SCIENTIFIC REPORT

2018

ACTIONS FOR CANCER RESEARCH

e-cancer.fr

INSTITUT NATIONAL DU CANCER

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

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e-cancer.fr

INTRODUCTION

ACTIONS FOR CANCER RESEARCH

INSTITUT NATIONAL DU CANCER

SCIENTIFIC REPORT 2018

In 2018, concrete and major progress was achieved in all areas of cancer control: prevention, screening, care, quality of life and research.

THE FRENCH NATIONAL CANCER INSTITUTE pursued its efforts to make innovation accessible to as many people as possible. This Scientific Report outlines all research initiatives in oncology, detailing the resources deployed and implemented. This report is a key element used by Scientific Advisory Board members to review the actions undertaken and subsequently advise and guide the Institute during its structuring processes and its initiatives. The structure of this document is intended to provide both a better reflection of the Scientific Advisory Board's advices and a focus placed on the recommendations of the 2014-2019 Cancer Control Plan, which will enter its final year. The French National Cancer Institute is without doubt indebted to all of the participating members, and we were delighted to welcome new members this year.

ALONGSIDE RESEARCH ACTIONS AND INITIATIVES, this year, we have finalised the regionalisation of screening schemes, and contributed to the publication of the decree authorising the extension of cervical cancer screening. In order to improve the quality, safety and relevance of care, ambitious work to modernise the cancer treatment activity authorisation scheme was initiated in 2018. The French National Cancer Institute has proposed to introduce additional quality criteria, in particular to facilitate access to innovation, to better define technical platforms and grading of care, and to promote cooperation between stakeholders. Nearly 900 health facilities are until now authorised to treat cancer.

EVEN THOUGH OUR PRIORITY IS TO CURE, quality of life is a major endpoint for patients and is part of their recovery process. Therefore, it is key to support patients in all aspects of the disease, whether these are psychological, economic, and social. In this context, the right to be forgotten has been a major step forward and the involvement of the French National Cancer Institute has enabled an extension of this scheme to other long-term remission patients suffering from certain leukaemias, kidney and prostate cancers.

THESE ADVANCES ARE THE FRUIT of combined efforts and are intended to be enduring. We are committed to continuing them in 2019 and beyond, with all of our partners.

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

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ACTIONS FOR CANCER RESEARCH

INSTITUT NATIONAL DU CANCER

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In 2018, INCa launched and operated

13 calls

for research proposals

1,019 projects submitted

146 projects funded

826 reviewers involved in the scientific review of the programmes including

456 international reviewers

ITMO Cancer-Aviesan launched and operated

5 calls for research proposals:

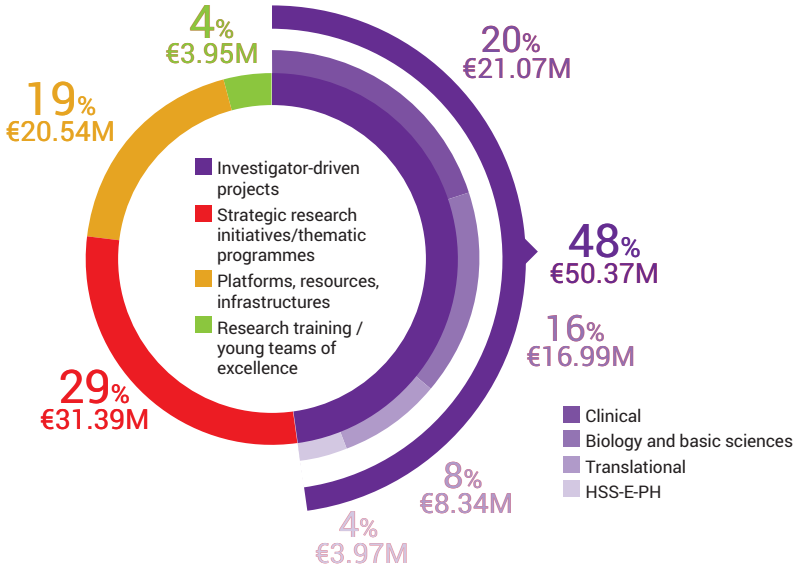
358 projects submitted

80 projects funded

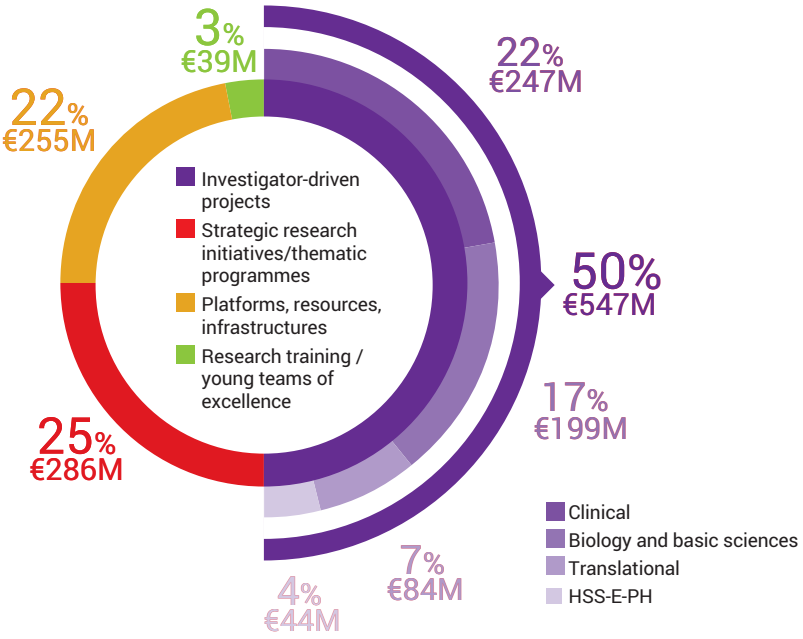
570 reviewers involved in the scientific review of the programmes including

405 international reviewers

2018 multi-year cancer funding by programme type (INCa, DGOS and ITMO Cancer-Aviesan): €106.26M invested



2007-2018 multi-year cancer funding by programme type (INCa, DGOS and ITMO Cancer-Aviesan): €1.15Bn invested



Total investments over the 2007-2018 period:

€454M
in biology and basic sciences

€260M
in translational and integrated cancer research

€318M
in clinical research

€119M
in research in human and social sciences, epidemiology and public health

1

The international scientific advisory board

This 13th 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 2018 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. Appendix 1 summarises previous key recommendations and describes the actions conducted to implement novel initiatives and/or to reinforce the major existing programmes.

THE INTERNATIONAL SCIENTIFIC ADVISORY BOARD MEMBERS

The members of the Scientific Advisory Board are:

- **Dr. Geneviève Almouzni,** PhD, Institut Curie, Paris, France
- **Prof. Cécile Badoual**, MD, PhD, Hôpital Européen Georges Pompidou, Paris, France
- **Dr. Jean-Pierre Bizzari**, MD, Celgene, Summit, USA
- **Prof. Cédric Blanpain,** MD, PhD, Université Libre de Bruxelles, Brussels, Belgium
- **Ms. Dominique David**, Founder and Chairperson of the Association pour la recherche sur les tumeurs cérébrales, Aix en Provence, France
- **Prof. Johann de Bono**, MD, PhD, The Institute of Cancer Research and the Royal Marsden, London, United-Kingdom
- **Prof. Olivier Delattre**, MD, PhD, Institut Curie, Paris, France
- **Prof. Anne Eichmann,** PhD, Yale School of medicine, New Haven, USA
- **Dr. Elizabeth A. Eisenhauer,** MD, Queen's University, Kingston, Canada
- **Prof. Yann Gauduel,** PhD, Ecole Polytechnique - ENS Techniques Avancées, Palaiseau, France
- **Dr. Ivo G. Gut**, PhD, Centro nacional de analisis genomica (CNAG), Barcelona, Spain
- **Dr. Mette Kalager**, MD, PhD, Harvard T.H. Chan School of Public Health, Boston, USA
- **Prof. Catherine Lacombe**, MD, PhD, Institut Cochin, Paris, France
- **Ms. Estelle Lecointe-Artzner,** Founder and Chairperson of the Association Info Sarcomes, Rennes, France
- **Dr. Douglas R. Lowy**, MD, NCI Acting Director, Bethesda, USA
- **Prof. Marc-André Mahé**, MD, PhD, General Director, Centre François Baclesse, Caen, France
- **Dr. Bernard Malissen**, PhD, Centre d'Immunologie de Marseille-Luminy, Marseille, France
- **Prof. Dame Theresa Marteau**, PhD, University of Cambridge, Cambridge, United-Kingdom
- **Dr. Patrick Mehlen,** PhD, Centre de recherche en cancérologie de Lyon, Lyon, France
- **Prof. Stefan Pfister**, MD, German Cancer Research Centre (DKFZ), Heidelberg, Germany
- **Prof. Louise POTVIN**, PhD, Institut de recherche en santé publique de l'Université de Montréal, Université de Montréal, Montréal, Canada
- **Prof. Gérard Socié**, MD, PhD, Hôpital Saint Louis, Paris, France
- **Dr. Naomi Taylor**, MD, PhD, Institut de Génétique Moléculaire de Montpellier, Montpellier, France
- **Prof. Robert A. Weinberg,** PhD, Massachusetts Institute of Technology (MIT), Cambridge, USA
- **Prof. Laurence Zitvogel**, MD, PhD, Gustave Roussy, Villejuif, France

2018 RECOMMENDATIONS

Following their meeting in September 2018, the members of the International Scientific Advisory Board issued the following recommendations.

1 The SAB thanks the French National Cancer Institute for the excellent Scientific report for 2017 and appreciates its new format and the clarity of its content. The comparison of 2007 vs 2017 is appreciated and underscores the progress achieved in the last ten years.

2 Some of the key initiatives such as PLBIO, CLIP², SIRIC have been instrumental and should pursued for the next five years.

3 The SAB appreciates the work undertaken on starting to implement the 2017 recommendations. The presentations of the SAB working groups are appreciated.

4 The scientific report should include a comprehensive analysis on specific themes: for example, intervention research nationwide.

5 The SAB strongly encourages links with behavioural science expertise at NCI and coordinating with other relevant agencies in France to achieve this.

6 In setting new strategic directions, INCa should consider the following priority areas:

- **a.** improvement in outcomes of high mortality cancers or cancers with poor outcomes compared to other countries;
- **b.** building on the unique strengths of the French cancer research community and infrastructures (e.g. BCB data);
- **c.** robust evaluation of the anticipation of emerging technologies (e.g. NGS, proton therapy, cancer microenvironment exploration);
- **d.** increasing the importance of holistic integration of multi-omic, immune, imaging, and other cancer/host markers in understanding cancer biology and driving treatment development;
- **e.** exploiting previous efforts and cohorts coordinated by UNICANCER/INCa bringing together genomics, immunometrics and clinical data: specifically to analyse the power of NGS in the stratification of patients for future pilot trials.

7 The SAB was concerned that France's strong cancer clinical trial community may be under threat. This requires further investigation and actions.

8 The SAB would welcome the opportunity to review the next draft cancer strategy and contribute to its final version.

2

2018 cancer research activity report

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

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

Every year, INCa issues investigator-driven calls for proposals to the scientific community in the 4 main research areas: cancer biology, translational research, clinical research and research in human and social sciences, epidemiology and public health. INCa has renewed the call for proposals for population health intervention research on reducing cancer-related inequalities and initiated two specific calls on Integrated Research Action Programme (PAIR programme) in paediatrics and pancreatic cancer. The Cancer control plans focus on specific research priorities, in collaboration with institutional partners, which are mostly planned by ITMO Cancer-Aviesan through multiple calls for proposals.

This section presents a detailed review of the research programmes conducted in 2018, 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 new prospects for advances in treatment, inhibition of resistance mechanisms and the development of tools through the establishment of projects involving physics, mathematics or information technology.

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

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

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

THE PROGRAMME IN 2018

In 2018, 32 projects were selected out of the 374 proposals submitted for a total amount of €16.99M. Importantly, the number of submitted applications represented a 25.5% increase compared to 2017, thus impacting the selection rate (8.6%) (Table 1).

The majority of the funded projects (85.9%,) aim to study the biological mechanisms of cell transformation and disease progression, according to the international CSO classification[1] (CSO1), and 10.9% study either molecular mechanisms of response and resistance to treatments, or identification of new therapeutic targets (CSO 5). One project aims to identify the causes or origins of cancer (genetic, environmental, and lifestyle, and the interactions between these factors) (CSO 2).

2018:
32 projects
funded out of the 374 proposals submitted for a total budget of
€16.99M

1. The detailed description of the CSO classification is presented in Appendix 2.

TABLE 1
FEATURES OF THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2018

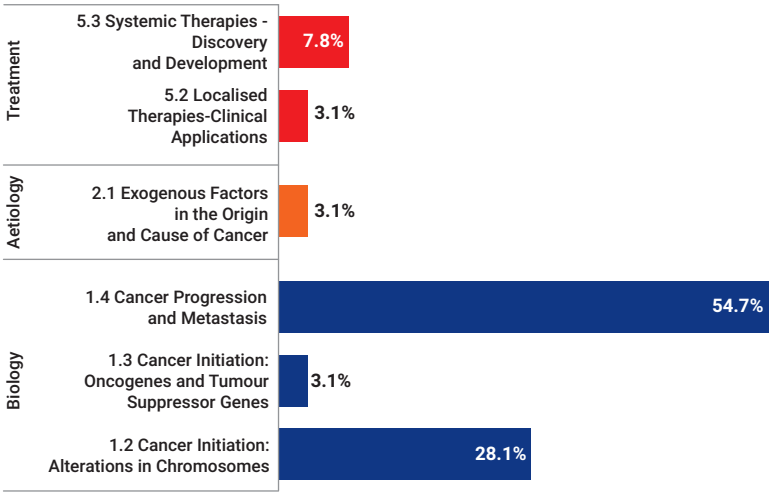
Objectives	To acquire new knowledge and develop new tools to create new therapeutic approaches. Open to all areas of basic research and to scientific disciplines involved in tumour biology research, this call has been launched to: • Enable the achievement of original projects; • Strengthen multidisciplinary collaborations; • Develop research in emerging areas.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€16.99M
Proposals submitted	374
Projects selected	32
Selection rate	8.6%

Figure 1 presents a detailed analysis of the funded projects and shows that nearly 55% 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 has a greater representation in 2018 compared to 2017 (45%) which was already higher than 2016 (21.1%). This trend reflects the increased interest of these research fields in cancer biology.

Projects studying the mechanisms of DNA repair and the regulation of gene expression (epigenetic regulation or transcription, CSO 1.2) or oncogenes, tumour suppressor genes and signalling pathways involved in cell proliferation and cell transformation (CSO 1.3) represented 31.2% of the funded projects.

Besides the CSO classification, the analysis of the main themes addressed by the selected projects shows that 25% of these aim to study the role of the immune system in cancer initiation and development:
- Immune microenvironment;
- Escape mechanisms from immune surveillance;
- Innate immune recognition of cancer cells;
- Role of microbiome;
- Role of inflammation in tumorigenesis.

FIGURE 1
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2018



THE PROGRAMME OVER THE 2007-2018 PERIOD

Since 2007, 407 projects have been selected out of the 2,933 proposals submitted to the Biology and basic sciences for cancer research programme, for a total budget of €198.79M (Table 2).

TABLE 2

TRENDS IN SELECTION AND FUNDING OF THE RESEARCH PROGRAMME IN BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH OVER THE 2007-2018 PERIOD

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	TOTAL
Funding (in €M)	14.46	13.52	13.56	20.80	14.44	15.89	15.07	19.97	17.21	20.26	16.65	16.99	**198.79**
Proposals submitted	106	145	342	241	203	191	208	284	267	281	291	374	**2,933**
Projects selected	40	30	27	43	30	32	33	38	34	38	30	32	**407**
Selection rate (%)	37.70	20.70	7.90	17.80	14.78	16.75	15.80	13.40	12.73	13.50	10.30	8.6	**13.9**

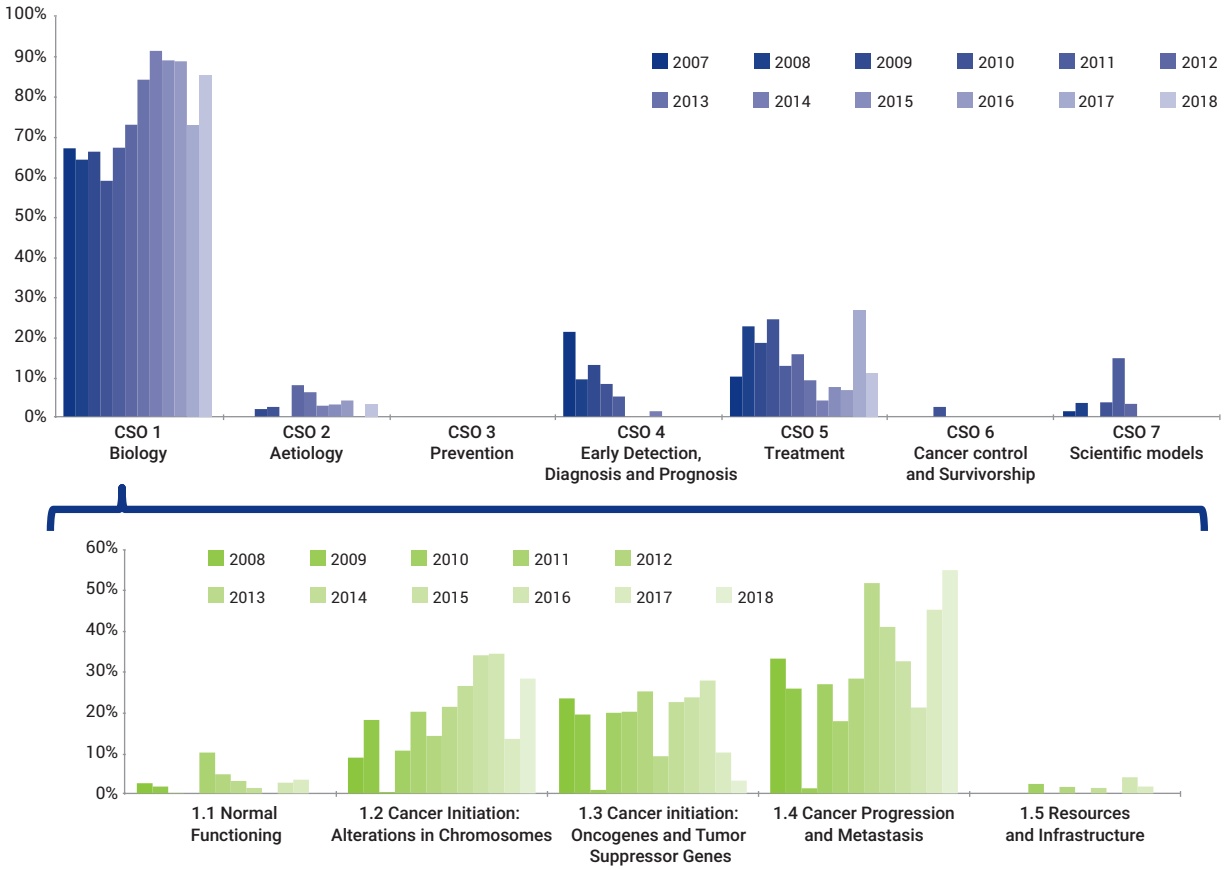
The number of letters of intent has been increasing steadily since 2011, reaching a peak of 374 applications submitted in 2018. This programme is, more than ever, the Institute's most attractive programme in terms of the number of applications. This observation highlights the importance of PLBIO for cancer-related basic science support. 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.

The analysis of the projects funded over the 2007-2018 period according to the CSO classification shows that the projects mainly focus on the biological mechanisms of cell transformation and disease progression. This trend has been quite stable over the years (Figure 2).

The majority of these projects study cancer progression and metastasis, especially the regulation of processes in tumour invasion, metastasis, angiogenesis and immune microenvironment (Figure 2, bottom panel).

FIGURE 2

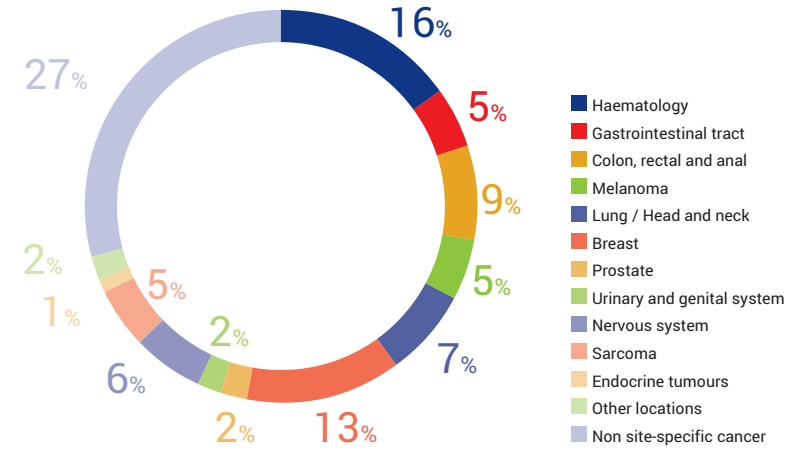
DISTRIBUTION OF SELECTED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2018 PERIOD



Nearly 30% of the projects are non-specific to a tumour type, highlighting the fact that the projects are more focused on general mechanisms of cancer initiation, development, and/or progression together with research on molecular targets and therapies that could be applied to several pathologies. Projects studying haematological malignancies (16%), breast cancer (13%) or colorectal cancer (9%) are also well represented (Figure 3).

FIGURE 3

DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO CANCER SITES STUDIED FOR THE BIOLOGY AND BASIC SCIENCES PROGRAMME OVER THE 2007-2018 PERIOD



Since 2007, projects addressing the role of the immune system in cancer initiation and development have represented approximately 20% of the total funded projects, for an overall amount of €41M. Figure 4 highlights that project funding in this research field has increased over the years. Indeed, immunology projects represented 18% of the funded projects in 2007, as opposed to 25% in 2018. Additionally, the average budget has progressed from €382,857/project to €572,503/project in 2018.

The detailed analysis of these projects shows that the most represented fields are: study of escape mechanisms of cancer cells from immune surveillance (20%), and study of the immune microenvironment (19%) (Figure 5). Considering the profile of the funded projects on immunology in 2018 (31% on immune microenvironment, and 25% on cancer cell immune escape), these fields remain of great interest for cancer research.

FIGURE 4

TRENDS IN FUNDING OF PROJECTS STUDYING THE ROLE OF THE IMMUNE SYSTEM IN CANCER INITIATION AND DEVELOPMENT

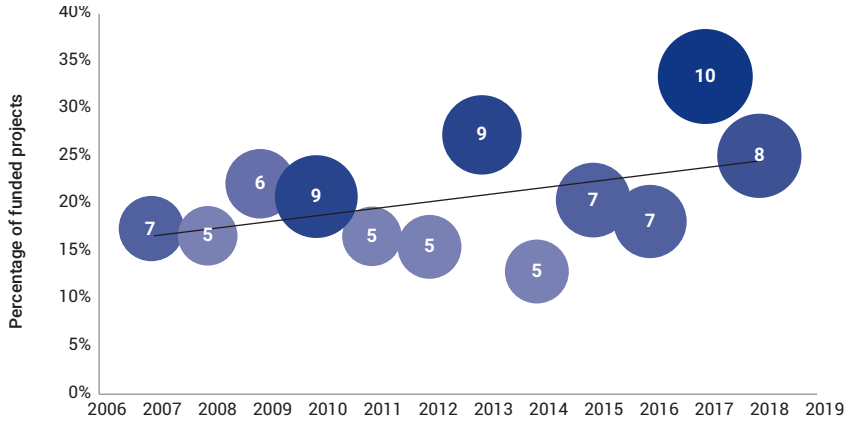
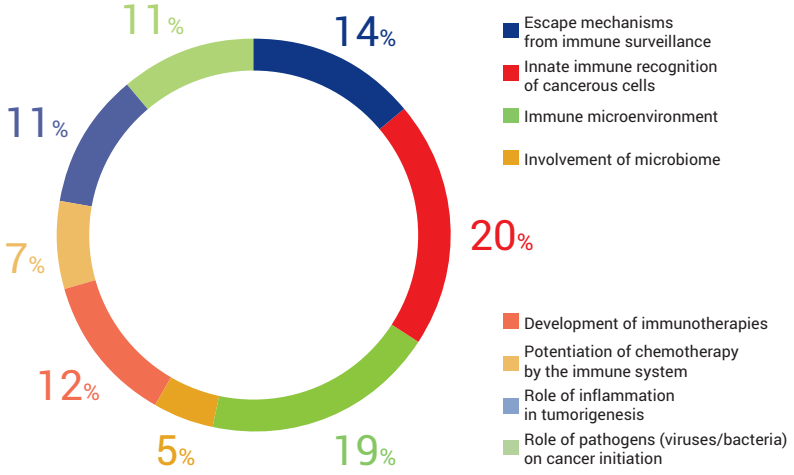


FIGURE 5

DETAILED ANALYSIS OF PROJECTS STUDYING THE ROLE OF THE IMMUNE SYSTEM IN CANCER INITIATION AND PROGRESSION OVER THE 2007-2018 PERIOD



Launch of preneoplasia call for proposals

Through strategic discussions, INCa and ITMO Cancer-Aviesan raised the importance of early diagnosis to cure a greater number of patients and the increasing interest of preneoplasia as a model in studying cancer initiation and cancer prevention. A task force was set up in March 2018 by INCa and ITMO Cancer-Aviesan to define the possibilities in developing such collaborative research in France.The Task Force's aim is to create a research area on preneoplastic biological processes and to consider ways of developing precision preventive medicine. Its action is targeted at scientific facilitation of research on "preneoplasia" in France and abroad.

Following meetings of this task force, a seminar was held on November 2018. This led to discussions on this topic and addressed different questions such as the definition of preneoplasia, the genesis of prelesions and their oncogenic mechanisms, as well as the different techniques for their study.
To boost this research field, INCa and ITMO Cancer-Aviesan plan to launch a call for proposals in early 2019. The general objective will be the characterisation, in space and time, on a molecular, cellular, and tissue level, of lesions with malignant potential. The aim is to contribute to a better understanding of their outcome (transition from pre-malignant to malignant state, stabilisation, regression) by characterising the underlying mechanisms, the formation sequence and the factors involved in risk emergence and progression, so as to identify targets to intercept and prevent the development of cancer and stratify lesions based on the risk of progression.

The International cancer genome consortium

The international cancer genome consortium was launched in 2007 to bring together researchers worldwide to comprehensively analyse the genomic, transcriptomic and epigenomic changes in 50 different cancer types or subtypes that are of clinical and societal importance across the globe and make the data available to the entire research community, to accelerate research into the causes and control of cancer.
Its initial aim was to define the genomes of 25,000 untreated primary cancers (the 25K Project).
The second ICGC project, the Pancancer Analysis of Whole Genomes (PCAWG), launched in 2013, is an international collaboration aimed at identifying common patterns of mutation in more than 2,800 cancer whole genomes.
The latest initiative, ICGC-ARGO (Accelerating Research in Genomic Oncology), will link genomic data that have already been amassed, new genomic data generated through the 10 years of ARGO, with clinical and health information to improve diagnostic and prognostic tools with genomic testing, and to make further progress in patient treatment and care.

14th ICGC scientific workshop

In May 2018, the 14th International Cancer Genome Consortium (ICGC)/1st ICGC-Accelerating Research in Genomic Oncology (ARGO) Scientific Workshop was held in Paris. This ICGC/ICGC-ARGO meeting brought together over 150 scientists from about fifteen countries.

This workshop discussed and coordinated a range of issues relating to the implementation and development of the ICGC, PCAWG and ICGC-ARGO projects. This meeting provided an opportunity to report on the progress of the ICGC-ARGO working groups:

- Technological Advancements: Harmonised ICGC-ARGO Clinical Genome;
- Consortium Development: Partnerships;
- Tissue and Clinical Annotation: Mandatory Clinical Dataset; Trials and Cohorts;
- Communication and Outreach: Patient Involvement; Media Strategy;
- Ethics and Governance: Complexity of the Clinic;
- Phenomics: Real World Data and Artificial Intelligence;
- Data Coordination and Management: Enhancement of Data Systems and Strategies.

It also reported on the progress of the ICGC-ARGO projects from different countries. At the time of the workshop, 17 programmes had been received.

The 8th edition of the International R&D Dating - "Immuno-oncology"

Aviesan, (French National Alliance for Life Sciences and Health) and ARIIS (Alliance for Research and Innovation in Health Industry) hold a partnership aiming to foster innovation in healthcare sector. Since its first edition in 2009, the International R&D Dating brings together excellence in the field of academic research and the world's R&D decision-makers from the healthcare sector with this purpose in mind. In line with this main strategic objective, ARIIS and ITMO Cancer of Aviesan co-organised the 8th edition of the R&D Dating in February 2018 on the theme of "Immuno-oncology". This event was a unique opportunity to highlight the excellence and expertise of French academic research teams, to discuss innovative projects, and to foster partnerships and collaboration between public authorities, academic researchers and industrials on this topic. It was attended by more than 360 participants including 151 R&D decision-makers from the healthcare sector representing 18 international delegations and 156 academic researchers and was considered a success. This one-day event, introduced by the Minister for Higher Education, Research and Innovation, Fréderique Vidal, allowed more than 30 industrials and academic speakers to discuss the different issues in immuno-oncology. In the afternoon, a B2B session was held, where 150 face-to-face Business meetings between industry representatives and researchers took place.

2018:
13
projects funded
for a total budget of
€5.51M

Thematic cancer research programmes

THE PROGRAMME FOR RESEARCH IN PHYSICS, MATHEMATICS AND ENGINEERING SCIENCES RELATED TO CANCER

Initiated in 2011, this programme aims to boost multidisciplinary partnerships to provide a different point of view and a different way to tackle the understanding of cancer progression and to improve the detection, diagnosis and management of the disease.

The programme in 2018

In 2018, 79 proposals were submitted and 13 projects were selected for a total amount of €5.51M (Table 3).

In 2018, projects were focused on developing new methods/devices for imaging (brain, skin, tumour microenvironment, endoscope), for tumour biomarker analyses, for treatments targeting (to the brain, antibodies for immunotherapy), for studying the mechanical properties of tumour progression (in order to develop treatments such as compressive stress), for better controlled radiotherapy (especially hadron therapy) with dosimetry. Mathematical models aimed at exploring the tumour microenvironment or studying the differentiation of a lineage in vivo also fell within the scope of selected projects.

