

SCIENTIFIC REPORT

2020

ACTIONS FOR CANCER RESEARCH

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

Working group

Scientific coordination

Karima BOUROUGAA, PhD, Research and Innovation Division, French National Cancer Institute

Contributions

Research and Innovation Division, French National Cancer Institute

ITMO Cancer-Aviesan

This document should be cited as: © Scientific report 2019, Institutional Document Collection, INCa, octobre 2021.

This document is published by the French National Cancer Institute, which holds the rights.

The information contained in this document may be reused if:

- 1) their reuse falls within the scope of Law N° 78-753 of 17 July 1978 as amended;
- 2) this information is not altered and their meaning distorted;
- 3) their source and the date of their last update are mentioned.

This document was published in October 2021. It is available at the following address:

Institut national du cancer (INCa)

Pôle recherche et innovation

52, avenue André Morizet – 92100 Boulogne-Billancourt

e-cancer.fr

© 2021. Institut national du cancer (INCa)

INTRODUCTION

ACTIONS FOR CANCER RESEARCH



SCIENTIFIC REPORT 2020

2020

was a year of challenges for everyone. Facing the health crisis caused by the COVID-19 pandemic, the French National Cancer Institute has both worked to maintain the activities of the oncology sector and continued with the projects underway, while remaining attentive to the needs of the French people. All these challenges were met thanks to the exemplary mobilisation of all our teams.

IN ADDITION TO THE RESEARCH ACTIONS PRESENTED IN THIS SCIENTIFIC REPORT, the Institute has pursued several projects, such as the work on limiting tensions in the supply of anti-cancer drugs, the completion of the second Horizon Scanning cycle to identify breakthrough drugs in development, and the implementation of our Living Lab, the first of its kind run by a public institution. These projects and actions testify to our will to continue to act, to adapt, to listen and to project ourselves, despite the very particular context of this past year.

BY EARLY 2020, the pandemic had taken over almost all public space, leaving very little room for prevention messages about other diseases. This lack of information was regretted by a large number of French people. As soon as the first lockdown period was over, INCa decided to relaunch its communication campaigns in response to their demand and to continue to support health professionals and patients in this very special health context. By choosing to have a strong presence in this very special year, the Institute has continued to change the way the French think about their lifestyles, the first step towards changing their behaviour. The evaluations carried out at the end of the campaigns attest to their effectiveness in this area.

NEVERTHELESS, this pandemic has opened up new opportunities and encourages us further to adapt. For example, the emergence of telemedicine could be expanded to cancer patient-related activities, such as prevention, screening, treatment, etc. In addition, it would be worthwhile taking advantage of the eagerness for the COVID-19 vaccine to increase cancer vaccination uptake further, while supporting and strengthening cancer research on infectious risks.

FINALLY, 2020 ALSO MARKED THE COMPLETION OF THE TEN-YEAR CANCER CONTROL STRATEGY PROJECT. In September, INCa launched an unprecedented citizen consultation to ensure that the strategic orientations and actions envisaged by the Institute met the expectations of the French people. This consultation also provided an opportunity to comment on all the proposals and to add new ones. A large-scale communication campaign invited citizens to read the Institute's entire proposal and to share their opinions and proposals and more than 23,200 votes were cast. The qualitative study revealed that the participants were very supportive of the ten-year cancer control strategy project. Indeed, 91% of them considered the Institute's overall proposal to reduce cancer in France to be relevant. During the online consultation, positive votes ranged from 85% for prevention to 95% for cross-cutting measures, with strong support for cancer research actions. In addition to this strong support, the consultation also enabled the Institute to enhance its initial roadmap. After an analysis of the 561 contributions submitted, 11 actions were added, based on proposals from Internet users, mainly in the areas of prevention, limiting after-effects, and improving quality of life. Thirty-five actions from the strategy have been completed thanks to the many contributions. In November 2020, this enhanced version of the draft cancer control strategy was presented and unanimously approved by the Institute's Board of Directors. The draft version was submitted to the French government in December.

ON 4 FEBRUARY 2021, THE PRESIDENT OF THE FRENCH REPUBLIC set out the content of the new ten-year cancer control strategy, setting ambitious targets, and granting a 20% increase in the funding to be devoted to it. Of the 234 actions proposed by the strategy, 78 will be launched from 2021. All of them will serve our fellow citizens.

Professor Norbert Ifrah, MD

■ Chairman and CEO of the
French National Cancer Institute

TABLE OF CONTENTS

ACTIONS FOR CANCER RESEARCH



INSTITUT
NATIONAL
DU CANCER

SCIENTIFIC REPORT 2020

Introduction	03
Key figures	06

1

**The international
scientific advisory board**

8

2

**2020 cancer research
activity report**

16

3

**Strategic topics for
advancing cancer research**

144

4

Appendices

160

KEY FIGURES

ACTIONS FOR CANCER RESEARCH



INSTITUT
NATIONAL
DU CANCER

SCIENTIFIC REPORT 2020

2020 total investments:

€44.51M in biology and basic sciences including

€5.02M dedicated to specific paediatric cancer research programmes

€23.57M
in clinical research

€8.17M

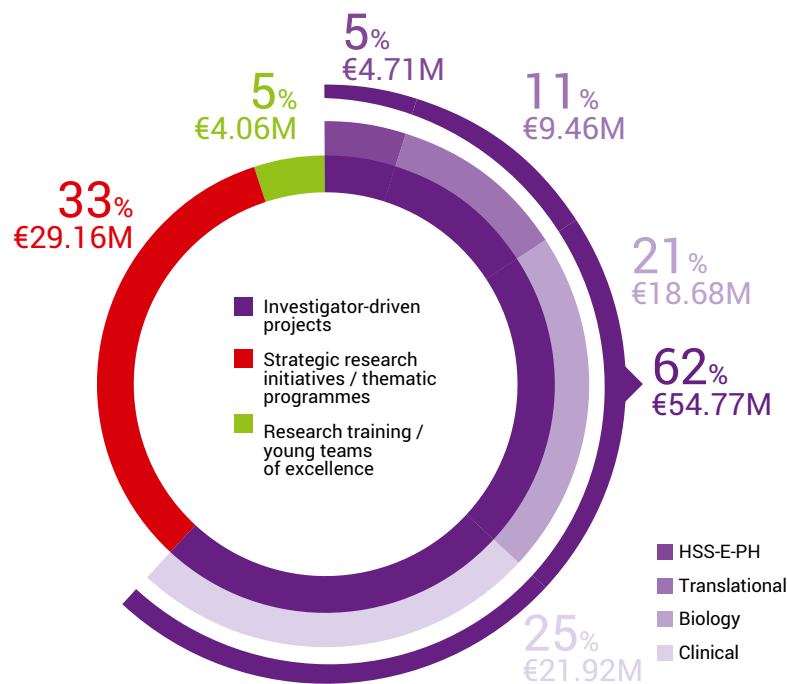
in research in human and social sciences, epidemiology and public health to cancer

€11.75M

in translational and integrated cancer research

2020 multi-year cancer research funding by programme type

(INCa, DGOS and ITMO Cancer-Aviesan): **€87.99M** invested



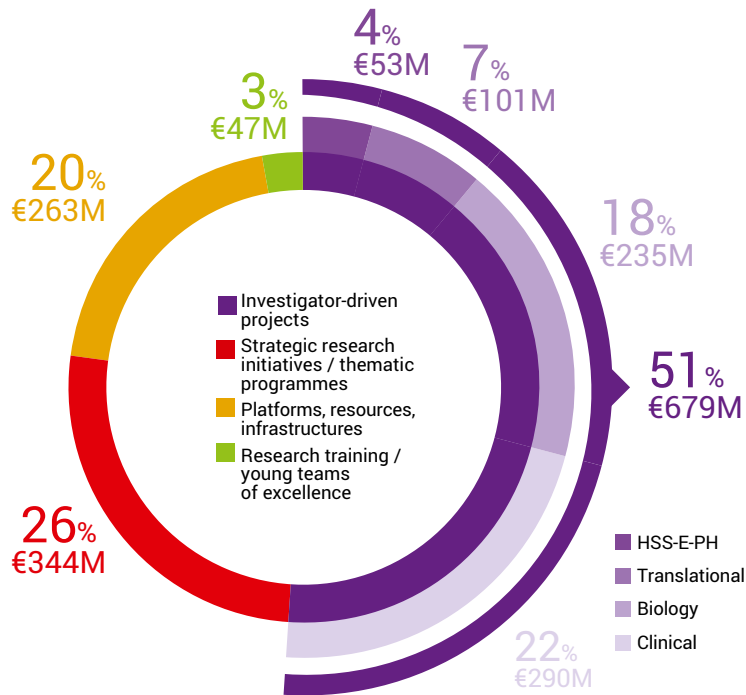
Total investments over the 2007-2020 period:



€281M in translational and integrated cancer research

€374M in clinical research

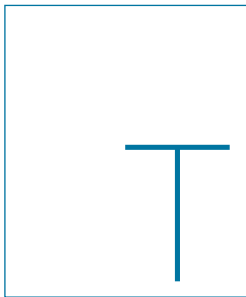
2007-2020 multi-year cancer research funding by programme type (INCa, DGOS and ITMO Cancer-Aviesan): €1.33Bn invested





- The international scientific advisory board members **10**
- 2020 recommendations **11**

The international scientific advisory board



This 15th 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 2020 recommendations of INCa's SAB. The SAB's recommendations are central to the Institute establishing an action plan and proposing a strategy to handle cancer research challenges over the years.

THE INTERNATIONAL SCIENTIFIC ADVISORY BOARD MEMBERS

The members of the Scientific Advisory Board are:

- **Dr. Geneviève Almouzni**, PhD, Institut Curie, Paris, France
- **Mrs. Pascale Altier**, VBO Consulting, Saint-Rémy-Lès-Chevreuse, France
- **Prof. Cécile Badoual**, MD, PhD, Hôpital Européen Georges Pompidou, Paris, France
- **Dr. Jean-Pierre Bizzari**, MD, Celgene, Summit, USA
- **Prof. Cédric Blanpain**, MD, PhD, Université Libre de Bruxelles, Brussels, Belgium
- **Prof. Johann de Bono**, MD, PhD, The Institute of Cancer Research and the Royal Marsden, London, United Kingdom
- **Dr. Franck Bourdeaut**, MD, PhD, Institut Curie, Paris, France
- **Dr. Elizabeth A. Eisenhauer**, MD, Queen's University, Kingston, Canada
- **Prof. Yann Gauduel**, PhD, Ecole Polytechnique - ENS Techniques Avancées, Palaiseau, France
- **Dr. Ivo G. Gut**, PhD, Centro nacional de analisis genómica (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
- **Dr. Douglas R. Lowy**, MD, NCI Acting Director, Bethesda, USA
- **Prof. Marc-André Mahé**, MD, PhD, General Director, Centre François Baclesse, Caen, France
- **Prof. Dame Theresa Marteau**, PhD, University of Cambridge, Cambridge, United Kingdom
- **Dr. Patrick Mehlen**, PhD, Centre de recherche en cancérologie de Lyon, Lyon, France
- **Prof. Stefan Pfister**, MD, German Cancer Research Centre (DKFZ), Heidelberg, Germany
- **Prof. Louise Potvin**, PhD, Institut de recherche en santé publique de l'Université de Montréal, Université de Montréal, Montréal, Canada
- **Mrs. Fabienne Renaud**, Europa Donna France, Nantes, France
- **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

2020 RECOMMENDATIONS

SAB discussion and recommendations RE: 2020-2030 Cancer Control Strategy

The SAB would like to first express that it is impressed by the breadth, scope and potential for real impact of the proposed cancer control strategy. We also are pleased to see that the comments made by the SAB earlier this year have been reflected in this updated version

The discussion of the SAB during its Oct 19, 2020 meeting focused on a number of topics:

- Where priorities for actions should be focused in the first few years of the strategy in each of the four Axes
- **Additional general comments** on the strategy as a whole – where clarity in the plan would be of value

SAB COMMENTS ON THE STRATEGIC PLAN PRIORITIES BY AXIS

Prevention axis

The SAB was impressed to see this level of emphasis on prevention and screening within the plan. We agreed that all of the Actions proposed under this Axis were of value and should be undertaken over the 10-year strategy, but that the following were **priorities for early action** in the next few years:

1 **Prevention Research** – is a priority and should also be a common thread throughout each activity found in this Axis. Of particular interest in this area is research not only into what works to change behaviour and how to implement it, but also what behavioural and policy interventions have not achieved their intended goals in France in the past and how to overcome that.

2 Prevention actions for both **Tobacco** and **Alcohol** are clear priorities – these are the two modifiable risk factors for a large proportion of cancers in France and indeed are the underlying causative factors for several of the Poor Prognosis Cancers found in Axis 3.

3 Screening access: It is clear that the COVID-19 pandemic has, in France and globally, reduced access to evidence-based screening. Thus the SAB endorsed the Screening Access action as an early priority

4 Obesity and Physical Activity: were also endorsed as actions of high priority to initiate within the early year(s) of this plan.

Additional general comments and recommendations vis-à-vis the Prevention Axis:

- Personalising prevention interventions (based on behavioural, socioeconomic, genomic, etc. risks) is an important area for research, evaluation and implementation. Individual risk is already affecting screening recommendations (e.g. BRCA-based strategies) and it clearly has a growing role in tailoring prevention strategies.
- Education for children and across the population, while not directly under INCa's purview, with clear messages about how to reduce risk for cancer as well as appropriate early detection will be central to communicating current and emerging knowledge.
- Telemedicine has emerged during the coronavirus pandemic as a means of delivering some aspects of health and cancer care. It could be explored as a tool for prevention and screening especially for more remote areas or those with limited services.
- Cancer Vaccines – with the public eagerness to embrace effective and safe SARS-CoV-2 vaccines once they are available, there is an opportunity to ramp up the information on safety and effectiveness of cancer vaccination such as hepatitis and HPV to improve uptake

Quality of Life Axis

The SAB was very supportive of the Actions within the Quality of Life (QoL) Axis. It was noted that is important to consider patient input into the definitions of what “good quality of life” means.

A few of the listed Actions in this Axis were felt to be of high priority to launch early within the timeline of the plan as follows:

1 Future-Focused Actions – the priority actions which were identified as future-focused were those of:

- a. Research
- b. Access to Innovation
- c. Evaluation of Innovation

2 Actions in these topics will guide the generation of knowledge and evidence to improve QoL.

3 In addition, actions were identified for early implementation because they will maximise the impact on patient QoL based on **current best knowledge**. These include:

- a. Supportive Care
- b. Rehabilitation

4 Finally, **therapeutic de-escalation questions** were highlighted. Research into this with appropriate implementation will have important potential impact on late effects of treatments.

It was emphasised by the SAB that both **adult cancer and paediatric cancer perspectives** are important to include as each of the actions in this axis are implemented.

Cancer predisposition/genetic counselling was put into this axis. The SAB feels that this is indeed an important topic with a high medical need in France, but should rather be moved into axis 1.

Poor Prognosis Cancers Axis

The SAB was very supportive of this Axis which is focused on reducing the mortality and improving quality of life outcomes of poor prognosis cancers. It is noted this will require a multi-pronged, multidisciplinary approach – so must include fundamental, prevention, early detection, treatment and supportive care research.

All the actions in this Axis were considered of high priority. The poor prognosis cancers show differences in terms of the current state of knowledge and the type of actions deployed for each will depend on this factor. The SAB focused on identifying which poor prognosis cancers would have the biggest potential for impact given the **burden of cancer they represent within France. Smoking and alcohol-related cancers** were thus highlighted as critical to address. These include **lung and liver cancers** in particular, seamlessly linking axis 1 and axis 3. The SAB agreed that **all** of the poor prognosis cancers are in need of more research to improve survival. Research priorities in different high-risk cancers might be very diverse (basic research, preclinical research, diagnostics, innovative treatments, etc.). The SAB anticipates that actions on smoking and alcohol-related cancers highlighted above have substantial potential for impact through prevention, early detection and/or treatment research.

Transformative and Cross-Cutting Priorities Axis

The SAB recommended the title of this Axis be expanded to include the term “Transformative” since not all the areas listed were truly “cross-cutting” in all Axes – whereas they were all potentially transformative.

The SAB did not recommend that some of these actions be prioritised for earlier action than others – they are all worth moving forward in the early year(s) of the plan.

A few comments on specific Actions were noted:

- **European and International collaboration** – it is clear that many aspects of cancer research and control activities will be achieved more quickly through collaborative action with European and international partners. Understanding in which areas of research this will have the greatest impact and in which areas France could lead the international collective will be helpful in giving this particular Action item focus. As a corollary to the discussion about international collaborations, there is the question of in which areas of research is France the leader internationally where additional investment within France will add important value.

- **Vulnerable Populations** - as for international collaboration, the COVID-19 pandemic has underscored the fact that there are specific populations that repeatedly bear the brunt of the effects of illness, so a focus on vulnerable populations across the plan is important. The key issue here is how to ensure that efforts to tackle vulnerable populations are truly multidisciplinary and not siloed.
- **Artificial Intelligence** – the outputs and tools created from machine learning and artificial intelligence algorithms may indeed be transformative across a number of areas related to health and cancer care delivery and research. Key to realising the potential of AI is the availability of high-quality, broad and well organized/annotated datasets to be used for this research. Leveraging and expanding beyond clinical datasets will be critical.

ADDITIONAL GENERAL COMMENTS AND RECOMMENDATIONS

Members of the SAB also raised a number of topics that were not specifically linked to individual Axes in the plan. These were:

Infrastructure Investment: As new research or treatment technologies and approaches emerge, there will be the need to consider more substantial investments in infrastructure across the French health care and research community. Examples relevant today could include: how to scale up research in CAR-T therapies (without relying only on industry); how to expand the network of researchers engaged in single cell or liquid biopsy research.

How to be sure that the 220 measures work together – The 2020-2030 strategic plan is broad, inclusive, ambitious and exciting. The SAB raised the question of how best to ensure that measures tackling various facets of the same cancer problem can be connected to maximise impact. The fact that there are 220 distinct measures will make this challenging and speaks to the need to consider this plan as a matrix to avoid siloes that could limit the potential impact of this work. In addition, consolidation of overlapping programmes would promote efficiencies and avoid siloes.

Finally, for the ambitious goals of this 10-year plan to be achievable, appropriate and increased funding as well as support (human resources) from Government will be needed. Furthermore, it will be necessary to actively monitor the impact of the plan (e.g. annual tracking of key goals) to ensure INCa can achieve the targets in the timeframe described. If not, some adjustments to the actions may be required.

SAB discussion and recommendations RE: 2019/20 report

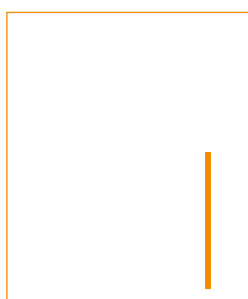
INCa is to be congratulated for its strong and comprehensive programmes across the spectrum of cancer research which have incorporated responses from previous SAB and other reviews.

However, the wide array of ongoing programmes also present challenges in capacity within the organisation to both manage these and launch the new plan. Thus, the SAB recommends streamlining of existing programs wherever possible – through consolidation, or sunsetting of programmes that have achieved their goals. To do so will increase the capacity of the organisation to launch the new plan.



● Biology and basic sciences for cancer research	18
■ The biology and basic sciences for cancer research programme (PLBIO)	19
■ Thematic cancer research programmes by ITMO Cancer-Aviesan	24
■ Support for paediatric cancer research	35
■ Support for professional careers in cancer research	43
● Translational and integrated cancer research	46
■ National translational cancer research programme (PRT-K)	47
■ European translational cancer research programme (TRANSCAN)	50
■ Integrated research action programme (PAIR)	56
■ Support for integrated cancer research structuring	58
■ Translational and multidisciplinary training programmes	62
● Clinical cancer research and access to innovation	68
■ National programme for hospital clinical research on cancer (PHRC-K)	69
■ Public-private partnerships	75
■ Precision medicine initiatives	80
■ Clinical cancer research organisation: structures, infrastructures, and tools	92
● Research in human and social sciences, epidemiology and public health	104
■ Research programme for human and social sciences, epidemiology, and public health applied to cancer (PLSHS-E-SP)	105
■ Population health intervention research programme (PHIR)	108
■ Support for research on environmental risk factors	111
■ Support for professional careers and training	115
● International commitments	121
■ European actions	121
■ Europe's Beating Cancer Plan: A new EU approach to prevention, treatment and care	126
■ International cooperation	128
● Review of cancer research funding and evaluation	131
■ Review and trends in cancer research funding	131
■ Evaluation of the 2014-2019 Cancer control plan – summary of interviews and recommendations with a research focus (Official report)	136
■ Joint Statement by the French National Research Funding Agencies to support Open Science	141

2020 Cancer Research Activity



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. The Institute completes its cancer research support through specific actions and allocations to support cancer research structuring and strategic research initiatives, such as fostering precision medicine, to promote access to innovation for all patients.

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

This following section presents a detailed review of the research programmes conducted in 2020, 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.

IN 2020, SUPPORT FOR BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH AMOUNTED TO:

€44.51M

€18.68M dedicated to support investigator-driven projects (PLBIO programme);

€25.06M to support thematic research programmes such as multidisciplinary projects and emerging topics;

€0.77M to support young leaders and cancer research training.



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

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

THE PROGRAMME IN 2020

In 2020, 35 projects were selected out of the 279 proposals submitted for a total amount of €18.68M (12.5% of the submitted applications were selected) (Table 1).

■ TABLE 1

FEATURES OF THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2020

Objectives	To acquire new knowledge and develop new tools to create new therapeutic approaches. Open to all areas of basic research and to scientific disciplines involved in tumour biology research, this call was launched to: <ul style="list-style-type: none"> • Enable the achievement of original projects; • Strengthen multidisciplinary collaborations; • Develop research in emerging areas.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€18.68M
Proposals submitted	279
Projects selected	35
Selection rate	12.5%

Figure 1 presents a detailed analysis of the funded projects:

- The aim of the majority of the funded projects (67.1%) is to study the biological mechanisms of cell transformation and disease progression, according to the international CSO classification¹ (CSO 1). Among these:
 - Nearly 33% 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;
 - 34.3% of the projects study 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);
- 2.9% relate to cancer aetiology (CSO 2);
- 2.9% concern the early detection, diagnosis, and prognosis of cancers (CSO 4);
- 27.1% of the funded projects study either molecular mechanisms of treatment response and resistance, or the identification of new therapeutic targets (CSO 5).

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

2020:
35 projects funded out of the **279** proposals submitted for a total budget of **€18.68M**

FIGURE 1
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2020

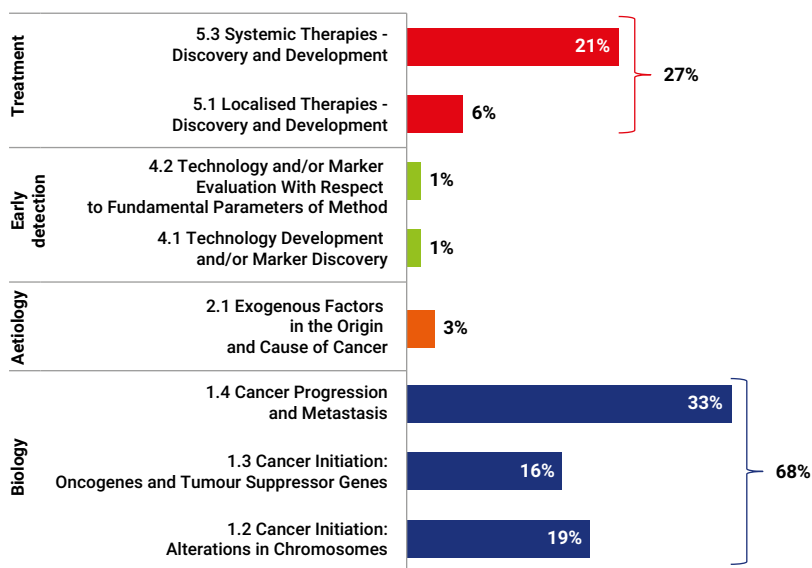


Figure 2 depicts a detailed analysis of the research topics of the selected projects:

- Microenvironment: 22% of the funded projects, with a majority of projects addressing the study of tumour infiltrating immune cells and the study of tumour–environment interaction;
- Cell signalling: 18% of the funded projects, with a particular emphasis on cellular metabolism and translation regulation;
- Genetics: 16% of the funded projects, mainly studying cell cycle regulation and/or senescence.

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

THE PROGRAMME OVER THE 2007-2020 PERIOD

Since 2007, 476 projects have been selected out of 3,503 proposals submitted to the Biology and basic sciences for cancer research programme, for a total budget of €235.30M (Figure 3).

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

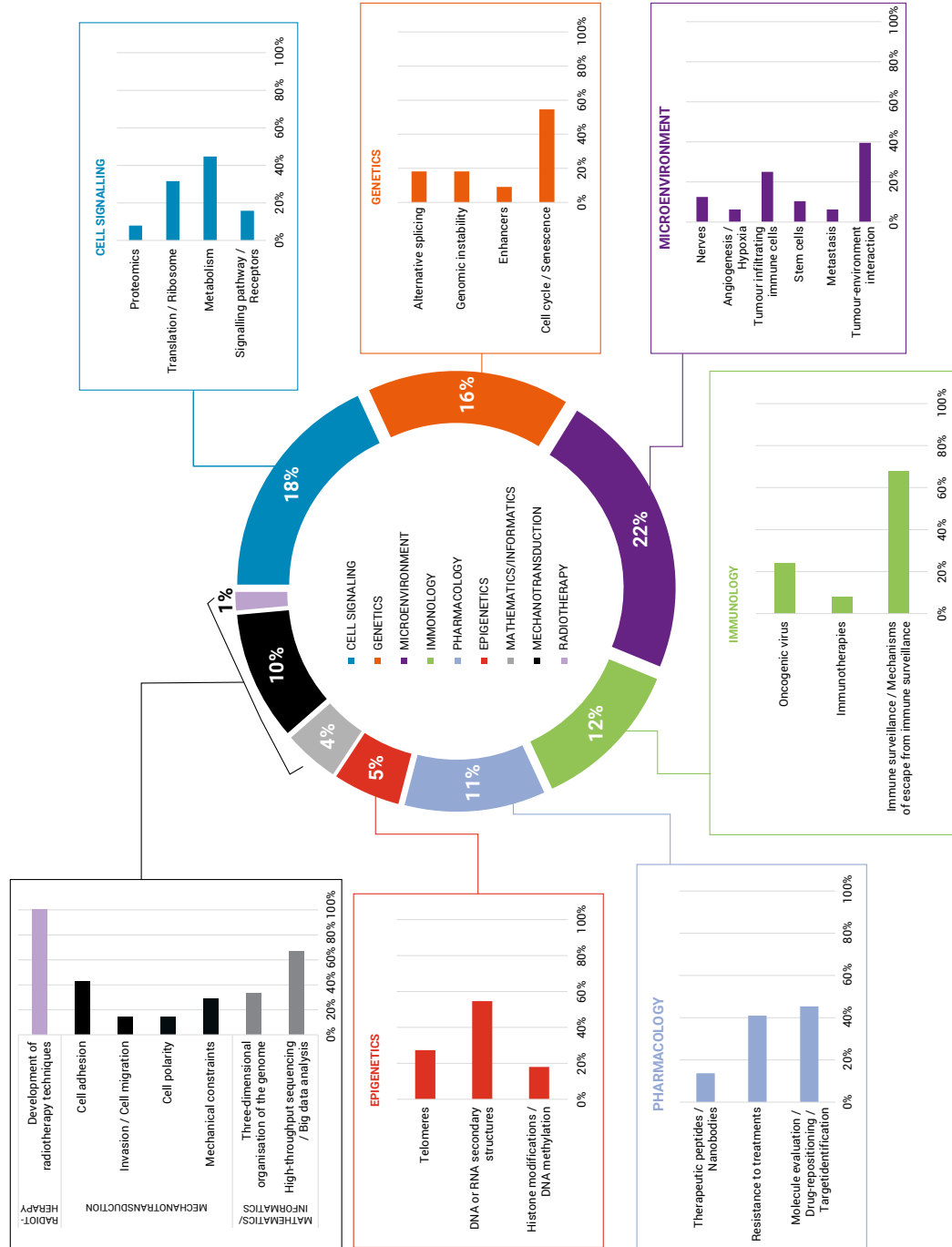
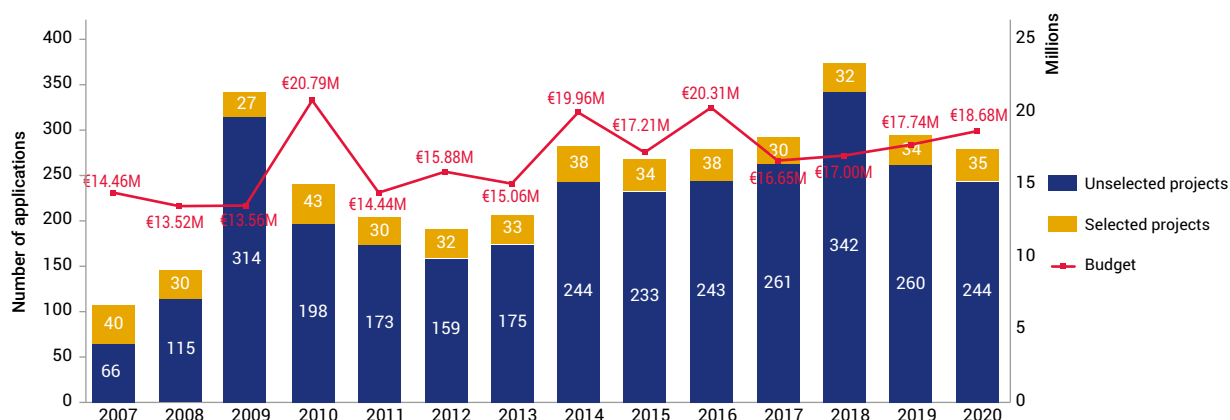


FIGURE 3
TRENDS IN SELECTION AND FUNDING OF THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME OVER THE 2007-2020 PERIOD



2007-2020:
476 projects
funded for over
€235M

The analysis of the projects funded over the 2007-2020 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).

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 (17%), breast cancer (13%) or colorectal cancer (9%) are also well represented (Figure 5).

FIGURE 4
DISTRIBUTION OF SELECTED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2020 PERIOD

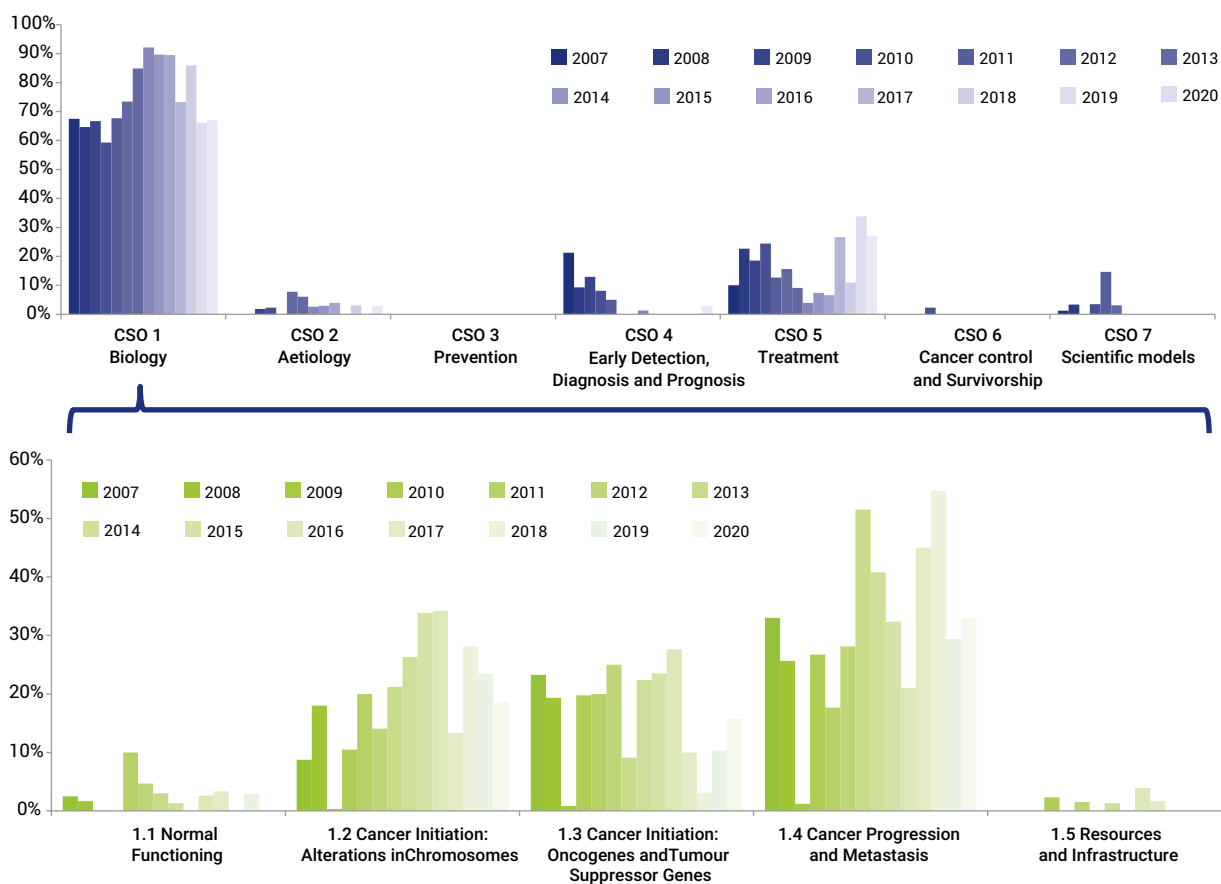
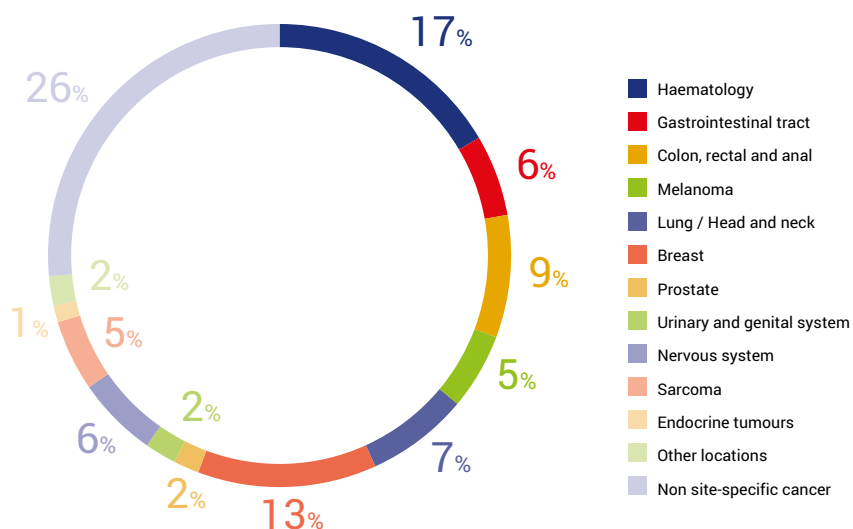


FIGURE 5
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO CANCER SITES STUDIED FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME OVER THE 2007-2020 PERIOD



Thematic cancer research programmes by ITMO Cancer-Aviesan

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

Initiated in 2019, this programme aims to support the implementation of the 3R rule in the field of oncology. Eligible projects should combine at least two entirely distinctive experimental models, 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.

The programme in 2020

■ TABLE 2
FEATURES OF THE 3R PROGRAMME IN 2020

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	€4.4M
Proposals submitted	42
Projects selected	10
Selection rate	24%

In order to replace (at least in part) rodent models, the selected projects focused on the development of alternatives to patient-derived xenografts (PDX) such as patient-derived organoids (sometimes in large numbers to constitute biobanks), spontaneous companion dog tumour organoids, spheroids and organotypic culture of cancer cells, 3D structures using cellular capsule technologies, organ-on-chip, C. elegans tumour models, etc. They were developed for the purposes of studying tumour biology, drug resistance and microenvironment effects, as well as evaluating the role of microstructures in tumorigenesis (e.g. P-bodies) and serving as drug screening platforms. Figure 6 presents the distribution of the selected projects according to the CSO classification.

Many poor prognosis cancers were concerned, such as pancreatic cancers, triple-negative breast cancer, small cell lung cancers, paediatric hepatoblastomas or acute myeloid leukaemias, cutaneous T-cell lymphomas, xenobiotic-sensitive testicular germ cells tumours, colorectal cancers, etc. These refined models, based on new technologies or new hypotheses, are intended to be compared to conventional PDX.

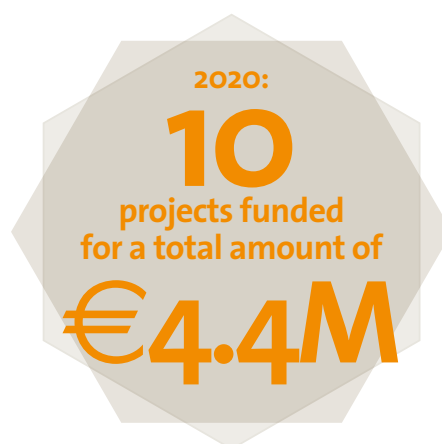


FIGURE 6
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE 3R PROGRAMME ACCORDING TO THE CSO CLASSIFICATION IN 2020

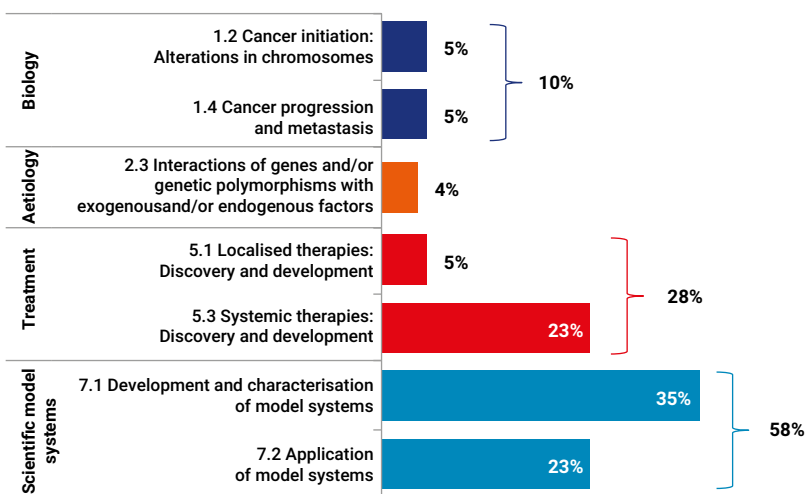
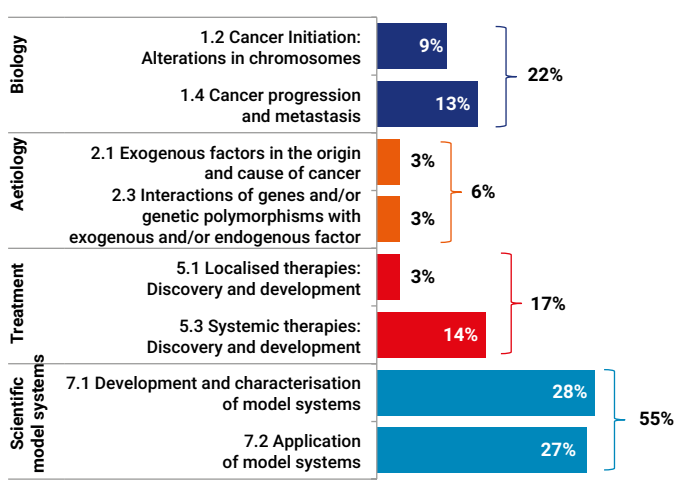


FIGURE 7
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE 3R PROGRAMME ACCORDING TO THE CSO CLASSIFICATION OVER THE 2019-2020 PERIOD



The programme over the 2019-2020 period

In 2 editions, 16 projects were selected for a total funding amount of €6.8M. In line with the objectives of the programme, 55% of the projects focused on model development, with the goal of deciphering tumour mechanisms and evaluating new treatments.

