Basic Sciences for Cancer Research-PL-BIO programme. In 2019, 3 cooperation projects between French and Taiwanese research teams were proposed.

ITMO Cancer-Aviesan and INCa at the AACR Annual Congress

As has been the case every year since 2017, ITMO Cancer-Aviesan had a booth in conjunction with INCa at the annual congress of the American Association for Cancer Research. In 2019, this event took place in Atlanta (Ga), and the aims were to:

- Represent the French cancer community
- Inform French and foreign young researchers of the funding opportunities in France
- Inform foreign researchers of collaboration with French public laboratories opportunities and collaboration funding
- Make available documents on:
  - French institutions and laboratories
  - Funding, mobility, team creation arrangements in France
  - Job and mobility offers in France
  - Upcoming colloquia in France

European and international commitments during the 2014-2019 Cancer Control Plan

The 3rd French National Cancer Control Plan sought to achieve 3 main objectives:

- Support the development of cancer control programmes of international agencies, in particular their actions in relation to the French-speaking countries of sub-Saharan Africa and the southern Mediterranean;
- Develop collaborative networks between France and Southern countries in the field of research and public health, drawing in particular on the infrastructures developed by Aviesan Sud's partners (IRD, Pasteur Institutes, Fondation Mérieux, etc.) in the target countries;

- Actively participate in the coordination actions of international cancer research funders and extend them with European countries and the US, and with emerging countries by proposing solutions shared by all.

INCa has developed several activities in order to respond to these objectives, participating in the structuring of international networks, including in LMICs, and in the development and implementation of international initiatives related to the continuum of care & research (table 37).

TABLE 37
GLOBAL PORTFOLIO OVER THE 2014-2019 CANCER CONTROL PLAN

	International consortia	Europe & High income countries	Low and middle-income countries
Cancer control		EPAAC – European Partnership for actions against cancer CANCON - European guidelines for quality improvement in comprehensive cancer control IPAAC – Innovative partnership for actions against cancer JARC (Joint action on Rare Cancers)	IAEA (International Agency for Atomic Energy) – PACT programme on cancer therapy/ (INCa is a contributor to PACT's comprehensive cancer control programmes)
Cancer biology / genomics	ICGC – International cancer genomic consortium (INCa was a founding member & sits on the ICGC executive committee/ INCa and ITMO Cancer-Aviesan support have funded 8 projects) GLOBAL ALLIANCE for Genomics and Health (dedicated to enabling secure sharing of genomic and clinical data)	BASIS – European research project on Breast cancer somatic genetic study	
Personalised medicine		CSA PerMed – European concerted action on personalised medicine (global objective is to develop a European strategic research agenda in personalised medicine)	
Translational research		TRANSCAN – European network on translational research (3 joint European calls for research proposals launched: "validation of biomarkers", "primary & secondary prevention", and "tertiary prevention") TRANSCAN 2 (4 new joint European calls)	

	International consortia	Europe & High income countries	Low and middle-income countries
Clinical research	US NCI CTEP – INCa coordinates French clinical research centre's participation in the US NCI mass solicitation for early phase clinical trials IRCI – International Rare Cancers Initiative (INCa to join the Board of the International Rare Cancers Initiative and contribute to the development of the initiative and delivery of its research objectives)		
Prevention	WHO (World Health Organization) - Framework Convention on Tobacco Control		
Diagnosis/ screening			Thailand : Research study funded by INCa: "PapilloV - Human papilloma virus (HPV) infection and cervical lesions in HIV-infected women receiving antiretroviral therapy in Thailand (Principal investigators: Institute for Development Research and Ministry of Public Health of Thailand) Laos: Research study funded by INCa: LaoCol-VP – Efficacy & cost/effectiveness of cervical lesion screening by HPV detection vs pap smear in HIV-infected women in Laos (principal investigator: Centre Infectiologie Charles Mérieux du Laos)
Cancer care / survivorship		CHRODIS PLUS (joint action dedicated to chronic diseases)	
Cancer registries			IARC/Global initiative for cancer registry development in LMIC (low and middle-income countries) – support to regional network hubs/ capacity-building in Sub-Saharan French-speaking countries/ development of training materials & modules in French (to be formalised)

	International consortia	Europe & High income countries	Low and middle-income countries
Capacity-building / training / research programmes		Flag-ERA (Era-net on digital medicine)	Senegal - cooperation agreement/ research & public health, capacity building, training, cancer control Ivory Coast - cooperation agreement research & public health, capacity building, training, cancer control Gabon – research programme on HPV/cervical cancer COFAC-Col (African Consortium for Cervical Cancer Control) MULTIETHNIC-PROSTABASE (Clinical and biological centralised database on ethno-geographic factors associated with metastatic prostate cancer progression in the Caribbean and Africa) WoRTH (strategy to enrol women in breast and cervical cancer screening programmes, in 3 Mediterranean countries)
Research & public health networking	IARC - Governing Council ICRP - International Cancer Research Portfolio ICISG International Cancer information service group Multilateral agreement (UICC, WHO) Bilateral agreement (US NCI, NCC China, NCC Japan, Taiwan Ministry of Research)	European Commission expert group on cancer control	Coordination with AORTIC - African organisation for research & training in cancer Setting-up of a Network for HPV/ cervical cancer control research with 5 French-speaking African countries
Global health	Cancer research funder annual meeting SUCCESS Project (Cervical cancer, Secondary prevention in 5 LMICs)		

