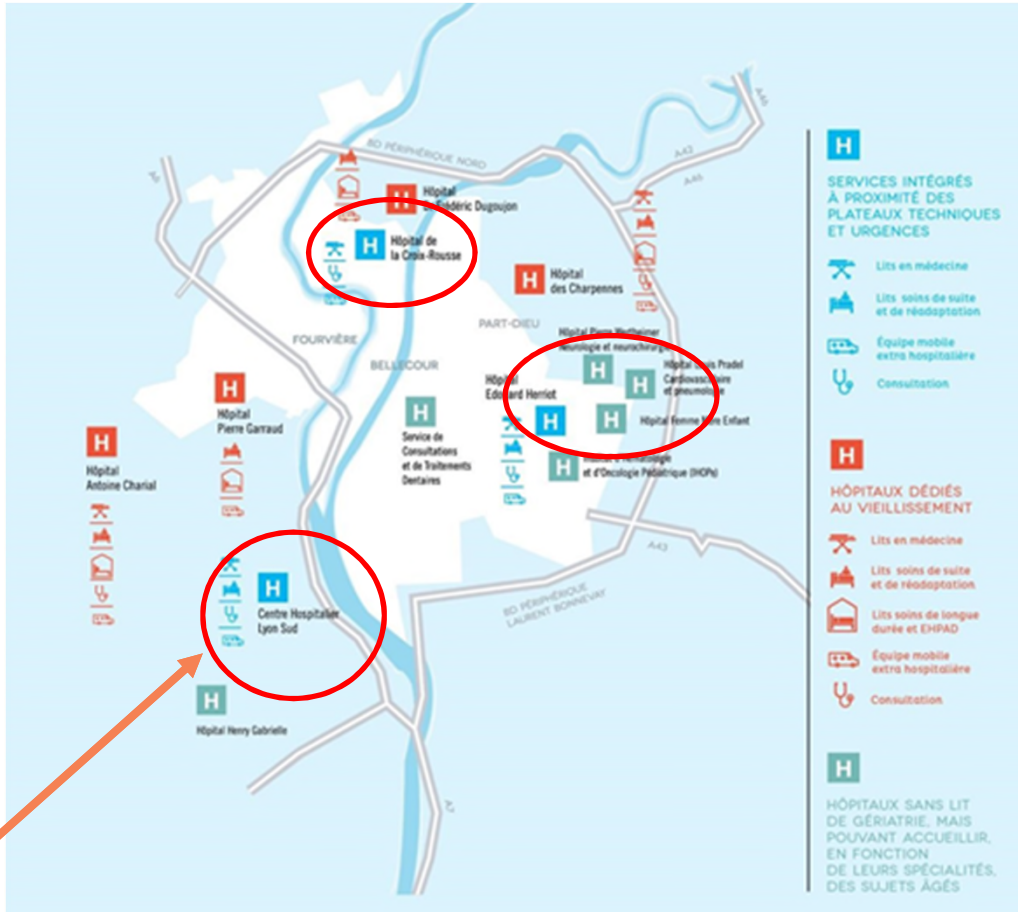
Hospices Civils de Lyon

INSTITUT DE
CANCÉROLOGIE

A COMPREHENSIVE CANCER CENTRE NETWORK BASED ON A UNIVERSITY HOSPITAL

Lyon University Hospital Cancer Institute : its missions at the origin - 2014

- Build a cancer care and research network
  - 15 000 patients a year
  - 250 physicians and biologists involved in oncology
  - 3 geographic sites (North, South, East)
  - 25 % of the hospital revenue per year



THE MAIN SITE :
LYON SUD HOSPITAL
2/3 of the overall activity
Medical Oncology, Radiotherapy, Hematology, Palliative Care departments

Lyon University Hospital Cancer Institute : its missions at the origin - 2014

- Improve patient's care process and care trajectories
- Face the demographic and scientific challenges of the coming years
- Promote patient's access to diagnosis and treatment innovations
- Contribute to the cancer care implementation at the territory level (the Auvergne-Rhône-Alpes Area)

