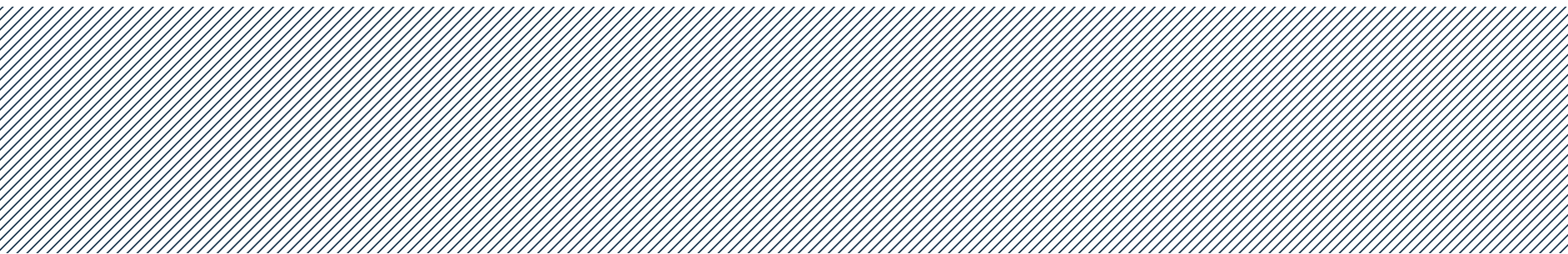
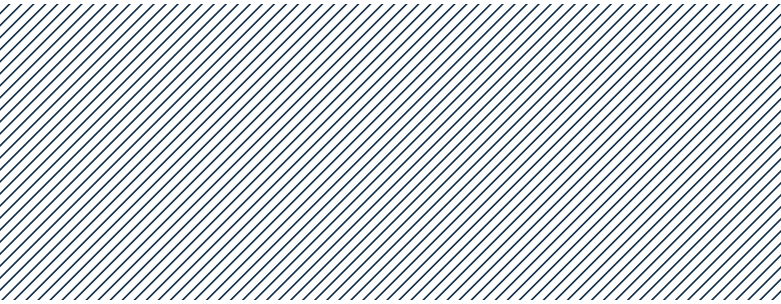


**LEEM'S  
COMMITMENT TO  
COMBATING CANCER**  
OUR 15 GOALS

**2018**





**LEEM'S COMMITMENT  
TO COMBATING  
CANCER**  
OUR 15 GOALS





**Jean-Christophe BARLAND**  
*Chairman of Leem's Cancer Committee*

## INNOVATION & DIALOGUE

Leem's Cancer Committee is made up of companies committed to combating cancer and has made it its mission to drive innovative advances in oncology and provide guidance on the choices made today that will in turn determine the health-care of tomorrow.

The field of oncology is experiencing a shake-up due to an unprecedented wave of innovations such as next generation immunotherapies, targeted therapies, genome sequencing, big data and its growing influence in research, and changes in the organisation and pathways of care as a result of digital transformation.

This accelerated pace of innovation in oncology presents France with a great opportunity to further enhance French excellence and simultaneously a formidable challenge.

Translating these innovations into a therapeutic reality for patients: such is our responsibility as a pharmaceutical industry engaged in education, outreach and dialogue with all stakeholders to combat cancer on the basis of concrete proposals. A national framework - three Cancer Plans - and the creation of the National Cancer Research Institute (INCa) have resulted in improved and structured research and healthcare initiatives across the country, providing a real impetus to cancer care in France.

France is at the forefront of Europe in leading research and care for cancer patients as well as in the distribution of innovative therapies.

Today, the challenging economic environment and the growing needs of patients mean that this unique model must be defended and strengthened. France can only continue its pioneering and leadership role in the field of cancer therapy through a partnership approach that encompasses all stakeholders - patients and their representatives, researchers, clinicians, healthcare professionals and manufacturers, and government.

This is the goal of this platform: to open up dialogue in a spirit of sharing, engagement and transparency with the same aim in mind, to roll back cancer.

# CONTENTS

<b>1</b> ▶ THE FIGURES FOR CANCER	p.9
<b>2</b> ▶ THE CANCER TREATMENTS	p.11
<b>3</b> ▶ THE CHALLENGES	p.13
<b>4</b> ▶ THE GOALS	p.15

## 4 ▶ OUR FIVE GOALS TO STIMULATE RESEARCH

---

### GOAL 1 p.20

Make the French regulatory framework for clinical trial setups more fluid

### GOAL 2 p.22

Speed up regulatory approvals for early-phase clinical trials

### GOAL 3 p.24

Optimise patient enrolment into clinical trials

### GOAL 4 p.26

Structure large clinical research programmes through public-private partnerships (PPPs)

### GOAL 5 p.28

Make the Research Tax Credit (CIR) a permanent fixture in order for France to remain fiscally attractive

## 5 ▶ OUR SIX GOALS TO FACILITATE EARLY PATIENT ACCESS TO INNOVATIVE MEDICINES

---

**GOAL 6** // p.34  
Anticipate innovative breakthroughs

**GOAL 7** // p.36  
Adapt assessment methodologies to the new challenges posed by cancer drug therapies

**GOAL 8** // p.40  
Optimise real-time data collection

**GOAL 9** // p.42  
Improve early access schemes (ATU - authorisations for temporary use - and RTU - recommendations for temporary use)

**GOAL 10** // p.46  
Develop performance-based contracts for innovative products

**GOAL 11** // p.48  
Reform the arrangements for funding in-hospital cancer drug therapies

## 6 ▶ OUR THREE GOALS TO IMPROVE THE CARE PATHWAY

---

**GOAL 12** // p.54  
Encourage the shift to outpatient care and ensure that the change is managed to improve the organisational impact of the treatments

**GOAL 13** // p.58  
Support integrated care initiatives

**GOAL 14** // p.60  
Put in place funding for the oncology pathway

## 7 ▶ PAEDIATRIC ONCOLOGY

---

**GOAL 15** // p.64  
A shared goal: paediatric oncology. Give the best chance of survival to the 2,500 children affected each year by cancer

1

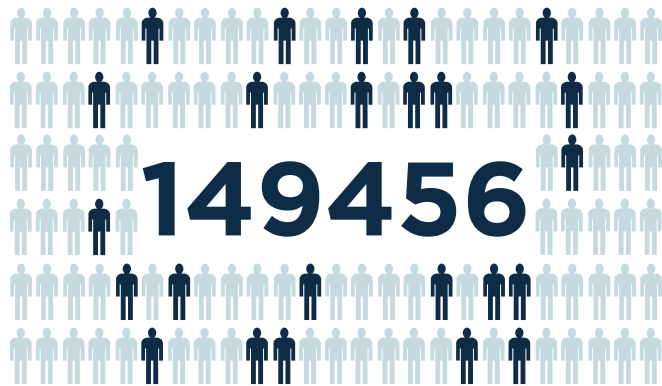


**THE FIGURES  
FOR CANCER**





**1,053:** the number of new cases of cancer diagnosed every day in France.



**149,456:** the number of deaths caused by cancer in France each year. Cancer is the leading cause of death in France.

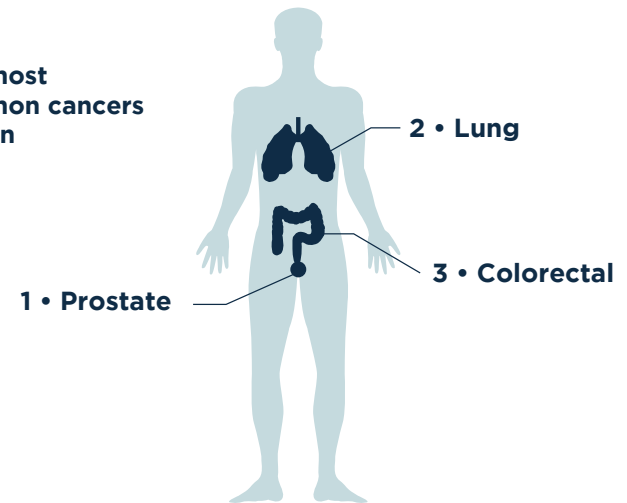


**More than half of all patients** recover from cancer

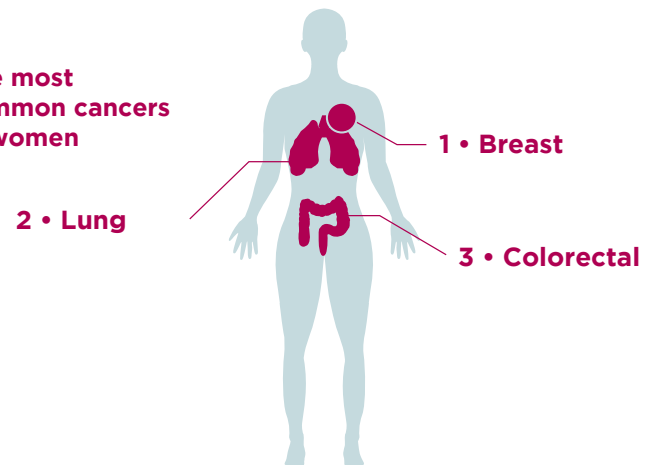
# 3 million

the number of people aged 15 and over, still alive in 2008, who have had cancer in their lifetime

**The most common cancers in men**



**The most common cancers in women**



2

▶ **THE CANCER  
TREATMENTS**

## The medicines in development

1,813 medicines are being developed to treat cancer. More than 70 new cancer drugs have been granted authorisation over the last 5 years, a large proportion of which have been targeted therapies.

France is the only European country to have set up an academic network of 28 molecular genetics platforms to perform molecular diagnostics for the approved targeted therapies. 100,000 molecular tests are performed each year for 75,000 patients.

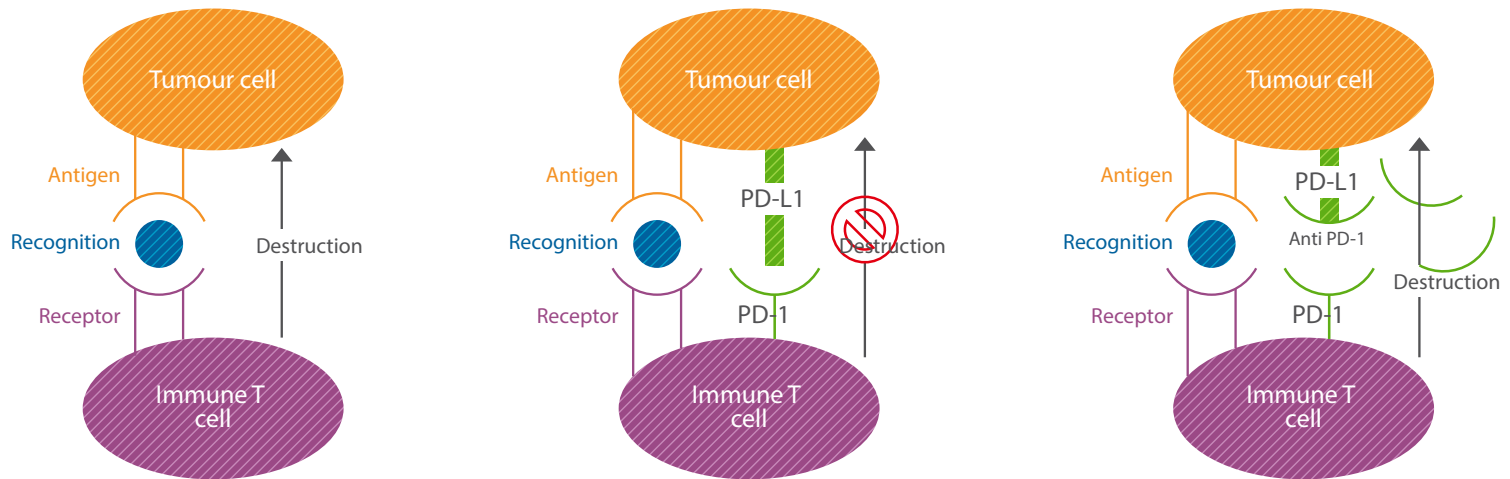
Over the course of 5 years, several immune checkpoint inhibitors (PD1/PDL1) have been indicated for the treatment of several advanced-stage cancers.

Source: EFPIA figures encompassing all drug development phases

## Innovative therapeutic drugs

The cancer drugs under development are at the forefront of innovation.

- 47% of the 804 clinical trials of innovative therapies underway in December 2016 worldwide are for cancer (Source Alliance for Regenerative Medicines).
- The term innovative therapies encompasses gene, cell (CAR-T cells), tissue and combination therapies.



1 • Normally, the immune system cells (self) recognise pathogens or tumour cells (nonself) and are able to destroy them.

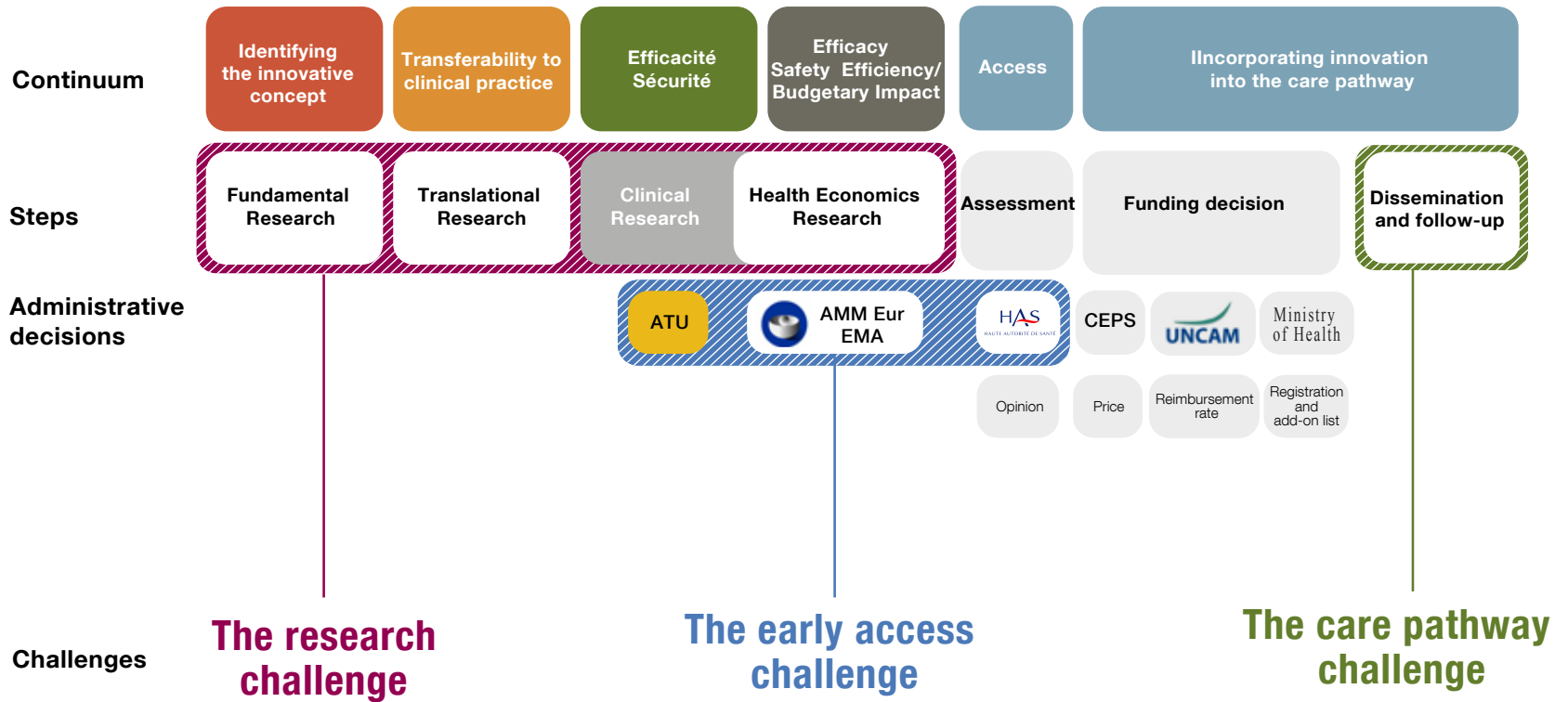
2 • The tumour cells can send a signal to block this destruction by binding one of their membrane proteins (PD-L1) to the immune cell receptor (PD-1).

