



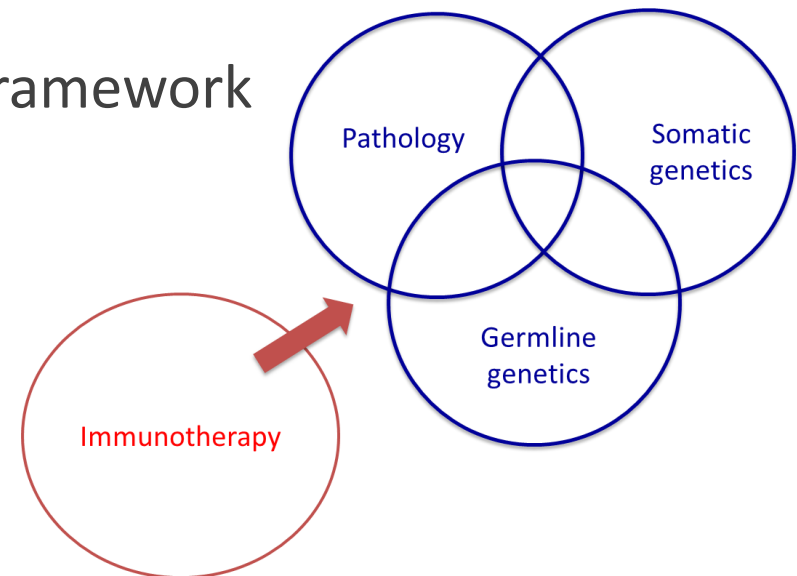
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# Rolling out personalised medicine for cancer in France

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Overall purpose is lead you through the continuous adjustments needed in the **organisational framework for personalised medicine in clinical routine in cancer**

- Targeted therapies – the starting point for the development of personalised medicine in cancer
- Organisational framework for PM
- New treatments & their impact on this framework

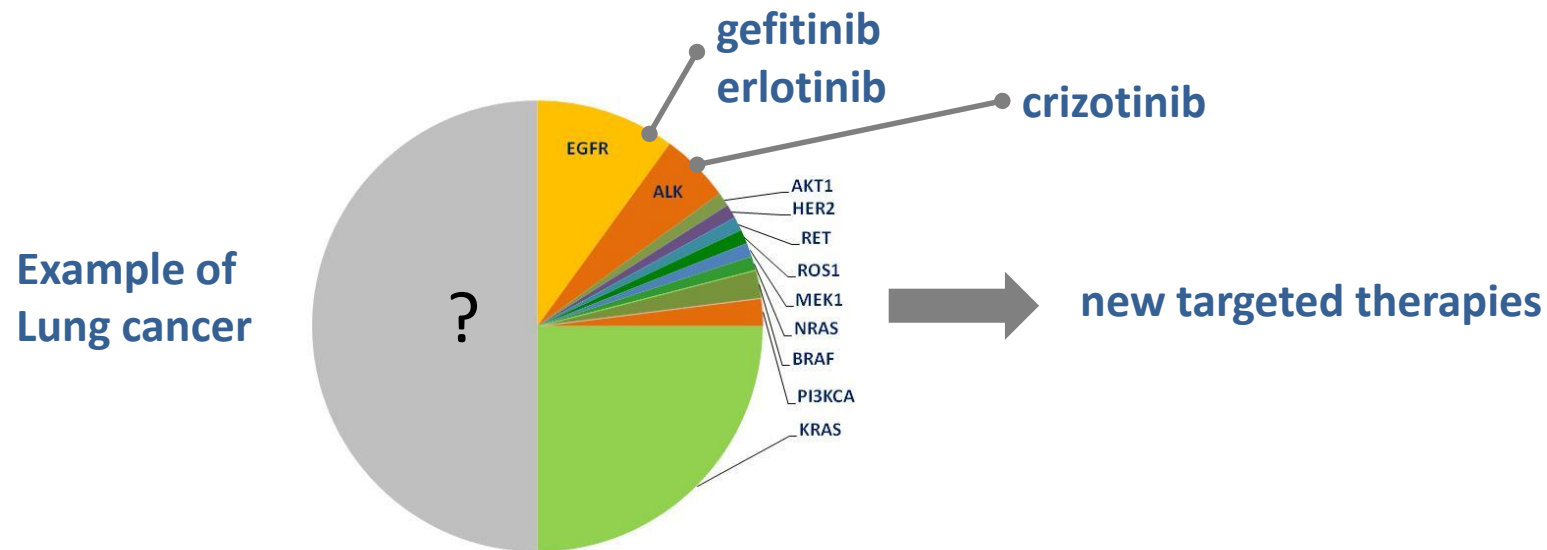


- ▶ **INCa is a National Health and Scientific Agency dedicated to cancer control** & reports to the Ministries of Health and of Research.
- ▶ **INCa's mission** is fulfilled through a **systematic implementation of evidence-based strategies across the cancer control continuum** (prevention, screening, early detection, diagnosis, treatment, supportive & follow-up care, palliation, and research)