STRENGTH AND WEAKNESSES

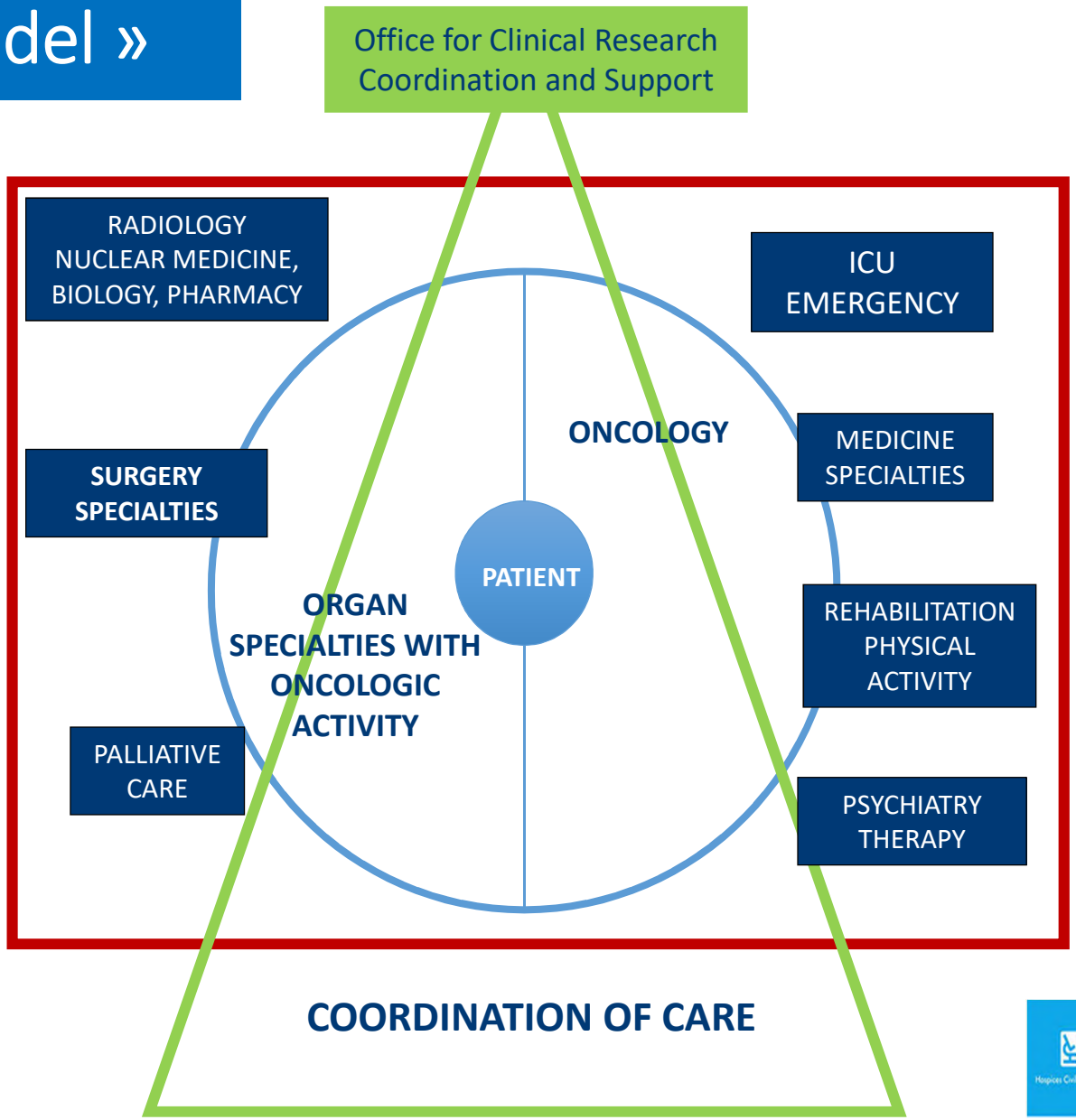
The Comprehensive Cancer Centre

The University Hospital

HOW TO ACHIEVE OUR GOALS ?