3 • By binding to PD-L1, the anti-PD-1 agents allow the immune cell to play its role (diagram 1) and destroy the tumour cell.

## Immunotherapy drugs

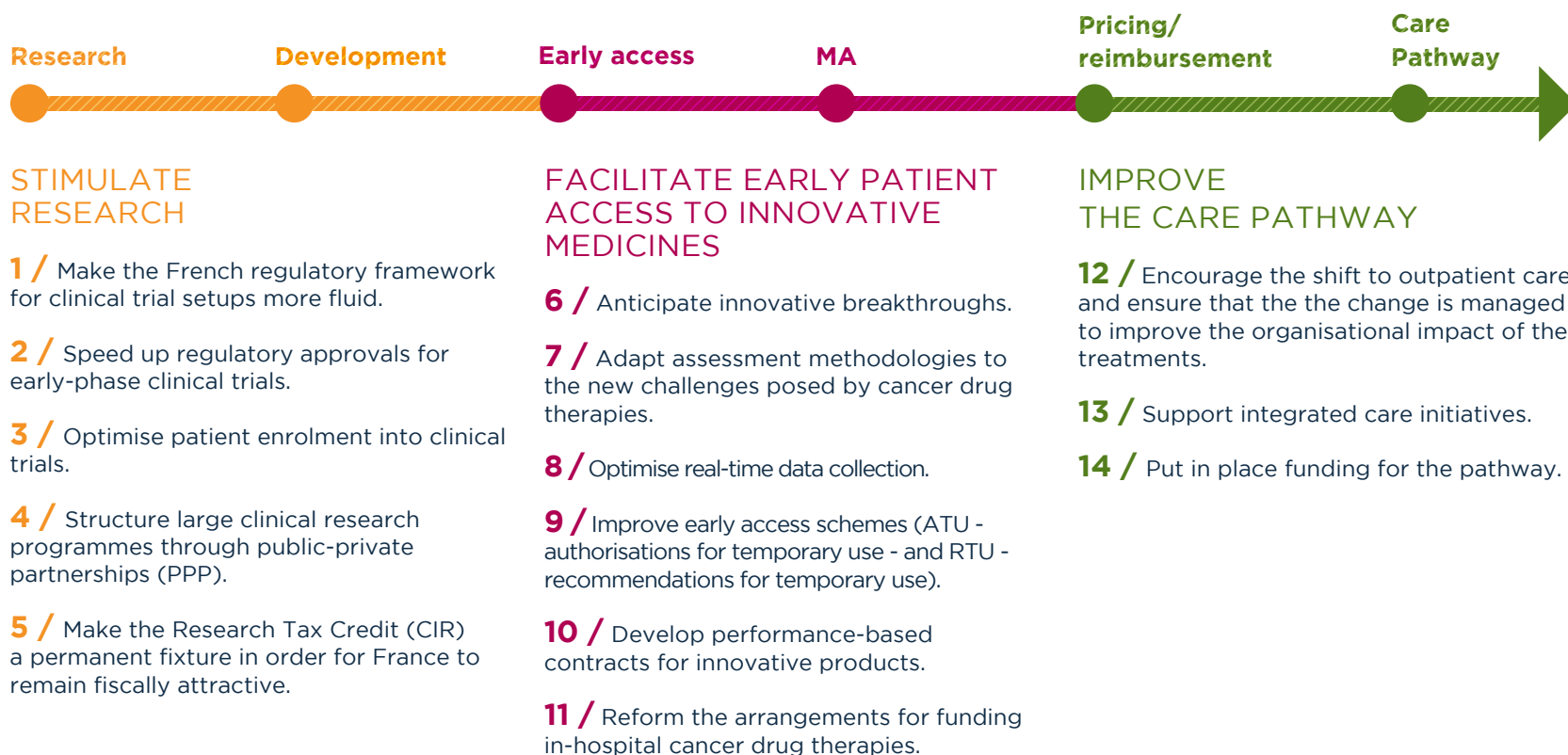
Immunotherapy involves using the patient's natural defences by mobilising the immune system to recognise and destroy cancer cells. The immune system responds when a virus, bacteria or other pathogen enters the body. It is thus able to recognise and destroy cells that have turned cancerous. Unfortunately, in some instances they are able to evade this immune reaction by activating another pathway. One of the major challenges of immunotherapy, therefore, is to restore the anti-tumour action of our defence system.

# 3 THE CHALLENGES



# 4 THE GOALS

## Drug life-cycle & ranking of the 14\* goals



**MA:** Marketing authorisation

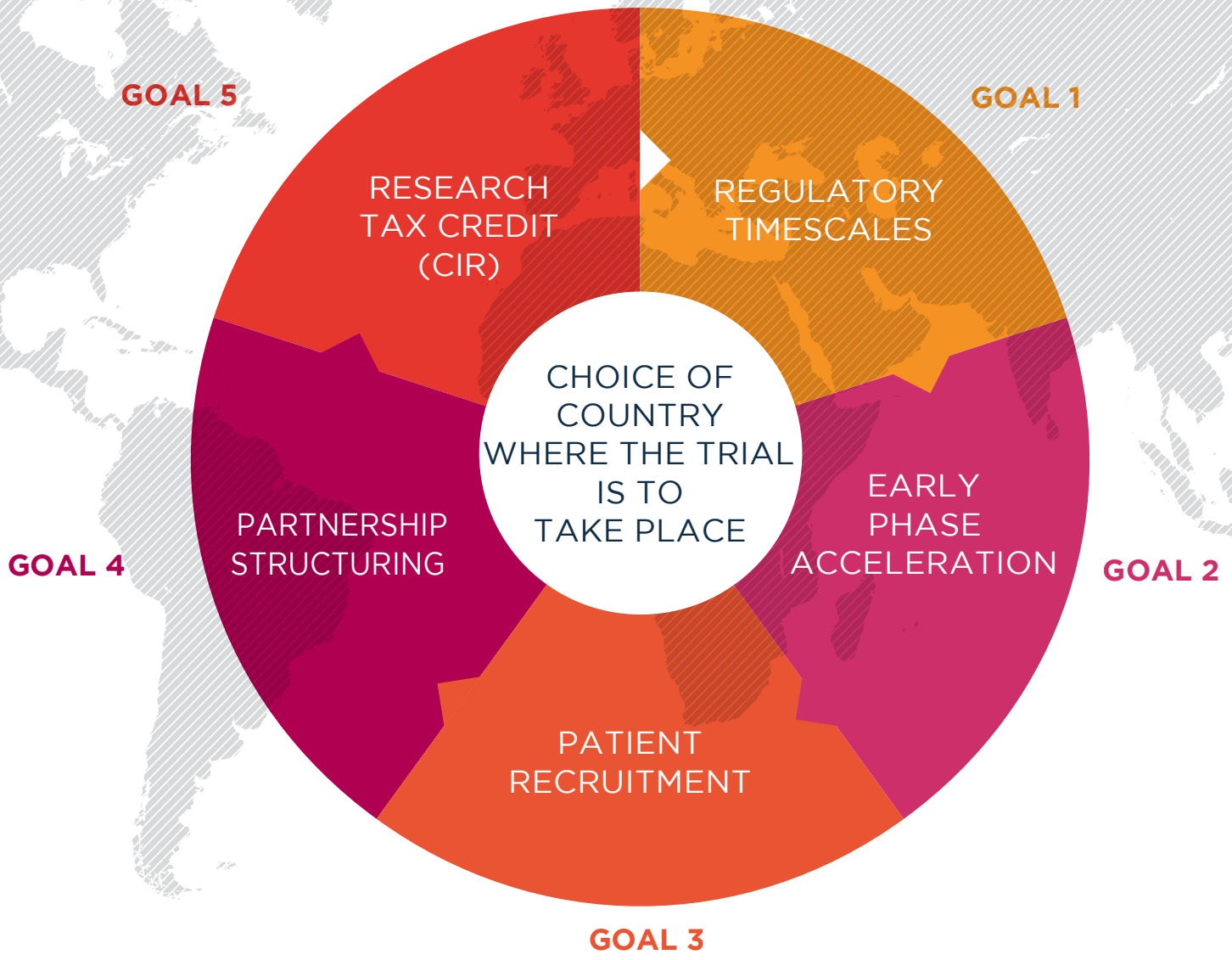
\* The 15th goal is a shared goal still under development

# 4 → OUR FIVE GOALS TO STIMULATE RESEARCH



Ensuring that France remains an attractive location for clinical research is a priority concern for patients, because rapid access to innovation is crucial, including at the early stages of development.

*Factors determining the choice of country  
where the trial is to take place*



**GOAL 1**  **p.20**

Make the French regulatory framework for clinical trial setups more fluid.

**GOAL 2**  **p.22**

Speed up regulatory approvals for early-phase clinical trials

**GOAL 3**  **p.24**

Optimise patient enrolment into clinical trials

**GOAL 4**  **p.26**

Structure large clinical research programmes through public-private partnerships (PPPs)

**GOAL 5**  **p.28**

Make the Research Tax Credit (CIR) a permanent fixture in order for France to remain fiscally attractive

## GOAL 1

# Make the French regulatory framework for clinical trial setups more fluid

### Regulatory timescales for setting up clinical trials in France

#### for setting up clinical trials in France Technical and regulatory authorisations (ANSM, CPP)



# 45%

The proportion of clinical studies for cancer conducted by industry. This figure was 41% in 2014.

# 60 days

The regulatory time limit set for 2019.

# 57 days

The median time for ANSM (National Agency for Medicines Safety) to give its approval.

# 62 days

The median time before the Comité de Protection des Personnes (CPP - equivalent to the Institutional Review Board in the US and the Ethics Committee in the UK) issues an opinion.

### Single agreement

To improve the timeliness of setting up clinical studies, France has made a single agreement mandatory for all industrial clinical trials since November 2016. It sets a time limit of 45 days for signing with the coordinating centre, plus an additional 15 days if other associated centres are taking part in the study.

## Overview

France is at the forefront of global clinical research and has the wherewithal to conduct high-quality clinical research: academic excellence, high-calibre clinical trial centres, research structuring, doctors with a high degree of scientific expertise, quality of care, etc.

However, the implementation of the Jardé Act in 2016 (research involving human beings), requiring the random distribution of dossiers among the different CPPs, poses the risk of further delaying the start of clinical trials. Indeed, some CPPs do not yet have the expertise required to investigate oncology dossiers, the bulk of which have been dealt with until now by only a small number of CPPs.

By way of illustration, 50% of studies (all diseases combined) have received a favourable opinion from only nine out of the forty CPPs in France and 80% of studies have received an opinion from 21 CPPs, which shows that dossier management is highly concentrated among some CPPs. The Jardé Act requires that all studies carried out on human beings be appraised by a CPP. These changes were not anticipated and risk increasing the time taken to start the studies.

ANSM is confronted by a rise in the number of dossiers for processing and by the growing complexity of oncology protocols. There is a risk that the arrival of advanced-therapy medicinal products (gene, cell, mixed) may increase the specific nature of the agency's work and extend the lead time as a result.

The longer regulatory timescales represent a loss of opportunity for cancer patients who are often faced with a survival issue. This is because clinical trial participation is often the last treatment alternative or allows them access to promising investigational treatments.

Often the difficulties encountered when obtaining approval for and implementing trials make France a less attractive destination and result in a lower number of clinical trials in the country. As a consequence, several biotechnology companies have decided to relocate their clinical trials because of the unreasonable regulatory timescales.

## Our proposals

> **1 / Pool the skills of the various CPPs** and increase their expertise in oncology by training them in the specificities of the clinical trial protocols and in the new mechanisms of action of the innovative technologies in an effort to shorten the dossier processing timescales

> **2 / Allow each CPP to capitalise on its experience** and handle the development plan covering the same molecule for a given indication or therapeutic area, especially where gene therapy and paediatrics are concerned.

> **3 / Provide the bodies which scrutinise the approval dossiers** (CPP, ANSM) with additional human and financial resources to shorten the administrative timescales for setting up clinical trials.

