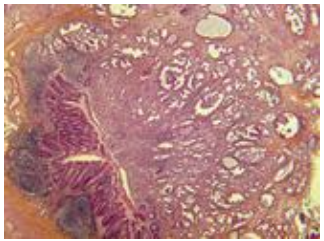
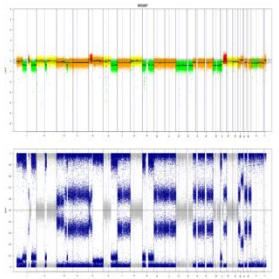
INSTITUT NATIONAL DU CANCER

Personalized Medicine
A nationwide initiative for an equal access to cancer treatment in France





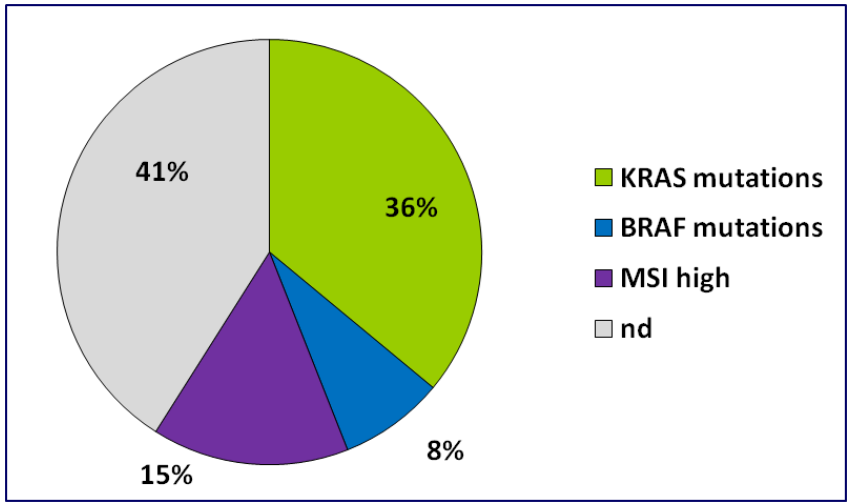
Fabien CALVO – Deputy Director General

The challenges of targeted therapies in cancer

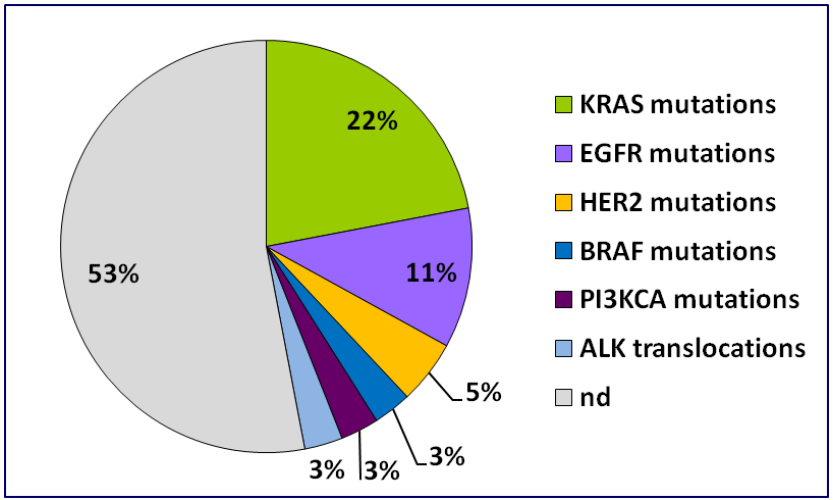
- Molecular genetics deciphers severe frequent cancers into specific rare cancers with specific treatment
- Molecular characteristics redefine tumor classification for molecular targeted therapies
- Ensuring equity of access to innovation
- Offering the best treatment to patients considering the cost – effectiveness ratio

The shift of paradigm : towards molecular subsets of cancers

Molecular subsets of **colorectal cancer** : 18,000 patients



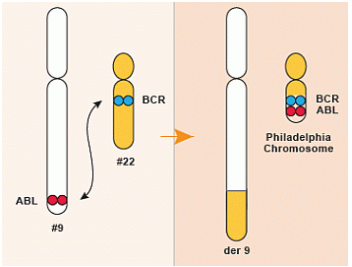
Molecular subsets of **non small cell lung cancer** : 16,000 patients



Molecular characteristics redefine tumor classification for molecular targeted therapies