REVIEW OF CANCER RESEARCH FUNDING AND EVALUATION

Trends in cancer research funding

CANCER RESEARCH FUNDING IN 2019

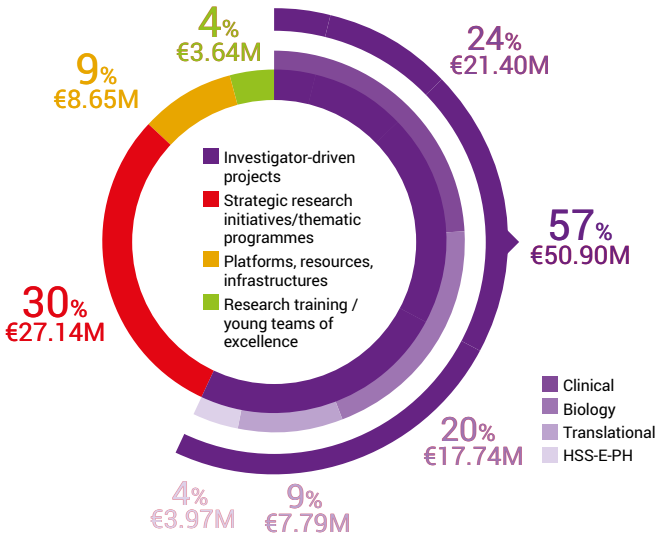
In 2019, the total funding awarded to cancer research programmes amounted to €90.32M (€39.42M from INCa, €24.28M from DGOS, €23.20M from Inserm for ITMO Cancer-Aviesan and €3.42M allocated by the French Cancer League and IReSP within the framework of the programmes in partnership with INCa, CLIP² designation and Tobacco programmes, respectively).

Figure 68 shows the breakdown of multi-year funding for 2019 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.

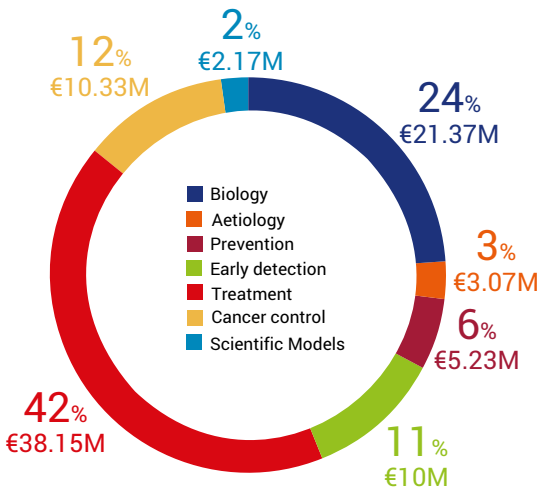
This figure shows that 57% of the allocated budget was devoted to competitive investigator-driven calls for proposals, managed by INCa, including funding from DGOS. Support for platforms, resources and infrastructures represented 9% of the funding in 2019 and include CLIP² designation and support for equipment. Strategic research initiatives and thematic programmes represented 30% of total funding in 2019 and also include the thematic research programmes managed and funded by ITMO Cancer-Aviesan.

FIGURE 68
2019 MULTI-YEAR CANCER FUNDING BY PROGRAMME TYPE (INCA, DGOS AND ITMO CANCER-AVIESAN): €90.32M INVESTED



The funding allocation according to the CSO classification highlights that research projects under the treatment category represented the most significant investment in 2019 (€38.15M) (Figure 69). The biology category represented €21.37M in 2019 (24% of 2019 investments) and decreased compared to 2018 (30% of 2018 investments). Cancer control, survivorship, and outcomes research issues represented 12% of investments (€10.33M), while the early detection, diagnosis and prognosis category represented 11% (app. €10M). The prevention category represented 6% of investments in 2019 (€5.23M) and is stable compared to 2018.

FIGURE 69
2019 MULTI-YEAR CANCER RESEARCH FUNDING ACCORDING TO THE CSO CLASSIFICATION (INCA, DGOS AND ITMO CANCER-AVIESAN): €90.32M INVESTED



CANCER RESEARCH FUNDING OVER THE 2007-2019 PERIOD

Since 2007, a total of 3,295 projects have been funded through the different competitive calls for research proposals and grants for designation for over €1.24Bn.

As shown in figure 70, the investigator-driven calls for proposals of the four main research areas represented a total of 50% of 2007-2019 investments, or approximately €625M. Strategic research initiatives aiming to primarily support precision medicine initiatives and thematic programmes represented 25% of cancer research investments (€312M). Importantly, support for resources and infrastructures represented 21% of total funding, approximately €263M, which highlights the determination 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.

FIGURE 70

2007-2019 MULTI-YEAR CANCER FUNDING BY PROGRAMME TYPE (INCA, DGOS AND ITMO CANCER-AVIESAN): €1.24BN INVESTED

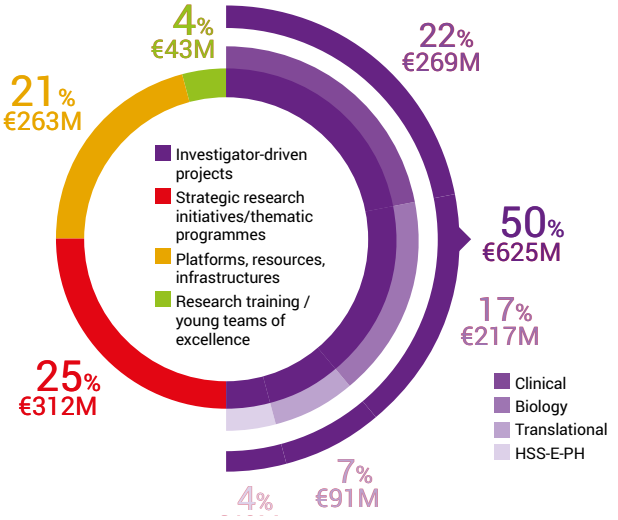
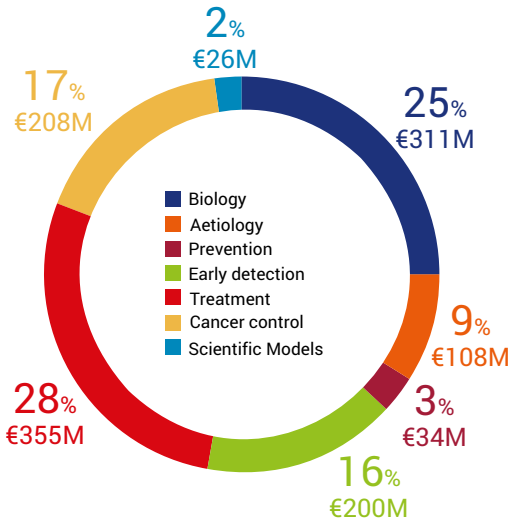