# Targeted therapies : a change of paradigm for cancer treatment

**Molecular abnormalities in tumour cells subdivide most frequent cancers  
in several rare entities**



**Different cancer types share the same genetic abnormalities**

→ A same targeted therapy can be used to treat different tumor types based on the expression of the molecular target

- Trastuzumab in breast and gastric cancers expressing HER2

# Predictive biomarkers for targeted therapies prescription

Biomarker	Cancer type	Targeted therapies	Patients nb in 2014
<i>KIT</i> mutations	GIST	Imatinib	<b>1189</b>
<i>HER2</i> amplification	Breast and gastric cancers	Trastuzumab, lapatinib, pertuzumab, trastuzumab emtansine	<b>9680</b>
<i>RAS</i> mutations	Colorectal cancer	Panitumumab, cetuximab	<b>22011</b>
<i>EGFR</i> mutations	Lung cancer	Gefitinib, erlotinib, afatinib, osimertinib	<b>24558</b>
<i>EGFR</i> expression	Squamous non small cell lung cancer	Necitumumab	
<i>ALK</i> translocations	Lung cancer	Crizotinib, ceritinib	<b>21183</b>
<i>ROS1</i> translocations	Lung cancer	Crizotinib (RTU)	<b>5414</b>
<i>BRAFV600</i> mutation	Melanoma	Vemurafenib, dabrafenib, trametinib, cobimetinib	<b>5534</b>
<i>BCR-ABL</i> translocation	Chronic Myeloid Leukaemia/ Acute Lymphoblastic Leukaemia	Imatinib, nilotinib, dasatinib, ponatinib, bosutinib	<b>7453</b>
<b>17p deletion / <i>TP53</i> mutation</b>	Chronic Lymphocytic Leukaemia	Ibrutinib, idelalisib	

# France organisational framework for personalised medicine

## Provides nationwide molecular diagnostic tests

### Objectives

- ▶ Perform molecular testing for all patients;
- ▶ Whatever the healthcare institution status (public hospitals, private hospitals...);
- ▶ Perform high quality tests;
- ▶ leukemia, solid tumours

### 28 regional centers

- ▶ Partnerships between several laboratories located in University hospitals and cancer centers
- ▶ Regional organization
- ▶ Cooperation between pathologists and biologists



The program is operated by INCa/French Ministry of Health since 2006

# Benefit & swift access to innovation for all patients

## Molecular tests are performed :

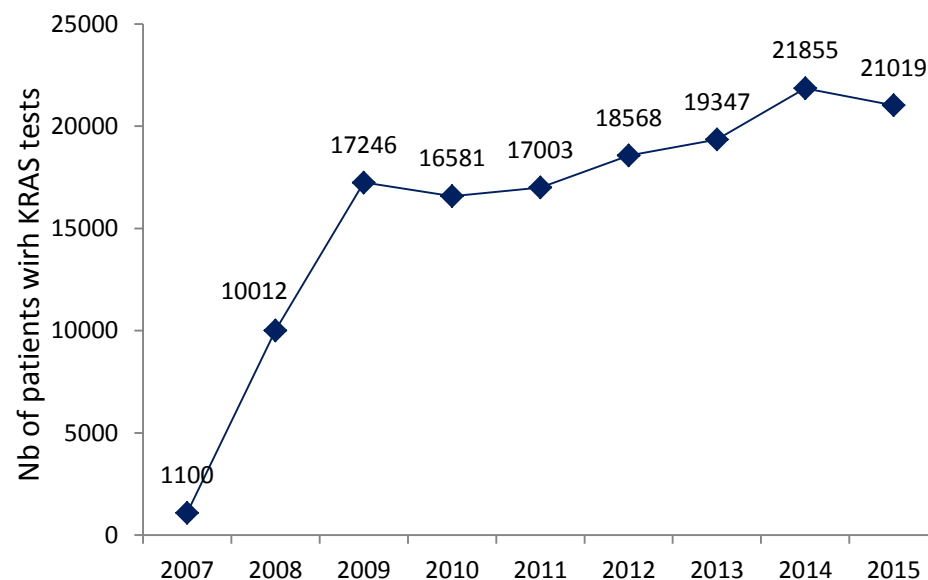
- ▶ for all patients
- ▶ No charge for patients & hospitals (covered by global budget allocated by INCa & Health Ministry to the centers)
- ▶ with compensation of local pathologists for sample shipments