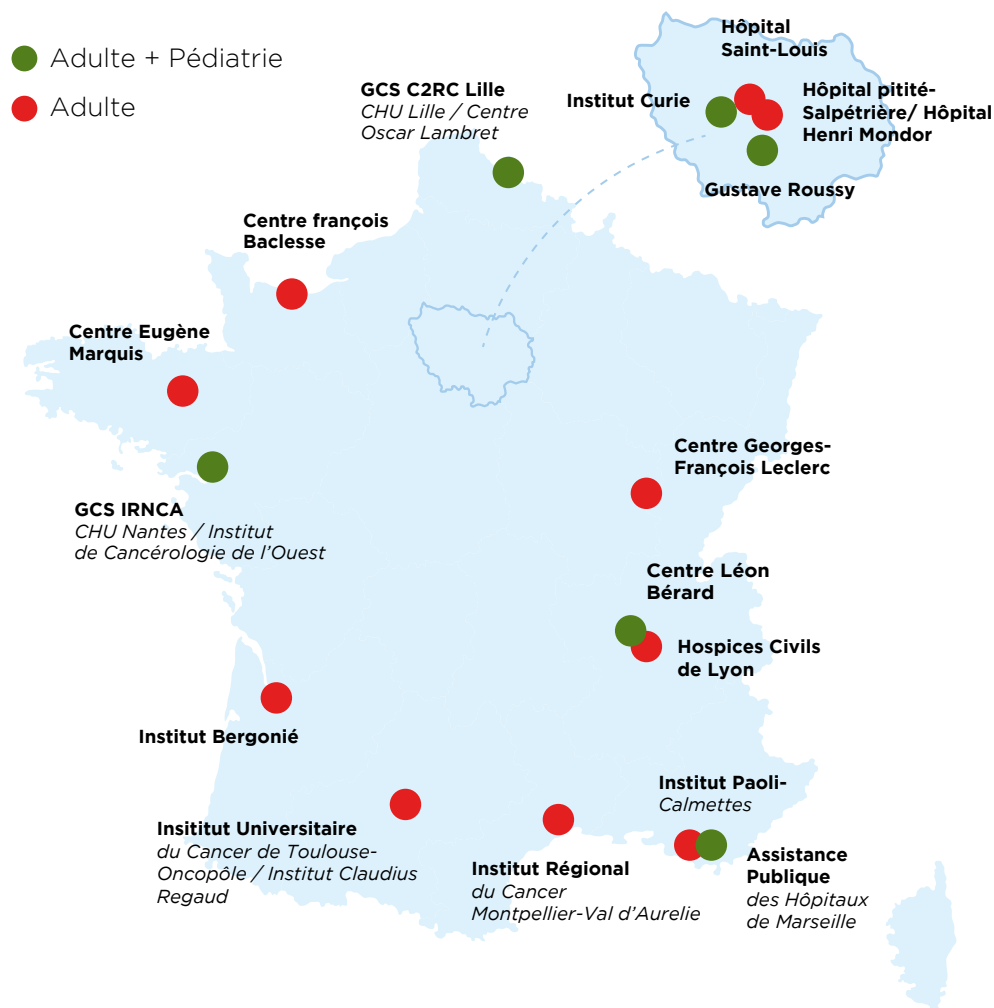
> **4 / Streamline approvals for observational trials:** simplification of requests for CNIL approval.

> **5 / Support the roll-out of the Single Agreement by providing new users** with information and training (via frequently asked questions or recommendations).

## GOAL 2

# Speed up regulatory approvals for early-phase clinical trials

### Map of INCa-accredited early-phase centres (CLIP)



# 60 days

The time taken for ANSM to approve early-phase trials in 2016. This figure was **54 days** in 2014.

### Early phase

An early-phase clinical trial (or phase 1 trial) involves an assessment of the safety profile of new agents (administered alone or in combination with another therapy), their effects on the body, and the adverse reactions they may cause in humans, and sets out to obtain initial information concerning their activity. It often coincides with the first administration of a medication in humans.

### The CLIP centres

These centres were first set up in 2010 and currently number 16. The CLIP centres are helping to improve the quality of clinical trials in France and to enhance the profile and attractiveness of France for early-phase studies among pharmaceutical companies<sup>1</sup>.

(1) Site: [www.e-cancer.fr](http://www.e-cancer.fr)

## Overview

As a country with outstanding expertise in the field of research and that benefits from initiatives recently introduced to improve the timescales for clinical trial setups (single agreement, new European regulation), France is well equipped to attract early-phase clinical trials to his soil. These strengths are bolstered by the existence of expert clinical trial centres dedicated to early-phase studies, the Accredited Early-Phase Centres (CLIP).

France, however, has to contend with regulatory difficulties to secure ANSM approval for early-phase trials, thereby resulting in overruns of the time limits set by the European Regulation (60 days) or a rejection.

In 2017, for example, one manufacturer waited 82 days for regulatory approval to launch its clinical trial, much longer than in previous years.

A lack of internal resources at ANSM is the reason for these lengthier timescales

The random assignment of dossiers to the newly established CPPs does not put their experience to full use and dilutes expertise. As a result, the CPPs are facing difficulties when analysing the often more complex early-phase dossiers, thus causing the regulatory timescales to overrun.

The issue of regulatory timescales is crippling France because the speed at which early-phase trials are set up is a key criterion in choosing a country. The harm to France is greater still as it is more likely to attract phase II and III trials if the phase I trial was conducted on French soil.

## Our proposals

> **1 / Support changes to the internal organisation of ANSM** for the creation of a unit dedicated to reviewing early-phase trial dossiers and provide it with the necessary resources to process cases within a competitive time frame.

> **2 / Allow certain CPPs** to specialise in early-phase trial dossiers so as to equip them with the expertise needed to analyse these often more complex dossiers.

> **3 / Promote early-phase trials by introducing an administrative fast-track mechanism** which allows prioritisation of their dossiers at ANSM and at CPP level.

**ANSM:** National Agency for Medicines and Health Products Safety

**CHU:** University Hospital

**CLCC:** Cancer Research Centre

**CLIP:** INCa-Accredited Centre for Early-Phase Trials

**CPP:** Institutional Review Board (USA) or Ethics Committee (UK)

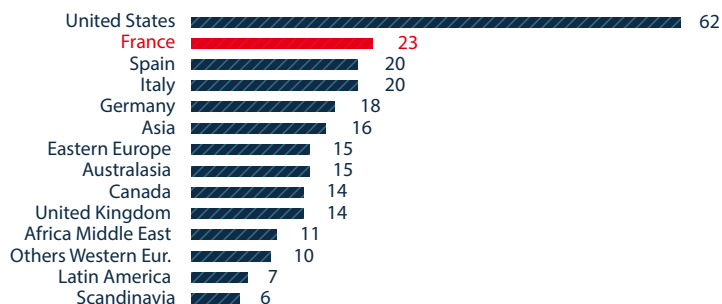
**INCa:** National Cancer Institute

## GOAL 3

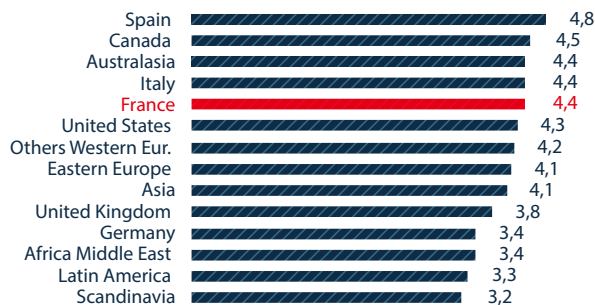
# Optimise patient enrolment into clinical trials

### Clinical trials

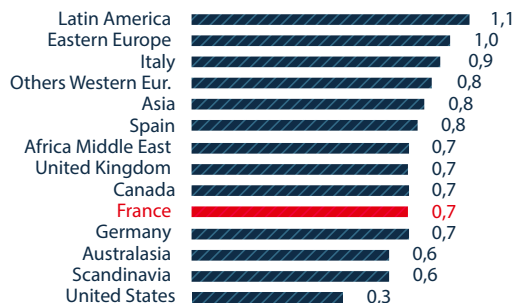
Average number of patients per trial



Average number of patients per centre



Rate of recruitment (number of patients recruited per centre per month)



### Recruitment

The recruitment of oncology patients in France has improved slightly since the Leem 2014 survey. The average number of patients per study rose from 22 in 2014 to 23 in 2016. The number of patients per centre increased from 4 in 2014 to 4.4 in 2016 and the recruitment rate from 0.6 in 2014 to 0.7 in 2016. France is thus still level pegging with its Western Europe and US competitors in oncology research. Patients now have a better understanding of clinical trials and associate them with early access to innovation.



## Overview

France must take action to maintain its position as a benchmark country. To optimise recruitment, 5 areas of improvement have been identified:

- urge clinicians or institutions to become involved in the recruitment process;
- provide stakeholders in the system (clinicians, patient associations, families, the general public, etc.) with better information on trials that are open to recruitment, so that better guidance is given to patients;
- challenge the geographical inequalities of access to clinical trials due to the uneven distribution of the clinical trial centres;
- address the shortage of human resources needed in order for the centres to include patients in the trials;
- Improve the INCa-run clinical trials database, which is still not comprehensive enough.

## Our proposals

### > 1 / **Continuously feed information into the INCa public** database on

clinical trials for adults and children and make it available on the online portal of the National Insurance Fund in a format that is easily readable by clinicians, associations, patients, families and the general public.

### > 2 / **Expand the tools already available to the multidisciplinary consultative meetings** (RCP) with the information contained in the database listing

all the relevant trials for each centre so that an alert can be triggered if a patient is eligible to join a trial.

### > 3 / **Identify patients who are eligible to join each clinical trial from existing databases** (the National Hospital Database made available on a

monthly basis, data from the genome platforms, etc.) and,

- determine in real time the number of patients eligible for a trial and relay this information through an alert system to the health centres and to the RCPs so they can increase the patient recruitment rate;
- relay this information via an alert system directly to patients (via the patient's cancer communication file) to inform them of the existence of the trial;
- optimise the resources of the oncology mobile clinical research teams led by the 7 GIRCI.

## GOAL 4

# Structure large clinical research programmes through public-private partnerships (PPP)

### New study designs



## UMBRELLA TRIAL

A clinical study involving multiple drugs and multiple biomarkers in a single cancer type (e.g.: SAFIR).



TRIAL 1



DRUG 1 DRUG 2 DRUG 3

TRIAL 2

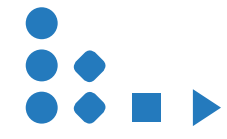
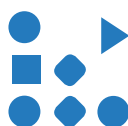


DRUG 1 DRUG 3 DRUG 4



## BASKET TRIAL

Clinical study involving a single agent and one or more biomarkers in several cancers (e.g.: AcSé).



DRUG 1



DRUG 2

# 2

The number of new programmes proposed in the Genomic Medicine France Plan 2025 that are due to be launched for sarcoma (Multisarc) and colorectal cancer (Acompli).

# 28

The number of INCa-accredited molecular cancer genetics platforms

### Basket trial

The paucity of therapies available for each biomarker means that the economic risk involved in a basket trial is huge. Pharmaceutical companies will therefore not commit to this type of trial on their own.

### MOSCATO

Example of a trial

Clinical trial involving multiple molecules and multiple biomarkers for several cancers.

## Overview

Personalised medicine demands new designs for specific clinical trials such as baskets trials.

The clinical research projects initiated in personalised medicine in recent years (AcSé, MOSCATO and other programmes) have proven their scientific value. Other trials of this type could also see the light of day by way of a new University Hospital Institute (IHU) specialising in oncology.

These programmes are based on an analysis of a patient's tumour profile using high-throughput sequencing to identify tumour biomarkers and direct the patient, where appropriate, to the most relevant clinical trial based on the biomarker expression in the tumour.

And yet studies such as AcSé experience a high rate of attrition in patient recruitment because they require that a large number of tumours be profiled to obtain a representative sample for a given alteration. Considerable human and financial resources are thus mobilised to form relatively small cohorts, which often culminates in insignificant results.

The paucity of therapies available for each biomarker means that the economic risk involved in this type of study is huge. Formalised partnerships with other manufacturers would spread the risk while also testing a larger number of agents. State intervention would strengthen their economic viability by pooling existing infrastructures and would allow them to benefit from a large-scale database provided under the Genomic Medicine France Plan 2025. The public-private partnership (PPP) framework is thus proving effective in ensuring the optimal implementation of basket or umbrella trials.

To optimise the generation of meaningful results, the Multisarc and Acomplis studies include the profiling of a much larger number of biomarkers and a trial design that involves the testing of several molecules according to identified biomarker. These two French government-sponsored clinical research programmes operate across the 28 INCa-accredited molecular cancer genetics platforms already in existence.

**INCa:** National Cancer Institute  
**Multisarc:** Personalised medicine programme for soft tissue sarcoma  
**AcSé:** Secure access to innovative targeted therapies  
**AMM:** Marketing authorisation

## Our proposals

**> 1 / Foster exchanges between academic and industrial researchers** in an effort to facilitate the implementation of joint fundamental and translational research projects such as RIR (International R&D Dating) and RIB (International Biotechnology Forum).

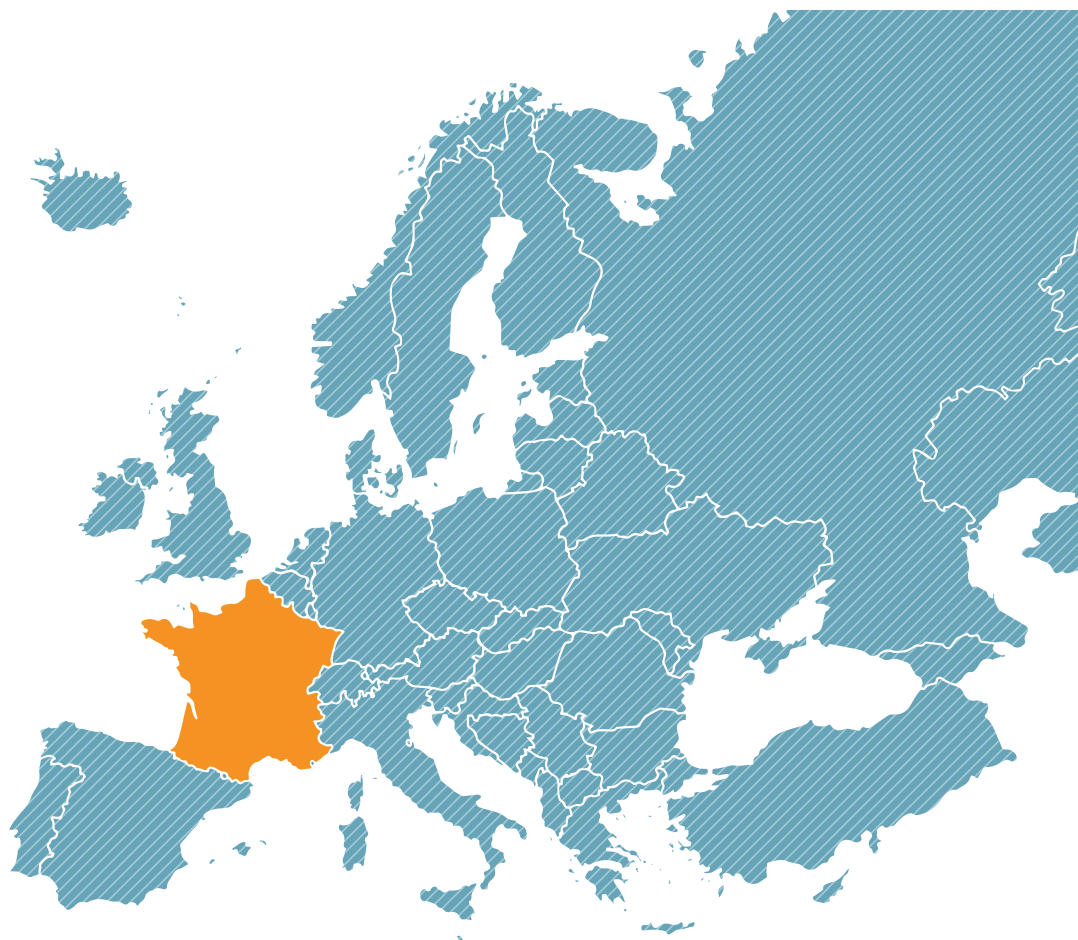
**> 2 / Deploy new clinical research programmes through the PPP model** with the aim of assessing multiple agents targeting different genetic alterations.