FIGURE 71

2007-2019 MULTI-YEAR CANCER FUNDING ACCORDING TO THE CSO CLASSIFICATION (INCA, DGOS AND ITMO CANCER-AVIESAN): €1.24BN INVESTED

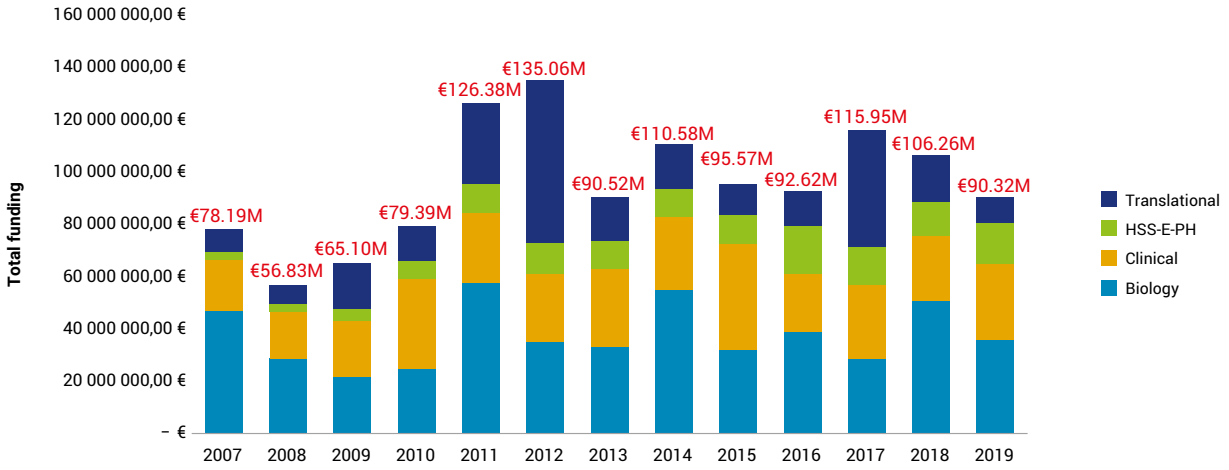


TRENDS IN CANCER RESEARCH INVESTMENTS OVER THE 2007-2019 PERIOD

Figure 72 presents the trends in total funding according to the cancer research fields over the 2007-2019 period. 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 72

TRENDS IN TOTAL FUNDING ACCORDING TO CANCER RESEARCH FIELD OVER THE 2007-2019 PERIOD (INCA, DGOS, ITMO CANCER)



Review of paediatric cancer research

Every year in France, 1,750 children aged 0-14 years and 800 adolescents and young adults are diagnosed with cancer. Despite improving survival rates of up to 80%, cancer is still the leading cause of death, and for some, there is no valid therapeutic option. In addition, two-thirds of survivors present with delayed side-effects or second cancers that could manifest throughout their lives. Research efforts must be pursued to overcome the challenges involved in increasing both the recovery and quality of recovery of young people with cancer..

For this reason, INCa is making the fight against childhood cancers a priority and proposes concrete measures aimed at boosting all research disciplines (fundamental, translational, clinical, social and human sciences/epidemiology/public health):

- Understanding the causes of paediatric cancers;
- Identifying new avenues for treatment, in particular for childhood cancers that are incurable or refractory to existing treatments;

- Fostering access to innovative medicinal substances for children;
- Reducing the adverse effects of treatments and long-term sequelae for children who are treated for cancer.

These take the form of structuring actions through different calls for proposals:

- The identification of new treatment targets requires an ever-greater understanding of tumour formation and development mechanisms. Achieving this detailed understanding involves, among other things, studying the genetic alterations present in tumour cells, which is made possible by tumour genome sequencing;
- The programme for all refractory tumours in French children has received specific funding for the MAPPY ACT trial since 2015, via the national programme for hospital clinical research on cancer (PHRC). The anomalies that are identified then serve to refer the sick children to the most suitable clinical trials;
- Within the framework of the ICGC International Consortium, France has undertaken to fund whole genome sequencing of two paediatric tumours, out of the eight that it is financing in total: one concerns retinoblastoma, and the other Ewing's sarcoma. A third programme on Leiomyosarcoma also concerns children;
- Two projects to sequence brain tumours in children are being undertaken by other partner countries within the framework of the ICGC: Canada and Germany.

In addition to research into new genetic targets, programmes targeting a better understanding of host-tumour interactions (in particular immunological aspects) or mechanisms regulating gene expression (epigenetics) are being developed in the field of paediatrics.

Those children suffering from particularly complex cancers or who find themselves in treatment failure situations must be referred rapidly to **clinical trials that allow them access to innovative drugs**.

Paediatric drug development was announced as one of five research priorities for the coming years by international public bodies and charities that fund cancer research, from 23 countries. They met at the Institute in January 2014 for the third International Cancer Research Funders' Meeting.