- Common wealth and project
  - Oncologists versus organ specialists
  - Rivalry between sites, schools, chapels…
  - « Our competitors are outside »… But emulation doesn't mean war !
- Efficient collaboration with administration and governance
  - Promoting the unique « voice of oncology »
- Creation of an original and integrative model of cancer care

The IC-HCL « Model »



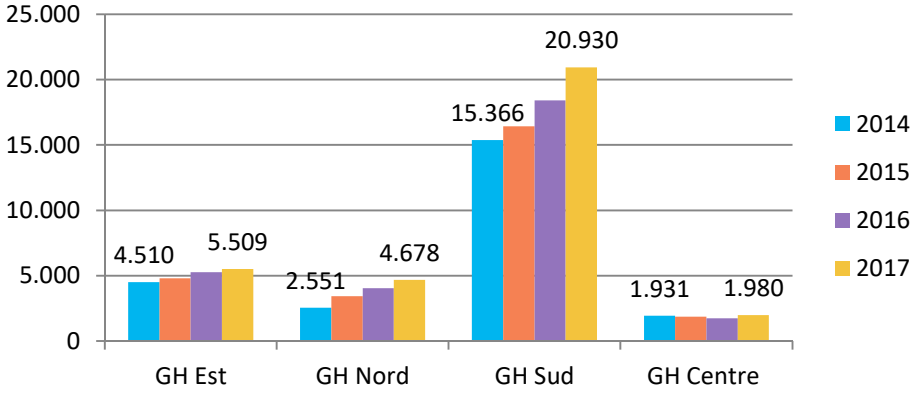
Building of « shared platforms » of ambulatory care in oncology

North Site
20 beds
Gyne oncol
Thoracic oncol
Head & Neck
Dig oncol

South Site
Med Oncol Dept
20 ambulatory beds
22 hospitalisation beds

East Site
20 beds
Gyne oncol
Thoracic oncol
Neuro-Oncol

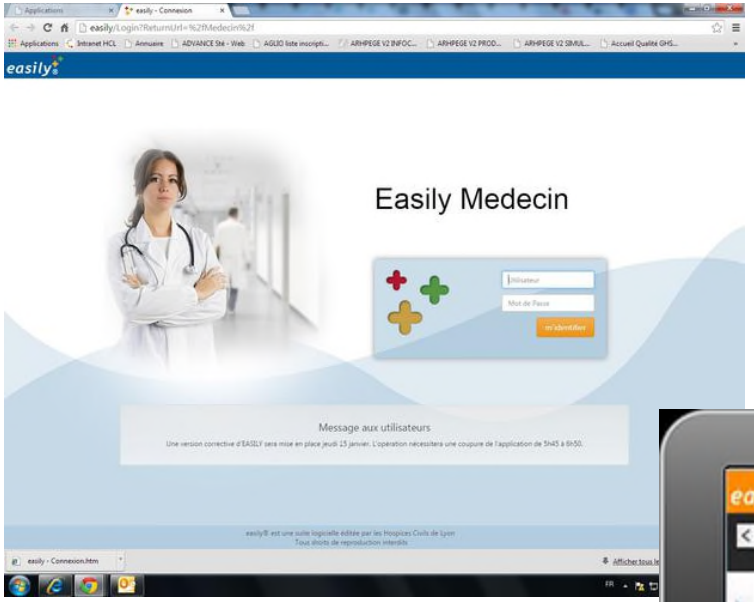
- Increase of overall activity
- Optimisation of resources
- Quality improvement
- Better access to supportive care
- Coordination by oncologists