TABLE 3
FEATURES OF THE PROGRAMME FOR RESEARCH IN PHYSICS, MATHEMATICS AND ENGINEERING SCIENCES RELATED TO CANCER IN 2018

Objectives	To attract physicists, mathematicians and engineers to cancer research in order to improve the understanding, diagnosis or therapeutic management of cancer
Programming institution	ITMO Cancer Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer Aviesan
Funding	**€5.51M**
Proposals submitted	**79**
Projects selected	**13**
Selection rate	**16.5%**

TABLE 4
TRENDS IN SELECTION AND FUNDING OF THE PROGRAMME FOR RESEARCH IN PHYSICS, MATHEMATICS AND ENGINEERING SCIENCES RELATED TO CANCER OVER THE 2011-2018 PERIOD

Years	2011	2012	2013	2014	2015	2016	2017	2018	TOTAL
Funding (in €M)	2.62	4.17	4.04	4.07	4.94	5.02	5.03	5.51	**35.41**
Proposals submitted	64	57	54	47	79	67	82	79	**529**
Projects selected	17	21	19	12	15	13	11	13	**121**
Selection rate (%)	26	37	35	25.5	19	19	13.4	16.5	**24**

The programme over the 2011-2018 period

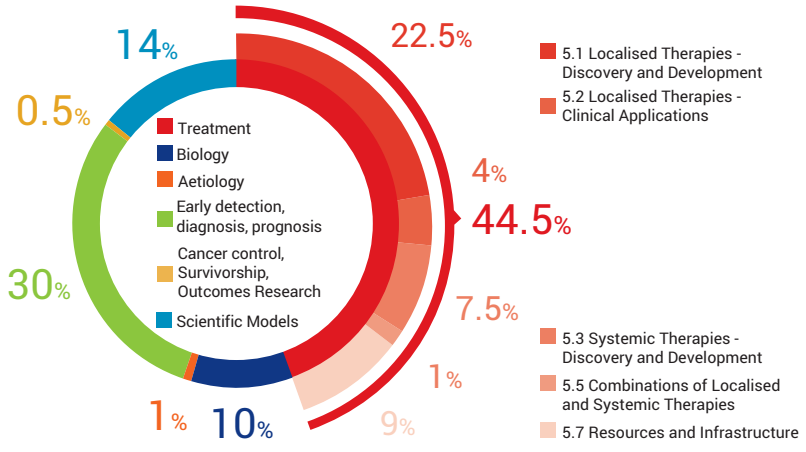
Over the 2011-2018 period, 121 projects were funded within the framework of this multidisciplinary programme for a total amount of €35.36M (Table 4).

The projects selected were generally ambitious and multidisciplinary with physicists involved. Many worked on developing tools for dosimetry in hadron or radiotherapy. Others worked on developing imaging or detection devices or tools for image processing or analysis. The effect of radiation on cells or molecules was also investigated under this programme. Nanotechnology developments or assessments of the effects of this technology were also well-represented among the projects. Nanotechnology is mostly used to enhance the effect of radiation specifically on the tumour. Since the inception of the programme, the number of projects dealing with innovative therapeutic approaches such as electroporation, plasma therapies or optical therapy approaches has increased.

2011-2018:
121
projects founded for just over
€35M

The distribution of the funded projects according to the CSO classification shows that almost half of these aim to develop new therapeutic approaches (Figure 6). Around a third of the projects related to the development of detection and diagnosis approaches. The remaining projects concerned the development of models or understanding cancer biology. Around half of the projects devoted to therapies fell within the subcategory of Discovery and development and clinical applications of localised therapies, representing 23% of the funded projects.

FIGURE 6
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2011-2018 PERIOD



Ex-post analysis of the programme for physics, mathematics and engineering sciences related to cancer

In 2018, an ex-post analysis of the 2011-2017 programme for Physics, mathematics and engineering sciences related to cancer was conducted by ITMO Cancer Aviesan. In brief, this programme has fostered a growing research community at the interface of physics, mathematics and biology that generates new knowledge on the processes in oncogenesis and new tools for cancer diagnosis and treatment. It has also demonstrated a leverage effect on teams who had benefited from the programme's funding. A reporting seminar involving laureates and experts from the 2012-2014 period was also organised in 2018 to complete this analysis.

2018:
8
projects funded for a total budget of
€3.97M

SINGLE CELL APPROACHES FOR THE STUDY OF ONCOGENIC PROCESSES

The "Single Cell" Programme was launched in 2018 by ITMO Cancer-Aviesan to promote research in oncogenesis based on new approaches harnessing genetic, epigenetic, transcriptomic and proteomic information at the cellular level to identify or characterise factors that promote the emergence and progression of tumours, be it tumour clone population or microenvironment cells.
In 2018, 37 projects were eligible and 8 projects were selected for a total amount of €3.97M (Table 5).

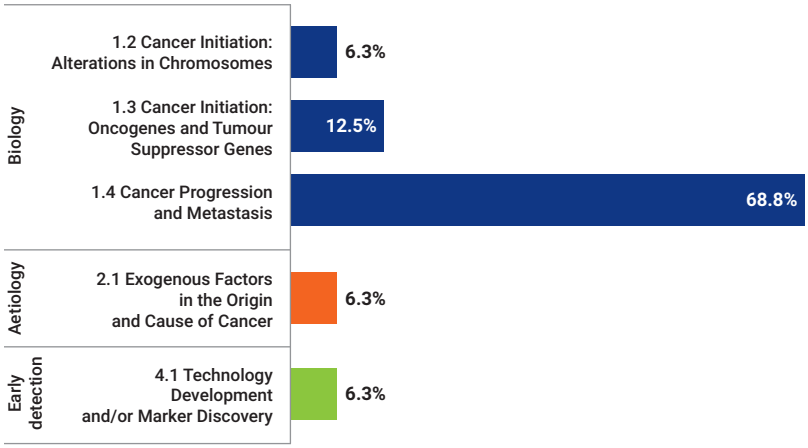
TABLE 5
FEATURES OF THE PROGRAMME IN SINGLE-CELL APPROACHES FOR THE STUDY OF ONCOGENIC PROCESSES IN 2018

Objectives	To promote research in oncogenesis based on "Single-Cell" approaches to identify or characterise factors that promote the emergence and progression of tumours
Programming institution	ITMO Cancer Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer Aviesan
Funding	**€3.97M**
Proposals submitted	**37**
Projects selected	**8**
Selection rate	**21.6%**

Projects focused on studying: intratumoral heterogeneity in cancer, which may promote tumour progression and resistance to therapies; differences between cells that give rise to tumours and those that do not; the cellular and molecular bases of secretory dysfunction in neuroendocrine tumours; the profiles of cancer-infiltrating B cells; the consequences of repeated nuclear envelope ruptures and DNA damage associated with cell deformation. Some projects also focused on inventory of intratumoral single-cell signatures. All proposals accounted for clinical transferability in order to improve both the diagnosis and treatment of the cancer studied.

The vast majority of the projects were aimed at understanding the basic biology of cancer according to the CSO classification, as 87% of them were classified in the Biology category (Figure 7). The remaining projects were either in the Early Detection and diagnosis or the Aetiology categories. The projects in the Biology category mostly investigated Cancer progression and metastasis.

FIGURE 7
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



NON-CODING RNAS IN ONCOLOGY: FROM BASIC TO TRANSLATIONAL RESEARCH

Many non-coding RNAs have been identified and implicated as key regulators in several biological processes. The "Non-coding RNAs" programme launched in 2017 by ITMO Cancer-Aviesan aims to promote the identification of non-coding RNAs (namely miRNA and lncRNA), 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).

In 2018, 48 proposals were submitted and evaluated and 9 projects were selected for a total amount of €3.75M (Table 6).

2018:
9
projects funded for a total budget of
€3.75M

TABLE 6
EATURES OF THE NON-CODING RNAS IN ONCOLOGY: FROM BASIC TO TRANSLATIONAL RESEARCH PROGRAMME IN 2018

Objectives	To promote study on non-coding RNAs, from their identification to their use in cancer diagnosis and treatment
Programming institution	ITMO Cancer Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer Aviesan
Funding	**€3.75M**
Proposals submitted	**48**
Projects selected	**9**
Selection rate	**18.8%**

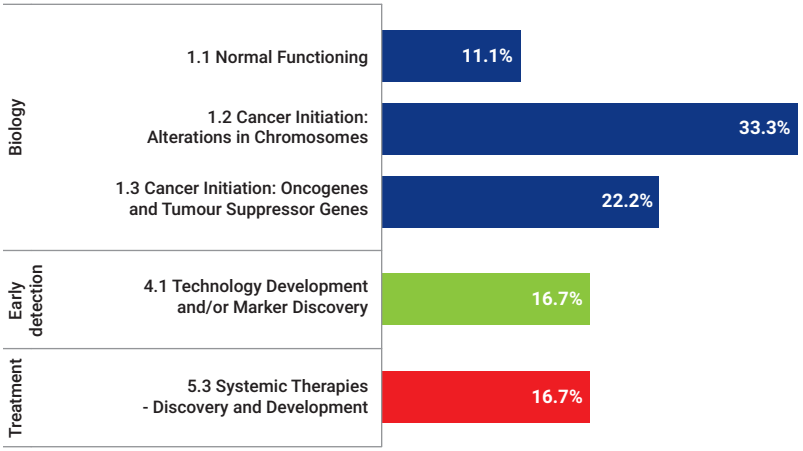
Ex-post analysis of the systems biology programme

The Systems biology programme was the subject of an ex-post analysis conducted by ITMO Cancer-Aviesan on the years 2012 to 2015. This analysis demonstrated that there is a growing community of researchers involved in systems biology and cancer. Furthermore, a variety of tools including mathematical models and analysis and integration pipelines have been generated by the research teams involved. These tools have been used to identify potential biomarkers, driver mutations and pathways involved in the development of cancer and some are now accessible to the research community. A reporting seminar on the Systems Biology programme covering the period from 2012 to 2014 was held in 2018 to complete the analysis report.

Projects focused mainly on identifying key ncRNAs (miRNAs, lncRNAs, rRNA, snoRNAs) involved in the regulation of specific cancer cell phenotypes, in oncogenic metabolisms, in chromatin organisation or in (targeted) therapy resistance, which could be used as innovative biomarkers for diagnosis and treatment monitoring, including in a circulating form. Networks and partners of these ncRNAs are also studied in many projects.

Two-thirds of the projects fell in the Biology category as per the CSO classification (Figure 8). The remaining projects were either in the early detection and diagnosis or treatment categories. The alteration in chromosomes subcategory represented half of the projects classified in the biology category.

FIGURE 8
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



SUPPORT FOR CANCER RESEARCH EQUIPMENT

In 2016, in compliance with Cancer Control Plan, the board of ITMO Cancer-Aviesan decided to launch a call dedicated to equipment acquisition in order to enable the development of ambitious research in the field of oncology, to encourage interactions between research teams and to increase the attractiveness and the position of French teams on the international arena.
In 2018, 67 proposals were submitted and evaluated and 17 projects were selected for a total amount of €3.39M (Table 7).

Since 2016, 71 grants for equipment were awarded for a total of €11.5M (Table 8).

The equipment requested in 2018 was particularly for cellular characterisation (i.e. cytometers) and imaging equipment (live-cell microscopy or devices for fluorescence imaging in small animals) (Table 9).

2018:
17
grant for equipment awarded for a total of
€3.39M

TABLE 7
FEATURES OF THE EQUIPMENT PROGRAMME IN 2018

Objectives	To give the laboratories the means in terms of equipment to lead an ambitious and innovative research policy. To encourage the acquisition of shared equipment, especially located on platforms.
Programming institution	ITMO Cancer Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer Aviesan
Funding	**€3.39M**
Proposals submitted	**67**
Projects selected	**17**
Selection rate	**25%**

TABLE 8
TRENDS IN SELECTION AND FUNDING OF THE EQUIPMENT PROGRAMME OVER THE 2016-2018 PERIOD

Years	2016	2017	2018	TOTAL
Funding (in €M)	4.93	3.18	3.39	**11.5**
Proposals submitted	119	34	67	**220**
Projects selected	38	16	17	**71**
Selection rate (%)	32	47	25	**32**

TABLE 9
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO EQUIPMENT CATEGORIES

Equipment categories	Projects selected 2016	Projects selected 2017	Projects selected 2018
Biochemistry and proteomics	5	1	4
Cellular characterisation and histology	**9**	**7**	**6**
Clinical	3	0	0
Genomics	**2**	**1**	**1**
Imaging	18	6	5
Animal models	**1**	**1**	**1**
TOTAL	38	16	17

TRANSLATIONAL AND INTEGRATED CANCER RESEARCH

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

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

Translational cancer research programmes

THE NATIONAL TRANSLATIONAL CANCER RESEARCH PROGRAMME (PRT-K)

The objective of this call for proposals (PRT-K), launched for the first time in 2007 and recurrent since 2009 in partnership with the 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.

2018:
13
projects funded out of the 116 proposals submitteds for a total budget of
€8.33M

The programme in 2018

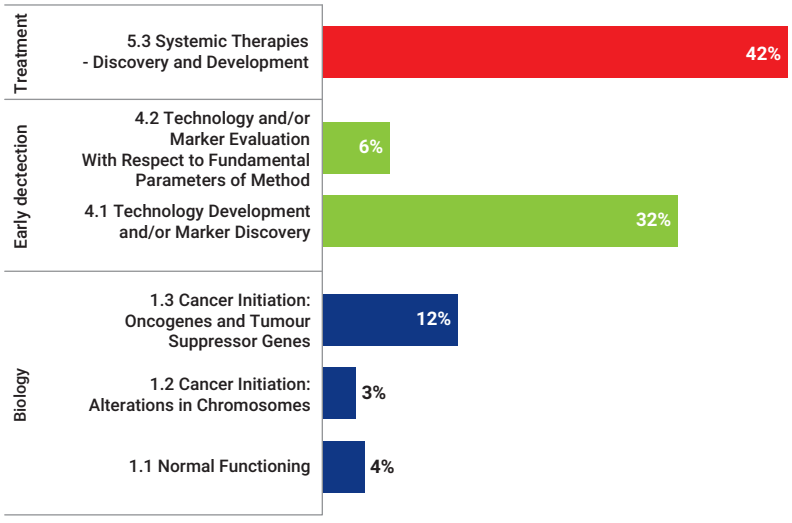
In 2018, 13 projects were selected for funding, out of the 116 submitted, representing an overall budget of €8.33M (€5.01M INCa + €3.32M DGOS) (Table 10).

In compliance with the objectives of the programme, about one-third of the projects selected in 2018 are studying new techniques and new biomarkers for early detection and diagnosis. More than 40% of the studies focus on the development of treatments, especially discovery and development of systemic therapies.

TABLE 10
FEATURES OF THE PRT-K PROGRAMME IN 2018

Objectives	To hasten the transfer of knowledge with a view to its prompt application in clinical practice for the benefit of patients, by giving researchers an incentive to develop multidisciplinary projects in close collaboration with clinical players, in order to improve prevention, early detection, diagnosis, treatment and comprehensive care of cancer patients.
Programming institution	INCa/Ministry of Health (DGOS)
Operating institution	INCa
Funding institution	INCa/Ministry of Health (DGOS)
Funding	**€8.33M** **INCa : €5.01M** **DGOS : €3.32M**
Proposals submitted	116
Projects selected	13
Selection rate	11%

FIGURE 9
DISTRIBUTION OF SELECTED PROJECTS IN 2018 ACCORDING TO THE CSO CLASSIFICATION



The programme over the 2007-2018 period

Since 2007, 1,432 proposals have been submitted to this call for proposals, and 190 have been selected and funded for a total amount of €83.3M. The overall selection rate for this call for proposals is 13% (Table 11).

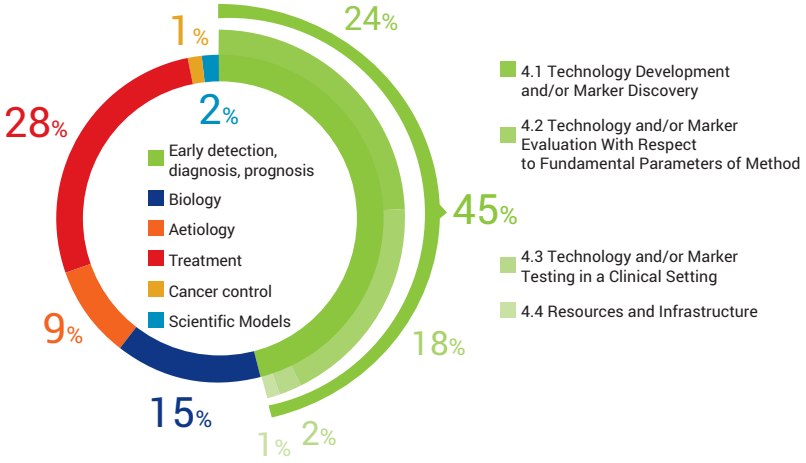
The CSO typology of the projects funded since 2007 corresponds to the characteristic profile for translational research (Figure 10), especially allocated to two main categories of research projects:

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

TABLE 11
TRENDS IN SELECTION AND FUNDING OF THE PRT-K PROGRAMME OVER THE 2007-2018 PERIOD

Years	2007	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	TOTAL
Funding (in €M)	3.70	9.82	6.54	5.15	8.95	8.81	8.53	8.44	7.62	7.65	8.33	**83.52**
Proposals submitted	56	147	83	118	163	163	138	162	151	135	116	**1,432**
Projects selected	14	24	16	12	26	20	16	21	15	13	13	**190**
Selection rate (%)	25	16	19	10	16	12	12	13	10	10	11	**13**

FIGURE 10
DISTRIBUTIONOF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2018 PERIOD



Study of data collection and biological resource organisation in candidate projects submitted to PRTK

For over ten years, INCa has pursued a policy of scientific valorisation of biological resources. Particularly, the Institute has published organisational recommendations and since 2011 has funded a specific organisation model to implement data and biological resource collection, biological and clinical databases (BCBs).
In order to evaluate the impact of these actions in the translational research programme, INCa carried out a study on projects reviewed and funded by the PRTK.
The main objectives of the study were:

- to determine the different types of structures and organisations involved for biological resource collection (data and biological samples) in research projects submitted to the PRTK;
- to determine how different organisations position in relation to each other, and particularly BCB structures.

2007-2018:
190
projects founded
for a total amount of
€83.52M

This was conducted on the projects selected after the letter of intent selection step in 2015, 2016 and 2017. In total, 140 full proposals were reviewed
The following data were identified and analysed:

- the type of collection structures and organisations;
- the notion of "longitudinal follow-up";
- the size of the collection or cohort of patients;
- the result of the application according to the collection structure (project funded or not funded).

Results

Types of collection structures and organisation
The analysis of the 140 applications helped identify 6 types of collection structures and organisation:

- Local organisation: recruitment and collection carried out by 1 or a few tumour banks, in a context where the research project involves teams from one health institution;
- Clinical service partners of the project: multicentric patient enrolment initiated by clinical partners of the project (partners with no apparent structural link);
- Structured care network: recruitment of patients in the framework of an accredited healthcare network (e.g.: rare cancer networks, oncogenetics system);
- Clinical trial: collection or cohort constituted during a clinical trial;
- Research Consortium (BCB): Recruitment and collection in the framework of a multicentric research network with a structured and "sustainable" organisation (excluding clinical trial);
- Large cohort: collection within a large national or international cohort (e.g. CONSTANCE, E3N).

Projects also exist for which no collecting organisation is involved. The research involves cell lines, animal models, PDX, or organoids already constituted, with no patient recruitment and with no human sample collection. These projects are classified as "NA" or without a collection structure.
The distribution of applications by collecting structures and organisations is presented in Table 12.
More than a third of submitted projects are based on a "local organisation" for recruitment and collection. Projects based on a "clinical trial" organisation repre-

TABLE 12
DISTRIBUTION OF APPLICATIONS BY COLLECTION STRUCTURES AND ORGANISATIONS

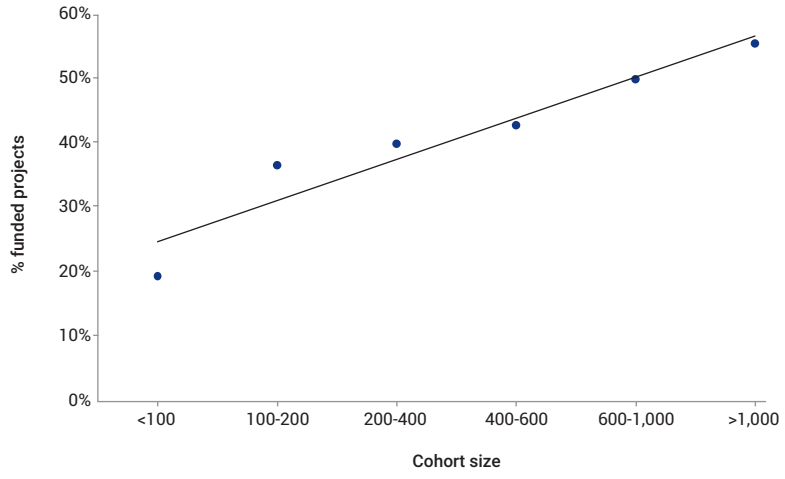
	Local organisation	Clinical service partners	Structured care network	Clinical trial	Research Consortium (BCB)	Large cohort	NA	Total
number of applications	47	17	9	39	17	1	10	140
% of applications	34%	12%	6%	28%	12%	1%	7%	100%
Number funded	7	8	2	19	9	0	4	49
Selection rate (in the category)	15%	47%	22%	49%	53%	0%	40%	35%
% funded (all projects)	14%	16%	4%	39%	18%	0%	8%	100%

sent 28% of applications. Projects with a BCB-type organisation are as frequent as projects organised with "clinical service partner" (12% of applications). Only one project is based on a "large cohort".
The analysis of the translational research programme results shows that projects based on a "research consortium" cohort have a higher selection rate. To a lesser extent, projects based on "clinical trials" and "clinical service partners" have a similar selection rate. The lowest success rate is observed for projects based on "local organisations".

The notion of longitudinal follow-up

For this study, we defined the notion of "longitudinal follow-up" as the following criterion: at least 2 points of biological analysis relating to different times or states of the disease.
The analysis of the applications shows that 83% of the research projects organise "longitudinal follow-up". This illustrates the importance of longitudinal follow-up in translational research studies, particularly for early detection biomarkers, theranostics or prognosis approaches.

FIGURE 11
FUNDED PROJECT RATES BY COHORT SIZE



The size of the collection or cohort

The size of the cohort is an important element in an application, since the number of cases helps provide a basis for statistical analyses. An analysis of the rate of funded projects by cohort size underscores that larger cohorts have a better chance of success in the call for proposals (Figure 11).

Conclusion

This analysis shows that "local strategy organisations" (isolated tumour bank) are no longer able to meet the needs of translational research. An isolated tumour bank often does not have the capacity to collect a sufficient number of cases, and it does not have the means to organise the collection of clinical data throughout the patient care pathway.

Healt democracy within Integrated Cancer Research Sites (SIRICs)

The development of health democracy is a national priority, not only in care, but also in the research field. Within the Integrated Cancer Research Sites (SIRIC), many actions are carried out in order to increase the participation of patients and health system users, by encouraging discussions between research organisations, researchers and the general public on scientific research and its challenges.

In November 2018, INCa organised a first meeting to bring together SIRICs representatives (managers, clinicians and researchers) and patient representatives, with the main objective to share experiences of the initiatives that are promoted within each SIRIC as part of the development of health democracy in research.

The findings of this first meeting indicate that all SIRICs now involve patient representatives in their steering committees. In order to bring their actions and the results of their work to the attention of the general public and patients, SIRICs have set up many communication actions through the dissemination of newsletters, organisation of patient-researcher-physician meetings (e.g.: awareness days, public events, workshops, etc.), and creation and uploading on the web of educational videos. At the research programme level, SIRICs tend to associate patient representatives as much as possible in the development and implementation of their scientific projects, particularly in human and social science research projects.

Following this meeting, several proposals for collaboration between SIRIC were discussed aiming, among other things, to set up common tools and a framework for the development of working methods and strategies to foster the involvement of patient representatives in the development of research projects conducted within SIRICs..

Projects based on BCBs have a better success rate at the PRTK call for proposals. BCB-type organisations are well-suited for translational research projects, as well as "clinical trial" and "clinical partnership service" multi-centre organisations.
Beyond the ability to convince a scientific evaluation committee of project feasibility, it would be important to determine whether the collecting structures have a real impact on research project success. Supplementary analyses will be carried out on completed projects, in order to determine the criteria for success and also to check whether collection structures and organisations genuinely guarantee logistical feasibility.

THE EUROPEAN TRANSLATIONAL CANCER RESEARCH PROGRAMME (TRANSCAN)

ERA-Net TRANSCAN-2 is a research funder network whose purpose is to establish coordination at a European level and support high-impact collaborative research projects in translational cancer research through joint transnational calls (JTC). With the support of the European Commission, under the EU framework programme Horizon2020, the ERA-NET TRANSCAN-2 has pursued its activities for a new five-year period (2015-2019). It is the continuation of the previous ERA-Net on translational cancer research TRANSCAN, funded from 2011 to 2014. This translational cancer research network involves 28 funding agencies and ministries from 15 Member States, 3 Associated Countries, and a third country (Taiwan).
Based on the recommendations of the TRANSCAN Scientific Advisory Board, TRANSCAN partners define the strategic research topics of the calls.

The programme in 2018

The 2017 TRANSCAN-2 call for research proposals, launched at the end of 2017 but operated in 2018, was dedicated to translational research on rare cancers.

TABLE 13
FEATURES OFTHE FOURTH TRANSCAN-2 CALL FOR PROPOSALS (JTC2017)

Objectives	To develop transnational innovative projects in translational research on rare cancers.	
Programming institution	**TRANSCAN-2**	
Operating institution	INCa	
Funding institution	**23 organisations / 17 countries**	
	All funding organisations	**France**
Funding	**€13.8M**	**€2.2M** **INCa : 1.5M€** **ARC Foundation : €0.7M**
Proposals submitted	92	73 Frenchs research teams involved in 56 LoIs 16 LoIs with French coordination
Projects selected	**12**	**9 French teams in 7 projects** **1 projects with French coordination**
Selection rate	13%	6.3%

This call led to the funding of 12 projects out of the 92 proposals submitted, including 6 French teams supported by INCa (in 5 projects), out of the 9 French teams participating in 7 selected projects. The total amount of French funding is €2.2M, including €1.5M from INCa and €0.7M from ARC Foundation for Cancer Research (ARC Foundation). The table below presents the main features and the results of this call for proposals.

Projects funded by INCa aim:
- To define biomarkers predicting PD-1/PARP inhibitor response in gynaecological carcinosarcoma and to identify resistance mechanisms;
- To clarify the clonal origin and to identify genomic alterations of upper urinary tract urothelial carcinoma and paired bladder recurrences;
- To identify novel marker signatures in pancreatic neuroendocrine tumour samples predicting individual patient response to approved therapies and to develop new models to identify novel opportunities for therapeutic intervention with substances used in the treatment of other cancers;
- To establish an advanced lesional map of T-cell prolymphocytic leukaemia, identify patterns of vulnerabilities from a comprehensive drug response chart, validate the most specific and active compounds and their combinations and to develop a prediction tool of drug sensitivities;
- To perform a comprehensive genetic and epigenetic characterisation of peripheral T-cell lymphoma samples to identify prognostic (epi-) genetic biomarkers, identify molecular targets and develop novel therapeutic strategies.

2018:
INCa funded 6 French teams out of the 12 European projetcs selected for a total budget of
€1.5M

The programme over the 2011-2018 period

Under the 2 TRANSCAN programmes, 7 JTCs have been launched, leading to the funding of 79 European projects, out of the 592 projects submitted, for €85M.

According to the CSO typology, the analysis of the projects that include French teams funded by INCa, over the 2011-2018 period, shows that the majority of the projects focus on early detection, diagnosis and prognosis, mostly for the development and evaluation of technology or biomarkers (31% and 20%,

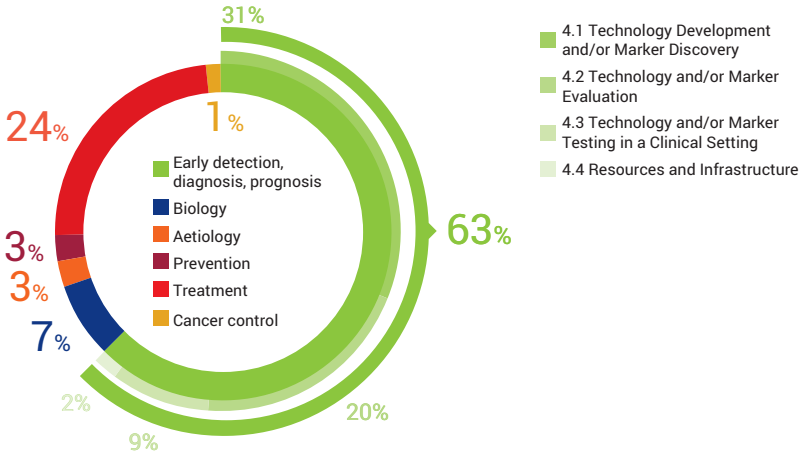
TABLE 14

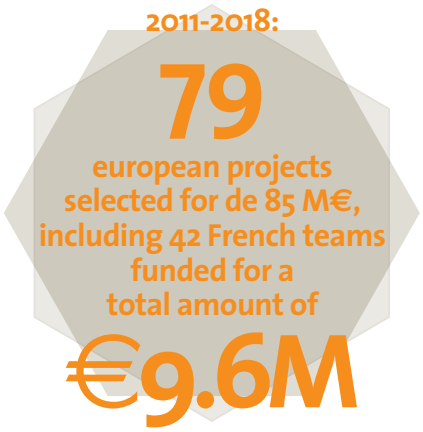
PREVIOUS CALLS FOR PROPOSALS OF THE ERA-NET TRANSCAN AND TRANSCAN-2 PROGRAMMES

ERA-NET TRANSCAN	
1st call for proposals : JTC-2011	**Topic: Validation of Biomarkers for Personalised Cancer Medicine** **Budget (15 funding partners):** €10.6M (INCa €1.3M) **Results:**10 projects selected out of 117 submitted pre-proposals ; 7 French teams (including 1 coordinator) participating in 6 selected projects.
2nd call for proposals : JTC-2012	**Topic : Translational Research on Primary and Secondary Prevention of Cancer** **Budget (15 funding partners)** : Total budget of €11.2M (INCa: €1.3M – ARC Foundation: €0.5M) **Results:** : 10 projects selected out of 55 submitted pre-proposals ; 9 French teams (including 1 coordinator) participating in 7 selected projects.
3rd call for proposals : JTC-2013	**Topic : Translational Research on Tertiary Prevention of Cancer** **Budget (15 funding partners)** : €11.4M (INCa: €0.8M – ARC Foundation: €0.57M) **Results** : 10 projects selected out of 68 submitted pre-proposals ; 4 French teams (including 1 coordinator) participating in 3 selected projects.
ERA-NET TRANSCAN-2	
1st call for proposals : JTC-2014	**Topic : Translational research on human tumour heterogeneity to overcome recurrence and resistance to therapy** **Budget (15 funding partners – 18 countries)** : €17.2M (INCa: €2.1M – ARC Foundation: €0.97M) **Results** : 16 projects selected out of 117 submitted pre-proposals ; 13 French teams (including 2 coordinators) participating in 11 selected projects.
2nd call for proposals : JTC-2015	**Topic : Translational research on immunology and immunotherapy of cancer** **Budget (15 funding partners – 11 countries)** : €6.3M (INCa: €1.17M – ARC Foundation: €0.53M) **Results** : 7 projects selected out of 33 submitted pre-proposals ; 8 French teams (including 2 coordinators) participating in 6 selected projects.
3rd call for proposals : JTC-2016	**Topic : Translational research onminimally and non-invasive methods for early detection and/or progression of cancer** **Budget (23 funding partners – 16 countries)** : €15.2M (INCa: €1.4M – ARC Foundation: €1.1M) **Results** : 14 projects selected out of 110 submitted pre-proposals ; 12 French teams (including 2 coordinators) participating in 9 selected projects.