NON-CODING RNAS PROGRAMME

Initiated in 2018, this programme aims to promote the identification of non-coding RNAs (namely micro RNAs and long non-coding RNAs), the study of their mechanism of action, their regulation in normal and cancer cells, and their involvement in oncogenesis (e.g. gene expression and genome stability regulation).

The programme in 2020

■ TABLE 3
FEATURES OF THE NCRNAS PROGRAMME IN 2020

Objectives	To promote the identification of non-coding RNAs, the study of their mechanism of action, their regulation and their involvement in oncogenesis
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€2.9M
Proposals evaluated	36
Projects selected	7
Selection rate	19%

The selected projects focused on the study (characterisation, role, mechanisms of action) of ncRNAs, long non-coding RNAs, micro RNAs or small nucleolar RNAs in different cancer-related conditions, such as:

- tumorigenesis (liver control of transcription-coupled double-strand break repair, liver cellular senescence, glioblastoma stem-like cells maintenance/differentiation and plasticity);
- metastasis (including preparation of bone pre-metastatic niches in breast cancers, tumour cells intra- or extravasation and angiogenesis control);
- resistance to treatment (hepatocarcinoma and melanoma epithelial-to-mesenchymal transition);
- antitumoral immune response (lymphocytes trafficking in high endothelial venules).

The programme over the 2018-2020 period

In 2 editions (2018 and 2020), 16 projects were selected for a total funding amount of €6.65M. In line with the objectives of the programme, the vast majority of selected projects (78%) focused on cancer biology to improve knowledge on oncogenesis processes (Figure 9). Others focused on biomarkers for cancer detection and diagnosis (9%) and systemic therapies (13%).

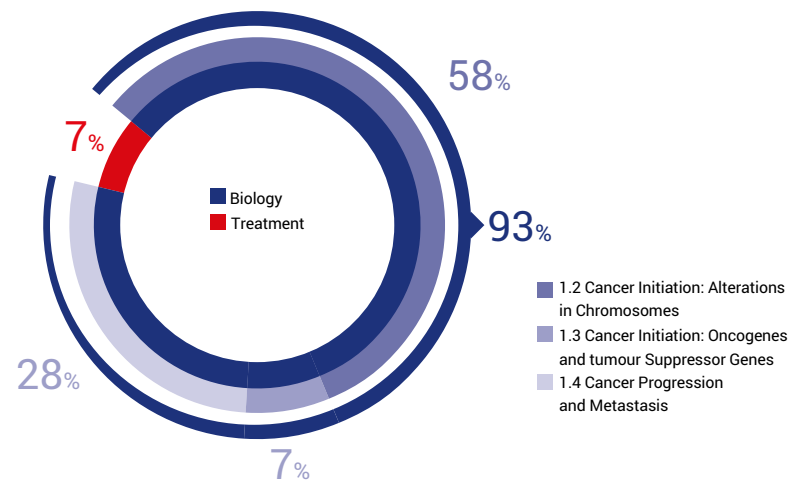
2020:
7
projects selected
for a total amount of
€2.9M

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

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

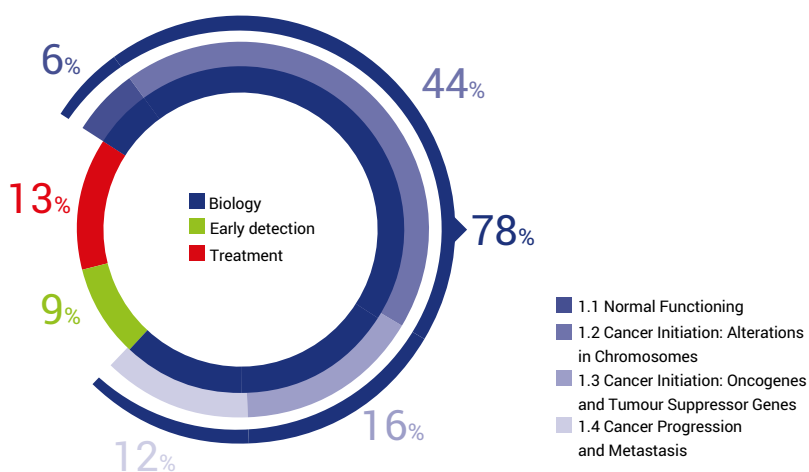


FIGURE 8
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE NCRNAS PROGRAMME ACCORDING TO CSO CLASSIFICATION IN 2020



2018-2020:
16
projects selected
for a total amount of
€6.65M

FIGURE 9
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE NCRNAS PROGRAMME ACCORDING TO CSO CLASSIFICATION OVER THE 2018-2020 PERIOD



The programme in 2020

TABLE 4
FEATURES OF THE MIC PROGRAMME IN 2020

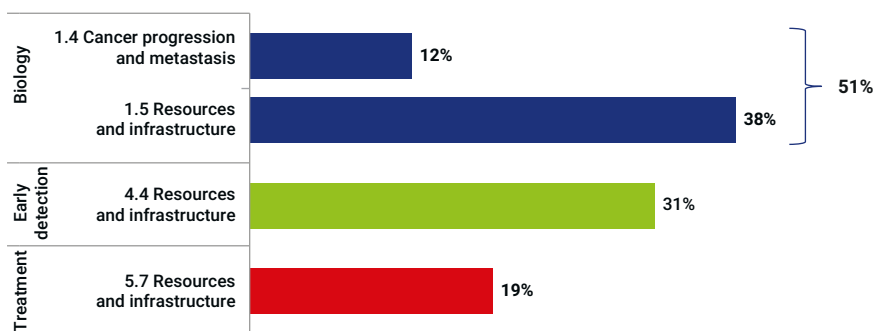
Objectives	To improve the understanding of tumour diseases and improve the prognosis of patients thanks to the contribution of mathematics and computer science
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€3.84M
Proposals evaluated	29
Projects selected	8
Selection rate	28%

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

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

- exploring mechanisms involved in oncogenesis, metastasis, treatment resistance or cell death processes: mechanical properties of cells and tissue architecture needed to initiate cancer processes, mechanical forces from actin to support macrophage tumour infiltration, metabolic plasticity of melanoma cell subpopulations associated with the emergence of targeted-therapy resistance, intra- and intercellular mechanisms involved in apoptosis-associated immunogenic cell death,
- producing and taking advantage of (big) data to uncover new facts relevant for cancer knowledge or clinical practice: profiles of plasma denaturation from cancer vs healthy patients, associations sought between a broad range of clinical variables, looking for pleiotropic effects in different cancers,
- developing a device able to visualise the risk of iatrogenic events in radiotherapy-treated areas.

FIGURE 10
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE MIC PROGRAMME ACCORDING TO CSO CLASSIFICATION IN 2020

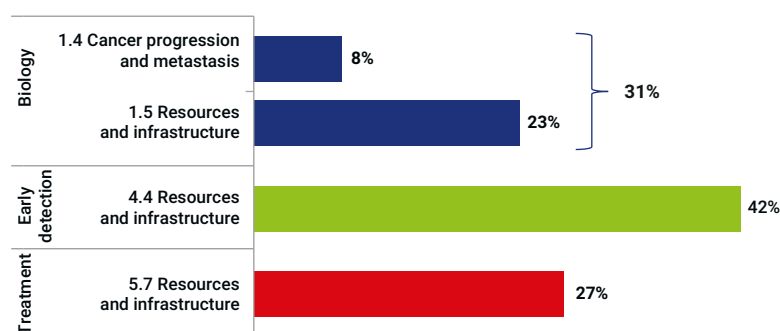


2020:
8
projects selected
for a total amount of
€3.84M

The programme over the 2019-2020 period

In 2 editions, 13 projects were selected for a total funding amount of €6.1M. In line with the objectives of the programme, most of the projects belonged to the CSO Resources and infrastructures categories, whether they focused on cancer biology, diagnosis or treatment (Figure 11).

FIGURE 11
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE MIC PROGRAMME ACCORDING TO CSO CLASSIFICATION OVER THE 2019-2020 PERIOD



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

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

The programme in 2020

■ TABLE 5
FEATURES OF THE PCSI PROGRAMME IN 2020

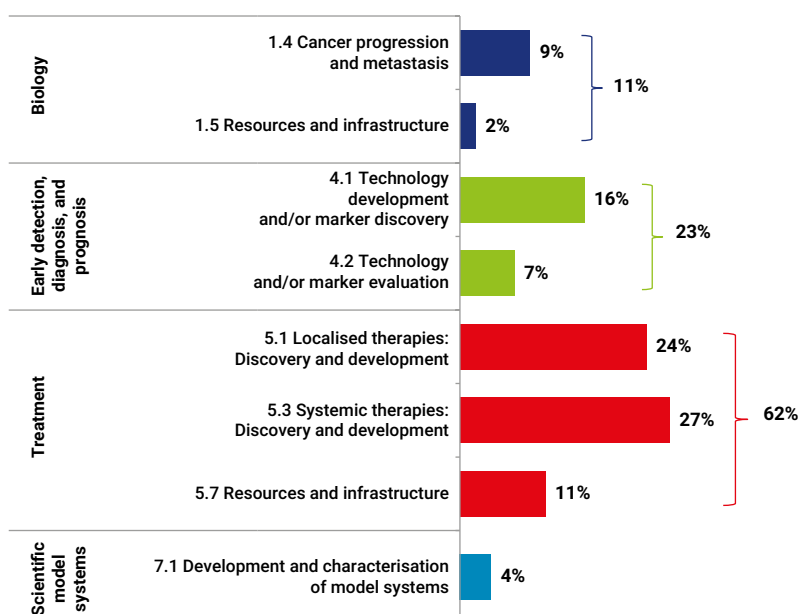
Objectives	To improve the understanding of tumour diseases and improve the prognosis of patients thanks to concepts or tools from physics, chemistry or engineering sciences
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€9.32M
Proposals evaluated	108
Projects selected	31 (20 Full projects & 11 Proof of concept projects)
Selection rate	29%

The selected projects focused on the development of systems based on cutting-edge physics technologies, aimed at

- exploring fundamental mechanisms of oncogenesis and improving cancer/metastasis diagnosis and follow-up:
 - acoustic levitation-made organoids to explore the spatial organisation of glioblastoma,
 - Raman imaging to explore lipid exchanges between stromal adipocytes and breast cancer cells in the invasive tumour front,
 - model of CAF-induced mechanisms of colorectal cancer cells budding in stroma,
 - model of circulating tumour cell signalling pathways affected by bloodstream deformation,
 - DNA nanopores to measure circulating miRNA single molecules,
 - magnetic nanoparticles to identify metastatic breast cancer cells and cancer-associated adipocytes,
 - lanthanide ions near-infrared II emission to link specific potassium channels to prostate cancer prognosis;
- developing new therapeutic avenues or improving existing ones:
 - Raman microspectro-imaging to explore the distribution of gemcitabine-squalene complex in cells and tissues,
 - cold plasmas evaluated to trigger cancer immunotherapy in non-small-cell lung carcinomas,
 - new hydrogen-generating electrochemical system to explore hydrogen effects on cancer cells and their microenvironment,
 - whole-body imaging to detect early metastasis in order to evaluate iron-oxide particle-based radiotherapy and magnetic field hyperthermia treatment,
 - dosimetric devices for FLASH therapy, biological dose modelling in radioelement-based therapies, and real-time control of hadrontherapy-treated tumour area to refine irradiation conditions during cancer therapy,



FIGURE 12
 DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE PCSI PROGRAMME ACCORDING TO CSO CLASSIFICATION IN 2020



- devices improving access to deep tumours such as glioblastomas (molecular activation systems based on nanoscintillator-photosensitiser, PET microbubbles-ultrasound, and prodrug-X Ray combinations) or pancreatic tumours (endoscopic cavitation for stroma access and disruption, nucleoline-based nanovectors),
- super-resolution microscopy to explore mechanisms of Tamoxifen resistance in breast cancer,
- tumour biomechanics-based model to predict treatment efficacy in liver metastasis,
- polymeric structure development combining 3 or more targeted drugs in ovarian cancer.

The selected projects also focused on the development and evaluation of chemical engineering-designed compounds targeting:

- histone chaperone antisilencing factor 1, by peptidomimetic chemistry and α -helix mimicry approaches,
- a sterol transport protein involved in cancer growth,
- PKC2 subunits interactions in overexpressing PKC2 cancers,
- a Bcl-2 family anti-apoptotic protein in ovarian cancer (small inhibitors with lowered platelet toxicity designed by Proteolysis targeting chimera (Protac) approaches),

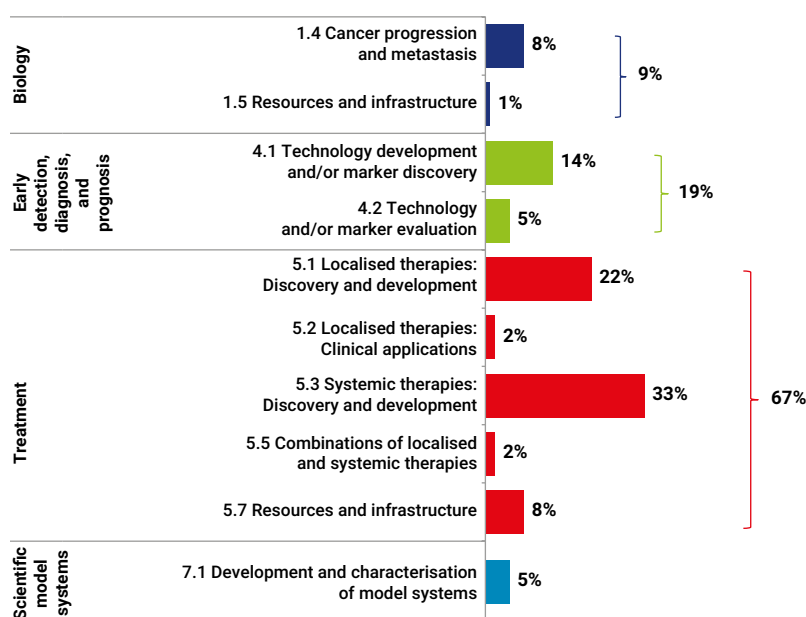


- insulin-degrading enzyme, to improve proteasome inhibitor-targeted therapy of multiple myelomas,
- DNA, with the generation of a broad library of iridium complexes and the evaluation of their efficacy in cisplatin-resistant breast, colon, ovarian, or liver cancer cells.

The programme over the 2019-2020 period

In 2 editions, 44 projects were selected for a total funding amount of €12.5M. New technology development for cancer diagnosis (19%) or treatment (67%) were at the core of the vast majority of the projects (Figure 13).

FIGURE 13
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE PCSI PROGRAMME ACCORDING TO CSO CLASSIFICATION OVER THE 2019-2020 PERIOD





Launch of the 1st Aviesan federative programme (PFA)

This first PFA edition of a PFA was organised in 2019 by ITMO Cancer and ITMO Molecular and Structural Bases of Life (BMSV) of Aviesan. Entitled “Towards a new subcellular map of the cancer cell”, it aims to pool expertise and skills between the cancer and structural biology/biophysics/biochemistry communities in order to unlock novel concepts in carcinogenesis requiring interdisciplinary cooperation. The Programme kick-off meeting took place in Paris on 6 March 2020. After an official launch by Aviesan’s Board and a brief review of its genesis by the ITMOs’ Boards, the “Nanotumor. Towards the tumor cell atlas” project was presented by the coordinators of the consortium and its 4 axes presented by their PIs.

Support for paediatric cancer research

COORDINATING PAEDIATRIC CANCER RESEARCH ACTIONS

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 per year, 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 2020, the Task Force met monthly at INCa and the collaboration work with the collectives took shape starting with the launch of three specific programmes (see section below).

These innovative interdisciplinary research programmes should make it possible to attract new scientific disciplines alongside researchers and clinicians.

Bibliometrics on French paediatric cancer research (2008-2018)

This study aims to:

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

A rudimentary first query was carried out in the Web of Science (WoS):

- 66,436 publications for the worldwide corpus;
- 3,347 for the French corpus.

At first glance, French paediatric cancer research represents 5.0% of global research, greater than the French share for research in all disciplines (estimated at 3.3% in 2018 according to the French Ministry of the Economy).

The methodology will include:

- numerous databases, including the WoS database, Unpaywall, etc.;
- a researcher survey;
- a peer-review exercise in order to qualify the effects and impacts.

The study should be available in early 2022.

Other actions have been implemented:

- The organisation of an International Meeting on Fundamental Research in Paediatric Cancer, by the French National Cancer Institute in partnership with ITMO Cancer -Aviesan. Initially planned in September 2020, this meeting has been postponed to June 2021 due to the Covid pandemic and will address 4 main topics:
 - Developmental biology, stem cell and paediatric cancer;
 - Paediatric cancer: from fundamental to modelling research;
 - Big data and management of paediatric cancer;
 - Immunology.
- The development of a website dedicated to childhood cancer with
 - Project portfolio;
 - Researcher mapping;
 - Articles on different diseases for families.
- A bibliographic study will be proposed in order to update the scientific knowledge on childhood cancers annually. The dedicated methodology was prepared in partnership with Inserm and the CNRS Institute for Scientific and Technical Information (INIST).

PAEDIATRIC CANCER RESEARCH PROGRAMMES

Thanks to the renewal of a €5M allocation by the French Minister for Higher Education, Research, and Innovation, 3 calls for proposals were launched this year.

Causes and origins of paediatric cancers

The aim of this new call for applications is to bring together, in a consortium, research teams from different disciplines, skills around the theme of the causes and origins of paediatric cancers. Interdisciplinary cooperation would appear to be necessary in order to define an integrated research programme that will make it possible to overcome the challenges related to this theme.

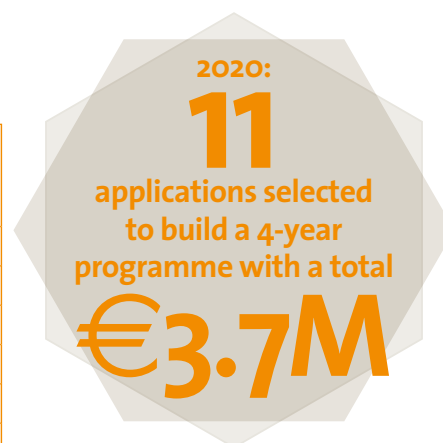
This call for applications first allowed the set-up of a research consortium, and then, in a second phase, the drafting, by the consortium, of a 4-year research programme.

In 2020, 11 applications out of a total of 31 were selected to form the consortium and then build a 4-year research programme, with an overall budget of €3.7M (Table 6).

The consortium, selected by the scientific evaluation committee, includes eleven basic research teams working in several research institutes and national cancer centres and whose research themes cover a broad field of research, including epidemiology, immunology, physiological modelling, genetic analysis, and molecular biology of paediatric tumour cells.

■ **TABLE 6**
FEATURES OF THE ORIGINS AND CAUSES OF PAEDIATRIC CANCERS PROGRAMME
IN 2020

Objectives	Formation of a new consortium dedicated to the study of the origins of paediatric cancers and drafting of a research programme
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€3.7M
Proposals evaluated	31
Projects selected	11
Selection rate	35.5%



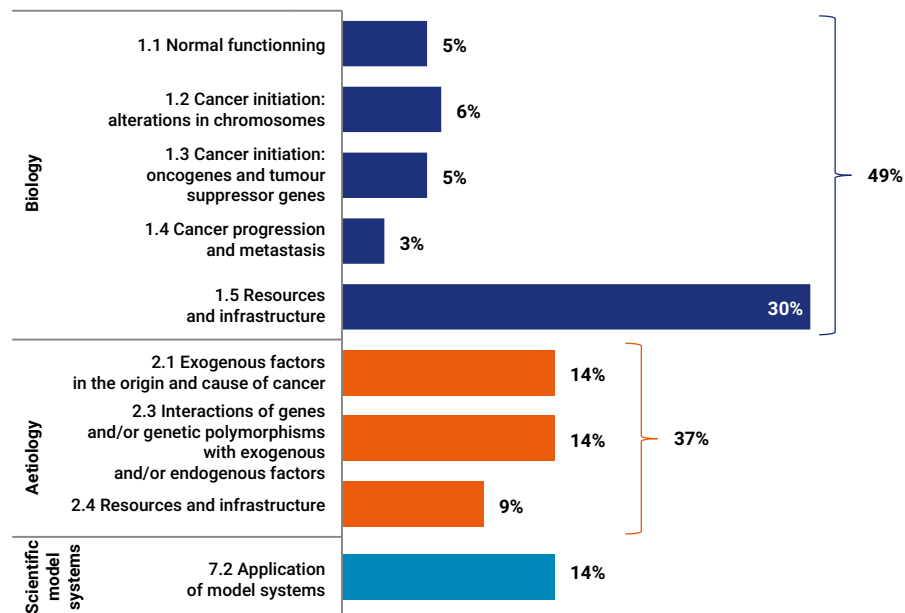
This consortium has built a multidisciplinary research programme taking into consideration the causes of paediatric cancers from an environmental to a molecular level, on different paediatric cancer entities. The specific objectives of the programme are to:

- Identify environmental and genetic risk factors, including those related to immunity, that may increase the risk of childhood cancer.
- Understand how changes in cell properties during the pre- and post-natal periods influence their susceptibility to genetic alterations frequently observed in paediatric cancers.
- Develop new models that mimic paediatric tumours more closely and that will make it possible to study the way cancer cells interact with surrounding cells.

At least once a year, the coordinator will present the progress of the programme to INCa and to the representatives of the Paediatric Task Force.

Furthermore, in order to ensure monitoring of the consortium, a mid-term review will be scheduled and will be carried out by a steering committee, composed of members of the scientific evaluation committee to analyse the progress of the project. One or more teams may be withdrawn from or added to the consortium at the mid-term stage if necessary.

■ FIGURE 14
DISTRIBUTION OF SELECTED APPLICATIONS ACCORDING TO CSO CLASSIFICATION



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

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

The aim is to fund original and audacious research projects, conceptually new and risky, considered as “High-Risk - High-Gain”, ineligible for funding in the context of traditional existing calls for proposals.

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

In 2020, 6 out of a total of 28 projects were selected for funding, for an overall budget of €899,519 (Table 7).



■ **TABLE 7**
FEATURES OF THE “HIGH-RISK - HIGH-GAIN” PAEDIATRIC ONCOLOGY RESEARCH
PROJECTS PROGRAMME IN 2020

Objectives	Enable the development of conceptually new and risky projects ineligible for funding in the context of traditional existing calls for proposals.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€899,519
Proposals evaluated	28
Projects selected	6
Selection rate	21.4%

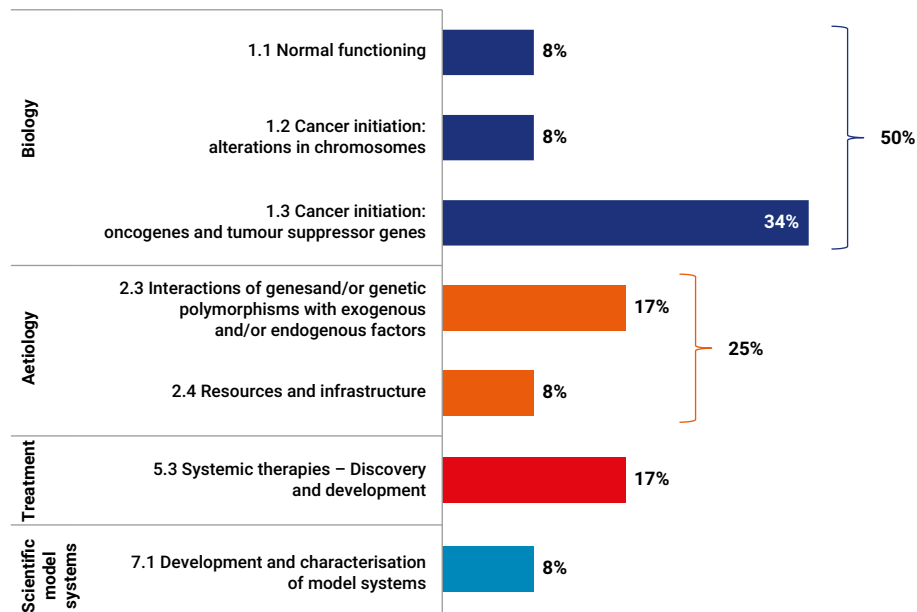
The selected and funded projects aim to:

- identify cells of origin of rhabdoid tumours by single cell genotyping and embryonic tissue cultures;
- study the epigenetic mechanisms at the origin of childhood leukaemia;
- identify dialogues between the cellular context and the exposome during tumour initiation and progression (using organoid models as tools);
- study the function and activity of a transcription factor in juvenile myelomonocytic leukaemia;
- conduct a preclinical animal study to define an immunotherapy strategy for the prevention of constitutional mismatch repair deficiency syndrome;
- study the progression of glioblastoma by combining brain organoid models with spatial transcriptomics.

The scientific evaluation committee unanimously highlighted the interest of this new programme and recommended its renewal for the year 2021 with a larger budget. The representatives of the Paediatric Task Force also unanimously underlined the interest of this call for proposals.

Thus, for the year 2021, this call for proposals will be renewed with a budget of approximately €2M, with projects lasting 2 years and funding authorised up to €200K per project.

■ FIGURE 15
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO CSO CLASSIFICATION



Research in paediatric oncology: post-doctoral fellowships and international mobility grants

The objectives of this call for applications are to boost the attractiveness of research in paediatric oncology to young talents, and to facilitate the career progression of junior researchers working in paediatric oncology research. It is also intended to enable statutory staff (researchers, medical doctors, engineers, etc.) to acquire new expertise for the development of paediatric cancer research projects.

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

It is also aimed to support statutory staff, young researchers and students already remunerated in France who wish to do an internship abroad as part of their training.

The programme in 2020

In 2020, 3 projects out of a total of 7 were selected for funding, with an overall budget of €425,100 (Table 8).

■ **TABLE 8**
FEATURES OF THE RESEARCH IN PAEDIATRIC ONCOLOGY: POST-DOCTORAL FELLOWSHIPS AND INTERNATIONAL MOBILITY GRANTS PROGRAMME IN 2020

Objectives	Reinforce the attractiveness of paediatric cancer research for young talent, facilitate the career of young researchers and enable statutory personnel to acquire new expertise in paediatric cancer research
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€425,100
Applications evaluated	7
Applications selected	3
Selection rate	42.9%



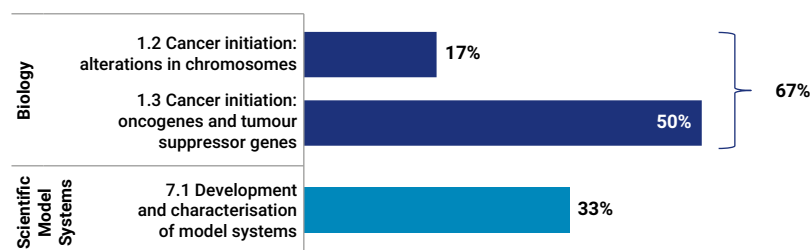
The three projects funded are post-doctoral fellowships (Table 9 and Figure 16).

■ **TABLE 9**
DISTRIBUTION OF THE SELECTED APPLICATIONS

Project aim	Country of the applicant's home laboratory	Country of the applicant's host laboratory
Study the cellular and molecular consequences of a specific fusion oncoprotein degradation in paediatric acute myeloid leukaemia	France	United States of America
Study the role of the ubiquitin-proteasome system in the tumorigenesis of medulloblastomas	Italy	France
Develop new ependymoma models for preclinical drug testing	Japan	France

Given the current health context, which has delayed the start date of certain projects, and considering the uncertainties about the development of the pandemic, INCa, in agreement with the Paediatric Task Force, has decided not to renew this call for applications in 2021.

FIGURE 16
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO CSO CLASSIFICATION



The programme over the 2019-2020 period

Since 2019, 10 proposals have been submitted to this call for applications and 5 have been selected and funded (2 projects in 2019 and 3 projects in 2020) for a total amount of €482,820. The overall selection rate for this call for application is 50%.

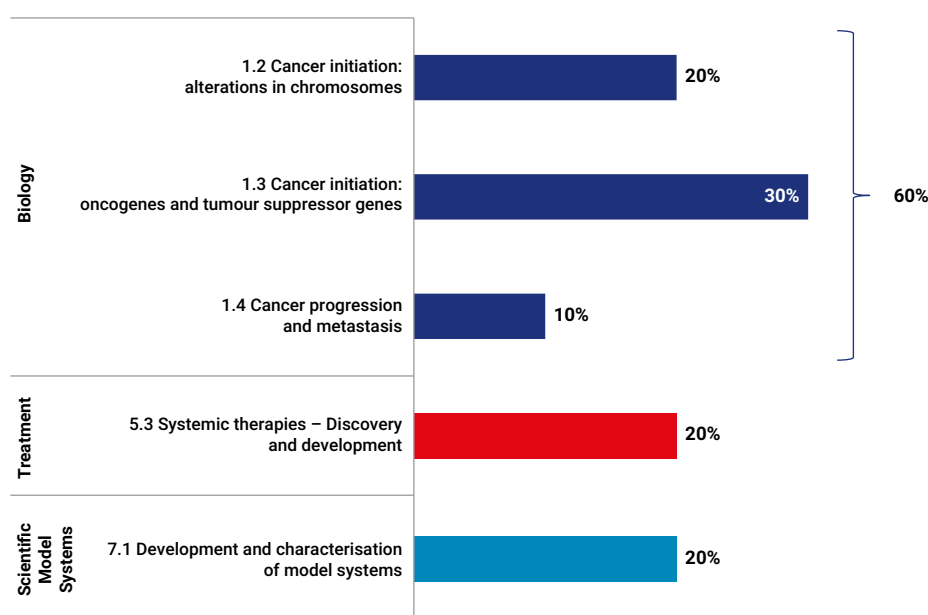
TABLE 10
TRENDS IN SELECTION AND FUNDING OF RESEARCH IN PAEDIATRIC ONCOLOGY: POST-DOCTORAL FELLOWSHIPS AND INTERNATIONAL MOBILITY GRANTS PROGRAMME OVER THE 2019-2020 PERIOD

Years	2019	2020	TOTAL
Funding (in €M)	57,720	425,100	482,820
Proposals evaluated	3	7	10
Projects selected	2	3	5
Selection rate (%)	66.7%	42.9%	50.0%

The CSO typology of projects funded since 2019 shows that projects are focused on basic research on cancer biology, therapeutics, and model development (Figure 17).

2019-2020:
5
applications selected
for a total amount of
€482,820

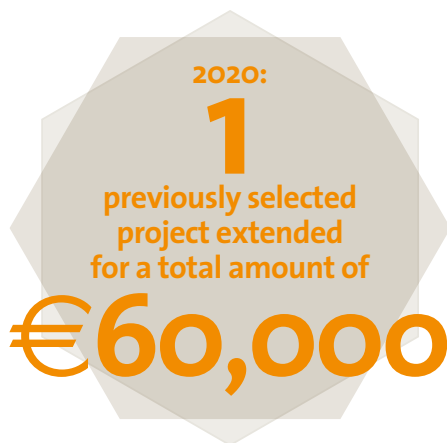
FIGURE 17
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO CSO CLASSIFICATION OVER THE 2019-2020 PERIOD



Support for professional careers in cancer research

SUPPORT FOR THE ATIP-AVENIR PROGRAMME

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



The programme in 2020

■ TABLE 11
FEATURES OF THE ATIP-AVENIR PROGRAMME IN CANCER RESEARCH IN 2020

Objectives	To promote the establishment of promising young PIs in cancer research by funding 3 years and/or a 2 year-extension of their starting team
Programming institution	CNRS and Inserm
Operating institution	CNRS and Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€60,000
Project extended for 2 years	1

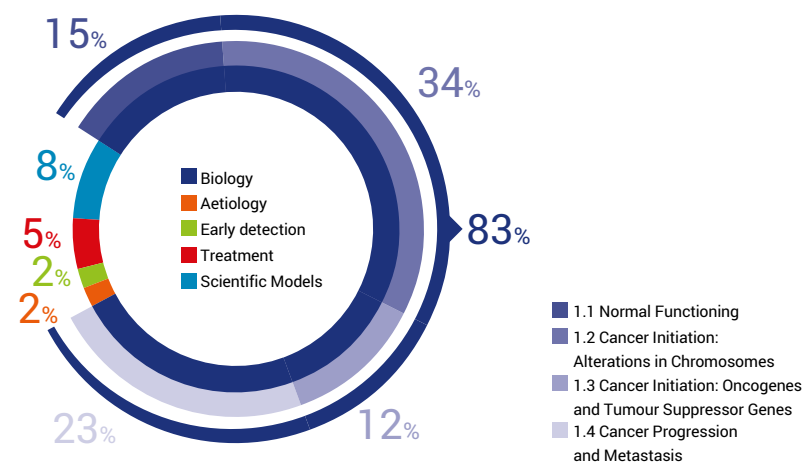
In 2020, one project selected in 2018 was extended for 2 additional years. This project is aimed at developing a dynamic model of epigenetic plasticity in cancer.

The programme over the 2007-2020 period

Over the 2007-2020 period, 52 grants were funded by ITMO Cancer-Aviesan for a total amount of €12.74M. More than 80% of the projects were devoted to cancer biology research (Figure 18).



■ FIGURE 18
DISTRIBUTION OF CANCER-RELATED PROJECTS SELECTED WITHIN THE SCOPE OF THE ATIP-AVENIR PROGRAMME ACCORDING TO CSO CLASSIFICATION OVER THE 2007-2020 PERIOD



SUPPORT FOR THE ANR JCJC PROGRAMME

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

■ **TABLE 12**
FEATURES OF THE JCJC PROGRAMME IN CANCER RESEARCH IN 2020

Objectives	To support established young researchers with additional funding of their project in the cancer field.
Programming institution	French National Research Agency (ANR)
Operating institution	French National Research Agency (ANR)
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€281,000 (1 project)

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



TRANSLATIONAL AND INTEGRATED CANCER RESEARCH



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

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

In 2020, support for translational and integrated cancer research amounted to

€11.75M:

€9.46M

dedicated to support investigator-driven projects (PRT-K programme);

€2.29M

to support translational and multidisciplinary cancer research training.



National translational cancer research programme (PRT-K)

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

THE PROGRAMME IN 2020

In 2020, 17 projects were selected for funding, out of the 106 submitted, representing an overall budget of €9.46M (€5.93M INCa + €3.53M DGOS) (Table 13).

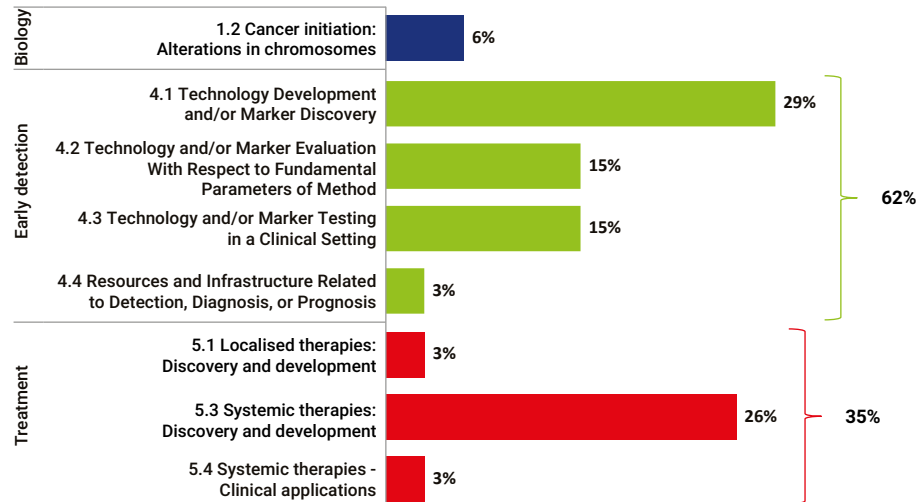
■ **TABLE 13**
FEATURES OF THE PRT-K PROGRAMME IN 2020

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	€9.46M INCa: €5.93M DGOS: €3.53M
Proposals submitted	106
Projects selected	17
Selection rate	16%

In compliance with the objectives of the programme, over 60% of the projects selected in 2020 are studying early detection, diagnosis, and prognosis. About one third of the studies are focusing on the development of treatments, especially discovery and development of systemic therapies (Figure 19).



■ **FIGURE 19**
DISTRIBUTION OF PROJECTS SELECTED IN 2020 ACCORDING TO THE CSO CLASSIFICATION



2007-2020:
223
projects funded for
a total amount of
€100.53M

THE PROGRAMME OVER THE 2007-2020 PERIOD

Since 2007, 1,657 proposals have been submitted to this call for proposals, and 223 have been selected and funded for a total amount of €100.53M. The overall selection rate for this call for proposals is 13.5% (Figure 20).

The CSO typology of the projects funded since 2007 corresponds to the characteristic profile for translational research (Figure 21), 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 treatment resistance mechanisms.