Clinical trials have been tailored to the arrival of targeted therapies supporting access to innovative drugs has been undertaken with the AcSé programme

Launched in June 2016, the AcSé e-SMART trial is aimed at children, adolescents, and young adults. It is the first clinical trial of its kind in paediatric oncology and is also sponsored within the framework of the European ITCC (Innovative Therapies for Children with Cancer) consortium. AcSé e-SMART aims to test several innovative drugs (targeted therapies, immunotherapies, alone or in combination) in one and the same trial according to the molecular profile of the child's tumour. The programme is sponsored by the Gustave Roussy Institute and co-funded by the French National Cancer Institute, the Imagine for Margo association, the ARC Foundation, and also pharma companies who provide funding, in addition to supplying their drugs.

The paediatric early-phase clinical trial centres (CLIP²) were the focus of a new call for applications for designation in 2014 and 2018 in order to extend their remit to paediatric cancers. Seven CLIP² with paediatric activity were designated in 2019 with financial support from INCa and the French Cancer League. Within the framework of the public-private partnerships and innovative drug-related calls for proposals, a project was selected in 2019 to test a drug developed by Roche.

The Institute is also active on a European level to foster the development of anti-cancer drugs for children. It helps identify clinical situations that should benefit from priority developments and propose them to the European Medicines Agency, and works on proposals for amendments to the European Regulation on medicinal products for paediatric use.

An SFCE (Société française de lutte contre les cancers et les leucémies de l'enfant et de l'adolescent) cooperative intergroup for paediatric oncology was designated at the end of 2014 and in 2017.

Its objectives are to:
- Develop and conduct therapeutic trials to **optimise treatments and test dose de-escalation, in order to reduce the side effects of treatments**;
- Accelerate and increase inclusions of children and adolescents in clinical trials;
- Take part in the development of multi-organ clinical trials and in personalised medicine projects organised by the Institute;
- Develop and submit translational research projects for the calls for proposals of the Institute;
- Help **structure** the research initiated and steered by the Institute, notably by helping to involve paediatric oncology researchers in multidisciplinary programmes.

To **boost research momentum and foster the links between fundamental and translational disciplines**, the 2016 edition of the Integrated Research Action Programme on cancer (PAIR) was dedicated to paediatric cancers in partnership with the French Cancer League and the ARC Foundation. Three projects have been supported since 2017. The programme is the subject of annual monitoring.

In 2019, 31 paediatric research proposals (projects and applications) were selected for funding, out of the 255 total funded projects, within the framework of the different research programmes launched. The total funding allocated to childhood cancer research represented €14.14M, representing 15.6% of 2019 investments (€90.32M).

Embracing the open science agenda through coordinated approach

The INCa Open Science policy, introduced in 2014, is fully aligned with the National Plan for Open Science launched by the French Minister of Higher Education, Research and Innovation, Frédérique Vidal, in July 2018.

In order to implement this national plan in our daily procedures, we have adapted our grant regulation which entered into force on 1 January 2020. These new articles were voted by the board of directors in December 2019.

Implementation of the roadmap coordinated by INCa to measure and assess the impact of biomedical research projects- French research funder statement (2017-2021)

Focus on

- pilot phase to test the template in 'real-life'
- support the implementation of ex-post impact studies (portfolio analysis)
- adopt impact assessment as a core strategy lobby to initiate a national forum

INCa developed his policy through cooperation with other French funding bodies: ADEME, ANR, Anses, ANRS and Inserm and in collaboration with the Centre for Direct Scientific Communication (CCSD), the Committee for Open Science, the Institute of Scientific and Technical Information (INIST) to better define and coordinate efforts to promote open access to publications and data.

Our policy has two main objectives:

Promote open access to publications

The funded project coordinator and partners must undertake to submit the scientific publications resulting from the research project to an open archive, either directly in HAL (the national repository) or via a local institutional archive. In addition, INCa recommends giving preference to publication in open access journals or books.

Contribute to open research data wherever possible

INCa supports European and international alignment efforts on the structure of open research data. In line with its policy, INCa will require all projects funded in 2021 onwards to produce a Data Management Plan (DMP), setting out how research data will be produced, reused, stored, protected, disseminated and, where applicable, retained for a significant period of time. The aim is to improve forward planning and rigorous monitoring throughout the research process. To be consistent, INCa follows the recommendations of the Committee for Open Science, and we will use the Science Europe DMP template, which aims to promote the international alignment of research data. The DMP will be updated as the project progresses in accordance with INCa's grant regulation.

In parallel, INCa has been an ORCID (Open Researcher and Contributor Identifier) member since 2014. We have chosen to integrate the French ORCID community launched in October 2019 with 34 institutions engaged in higher education and research. This membership is one of the French commitments of the Open Government Partnership (commitment 18: building an open science ecosystem).

The San Francisco Declaration on Research Assessment (DORA) - "Putting science into the assessment of research"

In October 2019, INCa signed DORA. It has become a worldwide initiative covering all scholarly disciplines and all key stakeholders, including funders, publishers, professional societies, institutions, and researchers.

More specifically for funding agencies, DORA recommends two measures addressing research assessment

When evaluating research proposals, INCa will place an emphasis on the quality of the applicants' research and not on journal impact factor or the journal in which the article was published. The suggested practices will be included in our application and review processes.

3

Strategic topics for advancing cancer research

In accordance with the missions assigned by the government, INCa have provided continuous financial support for research projects (and maintained and increased this support despite budget restrictions) based on transparent methods, international evaluation and participation of patient advocates in all the scientific evaluation committees for INCa's calls for proposals, in every field of cancer research.

The third part of this report presents the strategic research topics proposed by the French National Cancer Institute, in line with the recommendations issued by the International Scientific Advisory Board.