FIGURE 12

DISTRIBUTION OF THE SELECTED PROJECTS (WITH FRENCH TEAMS DUNDED BY INCA) ACCORDING TO THE CSO CLASSIFICATION OVER THE 2011-2018 PERIOD





respectively). This is in line with the general profile of translational research projects. Moreover, 2 calls of the 6 JTCs were specifically related to this topic (JTC2011: Validation of biomarkers and JTC2016: Methods for early detection). Additionally, 24% of the projects belong to the treatment category, especially on the discovery or the development of systemic therapies, primarily due to JTC 2014 (tumour heterogeneity to overcome recurrence and resistance to therapy) and JTC2015 (cancer immunotherapy).

In order to continue the ongoing European cooperation on translational research, a new proposal for a TRANSCAN-3 programme has been submitted to a new call under the EU programme Horizon 2020.

National preclinical radiotherapy research network

INCa launched a call for applications aiming to set up a national preclinical radiotherapy research network in 2017.

One application was received, and the international Scientific Evaluation Committee met in February 2018. The Committee welcomed the initiative of the network in France, but recommended that the project be resubmitted since some items needed to be clarified. The 2nd meeting of the Scientific Evaluation Committee took place on October 2018. INCa allocated €200,000 of funding over a 3-year period of designation to the selected proposal called RADIOTRANSNET.

TABLE 15
FEATURES OF THE CALL FOR APPLICATION TO SET UP A NATIONAL PRECLINICAL RADIOTHERAPY RESEARCH NETWORK

Objectives	To structure and to integrate fundamental and translational radiotherapy research. INCa's support is intended to: Promote multi and interdisciplinary grouping and to improve partnerships between various stakeholders in radiotherapy research at a national level; Foster academic capabilities in terms of innovation, design and management of preclinical projects; Enhance the international visibility and attractiveness of French radiotherapy research, and to develop European and international collaboration further in this field.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€200,000**
Proposals submitted	**1**
Projects selected	**1**

Integrated cancer research programmes

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

In France, in 2017, 26.9% of the population are daily smokers. In 2015, for all adults aged 30 years and over, more than 68,000 cases of cancers were tobacco-related (54,000 for men and 12 500 for women), which represented respectively 28% and 8% of all new cancers nationwide.

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

The Tobacco Fund decided to allocate €14M to INCa and to the Institute of Research in Public Health (IReSP) – €7M each – to co-launch a call for research and intervention proposals to reduce and control tobacco consumption.

The programme in 2018: the programme for research and intervention proposals to reduce and control tobacco consumption

This call for proposals covers all the aspects of research (fundamental, clinical or population depending on the sections) as well as a broad array of disciplines, ranging from clinical research to public health, and including information and communication technologies, economic and political science, social and human sciences, law, biology, epidemiology, etc.

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

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

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

- **Section 1 INCa/IReSP: Tobacco in the general population**
  - Area 1: Determinants & trajectories of smoking;
  - Area 2: Public policies, strategies and behaviours of stakeholders;
  - Area 3: Electronic nicotine delivery systems (ENDS).

2018:
25
projects selected for a total budget of
€7.21M

- **Section 2 INCa: Tobacco & cancer**
  - Area 1: Support for smoking cessation & cancer;
  - Area 2: Screening for tobacco-related cancers;
  - Area 3: Biology.

- **Section 3 IReSP: Diseases other than cancer**
  - Area 1: Tobacco cessation in patients with conditions other than cancer;
  - Area 2: Research on health services and systems other than oncology.

TABLE 16
FEATURES OF THE RESEARCH AND ACTION PROGRAMME FOR THE TABACCO CALL FOR PROPOSALS IN 2018

Objectives	To develop and put in place an integrated strategy to support research and actions related to tobacco and the cancers associated with it.
Programming institution	INCa / IReSP
Operating institution	INCa / IReSP
Funding institution	INCa / IReSP
Funding	**€7.21M** **INCa : €4.24M** **IReSP : €2.88M**
Proposals submitted	**55**
Projects selected	**25**
Selection rate	**45%**

TABLE 17
DISTRIBUTION OF THE SELECTED AND SUBMITTED PROJECTS RELATED TO THE TOTAL FUNDING FOR EACH SELECTION

Tobacco 2018 Call for Proposals	Section 1 INCa – IReSP*	Section 2 INCa	Section 3 IReSP	TOTAL
Proposals submitted	36	6	13	55
Proposals selected	11	5	9	25
Funding	€3.37M	€2.5M	€1.25M	€7.12M

*INCa: €1.74M; IReSP (Institute of Research in Public Health): €1.63M

Concerning section 2 (tobacco & cancer), 3 projects funded concerned the research on early detection and lung cancer screening (biomarkers, addictive process in e-cigarette, etc.). The 3 other projects related to existing links between tobacco and specific cancers, in a medical or biological way: impacts of tobacco on molecular characteristics in bladder cancer prognosis, social and genetic determinants in tobacco consumption, etc.).

As we need to reduce tobacco consumption in France, primary prevention and interventions in the general population are the first effective approach to include in a new call for research and intervention proposals to reduce and control tobacco. As such, we have received a large proportion of projects in this area, which included interventional research: mostly to delay the commencement of tobacco consumption in teenagers.

In addition, all the project proposers had the possibility to submit an "emerging project", which is a new alternative to the full project compared to previous years. It allows researchers to submit a scaled-down project (12 or 18 months) and test its feasibility before submitting a full project (36 or 48 months). The increase in the number of projects in 2018 is partly attributable to this new submission process.

2016 -2018:
43
projects selected for a total budget of over
€16M

The programme over the 2016-2018 period

Over the three years of calls for proposals on tobacco control, INCa provided funding for 26 projects, for a total budget of €12.1M. Year on year, more projects have been submitted compared to the previous call.

TABLE 18
TRENDS IN SELECTION AND FUNDING OVER THE 2016 - 2018 PERIOD

Years	2016	2017	2018	TOTAL
Funding (in €M)	3.52[1]	5.66[2]	7.21[3]	**16.39**
Proposals submitted	21	22	55	**98**
Projects selected	7	11	25	**43**
Selection rate (%)	33	50	45	**44**

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

FIGURE 13
DISTRIBUTION OF THE PROJECTS SUBMITTED AND SELECTED ACCORDING TO THE RESEARCH TOPICS OVER THE 2016-2018 PERIOD

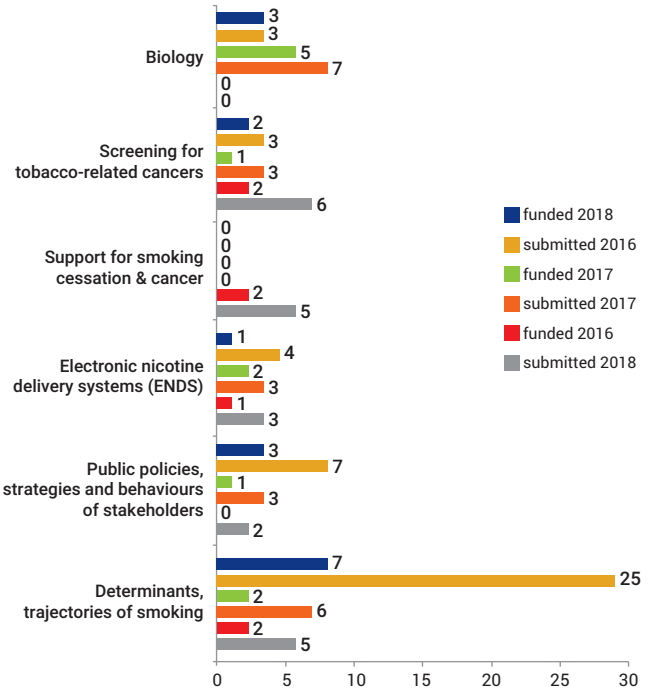
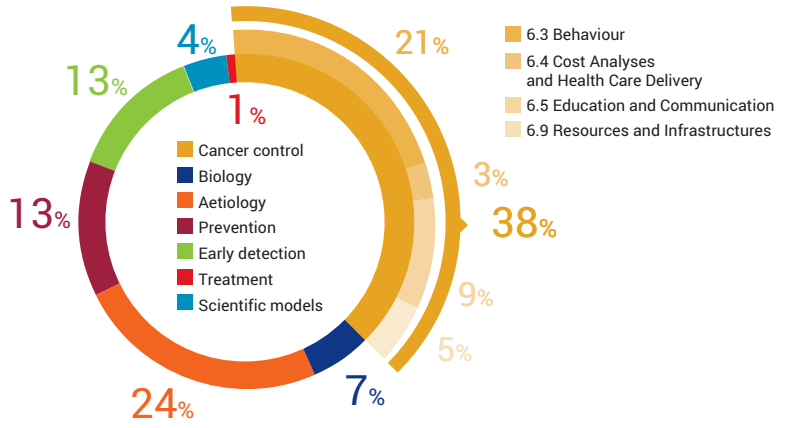


FIGURE 14
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2016-2018 PERIOD (FOR 2018, PROJECTS SELECTED IN SECTION 1 & 2)



Tabacco Workshop

In March 2018, INCa organised a report workshop on findings from previously funded projects. The aim of this meeting was to mark the end of the "PRIORITE Tabac" funding programme – which was initiated in 2016 by INCa – and to provide a space for researchers and stakeholders to exchange ideas.

This workshop included thirty attendees, from seven research teams and also associations, institutions, health services and state services.

In addition, it also provided an opportunity for INCa to introduce the Tobacco Fund and the launch of the new call for research and intervention proposals to reduce and control tobacco consumption.

The call for proposals has clearly evolved over the three last years, particularly in the area of "Determinants & trajectories of smoking". The recent change within the design of the call, the number of projects and the increasing mobilisation of the tobacco research field, demonstrate the developments in the general research community for this international issue aiming to help people to quit smoking. For 2019, the new call for proposals will be based and build on the Final Report from the Cochrane Tobacco Addiction Group: "Prioritising the unanswered questions in tobacco control", published in 2017.

THE INTEGRATED RESEARCH ACTION PROGRAMME (PAIR)

Since 2007, INCa has launched ten Integrated Research Actions Programme (PAIR) focusing on a specific type of cancer. The aim of this programme is to promote cooperation between all scientific disciplines (fundamental research, clinical research, epidemiology, public health and human and social sciences) around key structuring projects. This transversal programme aims to accelerate patient access to research progress. Since 2010, the PAIR programme is launched and funded in partnership with the charities ARC Foundation and the French Cancer League.

The programme in 2018

In 2018, 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.

Pancreatic adenocarcinoma is the sixth most common cancer in terms of incidence (3.9% of cases) with more than 11,600 new cases in 2012, equally distributed between men and women. The incidence of this cancer has risen sharply since 1980 with an increase of 2.3% and 3.9% per year respectively (+247.7% globally between 1980 and 2012). The causes of this increase are unknown. The increase in the incidence of these cancers is a worrying public health problem. It is estimated that, by 2025, it will be the third cause of cancer-related death in the EU after lung and colorectal cancer[2]. Mortality is almost stable in men, whilst a slight increase is observed in women. Survival at 5 years is very low (about 5%), due to late diagnosis in the absence of specific symptoms and methods for early diagnosis leading to delayed treatment of these patients, together with an absence of effective treatments.

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

Questions addressed by this call for proposals are focused on four main scientific areas:

- Epidemiology - genetics of pancreatic cancer;
- Biology of pancreatic cancer;
- Improving the techniques and strategies for the early diagnosis and typing of cancers, determining markers to predict and evaluate response to treatment;
- Access to diagnosis and care.

Out of the 45 projects submitted, 7 were funded for a total amount of €3.7M (Table 19). In total, the selected projects involved 39 research teams.

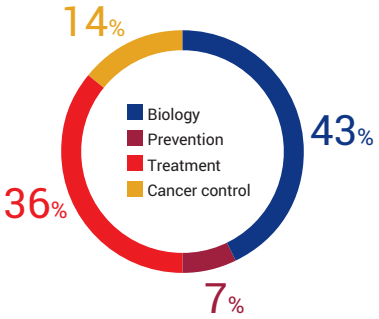
The distribution of the selected projects according to the CSO classification shows that a majority of projects concern biology (43%) and treatment (36%). For biology, one project aims to study cancer growth and metastatic development with innovative models, and one focuses on metabolic targeting of metastatic pancreatic cancer focusing on TGFβ-dependent metabolic pathways with the aim to proceed

7
projects were selected out of the 45 submitted for a total amount of
€3.7M
and involving 39 research teams

TABLE 19
FEATURES OF THE PANCREATIC CANCER PAIR PROGRAMME IN 2018

Objectives	To address issues arising from all disciplines by adopting a cross-disciplinary and integrative approach intended to improve the understanding and management of pancreatic cancer.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa / ARC Foundation / French League
Funding	**€3.7M**
Proposals submitted	**45**
Projects selected	**7**
Selection rate	**16%**

FIGURE 15
DISTRIBUTIONOF THE FUNDED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



2. Ferlay J., Partensky C. & Bray F. (2016). More deaths from pancreatic cancer than breast cancer in the EU by 2017. Acta Oncol. 2016 Sep - Oct;55(9-10):1158-1160. doi: 10.1080/0284186X.2016.1197419.

to a robust clinical validation of selected metabolic targets usable as therapeutic options to reverse metastatic PDAC progression. For treatment, the projects focus on chemo resistance and chemo sensitivity mechanisms.

The programme over the 2007-2018 period

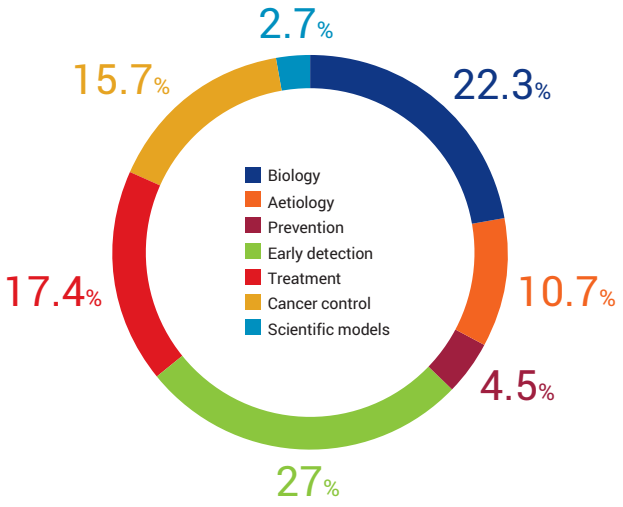
Since 2007, 10 PAIR programmes have been launched and funded, leading to the funding of 81 cancer research projects for a total amount of €46.30M (table 20). The analysis of the funded projects according to the CSO classification is consistent with the integrative aspects of the programme since all the cancer research fields are represented (Figure 16). The main categories are 27% for early detection, diagnosis, prognosis and 22.3% for biology.

In 2018, 3 report workshops were organised. These report workshops provide opportunities to federate research teams, leading to a high-quality translational research approach. These projects have led to numerous scientific publications in international journals and led to the development of new leads for innovative therapeutic strategies, the development of diagnosis tools and identification of new therapeutic targets.

TABLE 20
TRENDS IN SELECTION OF THE INTEGRATED RESEARCH ACTION PROGRAMME (PAIR) OVER THE 2007-2018 PERIOD

YEARS	CANCER SITES	FUNDING INSTITUTIONS	SELECTED PROJECTS	FUNDING (€ MILLIONS)
2007	Early colorectal cancers	INCa/Roche/Amgen	14	4.34
2008	Lymphomas	INCa/Roche/Amgen	7	5.21
2009	Hepatocellular carcinomas	INCa/ARC Foundation/ANRS	12	5.95
2010	Prostate	INCa/ARC Foundation/ANRS	8	5.62
2011	Upper aerodigestive tract cancers	INCa/ARC Foundation/French League	7	4.13
2012	Gyneacological	INCa/ARC Foundation/French League	6	3.41
2013	Melanomas	INCa/ARC Foundation/ French League	9	5.12
2014	Early breast cancer	INCa/ARC Foundation/French League	8	3.76
2017	Paediatric cancers	INCa/ARC Foundation/French League	3	5.04
2018	Pancreatic adenocarcinomas cancer	INCa/ARC Foundation/French League	7	3.68
TOTAL			81	46.30

FIGURE 16
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2018 PERIOD



2007 -2018:

10
PAIR programmes funded

81
projects selected for a total funding of

€46.30M

Gynaecological cancers PAIR Report Workshop

n November 2018, INCa and its partners, ARC Foundation and the French Cancer League, organised a workshop dedicated to the projects funded in the framework of the Gynaecological cancers PAIR launched in 2012. This report workshop was held during the 29th French Society of Gynaecological Oncology (SFOG) congress and brought together almost 150 attendees.

The findings of the six selected and funded projects were presented. These projects focused on issues concerning innovative approaches for specific molecular marker identification, new methods developed based on polarimetric imaging for diagnosis, new therapeutic targets such as dependence receptors, the development of new concepts in cancer immunotherapy and identification of proteins involved in the repair of damaged genes leading to innovative therapeutic strategies and the identification of social and territorial inequalities in HPV vaccine coverage.

Melanomas PAIR Report Workshop

In December 2018, INCa, ARC Foundation and the French Cancer League, organised a workshop dedicated to the projects funded in the framework of the Melanomas PAIR launched in 2013, during the Dermatological Days in Paris (JDP) congress. Approximately seventy people attended the workshop.

The findings of the nine funded and selected projects were presented. These projects focused on issues concerning the identification of new genetic factors to develop prevention or early detection strategies, identification of new biomarkers of response to immunotherapy, innovative therapeutic approaches (emphasising the central role of miRNA, using dependence receptors) and the identification of genomic profiles in the context of resistance to targeted therapies.

The Hepatocellular Cancers (HCC) PAIR Report Workshop

The HCC PAIR Report Workshop was held in December 2018 in Amiens during the First HCC National Days. Co-organised by INCa and its partners, ARC Foundation and the French agency for AIDS and viral hepatitis research (ANRS), this workshop offered an opportunity to present the findings of the 10 projects funded by this programme in front of more than 120 participants.

The results focused particularly on issues concerning:

- French prospective cohorts in HCC;
- Metabolic pathways;
- Identification of genes leading to HCC;
- Therapeutic innovations.

Furthermore, 4 lectures on hot topics in relation to HCC were included in the programme. The following topics were discussed:

- HCC epidemiology: strengths and weaknesses of French cohorts;
- Innovations in diagnostic imaging for HCC;
- New treatments for HCC;
- Overview: Past, present and future for HCC.

Significant changes have taken place in HCC in the last 10 years, allowing interdisciplinary and cross-institutional grouping of researchers and clinicians.

Translational and multidisciplinary research training programmes

THE BASIC AND TRANSLATIONAL RESEARCH TRAINING PROGRAMME

Support for basic and translational research is completed by an investment plan to promote training and career development for the next generation of investigators. These initiatives are supported by a dedicated call for applications in translational or basic research training for medical, pharmacy and veterinary science graduates through grants for Master's degrees, PhDs, and postdoctoral positions.

Led by ITMO Cancer-Aviesan, this programme aims to support complementary translational and fundamental research training of graduates of medicine, pharmacy, dentistry and veterinary science. The programme was amended in 2017 to include fundamental research.

In 2018, a total of €2.44M was awarded for 29 grants for 10 Master's students, 18 PhD theses, and 1 postdoctoral fellowship (Table 21). Since 2007, 262 training grants have been awarded to support training in translational cancer research for an overall funding of just over €21M (Table 22).

Over the 12 years of the programme, more than 40% of the grants were devoted to basic cancer research (understanding the general principles of cancer emergence or growth). Projects based on the development of therapeutic approaches accounted for 30% of grants, while detection and diagnostic approaches accounted for 21% of grants (Figure 18).

TABLE 21
FEATURES OF THE TRANSLATIONAL RESEARCH TRAINING PROGRAMME IN 2018

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 in	**€2.44M**
Proposals submitted	**106**
Projects selected	29
Selection rate	**27%**

TABLE 22
TRENDS IN SELECTION AND FUNDING OF THE BASIC AND TRANSLATIONAL RESEARCH TRAINING PROGRAMME OVER THE 2011-2018 PERIOD

Year	2011	2012	2013	2014	2015	2016	2017	2018	TOTAL
Funding (in €M)	1.53	2.11	1.31	2.37	1.85	1.93	1.97	2.44	15.53
Proposals submitted	35	36	49	101	96	111	108	106	642
Projects financed	19	25	22	30	25	29	24	29	203
Selection rate	54%	69%	45%	30%	26%	26%	22%	27%	32%

Support for training in interdisciplinary research - Frontiers in Life Sciences (FdV)

The FdV graduate school recruits students trained in various disciplines (e.g. biology, physics, mathematics, medicine, economy, linguistics, etc.) around the world. 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 aims to promote multidisciplinary training to adapt and to meet the needs of cancer research.

TABLE 23
FEATURES OF THE TRANSLATIONAL RESEARCH TRAINING PROGRAMME IN 2018

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

FIGURE 17

DISTRIBUTION OF SELECTED APPLICATIONS ACCORDING TO DEGREES OVER THE 2007-2018 PERIOD

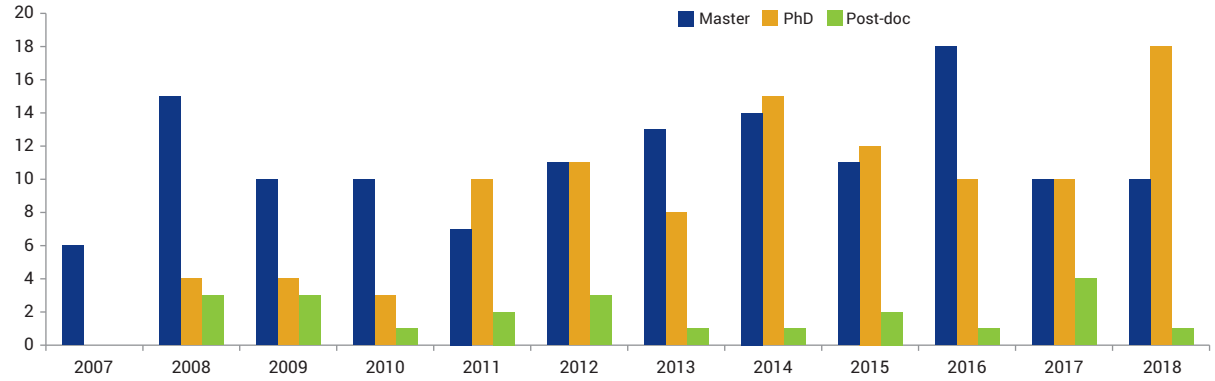
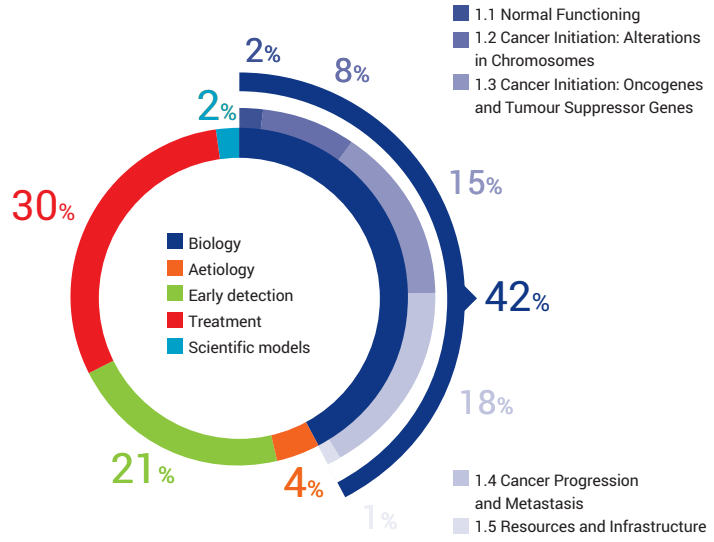


FIGURE 18

DISTRIBUTION OF SELECTED APPLICATIONS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2018 PERIOD



The projects aim to understand the role of cancer-associated fibroblasts (CAFs) in the initial stages of cancer cell invasion by using a multidisciplinary approach combining cancer cell biology and physics; and to improve drug delivery by using nanoparticle vehicles which are promising systems capable of decreasing drug toxicity while improving potentiation and targeting, thus offering key advantages in cancer therapies. Since 2010, 19 PhD candidates have received funding, for a total amount of €1.99M.

TABLE 24
TRENDS IN SELECTION AND FUNDING FOR TRAINING IN INTERDISCIPLINARY RESEARCH

Year	2010	2011	2012	2013	2014	2015	2016	2018	TOTAL
Funding (in €M)	0.21	0.21	0.21	0.21	0.21	0.31	0.42	0.21	1.99
Proposals submitted	4	7	5	6	4	4	5	4	39
Projects selected	2	2	2	2	2	3	4	2	19

Support for training in the Doctoral School of Information and Communication Sciences and Technologies (STIC)

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: control, signal processing, image processing, robotics, networks, telecommunications, data science, machine learning and artificial intelligence, human-machine interactions, programming, algorithmics, languages and architecture. In 2018, ITMO Cancer-Aviesan developed a partnership with the STIC Doctoral School to finance some PhD theses related to oncology within this school. The projects address modelling of the variation of key oncogenic pathways using radiomic and genomic data, and ultimately integration of their predictive outputs with the response to anticancer agents; and the study of drug resistance mechanisms to tumoral proliferation by computational modelling.

TABLE 25
FEATURES OF STIC DOCTORAL SCHOOL FUNDING IN 2018

Objectives	To promote dual training and foster innovative research by funding PhD theses at the interface of information technologies and oncology
Programming institution	Université Paris-Saclay
Operating institution	Université Paris-Saclay
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding in	**€0.19M**
Proposals submitted	**3**
Projects selected	2

Support for training in research for graduates of medicine, pharmacy, dentistry and veterinary studies ("Postes d'Accueil")

The Inserm "Poste d'Accueil" Programme allows students trained in medicine, pharmacy, dentistry and veterinary studies to do two years of research in an Inserm research unit within the framework of a PhD thesis. This programme is part of a policy to strengthen the links between fundamental, clinical and public health research.

The projects address the role of the Human endogenous retrovirus in myeloid blood disorders; the cytotoxic-induced anti-tumour immune response in breast cancer; and the role of telomere maintenance in low grade gliomas and osteosarcomas.

TABLE 26
FEATURES OF THE TRANSLATIONAL RESEARCH TRAINING PROGRAMME IN 2018

Objectives	To promote training of students or young medical, pharmacy and veterinary science graduates in translational research by funding 2 years of their PhD thesis
Programming institution	Inserm
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding in	**€0.26M**
Proposals submitted	**22**
Projects selected	**3**

Support for enabling young scientists to create and lead a cancer research team through the ATIP-Avenir programme

Under a partnership between Inserm and CNRS, a call for proposals is launched aimed at enabling young scientists to create and lead a 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 projects address the role of localised changes in chromatin compaction in oncogenesis; and the role of endothelial autophagy in chronic liver diseases. Two projects previously selected have also been extended for two additional years for €120,000.

TABLE 27
FEATURES OF THE ATIP-AVENIR PROGRAMME IN CANCER RESEARCH IN 2018

Objectives	To promote the establishment of young promising PIs in cancer research by funding 3 years of their starting team
Programming institution	CNRS and Inserm
Operating institution	CNRS and Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding in	**€0.6M**
Proposals submitted	**5**
Projects selected	**2**

CANCER CLINICAL RESEARCH AND ACCESS TO INNOVATION

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

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

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

PHRC-K funds clinical cancer 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);

- Combinations of several targeted drugs, or combinations of targeted drugs with chemotherapy or radiotherapy;
- Clinical validation of the efficacy of innovative health technologies for treatment or diagnosis;
- Reduction in the medium and long-term toxicity of treatments, and its assessment, especially for children and young adults and patients with breast cancer;
- Increase of survival;
- Palliative care;
- Meta-analyses addressing controversial issues in treatment efficacy.

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

THE PROGRAMME IN 2018

In 2017, 198 letters of intent were submitted to PHRC-K and 36 projects were selected for funding for a total amount of €21M (Table 28).

In compliance with the objectives of the programme, the selected projects are mainly intended to assess therapeutic innovations and to evaluate the efficacy of health technologies (Table 29).

TABLE 28
FEATURES OF THE PHRC-K PROGRAMME IN 2018

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	**€21M**
Proposals submitted	**198**
Projects selected	36
Selection rate	**18%**

TABLE 29
DETAILED ANALYSIS OF THE SELECTED PROJECTS IN THE 2018 PHRC-K PROGRAMME

	Number of projects selected
Drug therapy	**18**
Radiotherapy	**6**
Surgery and other innovative techniques	**4**
Immunotherapy	**3**
Imaging (included PET)	**2**
Biomarkers (diagnosis, prognosis)	**3**

2018:
36
clinical research projects funded out of the 198 submitted for a total budget of
€21M

Compared to 2017, there is an increase in the proportion of funded projects in supportive and palliative care: 5/14% compared to none in 2017.

Another feature for 2018 is a decrease in the selection rate: 18% in 2018 compared to 21% in 2017. This may be explained by an increase in projects' budgets, particularly those related to innovative technologies such as CAR-T cells.

THE PROGRAMME OVER THE 2007-2018 PERIOD

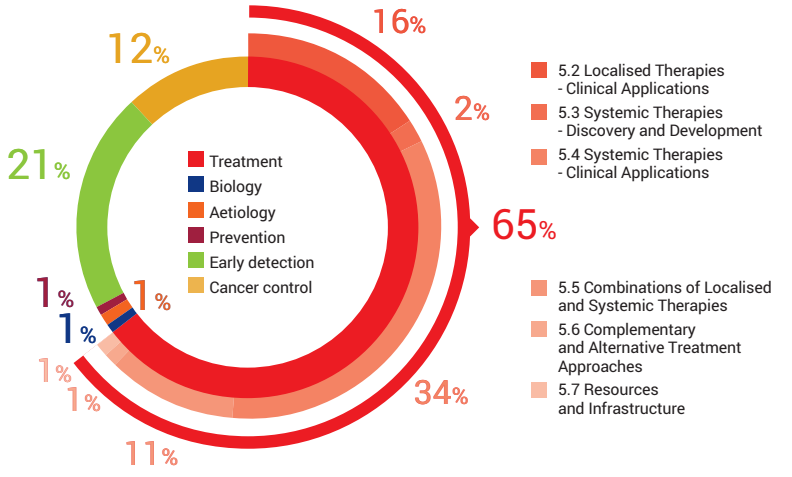
Since 2007, 2,553 proposals have been submitted to the PHRC-K programme and 596 projects have been selected for an overall amount of over €229M. The overall selection rate for this call for proposals is 23% (Table 30).