FIGURE 20
TRENDS IN SELECTION AND FUNDING OF THE PRT-K PROGRAMME OVER THE 2007-2020 PERIOD

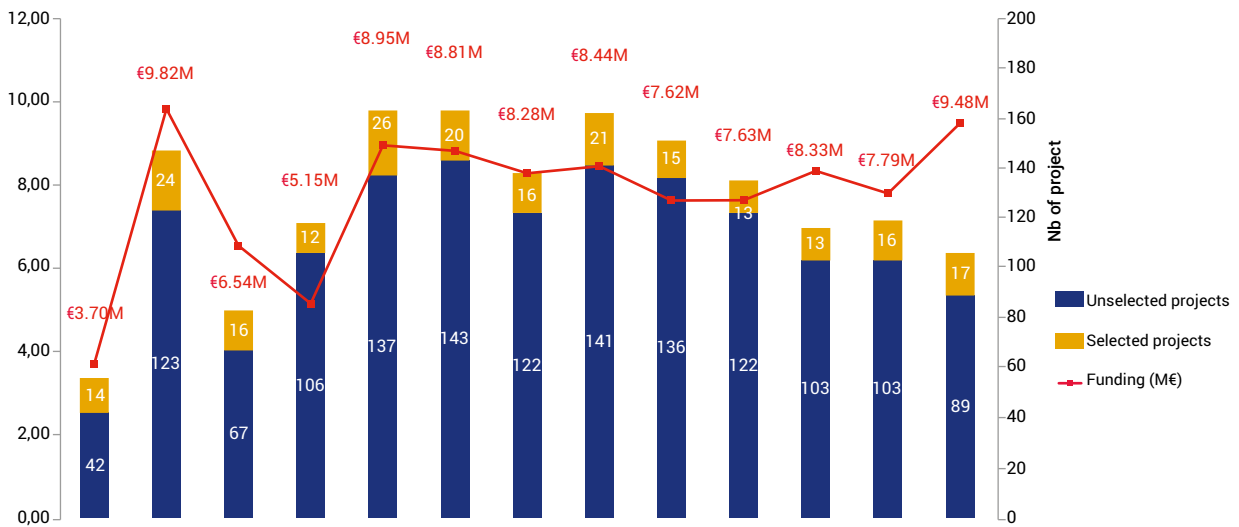
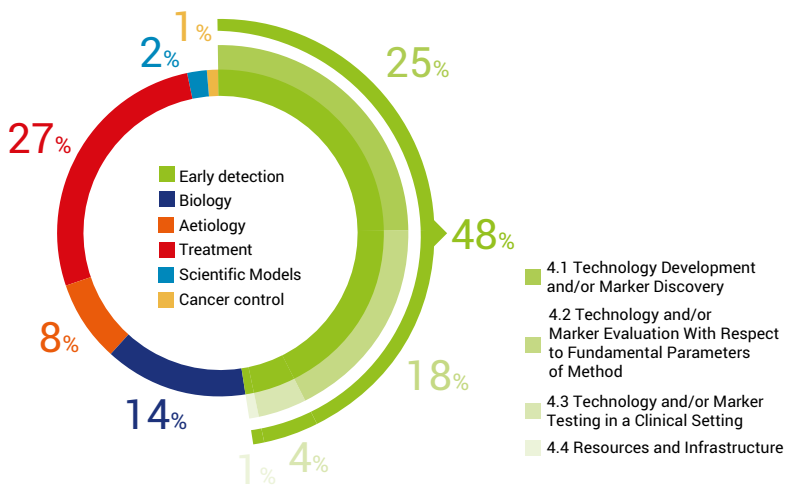


FIGURE 21
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2020 PERIOD



European translational cancer research programme (TRANSCAN)

THE PROGRAMME IN 2020

The European TRANSCAN network was created in 2011, under the Seventh Framework Programme of the European Commission, and continued under Horizon 2020 (TRANSCAN-2 from 2014 to 2020). The French National Cancer Institute has been participating in this network since the beginning. At the end of 2020, and after one year of active preparation with the European partners, the European Commission supported the continuation of this programme by approving the new TRANSCAN-3 ERA-NET for a 5-year duration (2021-2026). The Institute renewed its commitment to this project and will be, particularly, responsible for the third joint call for proposals in 2023. Indeed, each year, a different partner acts as Joint Call Secretariat to coordinate the application and selection process.

This ERA-NET aims to coordinate national and regional research funding programmes in the field of translational cancer research. The objective is to promote a transnational collaborative approach between scientific teams involved in cancer research, in order to produce significant results of higher quality and impact, to share data, and to pool infrastructures.

This consolidated network is now based on the cooperation of 31 regional and national, public and private funding organisations from 20 European and non-European countries (Figure 22). The majority of the partners have been collaborating since 2011 (within the 2 previous TRANSCAN and TRANSCAN-2 ERA-NETs).

TRANSCAN-3:

31

partners from

20

countries

■ FIGURE 22
TRANSCAN-3: PARTICIPATING COUNTRIES



For TRANSCAN-3, the network has been expanded with new partners, such as Canada, Hungary, Ireland or Romania, in accordance with the extension strategy included in the missions of this programme.

REVIEW OF THE TRANSCAN PROGRAMME OVER THE 2010-2020 PERIOD

Overview of the 7 calls

As a result of the 7 calls, 79 research projects were funded, involving 406 teams from 20 countries (including the US and UK, which are not participating countries) for a global funding of €85.2M (including the €3.4M EU contribution for the 2014 co-funded call) (Table 14).

■ **TABLE 14**

FEATURES OF THE DIFFERENT CALLS FOR PROPOSALS LAUNCHED OVER THE 2011-2017 PERIOD

JTC	Themes	Total budget spent (€M)	Number of funding organisations	Number of funded projects	Number of PIs in funded projects
2011	Validation of biomarkers	10.4	15	10	55
2012	Primary and secondary prevention	11.2	17	10	55
2013	Tertiary prevention	11.4	17	10	49
2014	Tumour heterogeneity	17.3	25	16	85
2015	Immunology and immunotherapy	6.0	15	7	35
2016	Minimally and non-invasive methods for early detection	15.1	23	14	70
2017	Rare cancers	13.8	23	12	57
Overall		85.2		79	406

The budget of the 2014 call was greater than the average budget thanks to a contribution from the European Commission (Figure 23). The limited number of applications and projects selected in 2015 is explained by a smaller number of participating partners than for the other calls for projects, with notably Germany and the Netherlands not taking part in this call.

FIGURE 23
NUMBER OF FUNDING ORGANISATIONS PARTICIPATING IN TRANSCAN AND TRANSCAN-2 CALLS AND TOTAL BUDGET



2011-2018:
17 calls
79 projects
406 teams
€85.2M

Selection rate

The 7 calls for proposals attracted nearly 2,800 researchers grouped together in 561 consortia. The overall success rate was about 15% (Figure 24).

Funding

An overall budget of €85.2M was spent by all funding organisations participating in the 7 TRANSCAN and TRANSCAN-2 calls. For some countries (Italy, Spain, France, Norway, the Netherlands, Belgium) several partner organisations are involved in the TRANSCAN network. France is the third largest funding country after Germany and Italy (Figure 25), which is consistent with its number three ranking in terms of funded teams (see Figure 28).

FIGURE 24
NUMBER OF PROJECTS SUBMITTED AND FUNDED AND TRENDS IN THE SELECTION RATE OF THE TRANSCAN AND TRANSCAN-2 CALLS

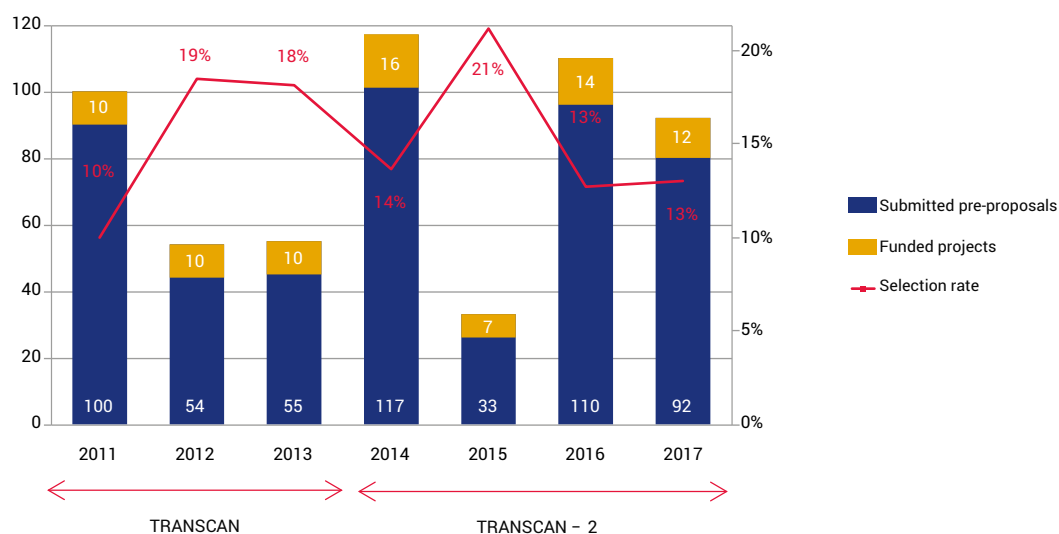
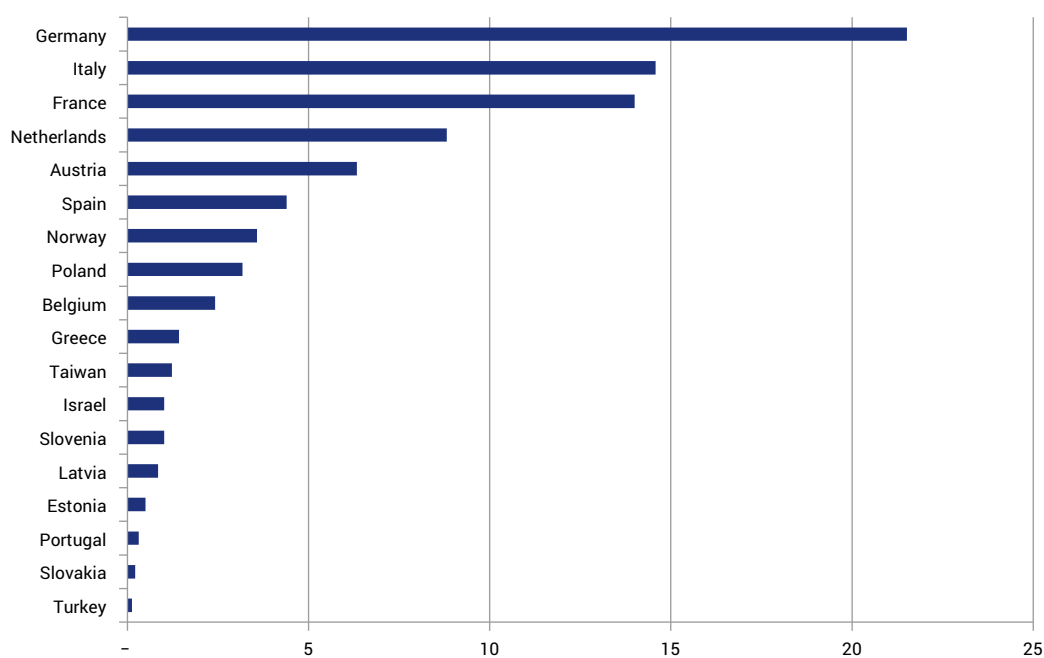


FIGURE 25
BUDGET SPENT BY COUNTRY IN TRANSCAN AND TRANSCAN-2 CALLS (IN €M)



Cancer types

Almost half of the projects selected in TRANSCAN and TRANSCAN-2 focused on haematopoietic and lymphoid malignancies, colorectal cancer, and breast cancers (Figure 26).

Clinical trials

Nearly a quarter of the TRANSCAN and TRANSCAN-2 projects included a clinical trial (early-phase only). The majority of these trials focused on breast, colorectal, lung, oesophageal, and thyroid cancers (Figure 27).

Number of funded researchers by country

Both in terms of the number of researchers participating in TRANSCAN projects (63 French researchers) (Figure 28) and the number of researchers coordinating projects (10 French coordinators), France ranks third behind Germany and Italy (Figure 29).

FIGURE 26
DISTRIBUTION OF FUNDED PROJECTS ACCORDING TO CANCER SITES STUDIED FOR ALL TRANSCAN AND TRANSCAN-2 CALL FOR PROPOSALS

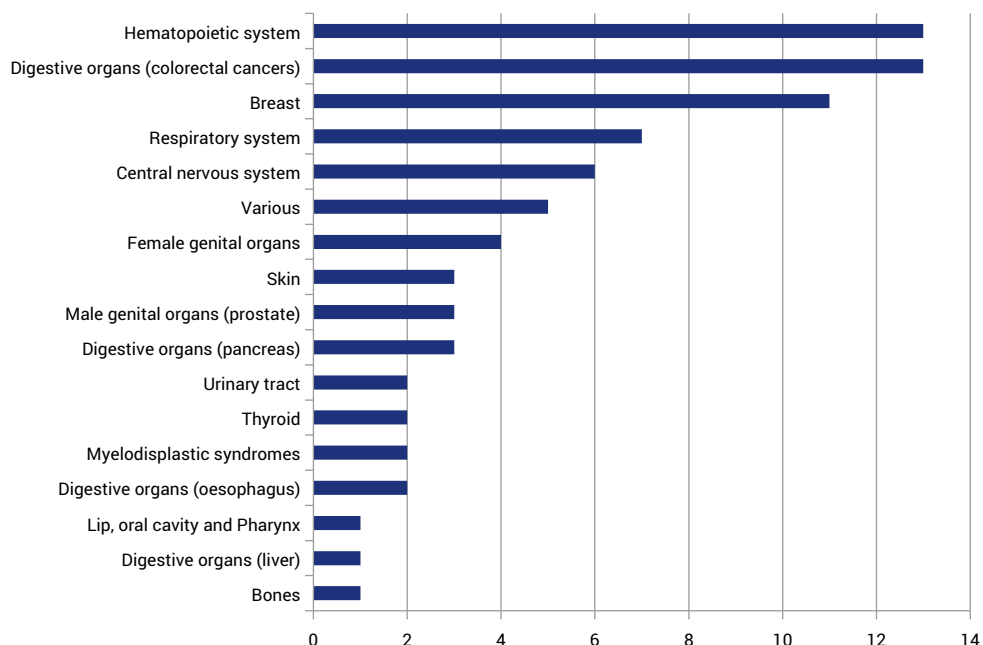


FIGURE 27
SHARE OF TRANSCAN AND TRANSCAN-2 PROJECTS INCLUDING A CLINICAL TRIAL AND NUMBER OF CLINICAL TRIALS BY CANCER SITE

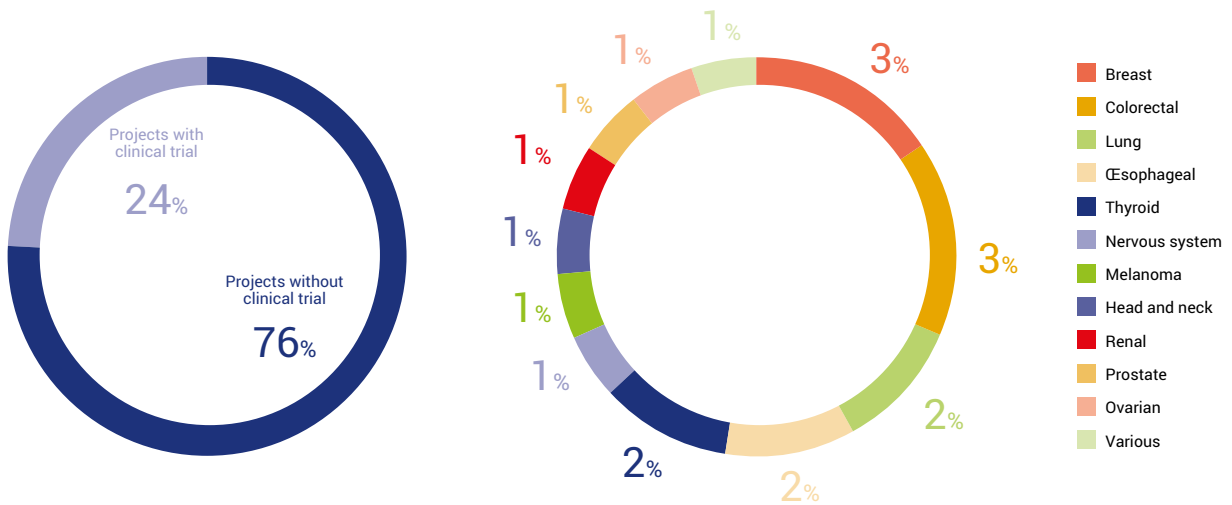
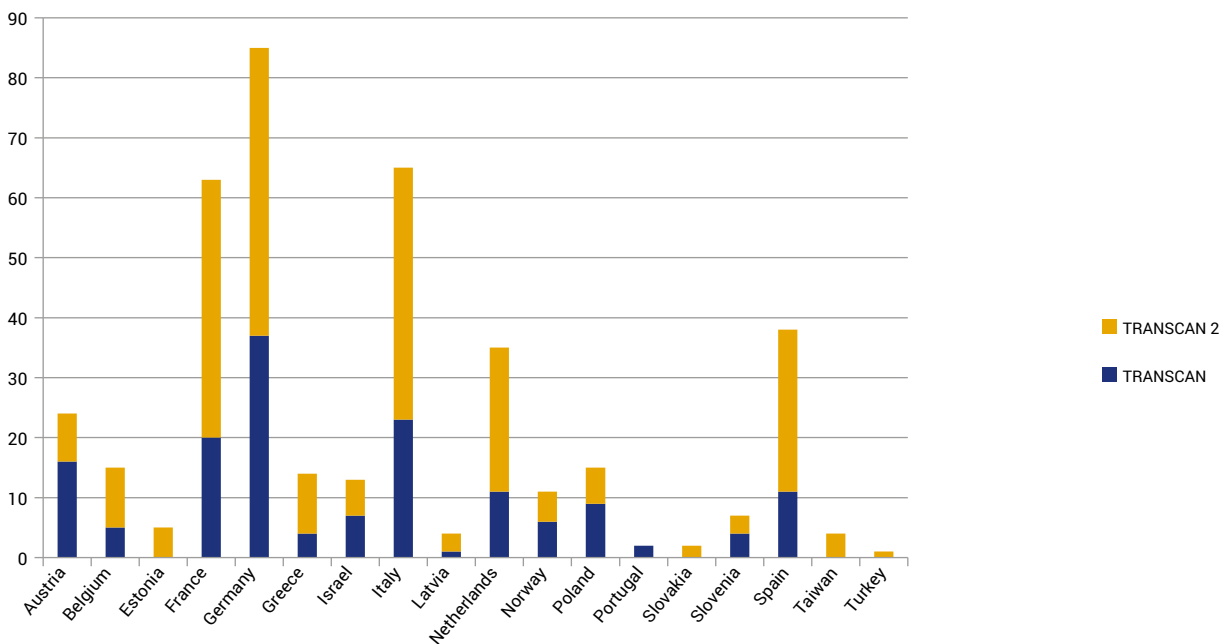
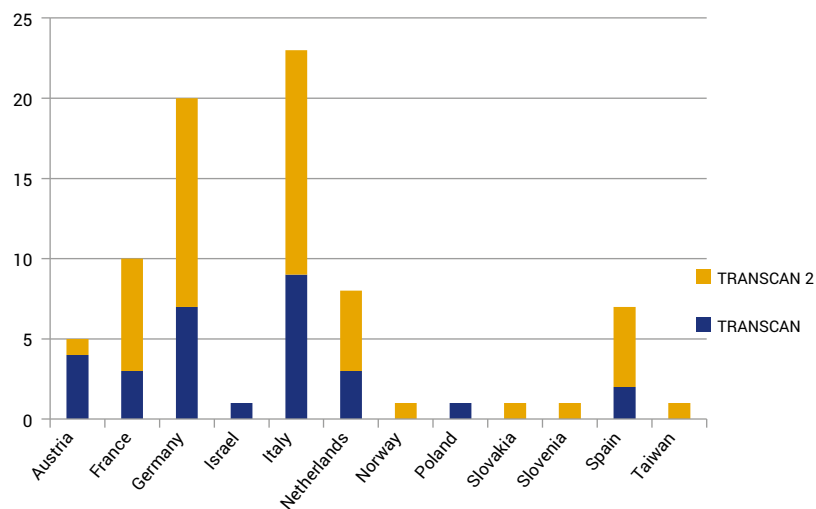


FIGURE 28
NUMBER OF FUNDED RESEARCHERS BY COUNTRY IN TRANSCAN AND TRANSCAN-2 CALLS



■ **FIGURE 29**
NUMBER OF FUNDED COORDINATORS BY COUNTRY IN TRANSCAN AND TRANSCAN-2 CALLS



Integrated research action programme (PAIR)

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

PAIR ON BRAIN TUMOURS

In 2019, INCa, ARC Foundation and the French Cancer League decided to renew their partnership in order to support, develop and co-fund a new PAIR devoted to brain tumours.

A dedicated Steering Committee was set up, particularly to define the scientific research priorities. Chaired by Professor Khê Hoang Xuan (AP-HP Pitié-Salpêtrière, Paris), this committee is composed by renowned experts in neuro-oncology, neuropathology, basic research, radiotherapy and imaging, paediatrics, epidemiology, human and social sciences.

From February to October 2020, the Steering Committee was split into 4 sub-groups to work on the research priorities, in the aim of helping INCa draft the most relevant call for proposals to be launched in 2021. Patient representatives were also involved in the discussions, and their opinions and recommendations were taken into account.

In October 2020, the brain tumours PAIR workshop was organised and attracted over 150 attendees. This national webinar promoted discussions around the 4 main issues of brain tumours research:

- Area 1: Improving fundamental knowledge through an integrative approach;
- Area 2: Improving diagnosis, treatment response assessment and monitoring;
- Area 3: Developing innovative treatments;
- Area 4: Considering quality of life and disability.

A call for proposals around these research areas will be launched in 2021.

FOLLOW-UP OF PREVIOUS EDITIONS

PAIR Pancreas

In 2017, INCa, ARC Foundation and the French Cancer League launched a PAIR dedicated to pancreatic cancer in order to increase and enhance dynamic research capabilities, to promote scientific excellence and the emergence of innovative projects, and to allow medical and scientific priorities to be defined.

In 2018, seven projects were selected for a total amount of €3.7M. The one-year follow-up meeting was held at INCa in February 2020. All the project leaders presented good progress of their research projects based on their initial milestones.

This meeting also offered an opportunity to address different points such as the relevant manner to transfer project results to practice, difficulties recruiting technicians, and problems due to PhD student funding.

A second-year follow-up meeting is scheduled in April 2021.

PAIR Breast cancer report workshop

In January 2020, INCa and its partners, ARC Foundation and the French Cancer League, organised a workshop devoted to the seven projects funded within the scope of the Early Breast cancers PAIR launched in 2014. This report workshop was held in collaboration with the French Breast Cancer Intergroup - Unicancer (UCBG) designated by INCa, as part of the "Breast cancer research day: from basic to clinical research". Approximately 170 health professionals and researchers attended.

The morning was devoted to the Breast cancer PAIR workshop and focused on basic research. This

session was chaired by Prof. David Cameron, Clinical Director of the Edinburgh University Cancer Centre. The afternoon was devoted to the scientific meeting of the French Breast Cancer Intergroup and focused on clinical research.

The results of the funded projects were presented. These projects have led to numerous scientific publications in international journals and led to the development of new leads for innovative therapeutic strategies and the identification of new therapeutic targets. This report workshop provided opportunities to federate research teams, leading to a high-quality translational research approach.

PAIR Paediatrics

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 over €5M.

In November 2020, a second annual virtual meeting with the 3 principal investigators was held. All three presented good progress of their research projects based on their initial milestones. However, due to the pandemic context, some objectives have been postponed resulting in a one-year extension.

Support for integrated cancer research structuring

INTEGRATED CANCER RESEARCH SITES (SIRIC)

The SIRIC (Integrated Cancer Research Sites) programme is a French National Cancer Institute research structuring policy initiated in 2011. The importance and priority of this flagship programme were reinforced in the 2014-2019 Cancer Control Plan with a second call for designation, launched in 2017. This second call was open to previously designated sites and to new applicants. It resulted in the designation of 2 new SIRICs (CURAMUS and ILIAD) and the renewal of 6 SIRICs (BRIO, CARPEM, CURIE, LYRICAN, MONTPELLIER CANCER and SOCRATE 2.0) for a 5-year designation period (2018-2022).

Organisation of mid-term evaluation

In 2020, a mid-term evaluation was organised by INCa with the objective of obtaining a scientific assessment of the progress and achievements made by the 8 SIRICs during the 1st designation period (from January 2018 to June 2020) in order to make recommendations to them on scientific objectives and/or strategies for the 2nd period (July 2020-December 2022).

An international Scientific Evaluation Committee (SEC), composed of 11 experts in different fields and disciplines, including 8 members who had participated in the selection committee for the SIRIC selection in 2017, and one patient representative were invited to perform this evaluation, which was carried out in a two-stage process, involving:

- the analysis of a written report presenting the SIRIC's activities and organisations by 4 different SEC members;
- an interview with each SIRIC director and some SIRIC representatives.

SIRIC designation aims to offer new opportunities for conducting translational cancer research, thus helping optimise, accelerate and disseminate the production of new knowledge and its application to cancer care. Therefore, the SIRICs were evaluated by the SEC according to the following 13 criteria:

1. SIRIC governance and management structure with executive and scientific committees

2. establishment of shared resource facilities to support the SIRIC integrated research programmes: platforms, databases, and teams with specific expertise (methodology, biostatistics, bioinformatics, regulatory and ethical procedures, etc). Establishment or development of high-quality biobanks with links to clinical and follow-up data
3. commitment to support the emergence of research projects (e.g. pump-priming grants)
4. commitment to a training programme in translational and integrated research
5. progress of the SIRIC multidisciplinary integrated research programmes
6. availability of a sufficient patient population or rate of patient recruitment to support bench-to-bedside studies in all integrated research programmes
7. effective integration between basic and applied scientists (e.g. clinicians, population scientists)
8. commitment to develop and integrate human and social sciences, epidemiology and public health studies
9. involvement of patient advocates
10. national and international synergistic collaborations as well as public-private partnerships
11. dissemination of new knowledge and best practices resulting from the research to professionals and patients, incentive for technology transfer for economic development
12. ability to leverage funding and/or resources obtained as a result of an “outstanding” designation
13. global vision of the SIRIC, scientific directions, goals and perspectives for the 2nd designation period.

General conclusions of the mid-term evaluation

Each SIRIC received a report with specific recommendations to be addressed during the 2nd designation period. In terms of general conclusions, the SEC underlined the important role played by the SIRICs in cancer research in France. They considered that this designation had a major effect on the structuring of sites and contributed to increased interactions between researchers and clinicians. The SIRIC programme promoted the integration of the different dimensions of research (basic, clinical, public health, epidemiology, and human and social sciences), leading to significant progress in the conduct of integrated multi-disciplinary research in oncology.

The Committee noted disparities between the SIRICs, both in terms of organisation and strategies. The call for applications gave some freedom in proposals, and partly explains these differences, with a different interpretation of the “SIRIC model” from one site to another. The SEC concluded that the majority of SIRICs made good use of the allocated funds with a large proportion of the grants used for the establishment of cutting-edge technological platforms.

In summary, SIRIC designation was undoubtedly recognised by SEC members as a great success. The SIRICs have made possible to considerably improve the quality of cancer research organisation, the production of knowledge, and the transfer of innovation in the practice and organisation of care. Based on the recommenda-

tions of the SEC and the results of this mid-term evaluation, INCa is considering updating the SIRIC model, while taking into account the actions planned in the 10-year cancer control strategy.

OSIRIS: Roll-out and real-life validation

- ***First publication of the inter-SIRIC OSIRIS group on the sharing and integration of clinical and biological data in oncology***



Pioneering and innovative molecular profiling trials conducted within SIRICs showed mixed results and led to the collective decision to boost data sharing and interoperability. The structuring of data, both biological and clinical, was an essential prerequisite for the work of the OSIRIS group (Inter-SIRIC group on the sharing and integration of clinical-biological data in oncology). The objective of this initiative was to enable various partner sites to share clinical, biological and genomic data in order to improve their use for research purposes. INCa has supported this national initiative by funding the “OSIRIS Proof of Concept” study which led to significant conceptual and technical achievements by the OSIRIS group, summarised below:

- the definition of a minimal set of 130 clinical and genomic items – “the OSIRIS set” (publicly available on the INCa website);
- the creation of a CDM (Common Data Model) – the “OSIRIS model” – able to capture the longitudinal progression of the disease;
- the demonstration of a federated system to remotely query databases in the participating institutions;
- the compatibility of the OSIRIS set with the HL7 Fast Healthcare Interoperability Resources (FHIR) format, an international standard for electronically exchanging healthcare information.

These findings were published in JCO Clinical Cancer Informatics in March 2021.

In order to promote the national initiative further, in 2021, the group will commence a follow-up project named MED-OSIRIS (Maintenance, Extension and wider Deployment of the OSIRIS dataset), also supported by INCa.

To access the publication: <https://ascopubs.org/doi/abs/10.1200/CCI.20.00094>

BIOLOGICAL AND CLINICAL DATABASES (BCBS)

From 2011 to 2013, INCa launched a call for applications to implement Biological and Clinical Databases (BCBs). This programme aimed to encourage, according to the recommendations made to the tumour banks, the federation of different players to set up, around a common pathology, biological and clinical databases associated with biological samples. In total, 14 projects were selected for funding for an overall budget of €8.1M.

Beyond the specificity of each BCB, an organisational model has been defined with the BCB teams to meet new research and public health needs.

The main objective and the added value expected of a BCB is to organise the set-up, development, and management of a national prospective cohort focused on a specific cancer pathology or cancer site to analyse its clinical, biological and genomic characteristics to improve the knowledge of the specific pathology, and secondly to study diagnostic modalities and therapeutic practices to refine patient care management.

The database consists of data from medical records and reports (clinical, histopathological and biological characteristics, monitoring data (treatments, treatment responses), and possibly associated with additional data (quality of life, working conditions, eating habits)) collected through patient surveys.

The collection of biological samples is based on the residue of samples taken in the context of routine care, and if necessary with additional samples, in order to characterise tumour status as much as possible at the key stages of care and treatment.

2020 has been a year of reflection and construction of the ten-year cancer control strategy. It is now obvious that the mastery and valuation of “data” are major challenges for achieving genuinely significant progress over the coming decade. Organisations like “BCBs” will have a significant role in our actions to structure care and research.

In October 2020, an experience-sharing seminar was organised with the BCB teams. This workshop offered an opportunity:

- to make an inventory of BCB activities and an assessment of organisations (valuations, expectations and difficulties, prospects);
- to address organisational perspectives that can be considered based on the ten-year cancer control strategy;
- to present the INCa data platform project and to discuss certain topics inherent to large-scale data sharing.

We confirm that BCBs could contribute to several measures of the ten-year cancer control strategy; particularly as members and partners of the networks of centres of excellence for “cancers with poor prognosis”. In this regard, 6 BCBs are positioned on this topic:

- Oesogastric carcinomas
- Liver
- Glioblastoma / Central nervous system
- Mesothelioma
- Pancreas
- Myeloproliferative syndromes (for cases of acute myeloid leukaemia following cancer transformation)

2011-2013:
14
BCBs supported for
a total initial funding of
€7.76M

2017-2018:
evaluation conducted
by a scientific evaluation
committee. A supplementary
budget of
€1.05M
has been allocated
to 8 BCBs.

2020:
**experience-sharing
seminar, to prepare
the ten-year
cancer control
strategy**

RADIOTRANSNET: National preclinical radiotherapy research network

In 2017, INCa launched a call for applications aiming to set up a national preclinical radiotherapy research network in order to structure and to integrate fundamental and translational radiotherapy research. RADIOTRANSNET, coordinated by Philippe Maingon and Vincent Marchesi, was designated by INCa and was granted €200,000 for 3 years.

The year 2020 was devoted to the following actions:

- Bringing together the principal players and stakeholders in the field of radiotherapy;

- 4th workshop dedicated to “combined treatment” was held in December 2020;
- Building a strategic research agenda for radiation oncology based on the 4 workshop reports;
- Links with national authorities (CNRS) and private companies;
- Participation in scientific events;
- Drafting a presentation leaflet of RADIOTRANSNET.

The project saw satisfactory progress in 2020, with a slight delay of 6 month due to the pandemic context.

Translational and multidisciplinary training programmes

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

Support for basic and translational research through project funding 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 post-doctoral 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 basic research training of graduates of medicine, pharmacy, dentistry, and veterinary science.

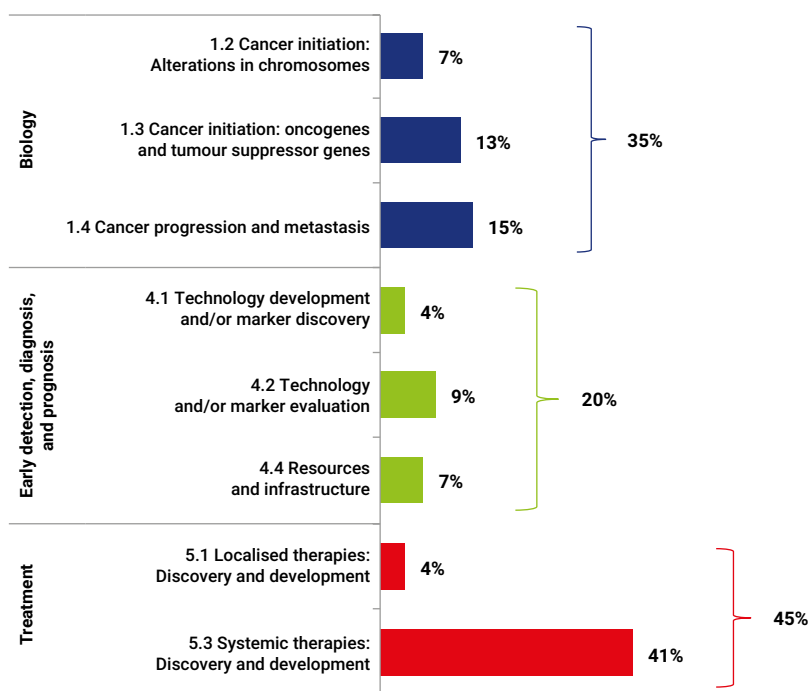
The programme in 2020

■ TABLE 15
FEATURES OF THE BASIC AND TRANSLATIONAL RESEARCH TRAINING PROGRAMME (FRFT) IN 2020

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	€1.97M
Proposals evaluated	48
Projects funded	23 (9 Masters, 13 PhDs & 1 Post-doctorate)
Funding rate	48%



FIGURE 30
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE FRFT PROGRAMME ACCORDING TO CSO CLASSIFICATION IN 2020



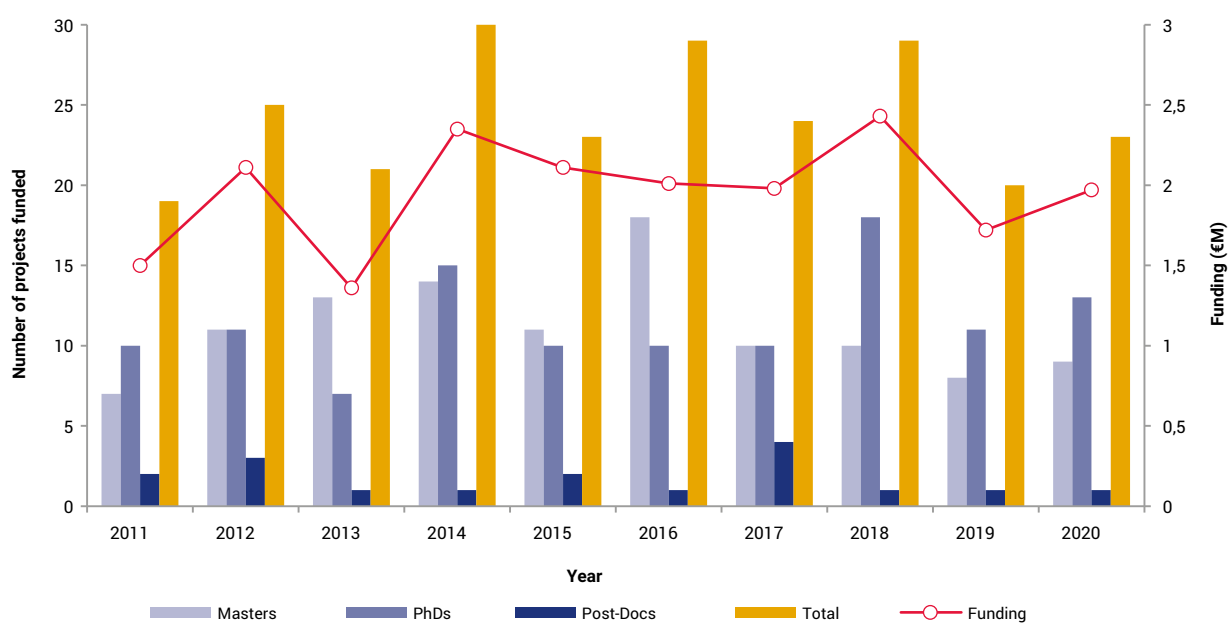
The programme over the 2011-2020 period

Since 2011, 243 projects have been funded from 779 evaluated projects (funding rate of 31%), for a total amount of €19.56M. Over this 10-year period, the FRFT programme funded 111 Masters, 115 PhD theses, and 17 post-doctorates (Table 16 and Figure 31).

TABLE 16
TRENDS IN SELECTION AND FUNDING OF THE FRFT PROGRAMME OVER THE 2011-2020 PERIOD

Year	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Total
Funding (in €M)	1.50	2.12	1.36	2.35	2.11	2.01	1.98	2.44	1.72	1.97	19.56
Proposals evaluated	35	36	49	101	98	111	108	106	87	48	779
Projects funded	19	25	21	30	23	29	24	29	20	23	243
Funding rate	54%	69%	43%	30%	23%	26%	22%	27%	23%	48%	31%

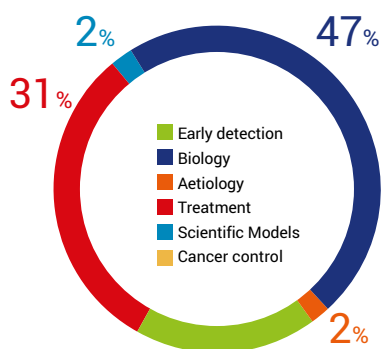
FIGURE 31
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE FRFT PROGRAMME ACCORDING TO QUALIFICATIONS OVER THE 2011-2020 PERIOD



2011-2020:
243
 projects selected for
 a total amount of
€19.56M

More than 45% of the grants were devoted to basic cancer research (understanding the general principles of cancer emergence or growth) (Figure 32). Projects based on the development of therapeutic approaches accounted for just over 30% of the grants, while detection and diagnostic approaches accounted for almost 20% of the grants (Figure). The Aetiology and Scientific model systems categories each concerned 2% of the projects.