**Ensure that all patients actually benefit from molecular testing**

## Colorectal cancer :

- ▶ **Mid 2008** : EMA approvals of panitumumab and cetuximab for patients with **wild type KRAS tumours**
  - ➔ INCa started funding the 28 centres by the end of 2008 (€2.5M)



**... as soon as a new therapy is available**

## Implementation of a quality assurance program

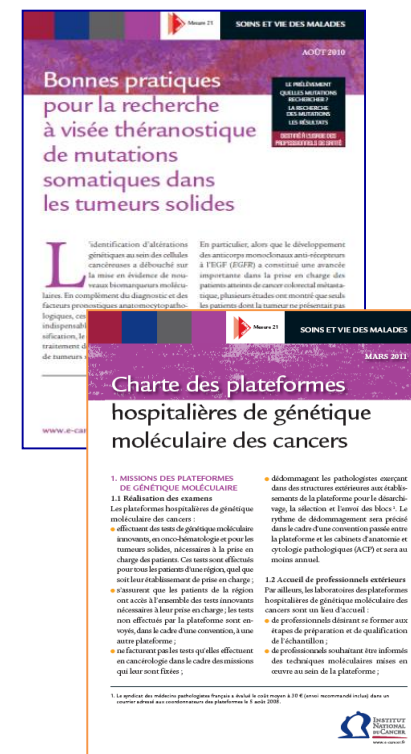
### Elaboration of guidelines for :

- ▶ the detection of mutations in solid tumours ;
- ▶ the organisation of molecular testing ;
- ▶ reports of molecular tests

### Implementation of national External Quality Assessment rounds for the main tests in the 28 centers

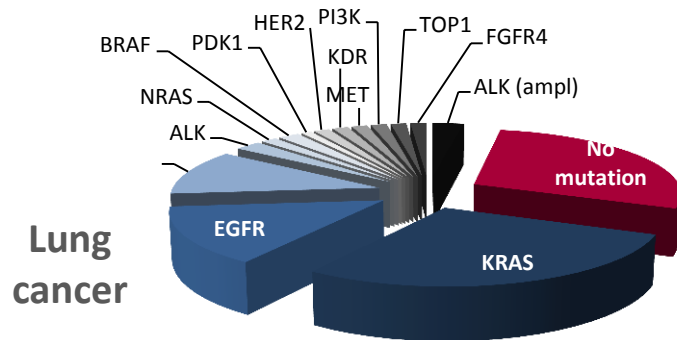


**Towards ISO 15189 accreditation**





# Increasing number of actionable molecular alterations & NGS



**Challenge : switch from the one by one approach to the targeted NGS approach**

NGS increases probability for a given patient to identify an actionable mutation in his tumour

- Increase the access to innovative drugs within the framework of clinical trials
- Facilitate the development of new targeted therapies