TABLE 30
TRENDS IN SELECTION AND FUNDING FOR THE PHRC-K PROGRAMME OVER THE 2007-2017 PERIOD

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	TOTAL
Funding (in €M)	14.1	15.68	17.94	20.18	21.00	19.30	17.14	21.06	20.14	19.69	21,89	21.07	229.26
Proposals submitted	213	193	218	222	285	226	240	196	186	192	184	198	2,553
Projects selected	76	50	52	59	62	54	44	45	37	42	39	36	596
Selection rate (%)	36%	26%	24%	27%	22%	24%	18%	23%	20%	22%	21%	18%	23%

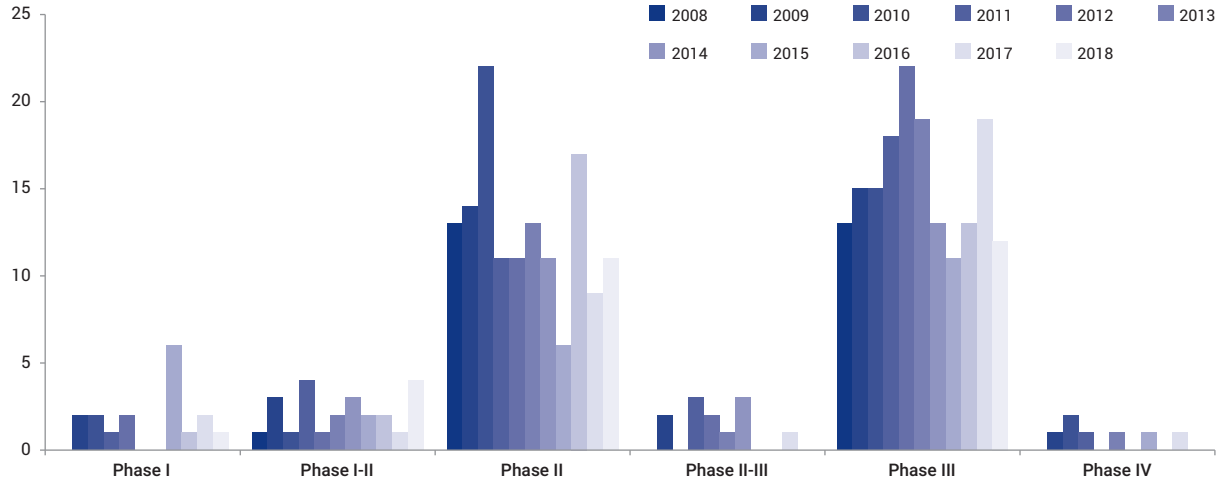
Over the 2007-2018 period, the CSO analysis of funded projects shows that the majority of the funded projects belong to the treatment category (66%) and, particularly, to clinical applications of systemic and localised therapies (52.5% and 17%, respectively). Moreover, the other topics studied are related to early diagnosis (21%) and care and survival (12%) (Figure 19).

FIGURE 19
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2018 PERIOD



Over the 2007-2018 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 20).

FIGURE 20
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO STUDY PHASE



REPORT WORKSHOP ON IMAGING

A focused annual report workshop is organised in order to valuate and improve communication regarding the projects funded by the PHRC cancer programme. In 2018, the topic of this workshop was imaging. It took place during the "Journées francophones de radiologie" in October 2018. The findings of 10 projects were presented, covering a wide range of topics (early detection, diagnosis, treatment follow-up) and organs (prostate, lung, kidney, liver (primary and metastatic), pancreas, colon, and brain (metastatic).

2007-2018:
596
projects funded for a total amount of
€229M

PROGRESS OF PROJECTS FUNDED THROUGH THE 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 programme.

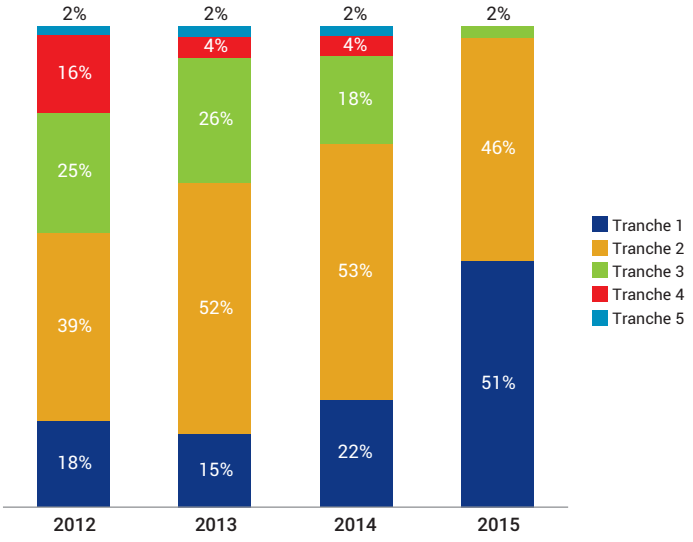
The funding is split into 5 funding tranches corresponding to 5 key stages of the clinical trial implementation process:

- Tranche 1 is paid 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 collection 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.

Over the 2012-2015 period, 192 projects were selected. Figure 21 presents the distribution in 2018 of the projects selected over the years according to their respective status, represented by their funding tranche.

FIGURE 21

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



In total, in 2018:

- 47% of projects requested tranche 2, corresponding to the regulatory authorisation stage;
- 27% of projects requested tranche 3, 4 and 5, corresponding to "50% inclusion" status, complete monitoring of all inclusions and publication status;
- 25% of the funded projects did not start the clinical study since the regulatory authorisations were not obtained;
- 4 to 6 years after project selection, only 3 projects reached publication status.

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

- To develop new models of study to reduce the duration of patient inclusion;
- To reduce the delay for obtaining authorisations. This subject is in progress and ANSM is working actively to achieve this improvement with fast-track procedures – to be able to start inclusion;
- To solicit project sponsors and/or investigators to obtain information on the different difficulties faced while increasing the steering of the clinical trials launched for a better assessment of feasibility in the future.

Public and private partnerships

Since 2011, INCa has promoted early access to innovative drugs for patients via cooperation with pharmaceutical laboratories that supply and distribute innovative drugs under the cooperation agreement 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 to offer patients, for indications which would probably not have been investigated by pharmaceutical firms.

At the end of 2017, INCa signed a new agreement with Roche Pharmaceuticals to provide three innovative drugs to the 16 CLIP²s:

- Atezolizumab, an anti-PD-L1 Mab;
- Cobimetinib, a MEK inhibitor;
- Ipatasertib, an Akt inhibitor.

This agreement enabled the launch of a call for proposals in 2018: 36 projects were submitted from 13 CLIP²s, three of which are paediatric projects. Among the 13 preselected projects, 4 of these were selected for a total amount of €2.8M (Tables 31 & 32).

TABLE 31
FEATURES OF THE CALL FOR PROPOSALS FOR EARLY-PHASE CLINICAL TRIALS

Objectives	The purpose of this call for proposals is to select, based on applications, early-phase clinical trial proposals aimed at assessing the drugs Atezolizumab, Cobimetinib and Ipatasertib, administered in monotherapy or combination therapy.
Programming and operating institution	INCa
Funding institution	INCa /ARC Foundation
Funding	**€2.64M** **INCa: €1.57M** **ARC Foundation: €1.07M**
Proposals submitted	**36**
Projects selected	**4**
Selection rate	**11.1%**

TABLE 32
MAIN FEATURES OF THE SELECTED PROJECTS

Agent	Title	CLIP² centre and PI
UCPVax : a CD4 TH1-inducer cancer vaccine – INSERM **Atezolizumab: anti-PD-L1 monoclonal antibody - Roche**	VolATIL: A phase II study evaluating the interest of combining UCPVax, a CD4 TH1-inducer cancer vaccine, and atezolizumab for the treatment of HPV-positive cancers	CLIP² Bourgogne Franche Comté - CHU de Besançon Prof. Christophe BORG
Atezolizumab: anti-PD-L1 monoclonal antibody – Roche **Cobimetinib: MEK inhibitor - Roche**	COBIATEZOSARC: A multicentre Phase I-II study evaluating the combination of an MEK inhibitor and a PDL1 inhibitor in paediatric and adult patients with locally advanced and/or metastatic soft tissue sarcoma	Centre Léon Bérard Dr. Nadège CORRADINI
Atezolizumab: anti-PD-L1 monoclonal antibody – Roche **G100 TLR4 agonist - Immune design**	AGADIR: Atezolizumab combined with intratumoral G100 AnD Immunogenic Radiotherapy in patients with advanced solid tumours	Institut Bergonié Dr. Paul SARGOS
Atezolizumab: anti-PD-L1 monoclonal antibody – Roche **Ipatasertib : Akt inhibitor – Roche** **Bevacizumab: anti-VEGF monoclonal antibody – Roche**	IMMUNOGAST: An umbrella phase 2 trial to assess personalised targeted IMMUNOtherapy-based regimens in recurrent advanced/metastatic GASTric adenocarcinoma patients	Hospices Civils de Lyon Prof. Benoit YOU

The aim of this programme is to assess innovative drugs outside pharmaceutical company development plans on academic questions, and to propose drug combinations. In compliance with the objectives of this programme, one project aims to evaluate drugs in the paediatric population (Dr. Corradini) and two projects will assess innovative associations:

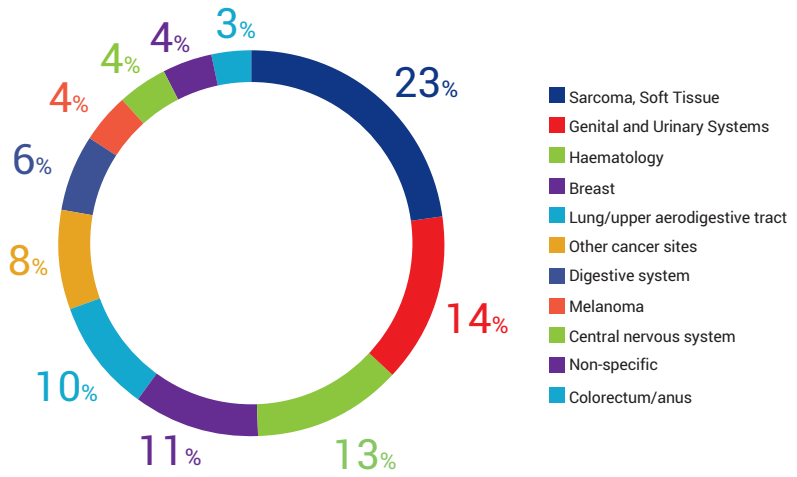
- one with drugs originating from academic research (Prof. Borg);
- the other combining drugs provided by two pharma firms (Dr. Sargos).

In total, INCa launched 13 specific calls for proposals to propose 24 drugs under development and 19 projects were funded for €12.48M to evaluate these molecules. Out of the 19 projects:

- 14 have actually started and the last 4 will start during 2019;
- 14 were co-funded by the ARC Foundation (INCa Funding: €7.91M; ARC Foundation funding: €4.56M).

The distribution of the funded projects highlights the specificity of this programme, with a large proportion of rare diseases. Sarcoma and Soft Tissue trials account for almost a quarter of funded projects compared to the PHRC-K programme where they account for 5%, and haematology and digestive system represent a large proportion of the funding (Figure 22).

FIGURE 22
DISTRIBUTION OF SELECTED EARLY CLINICAL TRIALS ACCORDING TO CANCER SITES STUDIED OVER THE 2009-2018 PERIOD



Precision medicine initiatives

THE AcSé PROGRAMME

As part of the 2nd National Cancer control plan, the AcSé programme (Secured Access to innovative therapies) was launched by INCa in 2013 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 development by 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. The first findings show the efficacy of crizotinib for which the indication could be extended to different cancer types, such as anaplastic lymphomas (presenting with an

Launch of the CLIP² designation

Following the two previous designations (2010-2014 and 2015-2019), the French National Cancer Institute in partnership with the French Cancer League, launched a third designation campaign in July 2018. This designation aims to renew and reinforce the national network of centres with expertise in early-phase clinical trials for cancers (solid tumours and malignant haemopathies) in adults and children, adolescents and young adults.

This call for applications was open to centres that were previously designated as well as centres conducting early-phase clinical trials and seeking designation.

AcSé-Crizotinib:
246 patients included

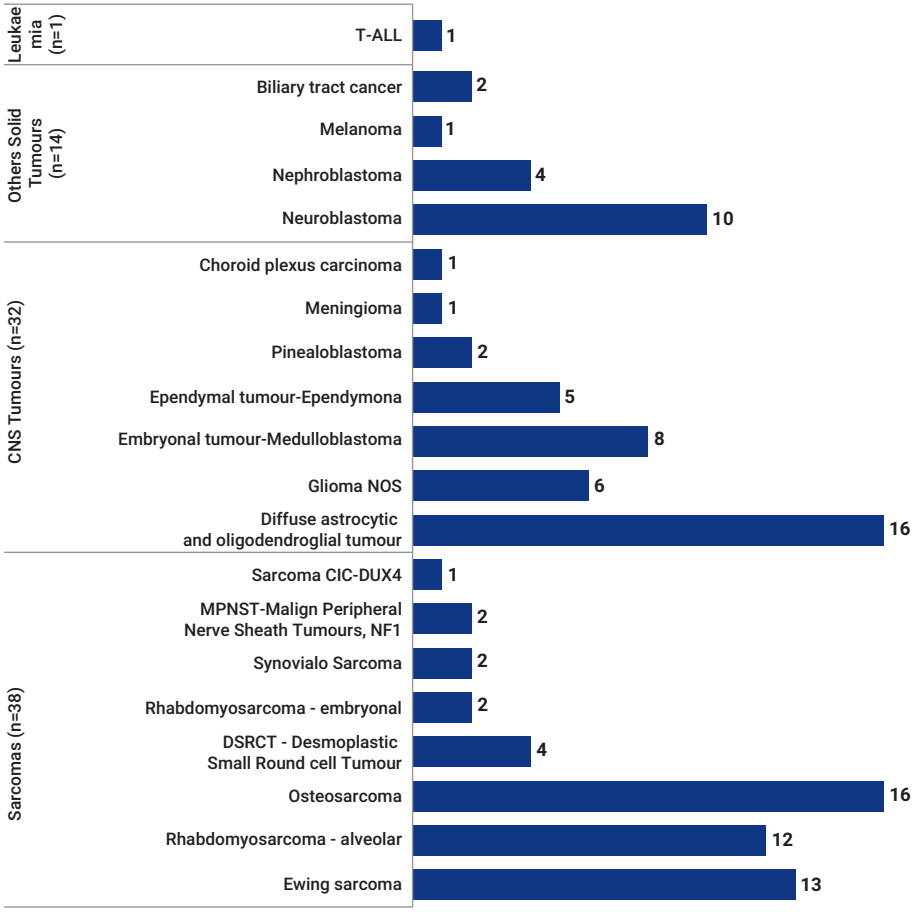
AcSé-Vemurafenib:
204 patients included

AcSé-eSMART:
110 children included

ALK translocation), oesogastric adenocarcinomas, stomach cancer, certain sarcomas or lung cancer (carrying a *MET* mutation);

- **AcSé-Vemurafenib,** launched in 2014, to evaluate the efficacy of vemurafenib, indicated in the treatment of melanomas in patients with the *BRAF V600* mutation. This trial, initially planned for 4 years of inclusion, was the subject of 2 extensions of 12 months and 6 months (i.e. the end of inclusions planned for 30 April 2019) and made it possible to treat **204 patients** with a non-specific *BRAF* mutation in more than 10 different cancer types. The first findings show 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 of Refractory Tumors 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 child-

FIGURE 23
AcSé-ESMART: DESCRIPTION OF RECRUITMENT BY STUDY ARM (DECEMBER 2018)



ren and adolescents with refractory or relapsed cancers, depending on the tumour molecular profile systematically screened within the framework of a specific PHRC-K project funded in 2014, the MAPPYACTS project. This innovative protocol has been already approved in 3 countries (France, Spain and Netherlands) and 2 of them are already active in recruitment, leading to the enrolment of **110 children** (Figure 23). The next European roll-out milestone is the opening of patient enrolment in Spain – depending on the next implementation of a national molecular analysis programme - Italy and UK;

- **AcSé-Nivolumab** and **AcSé-Pembrolizumab,** launched in May 2017, and aim to evaluate two anti-PD-1 agents in the treatment of rare cancers, based on the organisation of rare cancer networks designated by the French National Cancer Institute. In this context, patients with rare cancer also benefit from secure access to innovation through anti-PD-1 immunotherapy, and scientific data on these new drugs will be collected in controlled clinical trials. In total, 13 types of rare cancers (cohorts) are involved in these two trials, which aim to include almost 550 patients subject to therapeutic failure over three years. To date, **194 and 158 patients** have been respectively enrolled in AcSé-Nivolumab and AcSé-Pembrolizumab, while one cohort (Non-colorectal MSI-H cancer) has already reached the inclusion number target (n=50) (Figures 24 and 25).

AcSé- Nivolumab:
194 patients included
AcSé- Pembrolizumab:
158 patients included

FIGURE 24
AcSé-NIVOLUMAB: DESCRIPTION OF RECRUITMENT BY COHORT (DECEMBER 2018)

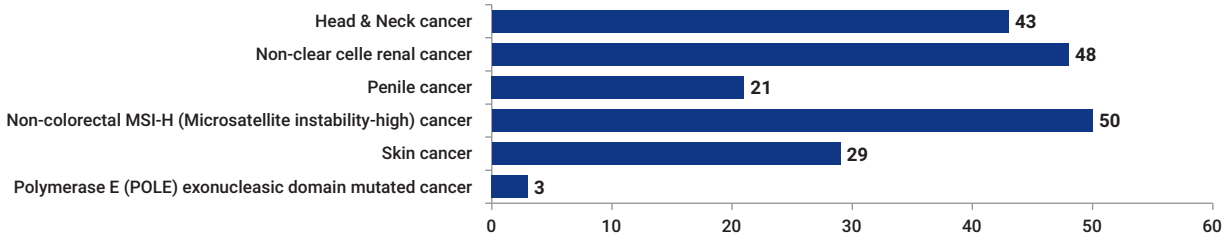
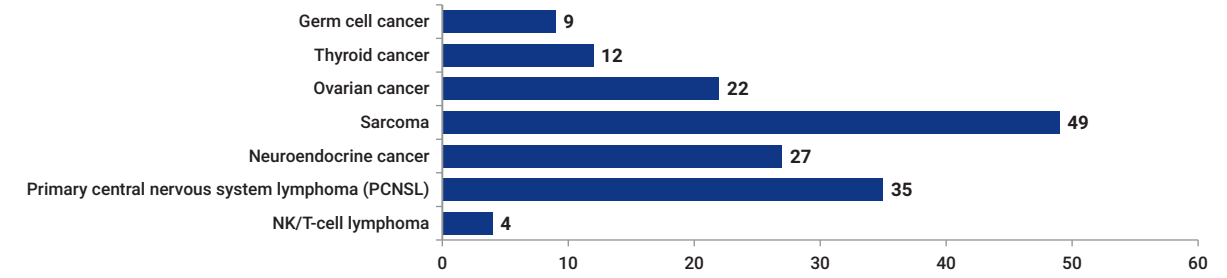


FIGURE 25
AcSé-PEMBROLIZUMAB: DESCRIPTION OF RECRUITMENT BY COHORT (DECEMBER 2018)



International visibility of AcSé programme

- **ASCO 2018**

Oral communication

AcSé crizotinib ASCO 2018 Biomarker-driven access to crizotinib in ALK, MET or ROS1 positive (+) malignancies in adults and children: the French national AcSé Program

Poster presentation

AcSé crizotinib ASCO 2018 The activity of crizotinib in chemo-refractory MET-amplified esogastric adenocarcinomas: results from the AcSé-crizotinib program

- **WCLC 2018**

Oral communication

Activity of crizotinib in MET or ROS1 positive (+) NSCLC: results of the AcSé trial

Vemurafenib in Patients Harboring V600 and Non-V600 BRAF Mutations: Final Results of the NSCLC Cohort from the AcSé Trial

- **ESMO 2018**

Poster

Biomarker-driven access to crizotinib in ALK, MET or ROS1 positive (+) malignancies in adults and children: the French national AcSé Program

Vemurafenib in patients (pts) harboring BRAF V600 mutation. Results of non-small cell lung cancer (NSCLC) cohort from the AcSé trial

ESMO Immuno-Oncology IO 2018

Poster presentation

AcSé-Nivolumab / AcSé-Pembrolizumab

AcSé immunotherapy trials: Anti-PD-1 therapy for adult patients with selected rare cancer types

- **ITCC 2018**

Oral communication

European pediatric precision medicine program in recurrent tumors: From molecular profiling trial towards AcSé-eSMART multiarm proof-of-concept study

- **AACR 2018**

Educational workshop

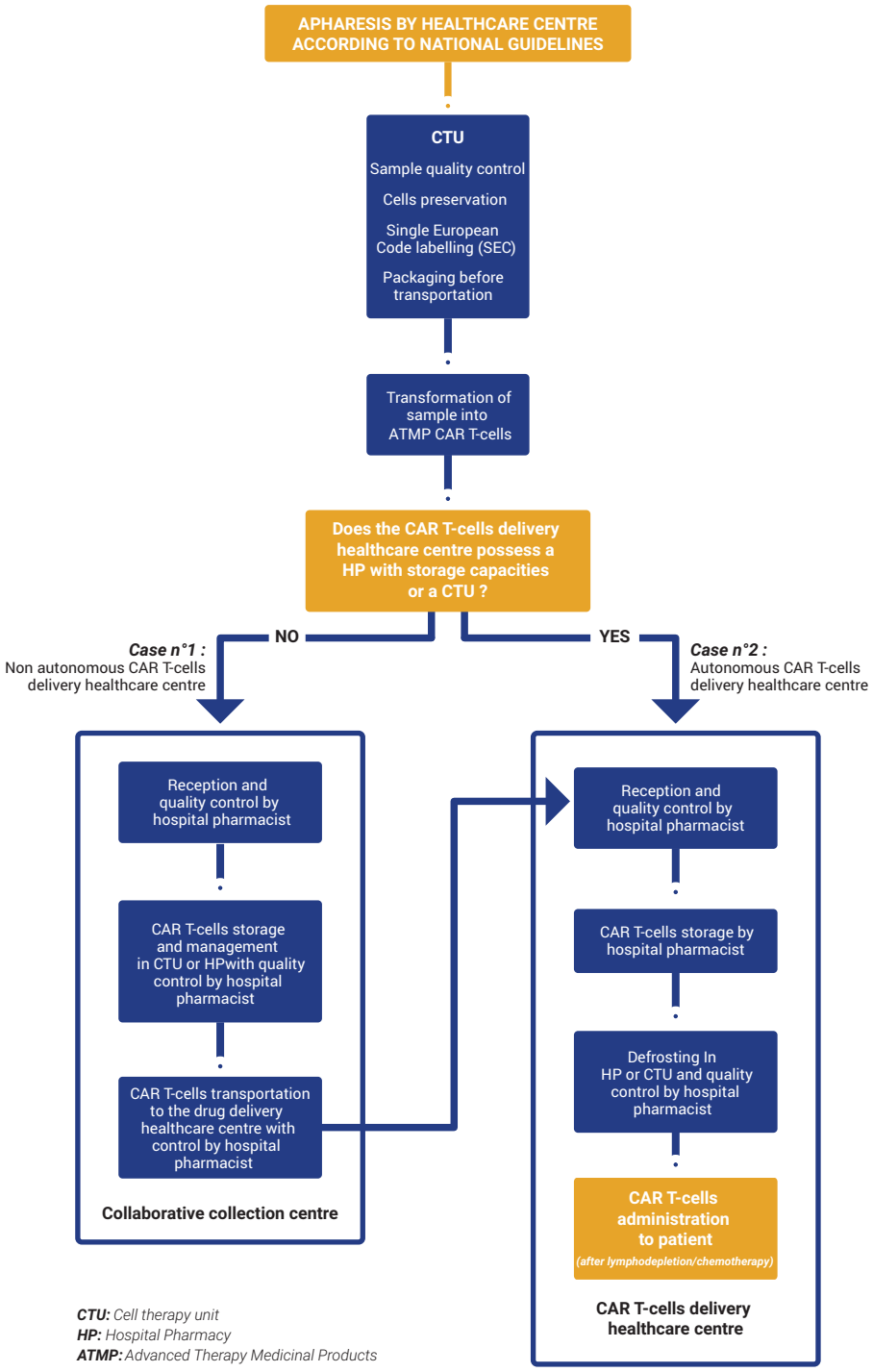
From the statistical bench to bedside: implementing proper designs in the eSMART paediatric combination phase I/II trials

CAR T-CELLS (RECOMMENDATIONS)

As the next generation in cancer immunotherapies, the potential of Chimeric Antigen Receptor T-cells (CAR T-cells) is recognised worldwide, first in acute lymphoblastic leukaemia and B-cell lymphomas. The FDA has approved two anti-CD19 CAR T-cells: tisagenlecleucel (Kymriah®) in August 2017, and axicabtagene ciloleucel (Yescarta®) in October 2017. The EMA recommended the first two marketing authorisations for Kymriah® and Yescarta® in the European Union in August 2018.

Since November 2017, while several industrial trials using CAR T-cells were conducted in France, INCa was commissioned by the French Minister of Health to anticipate a secured arrival of CAR T-cells on the market, and to support academic research in France in terms of quality, safety and efficiency. Throughout 2018, INCa brought together all the stakeholders (scientific, clinical, pharmaceutical and health care professionals, learned societies, national institutions) involved in the use of CAR T-cells. All the issues associated with CAR T-cells were discussed, particularly regarding their proper use including the management of therapeutic strategies and safety profile, as well as the organisation of care and academic research during a kick-off meeting organised with national institutions and agencies in November 2017.

FIGURE 26
CAR T-CELLS DELIVERY PATH



CTU: *Cell therapy unit*
HP: *Hospital Pharmacy*
ATMP: *Advanced Therapy Medicinal Products*

The Clinical Guidelines and Medicines Department at INCa led a collaborative project to define the criteria and the approval process to be used nationally. These guidelines aim to contribute to the building of a National legal framework based on article L.1415-2 of the French Public Health Code with dedicated criteria defining appropriate health care centres allowed to use CAR T-cells. This national legal framework is due to be published shortly.

In parallel, a working group dedicated to CAR T-cell academic research was set up with major scientists and researchers working in the field. A dedicated research kick-off meeting was organised in October 2018, and three sub-working groups were set up. These groups will specifically address basic and translational research, prerequisites for products and platforms, and clinical research, to draw up specifications to help INCa support this academic research. Beyond national priority areas for academic research, the major issues raised by the three academic research sub-working groups are as follows:

- vectors;
- good manufacturing processes for basic research;
- regulatory aspects and transfer to clinical research;
- funding of costly projects;
- follow-up of patients (epidemiological as well as biological monitoring).

The research field on CAR T-cells is now growing rapidly but it is still necessary to develop mature, fully understood and automated good manufacturing processes. It appears essential to coordinate a national policy on the issues regarding academic research on CAR T-cells and identify obstacles and incentives on which INCa could act. Academic research on CAR T-cells is a high priority for INCa, willing to boost and foster innovation in order to propose a global and comprehensive academic offering, non-competitive and complementary to the industrial offering. Work avenues still need to be developed nationally and internationally.

OSIRIS DATA SET

In the era of precision medicine, the interpretation of data, of increasing size and complexity, requires structured and interoperable databases, which will allow better stratification of patients for the management of their cancer. In this context, the OSIRIS group (inter-SIRIC group on data sharing and integration of clinical and biological data in oncology) was initiated by the SIRICs, with the aim of allowing the different centres to share biological, clinical and genomic data to foster their use in research.

The main difficulty associated with data sharing is the heterogeneity of the data and of information systems. The structuring of data, both biological and clinical, has thus constituted an essential requirement for the work of the OSIRIS group. The network has proposed a list of 130 clinical and omic items published on INCa's website in 2018 (https://en.e-cancer.fr/OSIRIS-a-national-data-sharing-project). This "OSIRIS set" establishes a minimum dataset for the sharing of clinical and biological data in oncology. The list is based on a conceptual and temporal cancer disease model agreed upon within the group.

The OSIRIS set has been organised with a terminology designed to be scalable and modular. In the future, other specific terminology aspects could be added according to tumour location (breast, lung, digestive tract etc.), treatment (chemotherapy, radiotherapy, and immunotherapy) and analysis (e.g. other genomic fields).

Following the first stage of structuring the clinical and omic dataset that led to the definition of the OSIRIS Set, several partners (Léon Bérard Centre, Institut Curie, Bergonié Institute, Georges Pompidou European Hospital, Montpellier Cancer Institute, Paoli-Calmettes Institute, Gustave Roussy, UNICANCER, Hôpital Saint-Louis) launched a project funded by INCa (budget 300 k€) to carry out a proof of concept. The goals are to:

- validate the dataset on genomic-guided clinical trials;
- set up a dedicated interface, within the centres promoting these programmes, allowing the effective sharing of data from about 250 patients from several precision medicine trials (ProfiLER, SHIVA, SAFIR, MOSCATO and PerMed);
- validate the approach proposed by the OSIRIS project by the regulatory authorities.

The proof-of-concept study is currently in progress and will end in June 2019. The key technical milestones have been completed as the warehouse network of searchable federated databases is now operational. The proposed structuring of clinical and biological data could be rolled out beyond the scope of this project. It would allow the interoperability of different sets of clinical and biological data collected as part of research projects, either academic or from industry. As such, the widespread use of the OSIRIS Set would have a major leverage effect for data sharing.

MOLECULAR GENETICS CENTRES UPGRADE AND IMMUNOTHERAPY DEVELOPMENT

Since 2006, INCa has supported the structuring of the 28 molecular genetics centres in order to ensure equal access to molecular diagnosis in France. 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. The new challenge is now to adapt to the rapid development of immunotherapy. The identification of biomarkers predicting the efficacy of checkpoint inhibitors is a major research challenge since only some patient subgroups respond to that therapy.

Two biomarkers, PD-L1 status and Microsatellite instability (MSI), are already used in care settings to determine the prescription of immunotherapies. Another biomarker, the Tumour Mutation Burden (TMB), is being tested in several clinical trials, and could be used in the near future.

INCa is supporting actions to accelerate the development and the roll-out of these tests in the 28 molecular genetics centres in France.

PD-L1

Pembrolizumab (monoclonal antibody anti-PD-1) was granted a marketing authorisation as a first-line treatment for adult patients with metastatic non-small cell type lung cancer where more than 50% of the tumour cells express PD-L1. It is now necessary to test this biomarker in routine clinical practice for a large number of patients. As early as 2015, INCa set up a working group with pathologists from

molecular genetics centres, in collaboration with the French Society of Pathology (Société française de pathologie, SFP) and the French Association for Quality Assurance in Pathological Anatomy (Association française d'assurance qualité en anatomie pathologique, AFAQAP), in order to tackle the quality assurance challenges of PD-L1 testing in clinical practice in a coordinated way. More specifically, in 2018, INCa funded AFAQAP to implement inter-laboratory external PD-L1 quality control.

Microsatellite instability

Errors in microsatellites, repeated DNA sequences particularly exposed to replication errors, are found very often when the MMR system (mismatch DNA repair protein system) is faulty (up to a 100-fold increase in the somatic mutation rate). The MMR status of a tumour can be investigated by IHC on the genes of the MMR system and/or by a molecular biology test evaluating microsatellite instability (MSI test).

Several clinical trials are currently evaluating the efficacy of checkpoint inhibitors on patients where the tumour presents a faulty MMR system. These molecules have not yet been granted a European marketing authorisation. However, the clinical trial, AcSé-Nivolumab, includes a cohort, now closed to enrolments, with non-colorectal cancer patients where the tumour presents high-status MSI. This status measurement was performed by the 28 molecular genetics centres, through specific funding support. Conducting these tests in different types of cancers highlighted technical problems, since immunohistochemistry and molecular biology markers were firstly developed in colorectal cancer. In this context, a specific task force, including pathologists and molecular biologists, was set up in 2018 to ensure the quality of the tests in the different cancer sites concerned.

Tumour Mutation Burden (TMB)

Another predictive biomarker of the response to immuno-oncology therapy, the TMB aims to measure the number of mutations carried by tumour cells over the whole genome and could be used in standard care in the near future. Its implementation requires analyses of large panels of genes (several hundred genes); however, most molecular genetics centres are only equipped to test a few dozen genes per patient. Even though no TMB-conditioned market authorisation exists in Europe yet, several clinical trials are currently evaluating the value of this biomarker for predicting the rate of response to immunotherapies. To anticipate the possible arrival of this biomarker, in 2018, INCa organised a task force with pathologists and molecular biologists to compile the needs of molecular genetics centres and devise ways to overcome the technology gap due to be created.