FIGURE 32
DISTRIBUTION OF PROJECTS SELECTED WITHIN THE SCOPE OF THE FRFT PROGRAMME ACCORDING TO CSO CLASSIFICATION OVER THE 2011-2020 PERIOD



SUPPORT FOR THE “FRONTIERS IN LIFE SCIENCES (FDV)” INTERDISCIPLINARY RESEARCH PROGRAMME BY ITMO CANCER-AVIESAN

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 2020

TABLE 17
FEATURES OF THE TRAINING IN INTERDISCIPLINARY RESEARCH - FRONTIERS IN LIFE SCIENCES (FDV) PARTNERSHIP IN 2020

Objectives	To promote ambitious cancer 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	€210,000 (2 projects)
Proposals submitted	39
Projects selected	23
Selection rate	59%

In 2020, 2 projects were selected for a total amount of €210,000. They were aimed at deciphering the role of tumour-associated macrophages on the tumour extra-cellular matrix structure, and at exploring the role of the metabolism of different subsets of cancer-associated fibroblasts (CAFs) on their identity and function.

The programme over the 2010-2020 period

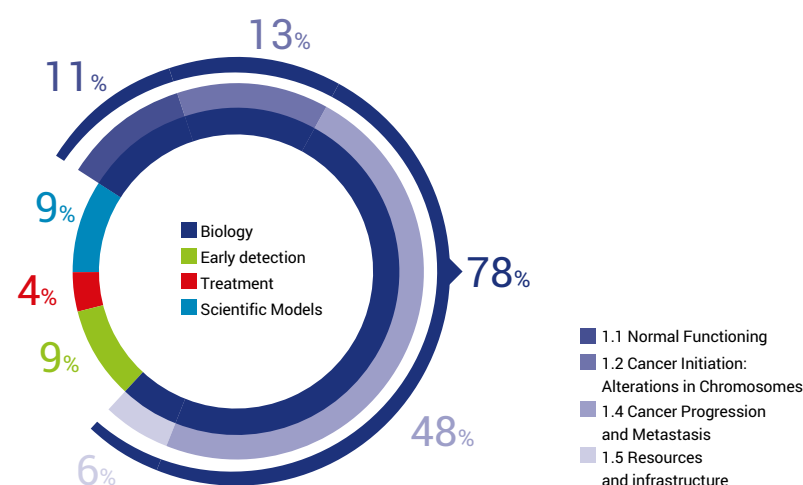
Over the 2010-2020 period, 23 grants were funded by ITMO Cancer-Aviesan for a total amount of €2.41M (Table 18). Almost 80% of the projects were devoted to cancer biology research (Figure 33).

■ **TABLE 18**
TRENDS IN FUNDING OF CANCER-RELATED PROJECTS WITHIN THE SCOPE OF THE FDV PROGRAMME OVER THE 2010-2020 PERIOD

Year	2010	2011	2012	2013	2014	2015	2016	2018	2019	2020	Total
Projects funded	2	2	2	2	2	3	4	2	2	2	23
Funding €M	0.21	0.21	0.21	0.21	0.21	0.31	0.42	0.21	0.21	0.21	2.41



■ **FIGURE 33**
DISTRIBUTION OF CANCER-RELATED PROJECTS SELECTED WITHIN THE SCOPE OF THE FDV PROGRAMME ACCORDING TO CSO CLASSIFICATION OVER THE 2010-2020 PERIOD



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

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

The programme in 2020

■ TABLE 19
FEATURES OF THE STIC DOCTORAL SCHOOL PARTNERSHIP IN 2020

Objectives	To promote dual training and foster innovative research by funding PhD theses at the interface of information technologies and oncology
Programming institution	Paris-Saclay University
Operating institution	Paris-Saclay University
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€102,421 (1 project)

In 2020, 1 project was funded for a total amount of €102,421. It was aimed at developing machine learning-based tools helping health professionals to extract and gather relevant data for multidisciplinary tumour boards meetings.

The programme over the 2018-2020 period

In 2 editions (2018 and 2020), 3 projects have been funded within the ITMO Cancer-Aviesan/STIC Doctoral School partnership, for a total amount of almost €300,000 (Table 20). Two projects belonged to the CSO Scientific model systems category, while the other one belonged to the CSO Treatment category.

■ TABLE 20
TRENDS IN FUNDING OF CANCER-RELATED PROJECTS WITHIN THE SCOPE OF THE STIC PROGRAMME OVER THE 2018-2020 PERIOD

Year	2018	2020	Total
Projects funded	2	1	3
Funding (€)	192,044	102,421	294,465



CLINICAL CANCER RESEARCH AND ACCESS TO INNOVATION



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

In 2020, support for clinical cancer research amounted to

€23.57M:

€21.92M dedicated to support investigator-driven projects (PHRC-K programme);

€1.65M to support strategic cancer research initiatives, such as RNAseq technique roll-out in molecular genetic centres.



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;
- 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 (de-escalation studies);
- Increase of patient 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.
- Research in primary care and prevention (French national health strategy).

In addition, 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 side-effects and delayed effects of treatments.

2020:
36
clinical research projects funded out of the 188 submitted for a total budget of **€21.9M**

THE PROGRAMME IN 2020

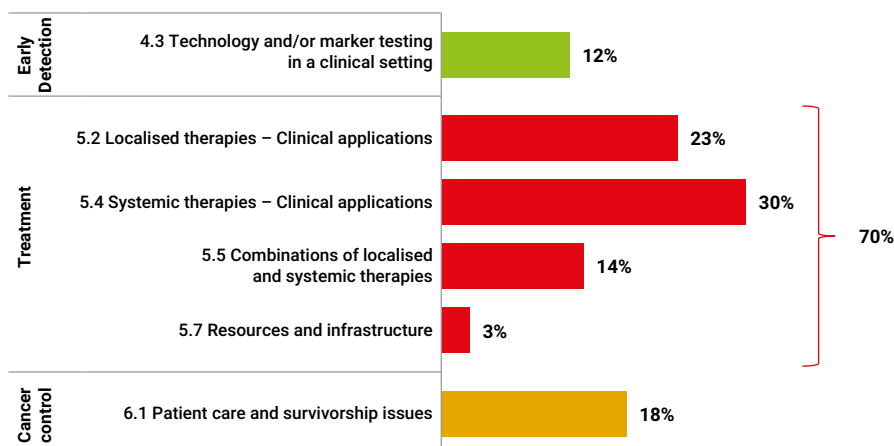
In 2020, 188 letters of intent were submitted to PHRC-K, and 36 projects were selected for funding for a total amount of €21.9M (Table 21).

■ **TABLE 21**
FEATURES OF THE PHRC-K PROGRAMME IN 2020

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	€21.9M
Proposals submitted	188
Projects selected	36
Selection rate	19%

For 2020, the CSO analysis of funded projects shows that the majority of the funded projects belong to the treatment category (69.4%) and, particularly, to clinical applications of systemic and localised therapies (42.8% and 33.2%, respectively). The other topics studied are related to early diagnosis (12.5%), and care and survival (18.1%) (Figure 34).

■ **FIGURE 34**
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION IN 2020



THE PROGRAMME OVER THE 2007-2020 PERIOD

Since 2007, 2,915 proposals have been submitted to the PHRC-K programme, and 668 projects have been selected for an overall amount of over €272M (Figure 35). The overall selection rate for this call for proposals is 23%.

Over the 2007-2020 period, the CSO analysis of funded projects shows that the majority of the funded projects belongs to the treatment category (65.6%) and, particularly, to clinical applications of systemic and localised therapies (52.3% and 25.7%, respectively). Moreover, the other topics studied are related to early diagnosis (20%), and care and survival (12.6%) (Figure 36).



FIGURE 35

TRENDS IN SELECTION AND FUNDING FOR THE PHRC-K PROGRAMME OVER THE 2007-2020 PERIOD

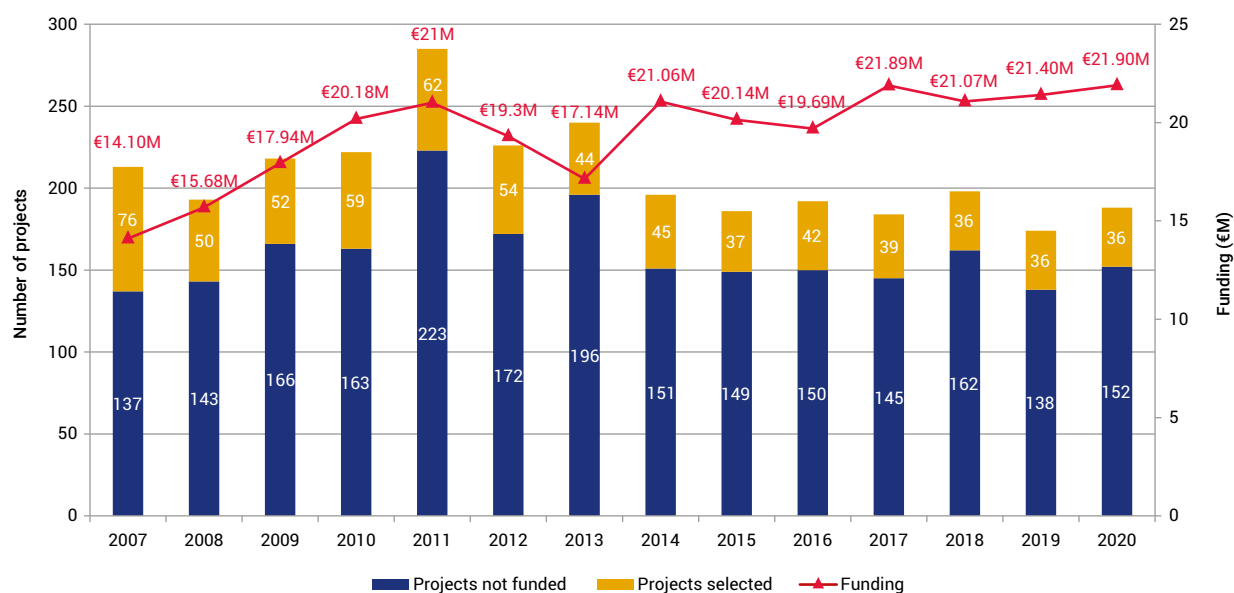
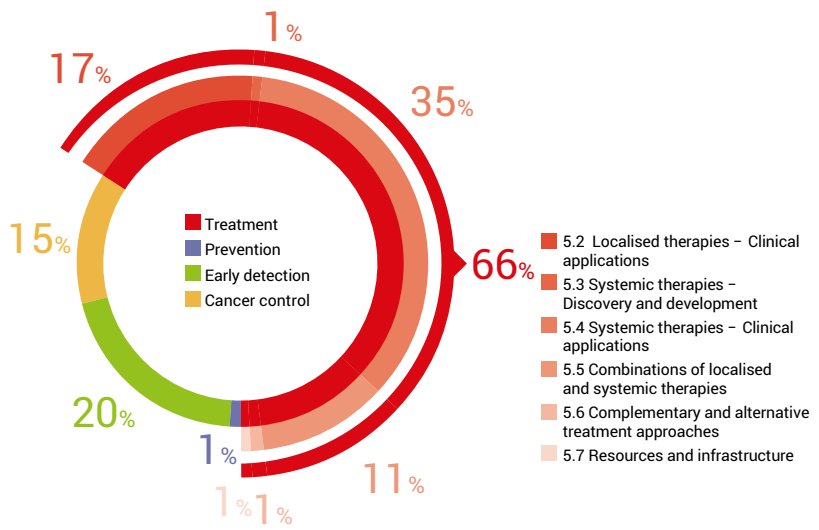




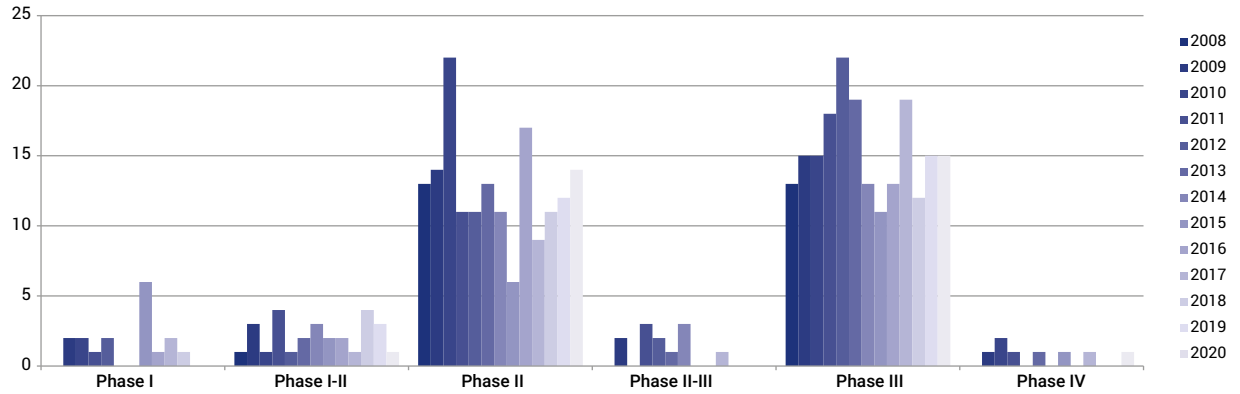
FIGURE 36
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2020 PERIOD



Over the 2007-2020 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



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 the 5 key stages of the clinical trial implementation process:

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

For the period of 2011 to 2019, 384 projects are concerned by monitoring according to funding tranches (figure 38).

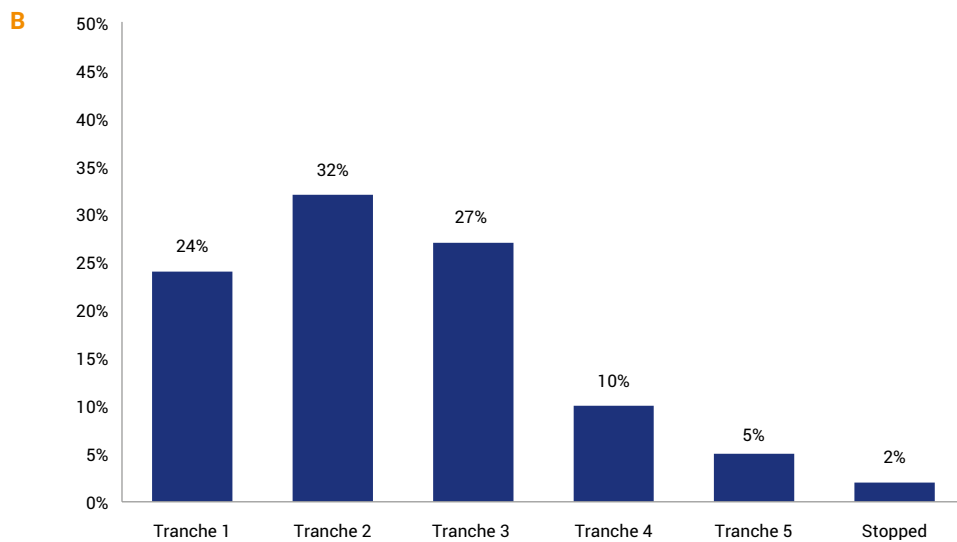
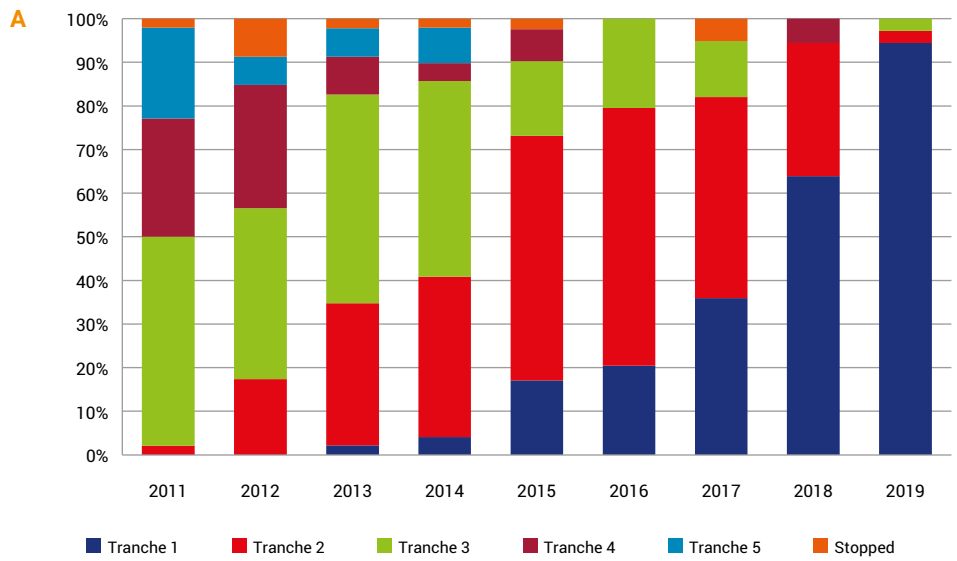
In 2020, for projects funded during the 2011-2019 period:

- 31.5% of projects requested tranche 2, corresponding to the approval stage.
- 28% of projects reached tranche 3, meaning that they have reached the “50% inclusion” stage.
- 5% of projects published based on their primary results, corresponding to 15 projects selected over the 2011-2014 period.
- 23.5% of funded projects did not start the clinical study either due to non-approval, or another reason (lack of human resources, no longer having support from the pharmaceutical industry, etc.).

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

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

FIGURE 38
DISTRIBUTION OF FUNDED PROJECTS ACCORDING TO THEIR PROGRESS AND THE YEAR OF SELECTION (PANEL A)
AND PERCENTAGE OF TOTAL PROJECTS ACCORDING TO THE TRANCHE STATUS (PANEL B)



A survey was conducted in 2020 in order to identify the reasons for which projects are still blocked in tranche 1 for more than 2 years after the funding allocation. Over the 2012-2017 period, 52 projects were concerned and different reasons have been identified (Figure 39):

- 48% of the projects experienced an administrative delay, the request for tranche 2 was on-going;
- 23% of the projects encountered difficulties blocking the advancement of their studies:
 - investigator's departure, or changing or lack of investment;
 - difficulties linked with the management of coordination, particularly for international promotions;
 - difficulties with pharmaceutical industry (i.e. supplying the study drug)
 - modifications of the research question, leading to a delay for the modified protocol validation.
- 17% of the projects experienced a delay in obtaining authorisations;
- 8% of the projects were discontinued.

Public-private partnerships

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

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

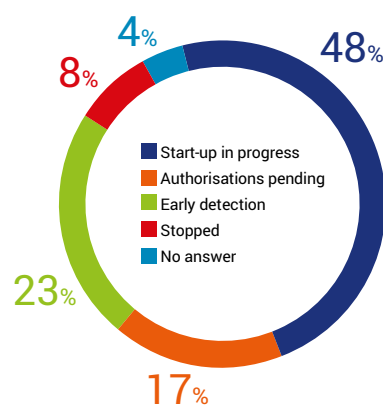
THE PROGRAMME IN 2020

In June 2019, INCa signed a new agreement with Novartis Pharma to supply the 16 CLIP² with four innovative drugs:

- HDM201, HDM2-P53 inhibitor
- Spartalizumab (PDR001), anti-PD1
- Capmatinib (INC280), c-Met inhibitor
- LSZ102, selective oestrogen receptor degrader

This agreement made it possible to launch a call for proposals in July 2020. Among the 35 projects submitted by 15 CLIP² centres, 6 were selected for a total amount of €2.97M.

■ **FIGURE 39**
SURVEY ANALYSIS: REASONS GIVEN
FOR PROJECTS BEING ON STAND-BY



■ **TABLE 22**
FEATURES OF THE INNOVATIVE DRUGS PROGRAMME IN 2020

Objectives	The purpose of this call for proposals is to select, based on applications, early-phase clinical trial proposals aimed at assessing the drugs HDM201, Spartalizumab, Capmatinib , LSZ102, administered in combination therapy.
Programming and operating institution	INCa
Funding institution	INCa /ARC Foundation
Funding	€2.97M INCa: €2.08M ARC Foundation: €0.89M
Proposals submitted	35
Projects selected	6
Selection rate	17.1%

The aim of this programme is to assess innovative drugs outside pharmaceutical company development plans on academic questions, and to propose drug associations. In compliance with objectives of this programme, the following were specifically selected:

- Two projects aiming to evaluate molecules in the paediatric population (Dr. De Carli and Dr. Ducassou)
- One project targeting metastatic soft tissue sarcomas, a disease of limited interest for industry (Prof. Blay)

■ TABLE 23
FEATURES OF THE SELECTED PROJECTS

Agents	Title	CLIP ² centre and PI
Spartalizumab : anti-PD-1 monoclonal antibody – Novartis Chemotherapies	SPARTANA: A phase IIA study evaluating the feasibility to combine radiotherapy, chemotherapies (docetaxel, cisplatin and 5-fluoro-uracil) and Spartalizumab in patients with locally advanced or oligometastatic squamous cell anal carcinoma	CLIP ² Bourgogne franche Comté CHU de Besançon Dr. Stefano KIM
Spartalizumab: anti-PD-1 monoclonal antibody – Novartis Capmatinib: c-Met inhibitor – Novartis	METIMGAST: Phase II to evaluate combination of capmatinib and spartalizumab in advanced gastric adenocarcinoma	CLIP ² Saint-Louis Paris Nord Assistance Publique des Hôpitaux de Paris Prof. Thomas APARICIO
Spartalizumab: anti-PD-1 monoclonal antibody – Novartis Pazopanib: tyrosine kinase inhibitor – Novartis	SPARTO: Spartalizumab and low-dose Pazopanib in Refractory or relapsed solid Tumors of pediatric patients and young adults	Cancer Innovation Nouvelle Aquitaine Hôpital des Enfants CHU Bordeaux Dr. Stéphane DUCASSOU
Spartalizumab: anti-PD-1 monoclonal antibody – Novartis Chemotherapies	GASPAR: A Single Arm Multicenter Phase 2 Study of Spartalizumab (PDR001) in Combination with fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) in perioperative for resectable gastric or gastroesophageal junction adenocarcinoma.	Centre François Baclesse Dr. Mélanie DOS SANTOS
Capmatinib: c-Met inhibitor – Novartis Everolimus : mTOR inhibitor – Novartis	ESMART capmatinib: Phase I/II trial of the cMET inhibitor Capmatinib (INC 280) combined with everolimus in pediatric, adolescent and young adult patients with refractory or relapsed cancer	CLIP ² -ILIAD Centre Hospitalier Universitaire d'Angers- Dr. Emilie DE CARLI
Pazopanib: tyrosine kinase inhibitor – Novartis HDM201 : HDM2-P53 inhibitor – Novartis	AMPHISARC: A multicentre, Phase I/II study evaluating the clinical impact of HDM201 + Pazopanib in patients with P53 wild-type advanced/ metastatic soft tissue sarcomas	Centre Léon Bérard Prof. Jean-Yves BLAY

THE PROGRAMME OVER 2010-2020

Since 2011, the Institute has launched 14 specific calls for proposals to propose 28 drugs under development, and 25 projects have been funded for €14.86M to evaluate these drugs, 17 have been co-funded by the ARC Foundation.

INCa Funding : €9.32 M

ARC Foundation funding: €5.54 M

Out of the 18 projects, 15 have actually started and the final 6 selected are planned to start in 2021 (Figure 40).

In this programme, the trials that have been able to start have enrolled nearly 500 patients.

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

FIGURE 40
OUTCOMES OF SELECTED PROJECTS

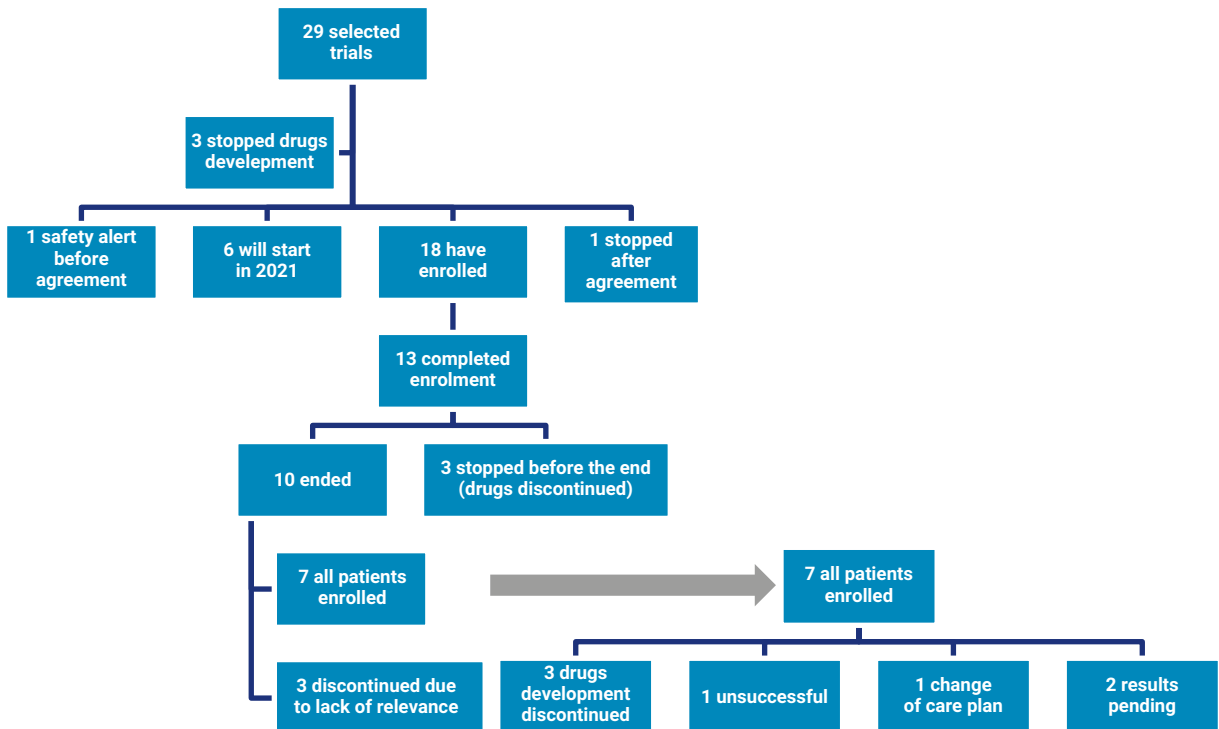
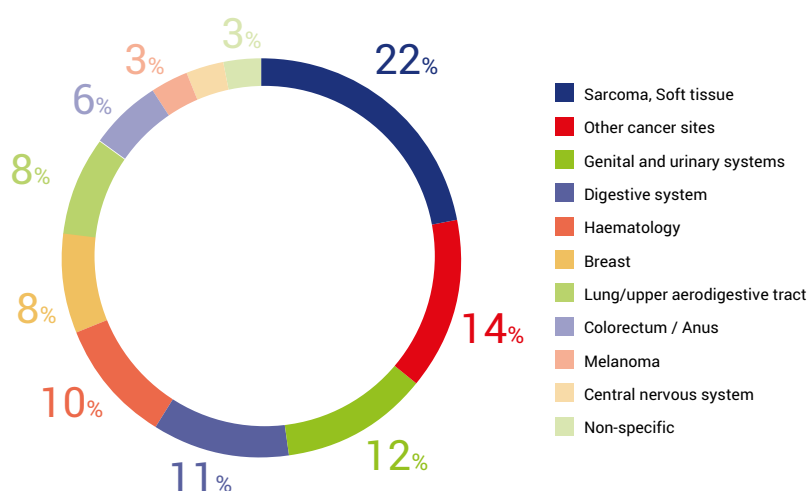


FIGURE 41
DISTRIBUTION OF SELECTED EARLY CLINICAL TRIALS ACCORDING TO CANCER SITES STUDIED OVER THE 2011-2020 PERIOD



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

In 2020, the Institute and the firm AstraZeneca signed a collaboration agreement to make innovative drugs available to the CLIP². Most of these innovative drugs from the AstraZeneca development pipeline are still in early development and thus have not yet received marketing approval. The nine proposed drugs are:

- AZD5153, BRD4 inhibitor
- AZD1390, ATM inhibitor
- Capivasertib (AZD5363), pan-AKT inhibitor

- AZD4635, A2aR inhibitor
- Ceralasertib (AZD6738), oral ATR inhibitor
- MEDI5752, anti-PD-L1/CTLA-4 bispecific antibody
- Monalizumab (IPH2201), anti-NKG2A antibody
- Savolitinib (AZD6094), cMET inhibitor
- Acalabrutinib, BTK inhibitor

Following the signing of this agreement, the Institute published a call for proposals for the 16 CLIP² in July 2020. The selection and funding of projects will proceed in 2021.

Precision medicine initiatives

CAR T-CELLS

INCa is involved in T²EVOLVE “Accelerating development and improving access to CAR and TCR engineered T cell therapy”, a new breakthrough alliance of academic and industry leaders in cancer immunotherapy.

This project was submitted to Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU) 18th Call for proposals (Topic 6: Supporting the development of engineered T cells). The IMI2 JU is a jointly funded partnership between the European Union, represented by the European Commission, and the European Federation of Pharmaceutical Industries and Associations (EFPIA). The IMI2 JU objectives are usually implemented through research and innovation actions where public and private partners collaborate, combining their expertise, knowledge and resources. The overall objective of this Call topic is to support the development of autologous and allogeneic engineered T-cell therapies, including CAR and TCR engineered T cells.

Selected in June 2020 by IMI2 JU, the full T²EVOLVE proposal has been granted with IMI funding of €7.8M for a period of 5 years (2021-2025).

Coordinated by Prof. Michael Hudecek, MD (Universitätsklinikum Würzburg, Germany) and Dr. Hélène Negre, PhD (Servier Iris and EFPIA project leader), the interdisciplinary T²EVOLVE consortium is made up of 27 European partners from 9 different countries:

- 15 Universities, research organisations, public bodies, non-profit groups (including INCa and Inserm);
- 6 EFPIA partners;
- 4 Small and medium-sized enterprises (SMEs) and mid-sized companies;
- 1 patient organisation;
- 1 associated partner.

The key objectives of T²EVOLVE are:

- to develop an innovation ecosystem that will accelerate the development of engineered T cell therapies (TCR and CARs) in the European Union;
- to grant EU patients access to the most ground-breaking and best available medical care, while providing guidance on the implementation of these novel treatments into the European Union healthcare system in a sustainable way, and to help alleviate the financial burden of health care on the economy and society.

INCa is involved and leads tasks in WP2 “Patient Involvement” and WP5 “Gold standard analytical methods used both pre- and post- infusion of engineered T cells”.

Additional information is available on <https://t2evolve.eu/>.

MOLECULAR GENETICS CENTRES: DEVELOPMENT OF SOMATIC GENETIC TESTING IN CANCER

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 genetic centres.

However, the number of therapies requiring a biomarker prescription is rising, and a variety of new biomarkers are in development. In this context, the Institute continues to propose and implement actions in order to support improvements in molecular genetics.

RNAseq roll-out

RNA analysis by New Generation Sequencing (NGS), also known as RNAseq, has demonstrated its usefulness, and is now starting to be used in routine care. Indeed, RNAseq analysis results are required in the marketing authorisations of several therapies, in particular to identify fusion transcripts.

Some molecular genetics centres have already mastered this technique and use it for routine care, but most centres still need to accredit it. In order to ensure equal access to RNAseq for all patients who would benefit from this analysis, the Institute has launched a programme to enable molecular genetics centres to validate and/or sustain the ramp-up and accreditation of such tests. This programme, representing a total funding of €1.5M over 18 months, aims to enable at least one laboratory from each of the 28 molecular genetic centres, throughout France, to perform RNAseq analysis routinely in 2022.

Recommendations for somatic testing

The landscape of molecular somatic testing in cancer is becoming increasingly complicated, and it is necessary to issue recommendations for the prescription and/or conduct of these tests to guide professionals in their practice and ensure the best care possible for patients in France. Accordingly, the Institute has been working with experts to issue several recommendations.

Recommendations for the prescription and conduct of MMR testing

In 2016, INCa issued recommendations for the “somatic testing of a deficiency of the MMR system, in Lynch syndrome-spectrum tumours”². Since that time, the testing of MMR deficiency, initially only used to detect Lynch syndrome patients, has been shown to be predictive of the response to some immunotherapies in specific cancers, while being a prognostic or diagnostic marker in some others. Thus, the use of this test has evolved and it is time to update these recommendations. A group of experts has been formed to draft the updated recommendations.

2. Tests somatiques recherchant une déficience du système MMR au sein des tumeurs du spectre du syndrome de Lynch, collection Outils pour la pratique, INCa, juin 2016.

Recommendation for the prescription of somatic tests

Given the fast-paced development of treatment options for different cancer sites, it could be difficult for clinicians to stay up-to-date and to 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 to optimise the number of tests performed in France yearly, INCa has set up working groups with pathologists, molecular geneticists, and clinicians to produce recommendations on the prescription of somatic tests in colon cancer, lung cancer, and melanoma. The recommendations aim to list all the different stages of the disease, and to recommend which tests should be carried out at which stage to ensure the best treatment for each patient.

NATIONAL ONCOGENETICS SYSTEM

Almost 5% of diagnosed cancers are related to hereditary cancer syndromes. Often discovered at an earlier age compared to the general population, with a risk of developing multiple tumours of the corresponding spectrum throughout their lifetime, these hereditary forms of cancer are due to constitutional genetic anomalies affecting transmissible predisposing genes. 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 coordinated through the national oncogenetics system. In 2019, it was organised around:

- 145 consultation sites in 101 cities across the country (mainland France and overseas departments);
- 25 laboratories, in charge of carrying out the genetic tests prescribed during consultations;
- 17 specific monitoring centres for those at a very high risk of cancer.

The purpose of this system is to identify people who have a hereditary predisposition to cancer (index or related patients) in order to offer them specific follow-up (appropriate monitoring and/or preventive surgery).

Since 2002, funding has been allocated by the DGOS/French Ministry of Health to allow the creation of new oncogenetic counselling services, or to strengthen already existing counselling (annual envelope of €6.67M supplemented by additional budget of €0.86M granted in 2015, and renewed in 2016, 2017, 2018 and 2019). Since its creation, the Institute 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 in improving its access.

The aims of the Institute's oncogenetic mission, supported by action 6.1 of the Cancer Plan 3, are to:

1. 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;
2. Develop activity in regions with the least services, and ensure access to oncogenetic counselling for the greatest number;
3. Support the arrival of new targeted therapies, such as PARP inhibitors.

2019 activity

● Increase in oncogenetic counselling and genetic testing (table 24)

In 2019, counselling locations and laboratory activity increased. The total number of consultations was 87,367 in 2019 *versus* 79,892 in 2018, reflecting an increase of 9% (+8% between 2016 and 2017, and +3% between 2017 and 2018). Regular progress has been observed since 2003.

Since 2013, to cope with the growing number of required analyses, the Institute has supported the development of targeted high-throughput sequencing (NGS) for diagnostic purposes. In 2019, 25 oncogenetics laboratories performed NGS analyses which allowed tests to be carried out on 34,032 patients (99% of all patients, *versus* 95% in 2018). NGS is now implemented in routine practice in all oncogenetics laboratories.

● Improved regional access

The regional average of the number of consultations per 100,000 inhabitants was 117 in 2019 *versus* 107 in 2018 (99 in 2016, and 105 in 2017).

● Increase in the time to the first consultation

In 2019, the median time to obtain a first oncogenetic counselling appointment for an index patient was 12 weeks, while it was 11 weeks in 2018. At the same time, the median time to obtain a first oncogenetic counselling appointment for a related patient was 8 weeks, *versus* 6 weeks in 2018. This increase could be explained by saturation of the system and higher activity with constant human resources.

● Significant increase in accelerated processes

Accelerated processes have been implemented when the result of genetic testing has a direct impact on the patient's care pathway (prescription of a PARP inhibitor, surgical procedure based on the presence of a *BRCA* anomaly, inclusion of patients with therapeutic failure in a clinical trial, life-threatening situation, etc.), counselling teams (and laboratories).

■ TABLE 24

ACCESS TO CONSTITUTIONAL GENETIC TESTING IN ONCOGENETICS LABORATORIES

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

* Results for 25 out of 26 laboratories

In 2019, index patients receiving emergency counselling increased considerably (5,171 versus 4,103 in 2018, an increase of 26%). The median time to obtain a first oncogenetic counselling appointment for these patients has been reduced to 8 days.

Despite the strong increase in activity in 2019, several coordinators have raised concerns about the limitations of the system and the lack of resources, particularly human resources (medical time, genetic counsellors), with the risk of increasing

October 8, 2020 workshop on the follow-up of those at a very high-risk of cancer

Follow-up centres were first operated as pilot projects from 2009, and then responded to calls for projects in 2012 and 2013.

On the recommendations of the Institute, the DGOS (the French General Directorate of Care Provision) granted an envelope of €4.34M to 17 regional and interregional programmes located throughout the territory (mainland France and overseas departments). These centres are responsible for:

- Setting up individualised monitoring;
- Ensuring and facilitating access to multidisciplinary expertise;
- Coordinating regional or interregional follow-up;
- Offering referral and expertise activity for difficult cases.

As part of its mission of monitoring and facilitating the oncogenetics system, the Institute organises a feedback seminar every two years.

The workshop held in October 2020 offered an opportunity to present and discuss the major advances and the problems encountered:

Major advances

- Improved quality of follow-up and adjustment of patient care through medical validation of examination reports;
- An increase in multidisciplinary care;
- Development of the sharing of computerised and secure health data;
- Stronger partnerships with regional cancer networks;
- Improved communication tools for patients and local health professionals (information brochures, dissemination of recommendations, websites, etc.);

- Implementation of research work, particularly to assess the quality of monitoring and patient compliance.

Main challenges

- Retrieval of reports of follow-up examinations carried out outside centres (patients, private practices);
- Highly time-consuming activities to the detriment of other missions;
- Organisation and coordination of networks covering larger territory, with the risk of heterogeneity of care;
- Weak national and international collaborations;
- Heterogeneous organisation of centres and lack of new directives from the Institute since 2012;
- Increased activity in a context of a fixed budget envelope with the risk of discontinuing the inclusion of new patients and territorial inequality.

Suggestions

- For national coordination and standardisation of practices:
 - To support centres to centralise and share their data;
 - To update follow-up guidelines based on national benchmarks and international recommendations;
 - To disseminate them in the Institute's publications.
- For an evaluation of the system: carry out a methodological study with specific health indicators to measure the efficiency of the monitoring programmes. This assessment will propose new guidelines expected by the coordinators of the centres, as well as a new allocation of funding from the DGOS.
- For the visibility and recognition of these follow-up networks which need strong institutional support: subsequently consider labelling programmes for monitoring those at a high risk of cancer based on the «Rare Tumours» centre model.

delays further. Indeed, this activity can only keep increasing with the development of precision medicine (future MA approvals of PARP inhibitors in new indications) and the implementation of the “Plan France Médecine Génomique” initiative (French initiative for genomic medicine).