The shift of paradigm : molecular alterations shared in several cancers

One drug is now efficient for the treatment of several « rare cancers »



Imatinib has granted European market approval 2001 for :

- Chronic myeloid leukemia and acute lymphoblastic Leukemia => BCR-ABL translocation
- Gastrointestinal Stromal Tumors => cKIT expression
- Hypereosinophilic Syndrome =>FIP1L1/ PDGFR re- arrangements
- Myelodysplastic-Myeloproliferative Diseases => PDGFR re- arrangements)
- Precursor Cell Lymphoblastic Leukemia-Lymphoma
- Dermatofibrosarcoma

Ensuring equity of access to innovation: France organisation of molecular platforms for personalised medicine

Provides nation-wide molecular diagnostic tests

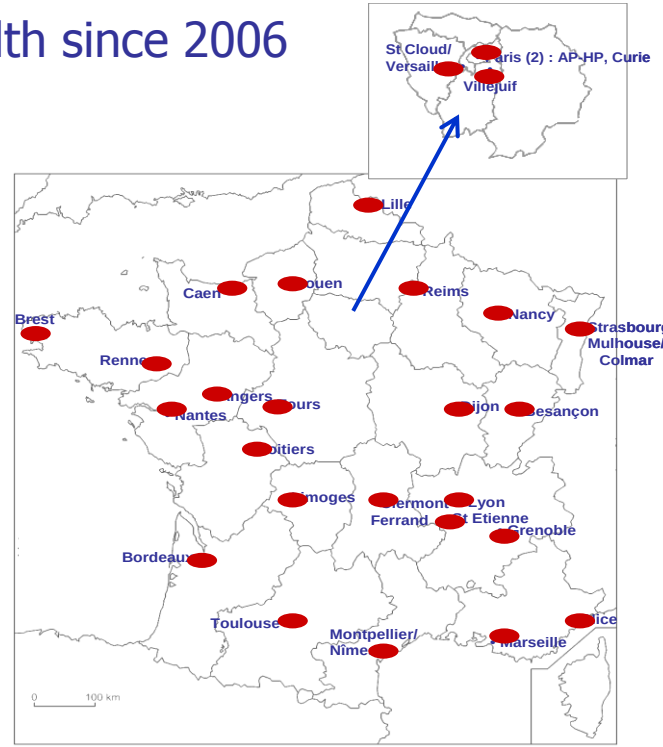
The programme is operated by the INCa/Ministry of Health since 2006

➢ 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 platforms

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



Predictive tests for targeted therapies prescription

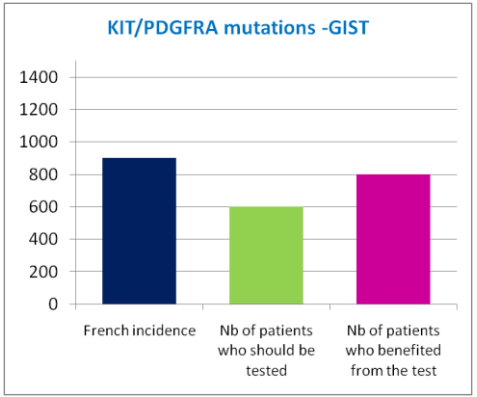
BCR-ABL translocation: 1- BCR-ABL detection 2- BCR-ABL quantification 3- ABL mutation	Chronic Myeloïd Leukemia/ Acute Lymphoblastic Leukemia	Imatinib prescription 1- Imatinib prescription 2- Monitoring of minimal residual disease 3- Resistance to Imatinib
KIT and PDGFRA mutations	GIST	Imatinib prescription
HER2 amplification	Breast and gastric cancers	Trastuzumab prescription
KRAS mutations	Colorectal cancer	Panitumumab and cetuximab prescription
EGFR mutations	Lung cancer	Gefitinib and erlotinib prescription
EML4-ALK translocations	Lung cancer	Crizotinib prescription
BRAF mutation V600E	Melanoma	Vemurafenib prescription