- The upstream organisation of these trials (choice of targets, molecules, target populations) would be a collaborative effort between clinicians and manufacturers;
- The government would provide the infrastructure (genetics and sequencing platforms and associated data) and the manufacturers would supply the molecules for testing;
- The data obtained at the end of these major research programmes could ensure the use of these treatments within the framework of a managed off-label MA (see proposal 10) or help to assess the molecule with a view to its market access.

## GOAL 5

# Make the Research Tax Credit (CIR) a permanent fixture in order for France to remain fiscally attractive

*Eligible expenditure under the CIR  
(rate of 30% and 5% over 100 million)*



€ **5,71**  
billion

The CIR budget for 2013

**20,000**

The number of French companies  
in receipt of the CIR

**30%**

The amount by which the cost of research  
activities is reduced as a result of the CIR

**12%**

The percentage of the total CIR allocated  
in 2015 which went to the pharmaceutical  
sector

### CIR

The Research Tax Credit (CIR) is a measure designed to support the R&D activities of companies, with no restrictions as to their sector or size. This scheme was introduced by the Finance Act 1983 and has undergone several changes over the past 15 years. Companies that allocate expenditure towards fundamental research and experimental development are eligible for the CIR by deducting such expenditure from their taxes subject to certain conditions. The CIR rate varies according to the investment sum (30% of R&D expenditures are eligible up to a ceiling of EUR 100 million and 5% above this figure).

### The German exception

The domestic R&D expenditure of German companies is double that of French companies. Nevertheless, Germany has no R&D tax incentives at present and has instead chosen to align itself with EU targets: raising of R&D expenditure to 3% of GDP, 2% of which financed by the private sector. Aid at federal or Lander level is targeted preferentially at SMEs and partnerships while more than 80% of R&D expenditure comes from industry, which is much more buoyant than in France. In addition, general taxation is more favourable to companies and seems to require no R&D incentive schemes.

## Overview

The French Research Tax Credit (CIR) scheme makes the country really attractive.

The project to introduce a common corporate tax base for the European Union (CCCTB Directive) is due to be rolled out in 2018. It would allow Research and Development (R&D) spending to be uniformly deducted from corporate tax in all European countries.

The competitive advantage afforded by the CIR that has until now made France fiscally attractive could be lost to this scheme; meanwhile strong competition is coming from Eastern European countries due in particular to the speed of patient recruitment.

## Our proposals

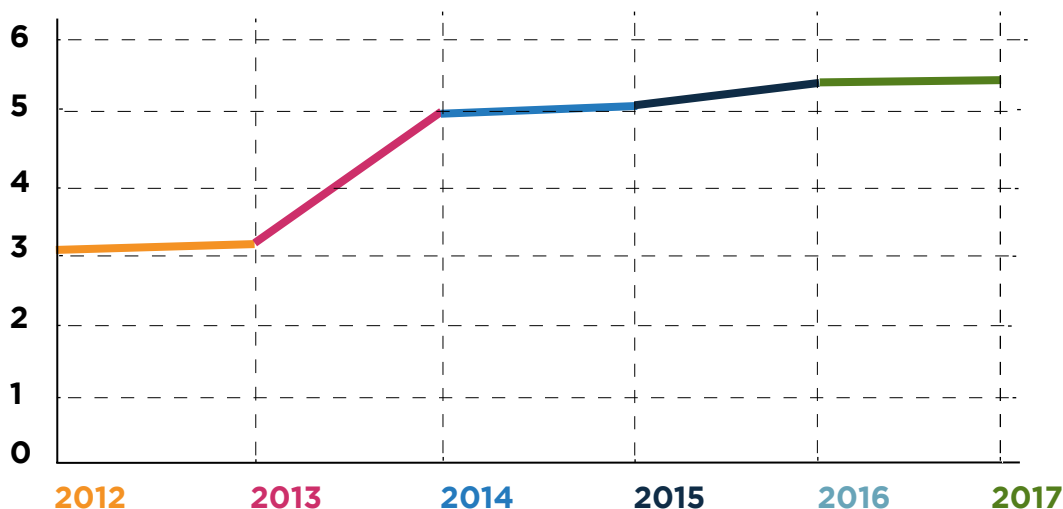
**> 1 / Maintain a CIR scheme** specific to France or consider a scheme which complements the European scheme to ensure that France remains more competitive than other European countries as a fiscally attractive destination.

**> 2 / Link up the French scheme with the European scheme** by establishing a one-stop-shop and by standardising the French eligibility criteria based on the European criteria.

**> 3 / Develop the schemes by making two improvements:**

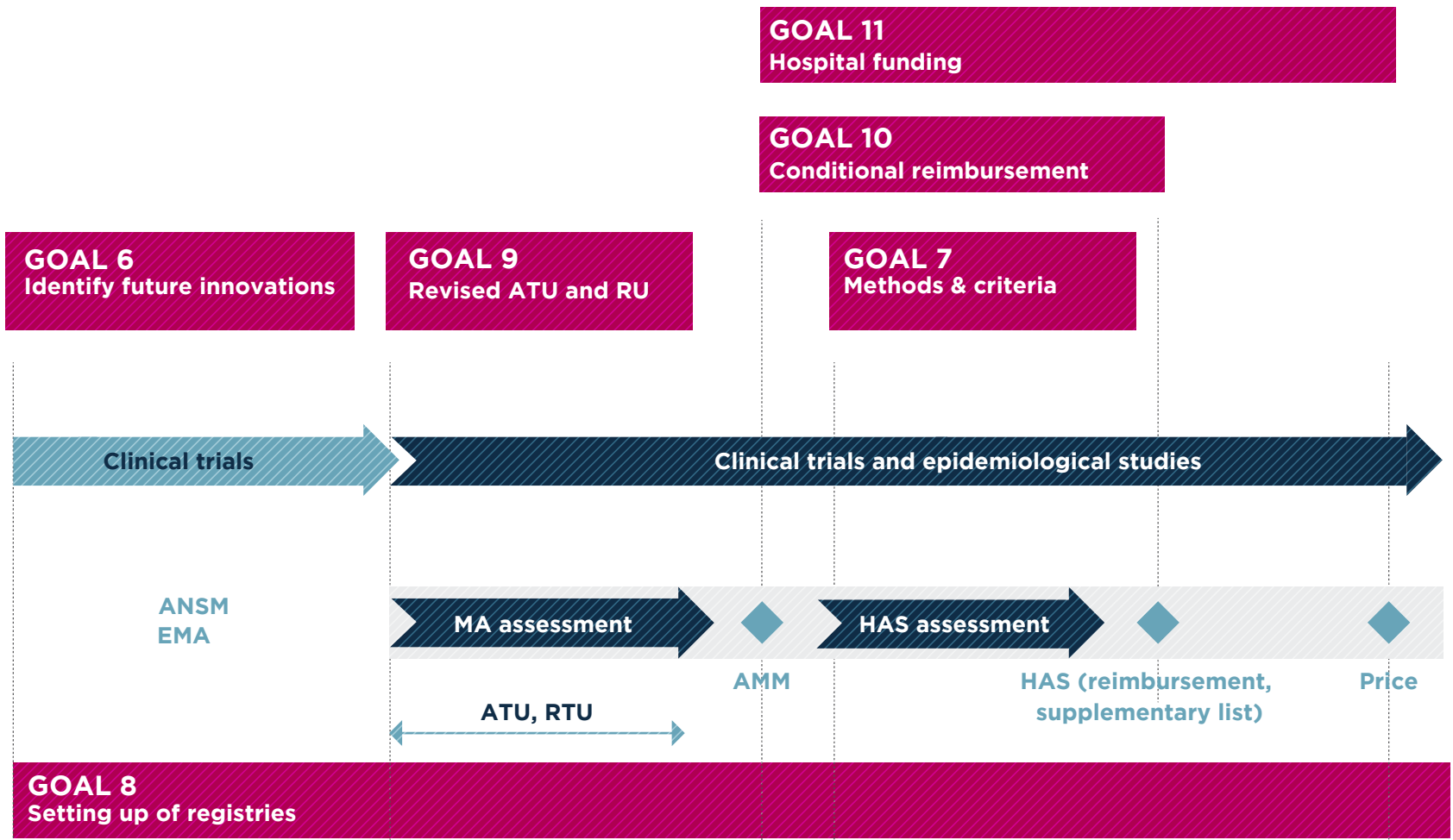
- more generally, by raising the cap for subcontracting;
- more specifically, by making health-care industries eligible to conduct epidemiological studies, including studies undertaken at the request of the authorities.

**Trend in the annual tax expenditure relative to the CIR (in € billion)**



**5 ▶ OUR SIX GOALS  
TO FACILITATE  
EARLY PATIENT  
ACCESS TO  
INNOVATIVE  
MEDICINES**

Many innovations in oncology are expected to emerge in the coming years and their specificities call for more suitable assessment methods.



**MA:** Marketing authorisation  
**ANSM:** National Agency for Medicines and Health Products Safety  
**ATU:** Temporary authorisation for use  
**EMA:** European Medicine Agency  
**HAS:** Haute Autorité de Santé (French National Authority for Health)  
**RTU:** Temporary recommendation for use



**GOAL 6**  **p.34**

Anticipate innovative breakthroughs

**GOAL 7**  **p.36**

Adapt assessment methodologies to the new challenges posed by cancer drug therapies

**GOAL 8**  **p.40**

Optimise real-time data collection

**GOAL 9**  **p.42**

Improve early access schemes (ATU - authorisations for temporary use - and RTU - recommendations for temporary use)

**GOAL 10**  **p.46**

Develop performance-based contracts for innovative products

**GOAL 11**  **p.48**

Reform the arrangements for funding in-hospital cancer drug therapies

## GOAL 6

# Anticipate innovative breakthroughs

### *Inspirational foreign models*

Other countries use prospective methods to gain an insight into the impact that innovations have. The UK horizon scanning exercise and the Canadian experience are two such examples.



In the **United Kingdom**, the aim of the Horizon Scanning Programme is to anticipate the introduction of emerging technologies 2-3 years prior to launch on the NHS. These studies are conducted jointly with academics to predict the clinical, economic or organisational impact of new innovative technologies.



**The Canadian** Agency for Drugs and Technologies in Health (CADTH) has implemented an horizon scanning programme specifically for cancer treatments: the pan-Canadian Oncology Drug Review (pCODR) process established in 2010. It tracks new cancer treatments in the pipeline based on information provided not only by the pharmaceutical companies but also by the FDA and other horizon scanning programmes already running in other countries. All the data is aggregated into a database and a summary report is sent to CADTH, which thus has knowledge of emerging drugs 1-5 years ahead of their introduction for an assessment of their potential impact.

# 110

The number of phase III cancer clinical trials in 2016. More than half are investigating tyrosine kinase inhibitors or monoclonal antibodies

# 3

The number of phase III trials involving cancer treatment vaccines

# 2 to 3 years

The lead time for emerging new medicines and new health technologies before their launch by the NHS in the UK

### Horizon Scanning

The information collected in the horizon scanning process (description of the technology, targeted cohorts, estimated number of potential patients, lists of comparators available on the market, clinical evidence of efficacy, clinical, financial and organisational impact presentations, etc.) is sent continuously to NICE and the NHS.

## Overview

Many innovations with a high economic, financial and organisational impact will come onto the market in the coming years.

In preparation for the introduction of these innovations, information sharing tools have been deployed on future innovations by the pharmaceutical laboratories and the government. The aim in the Cancer Plan 3 is to create an INCa-led Technology Watch Committee. A Prospective Committee for Drug Innovations has been set up at CEPS. In addition, the Genomic Medicine France Plan 2025 is expected to provide an initial prospective analysis on the impact of the new diagnostic test tools in the system and on the organisation needed to optimise their benefits.

## Our proposals

**> 1 / Set up a Horizon Scanning forecasting tool in France**, in conjunction with the other European countries and under the direction of a strategic committee which includes ANSM and the HAS, to bring all stakeholders on board (INCa, healthcare providers, researchers, manufacturers, patients, associations) and to be tasked with:

- periodically reviewing all technologies that impact funding by type of cancer from a clinical, organisational and budgetary perspective;
- prioritising the work carried out by the HAS to assess the most promising technologies in terms of public health;
- providing high-quality information to patients.

**> 2 / Anticipate the adjustments/transformations that the identified innovations will bring about in patients and patient associations as a result of the new treatments being rolled out in the coming years**

- assessment methodologies (especially for the internet of things, telemedicine, combined advanced-therapy medicinal products);
- training needs for healthcare professionals and assessors (ANSM experts and CPP members for example),
- care pathway organisations;
- financial impacts (loss of earnings compared with existing products in the case of substitutive innovations).

**CADTH:** Canadian Agency for Drugs and Technologies in Health

**CEPS:** Economic Committee for Health Products

**FDA:** Food and Drug Administration

**INCa:** National Cancer Institute

**pCODR:** Pan-Canadian Oncology Drug Review

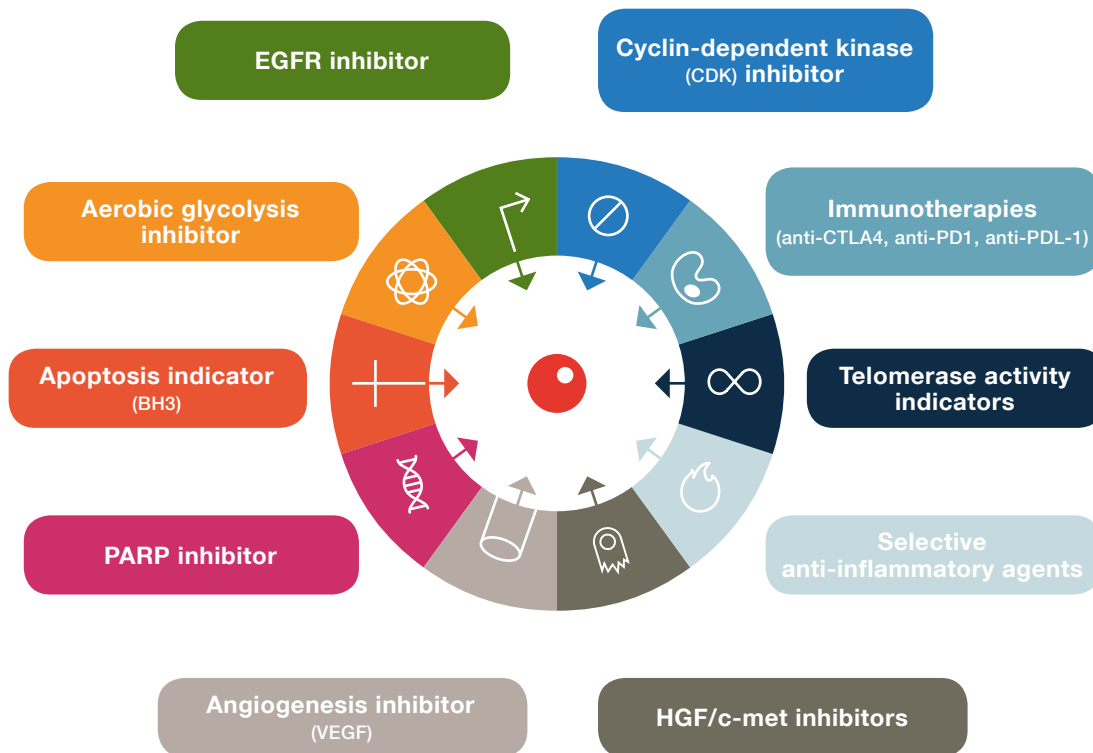
**NICE:** National Institute for Health and Care Excellence

**NHS:** the National Health Service

## GOAL 7

# Adapt assessment methodologies to the new challenges posed by cancer drug therapies

### Various therapeutic targets



# 1/3

The number of phase II cancer trials underway that do not include a comparison arm

# 87%

The proportion of phase II and II clinical trials involving targeted therapies  
64%

# 64%

The number of phase III trials in progress which involve molecules tested in several concomitant trials, in most instances covering several indications or several combinations.

