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

- gefitinib
- erlotinib
- crizotinib

Example of Lung cancer

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

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

... as soon as a new therapy is available

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)
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
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

- 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

- Targeted therapies € 1.7 billions
  - 47% of total cost

+ 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

Source: Rapport Thérapies ciblées, INCa 2014
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

Pathology

Somatic genetics

Germline genetics

Molecular genetics centres

Oncogenetic programme:
genetic counseling and laboratories
Towards a more integrated organisational framework

Pathology

Somatic genetics

Germline genetics

Integrated organisational framework
Change of paradigm in cancer treatment: a fast evolving scientific and medical environment

Targeted therapies
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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 adjustment integrated of the organisational framework

Pathology

Somatic genetics

Germline genetics

Immunotherapy
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.
plus d’informations sur

e-cancer.fr