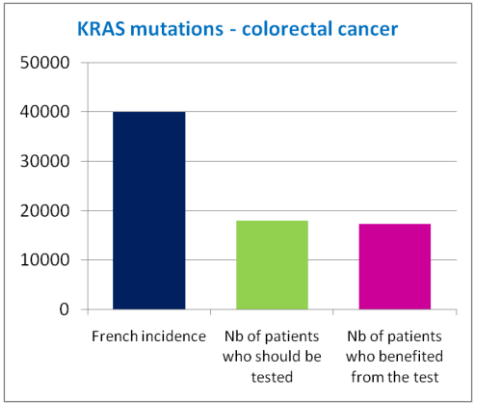
Benefit for all patients

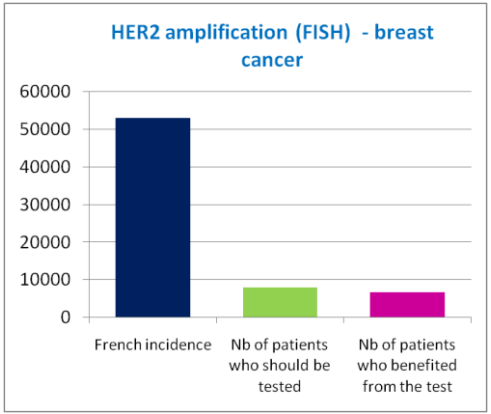
Measure 21.
Guarantee equal access to innovative and existing treatments.

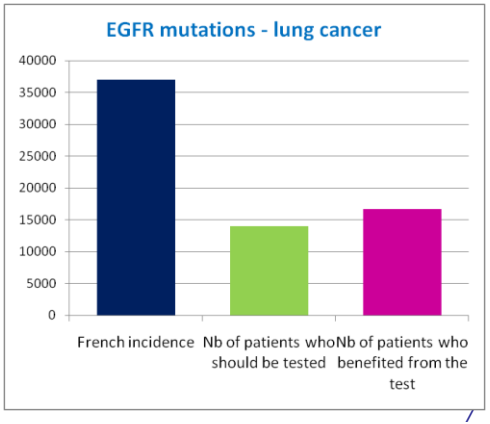
- For all patients
- free of charge for patients & hospitals
- compensation of local pathologists for sample shipments

⇒ Ensure that all patients effectively benefit from molecular testing





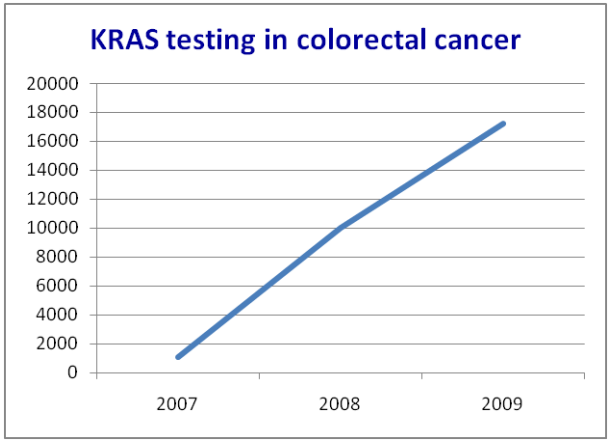




Offer each patient in France an equal access to molecular tests as soon as a new targeted therapy is available

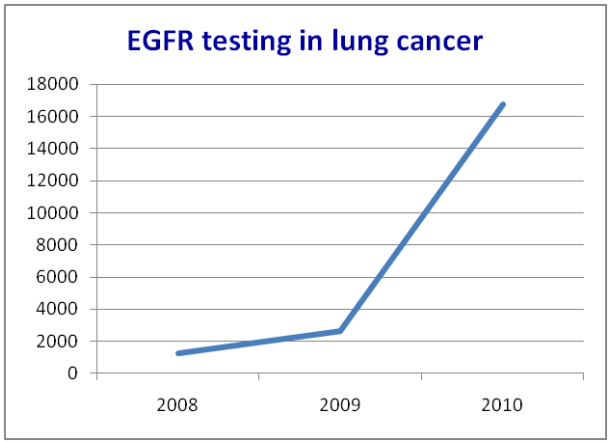
Mid 2008 : EMA approvals for Erbitux® and Vectibix® for patients with wild type KRAS tumours