## Overview

Clinical trials undertaken to assess innovations in oncology have new characteristics (personalised therapies, gene therapies, smaller populations, treatment sequences, etc.) with new designs (basket trials, large-scale PPP trials, etc.) and new primary endpoints.

This new reality has meant that the policy of registering cancer drug therapies with the EMA has evolved in recent years:

- the accepted endpoints are usually different from overall survival or progression-free survival;
- studies without a comparator arm are accepted;
- studies on small populations are accepted.

In France, the emergence of targeted therapies requiring the concomitant assessment of a drug and its biomarker test to identify the responder population has met with a number of setbacks. Firstly, the HAS methodological guide on targeted therapies with companion diagnostic testing was published in 2014<sup>1</sup>, almost 15 years after the MA was granted for the first targeted therapy for metastatic breast cancer. In addition, to ensure that the test is valid, the methodological guide recommends that the drug be assessed on both the biomarker-positive and biomarker-negative population. As this study design was never proposed by the pharmaceutical companies<sup>2</sup>, very few biomarker tests are assessed favourably at present, unlike in other countries. Moreover, the advent of genomic screening may increase this problem. Finally, the assessment process is increasingly opening up to contributions from stakeholders in the system.

Since November 2016, patient representatives have been invited to help assess health products by answering a questionnaire on their experience of the disease and their expectations for treatment. Yet these contributions have not been made public and this approach is not applied systematically to all products.

Similarly, although consultation of the scientific community on the methodology used by the HAS is indispensable, it is impeded in practice by the need to manage conflicts of interest.

These sweeping technological changes pose a human resource challenge to the HAS, which is responsible for incorporating these new approaches.

**PPP:** Private public partnership

**EMA:** European Medicines Agency

**AMM:** marketing authorisation

**HAS:** Haute Autorité de Santé (French National Authority for Health)

(1) French National Authority for Health Methodological Guide - Targeted therapies and their companion diagnostics: definition and assessment method. February 2014

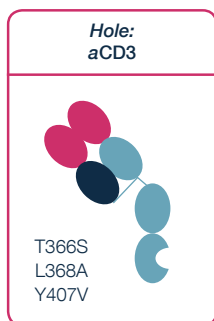
(2) The assessment of a drug on a biomarker-negative population is generally considered unethical by law.

## Other innovations

Example:

### Bispecific antibodies

TDB  
made up of two separate  
strands

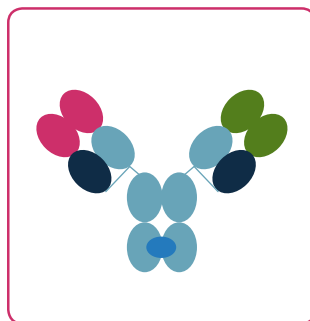


+



=

TDB  
Complete antibody



Products using a «Knob into holes» technique  
Low immunogenic potential  
Pharmacokinetic profile similar to a conventional IgG1 antibody

### Assessment criteria

Once the EMA has given its approval, these products may become stalled with the HAS: comparative phase III studies in particular with endpoints focused mainly on patient survival (overall or progression-free).

This inconsistency between the EMA and the HAS may result in unequal access to healthcare in France when compared to Europe. Thus, of the 49 treatments that were granted marketing authorisation between 2010 and 2014, 38 were accessible in Germany, 37 in England, 36 in Italy and 28 in France.

### Early-stage meetings

Although a one-off consultation is open to pharmaceutical companies to discuss certain methodological issues at early-stage meetings, such meetings are rare because in 2015 there were only 9 for every 232 notices of initial registration issued by the Transparency Committee(1). Moreover, the sole purpose of these meetings is to remind manufacturers of the current assessment methods adopted by the HAS. Innovations arrive with such speed as to require regular updating by the HAS of its assessment policies.

Indeed, taking targeted therapies as an example, the latest clinical developments demonstrate the advisability of targeting several biomarkers to increase the efficacy of precision drugs. This example shows the need for the HAS to change its assessment criteria in line with the methodological challenges posed by the assessment of new health technologies.

**EMA:** European Medicine Agency

**HAS:** Haute Autorité de Santé (French National Authority for Health)

**MA:** Marketing authorisation

**pCODR:** Pan-Canadian Oncology Drug Review

**INCa:** National Cancer Institute

(1) A recent publication shows just how widely the assessments of the national assessment agencies vary against the ESMO and ASCO systematic assessment scales (Oudard et al. 2017)



## Inspirational foreign models

One of the tasks of the pan-Canadian Oncology Drug Review (pCODR) in addition to Horizon Scanning is to develop its assessment policy on a participatory basis. It was established in 2010 to bring consistency to the assessment of cancer drugs in **Canada** by reviewing the clinical and economic evidence, while taking into account the views of all stakeholders in the system (patient groups, pharmaceutical companies, oncologists, etc.).

Thus, when an application to review a product is submitted to the Agency, patient representatives are asked to provide input via a dedicated website. Oncology-specific experts are then invited to share their recommendations via the same website. Subsequently, a Clinical Guidance Panel and an Economic Guidance Panel are formed to review the drug from these two perspectives.

The pCODR Committee comprises multidisciplinary experts (medical oncologists, doctors, pharmacists, economists, patients) and examines all the information collected on the website in addition to the clinical and economic guidance reports. Its reimbursement recommendations are made to the Canadian public health insurance systems and to the provincial cancer agencies and are published on the Canadian Agency's website, along with the comments submitted by the various parties.

## Our proposals

### > 1 / Regularly review the assessment methodologies and policies of the HAS:

- arrange for a full debate to be regularly held with the entire scientific community and other stakeholders, including patient representatives and industry, concerning the methodologies currently adopted by the HAS in an effort to identify areas where the agency's policy has changed;
- define, by drawing on the information provided by the horizon scanning tools, the work programme of the HAS with regard to the new methodologies or new assessment criteria and their implementation;
- construct a stronger ongoing dialogue between government, pharmaceutical laboratories and academic teams around scientific assessment issues and the basis of draft protocols through systematically organised early-stage meetings in oncology;
- provide medium-term visibility (over 3 years) of HAS policy changes and of the criteria for access to medicines with a high ASMR for major haemato-oncology diseases<sup>21</sup> in which recognition is given to therapeutic value.

### > 2 / Include the regular review of HAS methodologies and criteria in the HAS programme. A number of items should already be in the HAS programme and involve stakeholders (pharmaceutical companies, learned societies, patients, etc.):

- assessment of the value of treatment combinations;
- consideration of other assessment criteria (quality of life, etc.) in addition to conventional survival criteria;
- methods for the assessment of innovative treatments not compared in trials to a placebo or to another alternative treatment;
- consideration of the specific value of the last lines of treatment for non-responding patients.

### > 3 / Conduct a HAS-led overhaul of the assessment methodologies.

The debate on the overhaul of the assessment methodologies could be led by the HAS in consultation with INCa.

## GOAL 8

# Optimise real-time data collection

€ 1,2 billion

The annual number of treatment forms sent to the Health Insurance Fund

### What is the point of a complete registry?

A complete and unified registry makes it possible to:

- adapt cancer care according to the treatment given and patient characteristics;
- collect additional data to allow a full assessment to be made, within a specific time period, in implementation of contingent reimbursement mechanisms;
- collect data in implementation of payment by results mechanisms;
- facilitate patient recruitment to trials by determining their eligibility based on a specific biological marker;
- conduct more complete phase IV real-world studies more quickly.

500 terabytes

The density of the data contained in the medical administrative database

### Inspirational foreign models:

**Italy** established a national registry in 2005 for the collection of real-world data on medicines. The first registry was created in 2005 for the first targeted therapy for metastatic breast cancer, gradually expanding to other cancer drug therapies, and followed by the development of new registries for different therapeutic areas. This registry was the result of a public-private partnership (PPP) involving the Ministry of Health (authorities, doctors) and the pharmaceutical industry. Today, the registry's running costs are shared among all the stakeholders in the public-private partnership.

The registry provides overall patient monitoring, from diagnosis to drug dispensing at the hospital pharmacy. The computerised database contains the key data:

- the indication for which the treatment is used;
- disease progression, treatment-related side effects
- the costs incurred.

Healthcare professionals are required to participate in the registry. Their participation is needed so that the facility responsible for distributing treatment can be reimbursed by the Health Insurance Fund. The registry also allows pharmaceutical companies to access anonymised data with respect to their molecules.

### The national health data system

The SNDS (National Health Data System) came on stream in April 2017 alongside the creation of the INDS (National Institute of Health Data) tasked with ensuring health data quality.

**DCC:** Cancer communication file

**GHT:** Regional Hospital Group

**INCa:** National Cancer Institute

**INDS:** National Institute of Health Data

**MIG:** Mission of general interest

**PUI:** Hospital pharmacy

**PMSI:** Medical Information Systems Program, tool to describe and measure hospital activity from a health economic perspective

**RCP:** Multidisciplinary Consultative Meeting

**SNDS:** National Health Data System

**SNIIRAM:** National Health Insurance Cross-Scheme Information System



## Overview

The French computerised health databases of the National Health Data System are the most comprehensive in the world and the scope of SNIIRAM has been further broadened by the latest Health Act to become the SNDS in due course.

Although many studies already draw from the PMSI (hospital data), SNIIRAM (health insurance data) offers huge potential which has hitherto been underexploited in oncology. Indeed, its user base has long been very narrow and for-profit organisations were denied access to it.

In addition, the hospital information systems (chemotherapy software, PUI, data from the RCPs and data from molecular genetics platforms) show good potential thanks to the data they contain, and thus provide food for thought on the new arrangements for funding innovative cancer products and on the pricing of a medicinal product in line with its actual use. France also has a number of oncology registries but they are not comprehensive. They cannot therefore track the use of cancer treatments, their indication and line of therapy or toxicity, nor indeed off-label or non-reimbursable prescriptions.

## Our proposals

**> 1 / / Institute a dedicated oncology registry in France** which would be managed by the National Institute of Health Data (INDS) and by the National Cancer Institute (INCa) and which would allow the collection of product efficacy data as well as information on pathways and on organisational and budgetary impacts.

This registry would be fed with:

- data from the SNDS (SNIIRAM and PMSI) augmented with some additional criteria (treatment line, indications, etc.);
- data contained in hospital software (chemotherapy software, PUI software, DCC, RCP data);
- by the INCa platform software so as to capture biomarker data;
- data from future GHT software;
- data from existing registries.

**> 2 / / Introduce a mechanism of incentives and penalties** for healthcare professionals, comprising:

- a target-based payment for clinicians in healthcare institutions based on the IFAQ (Financial Incentive for Quality Improvement) pilot model;
- Payment for Public Health Objectives (ROSP) for clinicians;
- a more rigorous system whereby the facility is not reimbursed if information is not entered in the registry;
- a mission of general interest (MIG) of the «innovation» type that would attach value to the collection of clinical and health economic data in conjunction with the assessment of healthcare technologies.

Pharmaceutical companies could help to fund the registry by paying for access to anonymised data relating to their products.

## GOAL 9

# Improve early access schemes (ATU - authorisations for temporary use - and RTU - recommendations for temporary use)

Early access schemes do exist at present (temporary authorisations for use and temporary recommendations for use) but they face a number of obstacles and are unable to respond to every situation.

## RTU

### Overview

#### The Temporary Recommendation for Use

The RTU offers a secure prescribing framework for cancer treatments for off-label indications and makes it possible to gather real-world data on small cohorts (linkage to a particular biomarker or grouping of patients with a rare cancer). However, its implementation is difficult:

- requests for an RTU cannot be made by the pharmaceutical companies but must be sent by a third party (within ANSM, a learned society, INCa, etc.);
- requests for an RTU, unlike for an ATU, are administratively complex and lengthy, as are the timeframes for their implementation;
- the budgetary impact of products with an RTU may worry public authorities, thus making them less inclined to grant an RTU;
- The granting of an RTU is contingent on setting up a study protocol aimed at collecting efficacy and safety data. Pharmaceutical companies do not always plan for a phase III trial setup, thus rendering the mechanism unsuitable.

#### RTU

ANSM is able to accommodate off-label prescribing practices, provided that:

- there is a therapeutic need;
- and that the risk-benefit ratio of the medicinal product is presumed to be favourable, based chiefly on published scientific efficacy and safety data.

To this end, ANSM makes Temporary Recommendations for Use (RTU). RTUs are issued for a 3-year renewable term.

Their objective is to ensure that the medicines are being used safely through patient monitoring organised by the relevant laboratories.

# 23

The total number of medicines with cohort ATU status in 2016

# 6

The number of cancer therapies with cohort ATU status

# 11

The number of medicinal products currently granted RTU status, none of which in oncology

# 85%

The proportion of medicines covered by an ATU which were used in cancer care in 2016

**MA:** Marketing authorisation

**ANSM:** National Agency for Medicines and Health Products Safety

**ATU:** Temporary authorisation for use

**HAS:** Haute Autorité de Santé (French National Authority for Health)

**INCa:** National Cancer Institute

**RTU:** Temporary recommendation for use

# ATU

## Overview

### Temporary authorisation for use

The French ATU scheme is very attractive and the envy of many countries. Nevertheless, its application is restricted by several constraints:

- whereas oncology products have several indications, the ATU is approved only for the primary indication;
- moreover, the existing ATU scheme is threatened by the Social Security Financing Plan (PLFSS 2017), which caps the annual average cost per patient at EUR 10,000 for all products with sales in excess of EUR 30 million;
- due to the significant discrepancies in methodological requirements between the EMA and the HAS; trial results may well suffice for the EMA but rarely satisfy the HAS, which tends to draw out the time between the end of the ATU period and price setting, thereby increasing the time that patients have to wait before benefiting from treatment for all indications.