ASSESSING DELAYS IN PATIENTS CARE

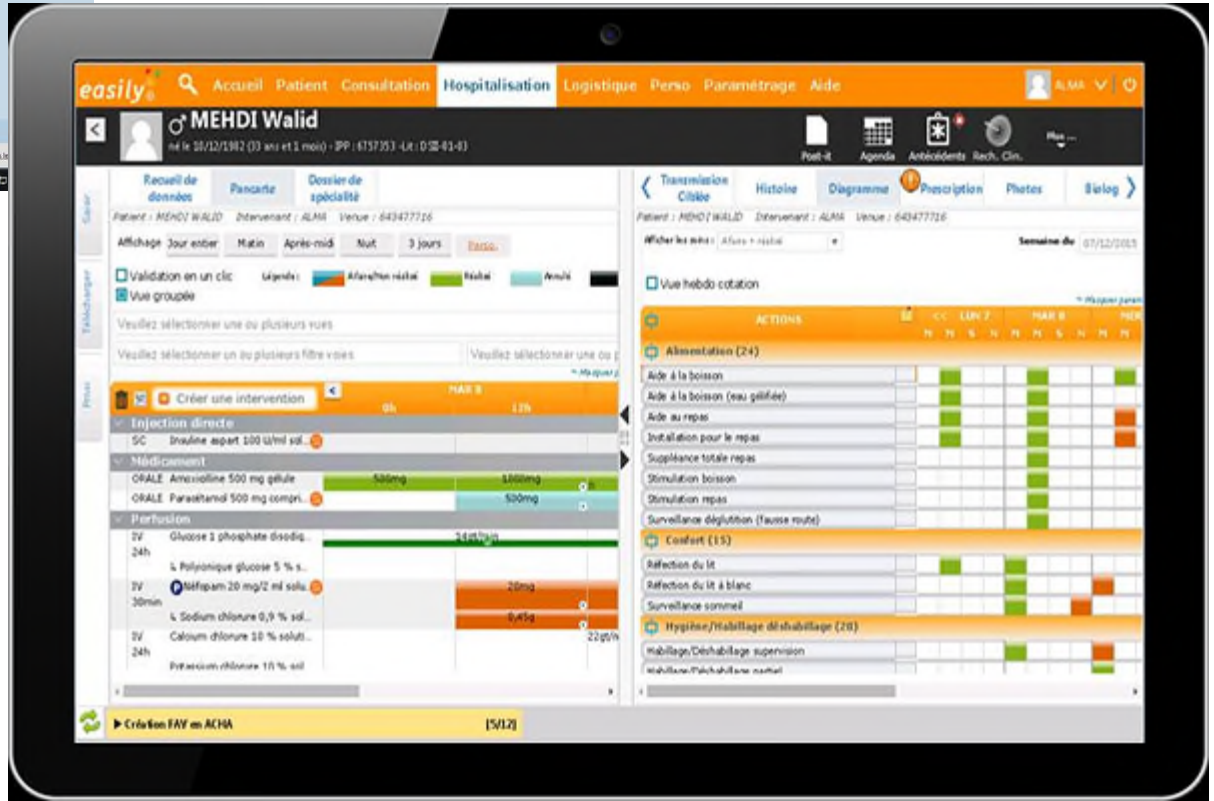
- Example of breast cancer patients
- Internal audit
- Delay between diagnosis and surgery
- Delay between surgery and adjuvant chemo
  - Considered non optimal if > 45 days
  - 2 months in the literature (LoE C)
  - Corrective measures
  - Automatic generation of data from the information system