⇒ INCa allocated €2.5M to the 28 platforms at the end of 2008

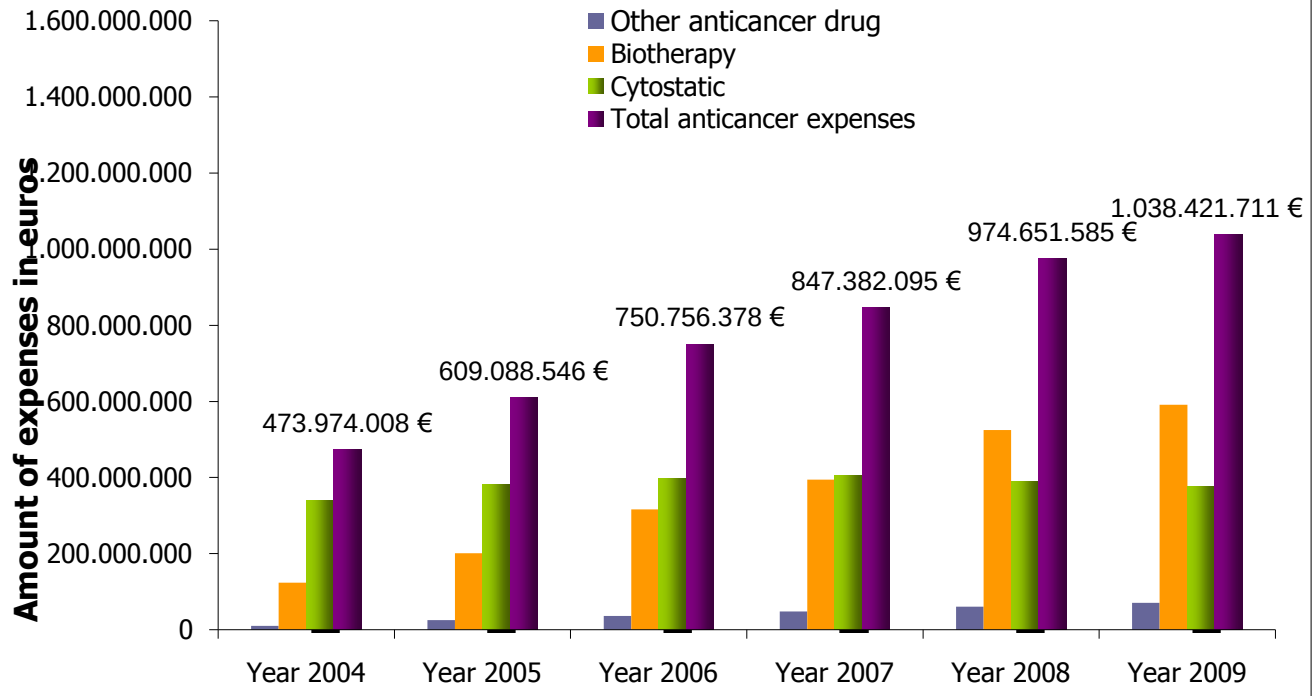


June 2009 : gefitinib approvals by EMA for patients with activating mutations of EGFR in their tumors

=> INCa allocated €1.7M to the 28 platforms at the end of 2009



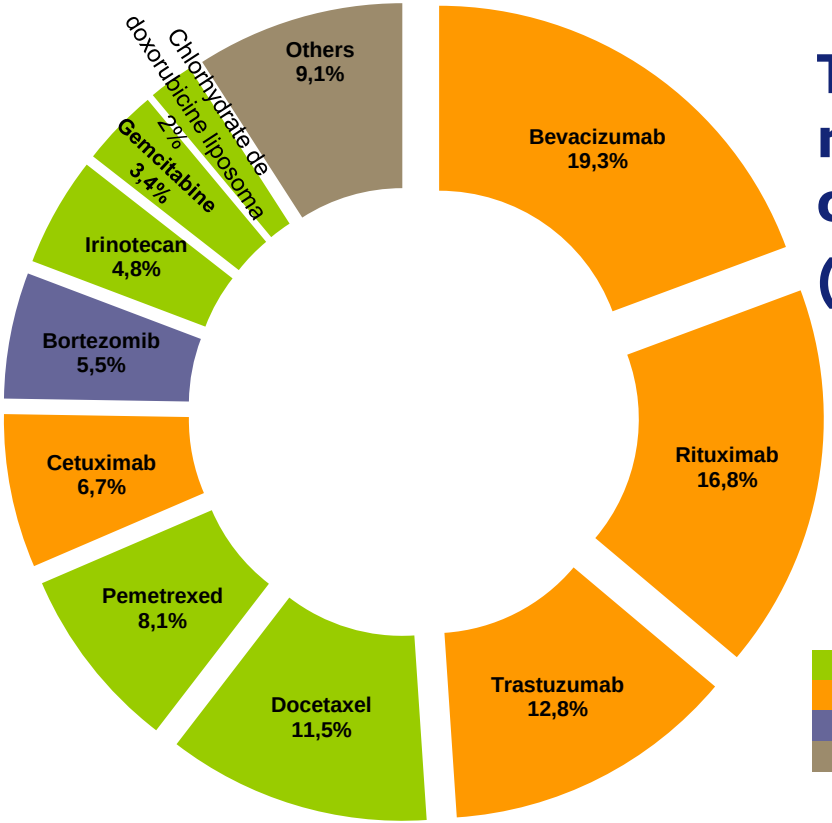
Offering the best treatment to patients considering the cost – effectiveness ratio:



