Cancer 2020 : The road to personalised cancer care

*Developing patient-centered cancer services for the 21st century*

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Disclosure slide

• I have no disclosure to declare
The french cancer plan 2009-2013: The road to personalised medicine

- **Patient centered approach**
  - Personalised therapeutic project (PPS)
  - Organized structures for specific cares
    - Rare tumours networks
    - Oncogeriatric centers/ Oncopeadiatric centers/ Young adults and adolescent centers
    - Oncogenetic consultations

- **Tumour centered approach**
  - Molecular diagnosis of tumours
  - Next Generation Sequencing

- **Clinical implications**
The personalised therapeutic project: a simplified and individualised path

• Each patient receives a personalised therapeutic project (PPS) and a post cancer personalised project (PPAC)

• Objectives:
  – Coordination of all the actors by a nurse
  – Early detection of supportive care and social needs
  – Explanation of the personalised therapeutic plan
  – Preparing the link with the actors outside the hospital and the general practitioner

• 35 centers participating to the first pilote phase
  – Over 3500 patients received a PPS
  – About 20% received a PPAC

• Evaluation in 2012 leading to a second experimental phase in 2013 before nationwide extension
The organization for rare cancers

- Too much diagnosis errancy and practice heterogeneity
- The organisation:
  - Clinical regional expert centres coordinated by a national expert centre,
  - National anatomopathological networks or groups of expert pathologists
- With the following tasks:
  - To set-up **multidisciplinary expert staff meetings** (decision of appropriate treatment)
  - To organize a **systematic double reading** (diagnostic certainty)
  - To contribute to **clinical research** (access to innovative treatments)
  - To set-up a rare cancer **database**
  - To disseminate **information to patients** and next-of-kin, through national patients organizations

**Measure 23:** Develop specific care management for patients with rare forms of cancer...
The organization for rare cancers

- Organisation started in 2009
  - Based on 3 calls for projects
  - 17 clinical networks
    - rare tumours
    - or tumours in a specific site (CNS, ocular)
    - or tumours on a particular background (pregnancy, viral post transplant, HIV)
  - 4 anatomopathological networks
- In 2011:
  - About 5500 patients with a rare cancer diagnosis benefit from this organization
  - 46 clinical trials initiated or ongoing and 17 achieved
  - 830 patients included in clinical trials
  - 10 websites dedicated to these rare cancers
  - 10 expert centres have formalized links to patients organizations
## 17 rare cancers clinical networks

<table>
<thead>
<tr>
<th>Rare cancers</th>
<th>Estimated incidence/y</th>
<th>Rare cancers</th>
<th>Estimated incidence/y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft tissue and visceral sarcomas</td>
<td>4 000</td>
<td>Refractory thyroid carcinoma</td>
<td>400</td>
</tr>
<tr>
<td>Rare malignant sporadic and hereditary neuroendocrine tumors</td>
<td>1 200</td>
<td>Primary ocular and cerebral lymphomas</td>
<td>300 - 400</td>
</tr>
<tr>
<td>Rare head and neck carcinoma</td>
<td>900</td>
<td>Lymphomas associated to coeliac disease</td>
<td>350</td>
</tr>
<tr>
<td>Malignant pleural mesothelioma</td>
<td>900</td>
<td>Malignant thymoma end thymic carcinoma</td>
<td>250</td>
</tr>
<tr>
<td>Cutaneous lymphomas</td>
<td>700</td>
<td>Trophoblastic gestational tumors</td>
<td>180</td>
</tr>
<tr>
<td>High grade oligodendroglioma</td>
<td>600</td>
<td>VHL disease and hereditary predisposition to renal carcinoma</td>
<td>160-240</td>
</tr>
<tr>
<td>Rare ovarian carcinoma</td>
<td>500</td>
<td>Rare peritoneal tumors</td>
<td>130-180</td>
</tr>
<tr>
<td>Cancers during pregnancy</td>
<td>500</td>
<td>Adrenal carcinoma</td>
<td>100-150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Viral-induced post-transplant neoplasia</td>
<td>100-110</td>
</tr>
</tbody>
</table>
## 4 Anatomopathological networks

<table>
<thead>
<tr>
<th>RARE CANCERS</th>
<th>NETWORK NAME</th>
<th>NATIONAL COORDINATOR</th>
<th>NATIONAL EXPERT CENTER (one or more sites)</th>
</tr>
</thead>
</table>
| Sarcomas of the soft tissues and viscera          | CRePS-TMV     | Prof Jean-Michel COINDRE           | Institut Bergonié, Bordeaux  
|                                                  |               |                                    | Institut Gustave Roussy, Villejuif  
|                                                  |               |                                    | Centre Léon Bérard, Lyon           |
| Malignant pleural mesotheliomas and rare peritoneal tumours | MESOPATH-IM@EC | Prof Françoise GALATEAU-SALLÉ     | CHU de Caen                                                     |
| Rare malignant neuroendocrine tumours             | TNEpath       | Prof Jean-Yves SCOAZEC             | Hôpital Edouard Herriot, HCL                                    |
| Lymphomas                                         | LYMPHOPATH    | Prof Georges DELSOL  
|                                                   |               | Prof Philippe GAULARD             | CHU Toulouse  
|                                                   |               |                                    | Hôpital Henri Mondor, AP-HP         |
Example of specialised organization: the elderly