Clinical research organisation: structures, infrastructures and tools

COOPERATIVE INTERGROUPS

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

The designation of the Cooperative intergroups 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.

Their strong involvement in Action 5.2 of the 2014-2019 Cancer Control Plan targeting the enrolment of 50,000 patients per year in 2019, is anticipated, particularly in clinical trials aimed at major therapeutic challenges, i.e. for increasing survival and reducing treatment side-effects and delayed effects.

In 2018, two further cooperative intergroups were designated, in the field of myeloma and urology, leading to a total of 13 designated cooperative intergroups (Table 33).

TABLE 33
COOPERATIVE INTERGROUPS DESIGNATED IN 2017 AND 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

PHARE findings

In 2006, INCa launched the national randomised controlled trial in breast cancer PHARE (Protocol for Herceptin® as Adjuvant therapy with Reduced Exposure). This study aims to compare the effects of 6 months *versus* 12 months of treatment with Herceptin® in terms of disease-free survival in patients previously treated with Herceptin® for 6 months.

The statistical analysis of the PHARE trial data published in 2013 in *Lancet Oncology*[3] did not demonstrate that 6 months of treatment with adjuvant trastuzumab is non-inferior to 12 months of such treatment for women with HER2-positive early breast cancer.

The final analysis of the PHARE trial data conducted in 2018 concluded that, definitively, the PHARE study failed to prove non-inferiority of 6 months versus 12 months of trastuzumab adjuvant therapy. The 12-month duration of trastuzumab therapy remains the standard in adjuvant treatment for patients with HER2-positive early breast cancer. These findings were presented by Prof. Xavier Pivot, the coordinating investigator of the PHARE trial, as part of the San Antonio Breast Cancer Symposium plenary session in December 2018.

In the field of cardiotoxicity, the analysis of the data from PHARE resulted in a publication in 2018: Jacquinot et al.[4] demonstrated that LVEF decreased during treatment with trastuzumab and rose again after the completion of treatment without returning to the initial values for a substantial subset. These findings would suggest investigating some strategies aimed to improve the ability to achieve a full recovery.

In October 2018, INCa organised the annual cooperative intergroup meeting. This meeting allowed intergroups to present their achievements in relation to the objectives of the designation call. It also allowed the intergroups to discuss future collaboration with INCa such as the promotion and the valuation of the clinical and translational research sponsored by the intergroups, and their contribution to the clinical and translational research strategy of INCa.

Enrolment of patients in clinical trials

Initiated under the 2003-2007 Cancer Control Plan and strengthened by the 2009-2013 Cancer Control Plan, INCa's annual survey assesses clinical research activities in oncology in France. This survey provides an estimation of the enrolment rate in cancer clinical trials each year in France. These data are presented annually to the French President. Data for year 2017 were reported by University Hospitals, Cancer Care Centres, Health Care centres and "EMRC" (Mobile Clinical Research Teams) through the 7 "GIRCI" (Interregional Clinical Research and Innovation Groups).

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

The results show a steady increase in the number of patients enrolled in clinical trials:

- There is a 15.6% increase in the number of patients enrolled in 2017 compared to 2016, with 60,602 patients included in cancer clinical trials for 2017 (figure 27), 31,179 of these were enrolled in a therapeutic clinical trial;

3. Xavier Pivot et al.(2013). 6 months versus 12 months of adjuvant trastuzumab for patients with HER2-positive early breast cancer (PHARE): A randomised phase 3 trial. 2013 Jul;14(8):741-8. doi: 10.1016/S1470-2045(13)70225-0.
4. Jacquinot et al (2018). Fluctuation of the left ventricular ejection fraction in patients with HER2-positive early breast cancer treated by 12 months of adjuvant trastuzumab. The Breast 2018 Oct 41:1-7. doi: 10.1016/j.breast.2018.06.001.

International Rare Cancer Initiative

The International Rare Cancer Initiative (IRCI) is a strategic partnership between the NCI (US), NIHR and CRUK (UK), the EORTC (Europe), INCa (France), CCTG (Canada), COSA (Australia) and JCOG (Japan). The driving mission of IRCI is to facilitate the development and delivery of hypothesis-driven interventional clinical trials for patients with rare cancer (see http://www.irci.info/http://www.irci.info/).

The initiative to date has convened working groups looking at twelve rare cancer types and opened seven trials, as well as stimulating a number of other publications on rare cancers.

In 2018, IRCI ran its second expression of interest (EOI) call for new working groups wishing to develop an international trial in a rare cancer. It was encouraging to see a high degree of interest from the international community, with 24 applications received. All the participating countries in IRCI had at least one lead applicant from their country submit an EOI, showing this initiative has true global reach and interest. Ten applications were successful:

- 3/10 applications to join to form the Rare Genitourinary (GU) Tumours group;
- 2/10 applications to join to form the Rare Haematological Tumours group;
- 1/10 applications to merge into Merkel Cell Carcinoma to become the Rare Skin Cancer group;
- 1/10 application to merge into the existing Relapsed/ Metastatic Anal Cancer Group;
- 1/10 application to merge into the existing Salivary Gland Cancer Group;
- 1/10 application to merge into the existing Small Bowell Adenocarcinoma Group.

The Board agreed to arrange a 1-day meeting for the lead applicant in synovial sarcoma.

Among the 10 applications, it is important to mention that 5 of these have a French leader, collaborator or co-applicant: Olivier Cussenot (APHP, Hôpital Tenon, Paris to join the Rare Genitourinary (GU) Tumours group, Juliette Thariat (Centre François Baclesse, Caen) to merge into the existing Salivary Gland Cancer Group, Richard Delarue (APHP, Hôpital Necker, Paris) to join the Rare Haematological Tumours group, Julien Haroche (APHP, Hôpital de la Pitié-Salpêtrière, Paris) to join the Rare Haematological Tumours group and Pierre-Laurent Puig (APHP, Hôpital Européen Georges Pompidou, Paris) to join the existing Small Bowell Adenocarcinoma Group.

Meeting spaces will be allocated to the working groups at ASCO each year to discuss memberships and trial concepts. Groups will be facilitated for up to three years, at which time it would be anticipated that trial set-up would be under way.

FIGURE 27
ENROLMENT OF PATIENTS IN CLINICAL CANCER TRIALS IN FRANCE ACCORDING TO THE TYPE OF SPONSOR 2008-2017 (INCA SURVEY)

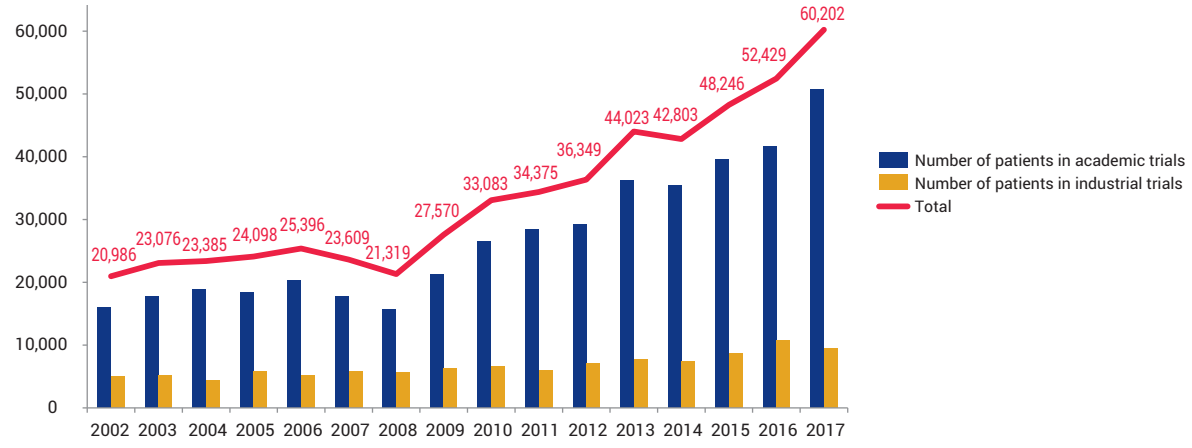
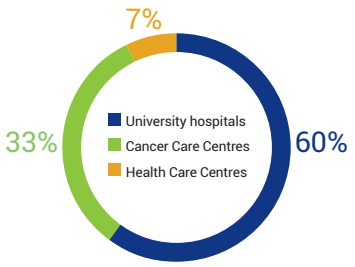


FIGURE 28
DISTRIBUTION OF PATIENTS ENROLLED IN CLINICAL CANCER TRIALS IN 2017 ACCORDING THE TYPE OF CARE PROVIDERS (INCA SURVEY)



- Over the last 10 years (2008-2017), the number of patients enrolled in cancer clinical trials has more than tripled, probably due to the Actions of the different Cancer Control Plans (figure 27);
- The ratio of enrolment in academic vs. industrial trials has remained stable over the years, with a significant predominance of inclusions in academic trials (82% vs. 18%). However, between 2008 and 2017, greater progression has been observed in academic trials (+ 223%) than in industrial trials (+ 69%) (figure 27);
- The distribution among the different care providers has been stable over the years: In 2017, 60% of patients were enrolled in University Hospitals, 33% in Cancer Care Centres, and 7% in Health Care Centres (figure 28).

INCa's cancer research clinical trial registry

Since 2007, INCa's cancer clinical trial registry has allowed easy access to clinical cancer trials conducted in France. It is freely accessible on INCa's website, and enables provision of regularly updated quality 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.

FIGURE 29
DISTRIBUTION OF CLINICAL TRIALS ACCORDING TO TYPE OF TRIAL (DECEMBER 2018)

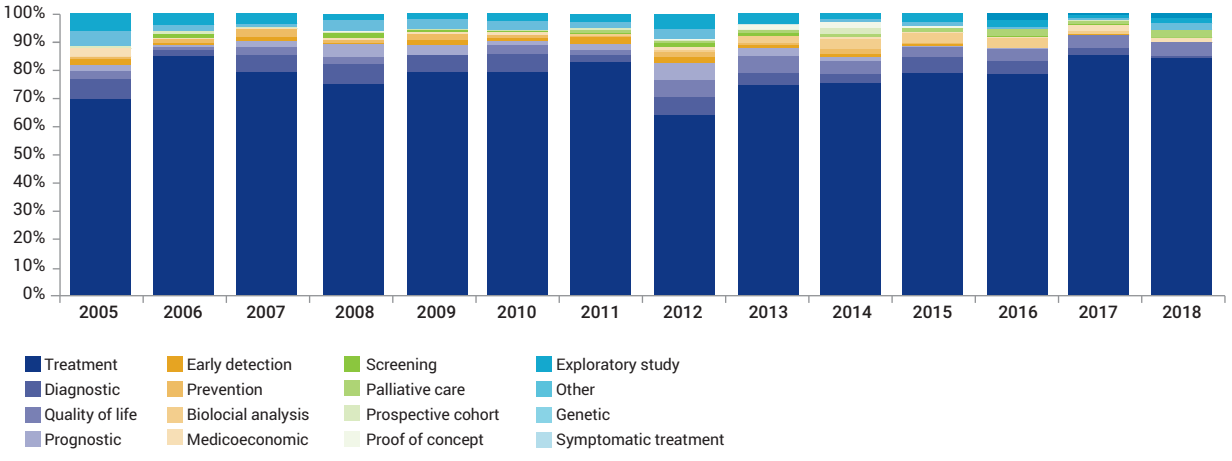


TABLE 34
INCA'S CANCER CLINICAL TRIAL REGISTRY

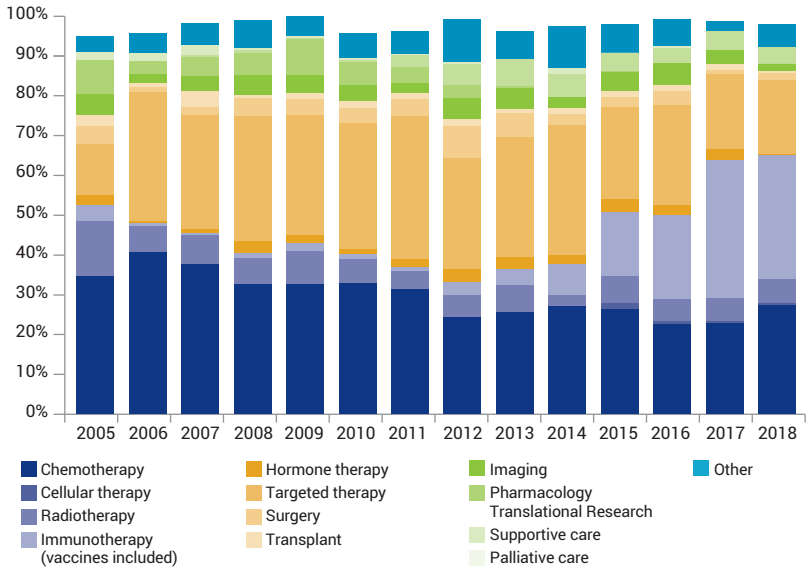
Objectives	Provide information on clinical cancer trials conducted in France.
Results	3,009 clinical trials advertised on INCa's website in December 2018, sponsored by more than 371 industrial and academic bodies. • 722 ongoing recruiting trials. – 60% are sponsored by academic bodies. – 77% are treatment trials. • 7% of trials posted are recruiting children, and 66% of these trials are mixed trials (recruiting both children and adults, among 37% of trials recruiting from 12 years of age) – In 2018, 80% of the trails including children were mixed trials. (60% of trials recruiting from 12 years of age)

Figure 29 presents the distribution of trials according to the type of trial and shows that therapeutic trials represent the majority. Interestingly, as of 2014, prognosis, medico-economic and prevention research studies are on the decline. This trend is also observed for studies on palliative care and genetics. From 2013 to 2017, there was an increase in trials addressing biological analysis in tumour sample in order to identify biomarkers.

The distribution of trials according to intervention highlights the increase in studies addressing immunotherapy from 2012 which represented 30% of the trials in 2018 (Figure 30). Trials testing targeted therapies increased over the 2006-2014 period (about 32% of trials), but since 2015 there are fewer trials on targeted therapies (about 20% of trials). We can also note a rise in trials in supportive care from 2011 (about 5% of trials). There were good proportions of trials in translational research from 2005 to 2012, but from 2013, there has been a drop in these trials in the registry.

FIGURE 30

DISTRIBUTION OF CLINICAL TRIALS ACCORDING TO TYPE OF INTERVENTION (DECEMBER 2018)



RESEARCH IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY AND PUBLIC HEALTH

One of INCa's goals is to bring human and social sciences, epidemiology and public health research on cancer in France up to the best international standards. In line with the 2014-2019 Cancer control plan, particular efforts are being devoted to increase basic and health intervention research. Specific emphasis is placed on reducing social inequalities related to cancer, as well as increasing the impact of cancer prevention measures, the participation rates in national screening programmes, and access to care.

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

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

2018:
15
projects were funded out of 115 submitted for a total amount of
€3.97M

THE PROGRAMME IN 2018

In 2018, 15 projects out of the 115 submitted were selected for a total amount of €3.97M. The selection rate is 13% (Table 35). Among the 115 projects, 7 were outside the scope and 8 not eligible.

TABLE 35
FEATURES OF THE HSS-E-PH PROGRAMME IN 2017

Objectives	To encourage the emergence of original research proposals, in terms of subject matter and approaches, and of scientific excellence in the various HSS-E-PH disciplines applied to cancer; To drive research on emerging and innovative topics to open new perspectives in our understanding of cancer issues in social and human sciences, epidemiology and public health; To develop and strengthen multidisciplinary scientific research by associating researchers from different disciplines around a specific question or objective, in order to develop the most relevant response.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€3.97M
Proposals submitted	115
Projects selected	15
Selection rate	13%

Among the 100 projects within the scope of the call, 3 main research themes can be distinguished:
- 9 projects in epidemiology and biostatistics out of 58 submitted;
- 3 in social sciences out of 25 submitted;
- 3 in psychology out of 17 submitted.

The subjects of these 15 projects are:
- risk factors for cancer occurrence (4 projects);
- comorbidities (3 projects);
- end of life and palliative care (2 projects);
- health care system and public policies (2 projects);
- patients and relatives' experience (2 projects);
- overseas territories facing cancer (1 project).

According to the CSO classification, among the 15 projects funded, 12 are in the "Cancer Control" category (patient care and survivorship, behaviour, cost analysis and health care delivery, end-of-life care), and 3 in aetiology.

THE PROGRAMME OVER THE 2007-2018 PERIOD

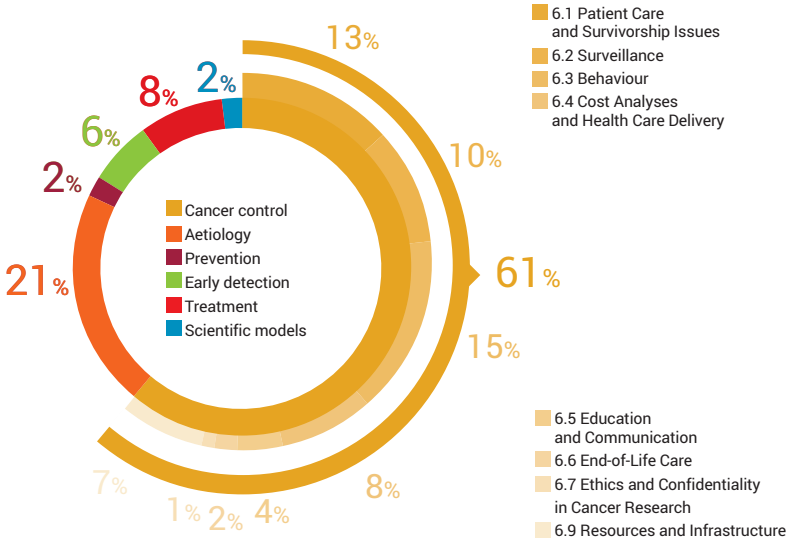
Since 2007, 209 projects out of 843 submitted have been selected for the investigator driven HSS-E-PH programme for a total amount of €44.14M (Table 36).

TABLE 36
TRENDS IN SELECTION AND FUNDING OF THE HSS-E-PH PROGRAMME OVER THE 2007-2018 PERIOD

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	TOTAL
Funding (in €M)	0.74	2.8	2.53	5.17	4.73	3.89	4.81	4.12	4.27	3.51	3.62	3.97	44.15
Proposals submitted	7	76	46	85	76	41	54	102	66	86	89	115	843
Projects selected	7	13	16	27	23	16	20	22	17	16	17	15	209
Selection rate (%)	100	17.1	34.8	31.8	30.3	39.0	37.0	21.6	25.8	18.6	19.1	13	24.7

Figure 31 depicts the distribution of projects funded according to the CSO classification and shows that Cancer control represents the main research category (60%) with projects focusing on patient care and survivorship, behaviours, surveillance, end-of-life care, ethics and confidentiality in the field of cancer research and awareness and communication. Then come aetiology projects (15%) allowing the identification of exogenous and/or endogenous factors related to the origin of cancers and risk factors.

FIGURE 31
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2007-2018 PERIOD



Population health intervention research (PHIR)

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

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

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

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

2018 :

9

projects selected for funding for an overall budget of

€2M

1/3 of the submitted proposals consisted of "emerging projects" highlighting growing interest in this funding track

50% of the selected proposals are emerging research projects, underscoring the validity of this funding tool.

TABLE 37
FEATURES OF THE POPULATION HEALTH INTERVENTION RESEARCH PROGRAMME IN 2018

Objectives	To promote the emergence of projects in intervention research applied to cancers, that are original and of scientific excellence, and likely to produce knowledge that is scientifically valid and socially useful; To encourage original partnerships between research teams in different disciplines (human and social sciences, public health [prevention/health promotion], epidemiology, biostatistics, etc.) and practitioners in the field (health promoters, medical, allied health, and social services personnel, community-based organisations, etc.), 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	**€2.00M**
Proposals submitted	**34**
Projects selected	**9**
Selection rate	**26.5%**

2010-2018:
47
projects have been funded (including 14 emerging research projects) for a total funding of
€12.14M

THE PROGRAMME IN 2018

In 2018, some significant changes were made to the call for proposals. The most important are:

- the types of "field" partners to involve, the role of patients and health care user associations, the addition of the notions of "empowerment", "shared decision-making" and "recovery", the accuracy of specifically disadvantaged population groups or the inclusion of a gendered approach;
- a point of attention on French overseas territories. A cross-cutting concern was included for the entire call for proposals coming from or covering these territories, in compliance with the objective to support the regional implementation of the Cancer Control Plan;
- some elements related to the dissemination and the use of the research project findings. A section was added in order to foster the methods for restitution and valorisation of findings further and to develop the necessary means through a process called "knowledge mobilisation". Moreover, so as not to overlap with the Tobacco control programme, projects addressing this issue were excluded, reducing the number of proposals submitted under this programme.

In 2018, out of 34 submitted projects, 9 were selected for funding, including 4 emerging projects, for a total budget of €2M. One-third of the submitted proposals consisted of "emerging projects", highlighting the growing interest in this funding track among the research community in the field of population health intervention research. However, it should also be noted that none of the proposals submitted in the form of "full projects" stemmed from previously funded emerging projects.

THE PROGRAMME OVER THE 2010-2018 PERIOD

Since 2010, out of 259 projects submitted, 47 projects were funded (including 14 emerging research projects) for a total amount of €12.14M (Table 38). On average, 29 projects are submitted each year with a 17.77% selection rate.

Although the "emerging research projects" funding track is recent, this kind of project accounts for almost a quarter of all selected and funded projects. Based on the experience of emerging projects converted to full proposals, INCa is expecting an increased number of high-quality full projects for the coming years.

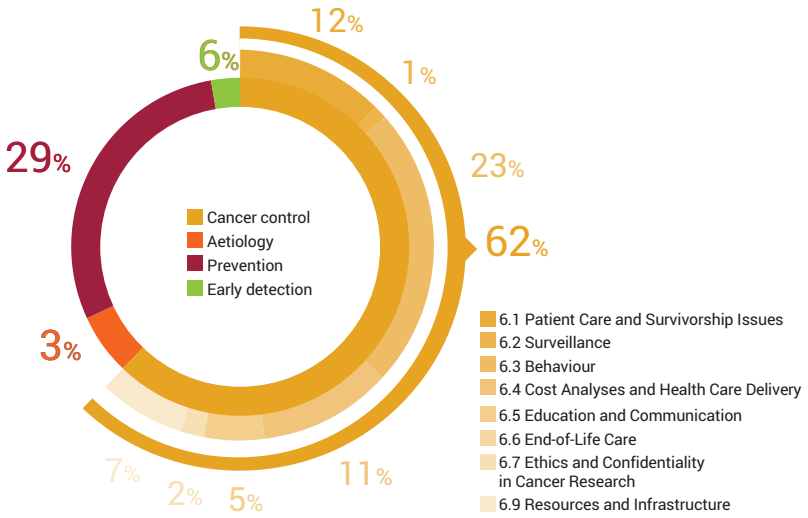
TABLE 38
TRENDS IN SELECTION AND FUNDING OF THE POPULATION HEALTH INTERVENTION RESEARCH PROGRAMME OVER THE 2010-2017 PERIOD

Year	2010	2011	2012	2013	2014*	2015	2016	2017	2018	TOTAL
Funding (in €M)	0.61	1.51	2.18	0.71	1.15	1.08	1.11	1.79	2	12.14
Proposals submitted	8	37	20	10	60	29	22	39	34	259
Projects selected	2	3	5	3	4	7	6	8	9	47
Selection rate	25%	8%	25%	30%	7%	24%	27%	20.5 %	26.5%	17%

*In 2014, partnership with IReSP, ARC Foundation, ANRS and MILDT.

Figure 32 highlights the distribution of the funded projects between 4 CSO categories: aetiology, prevention, early detection and cancer control. While prevention represents almost one-third of the projects in its own right, the projects dedicated to "behavioural change" within the "cancer control" category should also be taken into account to provide a more accurate figure. In doing so, research projects dedicated to prevention represent more than half of the total. Once again, in 2018, this "behavioural" subcategory increased significantly compared to 2017. With regard to the organs targeted, three groups of almost equal size can be identified: breast cancer, urinary tract and projects not targeting a specific organ.

FIGURE 32
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2010-2018 PERIOD



International symposium dedicated to Population health intervention research

The year 2018 was devoted to the preparation of a new international symposium whose theme was "contribution of PHIR to the reduction of inequalities". The event will be held in January 2019 as part of a partnership with IReSP and Inserm. The objectives of this international symposium are to foster exchanges between researchers, public decision-makers and healthcare stakeholders on intervention research practices in public health, to strengthen the capacities of the actors and to support the development of innovative research projects involving all these stakeholders.

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

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

THE PROGRAMME IN 2018

In 2018, 2 projects were selected for funding by ITMO Cancer-Aviesan for a total amount of €0.36M (Table 39). One of the projects aimed to characterise the effects of professional exposure to asbestos, strong inorganic acids, formaldehyde and wood or leather dust on the upper aerodigestive tract cancer risk. The other aimed to explore, in a mouse model, the validity of using circulating miRNAs profiles to evaluate chronic exposure to ultrafine particles.

2010-2018:
52
cancer-related projects funded for
€7.8M

TABLE 39
FEATURES OF THE 2018 RESEARCH PROGRAMME IN EMPLOYMENT-HEALTH-ENVIRONMENT IN THE FIELD OF CANCER

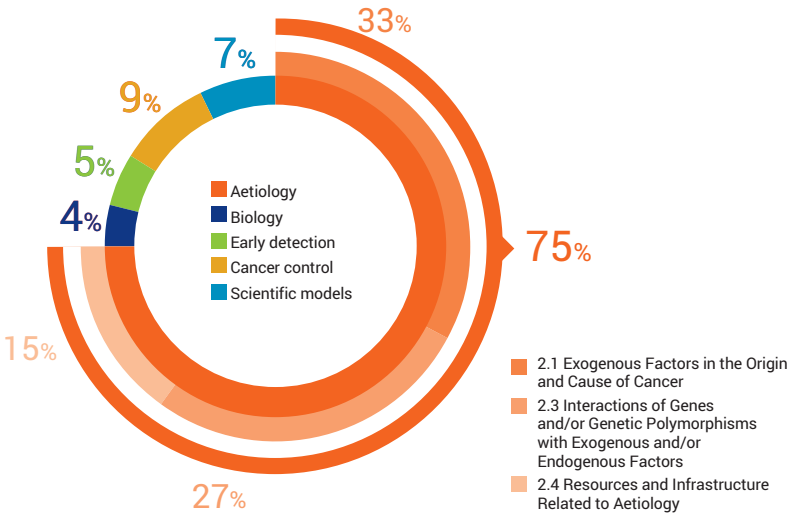
Objectives	To evaluate and analyse environmental risks for human health in the general population or at work. To address emerging and known risks, which can generate complex scientific debates, and for which a single approach can include concepts, methods and tools from different disciplines.
Programming institution	Anses
Operating institution	Anses
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€0.37M**
Letters of intent submitted	**42**
Full proposals submitted	10
Projects selected	**2**
Selection rate	4.8%

THE PROGRAMME OVER THE 2010-2018 PERIOD

Since 2010, 52 projects have been funded by the Cancer control plan within the framework of this programme for a total amount of €7.8M. The Ministry of Labour (DGT) and the French Environment and Energy Management Agency (ADEME) also funded cancer-related projects.

Over the 2010-2018 period, the funded projects primarily addressed the aetiology of cancer in accordance with the objectives of the call (75%). These projects largely aimed to assess the role of exogenous factors alone or in interaction with endogenous factors in the onset of cancer. The remaining projects dealt with cancer control, the development of model systems, or detection (Figure 33).

FIGURE 33
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OVER THE 2010-2018 PERIOD



Chlordecone issue in French Antilles

Chlordecone is a pesticide that was used for certain crops. Because of concerns about toxicity for humans, it was phased out or banned in most countries by the 1970s or 1980s. In France, particularly in the French Antilles, chlordecone continued to be used for banana farming into the 1990s. Furthermore, high prostate cancer (PC) rates are observed in the French Antilles.

This has given rise to concerns that exposure to chlordecone, both among banana plantation workers and in the general population via food, water and air, may have led to increased risks of PC.

In this context, the French Ministry of Social Affairs and Health requested INCa to provide the basis of novel research call that would answer whether there was a causal relationship between chlordecone exposure and prostate cancer risk in Martinique (another French archipelago in the Caribbean). The Institute will thus aim to support a scientifically robust and feasible study to provide scientifically-based evidence to clarify this relationship, underlying the putative relationship or not. To this end, INCa has set up a working group, bringing together first international renowned experts, and second all national stakeholders to discuss the manner in which to tackle this issue. Based on the recommendations issued, a call for proposals could have the following objectives and organisation:

- To build scientific communities and set up a national interdisciplinary consortium in order to create a new momentum in innovative fields, by developing complementary skills;
- The consortium will be organised based on work packages.

Support for training in HSS-E-PH: PhD programme

For the eighth consecutive year, the French National Cancer Institute, in partnership with the School for Advanced Studies in Social Sciences (EHESS) and the Doctoral Network in Public Health at the EHESP School of Public Health (EHESP), conducted 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 36 applications were submitted to INCa, slightly down on 2017 (43 applications). Out of these projects submitted, 5 were classified outside the scope of the call for applications. The 36 projects reviewed are divided into 3 research categories. Table 40 presents the distribution of the applications reviewed.

The distribution of projects according to discipline is substantially consistent between 2017 and 2018.

Following the review process, including interviews of applicants, four PhD theses were selected for funding (Table 41).

Over the 2007-2018 period, 38 PhD theses were supported for a total amount of €3.67M.

In 2018 : 4 PhD students were awarded: psychology, sociology and biostatistics.

TABLE 40
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.)	13
Epidemiology or biostatistics	13
Human sciences (psychology, cognition and learning, psychoanalytic studies, science of physical activity, etc.)	10

2007-2018: 38 PhD theses supported for an overall amount of €3.67M

TABLE 41
DOCTORAL FELLOWSHIPS FUNDED IN 2018

Title	Discipline
Understanding determinants of human papillomavirus (HPV) vaccine hesitancy among mothers in France: setting the stage for future successful interventions to improve primary prevention of cervical cancer through vaccination in France	Epidemiology
Drug exposures and risk of skin cancers in the E3N cohort	Epidemiology
Personalised medicine in oncohaematology: patients' representations and attitudes	Psychology
Study of the associations between lifestyle behaviours assessed by connected health wearables and psychological well-being after cancer in the French E4N cohort study	Epidemiology

INTERNATIONAL COMMITMENTS

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

Recent developments in research and innovation have improved our understanding of cancer. They are based on national and international cooperation between key players in cancer control. This cooperation can make a difference by creating new opportunities for research and innovation, by mobilising the international community in the fight against cancer, without forgetting the imperative of helping the least developed countries.

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

- implementing partnerships and strategic initiatives to encourage cutting-edge research and innovation;
- strengthening European cooperation in cancer control ;
- developing governance, international mechanisms and instruments for cancer control (WHO, IARC, UICC, etc.);
- providing international expertise in research, care and medicines with France's priority cooperation countries.