Source : ATIH-PMSI MCO base updated 2005-2008 / infography INCa and base 2009/ infographyINCa

Growth spending of drug therapy expenditure since 2004 in France (public hospital sector)

Offering the best treatment to patients considering the cost – effectiveness ratio:



Targeted therapy represents 57 % of the cost of anticancer drugs (public hospital sector)

Source : ATIH-PMSI MCO base 2009/ infography INCa

The anticancer targeted therapy portfolio

From 2004 to 2010 :

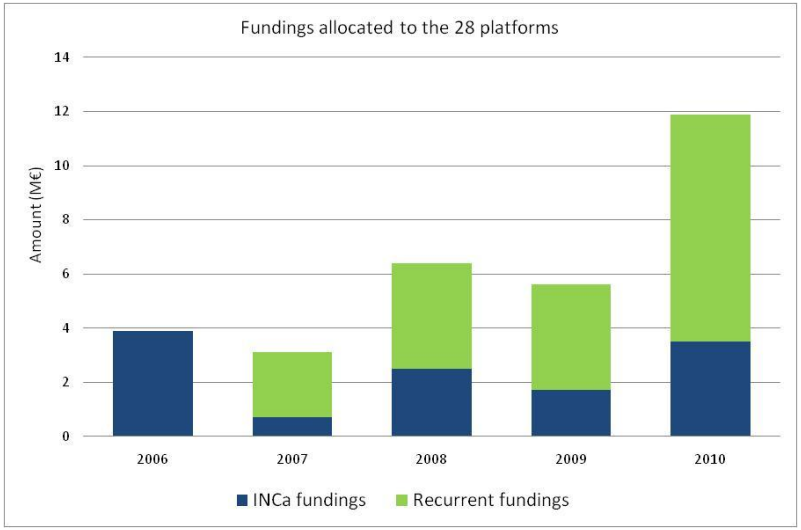
- **31 new drugs** in oncology got a first market approval in Europe.
- adapted to **49 therapeutic indications**
- Almost **half** of those new drugs are **targeted therapies**.

→ Impact on the **physician's practice** and on the healthcare's setting.