- Selection of 23 Oncogeriatrics coordination units after a call for project
  - covering 18 metropolitan regions and 1 overseas department
- with the following tasks:
  - To adjust cancer treatment in elderly people
    - Coordination between oncologic and geriatric teams, geriatric pre-screening test ± comprehensive geriatric assessment, geriatric propositions, multidisciplinary consultative meeting with the presence of a geriatrician...
  - To stimulate specific research in oncogeriatrics
  - To promote training of health professionals
  - To promote information

**Action 23.4**: Improve care management for elderly cancer patients

**Action 4.2**: Increase inclusion in clinical cancer trials with a participation rate of 5% in elderly (> 75 years) patients
The shift of paradigm for cancer treatment

- Towards molecular subsets of cancers
  - Molecular genetics deciphers severe frequent cancers into specific rare cancer

- Molecular alterations shared in several cancers
  - One drug is now efficient for the treatment of several « rare cancers »

Molecular subsets of non small cell lung cancer: 20,000 patients

Measure 21.
Guarantee equal access to innovative and existing treatments.

21.2 Develop cancer molecular genetics hospital platforms and expand access to molecular testing.
## Predictive tests for targeted therapies prescription

<table>
<thead>
<tr>
<th><strong>BCR-ABL translocation:</strong></th>
<th>Chronic Myeloïd Leukemia/ Acute Lymphoblastic Leukemia</th>
<th>Imatinib prescription 1- Imatinib prescription 2- Monitoring of minimal residual disease 3- Resistance to Imatinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>1- <em>BCR-ABL</em> detection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2- <em>BCR-ABL</em> quantification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3- <em>ABL</em> mutation</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>KIT and PDGFRA mutations</strong></th>
<th>GIST</th>
<th>Imatinib prescription</th>
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<tr>
<th><strong>HER2 amplification</strong></th>
<th>Breast and gastric cancers</th>
<th>Trastuzumab prescription</th>
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<tr>
<th><strong>KRAS mutations</strong></th>
<th>Colorectal cancer</th>
<th>Panitumumab and cetuximab prescription</th>
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<tr>
<th><strong>EGFR mutations</strong></th>
<th>Lung cancer</th>
<th>Gefitinib and erlotinib prescription</th>
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<th><strong>ALK translocations</strong></th>
<th>Lung cancer</th>
<th>Crizotinib prescription</th>
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<th><strong>BRAFV600 mutation</strong></th>
<th>Melanoma</th>
<th>Vemurafenib prescription</th>
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Ensuring equity of access to innovation:

French organisation of molecular centres for personalized medicine

Provides nationwide molecular diagnostic tests

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

- **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 centres**
  - Partnerships between several laboratories located in University hospitals and cancer centres
  - Regional organization
  - Cooperation between pathologists and biologists
Benefit for all patients

Molecular tests are performed:

- For all patients
- free of charge for patients & hospitals
- With compensation of local pathologists for sample shipments

⇒ Ensure that all patients effectively benefit from molecular testing
Rapid access to innovation

Offer each patient in France an equal access to molecular tests as soon as a new targeted therapy is available

Mid 2008: EMA approvals for Erbitux® and Vectibix® for patients with wild type KRAS tumours

⇒ INCa started to allocate €2.5M to the 28 centres at the end of 2008

June 2009: gefitinib approvals by EMA for patients with activating mutations of EGFR in their tumors

⇒ INCa started to allocate €1.7M to the 28 centres at the end of 2009
Offer the best treatment to patients considering the cost – effectiveness ratio

- Seed fundings from INCa for the test set-up
- Performance and cost evaluation
- Recurrent annual fundings from the French Ministry of Health insurance

This programme benefits also from INCa/private partnerships
Sparing cost for the health insurance

Example of gefitinib treatment in lung cancer

15,000 patients -
(gefitinib treatment: 8 weeks DFS; Mok 2009)

€ 69M

€ 1.7M

EGFR testing for lung cancer patients

1,724 patients +
(gefitinib treatment: 38 weeks DFS; Mok 2009)

€ 35M

Spared cost of gefitinib treatment

Cost of gefitinib treatment
Implementation of a quality assurance programme

- **Elaboration of guidelines for**:
  - the detection of mutations in solid tumors;
  - the organization of molecular testing;
  - reports of molecular tests.

- **Implementation of a national External Quality Assessment for the 28 centres**:
  - 2011: BCR-ABL quantification, KRAS and EGFR mutation screening;
  - 2012: BRAF mutation screening.