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

FIGURE 34
INCA'S GLOBAL PORTFOLIO

INCa's participation in European actions

In 2018, 1.9 million people died from cancer in Europe[5], representing one out five cancer-related deaths worldwide. Although health remains under national jurisdiction, the European Union has implemented numerous actions in cancer control, complementing the efforts of the Member States and improving coordination at a European level. This commitment will be reiterated in the next multi-annual financial framework (2021-2027), through new and continued initiatives: the Horizon Europe programme.

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

FIGURE 35
KEY ELEMENTS OF THE NEW EU RESEARCH AND INNOVATION PROGRAMME, HORIZON EUROPE

Horizon Europe is the new EU Research and Innovation Programme	
Previous Programme	Horizon 2020
Period	7 years (2021-2027)
Budget	€100 billion
Objectives	- To strengthen the EU's scientific and technological bases - To boost Europe's innovation capacity, competitivness and strengthen - To deliver on citizen's priorities and sustain our socioeconomic model and values
Structure	Three pillars: 1) Open Science 2) Global Challenges and Industrial Competitiveness 3) Open Innovation
Key Novelites	- Creation of the European Innovation Council - New R&I Missions - Extended association possibilities - Open science policy - News approach to Patnerships

In 2018, 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 5 joint or transnational actions in the areas of translational research (TRANSCAN-2, 2015-2020), rare cancers (JARC, 2016-2019), innovation (iPAAC, 2018-2021), and social and economic impacts of the disease (CHRODIS+, 2017-2020).

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.

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

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

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

As leader of WP9, the Institute convened all partners in July 2018 to Paris for the kick-off meeting. The institute has particularly made progress on the first task dedicated to clinical practice guidelines and reference frameworks related to the use of immunotherapies. Indeed, a mapping of existing clinical practice guidelines placing innovative immunotherapies (with a focus on checkpoint inhibitors and CART-cells) was performed gathering results from a literature review and from a questionnaire addressed to all iPAAC partners. Off-label recommendations were highlighted. The survey also enabled WP9 to collect information on immunotherapy reimbursement in European countries, according to their national potential restrictions of use as well as existing frameworks enabling early access to innovative immunotherapies for unapproved indications.

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

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

The TRANSCAN-2 ERA-Net is a unique European network of 28 research funding agencies and ministries from 15 Member States, 3 Associated Countries, and a third country (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.

The fourth TRANSCAN-2 (JTC-2017) call for projects on rare cancers was launched in December 2017 and projects were selected in October 2018. In total, 12 projects have been selected (see part 2.1.2. for more information), France is the second most represented country in number of research teams, behind Germany, and the third in number of coordination teams, behind Germany and Italy.

Furthermore, INCa acts as chair of the TRANSCAN-2 network steering committee and coordinates the work package in charge of the network's strategy and scientific research priorities. During 2018, most of the work package's missions were completed.

In response to the need for better European coordination of national efforts via ERA-Nets and to continue advancing translational cancer research, TRANSCAN-3 has been confirmed and should be implemented in 2021.

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

JOINT ACTION ON RARE CANCERS (JARC)

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

care, for patients with conditions requiring a particular concentration of resources or expertise regardless of where they are in Europe.

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

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

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

In 2018, the Institute participated in the development of the following deliverables:

- A map/database of expert centres and networks on rare cancers in Europe;
- A list of rare cancers;
- A list of differences and commonalities between rare cancers and rare diseases registration;
- Recommendations for the standardised estimation of rare cancer indicators on a European and national level;
- Report and survey on availability of clinical practice guidelines for all rare cancer families;
- A list of existing preclinical paediatric cancer models and skilled research teams involved in preclinical research.

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

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

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

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

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

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

The work package on "employment and back-to-work issues for people with chronic conditions" aims also to create policy recommendations targeting policy-makers to ensure that legislative frameworks provide better accessibility to existing employment support for those with chronic diseases. For further information, please consult the website: http://chrodis.eu/

INCa's global commitments

NATIONAL CANCER INSTITUTE – USA

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

The scope of the fellowship was discussed at this meeting and potential topics for enhanced collaboration between the US and France were identified as:

- Precancer;
- Rare cancers (common interest expressed in glioblastoma) and Paediatric cancers, in particular for initiating data sharing;
- Big data / real-life monitoring;
- Tobacco control and knowledge sharing on e-cigarettes;
- Proton therapy;
- CAR T-cells;
- Early-phase clinical trials;
- Joint training activities/programmes for students to develop the cooperation between French and American research and health institutions further, in particular in the field of clinical research.

In the months following this conversation, precancer and paediatric cancer emerged as two areas to highlight in discussions during the fellowship. A third area, the consortium application to UNITAID for cervical cancer screening and treatment (SUCCESS), was a priority focus due to meetings happening in Europe during Lisa Steven's fellowship.

INTERNATIONAL CONSORTIUM: "SUCCESS INITIATIVE"

Cervical cancer is one of the world's deadliest – but most easily preventable – forms of cancer for women, responsible for more than 270,000 deaths annually, 85% of which occur in developing countries.

In recognition of this, in May 2018, WHO Director-General, Dr Tedros Adhanom Ghebreyesus made a global call for action to eradicate cervical cancer. The eradication of cervical cancer as a public health issue is the objective set by the World Health Organization at the 2018 World Health Assembly meeting in Geneva.

Following this call for action, UNITAID issued a call for proposals to help eliminate cervical cancer. The HPV projects to be funded by UNITAID would improve and expand screening and treatment for cervical cancer, with special attention given to women living with HIV.

This HPV call seeks projects that would create a market for the best available tools to screen HPV and treat women at risk of developing cervical cancer in low- and middle-income countries, and help integrate these tools efficiently and economically, setting them up for large-scale expansion in the future.

Existing cervical cancer prevention initiatives in LMICs are failing to achieve a major impact in incidence and mortality reduction due to a combination of supply and demand-side constraints, such as a lack of market preparedness for adopting and scaling-up emerging evidence-informed tools and strategies, poor availability of accessible and acceptable cancer control services, insufficient number of trained providers, limited knowledge of cervical cancer among women, among others.

With the overall goal of paving the way to the eradication of cervical cancer, INCa proposed the formation of an international consortium to develop the SUCCESS project (Scale Up Cervical Cancer Elimination with Secondary Prevention Strategy). The project is set to increase women's access to evidence-based and quality assured secondary prevention services by catalysing the market for and supporting the introduction of emerging screening and treatment tools in seven countries - Bolivia, Kenya, India, Myanmar, Senegal, South Africa, and Tanzania. SUCCESS focuses strategically on markets with diverse capacities and readiness to maximise our global reach, as we expect to generate critical information on adoption and scale-up of technologies and service delivery models for a wide range of LMICs. The project was selected by UNITAID's board and is set to commence rolling out in 2019.

Partners involved in the consortium:
- Expertise France;
- International Agency for Research on Cancer (IARC);
- International Planned Parenthood Federation (IPPF);
- Union for International Cancer Control (UICC);
- French National Cancer Institute (INCa);
- National Cancer Institute (NCI), United States of America;
- National Cancer Center (NCC), Japan;
- National Cancer Institute (INCA), Brazil;
- Enhancing Care Foundation - (ECF);
- Women´s Health Equity Through Mobile Approaches Inc. (WEMA).

COOPERATION WITH IARC: CESTA PROJECT

In 2014, WHO updated the cervical cancer screening and treatment guidelines and included primary screening options with VIA and HPV testing. Although the guidelines were evidence-based, the available data that was used to derive the

recommendations was scanty, principally in low-resource settings. A research gap was identified for clinically relevant studies for the screening algorithms of interest.

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

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

NATIONAL CANCER CENTER – CHINA

INCa and the National Cancer Center of China (NCC) signed a Memorandum of Understanding in June 2016. Through this agreement, the two institutions wished to develop their collaboration in the prevention and fight against cancer.

In March 2018, meetings were organised in Beijing with NCC teams in order to identify areas of potential cooperation with China:

- mechanisms for monitoring and implementing the cancer plan;
- Authorisation criteria;
- Information systems at the national level;
- Complementary medicine for managing side-effects;
- Clinical research.

MINISTRY OF SCIENCE AND TECHNOLOGIES OF TAIWAN

The long-term relationship and exchanges with representatives of Taiwan's Ministry of Science and Technologies in France led to the signature of a MoU in 2017. The emphasis is placed on collaborative cancer research. The signature of this MoU has helped foster French-Taiwanese partnerships with the aim of co-funding joint cancer research projects within the scope of INCa's call for proposals on cancer biology, the Biology and Basic Sciences for Cancer Research-PLBIO programme. A first project "Comprehensive analysis of Immune microenvironment of soft-tissue sarcoma", bringing together French and Taiwanese teams, was selected in 2018.

INCA'S GLOBAL PROGRAMME FOR CERVICAL CANCER CONTROL - GPCCC - MEDITERRANEAN COUNTRIES

INCa funded the first steps of an ambitious project involving Mediterranean countries, conducted by the WHO collaborating centre for cancer early detection and screening

INCa is funding the first steps of an ambitious project involving Mediterranean countries, conducted by CPO, Piedmont - WHO Collaborating Centre for cancer early detection.

As part of INCa's global strategy for cervical cancer control, INCa has entered into an agreement with CPO, Piedmont - WHO Collaborating Centre for cancer early detection, to conduct a study entitled "Development of a strategy to enrol women in breast and cervical cancer screening programmes, in 3 Mediterranean countries, members of the Euromed Network". This study represents the first steps of a larger project called "WoRTH" (Women Rights To Health), which is the first health project to be granted designation status by the Union for the Mediterranean.

The study is currently ongoing in 2 Mediterranean regions (Balkans & Maghreb) and 3 countries (Albania, Montenegro and Morocco). Its main objective is to design the enrolment protocol in each country, taking into account the urban and rural context, local resources and societal acceptance. The strategy will be developed in line with national public policies and plans and in close coordination with national health authorities and healthcare practitioners.

The progress of the Worth project, including implementation, objectives already achieved, barriers, strengths and the future steps, was presented in April 2018 during the Marrakech International Women's Cancer Days.

The event was a joint venture organised by the Gynecological Cancer Intergroup (GCIG) (a collaborative network of international and national research groups performing clinical trials in gynaecological cancers), the Pan-Arabian Research Society of Gynecological Oncology (PARSGO), the Union for Mediterranean, INCa and CPO-WHOCC. It was an important opportunity to present the mid-term results of the project and to enhance the collaborative network, involving important local and international stakeholders.

On 19 and 20 June 2019 the final outcomes of the project will be presented and discussed among all partners. Future strategies and objectives will be included in the meeting agenda. Representatives of the three countries involved and international stakeholders will be invited to join the meeting that will be hosted in Marrakech, Morocco.

Summary of the actions conducted to date in each participating country

Albania

The actions were successfully completed in January 2018 with the support of the Albanian Institute of Public Health and the United Nations Population Fund (UNFPA) Albania. Activities were conducted in the Fieri district, the second Albanian district by number of inhabitants (Census 2011), and in 2013 had, the second highest value in terms of gross domestic product. In Albania, the two recruitment strategies compared were: face-to-face invitation (current invitation strategy) versus phone call: 1,196 women aged 30-49 were identified from general practitioners' (GPs) lists in 9 towns (3 urban and 6 rural) to be invited to have a screening test (Human papillomavirus test). Even though data analysis is currently in progress, the preliminary findings suggest a high acceptance of the screening test overall (82.6%), and confirm that the face-to-face approach is most effective strategy (95.3% of participation rate vs 80.4% through phone call). Acceptance was also higher in rural areas rather than urban areas (96.0% vs 85.1%). Lack of availability of phone numbers and unwillingness to be contacted by phone for health issues emerged as the main obstacles.

A survey was submitted to women accepting to participate in the project, and another to women refusing to participate in order to collect information on their perception of the screening programme, personal screening history, and existing barriers and facilitators to access and participation. The data collected suggest that around 15% of participating women had previously undergone a screening test and that the variables positively influencing the women's decision to participate were being invited by healthcare professionals and the availability of sample self-collection devices to collect vaginal samples as an alternative to having the sample taken by a healthcare professional.

To assess the attitudes and behaviour of women with respect to prevention strategies, a questionnaire was developed and sent to a different sample of 1,000 women. They were identified from GPs' lists in 18 towns (two urban and sixteen rural), and after being contacted by a trained fieldworker, 899 completed the questionnaire. The data collected are currently under analysis and an article will be submitted very shortly to a peer-reviewed journal. These data can be considered as baseline parameters after conducting awareness-raising actions as part of the WoRTH project.

Montenegro

Actions in Montenegro have been conducted by the National Institute of Public Health with the support of the WHO country office. Context analyses of Montenegrin demographics, epidemiological cancer profile, and organisation of the screening programme have led to agreement on the protocol to be applied. In Montenegro, the two strategies to be compared were phone call (current invitation method) vs invitation letter (alternative strategy): 3,156 still non-invited women aged 30-36 living in Podgorica (urban and rural areas) were selected from the Montenegrin Health Insurance Fund Informatics System. In the phone call arm, women were contacted by the nurse of the gynaecology consultant, while letters sent in the alternative strategy were sent by the Institute of Public Health. Missing data will be collected until 31 January2019, and data are currently being analysed.

Morocco

In Morocco, the project is rolled out in collaboration with the Ministry of Health and the Lalla Salma Foundation. Considering organisational as well as demographic differences within the country, national authorities identified three provinces to conduct the study: Tangier in the north, Kenitra in the midlands, and Marrakech in the south. In this country, two different strategies to invite women to undergo a VIA test will be compared: face-to-face invitation (current invitation method) vs "invitation made in Morocco". For the latter, women will be invited either by telephone (if available) or by home contact with a health professional or via a local NGO. Overall, 3,600 women will be invited to participate in the project. As for Albania and Montenegro, a questionnaire will be sent to women accepting to participate in the project, and another to women refusing to participate. As in Albania, a questionnaire will aim to assess the attitudes and behaviour of women with respect to prevention strategies. This survey will also be sent to a different sample of 900 women aged 20+. As in Albania, these data can be considered as baseline parameters after conducting awareness-raising actions as part of the WoRTH project. Actions in Morocco are currently being rolled out and will be completed by mid-March 2019.

REVIEW OF CANCER RESEARCH FUNDING

Trends in cancer research funding

CANCER RESEARCH FUNDING IN 2018

In 2018, the total funding awarded to cancer research programmes amounted to €106.26M (€58.06M from INCa, €24.39M from DGOS, €21.34M from Inserm for ITMO Cancer-Aviesan and €2.46M allocated by ARC Foundation, the French Cancer League and IReSP within the framework of the programmes in partnership with INCa).

Figure 36 shows the breakdown of multi-year funding for 2018 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, projects targeting a tumour type through the integrated research programme supported by INCa and the charities ARC Foundation and the French Cancer League, the integrated programme addressing tobacco control in partnership with IReSP and thematic research programmes managed by ITMO Cancer-Aviesan;
- Support for platforms, resources and infrastructures;
- Research training and support for young teams of excellence especially covering the PhD programme in human and social sciences, ATIP-Avenir and translational research training programmes for MDs, pharmacists and vets.

This figure shows that 48% of the allocated budget was devoted to competitive investigator-driven calls for proposals, managed by INCa, including funding from DGOS. Support for platforms, resources and infrastructures represented 20% of the funding in 2018 and include INCa's support for the Cancéropôles (regional cancer research hubs). Strategic research initiatives and thematic programmes represented 29% of total funding in 2018 and also include the integrated action research programme dedicated to pancreatic cancers launched and funded in partnership with ARC Foundation and the French Cancer League.

The funding allocation according to the CSO classification highlights that research projects under the biology and treatment categories represented the most significant investment in 2018, with €31.96M and €31.42M, respectively (Figure 37). The early detection, diagnosis and prognosis category represented 11% of investments in 2018 (€11.98M) and decreased compared to 2017 (21% of cancer research invest-

FIGURE 36
2018 MULTI-YEAR CANCER FUNDING BY PROGRAMME TYPE (INCA, DGOS AND ITMO CANCER-AVIESAN): €106.26M INVESTED

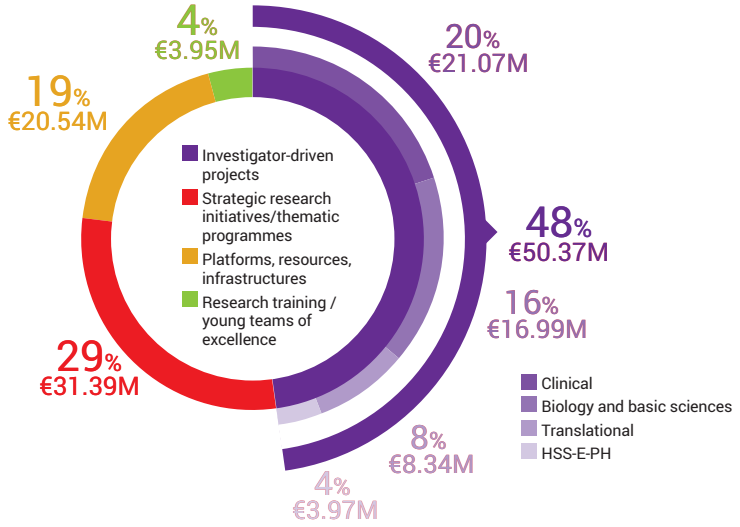
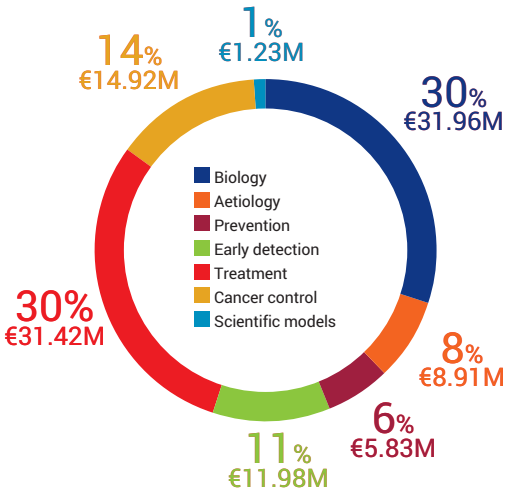


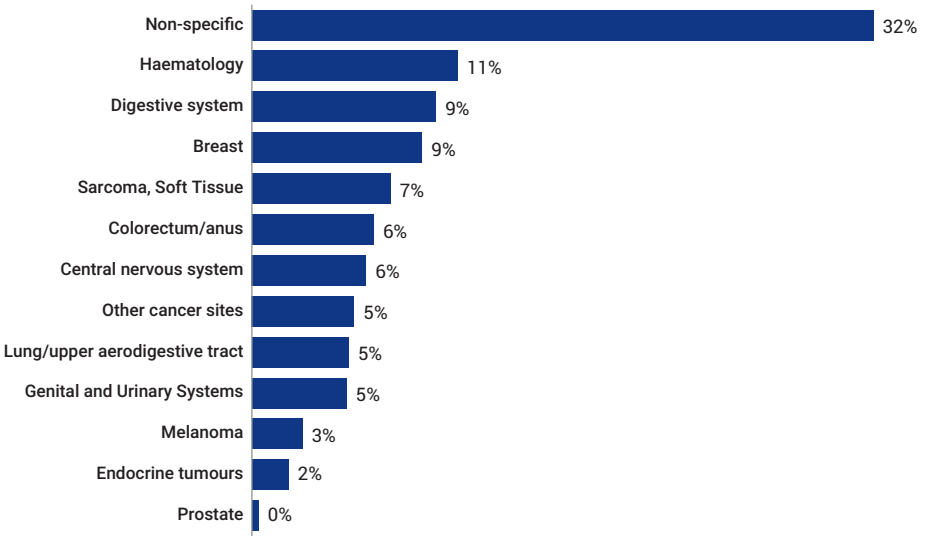
FIGURE 37
2018 MULTI-YEAR CANCER RESEARCH FUNDING ACCORDING TO THE CSO CLASSIFICATION: €106.26M INVESTED



ments). Investments in cancer control and survivorship issues represented 14% of cancer research investments with €14.92M. Importantly, research issues in cancer prevention represented 6% (€5.83M) and increased significantly compared to 2017 (0.3%).

The breakdown of 2018 funding by cancer sites studied shows that 32% of the allocated budget is non-specific to a tumour type (Figure 38). The main cancer sites studied are haematology, digestive system and breast. Sarcomas and soft tissue cancers represented 7% of cancer research investments, against 5% in 2017. Additionally, studies addressing lung and aerodigestive tract cancers represented 5% of the investments in 2018, compared to 9% in 2017.

FIGURE 38
2018 MULTI-YEAR CANCER RESEARCH FUNDING BY STUDIED CANCER SITES: €126.26M INVESTED



CANCER RESEARCH FUNDING OVER THE 2007-2018 PERIOD

Since 2007, a total of 3,041 projects have been funded through the different competitive calls for research proposals and grants for designation for over €1.15Bn.

As shown in figure 39, the investigator-driven calls for proposals of the four main research areas represented a total of 50% of 2007-2018 investments, or approximately €574M. Strategic research initiatives aiming to primarily support precision medicine initiatives and thematic programmes represented 25% of cancer research investments (€286M). Importantly, support for resources and infrastructures represented 22% of total funding, approximately €255M, and highlights the determination to reinforce the organisational framework and the coordination of cancer research activities. Alongside support for investigator-driven projects, INCa has developed a proactive policy for fostering cancer research excellence through the designation of and support for dedicated infrastructures aiming to promote coordinated, integrative and effective cancer research.

Figure 40 shows the breakdown of the projects funded and infrastructures according to CSO research categories, and highlights the importance of the fields of treatment and biology in cancer research investments, with 28% and 25%, respectively. Projects addressing cancer control and survivorship issues represented 17% of the overall funding during this period. The early detection, diagnosis and pro-

FIGURE 39
2007-2018 MULTI-YEAR CANCER FUNDING BY PROGRAMME TYPE: €1.15BN INVESTED

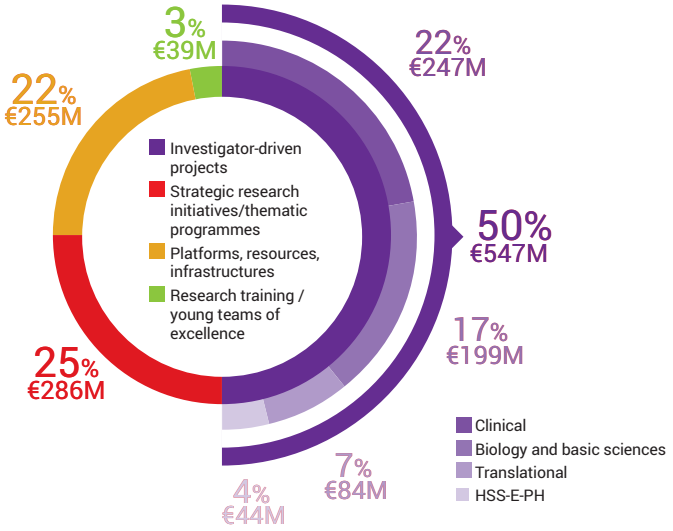
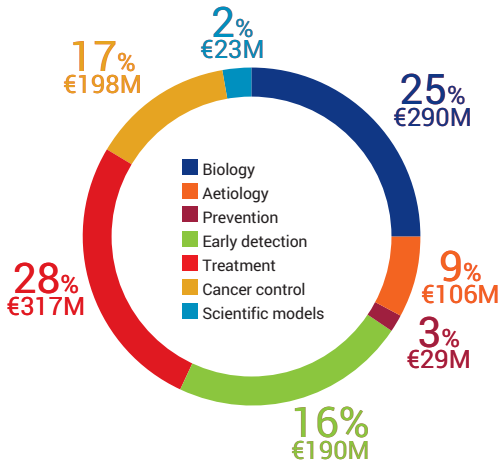


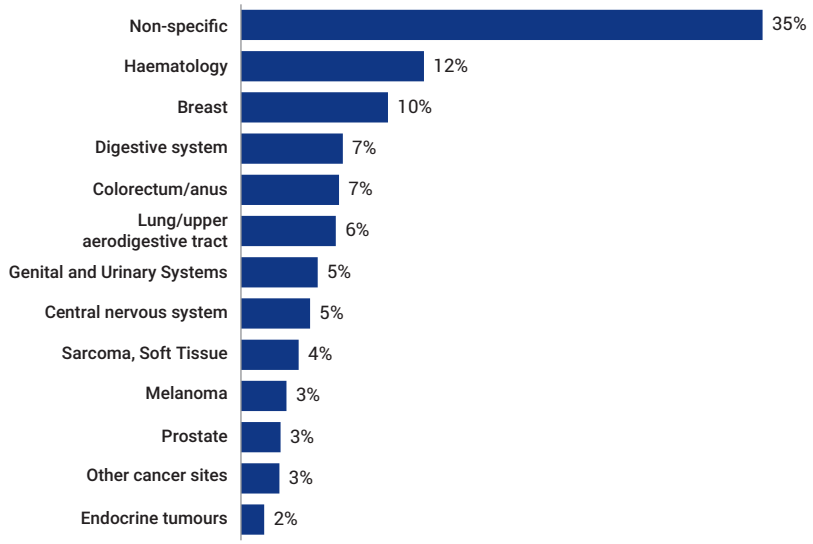
FIGURE 40
2007-2018 MULTI-YEAR CANCER FUNDING ACCORDING TO THE CSO CLASSIFICATION: €1.15BN INVESTED



gnosis category represented 16% and mainly encompassed translational research, support for molecular genetics centres and next-generation sequencing implementation.

Over the 2007-2018 period, 35% of the budget was allocated to non-specific cancer types (Figure 41). Haematological malignancies and breast cancer represented 12% and 10% of investments, respectively.

FIGURE 41
2007-2018 MULTI-YEAR CANCER FUNDING BY CANCER SITES STUDIED: €1.15BN INVESTED



TRENDS IN CANCER RESEARCH INVESTMENTS OVER THE 2007-2018 PERIOD

When comparing the breakdown of funding in 2007 and 2018 by programme type, it is interesting to note that even though investigator-driven programmes represent the majority of investments, allocations to priority-driven projects (strategic research initiatives and thematic programmes) have increased significantly since 2007 (figure 42). Indeed, priority-driven programmes represented 16% of the overall budget (almost €13M) and 29% (over €31M), in 2007 and in 2018, respectively. Additionally, support for cancer research training and young researchers has increased, reaching 4% of 2018 investments (€3.95M). These trends might be explained by the successive Cancer Control Plan objectives, e.g. strategic initiatives to support personalised medicine and rapid access to innovative therapies. Moreover, the dedicated funding allocated by ITMO Cancer aims to support cancer research in emerging topics and gap areas, as well as strengthen capabilities that may have been identified in investigator-driven programmes. As such, this assessment highlights the important challenge for cancer research funders in optimising the balance between investigator-driven and priority-driven programmes.

FIGURE 42
2007 AND 2018 MULTI-YEAR CANCER FUNDING BY PROGRAMME TYPE: €78.19M INVESTED IN 2007 AND €106.26M INVESTED IN 2018

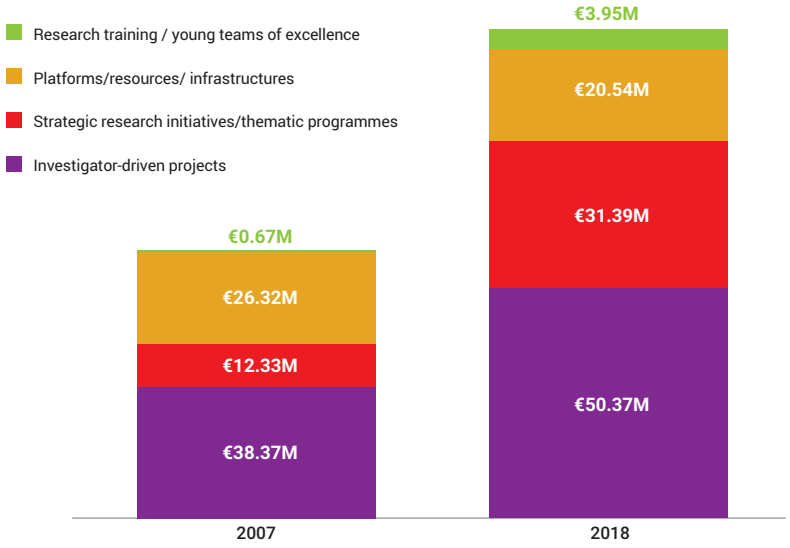
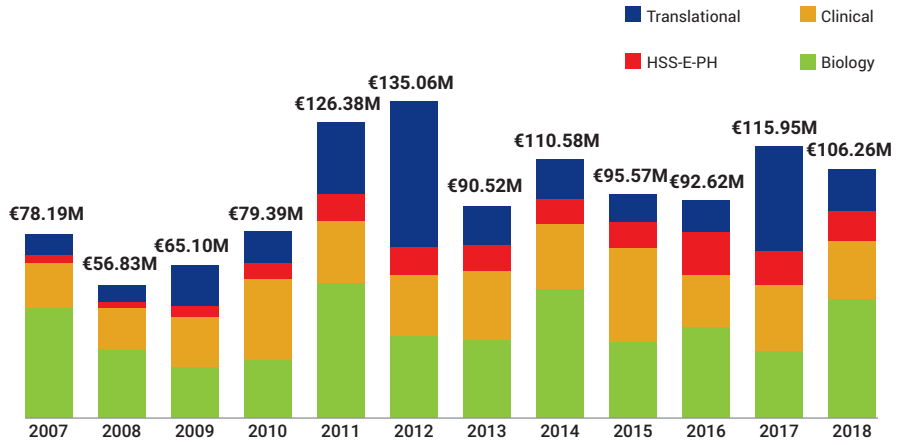


FIGURE 43
TRENDS IN TOTAL FUNDING ACCORDING TO THE CANCER RESEARCH FIELD OVER THE 2007-2018 PERIOD (INCA, DGOS, ITMO CANCER)

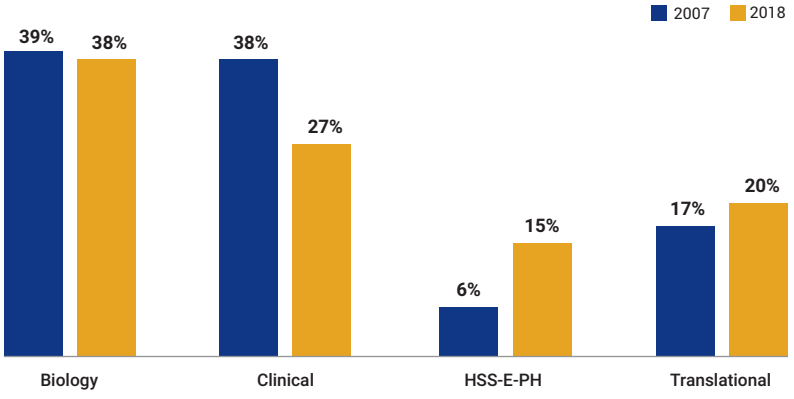


INCa's role in the coordination and support in cancer research cannot be achieved without providing strong parallel support whether at the funding or management level of structures and infrastructures. Support for cancer research structuring is thus a major endpoint and the investments saw slight changes between 2007 and 2018, corresponding to 34% and 20% of investments, respectively.

Figure 43 presents the trends of total funding according to the cancer research fields over the 2007-2018 period. The different structures supported in recent years have delivered significant multidisciplinary synergistic interactions for research funding and drug access to patients and have provided a basis for the coordination of clinical, fundamental and human and social science research at the 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.