⇒ NGS blurs the frontier between care & clinical research

# Targeted NGS in routine practice

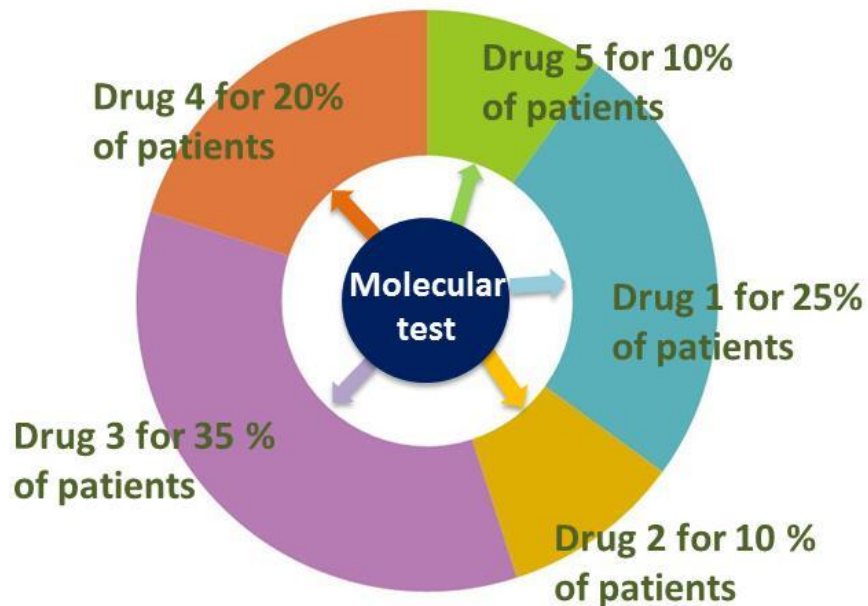
- ▶ Pilot phase launched in 2013 with 11 molecular genetic centres :
  - ✓ develop the necessary skills to use this new technology
- ▶ Monitoring led by INCa :
  - ✓ increase the sharing of experiences
  - ✓ Draft guidelines
- ▶ 5 referent teams in bioinformatics :
  - ✓ Validate & release existing data analysis pipelines, or develop better ones
  - ✓ support wet labs and their “embedded” bioinformaticians through network animation and training
- ▶ Economic impact of NGS evaluated at the same time

- ▶ Rolling out started in 2015 in all the molecular centres

Progressive shift from the standard approach towards targeted NGS for all patients

**This objective should be achieved by the end of 2016**

## Molecular screening allows the optimisation of treatments & expenditures



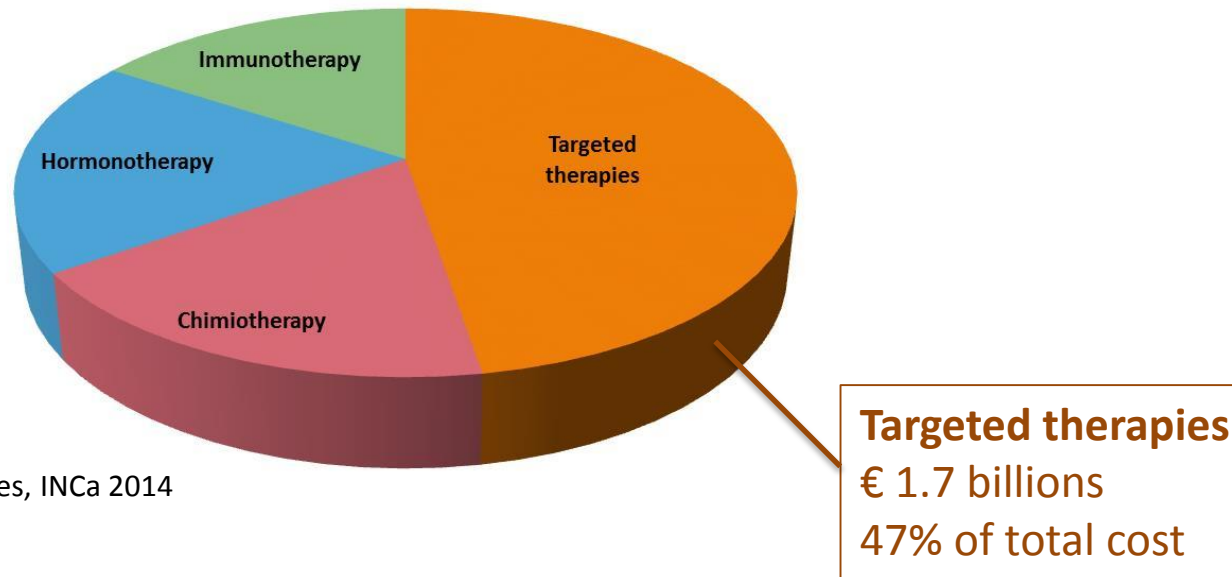
**AND**

No drug 1 for 75% of patients  
No drug 2 for 90% of patients  
No drug 3 for 65% of patients  
No drug 4 for 80% of patients  
No drug 5 for 90% of patients

- ✓ Molecular test (targeted NGS + FISH + IHC)  $\approx$  1000 €
- ✓ Targeted therapy  $\approx$  3000€ / month
- ✓ For a non responder  $\approx$  6000 € (2 months)
- ✓ For a responder  $\approx$  36,000 € (12 months)