The years 2019 and 2020 represent a pivotal period for French institutional cancer research planning. On one hand, 2019 marks the end of the third Cancer Control Plan and the preparation of a new ten-year strategy at the request of the government. On the other, the French Ministry of Research is preparing a multi-year research programming law (MYRPL), promising a significant and unprecedented financial effort, to further boost all areas of French scientific research.

These two coinciding events will provide INCa with a unique opportunity in the coming years, both to reinforce its recurrent actions and to launch new programmes, taking into account not only the priorities defined by the ten-year cancer control strategy (TYCCS), but also the recommendations of INCa's International Scientific Advisory Board, aimed at consolidating and improving the recurrent actions of INCa and its partners, ITMO Cancer-Aviesan and charities, that support French cancer research. Thus, INCa is currently working on the Institute's next objectives and performance contract with the State (COP), which will constitute the solid basis for the implementation of novel TYCCS actions.

INCa's Research & Innovation Division, together with ITMO Cancer-Aviesan, has played a key role in the preparation of both the COP and the TYCCS. Separate and common think-tank workshops have been organised to identify the research priorities for the next coming years and to propose new research actions addressing the three 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, and addressing poor prognosis cancers in adults and children. In the meantime, and in agreement with a previous recommendation by the SAB, INCa's Research & Innovation Division performed an internal SWOT analysis that helped identify new paths of improvement of INCa's recurrent actions in research funding and structuring. A number of these, such as for instance an increase in the success rate of the investigator-driven programmes, should be significantly improved within the context of an increase of the French Research budget required by the future MYRPL.

At the time of writing of this report, the government's decisions are still unknown regarding the level of financial support to be provided to the TYCCS. The possibility remains that setting priorities over time will be necessary, as underlined by INCa's SAB. Thus, the additional actions that have been detailed in the TYCCS will not be developed further in the following sections. However, while it the TYCCS is clearly a means to progress further in the three priority areas defined above, this does not mean that INCa has been inactive in these fields of research over the past 10 years. Although not specifically targeted, research on poor prognosis cancers is already supported by several actions. For example, a number of researcher-driven projects funded by INCa already tackling this question are funded by PLBIO, PRTK and PHRC-K grants. Again, an increase in the budget for these calls through the future MYRPL should contribute to the improvement in the knowledge and treatment of these cancers. Likewise, the recent or upcoming actions through the PAIR programmes (Pancreatic Cancers in 2018; Brain Tumours in 2021; Obesity & Cancer, in preparation) and the recent additional funding allocated to paediatric cancers, should be instrumental in this regard.

In addition, in order to take a quantum leap in this 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 in 2020 and 2021.

Prevention, which is one of the three priorities of the TYCCS, will be supported further through the SIRIC, PHRC-K, and HSS-E-PH programmes. Importantly, a recent effort has been made on cancer prevention through the programme for research and intervention proposals to reduce and control tobacco consumption. This programme will be continued and extended further to other addictions, such as alcohol, addressing a major recommendation of INCa's SAB. Another action regarding cancer prevention and early detection was jointly initiated by INCa and ITMO cancer Aviesan in 2019, to support basic research on preneoplasia. This programme will be renewed in 2020.

The following sections briefly describe the future directions of the research that will be further supported and improved by INCa's programmes. Obviously, this will be implemented as soon as more information becomes available as to the amount of support that the French government will provide to the TYCCS, as well as the roll out of the next objectives and performance contract within the MYRPL context.

PURSUING AND STRENGTHENING CANCER RESEARCH PROJECT FUNDING AND STRUCTURING

The year 2019 marks the end of the 3rd Cancer Control Plan. The evaluation of this plan and the results obtained in the course of this year help highlight the beneficial effects of the different programmes and projects promoted, and define measures and actions to be implemented to develop basic and translational research. These actions could be included in the new ten-year strategy and the objectives and performance contract.

In this context, and considering INCa's research missions:

- Recurrent actions related to the funding of basic cancer research (PLBIO, thematic AAP) and translational cancer research (PRTK, TRANSCAN) will be pursued as part of a global strategy to promote results (continuation of "successful" projects, assistance with transfer to clinical practice, communications with congress reporting, etc.), and by acquiring new tools for easier management of calls for proposals. A particular emphasis will be given to a possible increase in the PLBIO success rate, including by requesting further funding through the upcoming LPPR;
- A special effort will be made to utilise the data collected in the framework of research projects, through molecular genetics centres or in the framework of the biological and clinical databases. These data must be compatible with collation and interoperability (particularly in the context of the construction of the INCa database) but above all it must be possible to reuse them for new academic research projects or in connection with industry;
- Different evaluation methods will be implemented to assess the structuring effect of the SIRICs and Canceropoles:
  - Monitoring indicators will be defined to help the SIRICs implement their actions for the years 2021-2022 following the mid-term evaluation to be carried out in 2020. The third wave of designations could be the basis for a reflection on the changes to be envisaged in order to optimise and adapt structures to new issues,

  - A standardised survey will be conducted among all researchers who have benefited from funding between 2011 and 2018, as part of the "Emergence" call for proposals by all the Canceropoles, in order to evaluate the relevance and impact of this unique research support scheme;
- A general evaluation of the Canceropoles under the last designation process (2018-2022) will be carried out next year;
- Means will be provided to promote patient access to innovations: new measures will be proposed to develop the constitutional oncogenetics scheme in order to meet the expectations of healthcare professionals and to improve access to the system (taking into consideration heterogeneous practices, certain regions with insufficient coverage, or deficits in access for certain cancers such as digestive cancers for example):
  - Consolidate sites that provide local services in the face of increasing demand in order to identify a maximum number of people at a high risk of cancer and offer them personalised prevention and monitoring measures,
  - Control time limits (especially in the case of possible prescriptions for new targeted therapies),
  - Develop activity in the most poorly resourced regions by creating new consultation sites in areas with poor coverage or high demand,
  - Recognise the skills and the quality of the care provided (designation system through a call for applications);
- Increasing number of innovative drugs (whether associated with the evaluation of biomarkers or not) and new therapies for individuals with specific genetic abnormalities (germinal and/or somatic) are being developed and granted marketing authorisation. It is therefore necessary to define the key preliminary information for these individuals and their relatives and for health professionals. New expert groups will therefore be set up to develop and update new national recommendations;
- Incentive measures, through a non-competitive call for applications, will be offered to hospital molecular genetics platforms to implement new sequencing techniques (RNAseq) and deploy the analyses of new emerging biomarkers.