The data collected under the RTU and ATU schemes are used mainly to assess the benefit-risk ratio of a molecule and its clinical efficacy.

The ATU scheme does not currently allow for the collection and analysis of data that make it possible to comply with the binding timetable for application filing, reimbursements and pricing.

### ATU

In France, the exceptional use of medicinal products with no initial marketing authorisation (MA) and not subject to a clinical trial is contingent upon first obtaining a Temporary Authorization for Use (ATU).

ATUs are issued by ANSM under the following conditions:

- the medicinal products are intended to treat, prevent or diagnose serious or rare diseases;
- there is no suitable treatment;
- they are presumed to be effective and safe on the basis of current scientific knowledge.



## Inspirational foreign models:

In the United States, when a product has been registered by the FDA for its first indication, the National Comprehensive Cancer Network (NCCN) may issue a recommendation to approve reimbursement for an extended indication, thereby allowing the system to flow smoothly..

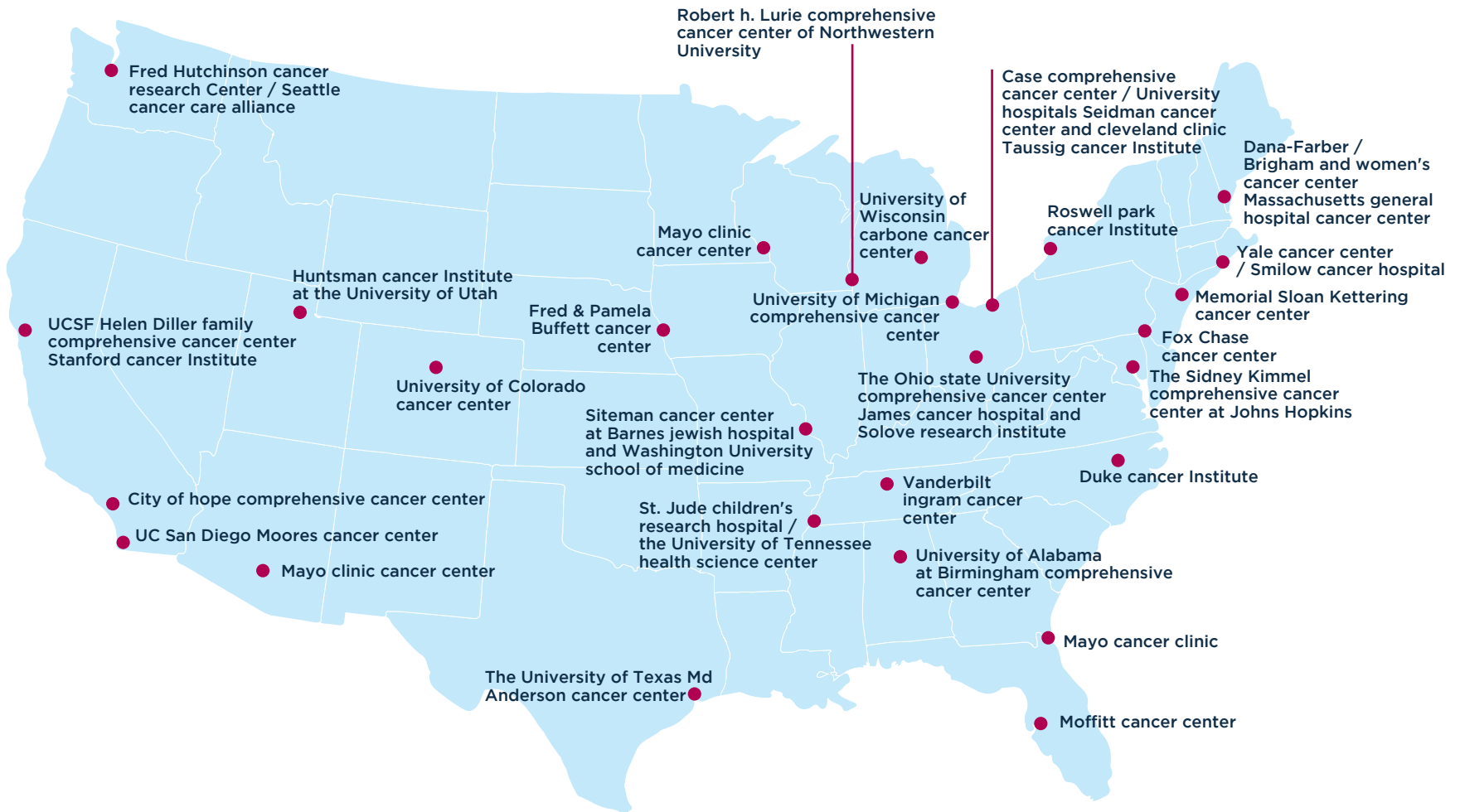


Illustration: The National Comprehensive Cancer Network (NCCN)

## Our proposals

Reform the two existing ATU and RTU schemes to lift the constraints, improve early patient access and regulate off-label products.

### Reform the ATUs:

> **1 / Open the ATU mechanism to indications** following the first indication to ensure that patients have early access to innovative cancer treatments where new indications can satisfy an unmet therapeutic need. An opportunity loss for patients between the clinical assessment and the funding decision is thus avoided.

### Reform the RTUs:

> **2 / Refocus the RTU on the regulation** of off-label indications for treatments in respect of which an MA extension application will not be made (introduction of a non-temporary recommendation for use - RU).

> **3 / Regulate off-label indications via an RU scheme**, especially for products resulting from major clinical trials conducted through public-private partnerships (PPP).

> **4 / Allow pharmaceutical companies to make RU applications** to ensure the correct use of their molecules and avoid unregulated off-label indications.

> **5 / Establish, under the guidance of the INCa and learned societies**, the procedures for ensuring the correct use of treatments within the RU scheme.

> **6 / Encourage the collection of efficacy data** within these two schemes.

**AMM:** Autorisation de mise sur le marché

**ATU:** Autorisation temporaire d'utilisation

**FDA:** Food and Drug Administration

**INCa:** Institut National du Cancer

**PPP:** Partenariat Public Privé

**RTU:** Recommandation temporaire d'utilisation

**RU:** Recommandation d'utilisation

## GOAL 10

# Develop performance-based contracts for innovative products

## Inspirational foreign models

### Les modèles étrangers qui nous inspirent



Since 2005, Italy's national registry for the collection of real-world data on medicines has proven to be a particularly useful means of financing innovations in cases where the manufacturer's information (efficacy, budgetary impact, etc.) on its product is insufficient to obtain funding.

Thus, the establishment of robust registries in Italy has prompted the systematic introduction of performance-based agreements.

Since 2012, almost 6% of total expenditure on costly treatments was reimbursed by pharmaceutical companies for failing to achieve the performance targets. The amount of discounts granted by pharmaceutical companies rose from nearly 80 million in 2012 to 200 million in 2015, reflecting the mounting success of the scheme.

Furthermore, almost half of the performance agreements in Italy are used to fund multi-indication cancer medicines. Lastly, performance-based payments significantly reduced patient access time to innovative therapies (median of 83.7 days with risk-sharing agreements versus 342.7 days without), thereby enabling patients in Italy to benefit more quickly from innovative therapies.



In England, where cancer treatments are concerned, the National Institute for Health and Care Excellence (NICE) has three options when deciding on a reimbursement claim. It can thus:

- > Grant reimbursement for a therapy;
- > Refuse reimbursement for a therapy;
- > Provisionally grant reimbursement for a therapy.

This third option, which was recently adopted via the Cancer Drugs Fund, allows therapies with a high reimbursement potential but whose clinical data and therefore cost-benefit ratio are not sufficiently mature to award an upfront fixed reimbursement agreement, to participate in a temporary reimbursement mechanism.

NICE thus approves funding on a provisional basis for a period of not more than 2 years. If, once this period has expired, the laboratory is unable to provide the trial results expected by NICE, reimbursement will be automatically suspended. If the opposite occurs, confirmation of the drug's reimbursement will be given subject to the usual conditions. The Cancer Drugs Fund's reimbursement conditions are regulated, each treatment being subject to a performance-linked agreement in which payment is adjusted according to the clinical results observed.

# € 200 millions

The amount of discounts granted in Italy by pharmaceutical companies in 2015

# € 80 millions

against in 2012 in Italy

# 83,7

The median number of days before patients were able to access innovative therapies under the risk-sharing agreements in Italy

# 342,7

The median number of days before patients were able to access innovative therapies without the agreements in Italy

**MA:** Marketing authorisation

**ASMR:** Improvement in medical benefit

**CEPS:** Economic Committee for Health Products

**HAS:** Haute Autorité de Santé (French National Authority for Health)

**NICE:** National Institute for Health and Care Excellence

## Overview

The framework afforded by the performance agreements is hugely advantageous in cases where payers are in doubt about the value of a product due to the potential variability in therapeutic benefit resulting from the uncertainties of the treatment populations, because it allows for the payment of treatments according to their real-world performance and not their theoretical clinical value as reported in clinical trials.

This funding mechanism is also useful for promising products whose value has yet to be determined from clinical findings. The clinical performance payment can then be combined with a conditional reimbursement mechanism. Although performance-based payments have begun to take hold in France for a number of years now, following the introduction of the Payment for Public Health Objectives (ROSP) for private doctors in 2011 and the Financial Incentive for Quality Improvement (IFAQ) for healthcare facilities in 2012, they are still seldom applied to health products.

The LEEM-CEPS framework agreement signed in late 2015<sup>(1)</sup> provides for the use of an outcomes-based agreement for health products, yet the French authorities are traditionally wedded to a «price/volume» negotiating logic and are less inclined to accept new funding methods, which is why this scheme has been slow to extend to medicines in France.

The development of this type of funding is also hampered in France by the weakness of the real-world performance measurement tools.

## Our proposals

### Encourage the establishment of funding mechanisms:

performance-based agreements and conditional reimbursements for innovations involving a degree of uncertainty for governments in order to facilitate early access to innovation.

#### Performance-based agreements:

> 1 / **Promote the introduction of performance-based agreements** for innovative cancer products whose real-world value is still uncertain or whose therapeutic benefit is expected to vary as a result of the treatment populations.

> 2 / **Focus performance-based agreements** on the attainment of clinical and/or economic objectives without assessments or reassessments by the National Authority for Health: simplify and specify the criteria and objectives to be met under the performance-based agreements along the same lines as the English model which uses the criterion of overall survival on treatment as a substitute for progression-free survival.

> 3 / **Clearly state the recompense and obligations** of each signatory. In addition, for transparency purposes, the existence of performance-based agreements and their operational mechanisms should be made public.

> 4 / **Set up a mechanism allowing for the periodic** renegotiation of clauses with CEPS following a period of real-world observation.

#### Conditional reimbursement mechanisms:

> 5 / **Set up a conditional reimbursement mechanism** for post-marketing products whose therapeutic value has still to be demonstrated and which do not meet the standard criteria of the HAS for determining reimbursement eligibility due to insufficient, but promising, clinical data (in the case of adaptive licensing for example) or due to unsuitable assessment methodologies (breakthrough innovations for example), subject to the mechanism satisfying the following general conditions:

- determination of the suspended ASMR level;
- obligation on the part of pharmaceutical companies to conduct the studies needed to provide additional data that will help determine the value of the product;
- funding would be possible through a payment by results mechanism (a fixed reimbursement rate can also be set).

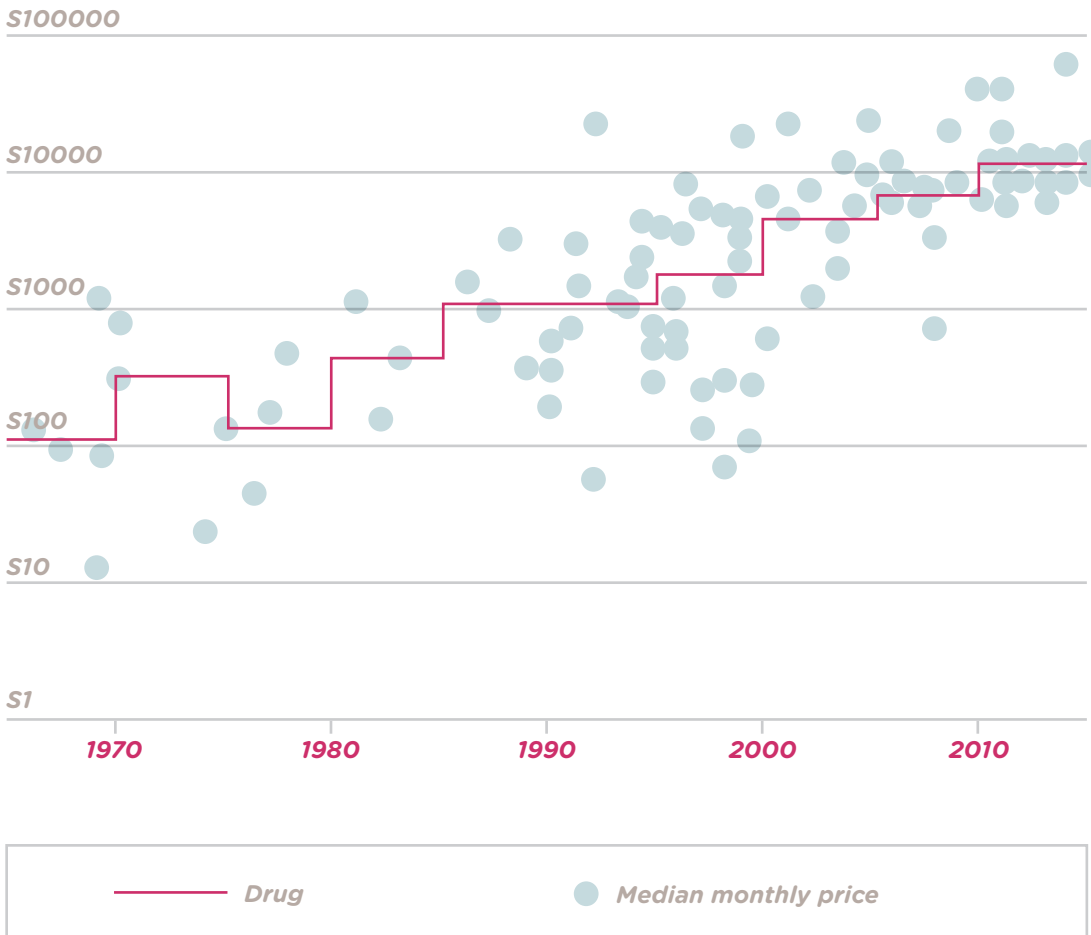
(1) Framework agreement of 31/12/2015 between the Economic Committee for Health Products and LEEM (Les Entreprises du Médicament)

## GOAL 11

# Reform the arrangements for funding in-hospital cancer drug therapies

### *The price of cancer drug therapies is on the rise*

Median monthly price of cancer drugs at the time of FDA approval (1965 - 2015)



# € 1,7 billion

The costs of cancer therapy agents charged on top of short-term inpatient services

# 50,8%

The proportion of the cancer therapy agents in the total expenditure of costly agents reimbursed on top of the GHS rate

### Homogeneous Group of Hospital Stays (GHS)

Hospital activity is defined through Diagnosis Related Groups (GHM) and Homogeneous Groups of Hospital Stays (GHS). For example, the hospital receives payment for a patient admitted for a certain number of days rather than admission to a specified hospital service.