An integrated tool for cancer patients



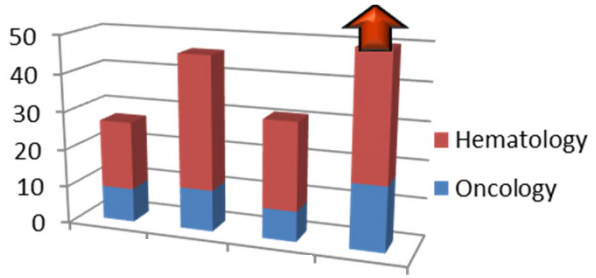
The IC-HCL Cancer Register Database

- **Based on the Easily Software**
- **Follow-up data : treatments, survival**

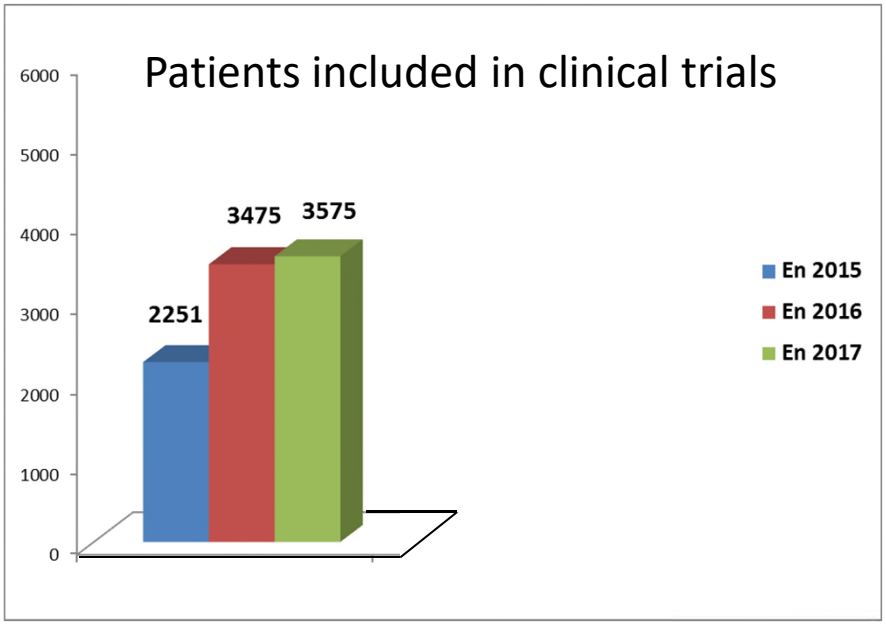


SOME ACTIONS

- Homogeneity in patients trajectory : radiotherapy, onco-urology
- Hotline dedicated to professionals
- Office for clinical research support :
  - Funding support : 5 M€
  - Coordination between sites
    - Investigators
    - Pharmacy
  - Medical writing : clinical trials protocols