ACSÉ PROGRAMME

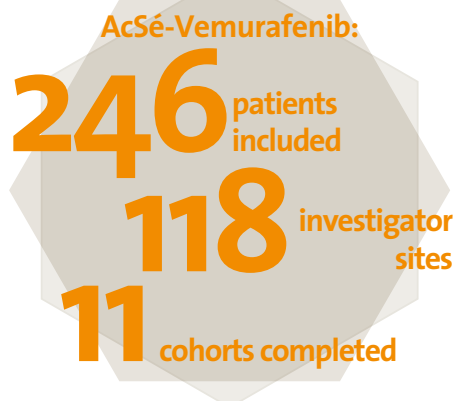
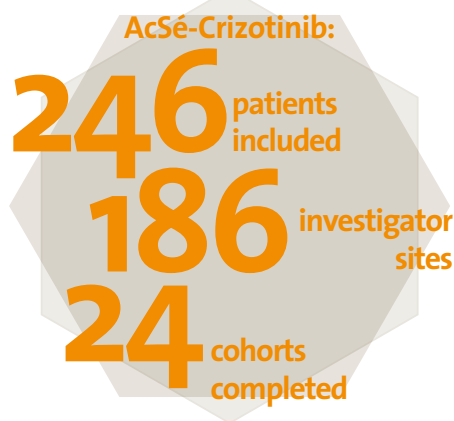
As part of the 2nd National Cancer control plan, the AcSé programme (Secured Access to innovative therapies) was launched by INCa in 2013, with the approval of the French Medicines Agency, to provide secured access to targeted therapies for patients in treatment failure situations, in non-authorised 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 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 planning 4 years of inclusion and the subject of 2 extensions of 12 months and 6 months, has been closed to enrolment since April 2019 and has enabled the treatment of 204 patients, with a non-specific BRAF mutation in more than 10 different cancer types (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-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

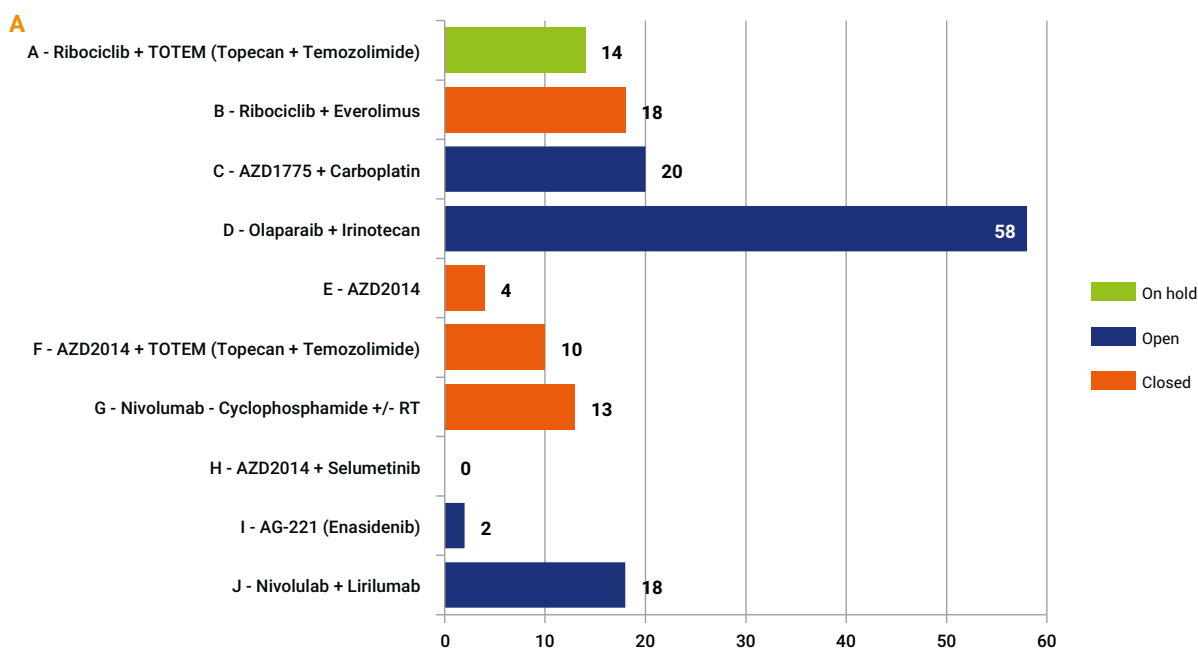


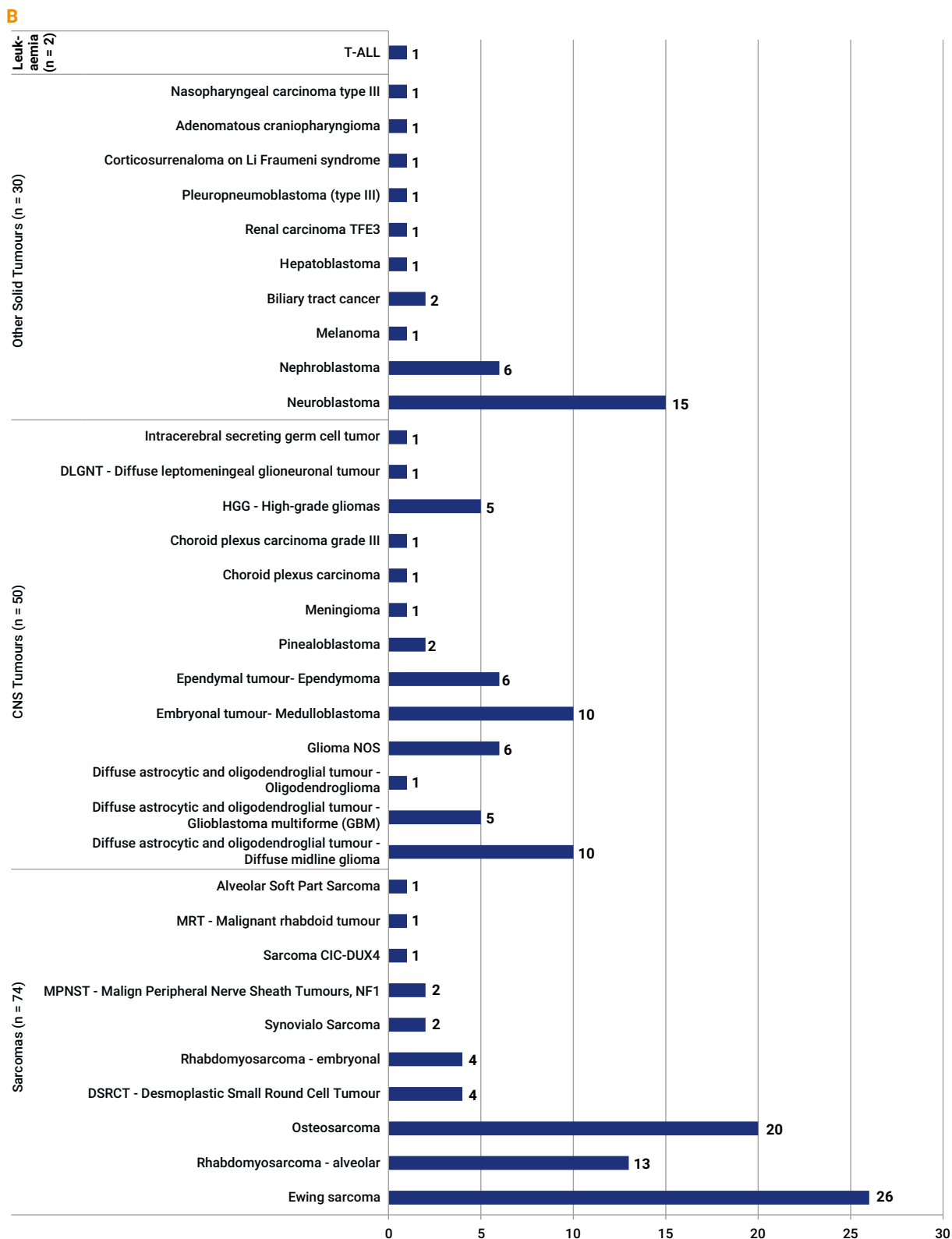
AcSé-Nivolumab:
269 patients included
654 investigator sites
6 cohorts follow-up

specific PHRC-K project funded in 2014, the MAPPYACTS project. This innovative protocol, approved and opened in 4 countries (France, Spain, Netherlands, and UK), has led to the inclusion and treatment of 157 children (136 in France, 4 in Spain, 8 in the Netherlands, and 9 in the UK) within 10 study arms, representing almost 30 different histological types (Figure 42).

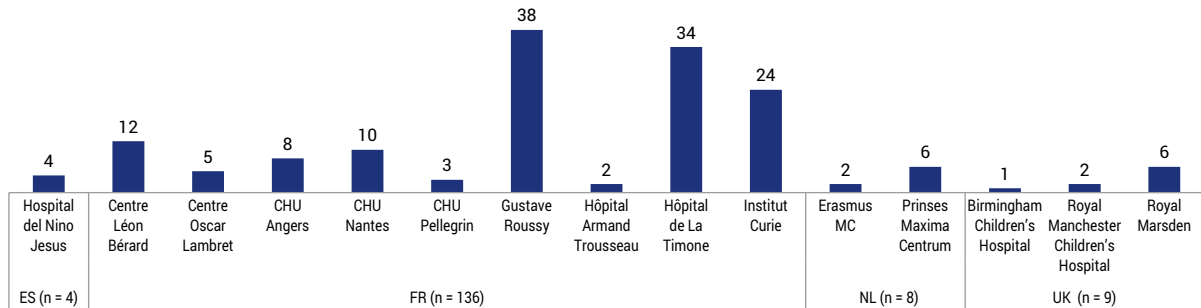
- AcSé-Nivolumab and AcSé-Pembrolizumab, launched in May 2017, to evaluate two anti-PD-1 agents in the treatment of rare cancers, based on the organisation of rare cancer networks designated by the French National Cancer Institute. In this context, patients with rare cancer also benefit from secure access 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.

FIGURE 42
ACSÉ-ESMART: DESCRIPTION OF RECRUITMENT BY STUDY ARM (PANEL A), BY COHORT (PANEL B) AND STUDY CENTRES/ COUNTRY (PANEL C) (DECEMBER 2020)





C



AcSé-Pembrolizumab:

334 patients included
48 investigator sites
7 cohorts follow-up

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

269 and 334 patients have been respectively enrolled in AcSé-Nivolumab and AcSé-Pembrolizumab, closed to enrolment since 31 December 2020 (Figures 43 and 44). Height cohorts have reached their objective (inclusion and treatment of at least 50 patients), and for one of these - the sarcoma cohort – the number of inclusions has been increased due to the various histological subtypes included in this cohort.

Based on the implementation of new types of clinical trials, the AcSé programme has clearly helped accelerate the emergence of innovation for the benefit of patients³.

All of the key features, principles, and objectives of the 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.
- 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, 1,222 patients, including 178 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 a 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 178 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 40 international communications, 3 press conferences, 1 patient guide, and 3 Temporary Use Recommendations (RTUs) filed.

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.

FIGURE 43
ACSÉ-NIVOLUMAB: DESCRIPTION OF RECRUITMENT BY COHORT (DECEMBER 2020)

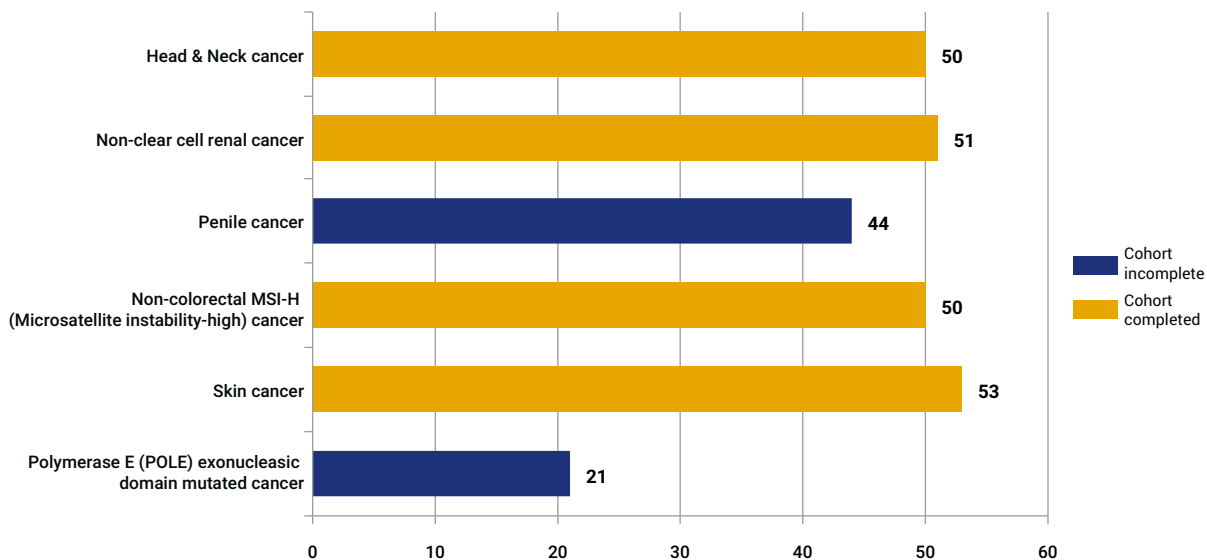
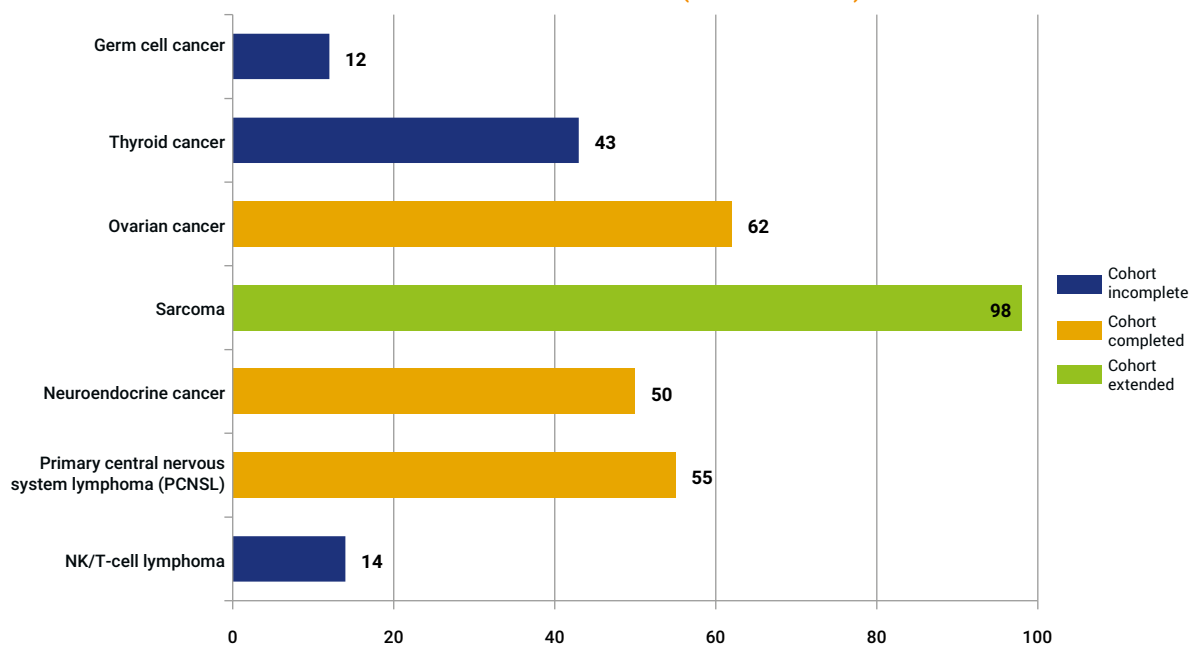


FIGURE 44
ACSÉ-PEMBROLIZUMAB: DESCRIPTION OF RECRUITMENT BY COHORT (DECEMBER 2020)



International visibility of AcSé programme

Publications

- Ortiz-Cuaran S et al. (2020) Circulating Tumor DNA Genomics Reveal Potential Mechanisms of Resistance to BRAF-Targeted Therapies in Patients with BRAF-Mutant Metastatic Non-Small Cell Lung Cancer. *Clin Cancer Res* 2020 Dec 1;26(23):6242-6253. doi: 10.1158/1078-0432.CCR-20-1037. Epub 2020 Aug 28
- Mazières J et al. (2020) *Vemurafenib in non-small cell lung cancer patients with V600 BRAF mutations and non-V600 mutations*. *Ann Oncol.* 2020 Feb;31(2):289-294. doi: 10.1016/j.annonc.2019.10.022. Epub 2020 Jan 3.

Oral communications

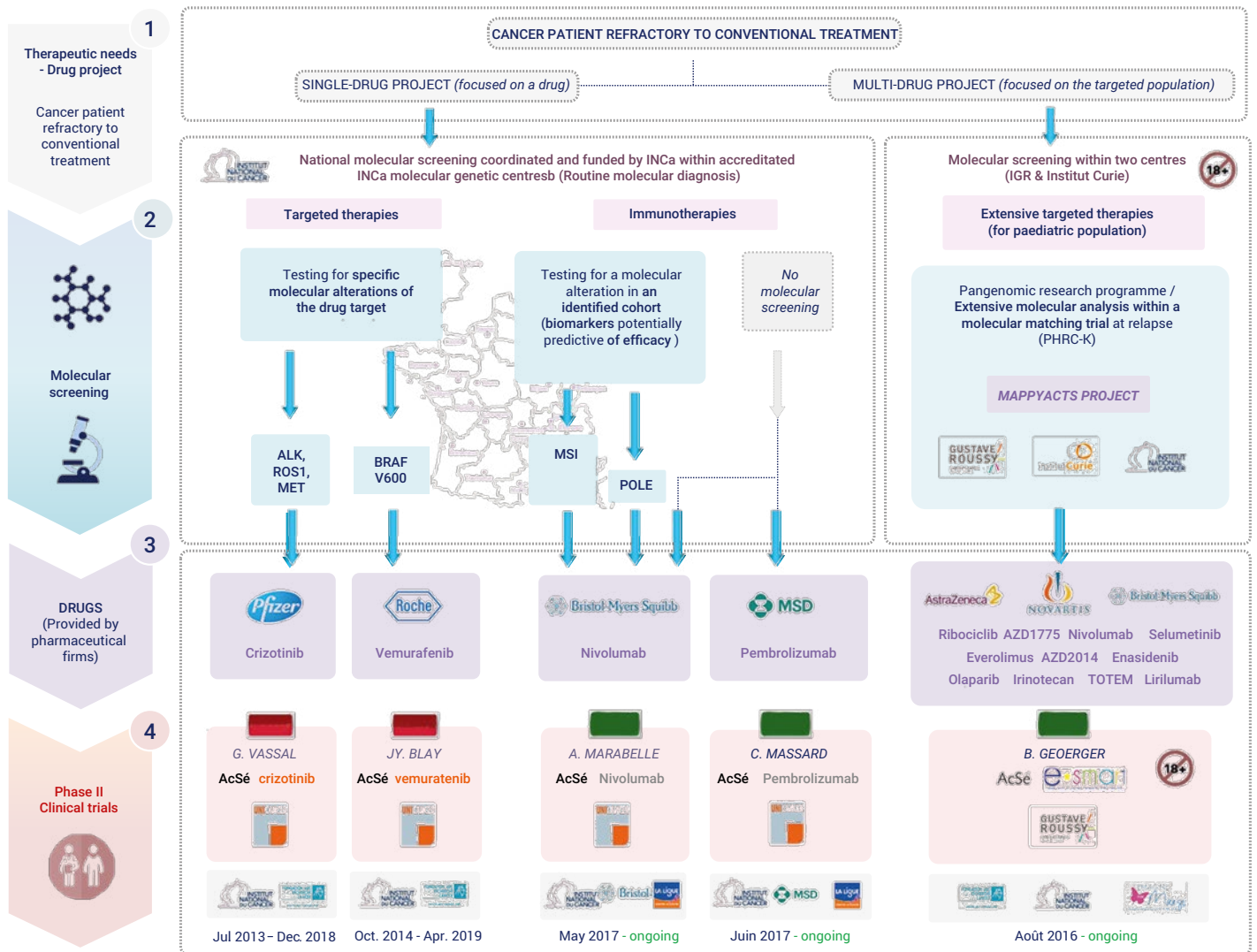
- “High activity of Nivolumab in patients with pathogenic exonucleasic domain POLE (edPOLE) mutated Mismatch Repair proficient (MMRp) advanced tumors”
ESMO 2020 (AcSé Nivolumab)
Rousseau B, Bieche I, Pasmant E, Simmet V, Hamzaoui N, Masliah-Planchon J, Pouessel D, Bruyas A, Augereau P, Grob J-J, Rolland F, Saada-Bouزيد E, Cohen R, Bouche O, Hoog-Labouret N, Legrand F, Simon C, Lamrani-Ghaouti A, Chevret S, Marabelle A.
- “High clinical benefit rates of pembrolizumab in very sarcoma histotypes: First results of the AcSé Pembrolizumab study”
ESMO 2020 (AcSé Pembrolizumab)
Blay J-Y, Ray-Coquard I, Penel N, Bertucci F, Bompas E, Saada-Bouزيد E, Eymard J-C, Lotz P, Coquand E, Schott R, Soulie P, Linassier C,

- Lecesne A, Brahmi M, Hoog-Labouret N, Legrand F, Simon C, Lamrani-Ghaouti A, Chevret S, Massard C.
- “AcSé Nivolumab: résultats préliminaires pour le carcinome baso-cellulaire avancé”
JDP (Journées Dermatologiques de Paris) 2020 (AcSé Nivolumab)
Veron M, Marabelle A, Grob J-J, Abi-Rached H, Chevret S, Simon C, Mortier L.
- “AcSé Nivolumab: résultats préliminaires pour le carcinoma trichoblastique”
JDP 2020 (Journées Dermatologiques de Paris) (AcSé Nivolumab)
Toulemonde E, Marabelle A, Fléchon A, Chevret S, Simon C, Beylot-Barry M, Mortier L.

Posters

- “Nivolumab in metastatic non-clear cell renal cell carcinoma: first results of the AcSe prospective study”
ASCO GU (AcSé nivolumab)
Albiges L, Pouessel D, Beylot-Barry M, Bens G, Pannier D, Gavaille C, Oudard S, Chevret S, Hoog-Labouret N, Legrand F, Simon C, Lamrani-Ghaouti A, Escudier B, Marabelle A, Flechon A
- “First results of the AcSé Pembrolizumab Phase II in the Primary CNS Lymphoma (PCNSL) cohort”
ASH 2020 (AcSé Pembrolizumab)
Hoang-Xuan K, Houot R, Soussain C, Blonski M, Schmitz A, Delwail V, Brachet P-E, Ghesquière H, Peyrade F, Tempescul A, Abraham J, Agape P, Ahle G, Baize N, Campello C, Gyan E, Jardin F, Oberic L, Rey P, Choquet S, Houillier C, Legrand F, Lamrani-Ghaouti A, Querel O, Hoog-Labouret N, Simon C, Chevret S, Massard C.

■ FIGURE 45
KEY FEATURES OF THE ACSÉ PROGRAMME



Clinical cancer research organisation: structures, infrastructures, and tools

CLIP²: EARLY-PHASE CLINICAL TRIAL CENTRES

Sponsored by the 2009-2013 Cancer control plan, the initiative to structure clinical and translational research is supported by INCa through a specific designation: early-phase clinical trial centres (CLIP² centres). The second 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, in partnership with the French Cancer League, a new designation of these structures in 2015, and identifying some centres dedicated to children including specific paediatric activities. The third and latest designation has made it possible to renew and bolster its support for expert centres in early phase clinical trials for adult and paediatric, adolescent and young adult cancers. Thus, among the 16 structures designated until 2024, 7 of these include paediatric oncology activities (figure 46).

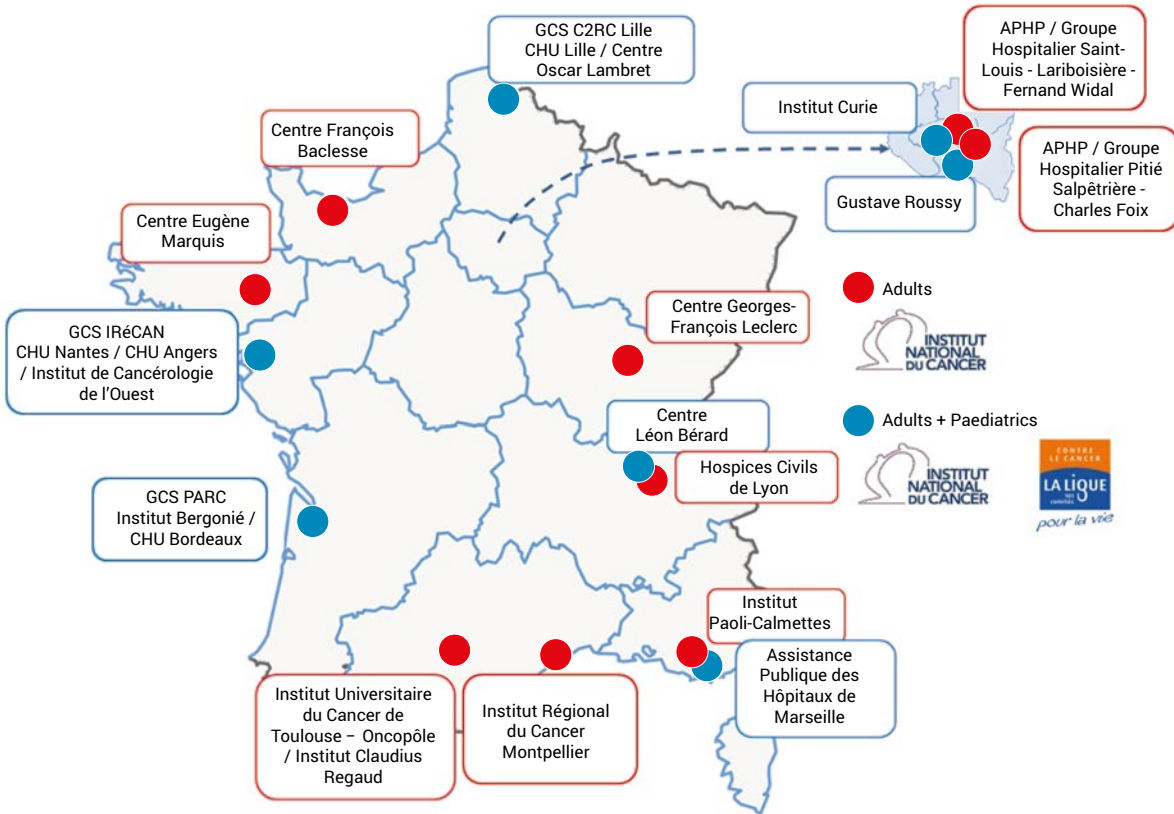
This programme has helped increase the visibility and attractiveness of these centres and also those of early-phase French clinical research (and should continue to do so), leading not only to an increase in the number of new trials launched, and the number of patients included every year within CLIP²,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

2019 activity report

Since 2010 (i.e. the first designation campaign), this initiative has contributed to the overall increase in the number of clinical trials initiated and the number of patients enrolled in CLIP² centres (Figure 47):

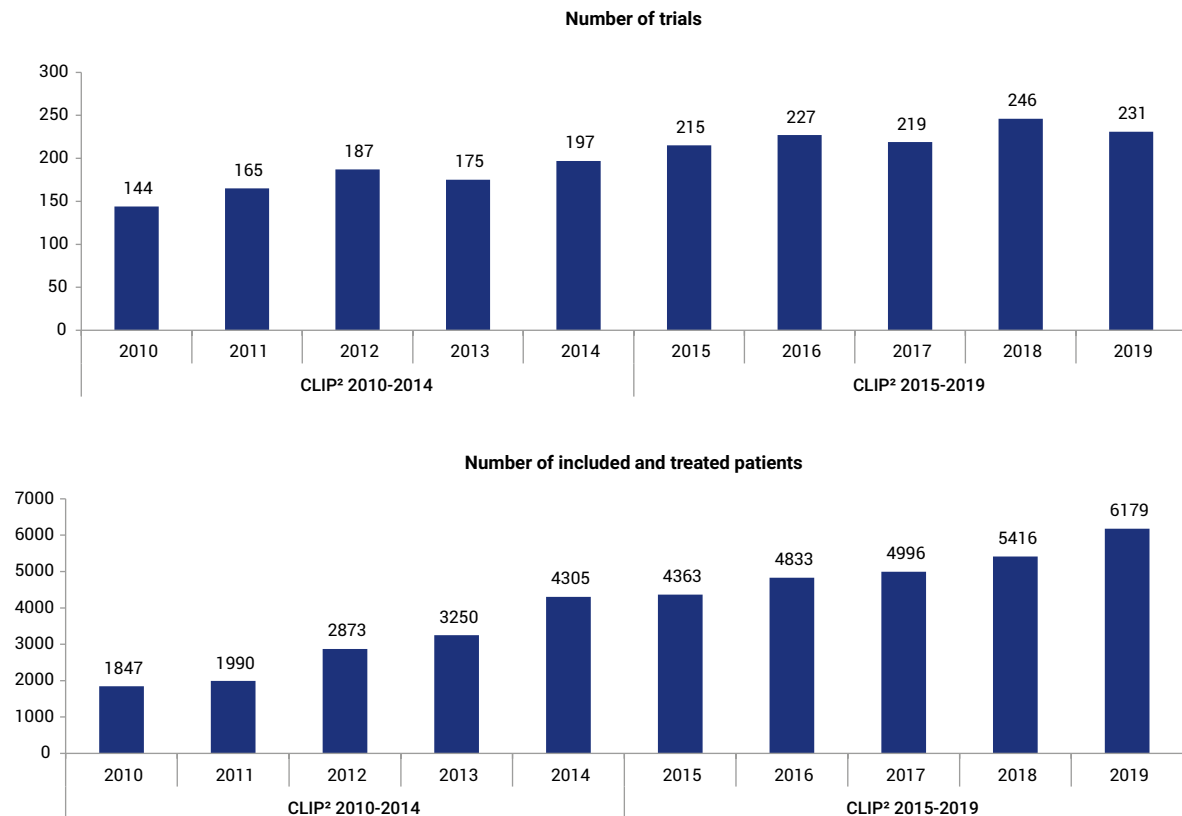
- + 60% increase in the total number of clinical trials launched with 231 in 2019;
- + 234% increase in the total number of patients enrolled, with 6179 patients enrolled and treated in 2019.

FIGURE 46
GEOGRAPHIC DISTRIBUTION OF CLIP² CENTRES (3RD DESIGNATION – 2019-2024)



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

■ **FIGURE 47**
TRENDS IN PROGRESSION OF THE NUMBER OF TRIALS INITIATED AND PATIENTS ENROLLED OVER THE 2010-2019 PERIOD



Since 2015 (i.e. the second designation), the total number of early-phase clinical trials has increased by about 8%, with the following distribution in 2019 (figure 48):

- 60% phase II trials;
- 22% phase I/II trials;
- 18% phase I trials.

The distribution of academically- versus industrially-sponsored trials has tended to balance out since 2015 (47% vs 53% in 2019), while nearly half of academic trials are sponsored by institutions hosting CLIP² (44% of trials in 2019), including trials under public/private partnerships developed and supported by INCa.

The distribution by type of therapy evaluated has been quite stable since 2017, with 94% of the trials corresponding to “drug study arms” and a balanced proportion of drug monotherapy and combination drug study arms in 2019 (Figure 50):

- 44% drug monotherapy experimental study arms;
- 45% drug combination experimental study arms;

FIGURE 48
DISTRIBUTION OF NEW TRIALS LAUNCHED ACCORDING TO STUDY PHASE

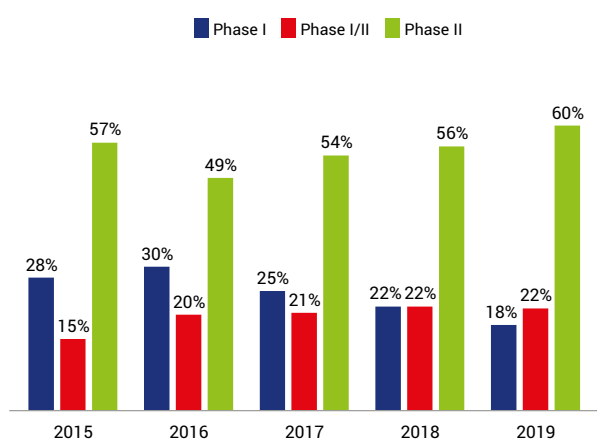
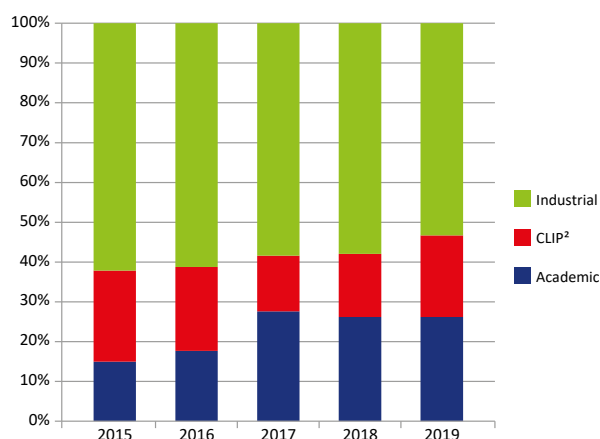


FIGURE 49
DISTRIBUTION OF NEW TRIALS LAUNCHED ACCORDING TO SPONSOR



- and 5% 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 5% correspond to “non-drug study arms”, which may evaluate one or more non-drug intervention such as radiotherapy, surgery, device, biomarkers, imaging techniques, etc.

Inter-CLIP² projects / working axes

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

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

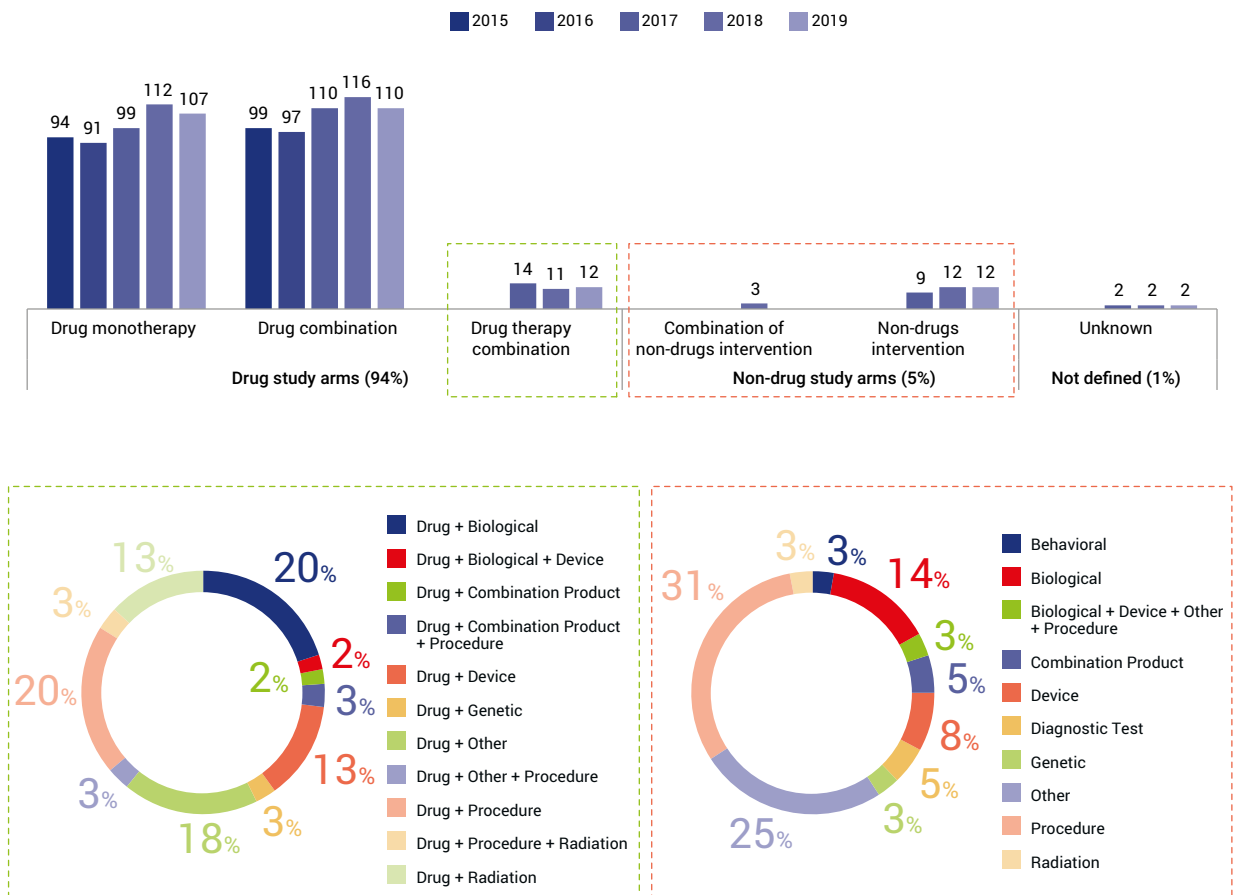
In 2018, an inter-CLIP² working group launched an initiative with all of the CLIP² centres, to improve the operational implementation of clinical research in oncology, by enhancing collaboration between investigator centres and industrial or academic sponsors, through shared recommendations.

Issued after nearly two years of consultation, these recommendations aim to improve the conditions of interaction between the two parties, and propose collaboration rules to be applied in reciprocal relations.

Firstly validated by all CLIP² centres and then favourably acknowledged by LEEM (“Les Entreprises du Médicament”), a pharmaceutical industry federation, these recommendations have now been agreed upon by both investigators and sponsors. They suggest an improvement in the quality of interactions and of work

Between 2010 and 2019 + 60% increase in the total number of clinical trials initiated, with 231 in 2019; + 234% increase in the total number of patients enrolled, with 6179 patients enrolled and treated in 2019.

■ FIGURE 50
TRENDS IN DISTRIBUTION OF EXPERIMENTAL ARMS IN NEW TRIALS LAUNCHED ACCORDING TO TYPE OF THERAPY ASSESSED



between CLIP² centres and sponsors, and should help focus the activity of the investigator centres on the care of patients involved in clinical trials.

The implementation of the recommendations should be effective in 2021

● **Patient referral networks**

Another CLIP² initiative focuses on the implementation of a shared common tool for referring patients between CLIP² centres, thus limiting the involvement of research actors in all anonymisation/de-anonymisation tasks, or of completing specific referral forms for each CLIP².

DATAVIZ clinical trial research database project (data visualisation in RSHINY interface)

Since 2010, the 16 CLIP² centres are required to annually report on their early-phase clinical trial activity, based on different indicators, such as:

- the trial NCT number (clinicaltrials.gov),
- the title of the trial and its acronym,
- the phase of the trial,
- the disease(s) addressed,
- the trial sponsor (academic versus industrial),
- the drugs being evaluated,
- the type of trial (paediatric, adult, geriatric, monotherapy or combination, number of inclusions, number of children accessing the innovative treatments, etc.)

In 2018-2019, a database dedicated to early-phase clinical trials was developed using the public data

available on the ClinicalTrials.gov website, listing all the clinical trials conducted internationally, to cross-reference these data with CLIP² centre activity.