**Cost of molecular tests << cost of targeted therapies**

## Cost of cancer drugs in 2014 in France : € 3.6 billions



Source : Rapport Thérapies ciblées, INCa 2014

## + 8.3% compared to 2013

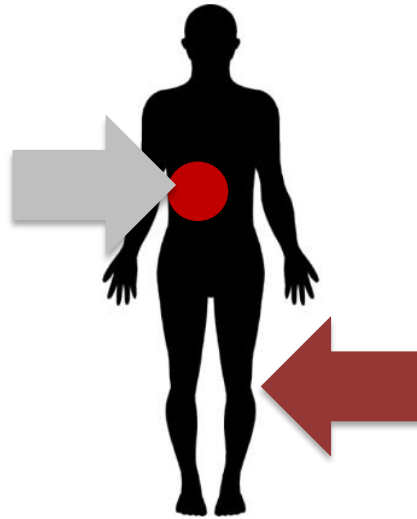
Main causes of steady increases of targeted therapies expenditures :

- Targeted therapies available for new subsets of patients
- Drugs combinations
- Patients stay longer under treatment

# Change of paradigm in cancer treatment : a fast evolving scientific and medical environment

## Targeted therapies

Molecular analysis of  
tumour cells



## PARP inhibitors

## Germline genetics analysis

2014 : Market autorisation of olaparib in  
ovarian cancer for patients with **BRCA  
mutations** (either somatic or germline)

## New challenges :

1. Patients information on the personal and familial impact of a positive BRCA test : ethics+++
2. Molecular tests integrating 3 complementary expertises : pathology, somatic genetics and germline genetics

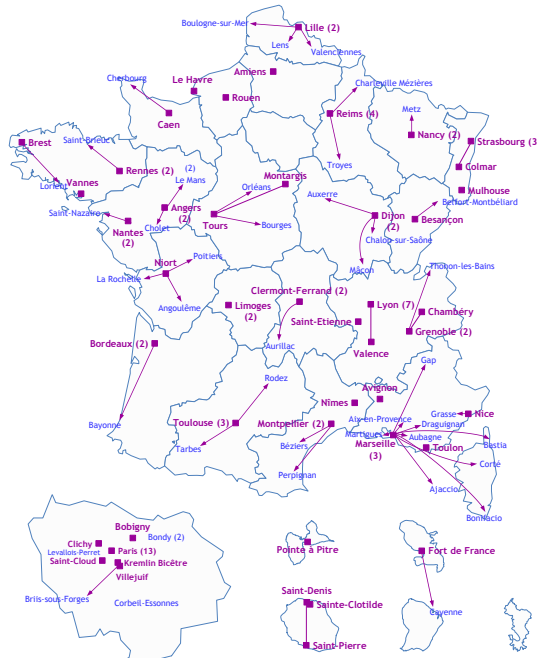
⇒ **Need to make current organisational framework evolve**

# French organisational framework for germline genetics in oncology

## Objectives :

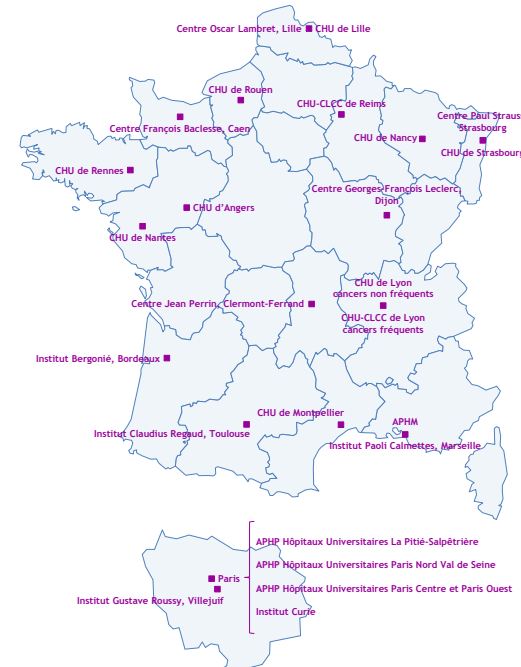
- ▶ identify people with genetic predisposition to cancer
- ▶ offer specific prevention programmes including risk-adjusted screening, preventive surgery and medicines.