Phase 1 trials



MOLECULAR BIOLOGY : activity in 2015

Lung *EGFR, KRAS, HER2, ALK, ROS1*
1165

Melanoma
BRAF Kit NRAS
285

CML
BCR-ABL
1466

CLL
76

Breast
Gastric
HER2
710

Glioma
Glioblastoma
444

CML/ALL
93

MPS non CML
989

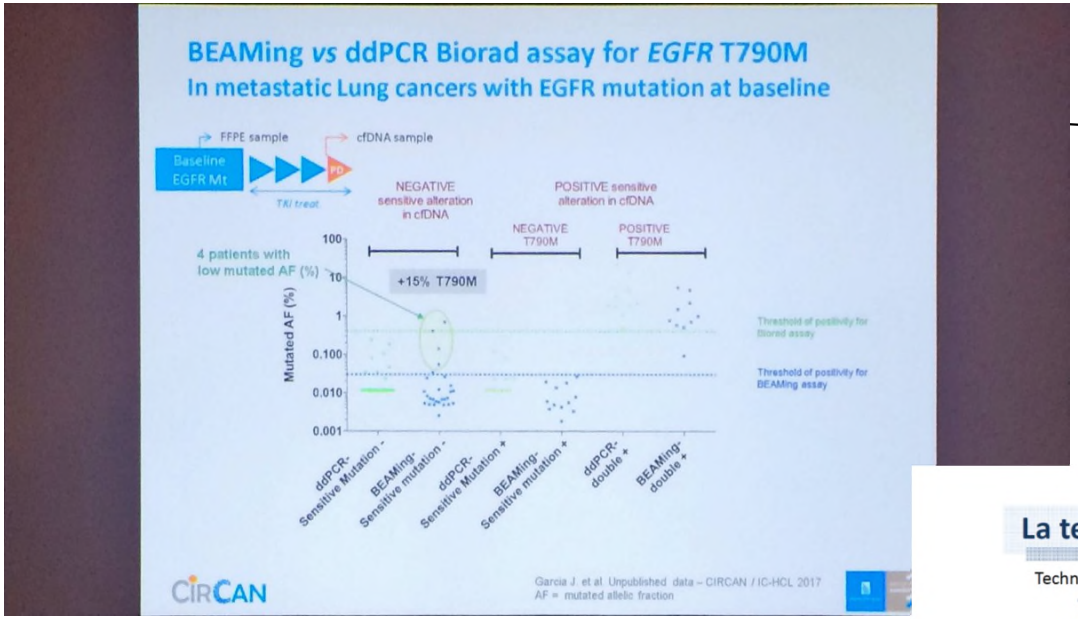
Colorectal
RAS, BRAF, MSI
1134

Lymphoma
B&T Clonality
501

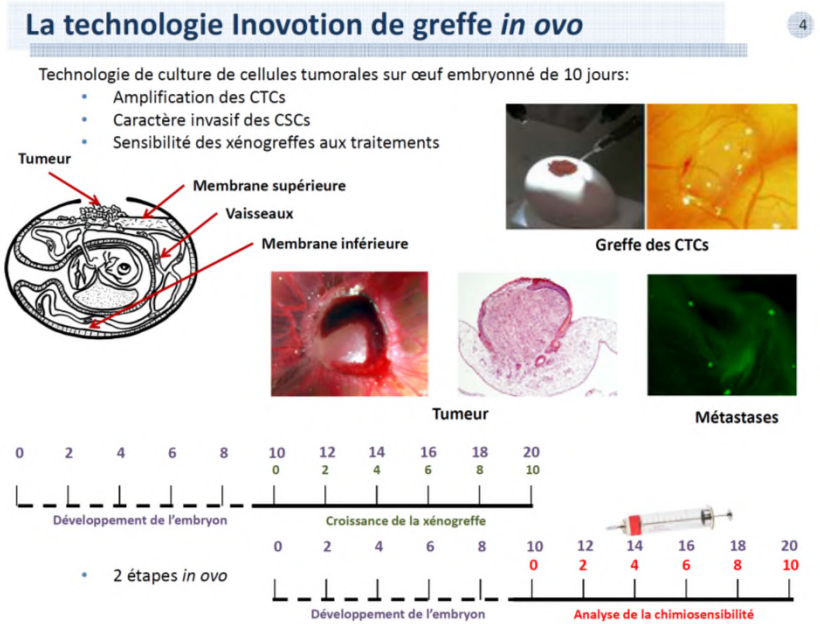
ALL/AML
1676

MDS
245

MOLECULAR BIOLOGY : ORIGINAL PROJECTS



CIRCAN : liquid biopsy in various tumor types



SENCIRTEG : CTC implanted in chicken embryo

MOLECULAR BIOLOGY : FROM CANCER SUSCEPTIBILITY TO TARGETED THERAPY IN BREAST / OVARIAN CANCER

COMPREHENSIVE CANCER CENTRE

Centre Léon Bérard
LYON ET RHÔNE-ALPES

Common Platform Genetic Counselling gBRCA

UNIVERSITY HOSPITAL (EAST)

UNIVERSITY HOSPITAL (SOUTH)

sBRCA ?

ORIGINAL PROGRAMS

- ONCORAL : oral anticancer treatments
- IMMUCARE : immunotherapy side-effects

« Networks inside the Network »

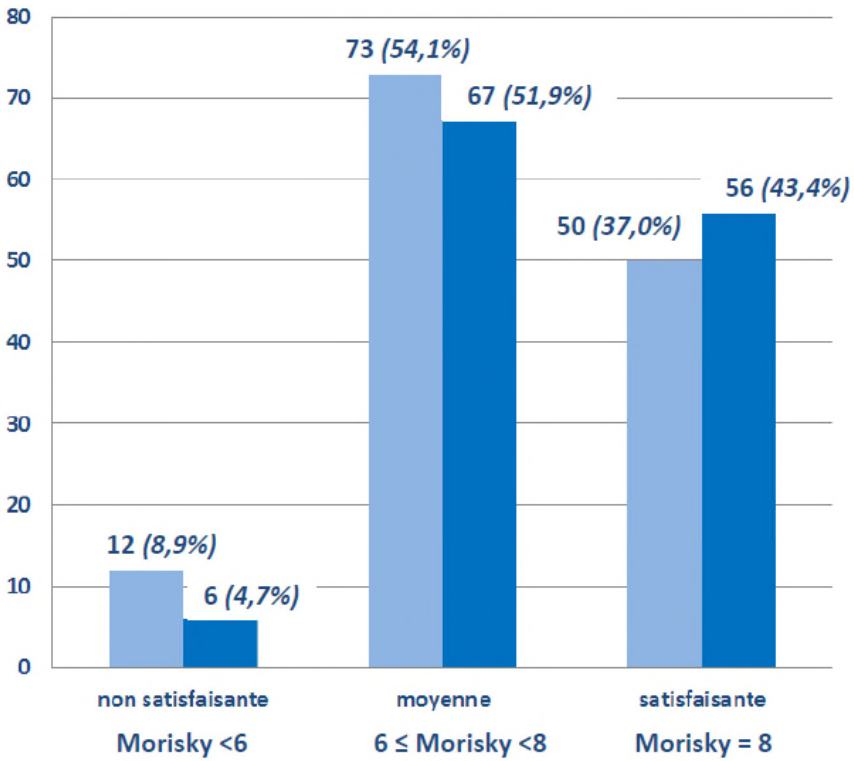
Promoting patient's adherence to oral therapy, home-hospital link and therapeutic education : the Oncoral Project