In order to meet the challenges of the future, it is therefore necessary to enhance valuation of the actions already undertaken and to consider how to improve them (in this context, for example, the definition of areas of collaboration between SIRICs and Canceropoles) in order to lay a solid foundation for future actions, to provide answers to questions in a transdisciplinary and complementary manner, and to provide the means for the quickest possible transfer of research findings to the patient's bedside.

STRATEGIC OUTLOOK IN CANCER CLINICAL RESEARCH

Conducting clinical studies has become more complex, time-consuming and costly. Recruiting appropriate participants is increasingly difficult, especially when it comes to new treatments targeting very specific abnormalities that affect only small patient populations. The AcSé programme is continuing and progressing for children (AcSé e-SMART), while the inclusions in the 2 ongoing adult AcSé studies (AcSé-Nivolumab and AcSé-Pembrolizumab) will soon be discontinued. It is now time to move forward, and analysis is underway within the framework of the next ten-year strategy to build new kinds of clinical trials, especially with regard to the evaluation of targeted therapies. This new concept can only be built in collaboration with clinical research experts (clinicians, statisticians, etc.), other agencies involved (ANSM, HAS), and also DGOS and CNAM. Another important stakeholder close to this field is the "Plan France Medecine Génomique" (PFMG), and we will have to work closely with its representatives to facilitate equitable access to innovative therapies in clinical trials for patients diagnosed on INCa's genomics platforms or on PFMG sequencing platforms. The challenges to be met will include:

- Identifying relevant indications;
- Obtaining drugs from the pharmaceutical industry;
- Working on treatments combinations and providing funding;

while respecting patient safety and reducing inequalities in access to treatment.

Another important objective is to improve cancer research structuring further. After bringing stakeholders together in the CART T-cell field in the last 2 years, it is time to build a national research network on CART T-cells, including fundamental researchers in immunology and in the field of cancer, researchers from the world of vectorology and production platforms and clinicians from the field of haematology and solid tumours in adults, and paediatricians. This continuum from fundamental to clinical research could certainly help improve the academic development of these targeted therapies and academic clinical trials in this field, in France.

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

The contribution of research on human and social sciences, public health, and epidemiology to the fight against cancer, has been supported by INCa since its creation. In the coming years, as a continuation of the work previously undertaken, INCa will mainly use three tools to support the boosting of research in this field: funding research; promoting and disseminating knowledge, and setting up researcher networks, evaluating calls, and producing HSS data on cancer.

Regarding research funding, the HSS-E-PH department will lead 5 calls for proposals/PhD candidates. Alongside these calls, a PhD research programme will be launched in collaboration with IReSP in the field of addiction. Moreover, in accordance with the prevention area of the next ten-year strategy, we will set up a research programme for young researchers on tobacco and alcohol. The missing link between the INCa-IReSP call for proposals and the call for PhD candidates, this project aims to propose a call for expressions of interest, in order to develop the scientific community around tobacco and alcohol, by encouraging young researchers to invest in these themes. The innovative approach proposed will make it possible to achieve this objective and guarantee the quality of research with support from international experts, and to build a network of researchers. The goal of 2020 is to set up a pilot version of this innovative scheme. The expected deliverable of this project is the involvement of and support for 8 young researchers and their projects on the themes of tobacco and alcohol. An analysis of this call will be carried out after the project funding phase to develop this system and roll it out if necessary, on priority research themes of the addiction fund for 2021.

Research chairs rely on excellence and offer a valuable framework for innovation and a motivating structure for top students and young researchers. The Institute's International Scientific Advisory Board has welcomed the use of such programmes. INCa has supported three chairs to date. In 2020, a chair on patient empowerment will be launched.

Developing links between researchers and promoting the spreading of knowledge are key forms of leverage for structuring research on human and social sciences, epidemiology, and public health. Regarding the setting up of researcher networks, we will organise PHIR seminars: one on emerging projects supported by INCa, and another one on methodological aspects in PHIR. We will launch a seminar on HSS-PH, which will include supported research from the "primary prevention: Diet, Alcohol, Physical Activity" call, and we will launch the first meeting of the PhD network initiated by INCa. In the field of tobacco, INCa-NCI will lead a workshop on the "Current State of Tobacco Cessation Interventions and Tobacco Prevention". 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 concrete research questions to reduce tobacco use among priority populations. Participants will work together to develop a path to reinvigorate tobacco control research by educating and motivating researchers on novel cessation interventions.

We have a lack of data and research in the field of Precision Medicine and oncogeriatrics form the viewpoint of human and social sciences: we will support a symposium on this topic.

Moreover, stimulating a drive for research on human social and sciences and public health in the "inter-cancéropole" and "interSIRIC" working groups and evaluating the value of one regular yearly event remain a priority.

Regarding the issue of programmes evaluation, it would seem necessary to initiate an in-depth study about discipline, problematic CSO classifications, research teams, etc. This research should include all projects submitted to and funded by INCa: call for proposals on human and social sciences, public health, and epidemiology, but also some specific projects, intervention research or calls for applications for PhD support. In 2020, we will start an evaluation programme focused on the projects funded in the call for research proposals on human and social sciences. This work will focus on identifying the knowledge produced through this call. It will also provide a status report of the research supported in these fields, identify gaps in uncovered areas, and analyse strengths and weaknesses.