In 2020, a data visualisation project of the early-phase clinical trials conducted in CLIP² centres was considered, as a further step in this database integration.

This Dataviz project will commence in 2021 in order to provide and share CLIP² activity data through a visual and dynamic interface, aiming to maximise the value of French early-stage cancer research conducted within CLIP² centres. This initiative would help meet clinical research actors' expectations, who request better use of their activity data reported to the various institutional supervisory bodies.

Currently, patient referral is based on regional or inter-regional networks. The first idea would be to maintain this local addressing process, while also considering a common national referral tool. This referral tool makes it possible to escalate local addressing requests to other CLIP²s in other interregions if no local alternative treatment is available.

This project, initiated at the end of 2020, is one of the inter-CLIP² working axes planned for the year 2021.

COOPERATIVE INTERGROUPS

The French cancer cooperative intergroups are independent and not-for-profit academic groups, including doctors and medical research professionals who collaborate to develop and conduct clinical trials.

The Cooperative intergroup designation process aims:

- To promote the grouping and improve collaboration between cooperative groups at a national level and to cover different cancer pathologies,
- To promote interaction between INCa and the cooperative groups in carrying out clinical trials and translational research, and help boost clinical research in France
- To improve the international visibility and attractiveness of clinical research in France, and to develop European and international cooperation in clinical and translational research in France.

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.

Study on screening-based trials

In 2017, the Institute, in collaboration with the CLIP² coordinators, highlighted the lack of information to identify clinical trials needing the presence of one or more specific biomarkers. This kind of information is now mandatory to guide patients into the most relevant clinical trials, considering the new kind of drugs tested, the implementation of NGS in routine clinical practice in molecular genetic centres, as well as the multiplication of molecular screening programmes on large panels developed in many centres.

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

In order to obtain an up-to-date list, a survey is carried out three times a year on CLIP²

centres, in order to implement the new trials opened and to remove the trials closed for inclusion.

This list is shared by e-mail to investigators and to members of Molecular Tumour Boards (approximately 350). It is also available on the Institute's website <https://www.e-cancer.fr/Professionnels-de-la-recherche/Recherche-clinique/Structuration-de-la-recherche-clinique/Les-CLIP2>

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

At the end of 2020, the list included:

- 507 trials (recruiting)
- 124 biomarkers with at least one trial recruiting, including innovative biomarkers

The last campaign aimed at designating French Cancer Cooperative Intergroups was held on 2017-2018 and 13 intergroups were designated (table 25).

■ **TABLE 25**
COOPERATIVE INTERGROUPS DESIGNATED IN 2017/2018

Cooperative intergroup	Diseases covered
ARCAGY-GINECO	Gynaecological cancers
CIGAL	Acute leukaemia
DIALOG	Geriatric oncology
GETUG-AFU Alliance	Urological cancers
GORTEC-GETTEC-GERCOR	ENT cancers
IFCT	Thoracic cancers
IGCNO	Neuro-oncology
IFM	Myeloma
INTERSARC	Sarcomas
LYSA-LYSARC	Lymphomas
PRODIGE	Digestive cancers
SFCE	Paediatric oncology
UCBG	Breast cancers

In 2020, at the request of the cooperative intergroups, a declarative survey on clinical research activity in oncology was specifically designed based on the national survey (see section 3.4.3). The aim of this survey was to quantitatively assess clinical research activities in oncology in France in these cooperative intergroups in 2019.

As a reminder, the cooperative intergroups can be sponsors, can be involved in academic trials, and/or in industrial trials: these 3 statuses were addressed⁴ (Table 26):

- 9 cooperative intergroups (or a group of the intergroup) (i.e. 2/3) were sponsors of 86 cancer clinical trials. They reported 7,192 inclusions in 2019, representing 14% of national inclusions in 2,063 French centres (see section 3.4.3). These 9 cooperative intergroups, as sponsors, participated actively at an international level with 188 participating centres abroad;
- All the cooperative intergroups have been involved in academic trials with 162 cancer clinical trials reported and 12,469 inclusions (24% of national inclusions);
- 7 cooperative intergroups have been involved in industrial trials with 39 cancer clinical trials and 714 inclusions reported (1% of national inclusions);
- Strong clinical research activity in early phases (phase 1 and 1/2) and phase 3: for example, 72% of inclusions are observed in phase 3 when the cooperative intergroups are involved in academic trials, and 9% of inclusions are observed in early phases when the cooperative intergroups are involved in industrial trials.

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

■ **TABLE 26**
MAIN RESULTS OF 2019 CLINICAL RESEARCH ACTIVITY IN ONCOLOGY AMONG COOPERATIVE INTERGROUPS

Status of cooperative intergroups	Number of cooperative intergroups	Number of trials	Number of inclusions
Sponsors	9	86	7,192
Involvement in academic trials	13	162	12,469
Involvement in industrial trials	7	39	714

ENROLMENTS OF PATIENTS IN CLINICAL TRIALS

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

These data are presented annually to the French President.

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

The actions promoted by the second Cancer Control Plan have led to an increase of more than 70% in patients enrolled in cancer clinical trials thanks to the structuring of clinical research sites, and an incentive policy, particularly via the INCa clinical trials 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 was to recruit 50,000 patients per year in therapeutic clinical trials by 2019.

In 2019, 52,502 patients were included in a clinical trial (Table 27):

- 32,897 patients in a therapeutic clinical trial;
- 75% were enrolled in academic trials;
- 42,944 patients in clinical trials addressing solid tumours;
- 9,558 in haematology.

■ **TABLE 27**

MAIN RESULTS OF CLINICAL RESEARCH ACTIVITY IN ONCOLOGY SURVEY IN 2019

	Academic	Industrial	TOTAL 2019
Number of inclusions	39,671	12,831	52,502
Number of inclusions in therapeutic clinical trials	21,882	11,015	32,897
Number of inclusions in clinical trials in solid tumours	32,159	10,785	42,944
Number of inclusions in clinical trials in haematology	7,512	2,046	9,558
Number of inclusions of children (0-18)	2,199	119	2,318
Number of adolescent and young adult inclusions (15-25)	2,034	287	2,321
Number of elderly adult (≥75 years old) inclusions	5,344	1,176	6,520

Childhood and adolescent cancers are a priority of the third Cancer Control Plan:

- 2,318 inclusions concern children in 2019, of which 95% are included in academic trials;
- 2,321 inclusions concern adolescents and young adults, 87% of these enrolled in academic trials.

Another indicator closely monitored by the third Cancer Control Plan is the inclusion of elderly subjects. In 2019, 6,520 inclusions concern patients over 75 years of age in total, 82% of these being included in academic trials.

The results of INCa’s annual survey in 2019 show a steady increase in the number of patients enrolled in clinical trials for the last 10 years between 2009 and 2019:

- There is a 4.6% increase in the number of patients enrolled in 2019 compared to 2018, with 52,502 patients included in cancer clinical trials in 2019. Therapeutic clinical trials increased between 2016 and 2019 from 28,222 to 32,897. The ratio of therapeutic trials grew significantly from 51.8% to 62.6% between 2017 and 2019 (Figure 51).
- Over the last 11 years (2009-2019), the number of patients enrolled in cancer clinical trials has doubled, probably due to the Actions of the different Cancer Control Plans (Figure 52).
- The ratio of enrolment in academic versus industrial trials has remained stable over the years, with a significant majority of inclusions in academic trials (75% versus 25%). However, between 2009 and 2019, greater progression was observed in academic trials (+ 86%) than in industrial trials (+ 59%) (Figure 50).
- The distribution among the different care providers is quite similar over the years: in 2019, 46% of the patients were enrolled in University Hospitals, 43% in Cancer Care Centres, and 11% in Health Care Centres (Figure 53).

FIGURE 52
PROGRESSION OF PATIENTS ENROLLED IN CANCER CLINICAL TRIALS (2009-2019)

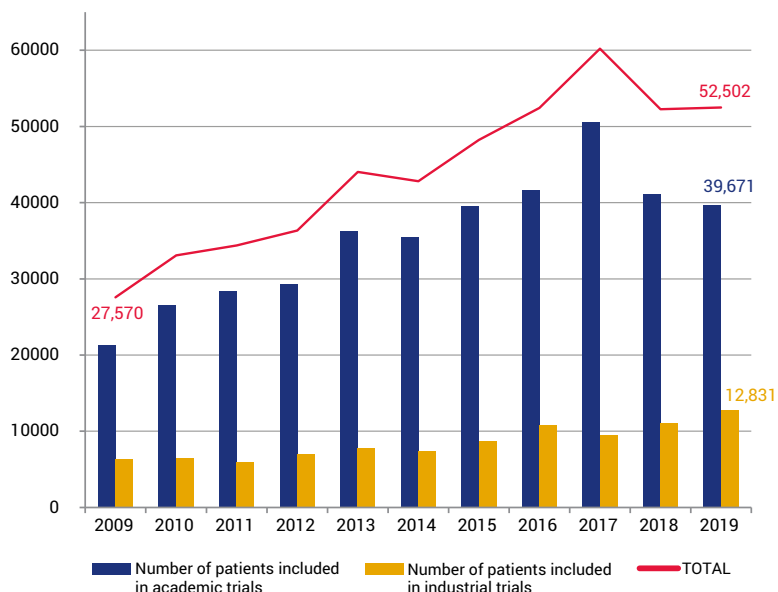


FIGURE 51
DISTRIBUTION OF CANCER CLINICAL TRIALS ACCORDING TO THERAPY OVER THE 2017-2019 PERIOD

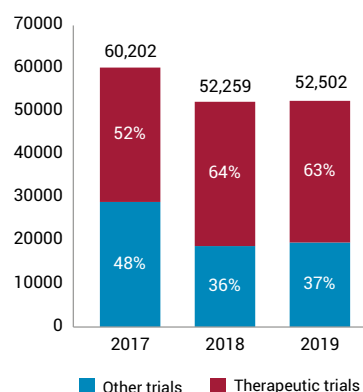
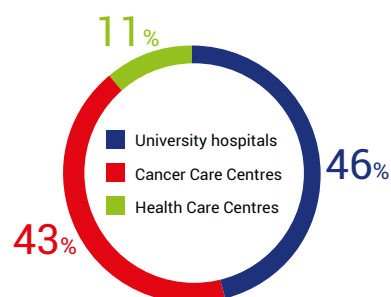


FIGURE 53
DISTRIBUTION OF PATIENTS ENROLLED IN CANCER CLINICAL TRIALS AMONG DIFFERENT CARE PROVIDERS IN 2019



“PHARE” and “SIGNAL” national clinical breast cancer trials sponsored by INCa

INCa is the sponsor of 2 national clinical trials on breast cancer:

- a randomised controlled trial, launched in 2006, to compare the effects of 6 months versus 12 months of treatment with Herceptin®: “PHARE, Protocol for Herceptin® as Adjuvant therapy with Reduced Exposure”;
- the “SIGNAL” protocol, launched in 2008, to set up a national prospective cohort in to identify genetic determinants that could influence resistance/sensitivity and/or toxicity to adjuvant cancer treatment and genetic determinants for developing breast cancer.

All declared trial sites in these trials were closed between 2019 and 2020.

Due to their sizes, these two trials have resulted in a unique and extensive collection of data consisting of:

- Patient clinical data, stored in a database hosted at INCa (11,846 patients included);
- Genomic data hosted at INCa;
- Biological samples (approximately 80,000: DNA, RNA, plasma, lymphocyte fractions and lymphoblastoid lines). Since 2012, these samples are stored in the Jean Dausset Foundation - Centre for Studies of Human Polymorphism (CEPH), located in Paris.

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

INCA’S CANCER CLINICAL TRIAL REGISTRY

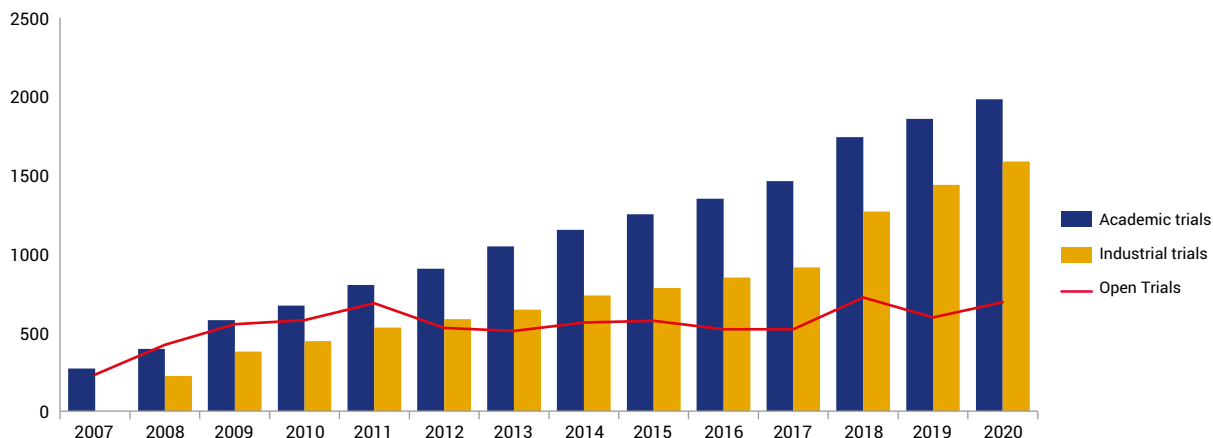
Since 2007, INCa’s cancer clinical trial registry has allowed easy access to cancer clinical trials conducted in France. On open access on INCa’s website, the registry enables provision of high-quality and regularly updated information to patients, health professionals and the general public.

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 28**
INCA’S CANCER CLINICAL TRIAL REGISTRY

Objectives	Provide information on cancer clinical trials conducted in France.
Results	3,567 clinical trials advertised on INCa’s website in December 2019, sponsored by more than 431 industrial and academic bodies. <ul style="list-style-type: none"> • 691 ongoing recruiting trials. <ul style="list-style-type: none"> - 57% sponsored by academic bodies. - 80% treatment trials.

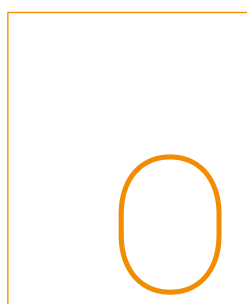
■ **FIGURE 54**
CLINICAL TRIALS IN THE REGISTRY (DECEMBER 2020)



As part of a total overhaul of the Institute's website, the future page of the registry must also be updated in order to allow better navigation for users, and will offer the possibility of importing information about posted clinical trials under a workable format.

In addition, 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 on the Internet for academic and industrial sponsors of clinical trials in oncology in order to register their trials directly in the webpage of the new database. This new registration portal will be available in the second quarter of 2021.

RESEARCH IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY AND PUBLIC HEALTH



One of INCa's goals is to bring human and social sciences, epidemiology, and public health research on cancer in France up to the best international standards. Particular efforts are being devoted to 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.

In 2020, support for human and social sciences, epidemiology and public health applied to cancer research amounted to

€8.17M:

€4.71M dedicated to support investigator-driven projects (PLSHS programme);

€2.45M to support thematic research programmes such as population health intervention research and environmental cancer risks factors;

€1.01M to support cancer research training.



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

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

Progress is also needed to 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.



THE PROGRAMME IN 2020

In 2020, 17 projects were selected out of the 74 projects submitted, for a total funding of €4.71M (Table 29).

■ **TABLE 29**
FEATURES OF THE HSS-E-PH PROGRAMME IN 2020

Objectives	<ul style="list-style-type: none"> • 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 the humanities 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	€4.71M
Proposals submitted	74
Projects selected	17
Selection rate	23%

Scientific animation

In order to promote and disseminate innovative knowledge on specific current and/or emerging themes, the Institute organised several events in 2020:

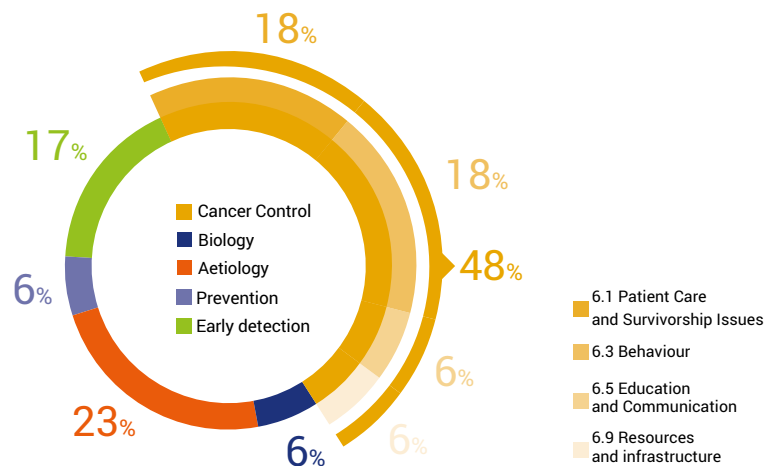
- The AAA research seminar (standing for “alcohol, diet and physical activity” in French) focusing on primary prevention and during which 9 research projects, previously funded through the HSS-P-PH programme, were presented and discussed by the scientific committee in order to provide a summary and draw up new research perspectives in primary cancer prevention. This webinar attracted 230 worldwide attendees.
- A thematic session was organised in partnership with the French-language oncogeriatrics society (SoFOG) in order to support interdisciplinary projects which represent a major challenge highlighted by the programme. Three researchers previously funded presented the status of their work in psycho-oncology, economics, and public health intervention research in the field of oncogeriatrics.

The topics of the 17 funded projects involve:

- Risk factors for the development of cancer (9 projects);
- Nutrition and Cancer (2 projects);
- Patients’ and relatives’ experiences (3 projects);
- Overseas territories facing cancer (1 project);
- Cancer prevention (1 project);
- Ethics (1 project).

Figure 55 shows the distribution of projects funded by CSO classification. The cancer control category is the largest (7 projects, representing 48%), with projects focusing on patient care and survivorship issues (3 projects for 18%), on a par with behaviours. Early detection and prevention categories represent 23% of funded project and increased compared to 2019. The aetiology category remains stable (23%).

■ **FIGURE 55**
DISTRIBUTION OF PROJECTS SELECTED IN 2020 ACCORDING TO THE CSO CLASSIFICATION



THE PROGRAMME OVER THE 2007-2020 PERIOD

Over the 2007-2020 period, 241 projects were funded for a total amount of €52.82M. With the exception of the first year and thanks to a regular increase in the funding budget over the last few years, the selection rate has been quite stable over the years (25%) (Figure 56).

FIGURE 56
TRENDS IN SELECTION AND FUNDING OVER THE 2007-2020 PERIOD

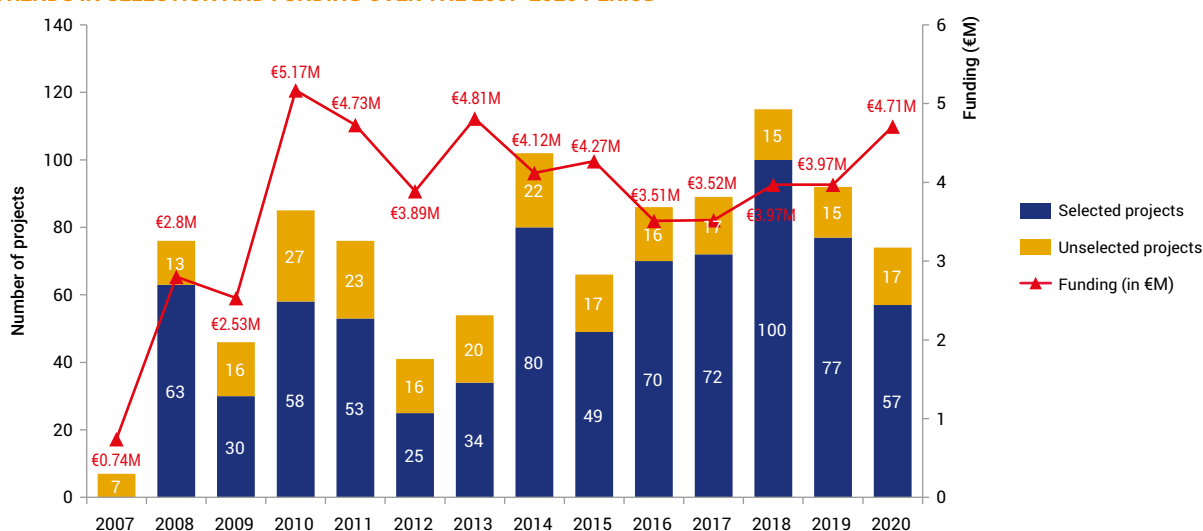
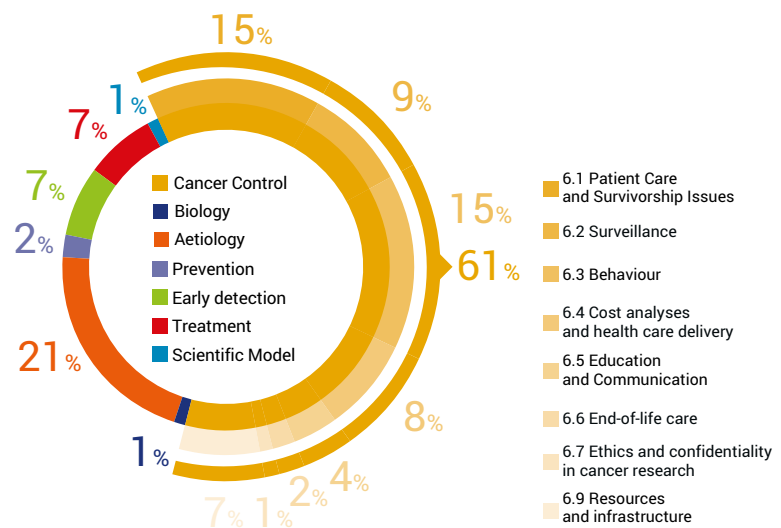


Figure 57 presents the breakdown of the selected projects according to the CSO classification over the 2007-2020 period. The cancer control category represents 61% of the selected projects (55% of total budget, over €29M), particularly with projects addressing patient care and survivorship issues and behaviour (30% of total projects). In addition, the Aetiology category represents 21% of the projects selected.

Project proposals in the field of paediatrics, teenagers or young adults are particularly welcomed, as well as projects dealing with cancers with poor prognosis, supportive care, or prevention.

2007-2020:
241
projects selected for
a total amount of
€52.82M

■ FIGURE 57
DISTRIBUTION OF THE SELECTED PROJECTS ACCORDING TO THE CSO
CLASSIFICATION OVER THE 2007-2020 PERIOD



Population health intervention research programme (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 to be funded for 12 or 18 months. 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 funding for this type of project was increased in 2020 by €30,000 to a maximum of €50,000, to bolster this scheme.

THE PROGRAMME IN 2020

In 2020, ten projects were selected for funding, including four emerging projects, for a total budget of €2.2M (Table 30) out of 34 submitted projects (22 emerging projects and 12 full projects). Two of these were full projects stemming from previously funded emerging projects, highlighting the interest of this funding track.

A third of the projects funded in 2020 concerned patient care and survivorship issues (CSO 6.1 category), another third involved research on education and communication (CSO category 6.5), and the remainder were research projects on surveillance, health care delivery and prevention with intervention on behaviour (CSO 6.2, 6.4 and 3.1).



■ **TABLE 30**
FEATURES OF THE POPULATION HEALTH INTERVENTION RESEARCH PROGRAMME IN 2020

Objectives	<ul style="list-style-type: none"> • 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
Selection of full projects	6 full projects selected / 12 submitted
Selection of emerging projects	4 emerging projects selected / 22 submitted

THE PROGRAMME OVER THE 2010-2020 PERIOD

Since 2010, out of 313 projects submitted, 63 projects have been funded (including 19 emerging research projects) for a total amount of €16.54M (Table 31).

Although the “emerging research projects” funding track is recent, since its creation, this kind of project accounts for 30% of selected and funded projects. Based on experience of emerging projects converted to full proposals, INCa is expecting an increased number of high-quality full projects.

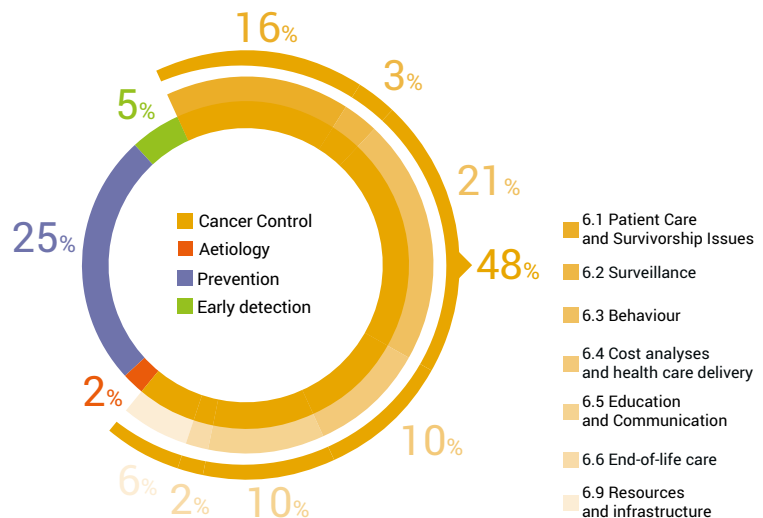
■ **TABLE 31**
TRENDS IN SELECTION AND FUNDING OF THE POPULATION HEALTH INTERVENTION RESEARCH PROGRAMME OVER THE 2010-2020 PERIOD

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Total
Funding (in €M)	0.61	1.51	2.18	0.71	1.15	1.08	1.11	1.79	2	2.20	2.20	16.54
Proposals submitted	8	37	20	10	60	29	22	39	34	20	34	313
Projects selected	2	3	5	3	4	7	6	8	9	6	10	63
Selection rate	25%	8%	25%	30%	7%	24%	27%	21%	26%	30%	29%	20%

2010-2020:
63
projects supported for
an overall amount of
€16.54M

Figure 58 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) represent nearly half of the funded projects (46%).

■ **FIGURE 58**
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2010-2020 PERIOD



Strengthening the PHIR community

The Institute plays an important role in developing the PHIR community, through the organisation of events to promote knowledge dissemination.

Emerging project webinar- July 2020

Organised in consultation with researchers, this webinar involved a presentation of the five emerging projects underway in 2020, and a round-table discussion putting the lessons learned from finalised emerging projects into perspective. Participants were then divided into four discussion workshops, led by members of the Institute, the co-chair of the scientific evaluation committee of the call for proposals (2019-2020), and senior researchers from the field. Nearly 60 PHIR researchers attended this event.

Connected devices for nutrition and physical activity webinar - November 2020

Organised to foster the PHIR community, this webinar focused on Olivier Aromatario's research work: the components and effective mechanisms required for a connected object or health application, to support the change of behaviour, taking Social Health Inequalities (SSI) into account. This seminar brought together nearly a hundred

people, researchers, but also administrators, health professionals, decision-makers, companies, etc., contributing to rich discussions around this work.

Coordination of a special issue in the Global Health Promotion journal

PHIR has an essential role in the development of policies and interventions to fight against inequalities effectively and not accentuate them. The Institute coordinated the production of a special issue in the journal Global Health Promotion, following the PHIR symposium organised in 2019. The aim of the issue is to present the diversity of PHIR practices to advance in the fight against inequalities and the development of equity in health. In particular, the issue examines the attitudes, theories and methods of research on interventions, terms of partnerships between researchers, decision-makers and actors involved in interventions, and planning and implementation practices of interventions. Opening with an institutional editorial co-signed by N. Ifrah (Chair of INCa), J. Salomon (National Chief Medical Officer, Ministry of Health) and G. Bloch (CEO of Inserm) and with a scientific editorial, this issue is composed of 7 original articles and 5 commentaries prepared by researchers, decision-makers and stakeholders in the field of health promotion.

Support for research on environmental risk factors

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.

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

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

The integrated and multidisciplinary cross-cutting research programme will aim to federate knowledge and skills through the cooperation of teams from different research fields, working as a consortium to implement several work packages. This collaborative programme would help optimise the production of knowledge and would promote its dissemination for a better understanding of the putative link between exposure to chlordecone and prostate cancer risk in the French Antilles.

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

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

A scientific evaluation committee was set up, composed of ten multidisciplinary experts: the national and international experts from the committee that made the initial recommendations for the issue of the call for applications, and additional experts from the fields of humanities and social sciences.

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

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

In response to this recommendation, the selected applicants will submit a proposal to the committee in 2021, before co-building the research programme.

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

This multi-agency programme addresses various public health issues related to the environment and workplace. ITMO Cancer-Aviesan has been funding cancer-related projects within this programme since 2010.

The programme in 2020

In 2020, 2 projects were selected for funding by ITMO Cancer-Aviesan for a total of €250,000 (Table). Projects focused on the effects of halogen compounds on nuclear receptors involved in tumour proliferation, and on the role of chronic exposure to cadmium on the activation of pancreas stellate cells and on the remodelling of stroma, both involved in the formation of preneoplastic pancreatic lesions.



■ TABLE 31
FEATURES OF THE PNR-EST PROGRAMME IN THE CANCER FIELD IN 2020

Objectives	<ul style="list-style-type: none"> • To evaluate the risk of cancer linked with exposure to potential carcinogens in the general population or at work. • To analyse low-dose or cumulative exposure effects of CMRs on cancer risks. • To identify environmental or occupational cancer risk factors. • To analyse the effect of genes/environment/behaviour interactions on cancer risks. • To develop cost/benefit assessment methods for cancer prevention or care. • To identify and validate biomarkers allowing cancer risk estimation in occupational or environmental settings.
Programming institution	Anses
Operating institution	Anses
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€250,000
Letters of intent evaluated	34
Full proposals evaluated	14
Projects selected	2 (1 Proof of concept & 1 Full)
Selection rate	6%

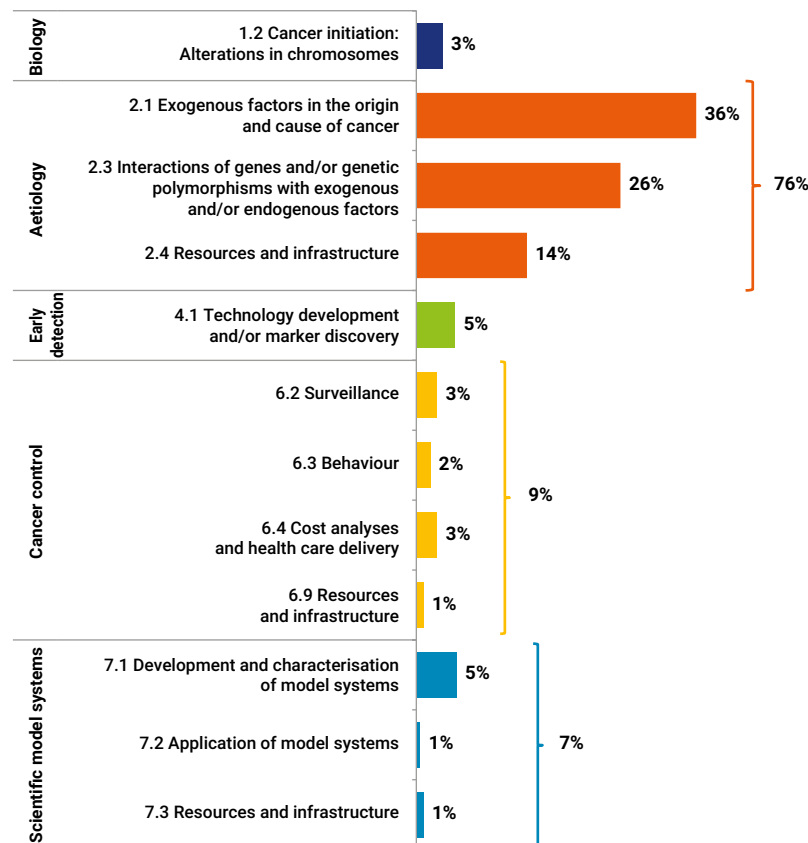
The programme over the 2010-2020 period

Since 2010, 56 projects related to cancer have been funded within the framework of this programme for a total amount of €8.5M. Funded projects primarily addressed the aetiology of cancer in accordance with the objectives of the call (more than 75%). These projects were largely aimed at assessing the role of exogenous factors alone or in interaction with endogenous factors in the onset of cancer. Other projects dealt with biology (cancer initiation), early detection (mainly marker discovery), cancer control, and scientific model system development and characterisation (Figure 59).



■ FIGURE 59

DISTRIBUTION OF CANCER-RELATED PROJECTS SELECTED WITHIN THE SCOPE OF THE PNR-EST PROGRAMME ACCORDING TO THE CSO CLASSIFICATION OVER THE 2010-2020 PERIOD



2020:
2
projects selected
for a total amount of
€530,000

SUPPORT FOR THE NATIONAL ÉCOPHYTO 2+ PROGRAMME FROM THE FRENCH OFFICE FOR BIODIVERSITY BY ITMO CANCER-AVIESAN

The French national Écophyto 2+ plan aims to reduce phytopharmaceutical compound use, dependence, risks and impacts by supporting changes in practices. In this context, the French Office for Biodiversity and the Ministries overseeing the Écophyto 2+ plan launched a call for proposals aimed at exploring the human health and ecosystem effects of exposure to these compounds. For the first time in 2020, ITMO Cancer-Aviesan funded 2 projects focusing on cancer research (Table 32). Both were aimed at exploring impacts of pesticide exposure on cancer, either hormone-dependent (prostate and breast cancers), or haematological (non-Hodgkin lymphoma).

■ **TABLE 32**
FEATURES OF THE ÉCOPHYTO 2+ PROGRAMME IN THE CANCER FIELD IN 2020

Objectives	To support projects exploring the effects of phytopharmaceutical compound exposure on cancer.
Programming institution	French Office for Biodiversity
Operating institution	French Office for Biodiversity
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	€530,000 (2 projects)

Support for professional careers and training

RESEARCH CHAIRS

Chair development and support policies are implemented proactively on the other side of the Atlantic and have been shown to be effective. Indeed, these systems are relevant for stimulating the creation of clusters of excellence, in particular in emerging sectors, by structuring a core of researchers on a developing theme. This is the objective pursued by the Institute with its research chair policy.

Health economics chair

Research in economics in the field of cancer is a discipline to be developed. The French National Cancer Institute innovated this year by creating a chair of excellence in this field of research, in partnership with the University of Paris-Dauphine and the Risk Foundation (Fondation du Risque). The main objectives will be to produce knowledge regarding:

- Questions related to drug shortages and strategies to secure supplies;
- Economic modelling applied to cancer treatment;
- Analysis of the effectiveness of financial incentives for preventive behaviour.

The chair was awarded to Ms. Brigitte Dormont, who is professor of economics at Paris Dauphine University and responsible for the “health and aging” axis of the Laboratory of Health Organisation Economics and Management. Her research focuses notably on regulatory health system policies, and particularly, on ambulatory medicine, and hospital pricing reform. She is a particularly renowned researcher in this field.

A dedicated steering committee has been set up to oversee the work of the research chair. This work began at the end of 2020 and will continue over a 3-year period. The budget allocated to the chair is €600,000.

Health democracy / empowerment chair

In 2020, the Institute launched a call for applications for the creation of a new chair of excellence in human and social sciences entitled “Health democracy/empowerment: involving citizens and people affected by cancer”, in partnership with Aix-Marseille University, the Paoli-Calmettes Institute, and the CANBIOS team (Cancers, Biomedicine and Society) at UMR1252 SESSTIM (Economic and Social Health Sciences and Information Processing).

Report meeting for the ITMO Cancer-Aviesan programme “Environmental risk factors exposure and cancer”

The aims of this programme were two-fold: to support the development of tools evaluating the role of environmental factor exposure in cancer risks, and to improve the understanding of mechanisms involved in such “environmental” cancers. Six editions of the programme took place during the 2012-2017 period. The report meeting took place in Paris on March 11th-12th 2020 and included laureates from the years 2012-2014 presenting their research funded by the programme. It was organised around 4 axes: contaminant cocktails (4 projects), gene/environment interactions (8 projects), endocrine disruptors (5 projects), and physical factors (5 projects). Discussion among laureates, selection committee members, and ITMO Cancer-Aviesan closed the session.



The overall objective of this research chair is to develop research in human and social sciences on health democracy and empowerment in the field of oncology. This objective aligns with the partners' research priorities, and aims to bridge a gap in research that has developed in this field, particularly in France.

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

Two applications were received and were deemed eligible. However, following the evaluation process, the evaluation committee stated they were not in favour of the selection of either candidate. As a result, the call for applications will be renewed in 2021.

The research chair programme over the 2015-2020 period

The Institute has been supporting the creation of research chairs of excellence since 2015 and has allocated a total budget of €1.5M to this end. Three research chairs have already 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 the social challenges of personalised medicine and innovation in oncology**.

An analysis of the first chairs and interviews with the chairholders and the host teams were carried out to identify areas for improvement. It appears to be necessary to propose an at least 5-year duration with an adequate budget and greater involvement of local partners. There is also a need to build-up perspectives for maintaining research themes after the period of funding for the chair by INCa (See Part III).

PHD PROGRAMME IN HSS-E-PH

The programme in 2020

For the 10th consecutive year, the French National Cancer Institute 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 17 applications were submitted to INCa, slightly down on 2019 and 2018 (25 and 36 applications received, respectively). Out of these projects submitted, 2 were classified out of scope and one was withdrawn. The 14 projects reviewed are divided into 3 research categories. Table 33 presents the distribution of the applications reviewed. The distribution of projects according to discipline is substantially consistent between 2019 and 2020.

■ **TABLE 33**
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.)	5
Epidemiology or biostatistics	6
Human sciences (psychology, cognition and learning, psychoanalytic studies, science of physical activity, etc.)	3

Following the review process, including interviews of applicants, five PhD theses were selected for funding, including a project that was subsequently reallocated to the PhD programme relative to psychoactive substances (Table 34).

■ **TABLE 34**
DOCTORAL FELLOWSHIPS FUNDED IN 2020.