FOLLOW-UP

Treatment schedule
Adherence
Side - effects
Interactions

Information of the pharmacist

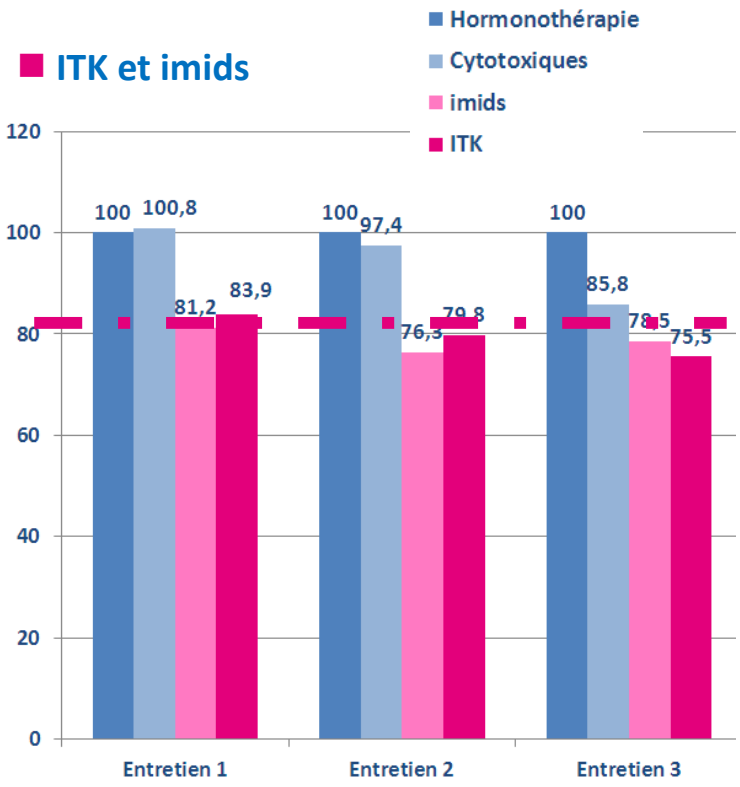
ASSESSMENT OF ADHERENCE IN THE ONCORAL PROGRAM