## 130 genetic counseling sites in 90 cities

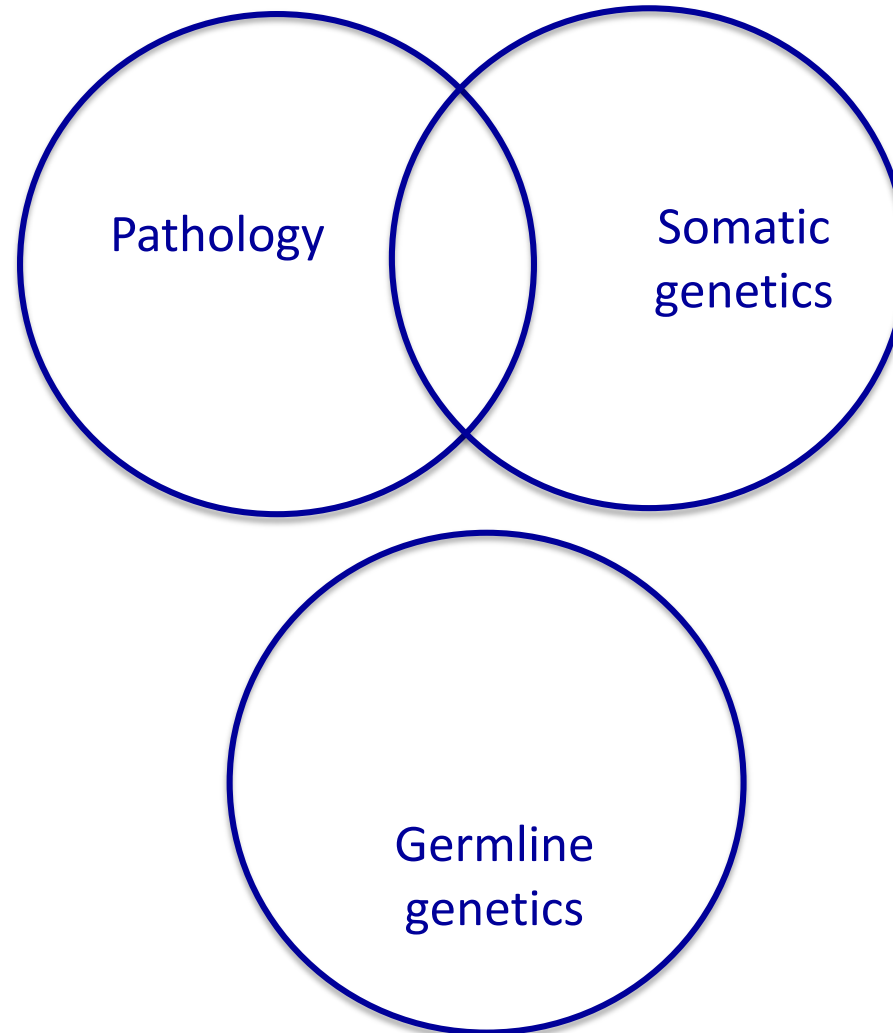


## 25 laboratories for genetic testing

Perform genetic tests prescribed by clinical geneticists



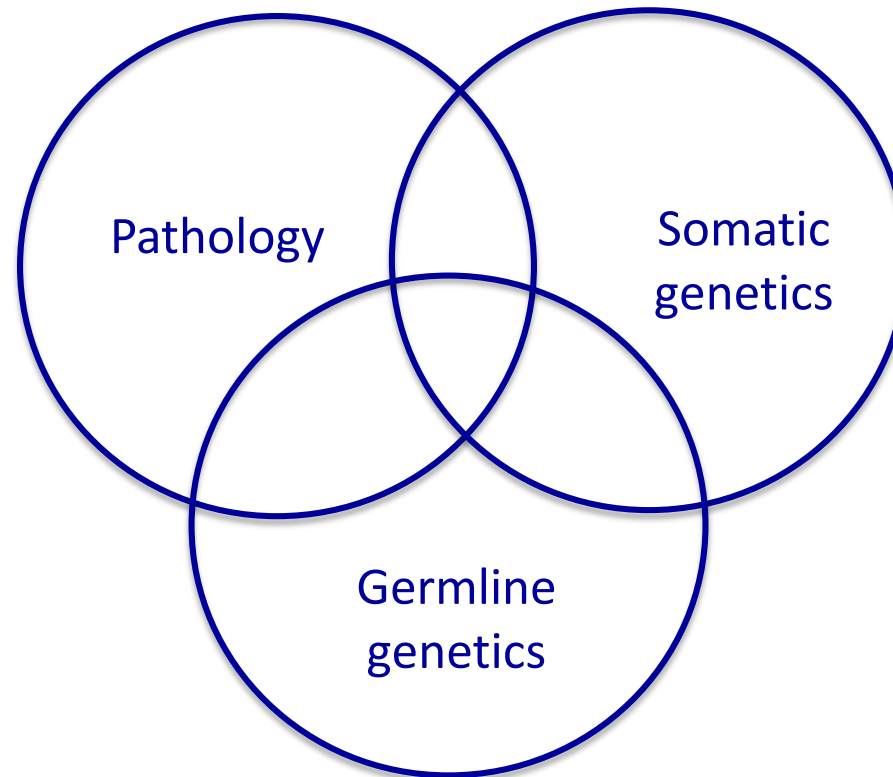
# Towards a more integrated organisational framework