Finally, the French Cancer Barometer, a population-based-survey, is carried out every five years and is, to date, one of the few national studies conducted to investigate individual perceptions linked to cancer risk factors. In 2020, we will commence the 4th edition of this national study.

RESPONSIBLE, ACCESSIBLE, TRANSPARENT AND RELEVANT RESEARCH AND INNOVATION

A country's ability to conduct cutting-edge research and technological development depends on researchers, innovative ideas, collaborations, structures, and tools. Thanks to these investments, research generates benefits for the population. Scientific policies needs reflection and evaluation, in particular with the aim of providing knowledge to help decision-making, inform public debate, etc. This is, moreover, a need expressed by decision-makers at national and international level, in particular because the increasing pressure on public budgets leads research funders to have to demonstrate their social utility (i.e. that research actually provides benefits to its beneficiaries). Moreover, we are currently seeing a substantial part of the research effort being directed towards major societal challenges.

Open science

Within the framework of our missions, it is necessary to build a long-term vision, and to evaluate the results of research in order to be able to highlight and enhance the impacts observed (socio-economic fallout, improvement in the incidence of cancer, life expectancy, etc.). Following the work carried out in recent years, impact assessment will continue thanks to the involvement of many research funders. This mobilisation will notably involve the use of various databases which will make it possible to describe the research and innovation supported by the Institute. Promoting scientific results could be an effective instrument to help decision-making in research and will allow us to inform scientific communities and society about our contribution to cancer research.

As part of our missions, we will continue our participation in the promotion of open science by adopting a concerted approach and joint commitments with partner research institutions. The Institute will also continue its engagement in national and international discussions to identify new ways of disseminating research results and accelerating their availability.

In addition, we will strengthen the Institute's prospective capacity to identify research fronts in order to be able to anticipate future research efforts as much as possible.

This strategy of openness will allow the Institute to get involved in new forms of societal participation in research processes through the implementation of projects. This will also allow all stakeholders to work together to better meet the needs and expectations of society and will help develop the role of science in society. Citizens must be involved in the design and production of research and in understanding the messages linked to research.

Defining a research agenda to define a new way of approaching translational research (transferring prospective innovations from laboratory to bedside)

It is increasingly acknowledged that ongoing interactions between basic researchers, the medical profession, public health professionals, patients and their advocates facilitated by multidisciplinary research organised on the same site (clinical and/or academic) have the potential to accelerate the transfer of scientific knowledge into innovations, and offer new avenues for prevention and medical treatment of diseases. This type of research is commonly named translational research.

Much is owed to these advances in translational biomedical research, constructed on the "bench-to-bedside" paradigm. However, scepticism remains about the short-term value of these emerging technologies in reducing the burden of cancer. In addition, little data is available on the best strategies for implementing "innovations" in clinical practice, ensuring the quality of testing and decision-making, informing practitioners, patients, and the general public, and measuring the impact of these applications on population health. This is mainly due to the consideration of translational research, by many institutions and researchers, as a process for transferring information from research laboratories to care facilities, resulting from close collaboration between fundamental researchers (including biologists) and clinicians. The main objective consists in translating preclinical results into clinical research, validating biomarkers, characterising the mechanisms of action of therapeutic targets, and establishing partnerships with the pharmaceutical industry in order to develop new anticancer agents.

However, the conceptualisation of translational research has undergone change in recent years, indeed, translational research is increasingly interpreted as the body of studies that ensures that new treatments and research knowledge will actually reach patients, improve quality of care in everyday clinical practice, and, eventually, have an impact on the healthcare system. The production of data and indicators on these aspects is critical for effective dissemination. This new perspective would allow us to go beyond the classic paradigm. This approach has seen very little development and financial support by health agencies worldwide to date.

To facilitate successful and responsible integration of innovations, the idea would be:

- To identify research-based evidence;
- To characterise the mechanisms enabling the adoption of these innovations;
- To support the integration of these innovations.

Through a multidisciplinary task force, we would like to work on disseminating some recommendations that will help develop, support, and encourage translational research in population health.

STRENGTHENING CHILDHOOD CANCER RESEARCH

Research on paediatric cancers has always been a constant concern for INCa. It is necessary to continue the ambitious research actions in the context of recurrent calls for proposals and the organisations already set up. In 2019, additional annual funding of €5M helped to strengthen this willingness to tackle childhood cancers. This additional funding will be renewed by the French Ministry of Research in the coming years and will contribute to INCa's ten-year cancer control strategy.

Proposing integrated and multidisciplinary projects

The fundamental, translational, clinical, human sciences, social science and epidemiology research programmes that have been initiated, as well as the monitoring and evaluation of specific organisations (CLIP² centres, cooperative intergroups, AcSé programme, etc.), will be continued.

Interdisciplinary research programmes will be set up. These programmes will address the following issues:

- The causes and origins of paediatric cancers;
- The onset of paediatric cancers;
- The mechanisms of early development;
- Treatment resistance in certain childhood cancers;
- The challenge of limiting treatment-related side-effects, including fertility preservation.

These innovative interdisciplinary research programmes should make it possible to attract new scientific disciplines alongside researchers and clinicians. Risk-taking will be encouraged, appealing for interdisciplinarity and originality through the support of "high-risk / high-gain" projects.

Sharing of clinical-biological data is essential for these rare cancers on a supranational level and the link with the PFMG programme will be guaranteed.

Guaranteeing access to the most appropriate therapies, clinical trials, innovation

New trial models, specifically devoted to childhood cancers, will be proposed, primarily based on existing structures and programmes: CLIP^2, SIRIC, AcSé programmes.