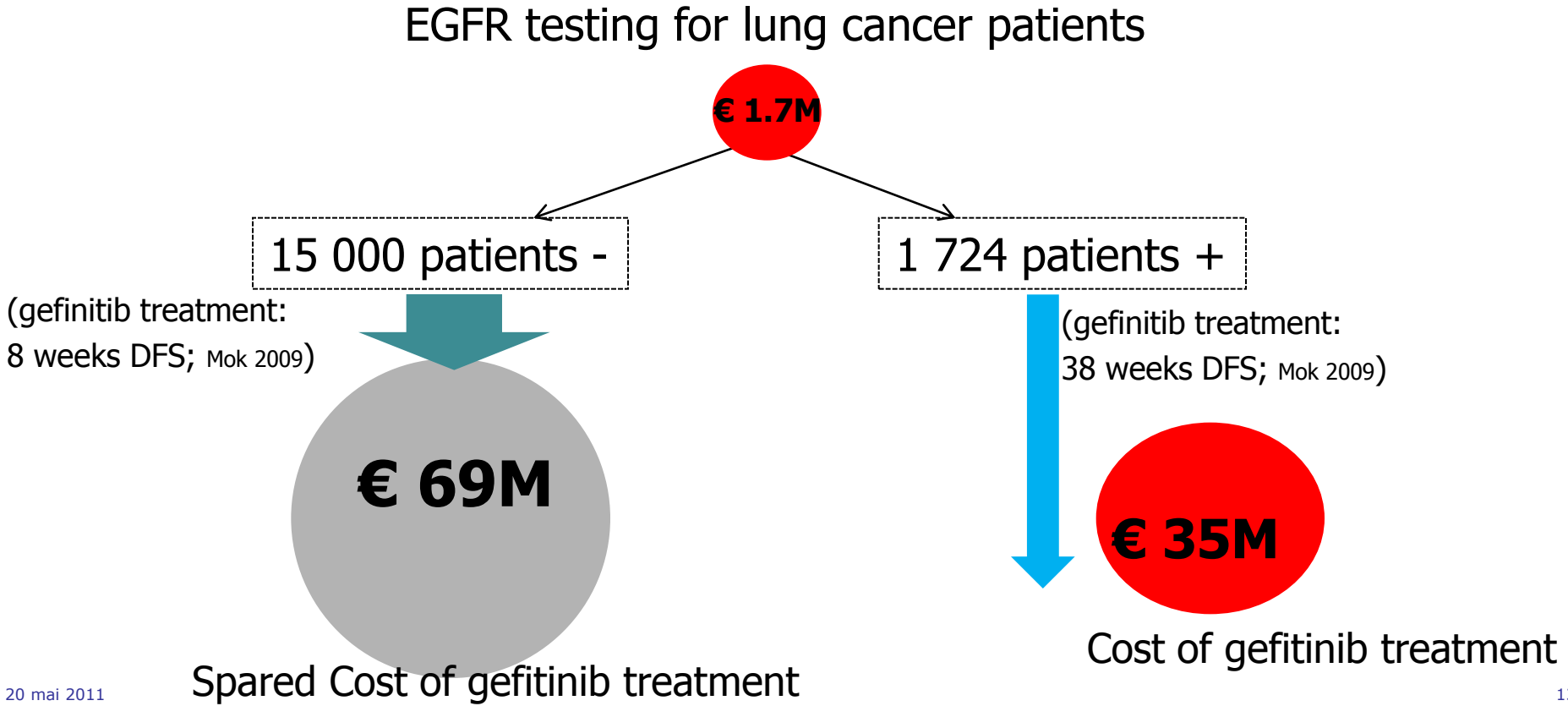
→ Need to have **access to molecular testing** for each patient in order to get a personalized medicine.

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



Example of gefitinib treatment : €69M spared cost for the health insurance



Some pending issues on targeted therapies

- **Is increased survival a legitimate end point?**

- Does tumor based molecular stratification exclude patients who could benefit from treatment?

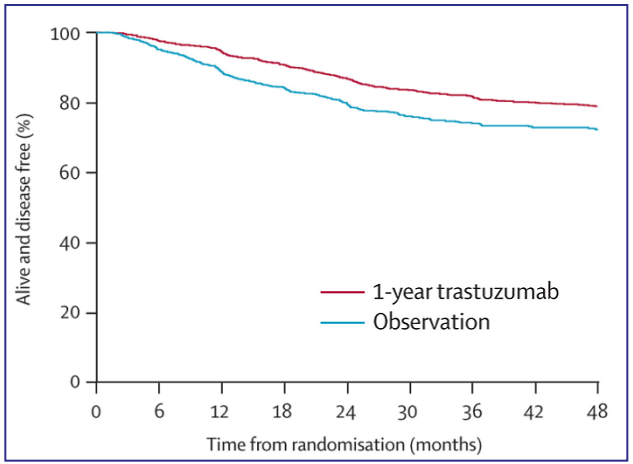
Is increased survival a legitimate end point ?

Trastuzumab for HER2 overexpressing patients with breast cancer

Metastatic setting

Clinical trial	Line of treatment	Type of administration	Median progression free survival (months)
H0649g	Second line and further	Monotherapy	3,2
H0648g	First line	Combination with chemotherapy	7,1
M77001	First line	Combination with chemotherapy	10,6

Adjuvant setting



4-year disease-free survival : 78·6% for 1-year trastuzumab *vs* 72·2% for the observation group.

(Gianni Lancet Oncol. 2011)

Some pending issues on targeted therapies

- Is increased survival a legitimate end point?

- **Does tumor based molecular stratification exclude patients who could benefit from treatment?**

Implementation of a quality assurance programme

2 types of action :

- Elaboration of guidelines for the detection of mutations in solid tumors before targeted therapies prescription :

- Implementation in 2011 of a national External Quality Assessment for the 28 platforms (BCR-ABL, KRAS, EGFR)

⇒ Harmonization of practices between platforms

⇒ Assurance quality optimization

Challenges ahead

- **Maintain the quality of molecular tests**
- **Anticipate the launch of new molecules** : reduction of time-to-access to molecule (In 2011, the INCa allocates €3.5M for the prospective detection of emergent biomarkers in lung cancer, colorectal cancer and melanoma).
- **Improve basic/clinical research interfaces** : Basic science to better understanding of mutations/variations/metabolic impact/redundancy of pathways and fostering translational research
- **Public/private partnerships** to optimize the implementation of new tests and sustain innovation.