## Overview

Products reserved for hospital use face the issue of access to the add-on list, and the rigidity of the GHS system leaves no room to fund the costly products.

Moreover, the recent enactment of a new decree prohibits de facto access to the add-on list for ASMR IV and V products (unless they are of significant public health value or their comparators are already registered on the add-on list).

However, therapeutic innovations with high efficacy potential have to contend with methodological assessment barriers that sometimes preclude the award of an ASMR reflective of their value. Accordingly, although these products promise very good results, they will not be eligible for reimbursement on the add-on list, thus acting as a barrier to access for patients.

What is more, the constraints imposed on hospital products place them on an unequal footing with retail pharmacy medicines, access to which is guaranteed regardless of ASMR level provided that the SMR (actual benefit) is not insufficient.

**ASMR:** Improvement in medical benefit  
**CEPS:** Economic Committee for Health Products  
**CCAM:** Common classification of medical procedures  
**GHS:** Homogeneous Group of Hospital Stays  
**SMR:** actual medical benefit

## Inspirational foreign models:

**Germany** has put in place working practices which allow it to conduct a real-world appraisal, at the earliest possible stage, of an innovation.

An OPS procedures code (equivalent to the French medical classification for clinical procedures) can be created for a procedure that includes the innovation or for the innovation alone, in order that the technology can be tracked.

Thus, throughout the funding period, the German system uses the corresponding code to carry out cost accounting. If, at the end of the interim coding period, the financial impact is negligible, the German equivalent of the GHS will not be changed. Conversely, if this is not the case, the GHS can be revised upwards or downwards more quickly using the data collected in full knowledge of the fact that the German GHS system is reviewed every year to update the amounts involved in new technologies.

## Our proposals

**> 1 / Provide funding for innovative and costly drugs on the add-on list:** include all hospital distributed cancer drug therapies with an average cost of more than 30% of the relevant GHS tariff on the add-on list as a transitional measure until such time as the prescribing volume is large enough for them to be permanently incorporated into the GHS system.

**> 2 / Adjust the GHS tariffs** and encourage the dynamic regulation of listed products to reflect actual hospital activity whilst maintaining an add-on list mechanism for the most costly products.

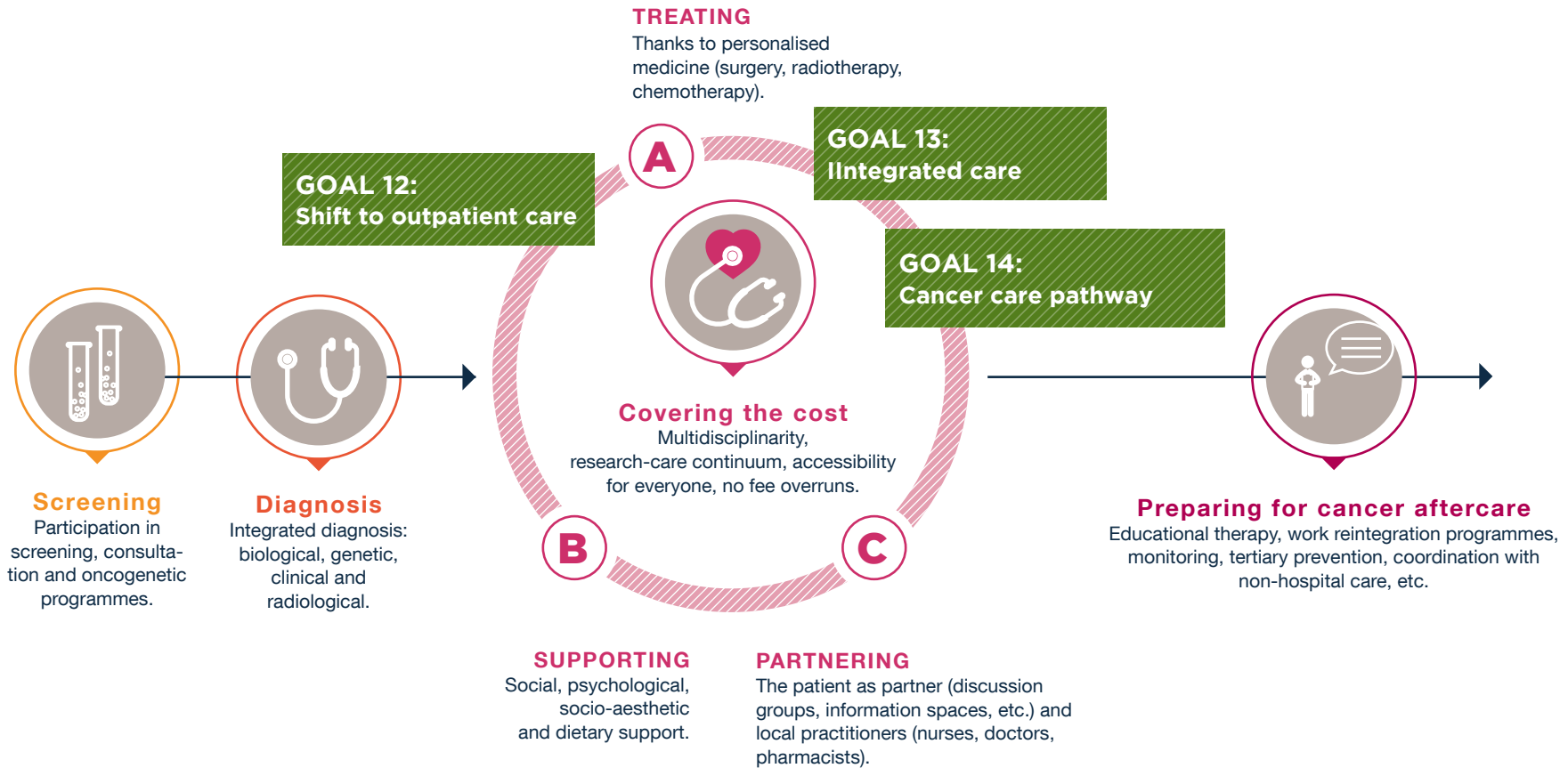
**> 3 / / Ensure that add-on list expenditures are objectively managed:** return the discounts obtained by CEPS for the products on the add-on list.

**6**

**▶ OUR THREE  
GOALS  
TO IMPROVE  
THE CARE PATHWAY**

Therapeutic advances and organisational developments require a restructuring of the care pathway to ensure equal access to care and innovations for all patients.

## The care pathway



**GOAL 12**  **p.54**

Encourage the shift to outpatient care and ensure that the change is managed to improve the organisational impact of the treatments

**GOAL 13**  **p.58**

Support integrated care initiatives

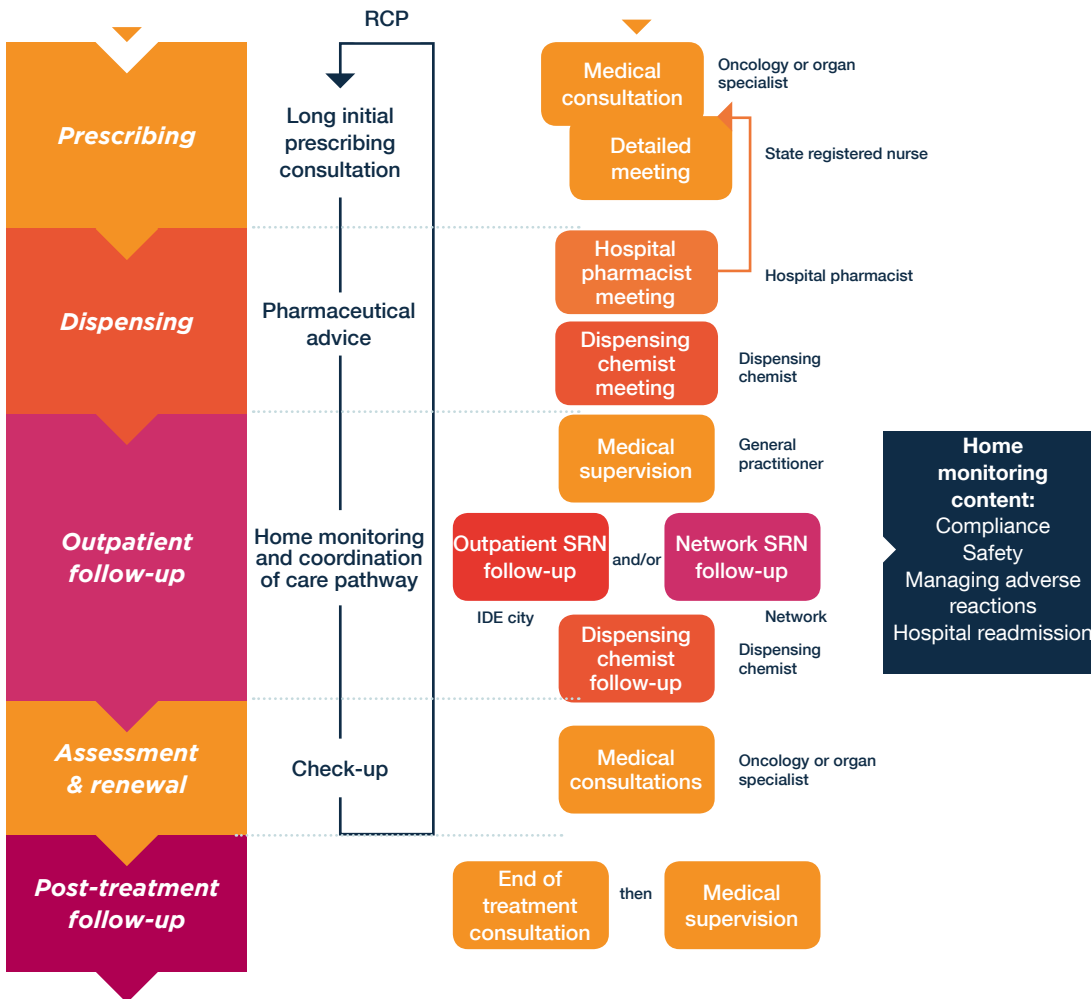
**GOAL 14**  **p.60**

Put in place funding for the cancer care pathway

## GOAL 12

# Encourage the shift to outpatient care and ensure that the change is managed to improve the organisational impact of the treatments

### Care pathway of a patient treated with oral cancer treatments

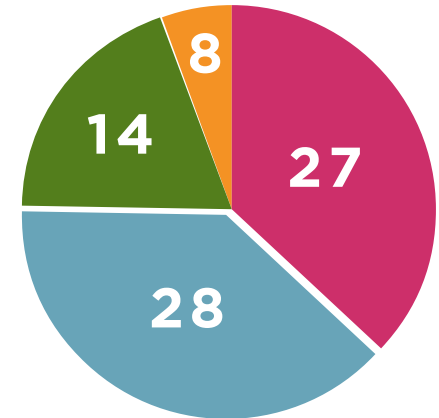


# 23

The number of oral chemotherapy agents newly available on the market between 2010 and the end of 2014

# 73

The number of oral cancer treatments available at the end of 2014  
One-third are targeted therapies



Cytotoxic agents

Targeted therapies

Hormone therapies

Other

## Overview

The administration of intravenous (IV) treatments to patients was, until recently, managed predominantly in a hospital setting but now the advent of oral cancer therapies has seen a transformation in care pathways and has supplanted inpatient with outpatient care.

This trend towards to outpatient care is very positive as it brings improvements to the quality of life of patients, lower direct and indirect costs and efficiency gains for facilities in the case of outpatient surgery. Nevertheless, it faces setbacks in several respects.

First of all, the shift to outpatient care has met with economic and financial challenges where oral therapies are concerned. Indeed, the introduction of oral therapies may lead to a bias in terms of offer of therapies available to patients, in light of the financial challenges facing health facilities.

Thus, there is a low take-up of hormone therapies in France, which are prescribed in 60% of cases compared to approximately 90% in other countries. Chemotherapies, on the other hand, account for approximately 1.5% administered in hospital-at-home care whereas this figure should be 14% according to estimates by the HAS(1). Such a bias is unfortunate for patients who could benefit to a far greater extent from outpatient or hospital-at-home care.

There is also an issue of quality of outpatient care owing to a lack of information on the part of primary care professionals (general practitioners, pharmacists) about the disease, innovative treatments, management of adverse reactions, etc..

Yet it is these professionals who are increasingly expected to care for patients receiving cancer therapies. The coordination between outpatient medical teams and hospital teams in cases of readmission due to serious adverse reactions is also a point of breakdown.

The provision of hospital-at-home care for the administration of IV chemotherapy is met with an organisational obstacle because the structures in place to administer IV chemotherapy are lacking.

An improvement in outpatient-hospital coordination and in information exchanges among professionals is one of the priorities of the 2014-2019 Cancer Plan. This is set in the context of developing outpatient surgery and oral chemotherapy, thus making the issue of coordination between hospital and private practitioners all the more crucial.

**CLCC:** Cancer Research Centres

**HAS:** Haute Autorité de Santé (French National Authority for Health)

**PUI:** Hospital pharmacy

(1) «Outpatient surgery and targeted therapies: two major ways forward in cancer care of the future for UNICANCER», Unicancer Press Release, 3 February 2015

**HAD:** hospital-at-home care

## ANAP

French National Agency to support performance in hospitals. Established by the Law of 21 July 2009 reforming the hospital organisation, and on patients, health and territories, «ANAP sets out to help healthcare and medico-social institutions improve the service they deliver to patients and users by developing, distributing, and monitoring the implementation of recommendations and tools that enable the institutions to modernise their management, optimise their property assets and monitor and increase their performance with a view to controlling their expenditure. (Extract from Law 2009-879 of 21 July 2009 - Art 18 (V)).



## Inspirational foreign models

### The NICE Health Technology Adoption Team (HTAT) in the UK.

#### Its mission:

- to identify innovative technologies with a high organisational impact;
- to detect barriers to their adoption (changes in processes, procedures, major changes to the care pathway, etc.).

NICE bases the development of such tools on the practical experience (prospective or retrospective) of early adopters who describe the steps taken by the teams to adopt the scheme: optimisation of the care pathway, training of care teams, etc.<sup>(1)</sup> The potential barriers to adoption are identified and the associated solutions explain how benefits to patients and the system (including cost savings) can be achieved in practice. The British system thus encourages the adoption of innovative health technologies with high impact potential.

Running alongside this programme, the National Homecare Medicines Committee (NHMC), which comprises the NHS, industry and Department of Health representatives, offers solutions to develop and improve homecare services by making this issue a key priority in the country.