Interestingly, support for cancer research structuring is reflected in the distribution of allocated funding according to the cancer research field, as depicted in figure 44. Indeed, when comparing the 2007 and 2018 portfolio, and excluding cancer research structuring, it is interesting to note that, alongside significant support for cancer biology and clinical cancer research, allocations for the translational and HSS-E-PH research fields have evolved significantly. While in 2007, over €8.65M was allocated to translational cancer research, in 2018, the investments represented 20% of the total budget (€17.66M). Allocations to research in human and social sciences, epidemiology and public health represented 15% of the overall 2018 budget (€13.09M), but merely 6% in 2007 with almost €3.3M.

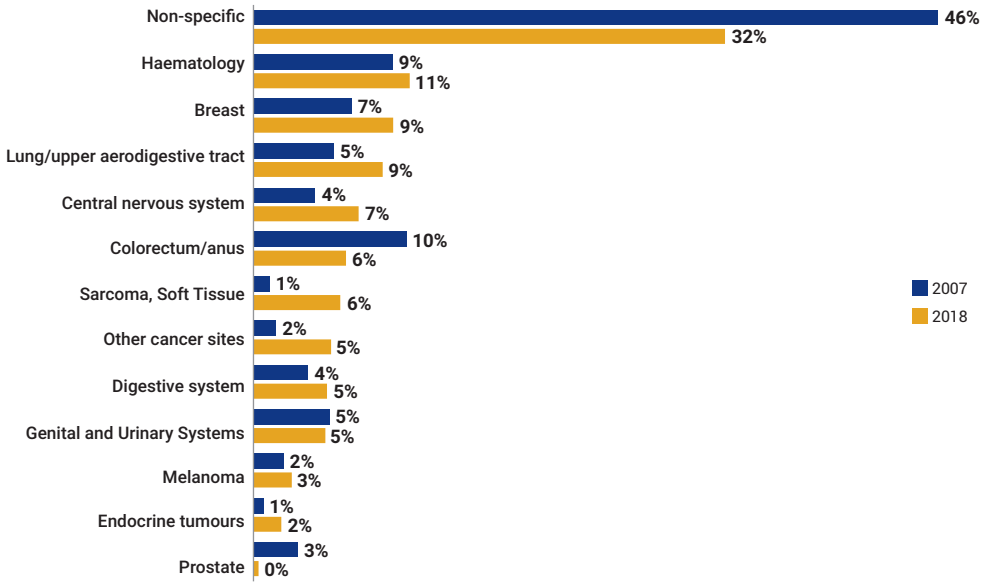
FIGURE 44
2007 AND 2018 FUNDING FOR CANCER RESEARCH PROJECTS BY RESEARCH FIELD AND EXCLUDING SUPPORT FOR STRUCTURING: €51.88M INVESTED IN 2007 AND €89.76M INVESTED IN 2018



These trends underscore developments in cancer research and more importantly the major role of cancer research studies related to cancer control, cancer care health management, beliefs and attitudes affecting behaviour; ethics, education and communication approaches, etc.

Investments according to cancer sites have also shown changes over the years (figure 45). Indeed, while allocations to non-specific cancer sites and colorectal cancers have decreased, support for studies related to lung and upper aerodigestive tract or the central nervous system has increased. Interestingly, support for sarcomas has seen a six-fold increase. Surprisingly, breast cancer and prostate cancer show opposite trends.

FIGURE 45
2007 AND 2018 MULTI-YEAR CANCER FUNDING BY CANCER SITES: €78.20M INVESTED IN 2007 AND €106.26M INVESTED IN 2018



Funding the most effective research in childhood cancers

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

Childhood cancer control has always been a priority in INCa's action plan through concrete measures to support and boost research:

- Designation of the cooperative intergroup SFCE (Société française de lutte contre les cancers et les leucémies de l'enfant et de l'adolescent) in 2017, working in close collaboration with other intergroups;
- Designation of 6 paediatric early-phase clinical trial centres (CLIP²) over the 2014-2019 period (Marseille, Paris, Villejuif, Lyon, Lille and Nantes-Angers). Supported by INCa and the French Cancer League, these centres are part of the European network dedicated to innovative therapies for children with cancer (Innovative therapies for children with cancer in Europe, ITCC);
- Adapting clinical trials to the arrival of targeted therapies and to provide secured access to innovative medicines through the AcSé programme;
- Launch of an Integrated Research Action Programme focusing on Paediatric Tumours in 2016;
- Support for paediatric cancer research projects: 14 projects funded out of the 66 projects submitted within the scope of the main investigator-driven pro-

grammes (biology, translational, clinical and human and social sciences, epidemiology and public health) for an overall amount of €9.2M. In 2018, the selection rate of paediatric projects was 21%.

Efforts to highlight paediatric cancers in all investigator-driven programmes will be pursued. Paediatric cancer research should, as in previous years, find support in our four main investigator-driven programmes.

In 2018, the mobilisation of parents' associations had driven an additional allocation of €5M per year by the Ministry of Research and Innovation to paediatric cancer research. This specific funding aims to support and coordinate basic cancer research in paediatrics through calls and actions not in existence to date. INCa coordinates, with three parents' association groups including various stakeholders, the calls and actions with feedback from INCa's paediatric interfaces. These include recommendations of a specific action group of the International Scientific Advisory Board. A new Health law of March 2019, mandates the Institute to make proposal, in coordination with research organisations, public and private operators in oncology, health professionals and other concerned persons, a decennial strategy for the fight against cancer, announced by decree.

The strategy defines the axes of oncology research and the allocation of corresponding resources and in particular the share of public funds allocated to research in paediatric oncology. INCa ensures the implementation. The INCa Scientific Advisory Board decides on this strategy. It reassesses its relevance at mid-term"

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

The societal demand for research evaluation is increasing. Indeed, the manner in which the research process is organised and funded is becoming increasingly scrutinised (due to budget constraints). There are also growing governmental demands to measure research impact (beyond academic publications), to understand how science works, who makes science, and to optimise its societal and economic impact, such as intellectual property, spin-out companies, health outcomes, public understanding and acceptance, policy-making, sustainable development, social cohesion, etc.

In this context, funding agencies are encouraged to produce analyses to assess the impacts of their actions quantitatively or qualitatively (relevance, effectiveness, efficiency, etc.). In line with one of the objectives of the 2014-2019 Cancer Plan (Objective 17.13), the French National Cancer Institute has set up a working group bringing together the majority of biomedical research funders (agencies, charities etc.) to discuss strategic evaluation and impact assessment of biomedical research projects.

INCa's approach is pluralistic and participatory, nineteen partner institutions have committed (not only in the oncology field).

The first meeting held in February 2017 highlighted the common objective and need to pursue this national expert knowledge and practitioner feedback. Therefore three working groups were put in place from September 2017 to December 2018

- to share strategies;
- to standardise grant applications and monitoring;
- to propose guidelines describing the impact pathway and describing, at all stages, the definitions, objectives, tools and research methodology tools available or that should be available etc.

Based on the willingness to build a community of practice, the recommendations of the different working groups are stated below.

- Provide a template for reporting scientific achievements with a minimal set of indicators;
- Implement impact indicators during and after the funding period to provide answers to stakeholders;
- Promote a mix of quantitative and qualitative approaches;
- Promote digitisation systems, data interoperability and open data through effective IT platforms;
- Promote the ORCID number and the ORCID researcher database;
- Promote text-mining and visualisation tools.

The contribution of a programme to a research field must be identified, described and valued by the research funders. However research funders must recognise that

- all the projects will not have a "societal" impact;
- it is difficult to attribute the effects of a project (programme) to a particular funder (project fallacy).

There is difficulty measuring impacts prospectively because they may be direct or indirect, expected or unexpected, positive or negative, immediate or distant.

A roadmap for the years 2019-2021 was also approved by all the partner institutions.

2019-2021 roadmap: foster and pursue the national initiative

- Pilot phase to test the template in "real-life";
- Support the implementation of ex-post impact studies (portfolio analysis);
- Provide a white paper to share with the funder community;
- Defend, on a national level, the requirement for the data to be kept for several decades after funding to be able to carry out ex-post impact studies (GDPR);
- Account for the open science / open data /open access movement;
- Research funders have committed to
  - evaluating the funded projects from the end of funding and beyond (there is often a significant time lag between conducting research and characterising impacts),
  - communicating science effectively by making researchers aware of our common interest to work together on this topic,
  - adopting impact assessment as a core strategy;
- Lobby to initiate a national reflection to adopt
  - national guidelines,
  - a national assessment tool (enter once: re-use many times).

3

Strategic topics for advancing cancer research

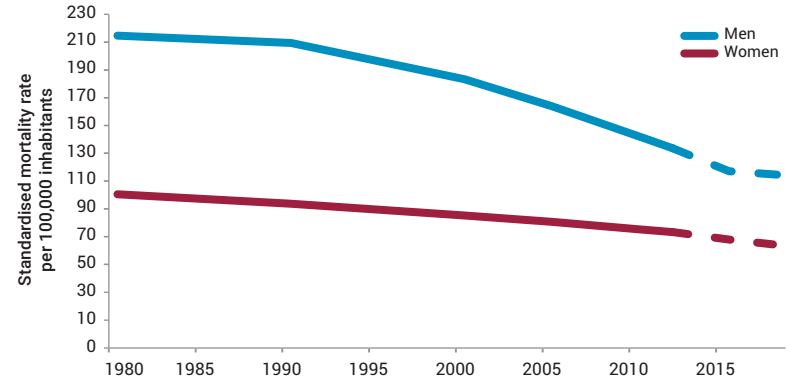
With support from the two supervising ministries, the International Scientific Advisory Board and the Board of Directors, INCa will have provided continuous financial support for research projects (and maintained and increased this support despite budget restrictions) based on transparent methods, international evaluation and participation of patient advocates in all the scientific evaluation committees for INCa's calls for proposals, in every field of cancer research.

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

STRATEGIC ORIENTATIONS FOR ADVANCING CANCER RESEARCH

Over 3.8 million people in France are currently living with or have recovered from cancer. While the number of new cases diagnosed is increasing year on year, progress made in diagnosis and treatments has led to a decrease in cancer-related mortality (figure 46). Indeed, in 2018, the number of new cancer cases for all cancer sites combined in Mainland France is estimated at almost 382,000 (204,600 in men and 177,400 in women). The number of cancer-related deaths is estimated at almost 157,400, of which 89,600 in men and 67,800 in women[6]. Nevertheless, the disease remains a difficult challenge for those affected, both physically and psychologically. It is also synonymous with disruptions in terms of social life and career (VICAN5 study)[7].

FIGURE 46
PROGRESSION OF MORTALITY SINCE 1980 (2018: PROJECTIONS)



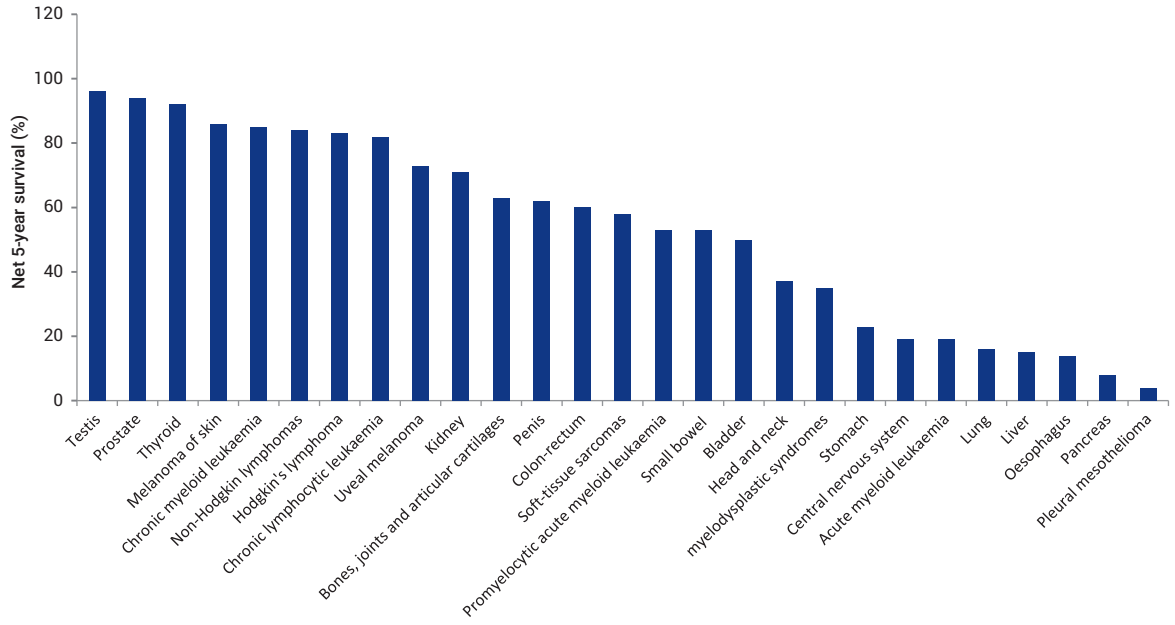
Furthermore, an improvement in the standardised net 5-year survival rate is observed for most cancers, regardless of sex. For all that, some situations continue

6. INCa (2018). Summary - National estimations of cancer-related incidence and mortality in Mainland France between 1990 and 2018 (Synthèse - Estimations nationales de l'incidence et de la mortalité par cancer en France métropolitaine entre 1990 et 2018).
7. INCa (2018). Life five years post-cancer diagnosis – Report.

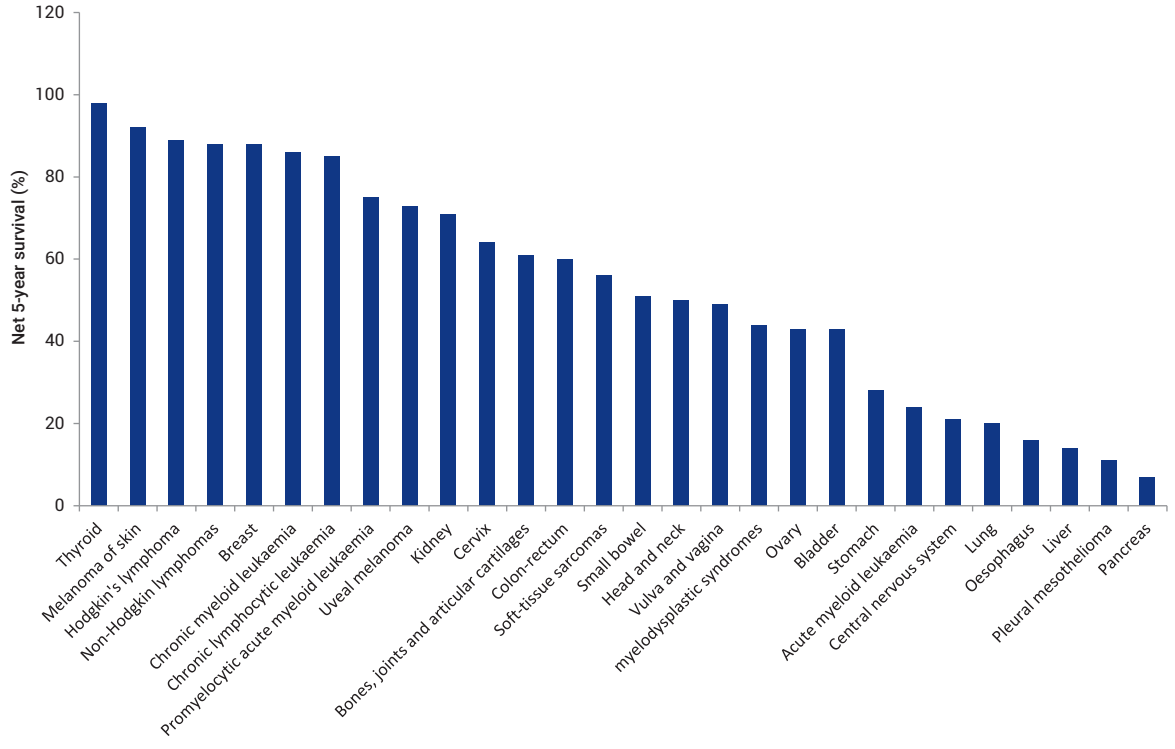
FIGURE 47

NET 5-YEAR SURVIVAL IN PATIENTS DIAGNOSED BETWEEN 2005 AND 2010 FOR SOME CANCER SITES (%)

Men



Women



to be of particular concern: some cancers have not seen any improvement (central nervous system and invasive brain stem cancers, pancreatic cancer, lung tumours or triple-negative breast cancers) (Figure 47).

These favourable trends are the result of long-term combined efforts that the French National Cancer Institute is committed to pursuing, within the framework of its duties set out by law and with all partners. For this reason, the Institute envisages, following on from the 2014-2019 Cancer Plan, adding further momentum to its duties, the strategy of which will be focused on key public health priorities.

Improving and strengthening prevention in order to reduce cancer incidence, to limit sequelae by providing less debilitating treatments, in order to offer patients, beyond recovery, the best possible quality of life, addressing poor prognosis cancers, endeavouring to offer disruptive developments with the potential to result in a paradigm shift, are now major challenges. These challenges should be displayed as the Institute's priorities for the coming years, in compliance with the national healthcare policy, while pursuing structuring actions to promote access to innovation.

Pursue and build on our efforts to promote access to innovation

Through its role as an accelerating force for progress, the Institute supports cancer research via various actions, more particularly including funding for high-quality and innovative research projects, coordinating, leading and structuring of research.

SUPPORT FOR CANCER RESEARCH PROJECTS

A source of scientific, technological and organisational innovation, support for cancer research will be maintained (investigator-driven and thematic calls for proposals, strategic initiatives, research facility, network designations, etc.).

The selected proposals must combine excellence, competitiveness and innovation. Nevertheless, further objectives must be defined within the scope of these missions set out by law for optimum support for the transfer of innovations for the benefit of patients and in order to adapt to cancer research needs.

As such, the level of research funding assigned to free investigator-driven proposals, over 4 to 5-year programmes, representing 50% of INCa's calls for research proposals, will be continued. Moreover, the model developed within the framework of thematic calls for proposals and strategic initiatives will be extended to support and promote experimental and accelerated translational research, particularly proof-of-concept studies for emerging or priority topics.

National, international and public-private partnerships will be set up with a view to optimising research allocations.

These resources will particularly help increase the attractiveness of France in all fields of cancer research (cancer biology, translational and integrated research, clinical research, human and social science research, paediatric oncology, etc.).

Moreover, these initiatives will make it possible to set up the necessary frameworks promoting skills and career development, while encouraging scientific expertise (researchers, medical practitioners, etc.) to meet new challenges and innovations in oncology.

CANCER RESEARCH STRUCTURING

In recent years, the cancer research and health landscape has seen major changes, providing France with new opportunities to step up its main programmes and launch new ones. Of the main initiatives, the creation of 8 SIRICs (integrated cancer research sites), 16 CLIP²s (early-phase clinical trial centres), 28 molecular genetics centres and 13 accredited cooperative intergroups have helped lay the foundations for high-quality research in France. INCa has implemented a very proactive policy, recognised by its peers in Europe, North America and Asia, to extend access to targeted therapies for patients identified as eligible using molecular testing.

The Institute's aim is to support the development of medicine based on tumour- and patient-specific biological parameters, providing large-scale facilities to enable new-generation molecular testing.

For all the facilities supported, the French National Cancer Institute intends to optimise the infrastructures provided based on further knowledge acquired and technological innovations while guaranteeing nationwide provision.

Since 2006, INCa and DGOS have supported 28 hospital cancer molecular genetics centres distributed throughout the country. They include several laboratories, possibly belonging to different institutions, making it possible to offer patients all of the key molecular genetics techniques for all the diseases involved. To date, the molecular genetics centres offer a catalogue of 60 tests, some of which are key for

- access to targeted therapies that are available or under development;
- guiding the diagnostic process;
- contributing to diagnosis, alongside clinical, morphological, biological parameters;
- guiding the patient's treatment strategy;
- enabling residual disease monitoring.

In targeted therapeutic strategies, innovations are no longer based solely on genetic abnormalities. The recent success of a set of immunotherapies enhancing the patient's antitumour immune response (checkpoint inhibitors) has prompted INCa to better prepare its 28 molecular genetics centres for the precise assessment of the immune microenvironment of tumours according to their immunocytochemistry and their mutational load. In this context, structuring of artificial intelligence will also be prioritised, with many parameters to be taken into account in order to describe each patient's immune response, for example.

PROGRESSION OF MOLECULAR GENETICS PLATFORMS TO INTEGRATED CENTRES:

➤ Implement new biomarkers (mutational load, MSI, targeted RNAseq, immunology, liquid biopsies, etc.) for new therapeutic and follow-up indications;
➤ Structure data and promote interoperability of patients' routine data;
➤ Strengthen and facilitate public-private technology partnerships to promote technology transfer;
➤ Organise interactions between molecular genetics centres and PFMG2025 platforms;
➤ Use molecular genetics centres for pre-cancer diagnosis standardisation and follow-up.

PUBLIC-PRIVATE PARTNERSHIPS

➤ Option of funding via private partners for proposals with a strong potential within the framework of public-private calls for proposals;
➤ Propose multipartner calls for proposals;
➤ Active process for companies and drugs: from one year to another, companies can join or leave the call for proposals;
➤ Option of offering multiple drugs via private partners.

In recent years, INCa has also helped anticipate the arrival and development of precision medicine through the designation of early-phase research centres (CLIP²) and the development of public-private partnerships with pharmaceutical firms, with a view to offering CLIP² centres innovative drugs under development. The aim is to select academic clinical trials intended to test these medicines in different indications or diseases from those foreseen in the pharmaceutical firms' development plans. This accreditation has helped raise the profile of these centres and of French early-phase clinical research, and aroused growing interest on the part of pharmaceutical firms in setting up early-phase trials and public-private partnerships within the framework of this programme.

Building on this success, the Institute intends to strengthen these public-private partnerships and optimise them in order to boost the innovative drug provision process.

Due to its resolute commitment to accelerating the emergence of innovation for patients' benefit, since 2013, the Institute has launched, with ANSM approval, a new type of clinical trials: the AcSé programme (Secured Access to innovative targeted therapies). An integral part of the second Cancer Plan, the AcSé programme provides patients having experienced treatment failure to Secured and assessed Access to innovative therapies, targeted on their specific biological characteristics outside approved indications.

The AcSé programme is based on several principles:
- patient safety, as it enables patients to receive, in a controlled context, cancer treatments that are adapted to the profile of their tumour and to any molecular targets identified by the 28 molecular genetics platforms, and makes it possible to study the benefit of these innovative drugs, in terms of efficacy and tolerance;
- equity of access to treatments throughout French territory;
- the non-competition principle, as this programme is only rolled out in addition to the clinical trials already available and is no substitute for pharmaceutical firms' research and development programmes.

PROGRESSION OF THE AcSé PROGRAMME

➤ Roll out the design of the AcSé e-SMART programme
- Develop multi-target trials, with multiple arms assessing different medicines, as monotherapy or combination therapy;
- option to launch new arms based on the arrival of new drugs;
- bring together and involve multiple private corporations;
- target multiple diseases or new diseases (e.g. leukaemia);
- provide earlier treatment for cancers with poor prognosis and paediatric cancers.

Since 2013, five clinical trials have been launched:
- AcSé-Crizotinib, launched in 2013, in which the first findings demonstrate the efficacy of crizotinib, the indication of which could be extended to various types of cancer, such as anaplastic lymphomas, oesogastric adenocarcinoma, stomach cancers or certain sarcomas;
- AcSé-Vemurafenib, launched in 2014;
- AcSé-eSMART (European Proof-of-concept Therapeutic Stratification Trial of Molecular Anomalies in Relapsed of Refractory Tumors in children), launched in 2016, making a number of targeted therapies available simultaneously in the same clinical trial for children and adolescents with refractory or relapsed cancers, based on the molecular profile of their tumour screened systematically within the framework of a clinical research project supported in 2014;
- AcSé-Nivolumab, launched in 2017;
- AcSé-Pembrolizumab, launched in 2017.

Six years on, the first results have demonstrated the value and feasibility of this programme, encouraging the Institute to propose rolling out this programme on a larger scale, particularly in the form of a call for proposals.

RESEARCH IMPACT EVALUATION

As a general rule, INCa and its partners have always been conscious of the need to optimise the balance between investigator-driven programmes, thematic and priority-driven programmes and cancer research structuring. The various evaluations conducted and the national initiative launched in partnership with the primary research funders will help outline the strengths and weaknesses of the various funding tools; prioritise actions and direct funding in a coordinated way towards hot topics and emerging research areas.

Evaluating the methods used to measure the impact of research is one of the Institute's priorities. In line with one of the objectives of the 2014-2019 Cancer Plan and in accordance with the emphatic recommendations of its Scientific Advisory Board, as of 2017, INCa brought together 16 funders of biomedical research to conduct a nationwide initiative. Working groups were formed with the aim of defining a "universal" scientific reporting model as well as a minimum set of qualitative and quantitative indicators. They were also intended to propose a review of the tools required and define various impact evaluation schedules and criteria. This nationwide initiative will help define a common institutional base by creating common practices extending beyond bibliometric indicators.

MEASURE THE IMPACT OF RESEARCH AND INVESTMENTS

➤ by focusing on people rather than documents.
➤ by constructing best practices for data capture.
➤ by setting up (national and/or international) comparison groups
➤ by adjusting for selection bias

THE NEW CHALLENGES IN CANCER RESEARCH LINKED WITH PROGRESS IN DIGITAL TECHNOLOGY: OPEN SCIENCE AND ARTIFICIAL INTELLIGENCE

Make science and innovation more open, collaborative and international

Open science is the unimpeded dissemination of research publications and data. It is based on the opportunity represented by the digital revolution for developing open access to research publications and, insofar as possible, data. The objective of open science is to take publicly funded research out of the confines of closed databases. This increases the effectiveness of research, particularly by reducing duplicated efforts in the collection, creation, transfer and reuse of scientific material.

Open science aims to build an ecosystem in which science is more cumulative, more strongly data-supported, more transparent, speedier, and offers more universal access. It helps democratise access to knowledge, necessary for research, training, economics, society, promoting scientific advances as well as innovation, economic and social progress, in France, in developed countries and in developing countries. Moreover, due to this transparency, open science provides leverage for scientific integrity and boosts the public's confidence in science.

Announced by the French Minister of Research and Innovation in July 2018, the National Open Science Plan makes open access mandatory for publications and for data obtained from research funded based on proposals. It sets up an Open Science Commission and supports major structuring initiatives of the landscape relating to publications and data. Finally, it includes a training section and an international section which are key to providing direction for scientific communities and to France's influence in this developing landscape.

DEVELOP OPEN SCIENCE POLICIES

➤ Make open access mandatory for research data
➤ Update the assessment system for researchers and research institutes (principles of the Leiden Manifesto and of the Declaration on Research Assessment, DORA)
➤ Keep scientific communities informed
➤ Define new skills, develop new training programmes and create new services for the next generation

INCa is one of the five national bodies involved in funding research tasked with rolling out the undertakings of France's national open science plan.

The National Open Science Plan implements the conditions for the development of open science and is made up of three key areas placing French research at the heart of the global movement for open access to data and transparency of public action:

- make open access to publications a widespread practice;
- structure and open up research data;
- be part of a long-term, European and international process.

Artificial intelligence and cancer research

As of 2017, the government sought to rally all the members of the French artificial intelligence (AI) community and create synergy between the many initiatives emerging in France to define a concerted national strategy. The aim of France's AI strategy is to confirm and support French momentum in the artificial intelligence sector. Health is one of the priority sectors for artificial intelligence development. In 2018, a preparatory project proposed a roadmap for the operational implementation of the Health Data Hub, intended to promote the use of health data and multiply the processing possibilities of such data. It will help develop new technologies, particularly those associated with artificial intelligence methods.

In oncology, a number of initiatives have shown the potential of AI in screening and diagnostics. One of the main challenges would be to explore the potential and added value of artificial intelligence in the analysis of research data, such as for example biological data with a view to supporting the functional analysis of genomic programmes (more refined classification of cancers) or the identification and assessment of biomarkers. AI also paves the way for real-time patient monitoring, with a complete and integrated view of the progression of symptoms, response to treatments as well as supporting the therapeutic decision.

ARTIFICIAL INTELLIGENCE AND ONCOLOGY

➤ Implement a long-term policy for supporting "upstream research" regarding artificial intelligence and promote transfer to the research sector, healthcare professionals and the population;
➤ Promote academic research by proposing calls for proposals for academic research and developing initial and/or continuous training in the field of AI in oncology;
➤ Promote partnerships with industry
➤ Guide healthcare professionals and the population in this transition;
➤ Evaluation and accreditation of the quality of the analytical algorithms/pipelines developed in all research fields, including human and social sciences
➤ Accreditation of structured sets/centres
➤ In compliance with GDPR and the Health Data Hub programme, handle data protection / data ownership / data security challenges via the INCa data platform

Step up research in prevention

PRIMARY PREVENTION

At the present time, 30% to 50% of cancers could be prevented by changing behaviours and implementing prevention strategies based on probative data and the clinical feedback available[8]. Given the initiatives already launched by the Institute to combat smoking and based on the previous recommendations of the International Scientific Advisory Board, the Institute will extend cancer prevention research to other important lifestyle-related factors, such as alcohol consumption and obesity, as well as environmental risk factors.

In this way, one of the primary objectives is to promote high-quality and multidisciplinary fundamental research on risk assessment. Moreover, it is important to develop European programmes, particularly to increase the power of findings, support and accelerate the roll-out of European action policies.

More specifically, for behavioural risk factors, it is important to improve knowledge, definition and assessment of attitudes and behaviours. In this way, neurosciences and international human and social and sciences studies can also support and reinforce knowledge for the benefit of health promotion research.

Regarding environmental risk factors, a matter of concern for the public, one of the priorities should focus on support for environmental research, particularly regarding exposures (e.g. strengthening molecular epidemiology) to facilitate personal and political decision-making and create a favourable health environment.

Moreover, infection with certain viruses, bacteria and parasites has been identified as a high risk factor for certain types of cancer. To date, some ten pathogens have been identified as carcinogenic by the International Agency for Research on Cancer (IARC). In France, 4% of cancers are thought to be caused by infectious agents (3.6% in men and 4.6% in women), whereas in Europe and in developing countries, this proportion is 7% and 23%, respectively. These cancers are preventable by implementing suitable prevention measures. These observations highlight the need to support infectious disease research to identify new carcinogenic factors and develop new vaccines.

Finally, in order to enable greater readiness for new potential risk factors or societal changes, it would seem necessary to set up a permanent international expert group tasked with supplying and influencing the research strategy with innovative initiatives regarding prevention.

SECONDARY PREVENTION

Secondary prevention focuses on screening and also helps, through early diagnosis, reduce cancer prevalence.

In this way, one of the priorities is to incentivise human and social sciences research to gain a better understanding of any reluctance felt, remove this reluctance and thus promote subjects' compliance with screening, particularly within the framework of existing, or future, nationwide programmes.