**Molecular  
genetics  
centres**

**Oncogenetic  
programme :  
genetic  
counseling and  
laboratories**

# Towards a more integrated organisational framework



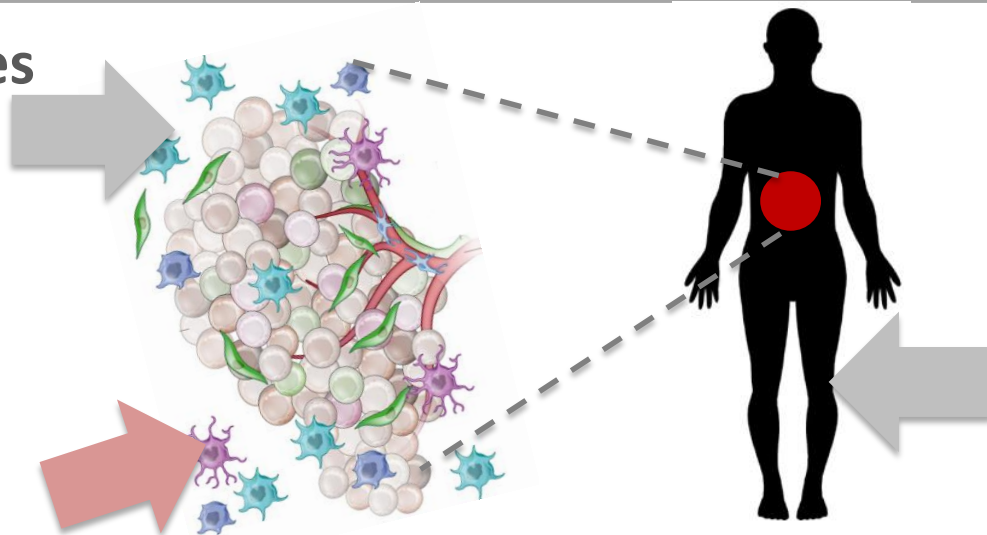
**Integrated  
organisational  
framework**



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## Targeted therapies

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## PARP inhibitors

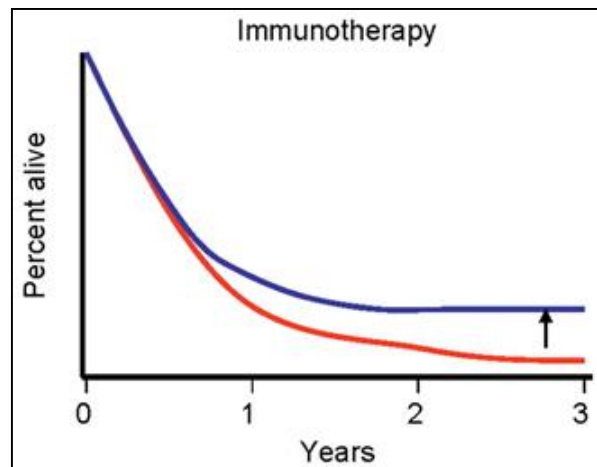
Germline genetics analysis

## Immunotherapy

Checkpoint inhibitors :