The Committee examines each product and identifies which could be administered at home, along with solutions such as engaging the services of homecare providers so that the transition occurs safely and securely.

Recommendations are then made to the NHS and key performance indicators are set to ensure that the services provided are of high quality and safe<sup>(2)</sup>.

(1) Adoption support resources overview, NICE, 2015

(2) Site: [www.sps.nhs.uk](http://www.sps.nhs.uk), National Homecare Medicines Committee, 2017



## Our proposals

**> 1 / Facilitate the shift to outpatient care** especially for oral chemotherapy, intravenous chemotherapy and outpatient surgery (prostate cancer, breast cancer).

**> 2 / Offer support**

and care for patients receiving oral therapy across both hospital and non-hospital settings:

- by assigning a key role to day hospitals through a coordinating nurse responsible for overseeing the care pathway;
- by forging a partnership with primary care professionals (general practitioners, retail pharmacists), who serve as external points of contact with the hospital team in the management of adverse reactions and drug interactions;
- by ensuring correct use of the medication and by optimising adherence to treatment so that the outpatient care is safe;
- by allocating dedicated and ongoing funding to coordination of the care pathway to ensure that the public interest is further served by initial prescribing of oral chemotherapy (MIG PPCO).

**> 3 / Realise the transformational potential** of portable outpatient treatments, the development of home IV chemotherapy and outpatient surgery, and organise procedures around a preference for outpatient care.

**> 4 / Encourage the development of organisations** adapted to the shift to outpatient care so that the gains intended for patients and the system are attained by transposing the role of the NHMC (National Homecare Medicines Committee) identified in the English model to ANSM and that of the Health Technology Adoption Team from NICE to ANAP.

**> 5 / Continuously assess the budget savings** achieved as a result of the shift to outpatient care and plough all or part of the savings made into innovation funding.

## GOAL 13

# Support integrated care initiatives

# 45

The number of teams of dedicated cancer care coordination nurses (IDEC) responsible for outpatient-hospital coordination

## French initiatives

### Gustave Roussy Institute

The CAPRI digital platform developed by doctors at the Gustave Roussy Institute sets out to improve coordination between the outpatient services and the hospital by facilitating interactions between the cancer patient's different caregivers. It helps to ease the flow of information between hospital and non-hospital healthcare professionals, and also between the follow-up nurse and patient through the action of two follow-up nurses and an internet portal<sup>1</sup>

### Curie Institute

The BILBAO programme initiated by the Curie Institute allows for highly integrated and accelerated management of the pre-therapy assessment phase of women newly diagnosed with breast cancer. All the professionals involved in this phase of the care pathway (nurses, medical oncologists, surgeons, radiotherapists and pathologists) work together at the Institute and intervene in groups or individually throughout the day as the assessment takes place.

### Grenoble University Hospital

The University Hospital has established the University Prostate Cancer Clinic in Grenoble. The Clinic brings together urologists, oncologists and radiotherapists where patient information can be shared, innovative approaches to treatment proposed and patient follow-up improved.

# Over 5,000

The number of supported patients

# 2/3

The proportion of IDEC teams that provide oral chemotherapy support

(1) Gervès-Pinquier, C. et al., «Impacts of a navigation program based on health information technology for patients receiving oral anticancer therapy: the CAPRI randomized controlled trial.» BMC Health Services Research 17.1 (2017): 133

**ARS:** Regional Health Agency  
**CPAM:** Primary Health Insurance Fund  
**INCa:** National Cancer Institute  
**PLFSS:** French Social Security Finance Bill

## Overview

Funding comes from INCa, ARS, and the care facilities themselves, with a possible contribution from industry. Nevertheless, the lack of sustainable funding and the regulatory difficulties preclude the more widespread adoption of this type of approach.

### Within the framework of the Cancer Plan

The IDEC trial involving dedicated coordination nurses was first piloted in 2014 within 35 facilities. These nurses are able to work alone, in teams or linked to external care coordination platforms. This scheme is still ongoing after the INCa-led pilot phase among complex targets (serious cancers, multiple diseases, psychological and social vulnerability, etc.).

### The actions of regional health agencies (ARS)

Several regional health agencies have worked on new organisations to reduce access times and to improve the quality and coordination of care. Prime examples are the creation of a new Breast Institute in Bastia (Corsica) which provides care within 72 hours; the establishment in Nouvelle-Aquitaine of a healthcare cooperation group between two cancer care institutions (Bordeaux University Hospital (CHU) and the Cancer Research Centre (CLCC)) with the aim of integrating the region's other two university hospitals; the adoption in Normandy of a regional medical cancer care project combining gradation of care and organisation of the care pathway, including post-treatment (2 CHU + 2 CLCC); a project to extend the AYA (adolescents & young adults) schemes in Auvergne-Rhône-Alpes.

## Inspirational foreign models:

**Germany** has introduced measures to encourage the development of integrated care models that allow for collaboration between outpatient and hospital care providers throughout the care pathway.

These are primarily financial incentives covered by the Special Care Cooperative Programme that pay projects achieving gains for the Health Insurance Fund. Thus, the support provided to these integration projects (institutions and health centres, industry) goes into the funding of investments.

These projects operate on a portion of the gains made by the Health Insurance Fund, which is thus relieved of all financial risk whilst recovering some of the gains. Additionally, these cooperation programmes are operated under the Special Care scheme pursuant to a contract between the supporters of these projects and the regional health insurance funds.

## Our proposals

**Develop new ways of coordinating care between disciplines and professions.**

> 1 / **Define the areas of care relevant** to the Cancer Plan and select projects in each of these areas.

> 2 / **Support innovation** in integrated care organisation through regional pilot programmes.

These proposals are part of an incentive measure, with performance-based funding for the integrated care initiatives.

## GOAL 14

# Put in place funding for the cancer care pathway

*The direction of the reforms:  
4 complementary goals to improve the care pathway  
Improve care quality and safety*



# 71,000

The number of new cases of prostate cancer in France each year

# 54,000

The number of new cases of breast cancer in mainland France each year

# 43,000

The number of new cases of colon cancer in France each year, of which 23,500 are men

# 39,500

The number of new cases of lung cancer in France each year, of which 28,000 are men

## Overview

A number of care pathways are now permanently established as a result of the adoption of standardised care protocols for localised cancers (breast, prostate, colon and rectum). However, the cost and quality of treatment/care provision vary widely.

Some care pathways are still disorganised and result in a discontinuity of care, preventable emergency care and, overall, a lack of advice and guidance on the best possible treatment.

Added to the problem of the quality of patient care is the considerable cost variability.

However, a number of standardised care protocols for localised cancers (breast, prostate, colon, rectum) could be used as pilots for funding the care pathway.



### Inspirational foreign models:

In the United States, Medicare has introduced an episode-based payment for cancer care.

The flat fee covers all the costs of a cancer care pathway. As a result, care facilities that manage to reduce their costs increase their results and those that reduce the quality of care are penalised.

The cost-effectiveness ratio of the standard care pathway is thus substantially optimised. As an illustration, a pathway funding system has been set up in the United States which packages the cost of treating a patient with breast, colon or lung cancer.

The introduction of this package, which excludes the cost of the drug, has reduced the cost of care by 34% through a reduction in the number of hospital admissions and unnecessary medical consultations, whilst maintaining the same standard of care.<sup>(1)</sup>

## Our proposals

**1 / Consider a permanent organisation** for funding the cancer care pathway for certain cancers with well-established protocols.

**2 / Describe the framework of the scheme** and the procedures for sharing any financial gains generated as well as the contractual arrangements between the project backers, the CPAMs (Primary Sickness Insurance Funds) and the region.

**3 / Put a scheme in place to re-deploy the savings generated** by the payment system for organised care pathways with a view to funding innovation. This scheme would act as an incentive to practitioners to optimise the efficiency of the care pathways.

7

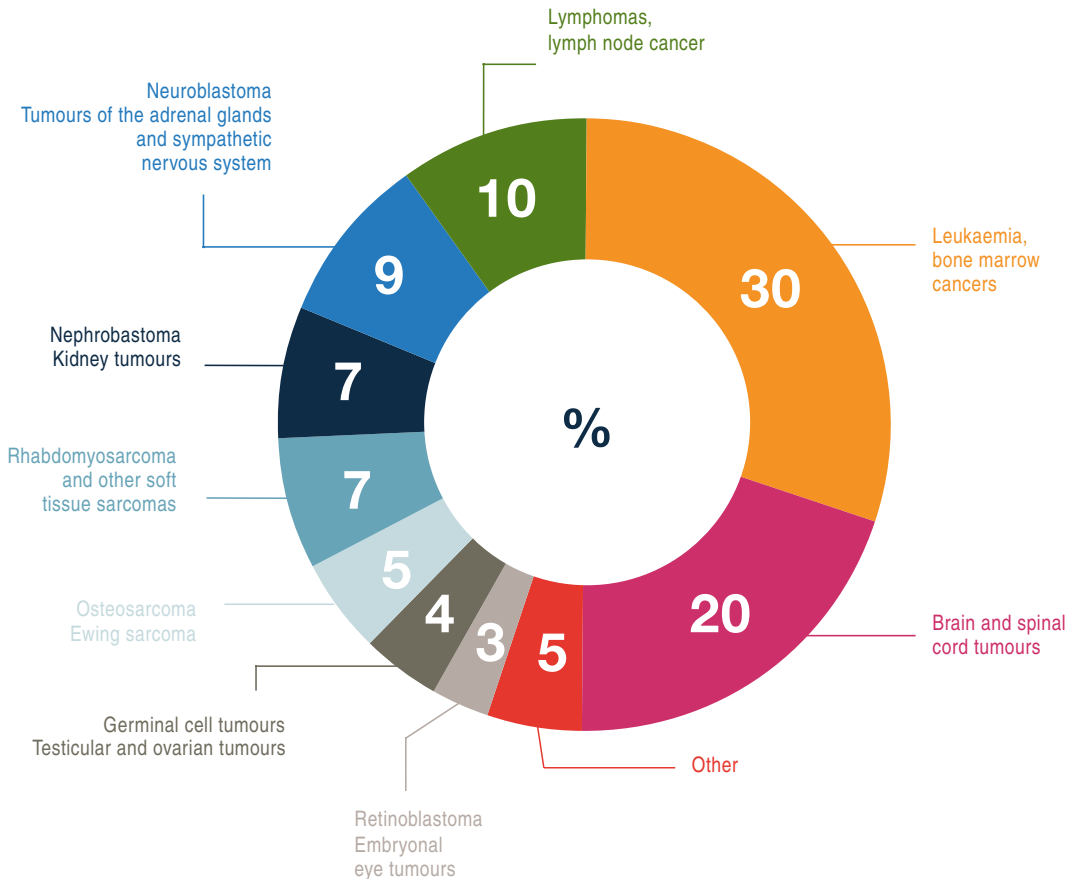
**PAEDIATRIC  
ONCOLOGY**

## **GOAL 15** **p.64**

A shared goal: paediatric oncology.  
Give the best chance of survival to the 2,500 children affected  
each year by cancer.

## GOAL 15

### Incidence of the different childhood cancers



# 37

The number of early-stage trials in paediatric oncology in France between 2010 and 2013

# 607

The number of patients included in these trials

# 2,200

The number of new cases of cancer in children each year in France

# 4 out of 5

The proportion of children who recover from their cancer

# 1

The number of therapies with cohort ATU status in paediatric oncology

### The worldwide one-of-a-kind AcSé-ESMART trial

Launched in June 2016, the trial includes over a 3-year period 260 children who have reached a therapeutic dead end. It is financed by Imagine for Margo and INCa. The Gustave Roussy Institute is the sponsor. 3 laboratories are providing 10 molecules for evaluation at no cost.



## Overview

Cancer is the leading cause of death from disease in children and adolescents. A number of initiatives in the field of paediatrics have been undertaken at European and national level. Since 2007, the European Paediatric Regulation has changed the landscape of drug development.

By introducing incentives for research, this regulation has now made it possible for France to become an agent of this change.

However, there is still scope to improve its implementation, particularly in the oncology field. The third Cancer Plan (2014-2019) has set a specific goal of meeting the needs of children, adolescents and young adults with cancer in order to improve:

- the quality and safety of care;
- access to research and innovation;
- full support for children and their families;
- preparation and follow-up for children and their families in the post-cancer period.

More recently the ESMART trial, set up to help children with cancer gain early access to innovative treatments, has been a major step forward..

## Our collaborative approach in paediatric oncology

The Cancer Committee has taken on board the persistent problems encountered by children, adolescents and their families in the care pathways.

The Committee has chosen to focus its work primarily on paediatric oncology. In particular, it has chosen to work on improving (i) the quality and safety of care, (ii) access to innovation, and also (iii) full support for children and their families during and after the illness.

To achieve these objectives, the Committee has decided to involve all stakeholders in a participative process to develop an action plan based on a shared analysis of needs.

Doctors, patient associations and families have been consulted to identify needs and elicit their suggestions.

This instructive approach has helped determine several courses of action to which industry can contribute.

At the end of a feedback workshop, it was decided collectively to pursue this course of action by developing a shared plan for paediatric oncology.

This plan, which is being jointly devised, will focus on three areas:

- further developing the offer of therapies available;
- promoting access to treatment for everyone;
- improving the quality of life of children and the support for their families.

# CANCER COMMITTEE

## Composition

Nom	Prénom	Entreprise
ANDRIEUX-BONNEAU	Aurélié	ABBVIE
BARLAND	Jean-Christophe	BRISTOL-MYERS SQUIBB
BOREL	Thomas	Leem
BOYAVAL	Gwendoline	MSD France
CHAUSSE	Aurélié-Anne	SANOFI France
COLLET	Frédéric	NOVARTIS
DELATTRE	Isabelle	Leem
DUPONT	Marianne	ABBVIE
GALAUP PACI	Ariane	Leem
GREGOIRE	Sylvie	IPSEN
GRUMEL	Olivier	JANSSEN-CILAG
KRULIK	Jérôme	PFIZER
LUKASIEWICZ	Michaël	ROCHE
MARECHAL	Christelle	Leem
MORALI	Monique	MERCK SANTÉ
PIRES-CARIUS	Nathalie	NOVARTIS
RAYNAUD	Catherine	PFIZER
SABATIN	Yannick	CELGENE
VAROQUEAUX	Nathalie	ASTRAZENECA

This platform has been created with the help of Care Factory at [www.carefactory.fr](http://www.carefactory.fr)





COMITÉ CANCER  
58, boulevard Gouvion-Saint-Cyr  
CS 70073  
75858 Paris Cedex 17  
T.: 33 (0)1 45 03 88 88

 [facebook.com/lemedicamentetmoi](https://facebook.com/lemedicamentetmoi)  [@LeemFrance](https://twitter.com/LeemFrance)

 [Leem](https://www.linkedin.com/company/leem)  [LeemFrance](https://www.pinterest.com/LeemFrance)

[www.leem.org](http://www.leem.org)