Conclusions and perspectives

- **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 platforms are key to help develop translationnal research and to sustain progress**
- **They are instrumental to facilitate access to the best care and improve patient's survival and quality of life**
- **Training of medical students and professionals to personalised medicine**

acknowledgements

- 28 pathologists and molecular biologists who run these platforms and their collaborators
- INCa departments of Health Care and Research – special thanks to Fréderique Nowak in charge of this program, Valerie Thibaudeau and Christine Berling
- Our previous president, Dominique Maraninchi
- The patients to whom this national contribution is dedicated

Prof Fabien CALVO – Deputy General Director
fcalvo@institutcancer.fr

Tel. +33 (0) 1 41 10 50 00 ● Fax +33 (0) 1 41 10 50 20
52, avenue André Morizet
92513 Boulogne-Billancourt Cedex France
www.e-cancer.fr

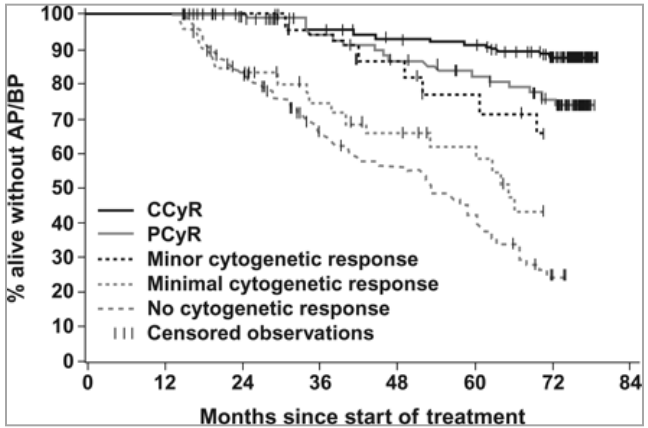
Economical impact of molecular testing

Cancer	Drug	Biomarker	% patients with mutation	Nb of tested patients	Number of spared prescriptions	Median PFS for non responders	Cost of treatment/ patient	Spared cost	Public fundings allocated for the provision of the test
lung cancer	gefitinib	EGFR mut	10,3%	16722	15000	8 weeks	4 600 €	€69 M	€1.7 M
	erlotinib				15000	8 weeks	4 600 €		
colorectal cancer	cetuximab	KRAS mut	36%	17250	6 210	8 months	32 419 €	€ 201 M	€2.5 M
						8 weeks	9 263 €	€57 M	
	Panitu-mumab					4 weeks	4 390 €	€27 M	

1- Is increased survival a legitimate end point ?

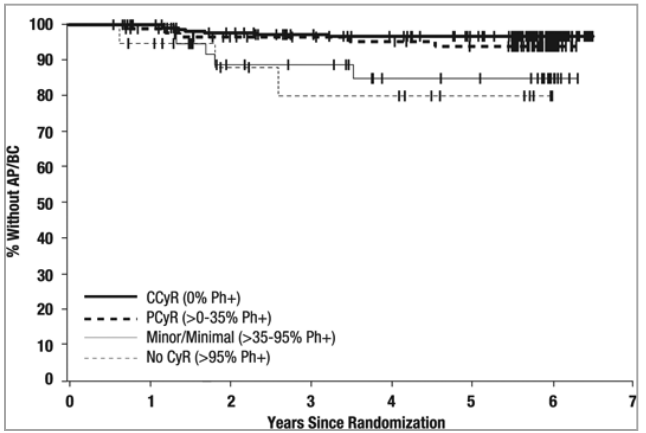
Imatinib for patients with CML (BCR-ABL translocation)

After failure of interferon -α treatment



6 year-survival rate = 76% (Hochhaus, Blood 2008)

Fist line treatment



6 year-survival rate = 88% (Hochhaus, Leukemia 2009)

CML patients taking Imatinib and in remission after two years of treatment have similar mortality rates to people in general population (Gambacorti-Passerini C, JNCI 2011)