Moreover, pharma companies will be encouraged to develop drugs to treat paediatric cancers. In this aim, INCa will continue to be involved in European regulatory measures to encourage paediatric drug development.

It is important that these actions conducted by INCa be coordinated with all parties involved in research, and promoted and linked to European initiatives

Fertility preservation

In this aim, INCa will prepare one or more interdisciplinary research programmes with the community on prevention and reduction of the risks of impaired fertility, and treatment for children and young adults.

INTERNATIONAL COMMITMENTS

Cooperation between key European and international players in cancer control and research opens up considerable opportunities for progress, both in basic research, prevention, screening, and early diagnosis, as well as in access to quality services and innovative therapies. The strengthening of international and European cooperation could constitute a strong objective of the next strategic framework for cancer control in France. INCa's international and European actions will be focused on a certain number of key areas where international cooperation could bring real added value (rare cancer, data sharing, exchange of good practices, research consortium, coalition for better regulation, drug prices, etc.) with the following priorities:

- Strengthen international regulations to better protect individuals and initiate joint actions at a European level;
- Strengthen research and care networks (rare cancers, paediatric cancers, cancers with poor prognosis);
- Perform and share benchmarks to identify innovative practices and thus encourage progress;
- Invest in international data sharing for the benefit of the patient;
- Strengthen bilateral cooperation with most developed countries;
- Develop international consortia on priority or promising research fields.

4 Appendices

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 110 worldwide organisations from Australia, Canada, France, Japan, the Netherlands, United Kingdom, and the United States. INCa joined this partnership in 2009.

ICRP International Cancer Research Partnership

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 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

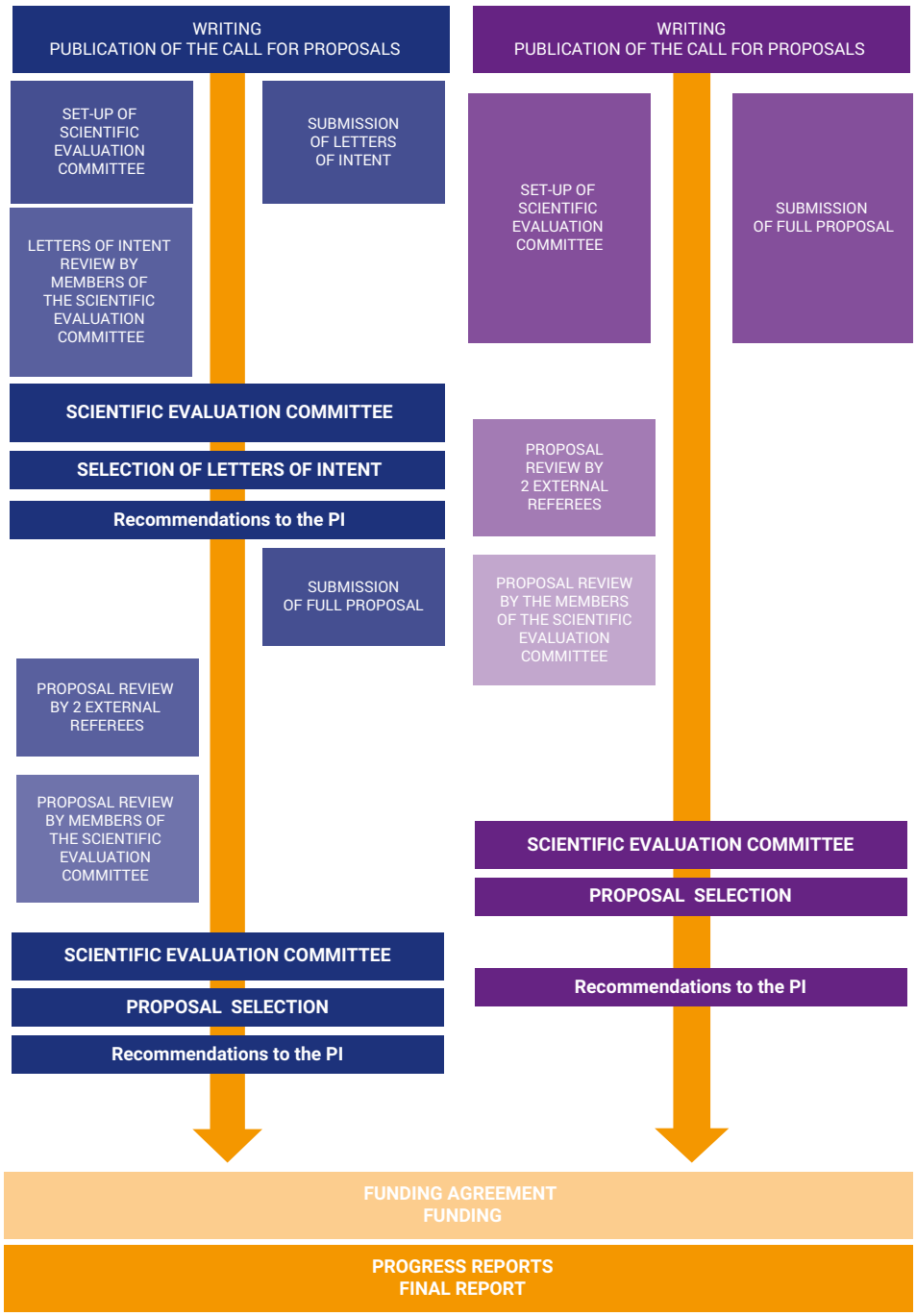
- **CSO 4 Early Detection, Diagnosis, and Prognosis**
  - **4.1** Technology Development and/or Marker Discovery
  - **4.2** Technology and/or Marker Evaluation with Respect to Fundamental Parameters of Method
  - **4.3** Technology and/or Marker Testing in a Clinical Setting
  - **4.4** Resources and 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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