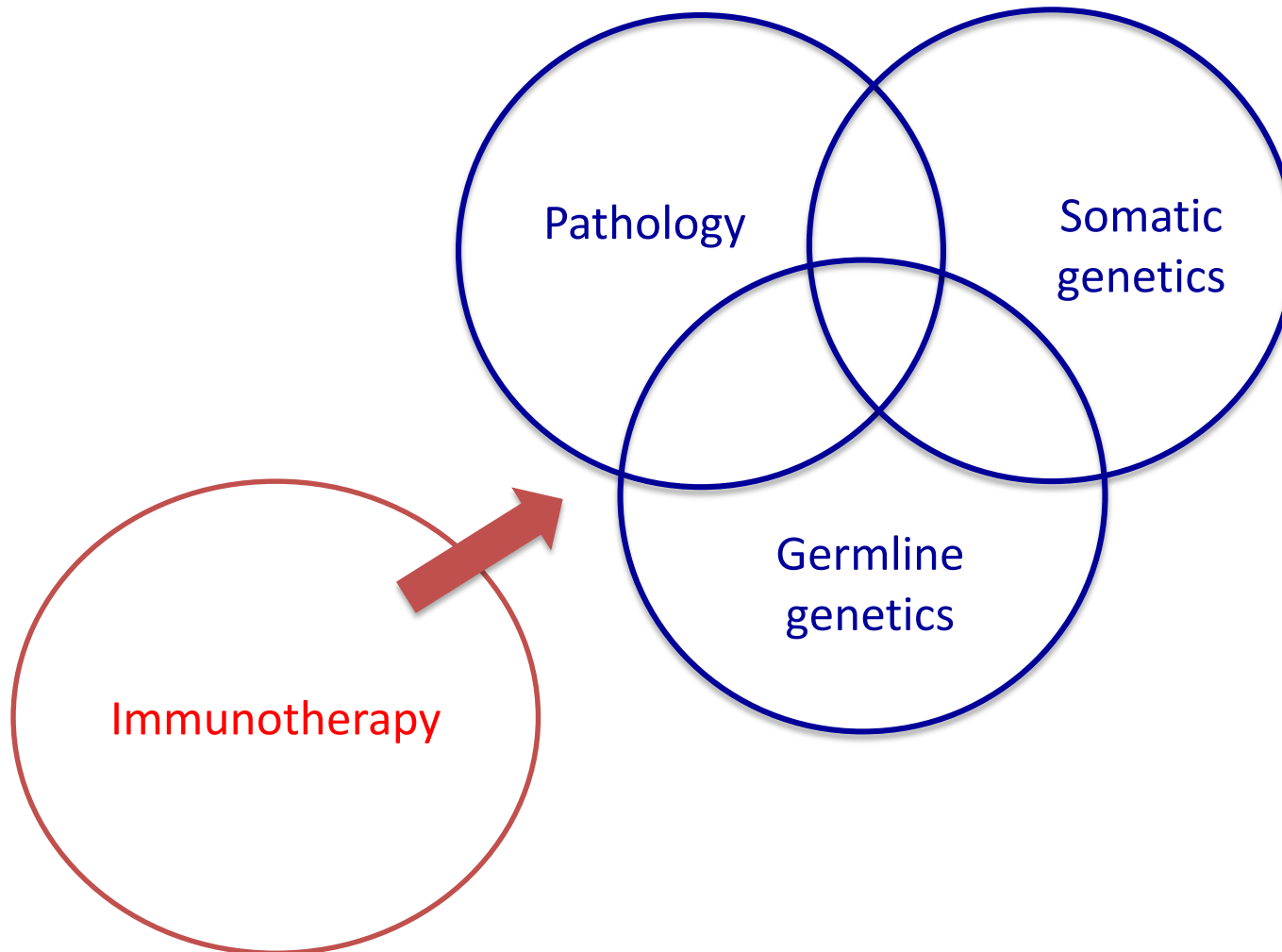
- Anti-CTLA4
- Anti-PD1 and anti-PDL1

Market authorization and ongoing clinical trials in melanoma, lung cancer, mesothelioma, kidney cancer, bladder cancer....



=> **Specific predictive biomarkers are under development and will enter soon into clinical practice**

# Towards next ajustment integrated of the organisational framework



## **France' organisational framework for precision medicine in oncology :**

- has been operating for 7 years;
- offers an equal access to molecular testing for all patients in France;
- shows that molecular stratification can be successfully integrated into the healthcare system;
- shows that such a national organisation has to be continuously adjusted in a context of a fast evolving scientific, medical and technological environment



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plus d'informations sur  
**e-cancer.fr**