Title	Discipline
CAR-T treatments as promises and disruption(s) in the French health system.	Social sciences
Mixed generalised linear models and pseudo-observations as alternatives to Bayesian survival analysis for the evaluation of therapies in rare cancers	Public health / biostatistics
Rethinking vaccine hesitancy; comparative study of HPV and HBV vaccinations.	Sociology
Influence of agricultural activities on the risk of embryonic tumours in children	Epidemiology

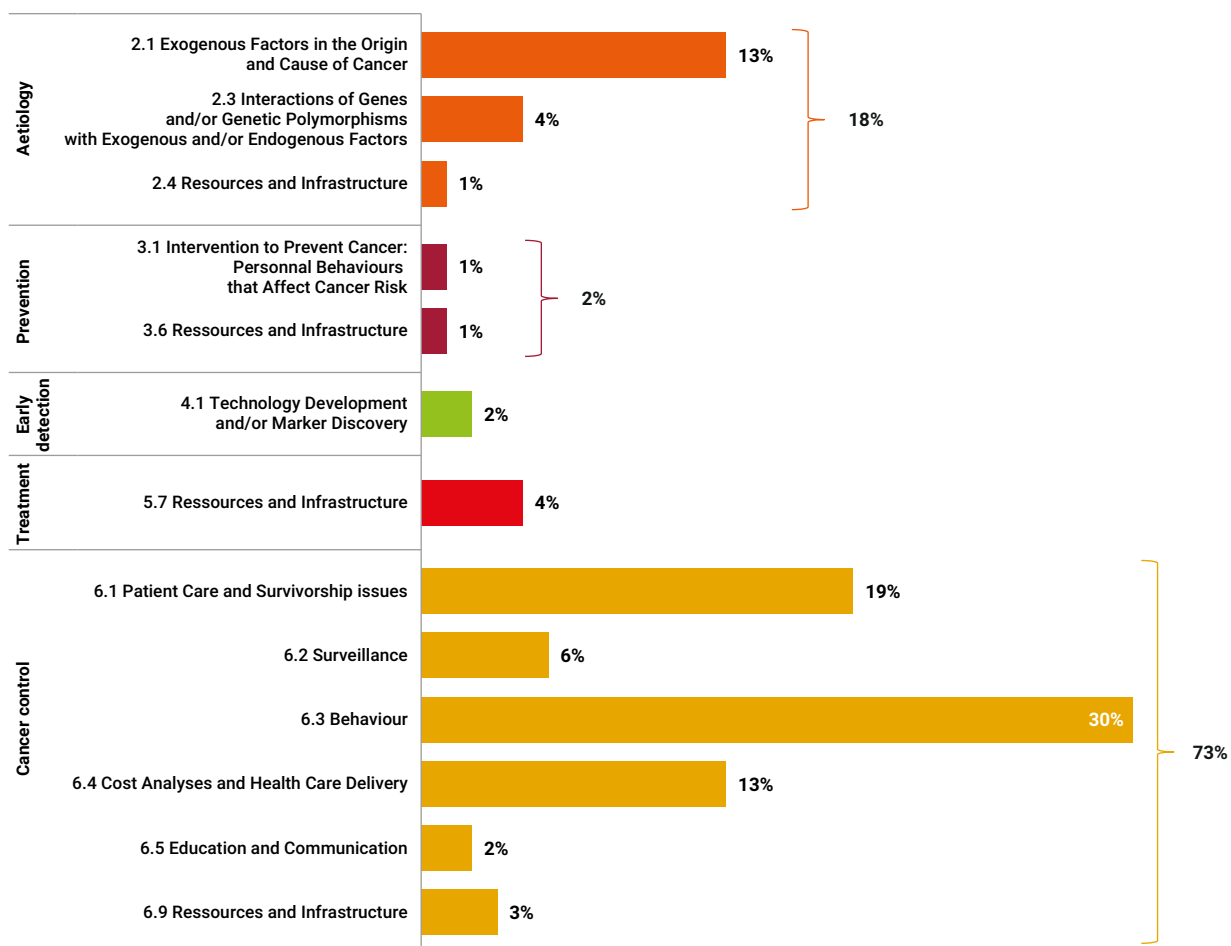
In 2020,
4 PhD students
 were awarded funding:
 epidemiology, sociology,
 social sciences,
 and biostatistics.

2007-2020:
46
 PhD theses supported
 for an overall amount of
€4.47M

The programme over the 2011-2020 period

Over the 2007-2020 period, 46 PhD theses were supported for a total amount of €4.47M (Figure 60).

FIGURE 60
DISTRIBUTION OF THE SELECTED GRANTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2020 PERIOD



PHD PROGRAMME IN ALCOHOL AND TOBACCO RESEARCH

Due to the COVID-19 pandemic, only the “Reduce and fight against psychoactive substances consumption and addictions” call for applications for doctoral grants was implemented in 2020.

Following on from the programme launched in partnership with the Institute of Public Health Research (IReSP), “Tobacco INCa-IReSP 2019”, this call is open to all psychoactive substances: tobacco, alcohol, and cannabis.

It covers all 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, humanities and social sciences, law, biology, epidemiology, etc.

It is divided into 3 sections:

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

Aimed to support PhD students with a 3-year grant, this call for applications targets all students with a Master’s degree in humanities and social sciences, public health, epidemiology, or biology, enrolled in first or second year in a doctoral school. The implementation of this call was adjusted due to the health crisis: flexibility in obtaining the necessary supporting documents from universities for the submission of applications, and schedule. The call was a success with 27 applications submitted (8 in epidemiology, 8 in neurosciences, 7 in humanities and social sciences, 4 in biology, and 3 in other disciplines).

- Finally, 9 PhD students were funded by INCa (5 applicants) and IReSP (4 applicants). The 5 PhD theses funded by INCa concern:
 - Judgement and stigmatisation of addictions in cancer patients;
 - Cravings: early and predictive marker of addiction to tobacco, alcohol, and cannabis;
 - Design and functional analysis of nicotinic acetylcholine receptor $\alpha 4\beta 2\alpha 5$ allosteric modulator for the treatment of nicotine addiction
 - Study of the cellular and molecular mechanisms involved in the pulmonary pathogenicity of heated tobacco emissions
 - Screening for bronchopulmonary cancer in subjects occupationally exposed to asbestos.



This last PhD was transferred after being selected for the call for applications aimed at supporting HSS-E-PH theses and will be funded through the addiction fund (Table 35).

■ **TABLE 35**
DISTRIBUTION OF THE SELECTED PROJECTS RELATED TO THE TOTAL FUNDING

2020 "Psychoactive substances" call for doctoral grant applications	Funding by INCa	Funding by IReSP	TOTAL
Projects selected	5	4	9
Funding	€596,916	€402,250	€999,166

"Tobacco: Population-based Research & Vulnerable Populations" webinar

Held in December 2020, the webinar attracted over 200 attendees.

The aim of this webinar was to present research projects dealing with intervention, prevention, and smoking cessation measures for vulnerable populations: adolescents, young adults, disadvantaged groups, pregnant women, cancer patients, and patients with mental health problems.

This scientific seminar offered an opportunity to present the initial research results of projects completed, as well as the methodologies and scientific approaches of projects currently being supported by the Institute in this area.

Eleven speakers presented their projects in 3 sessions:

- Session 1: Smoking cessation aids for vulnerable populations
- Session 2: Research methods and protocols
- Session 3: Perception and prevention of work amongst young people.

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.

R

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.

European actions

In the European Union, 2.7 million people were diagnosed and 1.3 million people died from cancer in 2020⁵. 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.

5. 2020 Cancer Estimates, source: European Cancer Information System.

In 2020, 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 joint or transnational actions in the areas of translational research (TRANSCAN-2, 2015-2020 & Transcan 3, 2021-2026), innovation (iPAAC, 2018-2021), Next Generation Sequencing For Oncology (OncNGS 2020-2025), CAR and TCR-engineered T cell therapy (T2Evolve, 2021-2025).

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 at providing 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 9 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. Within the framework of this WP some deliverables and milestones had been achieved:

- Report on Innovative cancer therapies in clinical practice guidelines;
- Report on Reference frameworks linked with the access to innovative immunotherapies;
- Report on Horizon scanning systems applied for cancer control in Europe;
- 1st draft of the report on Real life monitoring of innovative cancer therapies taking CAR-T cells as an example.

WP 5 on cancer prevention

INCa has contributed to the different tasks of this WP. 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. Within the framework of this WP, main milestones have been reached:

- Survey on attitudes for early diagnosis at a European level;
- Report of innovations, including harms and benefits from risk-stratified screening;
- Sustainability and Monitoring of the European Code Against Cancer: Recommendations by IARC subcontracted IPAAC contribution, which is posted on the Intranet but not yet public.

WP 6 on Genomics in Cancer Control & Care

The Institute contributed to the activities of the WP6, and more specifically to the activities of Task 6.2 *Concept for the implementation of risk-adjusted prevention: the breast cancer case*

WP 12 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.

Within the framework of this WP 12, one-pagers have been finalised by the Institute, describing examples of European initiatives and programmes considered interesting by partners, Member State representatives and/or stakeholders in the field of clinical practice guidelines, access to advanced therapies, and Horizon scanning schemes.

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

TRANSCAN- ERA-NET: ALIGNING NATIONAL/ REGIONAL TRANSNATIONAL CANCER RESEARCH PROGRAMMES AND ACTIVITIES (TRANSCAN-2 & TRANSCAN 3)

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.

At the end of 2020, the European Commission supported the continuation of this programme by approving the new TRANSCAN-3 ERA-NET for a period of 5 years (2021-2026). The Institute is renewing its commitment to this project, and will notably lead WP6 dedicated to joint calls for proposals, and will be responsible for the third joint call for proposals in 2023.

The TRANSCAN-3 network is now based on the cooperation of 31 funding organisations, regional and national, public and private, from 20 European and non-European countries. The majority of the partners have been collaborating since 2011 (within the 2 previous TRANSCAN and TRANSCAN-2 ERA-NETs), and the network has been expanded with new partners, such as Canada, Hungary, Ireland or Romania, in accordance with the extension strategy included in the missions of this programme.

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

**T²EVOLVE: ACCELERATING
DEVELOPMENT AND
IMPROVING ACCESS TO
CAR AND TCR-ENGINEERED
T CELL THERAPY**

The logo for T²EVOLVE features the text "T²EVOLVE" in a bold, sans-serif font. The "2" is a superscript. The "O" in "EVOLVE" is replaced by a stylized blue and green circular graphic. The logo is set against a background of two horizontal grey bars.

Immune cells that are empowered by gene-engineering to seek and destroy cancer cells (engineered T cell therapy) constitute a transformative novel treatment that has the potential to cure cancer. Multiple new versions of this therapy are being developed for distinct types of cancer, but their introduction into clinical practice is hampered by a lack of standardised and validated models to predict safety and efficacy, customised manufacturing and monitoring to scale up production and clinical use to industry standards, and strategies for optimal patient conditioning.

The interdisciplinary T²EVOLVE consortium is made up of 27 European partners from 9 different nations. Partners include university and non-university research facilities, pharmaceutical and biotechnology companies, as well as regulatory authorities and patients and professional associations.

A core feature of this approach will be the embedding of patient stakeholders as contributing members of the team across all levels of the R&D process. The overall aim is the development of an innovation ecosystem that will accelerate the process of developing engineered T cell therapy in the EU.

The project will deliver novel tools for education and for improving the communication between healthcare providers and patients, optimised laboratory models

that can help determine how safe and effective new therapies with engineered T cells are, standardised methods in which these therapies are produced and monitored during treatment. The consortium members are innovators and pioneers in this field that are dedicated to bringing the EU to the forefront of the global engineered T cell therapy movement. This effort will ensure that EU citizens will continue to have access to the most innovative and best-available medical care, provide guidance on how to implement this novel treatment into the EU health care system in a sustainable way, and secure a leading role for Europe in this emerging field in medicine and science, the economy and society.

INCa is involved in a WP dedicated to the “*Patient Involvement*” (WP2) aiming to:

- Promote engagement of patients and patient centricity all along the R&D process;
- Ensure adequate communication on engineered T-cell therapies to patients and their family/informal caregivers;
- Ensure that HCPs are sensitised to patient needs;
- Propose solutions for equitable patient access to engineered T cells;
- Propose solutions to guarantee broad patient access to engineered T cells.

The Institute is also involved in a WP dedicated to “*Gold standard analytical methods used*” (WP5) which aims to:

- Describe state-of-the-Art analytical assays used for in-process and release Quality Controls of engineered T cells, and immunomonitoring (survey and literature analysis);
- Develop innovative analytical tools and technologies;
- Produce a set of standardised analytical methods.

For further information, please consult the website: <https://tzevolve.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 for 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 diagnostic 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 acts, together with other organisations, as a supporting entity. Its role consists essentially in supporting the identification of needs, the feasibility analysis, and the evaluation of offers and the follow-up of contracts. INCa is more involved in WP2 devoted to the preparation of public procurement. The objective of this WP is to define the elements that will constitute the PCP:

- Define the content of the oncNGS solution (test kit and IT developments of the analysis system);
- Develop the business case for oncNGS;
- Publish the prior information notice and proceed with the market consultation;
- Establish the award criteria for the selection of the solution at each stage of the PCP process (device concept, prototype and solution).

The work will be continued in WP3 devoted to the tender itself.

INCa's participation in the project will ensure that the solutions developed in the project can be integrated into the French healthcare system.

For further information, please consult the website: <http://oncngs.eu/>

Europe's Beating Cancer Plan: A new EU approach to prevention, treatment and care

In February 2021, the European Commission launched "Europe's Beating Cancer Plan", which reflects a **political commitment to leave no stone unturned to take action against cancer.**

It contains concrete, ambitious actions that will support, coordinate, and complement Member States' efforts to reduce the suffering caused by cancer.

Europe's Beating Cancer Plan is also a key pillar of a stronger **European**



Health Union and a more secure, better-prepared, and more resilient EU. It outlines substantive actions to mitigate the impact of the COVID-19 pandemic on cancer care, and support structural improvements for a more sustainable cancer pathway.

The overall budget for Europe's Beating Cancer Plan is about €4 billion from different European programmes, such as:

- €1.25 billion from **EU4Health programme** will be used to support actions and initiatives outlined in the Cancer Plan;
- €2 billion from **Horizon Europe**, Framework Programme for Research and Innovation, to support the **Mission on Cancer** and other cancer related research projects including for research infrastructures;
- €500 million from **Erasmus+, the European Institute for Technology and Marie Skłodowska-Curie Actions** for projects in education, training, and research in the field of cancer;
- €250 million from **Digital Europe Programme** for cancer-related projects, and to support wider digital investments, such as relating to electronic data, cybersecurity and digital skills from which the health sector will benefit.

The aim of Europe's Beating Cancer Plan is to tackle the entire disease pathway. It is structured around four key action areas where the EU can add the most value:

1. prevention;
2. early detection;
3. diagnosis and treatment;
4. quality of life of cancer patients and survivors.

Over the coming years, it will focus on research and innovation, tap into the potential that digitisation and new technologies offer, and mobilise financial instruments to support Member States, and with its policy objectives, supported by ten flagship initiatives and thirty-two supporting actions, the Cancer Plan will help Member States turn the tide against cancer.

The first area of intervention of Europe's Beating Cancer Plan is to support a modern approach to cancer, using new technologies, research and innovation at the service of patient-centred cancer prevention and care.

According to the European Commission, the better we understand the biological processes, risk factors and health determinants driving cancer, the more effectively we can prevent, detect, diagnose and treat it. Stepping up research and innovation efforts will enable us to better understand cancer risk factors, as well as improve diagnoses, therapies, treatments, and prevention policies.

The Mission on Cancer, envisaged under Horizon Europe, will be a major component of the EU's investment in cancer research and innovation. It will deepen our understanding of the complexity of cancer, and Europe's Beating Cancer Plan will use the remarkable potential of new technologies and scientific progress, including insights from comorbidities, social and behavioural sciences, to better address cancer across the entire disease pathway through its flagships and actions, such as:

Following the 2020 SAB recommendations received, the Institute will seize the sizable opportunities provided by Europe's Beating Cancer Plan to achieve some objectives and goals of the Ten-Year Strategy at a European level.

- **Flagship 1:** Create a **Knowledge Centre on Cancer** to facilitate the coordination of scientific and technical cancer-related initiatives at EU level – 2021.
- **Flagship 2:** Launch a **European Cancer Imaging Initiative** to support the development of new computer-aided tools to improve personalised medicine and innovative solutions – 2022.
- **Other actions:**
 - Enable cancer patients to securely access and share electronic health records for prevention and treatment across borders through the European Health Data Space – 2021-2025.
 - Expand the European Cancer Information System – 2021-2022.
 - Launch Horizon Europe Partnerships to translate scientific knowledge into innovations – 2021.

International cooperation

Cancer is still on the list of diseases with high mortality (9.6 million in 2018, 8.2 million in 2012). Although some types of cancer can be cured and others can be transformed into chronic disease, around 1 in 6 deaths worldwide are due to cancer (WHO 2018), and its economic impact was estimated in 2010 at some US \$ 1,160 billion.

About 70% of cancer deaths occur in low- and middle-income countries. According to WHO estimates, cancer is the first or second cause of death before age 70 in 91 of its 172 member countries, and third or fourth in 22 countries. The increase in life expectancy, as well as the distribution of risk factors associated with economic development, is increasing the global incidence of cancer. Thus, according to GLOBOCAN 2018 estimates produced by IARC, cancer represented 18.1 million new cases annually in 2018. Lung cancer is the most commonly diagnosed (11.6% of cases) and the most common cause of mortality (18.4%), followed by breast cancer (11.6%), prostate cancer (7.1%) and colorectal cancer (6.1%) in terms of incidence, and by cancer colorectal (9.2%), stomach cancer (8.2%), and liver cancer (8.2%) for mortality. In ten of the most advanced countries in the fight against cancer, the five deadliest cancers together account for more than half of cancer-related deaths. An analysis of the five cancers for each country shows the high prevalence of lung and colorectal cancers in terms of mortality. Breast cancer is a major cause of death in all the countries concerned apart from Asian countries, which tend to face excess mortality linked to cancers of the stomach and liver. The fight against cancer therefore requires specific adaptation to the national and regional context. Across countries, the five deadliest cancers account for 50% or more of deaths from this disease.

However, the most frequently diagnosed cancers as well as the causes of death vary substantially between countries and within each country due to socio-economic factors. The position of cancer as a cause of premature death within a given country is directly correlated with the national level of social and economic development. Likewise, the mortality and incidence of different types of cancer differ considerably between countries with high HDI and countries with medium and low HDI.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER - IARC

Report on the relationship between France and the IARC

As the representative of France on the Governing Council of the International Agency for Research on Cancer (IARC), INCa contributes to the development of the international cancer research agenda, which constitutes a heritage and a vision, that of General de Gaulle, for whom the advancement of science and the progress of the human condition required international cooperation. This commitment was recently renewed with the support of the State, the Region and the City of Lyon for the construction of the “New Centre”, the first foundation of which was laid this year.

International Agency
Research on Cancer



The “New Centre” opens a new era in the development of the IARC and its activities. The need to strengthen international cooperation on global health issues has become, now more than ever, an imperative. Cancer is a global burden that requires a global response.

In this context, INCa and the IARC have published a report on the relationship between France and the IARC. It presents a description of the missions, strategic orientations, and activities of the centre, but also an inventory of cooperation with French institutions. These are all elements that will provide useful information for the pursuit of the partnership between French authorities and the IARC.

The establishment of the IARC in France has a positive impact on the research landscape in France, which must be enhanced. The French contingent of IARC scientists is the largest, including among doctoral students. They thus benefit from a high-level international environment to carry out their research. Among the projects developed by the IARC, nearly a third are the subject of collaboration with a French team. These mainly concern epigenetics, environment and radiation, nutritional epidemiology, biomarkers, and genetic predispositions of cancer. These international collaborations are undeniably a vector of scientific excellence, and of accelerating progress in key areas of cancer research. Between 2014 and 2018, the IARC worked with 55 French partner entities to carry out its projects. This shows the extent of the potential of the partnership between France and the IARC.

Scientific achievements of the IARC

IARC research reported that 18.1 million new cancer cases were diagnosed around the world in 2018, and 9.6 million people died from the disease. By 2040, those figures are expected to nearly double, with the greatest increase observed in low- and middle-income countries (LMICs). Prevention is the most cost-effective

long-term strategy for the control of cancer. Globally, approximately one third of all cancers could be prevented with evidence-based knowledge of established risk lifestyle factors (tobacco smoking, alcohol consumption, unhealthy diet, physical inactivity, and excess weight). Infectious pathogens are important and modifiable causes of cancer. IARC findings reported, for 2018, an estimated 2.2 million infection-attributable cancer cases diagnosed worldwide. Primary causes were *Helicobacter pylori*, human papillomavirus (HPV), hepatitis B virus, and hepatitis C virus. IARC research has shown that a single dose of HPV vaccine provides similar protection against persistent HPV 16/18 infection as the three- or two-dose vaccines. A new IARC Handbook of Cancer Prevention concluded on the efficacy of cervical cancer screening to reduce related mortality. Scientific evidence on primary and secondary prevention of cancer has been compiled and translated into a set of public health recommendations in the European Code Against Cancer. These recommendations have been used as a guide by countries to design their national cancer plans.

The IARC Biennial Report 2018–2019 provides an overview of the full range of IARC's scientific achievements in the two-year period (see Document GC/62/2).

COOPERATION (COVID-19 AND CANCER)

International meeting at the initiative of INCa (May 2020)

The Institute organised a virtual meeting with its international partners (Germany, Italy, South Korea, Japan, Canada / Quebec) to share information, tools, and recommendations on:

- General situation in the respective countries;
- Impact of COVID-19 on cancer management / organisation, including prevention, screening, treatment;
- Recommendations for cancer patients and professionals during the pandemic;
- Recommendations and criteria for post-containment.

Participants

INCa: Norbert Ifrah, Chairman, Thomas Dubois, International Affairs – DKFZ: Michael Baumann, Chairman, Claudia Mayer, International Affairs - NCC Japan: Hitoshi Nakagama, President, Tomohiro Matsuda and Kay Ohara, International Affairs - NCC South Korea, Lee Eun Sook, President, Han, Jong Soo, International Affairs .

Technical Cooperation with Quebec

This technical cooperation initiated between Dr. Jean Latreille (DQC Director) and Dr. Jean-Baptiste Meric (Director of Public Health and Care Division, INCa) enabled:

- monitoring of the evolution of the respective situations (Quebec being slightly ahead in the progression of the epidemic compared to France);
- sharing of experience on the measures put in place for the organisation of care during the crisis;
- the transfer of planning and care organisation tools.

REVIEW OF CANCER RESEARCH FUNDING AND EVALUATION

Review and trends in cancer research funding

CANCER RESEARCH FUNDING IN 2020

In 2020, 258 projects were selected and the total funding awarded to cancer research programmes amounted to **€87.99M**, including:

- €39.20M from INCa;
- €25.45M from DGOS;
- €23.33M from Inserm for ITMO Cancer-Aviesan.

Figure 61 shows the breakdown of multi-year funding for 2020 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;
- 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 62% of the allocated budget was devoted to competitive investigator-driven calls for proposals, managed by INCa, including funding from DGOS. Strategic research initiatives and thematic programmes represented 33% of total funding in 2020, and also include the thematic research programmes managed and funded by ITMO Cancer-Aviesan.

Figure 62 presents the funding allocation according to the CSO classification:

- Treatment category represented the most significant investment in 2020 with €34.01M (39%);

FIGURE 61
2020 MULTI-YEAR CANCER RESEARCH FUNDING BY PROGRAMME TYPE (INCA, DGOS AND ITMO CANCER-AVIESAN): €87.99M INVESTED

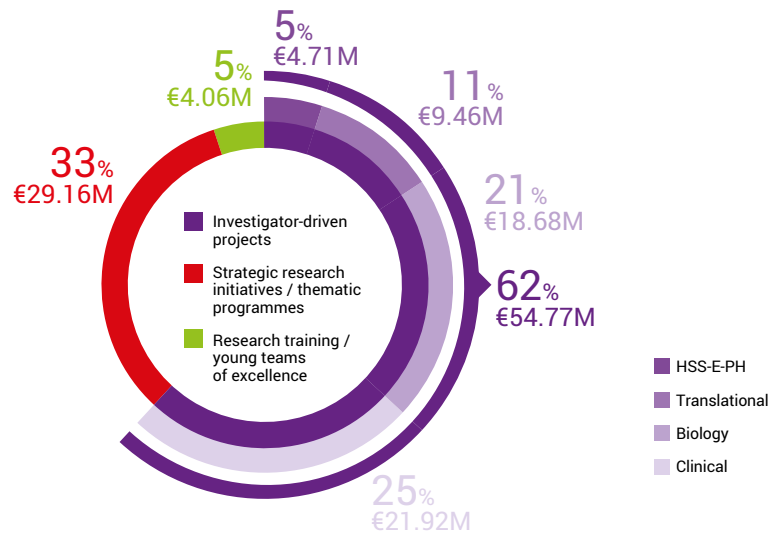
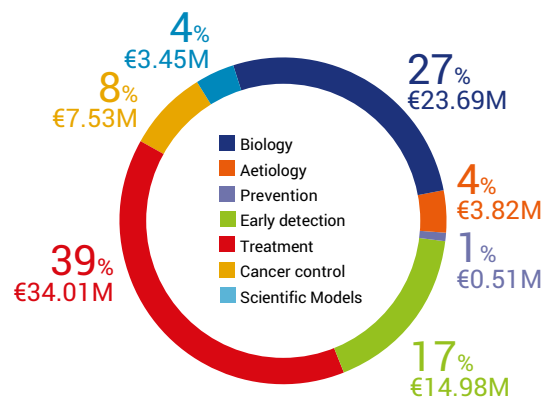


FIGURE 62
2020 MULTI-YEAR CANCER RESEARCH FUNDING ACCORDING TO THE CSO CLASSIFICATION (INCA, DGOS AND ITMO CANCER-AVIESAN): €87.99M INVESTED



- Biology and scientific model categories represented €23.69M and €3.45M in 2020, respectively (27% and 4% of 2020 investments);
- Early detection, diagnosis and prognosis amounted €14.98M (17% of 2020 funding);
- Cancer control, survivorship, and outcomes research issues represented 8% of investments (€7.53M), while the prevention category represented a mere 1% of investments in 2020 (€0.51M);
- Studies related to the aetiology category amounted to €3.82M in 2020 and represented 4%.

CANCER RESEARCH FUNDING OVER THE 2007-2020 PERIOD

Since 2007, a total of 3,561 projects have been funded through the different competitive calls for research proposals and grants for designation for over **€1.33Bn**.

Figure 63 shows the breakdown of 2007-2020 total funding by programme type:

- Investigator-driven calls for proposals of the four main research areas represented a total of 51% of 2007-2020 investments, or approximately €679M;
- Strategic research initiatives aiming to primarily support precision medicine initiatives and thematic programmes represented 26% of cancer research investments (€344M);
- Support for resources and infrastructures represented 20% 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;
- Support for young teams and cancer research training represented a total of 3% of total investments (€47M).

Figure 64 presents the distribution of 2007-2020 total funding according to the CSO classification:

- Treatment and biology categories represented the most significant investment, with €392M and €335M, respectively;
- Cancer control, survivorship, and outcomes research issues represented 16% of total funding (€216M);
- Early detection, diagnosis and prognosis categories amounted to €215M;
- Research aiming to identify the causes or origins of cancer – genetic, environmental, and lifestyle – and the interactions between these factors falls into the aetiology category, representing 9% of total funding with €112M;
- Prevention and scientific models categories amounted to €34M and €29M, respectively.

Review of support for paediatric cancer research funding in 2020

In 2020, a total of **24 paediatric research proposals** (projects and applications) were selected for funding, out of the 258 total funded projects, within the scope of the different research programmes launched. The total funding allocated to childhood cancer research represented €9.73M, corresponding to 11% of 2020 investments (€87.99M).

Measure and assess the impact of biomedical research projects - French research funder statement (2017-2021)

During 2020, the partners continued their efforts to implement the roadmap.

The priority actions were

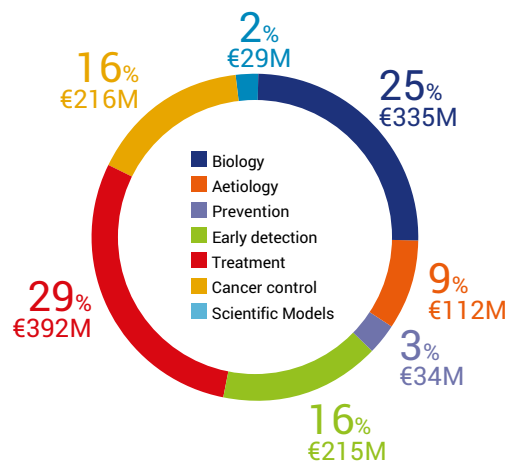
- to test templates and impact methodology
- to support the implementation of ex-post impact studies (portfolio analysis)

A reflection on the perspectives of the working group was also initiated.

FIGURE 63
2007-2020 MULTI-YEAR CANCER RESEARCH FUNDING BY PROGRAMME TYPE (INCA, DGOS AND ITMO CANCER-AVIESAN): €1.33BN INVESTED



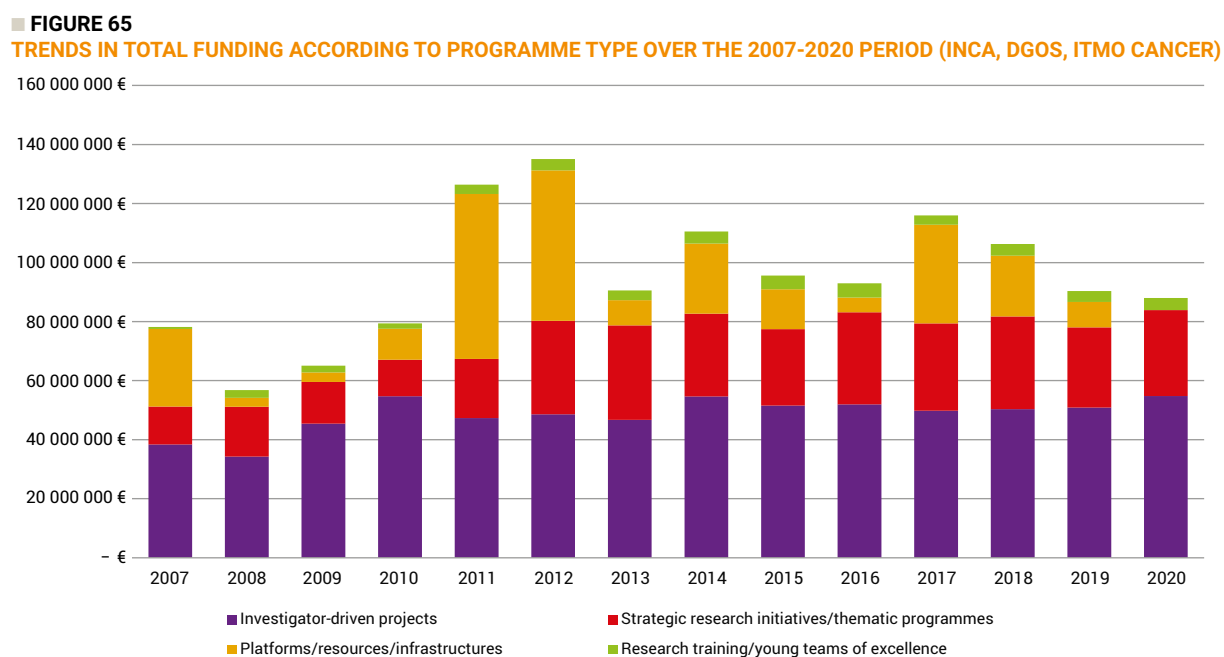
FIGURE 64
2007-2020 MULTI-YEAR CANCER FUNDING ACCORDING TO THE CSO CLASSIFICATION (INCA, DGOS AND ITMO CANCER-AVIESAN): €1.33BN INVESTED



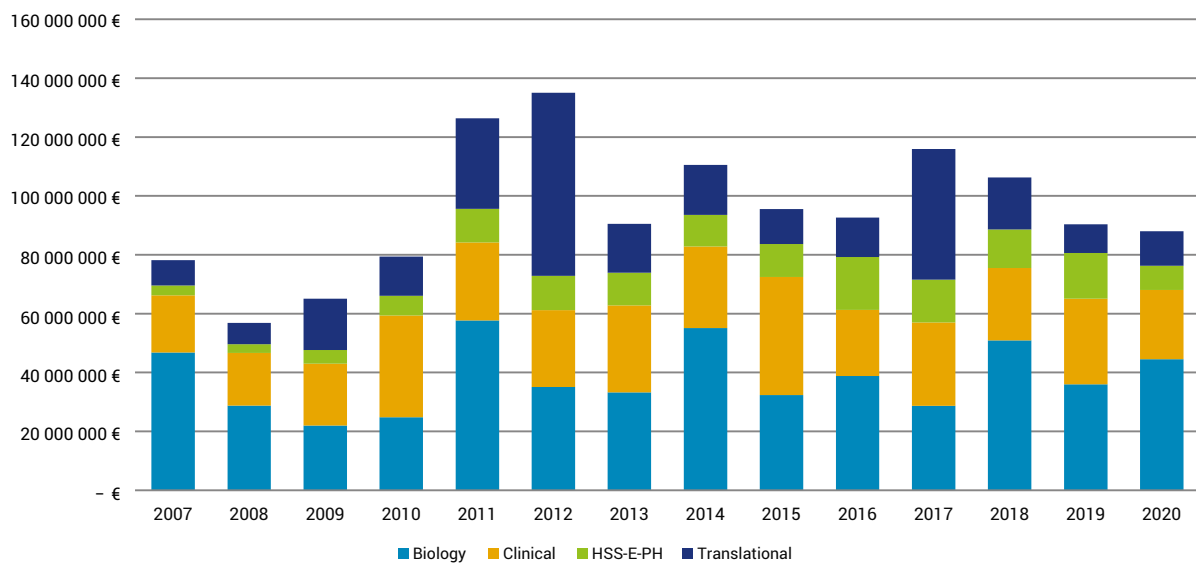
TRENDS IN CANCER RESEARCH INVESTMENTS

Figures 65 and 66 present the trends in total funding according to the programme type and cancer research fields over the 2007-2020 period, respectively.

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



■ **FIGURE 66**
TRENDS IN TOTAL FUNDING ACCORDING TO CANCER RESEARCH FIELD OVER THE 2007-2020 PERIOD (INCA, DGOS, ITMO CANCER)



Evaluation of the 2014-2019 Cancer control plan – summary of interviews and recommendations with a research focus (Official report)

The evaluation was conducted jointly by the General Inspectorate of Social Affairs (IGAS, Inspection générale des affaires sociales) and the General Inspectorate of Education, Sport and Research (IGSR, Inspection générale de l'éducation, du sport et de la recherche), as part of a global evaluation of the actions carried out over the five years of the plan. The following summary presents the main strengths, weaknesses, warning points and levers for research indicated by the inspectors.

The third Cancer control plan has enabled major advances in a large number of areas

In the field of research, the visibility of integrated cancer research sites (SIRIC) and their capacity for integration and consultation represent a major success of the plan, which embodies the realisation of translational research by bringing together clinicians and researchers on common subjects. This cancer control plan has continued the integrative dimension of research in SIRICs by involving research in human and social sciences (including epidemiology and public health) and by involving patients. This success is part of the structuring supported by

the successive plans (early-phase clinical trial centres, biological and clinical databases, cancerpoles, etc.). SIRICs have also been able to take advantage of the support offered by the Investing for the Future programme (“programmes d’investissements d’avenir”).

In France, cancer research made notable progress between 2003 and 2015 and is internationally recognised. The effort for disciplinary decompartmentalisation, driven by investigator-driven or thematic programmes, has been actively pursued and supplemented by the launch of specific research programmes focused on questions requiring special effort (e.g. tumour heterogeneity). This type of approach makes it possible to invest in the experts and the teams concerned in defining the programme at the upstream stage. In addition, the plan has enabled support for short-term, innovative and even risky projects developed in cancer sciences as well as in humanities, involving building a methodology for the selection and specific monitoring of these projects. Investigator-driven programmes were very attractive in the past, but the selection rate has dropped and is no longer compatible with current research standards. The PHRC-K with an 18% selection rate in 2018 is at the level of ANR calls for proposals. This situation needs to be resolved either by increasing funding or by redefining the scope of the programmes. In addition, ex-post analyses or scientific monitoring of programmes cannot replace a regular external scientific evaluation by the High Council for the Evaluation of Research and Higher Education (Hcéres), especially under the funding of the 172^e programme. This evaluation needs to be put in place.

The cancer control plan has made it possible to include cancer research in the current concerns of assessing the impact of short- and long-term research by promoting the implementation of a group of research operators, in order to move forward on these subjects in a coordinated manner. Likewise, real mobilisation on the issues of open science in the context of the National Open Science plan has been achieved, and these questions of sharing protocols and negative or positive results are crucial. The report highlights the relevance of these actions and underlines the strategic role that INCa can play at the core of these discussions, on the basis of the structuring achievements obtained in France thanks to previous plans.

Setting up a research workforce and expertise in oncology in the regions is an asset of the previous plans consolidated by the last cancer plan: in the last decade, cancer research has been impacted by unprecedented transformations, by technological developments, particularly in the field of imaging, high throughput sequencing, and the possibilities of fine genome manipulation and translational research. Researchers’ reactivity has been encouraged, for example for rapid developments in immunotherapies or issues related to data sharing raised by the development of precision medicine. Such cross-mobilisation initiatives between researchers and clinicians should be extended in order to consolidate a concerted strategy at the national level, which makes it possible to clear existing obstacles.

Progress has been made in the development of innovative therapeutic strategies, in particular with the AcSé programme, internationally recognised, and to be consolidated. France is also visible in the field of early-phase clinical trials in oncology, particularly in paediatrics. The effort should be pursued.

6. Funding line of the Ministry of Research dedicated to support “Multidisciplinary scientific and technological research”.

In the field of prevention, the third Cancer control plan played a decisive role in the adoption of a national smoking reduction programme in 2014 (one out of every five cancers is attributable to tobacco). Smoking remains marked by strong social inequalities in prevalence. However, the decrease in the number of smokers, after a decade of stability, is welcomed.

For healthcare aspects, precision medicine is a major advance of the Cancer control plan which has brought together the health and research sectors, with growth in innovative cancer drugs in haematology, immunotherapy, and targeted therapies. The early accessibility to innovative treatments through clinical trials or temporary authorisations for use, issued by the ANSM, have been real assets. The national oncogenetics system was strengthened with a 40% increase in counselling between 2014 and 2017, 25 oncogenetics laboratories (constitutional genetics) and 28 molecular genetics centres distributed throughout the territory, supported by INCa and the DGOS. According to INCa, 30 targeted therapies are now associated with a biomarker. The close links between research and care have allowed the development of precision medicine that is set to expand even further. The evaluation mission describes these developments as great successes. Gains in survival are measured in certain cases in years, and several innovations have helped increase life expectancy for patients subject to treatment failure. The development of CAR T-cell therapies, intended to treat certain haematological cancers for patients subject to therapeutic impasse, has thus represented a major innovation. It testifies to the capacity for adaptation and innovation that the French research and health system can demonstrate.