⇒ Assurance quality optimization

⇒ guide the molecular genetics centres to becoming accredited to ISO 15189 standard as soon as possible
Anticipate the launch of new molecules

The INCa allocated €3.5M in 2010 and €2.8M in 2011 for the prospective detection of emerging biomarkers

- For the 20,000 patients with lung adenocarcinoma, additional analysis of:
  - EGFR mutations conferring resistance to TKI-EGFR;
  - KRAS, HER2, PI3KCA and BRAF mutations;
  - ALK translocation.

- For the 17,000 patients with colorectal cancer, additional analysis of:
  - BRAF mutation;
  - MSI test.

- BRAF and cKIT mutations for patients with melanoma

⇒ Be ready to perform the test as soon as the therapy is available
Early Access to targeted therapies: the AcSe study

- To favour secured access to MA or near to market new drugs for all patients in all authorized cancer treatment centers in France (N=835)
- Facilitated criteria of inclusion and non inclusion
- Based on a defined molecular abnormality in any tumor types (excluding those of MA)
- Simple clinical protocol aiming at detecting efficacy and safety in new rare indications
- Stratification for Go – Stop in different tumor types
International cancer genomics consortium: ICGC
International Human Epigenome Consortium: IHEC

<table>
<thead>
<tr>
<th>Countries within the ICGC</th>
<th>Funding bodies</th>
<th>Types of tumours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>• Federal Ministry of Education and Research&lt;br&gt;• German Cancer Aid</td>
<td>• Brain</td>
</tr>
<tr>
<td>Australia</td>
<td>• National Health and Medical Research Council</td>
<td>• Ovary&lt;br&gt;• Pancreas</td>
</tr>
<tr>
<td>Canada</td>
<td>• Ontario Institute for Cancer Research&lt;br&gt;• Ontario Ministry of Research and Innovation&lt;br&gt;• Canada Foundation for Innovation</td>
<td>• Pancreas</td>
</tr>
<tr>
<td>China</td>
<td>• Chinese Cancer Genome Consortium</td>
<td>• Stomach cancer</td>
</tr>
<tr>
<td>Spain</td>
<td>• Spanish Ministry of Science and Innovation</td>
<td>• Chronic lymphocytic leukaemia</td>
</tr>
<tr>
<td>France</td>
<td>• National Cancer Institute</td>
<td>• Breast&lt;br&gt;• Liver&lt;br&gt;• Prostate</td>
</tr>
<tr>
<td>India</td>
<td>• Department of Biotechnology&lt;br&gt;• Ministry of Science and Technology</td>
<td>• Oral cavity</td>
</tr>
<tr>
<td>Italy</td>
<td>• University of Verona · Italian Ministry of Education&lt;br&gt;• University and Research</td>
<td>• Pancreas</td>
</tr>
<tr>
<td>Japan</td>
<td>• RIKEN · National Institute of Biomedical Innovation</td>
<td>• Liver</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>• The Wellcome Trust · Breakthrough Breast Cancer</td>
<td>• Breast</td>
</tr>
<tr>
<td>European Union</td>
<td>• European Commission FP7</td>
<td>• Breast · Kidney</td>
</tr>
<tr>
<td>Cancer genome Atlas (USA)</td>
<td>Funding bodies</td>
<td>Types of tumours</td>
</tr>
<tr>
<td>United States</td>
<td>• National Institutes of Health&lt;br&gt;• National Cancer Institute&lt;br&gt;• National Human Genome Research Institute</td>
<td>• Brain&lt;br&gt;• Colon&lt;br&gt;• Lung&lt;br&gt;• Ovary&lt;br&gt;• Leukaemia</td>
</tr>
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</table>
Liver Cancer genome programme

Guichard et al. Nature Genetics, 2012
Liver Cancer genome programme

Activated pathways according to the causal trigger

Guichard et al. Nature Genetics, 2012

www.esmo2012.org
Proof of concept for molecularly guided therapy: prospective trial for the future

- Need to demonstrate that sequencing tumours (Exome-Whole GS) is of interest for treatment decision
- A national cooperative randomized study in early metastatic patient in some tumour types
- Comparing therapeutic decision based on NGS to current diagnostic procedures including defined genetic tests
- With the help of Pharmas to provide drugs already in phase 2 trials
Conclusions and perspectives

- **Personalised medicine is a multiparametric and integrative approach**
  - Which should be the standard of care for any cancer patient
  - Taking into account several factors linked to the patient or the tumour itself
  - Leading to identify dedicated structures or organisations

- **This initiative for targeted cancer treatment in France shows that:**
  - Innovation can be successfully integrated into the healthcare system
  - Molecular stratification is cost effective
  - This organization could be easily expanded in other European settings

- **These molecular genetics centres are key to develop translational research and to sustain progress.**

- **All these approaches are instrumental to facilitate access to the best care and improve patient’s survival and quality of life.**