Moreover, it is also important to support research in favour of improving knowledge and developing tools to identify high-risk subjects. For example, one

STEP UP RESEARCH IN PRIMARY PREVENTION

- ➤ Promote high-quality and multidisciplinary fundamental research on risk assessment
- ➤ Behavioural risk factors: assess attitudes and behaviours
- ➤ Support research on environmental risk factors
- ➤ Support infectious disease research to identify new carcinogenic factors and develop new vaccines
- ➤ Set up a permanent international expert group tasked with supplying and influencing the research strategy with innovative initiatives regarding prevention

INTER- AND MULTIDISCIPLINARY SUPPORT FOR RESEARCH IN SECONDARY PREVENTION

- ➤ Incentivise research to gain a better grasp of behaviours so as to adopt a more suitable approach and thus promote subjects' compliance with screening
- ➤ Identify at-risk subjects
- ➤ Develop new screening and prevention models for hereditary cancers, therapeutic de-escalation, recurrences, etc.
- ➤ Support research on precancer
- ➤ Continue and innovate efforts in a European and international level
- ➤ Develop tools devoted to assessing early detection

8. IARC (2018). Setting priorities for cancer prevention in Metropolitan France: the proportion of cancers attributable to lifestyle and environmental factors. Funding: INCa (2015-002).

of the key priorities could be developing new screening and prevention models for hereditary cancers while supporting research to validate newly identified markers (functional genomics, mutational load, etc.).

Finally, research aimed at improving our knowledge of natural disease outcomes must be prioritised to:
- Develop early-detection tools and methodologies (research on precancer);
- Develop research on predictive tests enabling therapeutic de-escalation;
- Reduce overdiagnosis.

These endeavours and initiatives should also be promoted on a European and international level.

All of these initiatives should help develop personalised prevention.

Prevent side-effects and improve quality of life

PREVENT SIDE-EFFECTS AND IMPROVE QUALITY OF LIFE

- ➤ Support clinical research with the aim of optimising treatments
- ➤ Identify and define the cancers and therapies causing significant side-effects
- ➤ Support research in biology on side-effects and toxicities of new therapies (pharmaco-genomics, etc.)
- ➤ Prevent and treat after-effects presented by former paediatric cancer patients
- ➤ Promote and support on supportive care with a view to interdisciplinary research
- ➤ Define suitable quality-of-life measurement scales
- ➤ Study organisational procedures in respect of after-effect follow-up, monitoring and treatment
- ➤ Support interventional population health research
- ➤ Support patient empowerment

While, thanks to progress in research, recovery rates have increased significantly over the last 20 years, the disease remains a difficult challenge impacting both physical and psychological aspects.

In this way, in order to prevent and reduce side-effects and also improve quality of life, it is key to promote studies regarding dose validations and on treatment duration (phase III therapeutic de-escalation / phase IV long-term follow-up). More generally, the Institute proposes to step up and support clinical research aimed at optimising treatments and therefore also adapt the design of clinical trials.

In parallel with therapeutic advances, it is important to identify and define cancers and therapies causing significant side-effects, as well as support research in biology and translational research on side-effects, toxicities potentially caused by new therapies, etc. This research should also help prevent risks of recurrence.

Moreover, research on supportive care should be supported with a view to developing multidisciplinary medico-economic and sociological clinical research. These studies will also help define quality-of-life measurement scales suitable for different cancers (age, gender, therapy, disability-free survival, etc.), but also, for example, treat and prevent fertility problems in former paediatric cancer patients.

These goals underline the need to study the organisational procedures in respect of after-effect follow-up, monitoring and treatment involving patients, who need to play an active role in the cancer research continuum as a whole.

Moreover, population health intervention research will particularly be supported, principally in areas such as return to work, patient education and recovery.

Address poor prognosis cancers

Despite the progress achieved, improvements have yet to be seen for some cancers: pancreatic cancer, central nervous system tumours, oesophageal, stomach or liver cancer, for example as for rare subtypes of other cancer types.

In this way, supporting fundamental research is key to acquire more knowledge on cancers with poor prognosis, step up cancer research in poorly developed fields, and support studies on tumour cell dormancy and resistance. Moreover, this cancer biology research should be associated with the development of specific tools for monitoring these cancers.

More specifically, it will be necessary to identify, on a site-by-site basis, the research areas of interest and involve other scientific disciplines. For example, as mortality from pancreatic cancer is essentially due to its late diagnosis, research should help develop means of early detection (tumour biology, biomarkers identification, liquid biopsies, imaging etc.).

Moreover, some survival rates differ between countries, more particularly for stomach, oesophageal and central nervous system cancers (CNS) which are higher in Japan[9] (Figure 48). These observations highlight the need for sharing of experience and knowledge transfer with some of our partners in order to improve cancer care in France.

The knowledge gained should also help develop new therapies, more specific to these tumours and enable the progression of precision medicine to personalised care. Clinical trials should be conducted on a European scale with, in particular, a view to increasing the robustness of the results.

Furthermore, it is important to consider support for patients. In this way, it is envisaged to step up human and social sciences research in poorly developed cancer research fields (palliative care, healthcare system, patient and family well-being, etc.) and support the set-up of caregiver and carer associations for cancers with poor prognosis. Involving patients, citizens and carers in the design, follow up and results of research is now compulsory.

All of these endeavours and innovations will be supported on a European and international level.

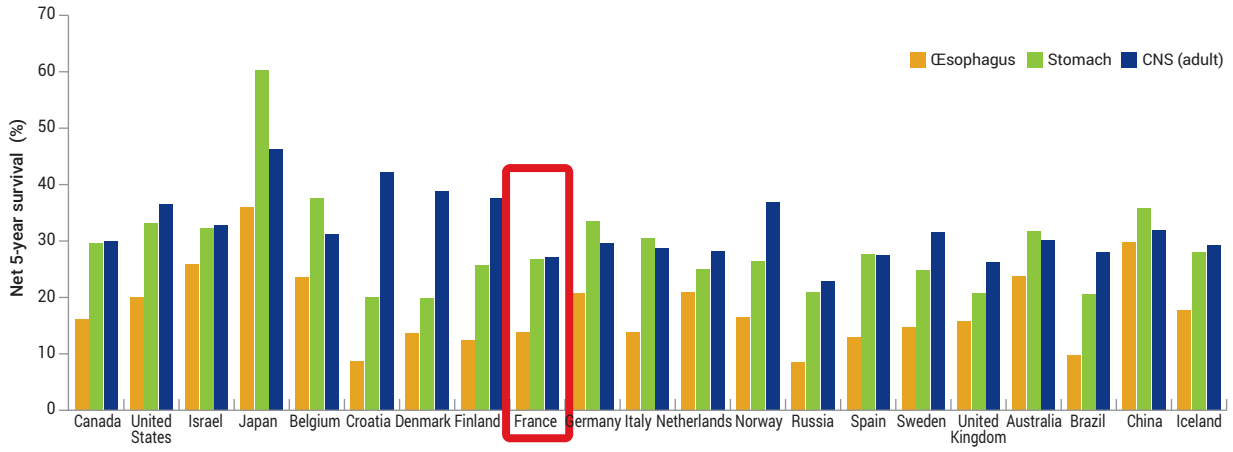
Through these actions, the Institute is targeting an improvement in net 5-year survival of at least 50% for cancers with poor prognosis by 2030.

ADDRESS POOR PROGNOSIS CANCERS

- ➤ Increase knowledge on these tumours
- ➤ Develop specific tools for the follow-up of cancers with poor prognosis
- ➤ Identify, on a site-by-site basis, research areas of interest
- ➤ Promote suitable and accelerated therapeutic innovations: transition from precision medicine to personalised care
- ➤ Adapt clinical trials to the small populations concerned
- ➤ Step up research on palliative care, the healthcare system, patient and family well-being, etc.
- ➤ Support the set-up of caregiver and carer associations to increase support
- ➤ Pursue efforts and innovate on a European / international scale

9. Allemani C. et al. (2018). Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. The Lancet 2018 Mar 17;391(10125):1023-1075. doi: 10.1016/S0140-6736(17)33326-3.

FIGURE 48
NET 5-YEAR SURVIVAL IN PATIENTS DIAGNOSED BETWEEN 2010 AND 2014 (CONCORD-3 STUDY)



INCREASE FRANCE'S ATTRACTIVENESS FOR RESEARCH AND INNOVATION

- Support young researchers and attract young talents
- Promote cross-disciplinary training and encourage scientific expertise to meet new challenges and innovations in oncology
- Develop international research and support a network of young researchers in social and human sciences
- Structure paediatric research, organise and structure data sharing
- Coordinate with ongoing actions in the field of childhood cancer research
- Raise the profile of cancer research in France

Increase France's attractiveness for research and innovation

In order to achieve these aims, it is necessary to set up the necessary frameworks promoting skills and career development in France.

Indeed, supporting young researchers, their mobility, and preparing the scientific community for new challenges, particularly arising from technological innovations, are key to guaranteeing expertise and quality research. Moreover, multidisciplinary training and interdisciplinary interactions, particularly through support for specific networks and infrastructures, will help raise the profile and increase the momentum of French cancer research.

More specifically, as regards paediatric, adolescent and young adult cancer research, it seems necessary to support and step up cooperation through well-established clinical research infrastructures, information systems, reference groups and research networks for paediatric cancers. They will be able to form national or international networks providing the critical mass needed.

In its capacity as a state agency, the French National Cancer Institute will pursue and step up its involvement in building international programmes, particularly on topical issues.

4 Appendices

KEY RECOMMENDATIONS OF THE INTERNATIONAL SCIENTIFIC ADVISORY BOARD AND ACHIEVEMENTS

Recommendations

2007

- The board supports the investment plan made by INCa in training of physicians/scientists and translational researchers.
- The board encourages financial incentives for cooperative research groups willing to consolidate and study specific topics.
- The board would encourage an integrated approach within the European Union
- The board encourages supporting tumour banking at the institution level but thinks it should be focused on collecting material which is annotated with high quality control
- The board thinks the number of call of proposals is too high and should be reduced. Among the high priority areas are genomics and epigenetics. Systems biology is considered by the board as a tool and is not considered as an independent research priority

Actions achieved:

Since 2007: recurrent support for translational research training of students or young medical, pharmacy and veterinary science graduates, provided by ITMO Cancer since 2012

2012: evaluation of the translational training programme

2012-2015: Designation of 13 cooperative intergroups

2017: Designation of 11 cooperative intergroups

Since 2008, INCa has been a partner in 7 European projects aimed at coordinating research: European Partnership for Action Against Cancer (EPAAC), Joint Actions on rare cancers, cancer control, chronic diseases, TRANSCAN, FLAG-ERA, etc.

2011: Publication of institutional recommendations for the creation of tumour collections for research programmes

2011-2013: support for 14 national biological and clinical databases

Reduction in the number of call for proposals, INCa proposes 4 main investigator-driven programmes with international peer reviewing:

- Biology and basic sciences for cancer research;
- Translational cancer research, co-funded by DGOS (Ministry of Health);
- Clinical cancer research, operated by INCa and funded by DGOS (Ministry of Health);
- Research in human and social sciences, epidemiology and public health.

Specific strategic cancer research initiatives and thematic programmes launched according to research priorities.

Recommendations

2008

- The SAB supports real engagement of INCa in translational research which can be defined by direct collaborations between clinicians and bench researchers (see definition from the Translational Research Working Group - NCI*).
- As part of its responsibility in cancer leadership in France, INCa should
  - sponsor international symposia
  - continue leadership in public education
  - take a leading role in cancer survivorship issues
- The SAB members endorse the key role of INCa in coordinating cancer care, prevention and cancer research.

Actions achieved:

Annual call for proposals for translational cancer research, in partnership with the Ministry of Health (DGOS) since 2009

Participation in the European ERA-Net initiative to support joint translational research projects through the TRANSCAN programme since 2012

Recurrent support for translational research training since 2008

2012: Joint strategic research orientations published by INCa and ITMO Cancer-Aviesan.

Organisation of national and international congresses:
- 2010: Quality of Life of Cancer Patients
- 2011: Symposium on environment and cancer, International conference on the tumour microenvironment
- 2012: Symposium on Cancer and Inequalities, International R&D Dating, International forum on prospective in cancer research and treatment
- 2013: International symposium on nutrition and cancer
- 2014: International symposium on intervention research, Cancer. Life two years post-diagnosis (VICAN2)
- 2016: International symposium on nanomedicine in collaboration with NCI, International symposium on intervention research, Integrated research actions programmes workshops (Paediatrics, pancreatic adenocarcinomas)
- 2017: Cancer immunotherapy, progress and challenges

2012: Web documentary on Cancer research for the general public in collaboration with ARC Foundation

2015: publication of a brochure for patients on taking part in clinical trials in oncology, in partnership with the French Cancer League

2016: Online report on precision medicine

Report publications:
- 2012: Strategic report on a programme for cancer prevention research: Changing Health Behaviours and their Individual and Collective Determinants
- 2012: Report on the main advances in the tumour microenvironment (programme co-funded by INCa/ARC Foundation in 2006).

INCa appointed to steer the 2009-2013 and 2014-2019 National cancer control plans launched by the French President

Recommendations

2009

- We recommend defining the criteria for the centres of excellence (comparable to the comprehensive cancer centres in Europe and North America) and setting a process before opening a national call.
- We encourage INCa to work with the charities dedicated to cancer to leverage funds on strategic research programmes.
- We recommend developing a specific strategy for research in prevention involving the core population sciences (including behavioural and social sciences, epidemiology, public health, statistics, economics, etc.).

Actions achieved:

2009-2011: discussion and sharing of practices with the US NCI on the set-up of Comprehensive Cancer Centers in order to define the necessary criteria, proposal of the framework to the supervising ministries and the Board of Directors and preparation of the call for applications in partnership with DGOS and Inserm,

Designation of integrated cancer research sites (SIRICs):
- 2 in 2011, 6 in 2012
- 2017: new designation campaign: 8 SIRICs designated, including 6 renewed

Set-up of integrated research programmes (PAIR programmes) dedicated to a specific cancer type, in partnership with ARC Foundation and the French Cancer League

2010 & 2015: Joint support with the French Cancer League for CLIP² centres designation

2012-2017: Joint funding with ARC Foundation for early-phase clinical trials on innovative drugs in CLIP² centres

2016: Launch of the call for proposal dedicated to prevention of risks of second cancer with ARC Foundation

2013-2017: Launch of the AcSé programmes, sponsored by Unicancer and supported in partnership with ARC Foundation

2015: Launch of the research and action programme to reduce smoking and change the current prevalence of Tobacco-related cancers (PRIORITE Tabac), in partnership with ARC Foundation and the French Cancer League (3 calls for proposals scheduled)

Strategic report on cancer prevention research: changing health behaviours and their individual and collective determinants

Launch of a new call for proposals on population health intervention research

2014: Primary prevention call for proposals in collaboration with IReSP (French Public Health Research Institute)

Launch of a research chair on cancer prevention

Recommendations

2010

- The Board fully supports the prospective establishment of "molecular portraits" (including sequencing) in tumour samples from cancer patients. The Board recommends reassessment of the number of molecular diagnostic platforms and strongly supports interaction with basic/translational research focusing specifically on information systems between platforms and clinical data. One of the major issues the Board would like to highlight is the need to properly train clinicians and scientists in the new skills associated with molecular diagnostics and prognostics of cancer.
- The Board recommends that epigenomics and tumour microenvironment be part of the priorities.

Actions achieved:

2015: set up of the inter-SIRIC working group on data sharing (OSIRIS)

2017: support for the proof-of-concept study addressing technical, regulatory and organisational validation

Launch of thematic programmes by ITMO Cancer-Aviesan

2011: research programme on projects in physics, mathematics, and engineering sciences applied to cancer;

2012: research programme on systems biology;

2013: research programme on epigenetics;

2011

- The SAB strongly supports and endorses the SIRIC Initiative. While keeping it highly selective, the SAB recommends an increase in the number of SIRIC sites. We encourage INCa to increase the budget of the SIRIC sites and develop networking of SIRIC sites.
- INCa should foster the development of bioinformatics and medical information processing as well as research in complex systems in collaboration with other research organisations.

Actions achieved:

2014: Set-up of inter-SIRIC working groups on data sharing, immunotherapy, radiotherapy, etc.

2015: mid-term evaluation of the 8 SIRICs designated in 2011 and 2012

Coordination between SIRICs and Cancéropôles officially included in Cancéropôle objective and performance contracts and as criteria in the SIRIC mid-term evaluation.

2008: INCa joined the ICGC Programme and funded the breast and liver projects

2011-2014: ITMO Cancer funded the prostate, Ewing sarcoma and rare tumour projects (Retinoblastoma, Gynaecological Carcinosarcoma, Leiomyosarcoma and Prolymphocytic B-cell leukaemia projects)

2016: INCa joined the signatories of the Global Alliance for Genomics and Health

2016: Launch of the 2025 Genomic Medicine France Plan and the pilot Cancer trial

Recommendations

2012

- In light of the shocking increasing prevalence of smoking in France, we specifically recommend dedicated programmes that aim to develop and evaluate interventions to reverse this trend.
- Next-generation sequencing (NGS) represents a highly promising technology with marked potential for personalising cancer treatment and prevention. We recommend that large-scale NGS facilities be implemented at some of the SIRIC sites and services shared with the oncology community. Complementary bioinformatics expertise and clinical data management must be available at these centres.

Actions achieved:

2014: INCa member of the French delegation at the 6th Conference of the Parties (COP 6) of the Framework Convention on Tobacco Control (FCTC), held in Moscow from 13 to 18 October 2014

Launch of the National Programme to Reduce Smoking (PRNT)

2015: Launch of the research and action programme to reduce smoking and change the current prevalence of Tobacco-related cancers (PRIORITE Tabac), in partnership with ARC Foundation and the French Cancer League (3 calls for proposals scheduled)

2016: Launch of the plain packaging evaluation, DePICT evaluation study, funded by INCa

2016: National Decree establishing a specific fund for tobacco control

2013: Selection of molecular genetics centres for implementing NGS technology

2015-2017: roll-out of NGS technology in all molecular genetics centres (28) and oncogenetics laboratories (25)

Recommendations

2013

- The Board is pleased by INCa's leadership in the planning of the preparation of Third Cancer Plan. INCa is encouraged to use this opportunity to refine its portfolio of projects to better reflect the strategic priorities of the Cancer Plan.
- The Board applauds the agenda of the INCa in expanding the infrastructure of next generation sequencing (NGS) and implementing the results in clinical practice. This investment will likely pay off handsomely over the next five years in terms of improving clinical practice and personalised medicine.
- The Board encourages INCa to take leadership in developing partnerships with other agencies in fostering research in prevention, especially concerning tobacco and related products.
- The Board would like to encourage INCa to continue to develop communication tools, and dissemination of science towards the layperson, and interactions with patients' advocacy groups.

Actions achieved:

2012-2017: Discussions/collaboration with the pharmaceutical industry and biotechnology firms

2015: INCa joined the signatories of the Melbourne Call launched by the International Consortium for Action and Research on Tobacco (ICART).

2016:
- Memorandum of Understanding signed with China's National Cancer Center
- Agreement signed with WHO– Department of Reproductive Health and Research

2017: Memorandum of Understanding signed with the Ministry of Science and Technologies of Taiwan

2013-2017: emphasis on strategic clinical initiatives to strengthen personalised medicine

2013: Launch of the AcSé programme

2015: start of the use of NGS in routine clinical practice in molecular genetics centres and oncogenetics laboratories

2015: Launch of the first joint programme of actions in research/public health to combat tobacco-related cancers with ARC Foundation and the French Cancer League (in collaboration with Inpes, MILDECA and DGS)

2007: Cancer clinical trial registry available on INCa's website to provide information on open trials launched in France (academically and industrially sponsored trials)

Participation of patient representatives in all of INCa's scientific review committees

2015: 2 patient representative members of the International Scientific Advisory Board for a 5-year term

Involvement of patient representatives and associations in the drafting of specific calls for proposals (objectives and application forms)

2016: Launch of the Paediatrics PAIR, prepared and supported in partnership with the association Imagine for Margo

2016: Launch of AcSé-eSMART, funded in partnership with the association Imagine for Margo and ARC Foundation

Recommendations

2014

- The Board is fully impressed by the achievements made by the molecular screening programme (28 molecular genetics centres) and wishes to proceed to this 'omics' programme as this is a unique programme. We strongly endorse the proposal to establish a network linking the major established platforms.
- The Board encourages INCa to leverage the on-going precision medicine trials with tumour microenvironment and immune read-outs.
- The Board acknowledges INCa's efforts to build capacity in the area of prevention/ intervention research implementation. However, it is concerned that this multidisciplinary domain still needs to be further developed in collaboration with other relevant agencies. The Board strongly suggests that the priority about tobacco control should be used to strengthen this field.
- The Board strongly encourages INCa to continue to hold French authorities to account to ensure they meet all their obligations as signatories of the WHO Framework Convention on Tobacco Control.
- The Board strongly supports the priority on basic understanding of the tumour ecosystem and looks forward to seeing specific implementation plans.

Actions achieved:

2013-2016: Launch of the AcSé programme to provide secured access to targeted therapies
- 2013: Launch of AcSé-Crizotinib
- 2014: Launch of AcSé-Vemurafenib
- 2016: Launch of AcSé-eSMART clinical trial for paediatric patients
- 2017: Launch of two immunotherapy clinical trials: AcSé-Nivolumab and AcSé-Pembrolizumab

2015: Launch of a research chair in cancer prevention (in collaboration with EHESP and IResP)

2017: Preparation of the call for applications dedicated to the roll-out of the TABADO campaign to support smoking cessation targeting young people in vocational high schools and apprentice training centres scheduled for 2018

2016: in May, the French Minister of Health announced several measures under the PRNT programme, such as the roll-out of plain packaging

2016: Launch of the 2nd Tobacco related-cancer programme including areas focused on biology and inflammation and tobacco substitution

2017: increase in cigarette pack price

2015: Launch of the research programme on tumour heterogeneity and ecosystems by ITMO Cancer

Recommendations

2015

- Investing in the next generation of young independent investigators and the training of clinicians, pharmacists and veterinarians will ensure the future of basic and translational cancer research. While the Board appreciates what INCa has achieved so far on this front, we recommend a strong increase in the number and the duration of grants awarded to young researchers. It will be also important to develop new actions for the continuous training of clinician scientists.
- The Board applauds the creation of a Chair dedicated to cancer research prevention. It congratulates INCa for its leadership in developing the required partnerships with other French agencies and institutes. The Board encourages INCa to continue its work in capacity building for cancer prevention research in France.
- The Board applauds the comprehensive approach to precision cancer medicine for paediatric patients across France.

Actions achieved:

2015-2017: 2-year extension in the support for young researchers granted in the ATIP-Avenir programme

2016: Launch of a university research chair in human and social sciences (in collaboration with University Lille 3 and ONCOLille SIRIC).

2016: Launch of the integrated research programme PAIR on paediatrics, in partnership with ARC Foundation and the French Cancer League in order to increase and enhance dynamic research capabilities, and strengthen bridges between different disciplines in paediatric oncology

Recommendations

2016

- The expansion of clinical trials should not come at the expense of a reduction of phase I and II trials.
- INCa should discuss with ANSM an efficient way to reduce timelines for the evaluation and activation of clinical trials.
- As a general rule for all programmes supported by INCa and the dissemination of results, the involvement of patients should be strengthened.

Actions achieved:

2010 & 2015: designation of early phase CLIP² centres

2011-2016: 12 calls for proposals, 21 drugs, 18 early-phase clinical trials funded and conducted in CLIP² centres

2017: discussions with pharmaceutical firm to launch new calls for proposals for innovative drugs

2017: INCa requested all CLIP² centres to review the actual timelines for early-phase clinical trials assessing innovative drugs

Support for the proofreading of briefing notes, preliminary proposals or letters of intent, and patient information documents launched by the French Cancer League

2016 Nanotechnology congress: Dedicated Round table on Ethics and societal issues

2017: Set-up of the Health Democracy Committee involving
- representatives of health system users;
- people who have or have had cancer;
- relatives or caregivers;
- representatives of palliative and end-of-life aspects;
- representatives of the social vulnerability issue.

Recommendations

2017

- The Board is pleased and eager to serve in a more strategic advisory role and is in favour of the constitution of ad hoc action groups around specific strategic topics.
- The Board underscores the need for systematic assessment of impact and return of investment of the INCa research funding programmes (Scientific report 2017 should include some of these analyses). A specific impact report should be presented in the two years, the framework should be presented in 2018 and the final report in 2019.
- Building on the progress made on tobacco control research, the Board recommends expanding the prevention research focus to include the three main modifiable behavioural risk factors that are obesity, alcohol and physical inactivity.

Actions achieved:

A first action group of the International Scientific Advisory board has been set up to address paediatric cancer issues and to define a strategic roadmap

The design of the Scientific report have been revamped and the 2017 Scientific report presented trend analyses, with a particular emphasis on the comparison of 2007 vs 2017, acknowledged by the International Scientific Advisory Board

INCa is organising an international congress on the added value of population health intervention research to foster discussions to support the development of innovative research projects involving all stakeholders, particularly on lifestyle factors

COMMON SCIENTIFIC OUTLINE

Established in 2000, the International Cancer Research Partnership (ICRP) is a unique alliance of cancer organisations, working together to enhance global collaboration and strategic coordination of cancer research. It includes 110 worldwide organisations from Australia, Canada, France, Japan, the Netherlands, United Kingdom, and the United States. INCa joined this partnership in 2009.

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

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

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

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

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

THE DIFFERENT CSO CATEGORIES INCLUDE:

- **CSO 1 Biology**
  - **1.1** Normal Functioning
  - **1.2** Cancer Initiation: Alterations in Chromosomes
  - **1.3** Cancer Initiation: Oncogenes and Tumour Suppressor Genes
  - **1.4** Cancer Progression and Metastasis
  - **1.5** Resources and Infrastructure

- **CSO 2 Aetiology**
  - **2.1** Exogenous Factors in the Origin and Cause of Cancer
  - **2.2** Endogenous Factors in the Origin and Cause of Cancer
  - **2.3** Interactions of Genes and/or Genetic Polymorphisms with Exogenous and/or Endogenous Factors
  - **2.4** Resources and Infrastructure Related to Aetiology

- **CSO 3 Prevention**
  - **3.1** Interventions to Prevent Cancer: Personal Behaviours that Affect Cancer Risk
  - **3.2** Nutritional Science in Cancer Prevention
  - **3.3** Chemoprevention
  - **3.4** Vaccines
  - **3.5** Complementary and Alternative Prevention Approaches
  - **3.6** Resources and Infrastructure Related to Prevention

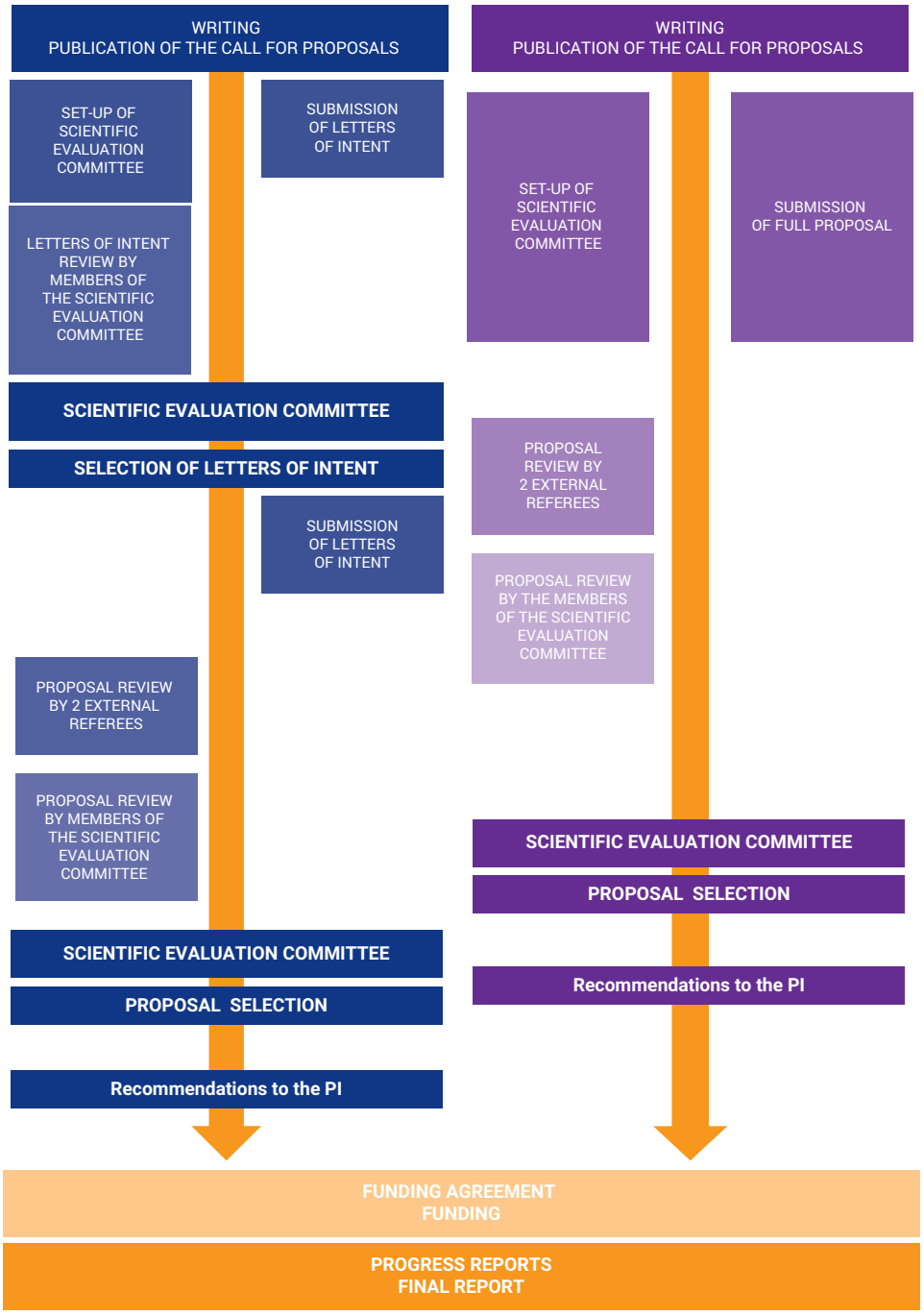
- **CSO 4 Early Detection, Diagnosis, and Prognosis**
  - **4.1** Technology Development and/or Marker Discovery
  - **4.2** Technology and/or Marker Evaluation with Respect to Fundamental Parameters of Method
  - **4.3** Technology and/or Marker Testing in a Clinical Setting
  - **4.4** Resources and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

- **CSO 5 Treatment**
  - **5.1** Localised Therapies - Discovery and Development
  - **5.2** Localised Therapies - Clinical Applications
  - **5.3** Systemic Therapies - Discovery and Development
  - **5.4** Systemic Therapies - Clinical Applications
  - **5.5** Combinations of Localised and Systemic Therapies
  - **5.6** Complementary and Alternative Treatment Approaches
  - **5.7** Resources and Infrastructure Related to Treatment

- **CSO 6 Cancer Control, Survivorship, and Outcomes Research**
  - **6.1** Patient Care and Survivorship Issues
  - **6.2** Surveillance
  - **6.3** Behaviour
  - **6.4** Cost Analyses and Health Care Delivery
  - **6.5** Education and Communication
  - **6.6** End-of-Life Care
  - **6.7** Ethics and Confidentiality in Cancer Research
  - **6.8** Complementary and Alternative Approaches for Supportive Care of Patients and Survivors
  - **6.9** Resources and Infrastructure Related to Cancer Control, Survivorship, and Outcomes Research

- **CSO 7 Scientific Model Systems**
  - **7.1** Development and Characterisation of Model Systems
  - **7.2** Application of Model Systems
  - **7.3** Resources and Infrastructure Related to Scientific Model Systems

INCA'S CALLS FOR PROPOSALS: SCIENTIFIC AND OPERATIONAL MANAGEMENT



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