A cross-cutting priority of the Cancer control plan 3, paediatric research has seen major advances. Parents' questions about the causes of these cancers often remain unanswered, beyond the genetic causes (around 5% of cases). The often-raised question of the role of the environment deserves further study. Supportive care (treatment of pain and dietary problems, psychological support, social monitoring during illness, and palliative care) is also progressing. Improving the recovery rate remains a major challenge. The long-term follow-up of patients, the possibility of a life with fewer after-effects, taking into account the social impact, are all objectives identified in the third Cancer control plan, the implementation of which is progressing but still requires considerable work. INCa devoted 12% of its funding over the 2014-2018 period to paediatric cancer research, including support from Aviesan. Seven early-phase clinical trial centres with paediatric activity were designated, and an integrated paediatric research programme (PAIR paediatrics) was launched in 2016. Since 2019, the additional €5M support from the French Ministry of Research, earmarked for paediatric cancer research implemented in a task force, helped launch actions in 2019-2020, particularly in relation to the collection and sharing of data in paediatric oncology. In this instance, INCa is funding a study on the strengths of paediatric cancer research in France and is launching a bibliometric study, which together will provide support for the definition of a long-term strategy.

Constructive orientations should be reinforced by monitoring their implementation.

The third Cancer control plan can be credited with further designating of programmes and with having clarified or redefined their missions as well as the

national coordination (this particularly concerns SIRICs, early-phase clinical trial centres and cancerpoles). Cancerpoles are the first step in the policy of structuring cancer research initiated in 2003 with the first Cancer control plan (2003-2007). Their missions were updated and refocused during the designations in 2014 and 2017. Close coordination between INCa and cancerpoles was essential for the implementation of the plan, and would have benefited from more pooling of best practices and sharing tools. An inventory of research in oncology, of all its supports and territorial and regional stakeholders in the context of the national research landscape in France such as that INCa recently undertaken for research in oncopaediatrics, would help better define the needs for regional or interregional structuring.

In a number of areas, the achievements of the third Cancer plan have not been up to the challenge.

Knowledge of the links between cancer and the environment and the protection of the population from exposure must be increased.

Improving the survival rate for cancers with a poor prognosis (net 5-year survival of less than 33%), patients' pathways and overall care are a major issue.

Despite the many actions undertaken, the area of job retention and return to employment is struggling to move from a disability-focused approach to a vision more broadly open to workers' vulnerabilities. More generally, for all themes related to life during and post-cancer, the impact of the actions carried out has yet to be assessed from the point of view of patients, in line with the provisions in the Cancer control plan.

Finally, the reduction of inequalities, which was one of the two transversal priorities of the plan, is progressing, but in a dispersed and insufficiently structured way, both in terms of social and territorial inequalities (similar observation made at the end of the second Cancer plan). It is often not possible to assess the effectiveness of previous achievements or, worse, there are reasons to believe that inequalities have worsened (e.g. access to MRIs). Better targeting of audiences and making expected results more explicit, while relying more closely on regional health boards, and mobilising a multi-exposure view of individual risks, would make it possible to have actions that are both more useful and more suitable for evaluation.

Some regressions observed during the implementation of the third Cancer control plan require immediate attention.

In addition to the fact that the plan was singularly lacking in ambition in the fight against alcohol, the period was marked by several setbacks in this fight (including the relaxation of the Evin law). Cancer is the leading cause of alcohol-induced death (16,000 deaths per year); 8% of cancers are attributable to alcohol, and of these the most frequent site is breast cancer (nearly three out of every ten cancers attributable to alcohol are breast cancer). Alcohol consumption has seen a scant decline, placing France among the largest consumers of developed

countries (OECD). However, it is now established that all alcohol consumption is a risk to health. This situation requires the adoption of an ambitious public policy to prevent alcohol risk, as requested by the court of auditors in 2016. The cancer community would benefit from acting as an initiator.

Real problems of accessibility are observed both for drugs and innovative procedures despite a sharp increase in spending in this area. The reality is that accessibility to innovative medicines is declining and a source of considerable inequalities nationwide, to such an extent that the chairpersons of INCa and HAS have alerted the public authorities. In fact, since 2016, the reimbursement of innovative molecules has required a moderate “improvement in actual benefit” but this is subject to having long-term results on survival, often not possible, particularly for rare cancers, paediatric cancers or poor-prognosis cancers. The criterion of no cancer progression is not enough. Moreover, even when the decision is favourable, the post-European marketing authorisation period is sometimes counted in years, which is not the case in other European countries. Access to innovative procedures is also of great concern, again with nationwide inequalities of access. Addressing these issues is a matter of urgency. Finally, the evaluation mission noted that certain objectives of the first and second Cancer plans were implemented differently across the territory. It recommends working simultaneously on the leverage to achieve these objectives and those of the current Cancer control plan which have not been achieved. Feedback from the regions, in terms of health as well as research, should also be taken into account.

67 recommendations were issued, with some 14 related to research

1. With regard to basic research programmes and the investigator-driven research programme in biology and basic sciences for cancer research (PLBIO), ensure the external scientific evaluation of research support programmes by Hcéres prior to a new programme and with a view to their possible development.
2. Strengthen support for promising young cancer researchers. Based on an inventory, current and emerging cancer research training needs should be considered in order to strengthen their effectiveness.
3. Consolidate support for SIRICs in order to ensure their full development, the success of translational research, and strengthen the link with clinical research. Their expertise represents an asset for the implementation of the ten-year cancer control strategy.
4. Improve the scientific management and monitoring of PHRC-K and develop an integrated vision of clinical research in oncology.
5. Strengthen long-term follow-up of children who have had cancer.
6. Accurately detail the expected results of reducing inequality.
7. Define actions to reduce inequality on medical and population-based approaches that specifically target the public to be prioritised.
8. Develop comprehensive approaches that take into account the accumulation of risk factors at the individual level and combine different behaviours identified as healthy.
9. Define the main orientations for the next 10 years, and a specific plan for 3 years
10. Plan from the construction of the ten-year cancer control strategy its external evaluation process and a scientific evaluation schedule by Hcéres for research programmes funded by programme 172.

11. External evaluations will be useful for the INCa's International Scientific Advisory Board. Indeed, the law of March 8, 2019 stipulates that they have to provide a mid-term review on the relevance of the ten-year cancer strategy.
12. Define the methods of ex-ante evaluation and scientific monitoring through sharing of experience from emerging so-called high-risk projects; in their different configurations, in a specific scheme in order to anticipate their impact assessment.
13. Pursue a collaborative approach between cancerpoles and organise the necessary tools for information sharing and feedback. The flexibility of the cancerpole model – regional and inter-regional — and on their missions should be considered.
14. The third Cancer control plan continued efforts to support cancer research by relying on a specific and evolving programme of research activities. It has enabled real success, particularly in the development of translational research, which guarantees a continuum from basic research to clinical research. The report underlines the need to continue developing an ambitious cancer research policy in a context of international collaboration and competition, and integrated into the national research system.

Joint Statement by the French National Research Funding Agencies to support Open Science

Under the National Open Science Plan established in July 2018, the French Research Funding Agencies have set up a collaborative network to define a joint approach to support knowledge sharing and dissemination.

Aware of the increasing importance of developing open access to research publications and data, this network of funding agencies⁷ is today highlighting its commitment to open science in accordance with the following values and principles:

- **Promoting open access to scientific publications**

We are asking our grantees to deposit scholarly publications that result from projects that we have funded, directly in an open archive, either in the French national archive HAL or through a local institutional archive. We also recommend preference be given to publishing in open-access journals or books.

- **Fostering the opening of research data under the principle of “as open as possible, as closed as necessary”**

To support management, structuring, access, interoperability and where possible openness and re-use of research data, we are asking our grantees to draw up a Data Management Plan (DMP) as soon as their research project starts, and recommend regular updates, particularly at the end of the project. We also recommend using the DMP template developed by Science Europe, available on the DMP OPIDoR tool.

7. French Agency for Ecological Transition – ADEME; French National Research Agency – ANR; National Food, Environment and Occupational Health Safety Agency – ANSES; French National Cancer Institute – INCa; National AIDS and Viral Hepatitis Research Agency – Inserm/ANRS.

- **Sharing our practices and procedures for evaluating the scientific quality of projects in accordance with** the recommendations of the **San Francisco Declaration on Research Assessment** (or DORA).
- **Informing our grantees and raising their awareness of Open Science by sharing best practice**, in collaboration with the actions of the French Open Science Committee and national higher education and research stakeholders.
- **Opening up data from projects funded by our institutions** in accordance with the Open Government Partnership, which promotes transparency in public affairs and in accordance with the law for a Digital Republic which provides for data generated by the Government to be openly available by default. This initiative will make it possible to provide data to ScanR, the French search engine for exploring the research and innovation landscape and, at an international level, to European infrastructures such as OpenAire.
- **Publishing an annual report on our activities and the different measures taken to promote open science.**

3

● Support for biology, translational and integrated cancer research	148
● Clinical cancer research	150
● Strategic outlook in human and social sciences, epidemiology and public health	152
● Strategic foresight to analyse research and innovation portfolios	155
● European and international commitments	157

Strategic orientations for advancing cancer research

2

2020 will be remembered as a unique year owing to the health crisis triggered by the COVID-19 pandemic. French research as a whole, and cancer research in particular, has been strongly impacted by this crisis. As a consequence of the lockdown, most of the laboratories had to postpone a large part of their projects and programmes.

The French National Cancer Institute has done its best to help the research community, notably by extending the duration of funding.

Despite this unprecedented event, INCa managed to run all the recurrent calls for research proposals on time and provided continuous financial support for research projects based on transparent methods, international evaluation and participation of patient advocates in all the scientific evaluation committees for INCa calls for proposals, in every field of cancer research. Of course, this required significant adaptability of the teams and a reorganisation and renewal of the processes which in some instances could be further exploited in the future.

Among the highlights of this past year in terms of new actions implemented in 2020 and described in detail in the previous sections, one should mention, among others, the launch of the brain tumours PAIR (in partnership with ARC Foundation and the French National Cancer League), and the launch of novel and original programmes in Paediatrics (Consortium; High Risk-High Gain project funding; organisation of an international meeting postponed in 2021). ITMO Cancer-Aviesan also renewed for the second year the MIC programme (contributions to oncology of mathematics and computer science programme), which proved to be successful in 2019.

2020 also saw the launch of competitive calls of proposals for the constitution of research consortiums on the causes and origins of paediatric cancers, on one hand, and on exposure to chlordecone and prostate cancer risk in the French Antilles, on the other. We organised a number of seminars and workshops in Human and Social Sciences and Public Health, in order to promote and disseminate knowledge in these fields and to set up researcher networks to further strengthen the cancer research workforce. Regarding clinical research, mention should be made of the RNAseq roll-out to the 28 molecular

genetic centres and INCa's involvement in the in T²EVOLVE IMI2 European programme ("Accelerating development and improving access to CAR and TCR engineered T cell therapy"), another action in line with the SAB recommendations.

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 2020 and 2021 represent a pivotal period for the institutional planning of French cancer research. It marks the alignment of two important events: the finalisation of the new ten-year cancer control strategy (TYCCS) and that of the multi-year research programming law (MYRPL) of the French Ministry of Research. For the first time for over a decade, this will help boost all areas of the French cancer research further thanks to a significant and unprecedented financial effort from the French government.

New research actions in the four axes of the TYCCS have been proposed and approved by the SAB: improving cancer prevention; limiting the side-effects of treatments and improving the quality of life of those affected by the disease; addressing poor prognosis cancers in adults and children, and ensuring that progress benefits everyone. Obviously, these actions are complementary and would not be sufficient without reinforcing the recurrent core actions supporting cancer research, enabled by a financial effort enshrined in the MYRPL law. This has led INCa, with the help of the SAB recommendations and its partners, ITMO Cancer-Aviesan and charities that support French cancer research, to reconsider its core actions, within the scope of the objectives and performance contract of the Institute with the State (COP), in order to improve them and to link them with the priorities defined by the TYCCS.

With respect to the recurrent core actions, we have undertaken an evaluation of the structuring programmes such as Canceropoles and SIRIC, with the help of external committees, in order to propose a new designation campaign in 2023, considering not only the new landscape and recent developments of French cancer research, but also the priorities of the TYCCS.

We are also working on the design and simplification of some of our recurrent calls, for example by merging them to provide better visibility, thereby complying with SAB recommendations.

In the meantime, an increase in the success rate will apply to all investigator-driven programmes (PLBIO, PRT-K, PHRC-K and PLSHS), as a result of a significant contribution from the government as early as 2021.

Regarding the ten-year cancer control strategy, the year 2020 was used to define the priorities and to prepare the actions to be launched in 2021, with two main considerations:

- 1/ to design new types of actions and programmes that could complement the core actions in the different axes of the TYCCS;
- 2/ to ensure that the numerous actions proposed in the TYCCS will be connected and coordinated: as pointed out by the SAB, the high number of separate measures gives rise to a need for consolidation of overlapping programs to promote efficiencies and avoid siloes.

To meet these concerns, which were shared by the French Ministry of Research, INCa and ITMO Cancer-Aviesan have been engaged in brainstorming sessions internally and with their partners to establish a roadmap and a blueprint of the new programmes. In this context, some of the new 2020 actions mentioned above, which are already part of the ten-year strategy, have been useful experiments for setting up new designs of research support.

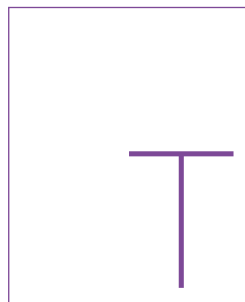
In the following sections, we provide several examples of actions that will be launched by 2021 and beyond, in the four axes of the TYCCS. These include both new calls for proposals of research projects and calls for expressions of interest in the setting up of research consortia or networks.

Within the Prevention and Quality of Life axes, cross-cutting multithematic and multidisciplinary calls for proposals will encompass personalising prevention, supportive care, surgical reconstruction, preservation of fertility and its restoration, etc. In line with the first High Risk-High Gain calls for proposals in paediatric cancers launched this year, we also plan to extend the concept to poor prognosis cancers.

In addition, in order to take a quantum leap in the poor prognosis cancer research area, there is a clear need for strengthening interdisciplinary research, which has been one of the main priorities of 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 2021. Moreover, the first edition of the INCa-ITMO joint call on precancerous lesions launched in 2019 will be renewed in 2021, as we are convinced that this topic is likely to feed all four TYCCS axes, and especially poor prognosis cancers, secondary prevention, and reduction of sequelae.

All these actions will be also considered in the international context, and structuring ones should prove useful to prepare French cancer research for worldwide development and cooperation. Indeed, the French Ten-Year Cancer Control Strategy coincides with the next Europe’s Beating Cancer Plan, displaying many overlapping and converging features, both in health and research areas, with a strong emphasis on prevention and equal access to innovation and personalised treatments.

SUPPORT FOR BIOLOGY, TRANSLATIONAL AND INTEGRATED CANCER RESEARCH



The year 2020 was marked by several major actions regarding basic research in biology, translational and integrated research, including the mid-term evaluation of the SIRIC programme, the decision of the European Community to support a new TRANSCAN ERA-NET (the third one), the launch of three calls for proposals or applications dedicated to paediatric cancer research, the deployment of pilot projects (for example “OSIRIS”), several seminars for monitoring and reporting on current actions (biological and clinical database, the national oncogenetics system), and the funding of the implementation of RNAseq in molecular genetics centres.

Several issues were identified that will need to be considered for future actions:

- The difficulty of attracting new disciplines, outside of biology, for cancer research and especially in paediatrics. Interdisciplinary and complementary approaches could accelerate innovation, overcome methodological barriers, and potentially provide part of the solution to currently unresolved scientific questions. New calls for proposals will be launched to encourage research teams with different scientific skills to work together.
- The need for further support for research that is conceptually disruptive and risky, and that would be ineligible for funding through more “conventional” calls for proposals. INCa was the first research agency in France to launch, in 2020, a “High Risk-High Gain” call for proposals for paediatric cancer research. Considering the results of this first edition and with the aim of renewing this call, brainstorming will be carried out to give applicants a better appreciation of the objectives and expectations of these calls, and to help the committee to better review these projects. Through this trial, such high-risk, high-gain calls for proposals, could represent a valuable blueprint for future research actions of the 10-year cancer control strategy, not only for paediatric cancers, but also, for example, to boost research on poor prognosis cancers of all ages.

- How to evolve and improve structuring actions and programmes such as the SIRIC or Canceropole programmes? This is particularly important since the 10-year cancer control strategy aims to designate new centres, structures or networks of excellence on prevention, screening and poor prognosis cancer research, which will need to be linked with or rely on existing features or programmes. In partnership with the stakeholders concerned, reflections will be carried out in 2021 to design new models and define the specifications for future calls for applications for the new waves of designations planned for 2022.
- How to optimise the identification and follow-up of people who have a hereditary predisposition to cancer? It appears necessary to adapt the national oncogenetics system in order to improve control of the time-frame for obtaining appointments for genetic counselling and analysis, and to offer innovative treatments to patients with constitutional genetic alterations. It is therefore necessary to take stock of the situation, and a thorough evaluation of the system is needed in order to measure its efficiency and to propose an organisation more suited to recent changes in the course of oncogenetics and new treatments.

In view of the results already achieved and in a context of strong momentum both with the increase in funding allocated for basic research under the new research programming law (which will allow an increase in selection rates for calls for proposals), and the setting up of the first actions of the 10-year strategy in 2021, we will be able to both valorise previous actions and build new actions to best meet future goals.

CLINICAL CANCER RESEARCH



linical cancer research will represent an essential pillar of the ten-year cancer control strategy starting in 2021. In addition to strengthening the recurrent core actions, the clinical research department has started to launch new specific actions.

In order to address the global action **Developing research to reduce sequelae and improve patients' quality of life**, a new call for proposals will be launched for thematic projects on supportive care, surgical reconstruction, preservation of fertility and its restoration, quality of life. The prioritisation of this action is in line with SAB recommendations. In order to promote multidisciplinary, projects must be carried out by 2 teams from 2 different disciplines from the fields of fundamental, clinical research or in human and social sciences-epidemiology-public health, with the aim of this programme enabling the emergence of research projects of excellence in topics that may be under-represented in our usual call for proposals.

As early as 2021, we also expect to be able to foster new projects specifically addressing therapeutic de-escalation questions, through the PHRC-K call thanks to funds secured from the French Ministry of Health, which was also a recommendation of the SAB.

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

- **Encourage manufacturers to invest in the field of poor prognosis cancers**

A framework for discussions with manufacturers will be set up, in compliance with the ethical rules of the French National Cancer Institute, so that they are encouraged to invest in the field of poor prognosis cancers and they can in particular make molecules available free of charge. The measure should benefit all of the actions carried out by INCa around access to therapeutic innovations, including its support for innovative early-phase clinical trial programmes.

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

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

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

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

Serving the action **Ensuring that vulnerable populations are included in the conduct of clinical trials**, a bibliographic report will be drawn up in order to identify the barriers and leverages to inclusion in clinical trials. Based on this report, a reflection on driving research in sociology will be carried out.

Finally, within the framework of the transversal axis and the global action **Combating loss of chance by paying specific attention to the continuity of actions to fight cancer in times of crisis**, a REX (return of operating experience) will be organised to identify the barriers and leverages for continuing clinical trials during the COVID pandemic. Indeed, whether in respect of on-going trials or the setting up of new trials, the continuation of clinical research or its disruption for all or some is considered in coordination with care provision maintenance. The monitoring of subjects enrolled in trials is the subject of special provisions to limit loss of chance, including the continuation of the administration of the trial treatment through adverse event reporting.

In a more global and medium-term perspective, we are currently carrying out an analysis with all stakeholders, including the national *Plan France Médecine Génomique 2025*, to renew the AcSé programme and extend the AcSé e-SMART model to adult cancers, especially of poor prognosis.

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



Given that the ten-year cancer control strategy is largely focused on prevention, it will actively rely on contributions from research in Human and Social Sciences (HSS) and Public Health. In the coming years, as a continuation of the work previously undertaken, INCa will mainly use three tools to develop research in this field: research funding; promoting and disseminating knowledge; setting up researcher networks; evaluating funding schemes, and producing HSS data on cancer.

Regarding research funding, the HSS-E-PH department will continue the chlordecone research programme, for which the research consortium is set to begin its research in Q1, with programme validation scheduled for Q4. The call for applications for HSS-E-PH PhD grants and for Psychoactive Substances and Addictions will be renewed. The research programme for junior researchers in the field of tobacco and alcohol trialled⁸ in 2020 was a resounding success and will be offered again this year. 2021 is a pivotal year for two of the three INCa recurrent calls for proposals, set out above⁹. In fact, this is the final year that the HSS-E-PH and PHIR calls for proposals will be held in the format known for over 10 years: at the end of H1, a project will be led to merge these two programmes into one, to achieve greater visibility and cohesion, and also capitalise on the scientific evaluation processes. The specific aspects of PHIR will be bolstered with the creation of a section targeting this theme in the new format of this call for proposals. Three actions from the ten-year cancer control strategy will be developed in the context of this merging process:

1. action IV.3.6 (HSS and intervention research on determinants and innovative patient support);
2. action IV.2.2 (HSS & PHIR research on care and support for children and AYAs);
3. action III.1.5 (tertiary prevention research for cancers of poor prognosis) of the ten-year strategy.

These actions will be developed in a targeted section of this new CFP. Finally, the HSS-E-PH department is steering the implementation of action I.1.1. of the

8. The missing link between the INCa-IReSP call for proposals and call for PhD applications, the aim of this project is to offer a call for expressions of interest, with a view to developing the scientific community in relation to tobacco and alcohol, by encouraging junior researchers to invest in these topics. This innovative scheme includes a pre-selection phase, a discussion seminar involving international experts and interviews to select 8 candidates.

9. These are 1- the free call for proposals in Human and Social Sciences, Epidemiology and Public Health; 2- call for proposals in the field of population health intervention research; 3- combatting psychoactive substance use and addiction.

ten-year strategy. This action is aimed at bolstering and structuring primary cancer prevention research. It particularly involves boosting the appeal of this field for junior researchers, encouraging multidisciplinary, supporting the production and dissemination of new knowledge, and application for the benefit of the population. To develop this action with a budget of €3.2M over a 4-year period, a review of existing schemes internationally and within France will be conducted and a steering committee will be enlisted to examine the scope and type of scheme to focus on, before a call for applications is drafted by INCa.

Research chairs offer a valuable framework for innovation for developing HSS and PH research on cancer prevention. This scheme above all makes it possible to develop teams for relatively unexplored or emerging themes, and develop collaborations to sustain them over time. In addition, in its new format, this scheme will benefit from support from INCa, over a 5-year period, financial contribution from the partners and an agreement in principle between the academic partner structures to create a position in this area after the 5 years have elapsed. In 2021, the Patient Empowerment Chair will be renewed (University of Marseille), a “Psycho-oncology innovations and intervention research” Chair (University of Lille) will be set up, along with another on tobacco and cancers.

Developing discussions between researchers and providing spaces for disseminating knowledge are key forms of leverage for structuring research in human and social sciences, epidemiology, and public health. Regarding PHIR development, we will organise a seminar in H1. Developed for and with researchers, this webinar will include 2 phases. The first phase will relate to projects supported by INCa in 2020, and the second to the issue of participatory methods and the role of beneficiaries in research. In line with the ten-year strategy, a seminar on human and social sciences and public health in the field of tertiary prevention will be organised for specific cohorts (AYA, poor prognosis, vulnerable individuals). Its objectives will be to present research supported within the framework of the Institute’s calls for research proposals, prepare a review, and suggest prospects. The PhD network initiated by INCa last year will be developed. In the field of tobacco, which was highlighted as a priority among the SAB recommendations, INCa-NCI will facilitate a workshop on “tobacco cessation interventions and tobacco use 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. This action has been postponed due to the health crisis. The bi-annual PHIR conference is a key event, popular among the scientific community. It will take place at the end of the year online and in-person on the following theme: “support schemes for those affected by cancer and their relatives: input from population health intervention research”. The objective of this conference prepared with researchers, practitioners and patients is to review the intervention research and knowledge available to date on support schemes for patients and their relatives, promote discussions on practices, and identify the challenges to be tackled in developing this field of PHIR. Researchers, decision-makers, civil society, contributors, caregivers, patients, former patients, family member carers and expert patients will share practical research and ideas through oral paper and poster presentations selected under the aegis of a scientific committee.

Finally, in partnership with CRUK, DKFZ and Anses, work will particularly be carried out on organising the Vaping conference. The objective of this conference will be to review the status of on-going research on vape user pathways and the impact of vaping on health.

Moreover, in order to stimulate a drive for research in human and social sciences and public health in the “inter-canceropole” and “inter-SIRIC” working groups, an annual event will once again be organised. Also, in conjunction with the canceropoles, a new format will be trialled to set up a space for discussion between researchers and the HSS-E-PH-IR team on support schemes: Research Cafés. Lasting 90 minutes, the purpose of these virtual events is to present support schemes (for example Chairs, junior researcher CFA, the new merged CFP), and to provide an opportunity for discussion between researchers and INCa.

Regarding the issue of research support scheme evaluation, it would seem necessary to initiate an in-depth study about disciplines, issues, research teams, and their CSO classifications. Following on from the preparatory work conducted in 2020, we will launch an evaluation programme in 2021, focused on the projects funded in the call for research proposals in human and social sciences. This work will enlist an international scientific committee to fine-tune the research questions in terms of identifying the knowledge produced through this call for proposals.

Finally, in 2021, we will complete our validation of the 2015 Cancer Barometer in the area of screening, and we will commence our analysis of the data from the 4th edition of the Cancer Barometer. This population-based survey carried out every five years is one of the few national studies conducted to investigate the French population’s perceptions of cancer risk factors. The department steered the scientific drafting of the questionnaire in concert with researchers, stakeholders from the field, and user representatives. The survey conducted in conjunction with Santé Publique France will take place during Q2 and the analysis of the results will commence in September.

STRATEGIC FORESIGHT TO ANALYSE RESEARCH AND INNOVATION PORTFOLIOS

S

Scientific discoveries with potentially large impacts on science and technological innovations are of particular importance to research funding agencies. We wish to capitalise on the future impact studies that will be carried out over the next few years to implement a foresight programme. In fact, cancer research lends itself particularly well to prospective exercises since it deals with long-term issues.

Foresight is the discipline of exploring, anticipating, and shaping the future. This discipline contributes to the identification and better anticipation of trends, disruptions, weak signals or emerging topics likely to represent key issues in the future. Strategic foresight sheds light on future science fronts.

To achieve these ambitions, the Institute will develop prospective analyses. These prospective analyses will anticipate new research programming needs. Predictive approaches represent an essential step in the acquisition of knowledge. They are based on big data, interdisciplinarity, digital transition, artificial intelligence, and open science.

Finally, these predictive approaches prompt new questions considering the evolution of scientific, technological, social, economic contexts, etc.

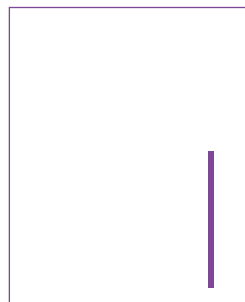
In brief, the strategic foresight programme will help us to guide our future research programmes by allowing us to

- understand how past developments have led to the current situation;
- understand the transformations in progress;
- debate future challenges;
- explore alternative possible futures;
- align science fronts and societal demand;
- involve key stakeholders;
- define adequate monitoring indicators, so that actions can be adapted along the way.

Benchmarking will be carried out to identify best practices among the health agencies that have implemented this kind of approach.

As a starting point, a scoping study could be considered to provide an overview of relevant trends, drivers, developments and challenges influencing our understanding of cancer. We also plan to be supported by those who have developed expertise in these fields.

EUROPEAN AND INTERNATIONAL COMMITMENTS



Internationally, the rise in the incidence of non- or indirectly - communicable diseases is one of the challenges for global health. The international community must face the challenges associated with this global epidemiological transition with many impacts to be expected on health systems and populations in all countries of the world, in terms of the organisation of care and the development of research, access to medicines.

Pursuing this objective, INCa is initiating in 2021 a consultation of its main partners (10 countries, the UICC, the IARC, and the European Commission) with a view to strengthening international coordination in cancer control. INCa will also actively contribute to the development of the activities of Europe's Beating Cancer Plan, to their implementation and monitoring, in particular with a view to ensuring synergistic action and complementarity with the French ten-year strategy. These two forms of leverage will be explored through the following axes of intervention:

- **Strengthen international regulations** in order to protect the population better and initiate common actions at a European level. Regulations will be strengthened, on the basis of scientific data, in order to protect the population against environmental and infectious risk factors in particular. Joint actions could be considered to reduce the population's exposure to environmental risk factors.
- **Networks between research and care infrastructures**, in particular for rare, paediatric and poor prognosis cancers, will be strengthened in order to meet the challenges of critical masses through multicentre clinical trials.
- **Carry out and share benchmarks to identify innovative practices and thus encourage progress.** The achievement of systematic benchmarks will be supported, as leverage for progress, with a view to identifying innovative practices in the various countries in terms of prevention, screening, care, research, post-cancer, and quality of life. The probative nature of these practices will be assessed in order to consider their transferability, if necessary.

- **Invest in international data sharing for the benefit of the patient.** Investment in international data sharing is essential, at the service of knowledge and for the benefit of the patient. Data sharing should make it possible to accelerate research and ensure quality of care, especially for complex cases.
- **Develop international consortia in promising research fields.** The development of multidisciplinary international consortia in promising or priority fields of research will make it possible to address the challenges of the complexity of cancer biology (oncogenesis, aggressiveness, metastatic process, resistance, cellular immunotherapy, etc.), emerging risk factors, or even cancers with a poor prognosis (precancer, risk factors for specific cancers, new tests and screening opportunities, innovative treatments).

4

Appendices

- Common scientific outline **161**
- INCa's calls for proposals: scientific and operational management **163**

COMMON SCIENTIFIC OUTLINE



Established in 2000, the International Cancer Research Partnership (ICRP) is a unique alliance of cancer organisations, working together to enhance global collaboration and strategic coordination of cancer research. It includes 150 worldwide organisations from Australia, Canada, France, Japan, the Netherlands, United Kingdom, and the United States. INCa joined this partnership in 2009.



This consortium aims to improve access to information about cancer research being conducted, explore opportunities for cooperation between funding agencies, and enable our members to maximise the impact of their independent efforts.

ICRP organisations share funding information in a common format (known as the Common Scientific Outline or CSO) to facilitate pooling data and evaluating data across organisations.

The Common Scientific Outline, or CSO, is a classification system organised around seven broad areas of scientific interest in cancer research. The development of the CSO is laying a framework to improve coordination among research organisations, making it possible to compare and contrast the research portfolios of public, non-profit, and governmental research agencies. This classification is subdivided in 7 categories:

- Biology
- Aetiology (causes of cancer)
- Prevention
- Early Detection, Diagnosis, and Prognosis
- Treatment
- Cancer Control, Survivorship, and Outcomes Research
- Scientific Model Systems

As a member of the ICRP consortium, INCa and its partners use this classification. The types of research projects funded by INCa, the French Ministry of Health (DGOS) and Inserm for ITMO Cancer-Aviesan that are presented in this report are based on this CSO classification.

THE DIFFERENT CSO CATEGORIES INCLUDE:

● CSO 1 Biology

- 1.1 Normal functioning
- 1.2 Cancer initiation: alterations in chromosomes
- 1.3 Cancer initiation: oncogenes and tumour suppressor genes
- 1.4 Cancer progression and metastasis
- 1.5 Resources and infrastructure

● CSO 2 Aetiology

- 2.1 Exogenous factors in the origin and cause of cancer
- 2.2 Endogenous factors in the origin and cause of cancer
- 2.3 Interactions of genes and/or genetic polymorphisms with exogenous and/or endogenous factors
- 2.4 Resources and infrastructure related to aetiology

● CSO 3 Prevention

- 3.1 Interventions to prevent cancer: personal behaviours that affect cancer risk
- 3.2 Nutritional science in cancer prevention
- 3.3 Chemoprevention
- 3.4 Vaccines
- 3.5 Complementary and alternative prevention approaches
- 3.6 Resources and infrastructure related to prevention

● CSO 4 Early Detection, Diagnosis, and Prognosis

- 4.1 Technology development and/or marker discovery
- 4.2 Technology and/or marker evaluation with respect to fundamental parameters of method
- 4.3 Technology and/or marker testing in a clinical setting
- 4.4 Resources and infrastructure related to detection, diagnosis, or prognosis

● CSO 5 Treatment

- 5.1 Localised therapies - Discovery and development
- 5.2 Localised therapies - Clinical applications
- 5.3 Systemic therapies - Discovery and development
- 5.4 Systemic therapies - Clinical applications
- 5.5 Combinations of localised and systemic therapies
- 5.6 Complementary and alternative treatment approaches
- 5.7 Resources and infrastructure related to treatment

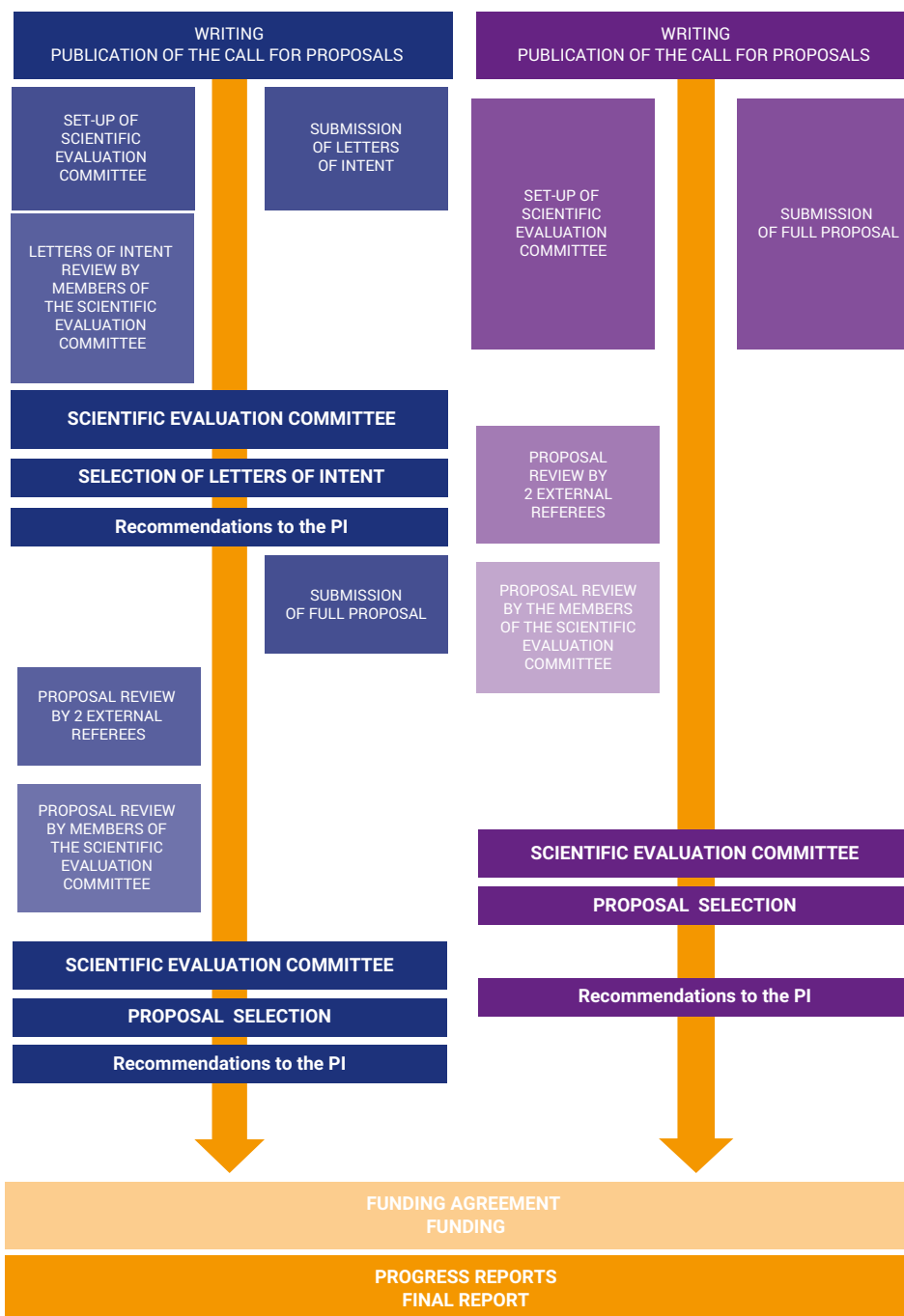
● CSO 6 Cancer Control, Survivorship, and Outcomes Research

- 6.1 Patient care and survivorship issues
- 6.2 Surveillance
- 6.3 Behaviour
- 6.4 Cost analyses and health care delivery
- 6.5 Education and communication
- 6.6 End-of-life care
- 6.7 Ethics and confidentiality in cancer research
- 6.8 Complementary and alternative approaches for supportive care of patients and survivors
- 6.9 Resources and Infrastructure related to cancer control, survivorship, and outcomes research

● CSO 7 Scientific Model Systems

- 7.1 Development and characterisation of model systems
- 7.2 Application of model systems
- 7.3 Resources and Infrastructure related to scientific model systems

INCA'S CALLS FOR PROPOSALS: SCIENTIFIC AND OPERATIONAL MANAGEMENT



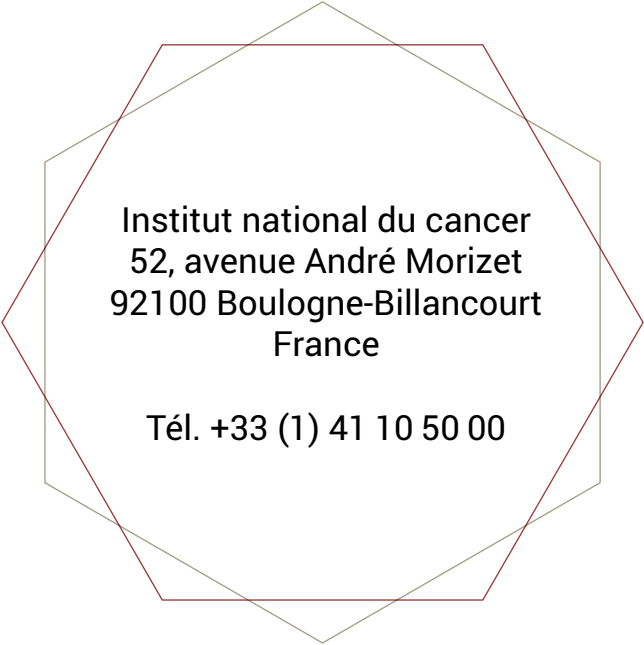


52, avenue André Morizet
92100 Boulogne-Billancourt
France

Tel. +33 (1) 41 10 50 00
diffusion@institutcancer.fr

Published by the French National Cancer Institute
All rights reserved – Siren 185 512 777
Conception : INCa
Realised by Desk (www.desk53.com.fr)
ISBN : 978-2-37219-792-2
ISBN net : 978-2-37219-793-9

DEPÔT LÉGAL NOVEMBRE 2021



Institut national du cancer
52, avenue André Morizet
92100 Boulogne-Billancourt
France

Tél. +33 (1) 41 10 50 00

For more information e-cancer.fr