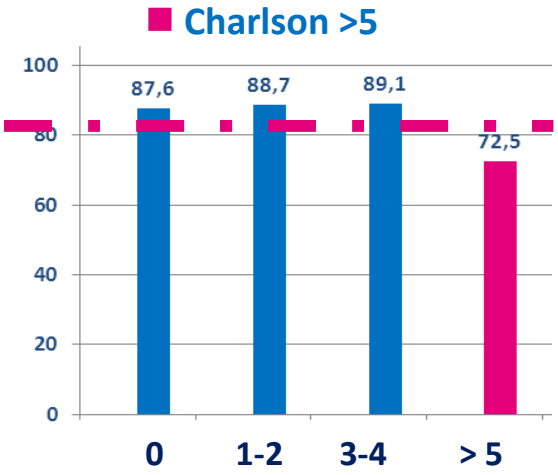


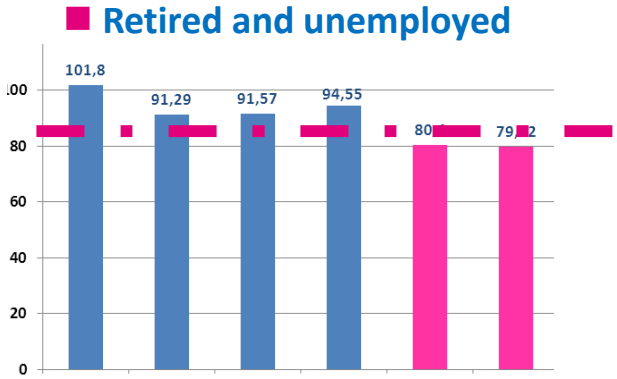
Bad Intermediate Good

3 sessions

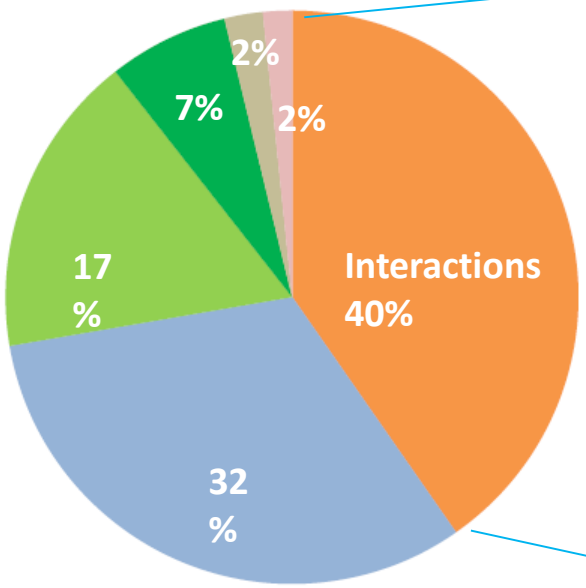
Mean Relative Dose - Intensity : 84,04%







PHARMACEUTICAL INTERVENTIONS



- interactions
- Treatment schedule
- home-hospital link
- Green light for treatment
- Comedications
- posology

1/4
not recommended or contra-indicated

1/ 3
⇘ efficacy

1/3
⇗ toxicity

Drugs at risk
anticoagulants – anti-acids

794 interventions
Acceptation rate : 90%

Hospices Civils de Lyon

INSTITUT DE CANCÉROLOGIE

IMMU CARE

IMMUCARE

A network for patients and physicians : early diagnosis and treatment of immunotherapy side-effects

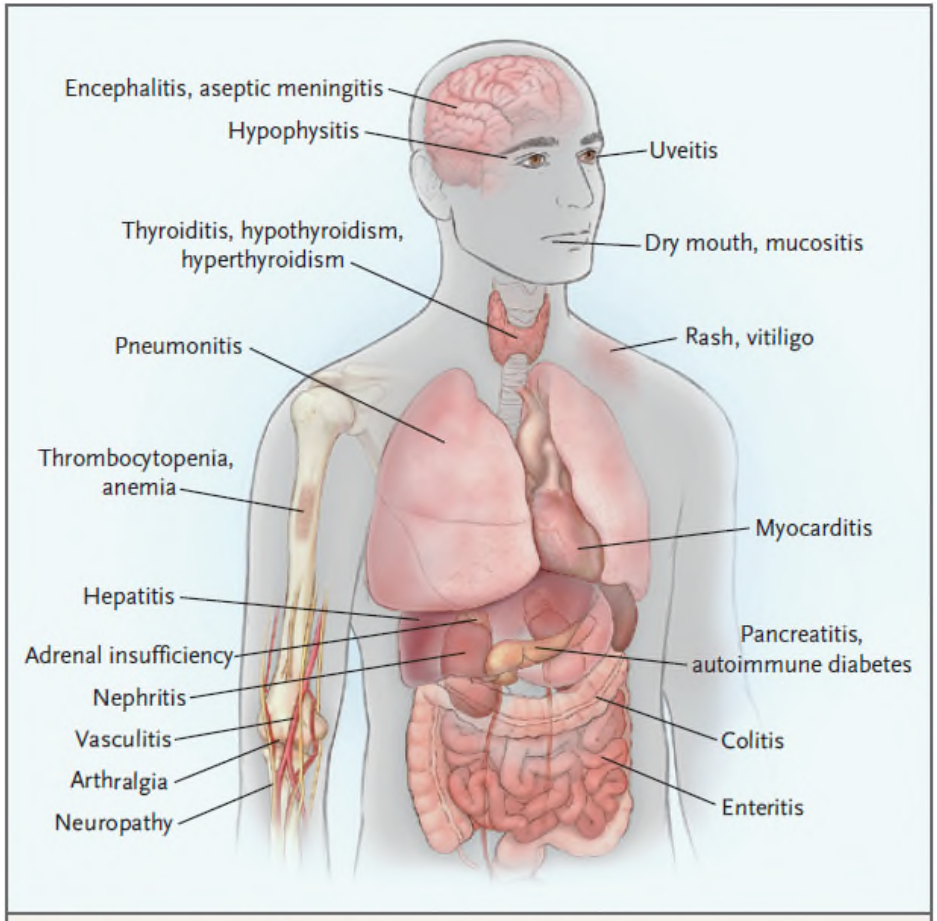
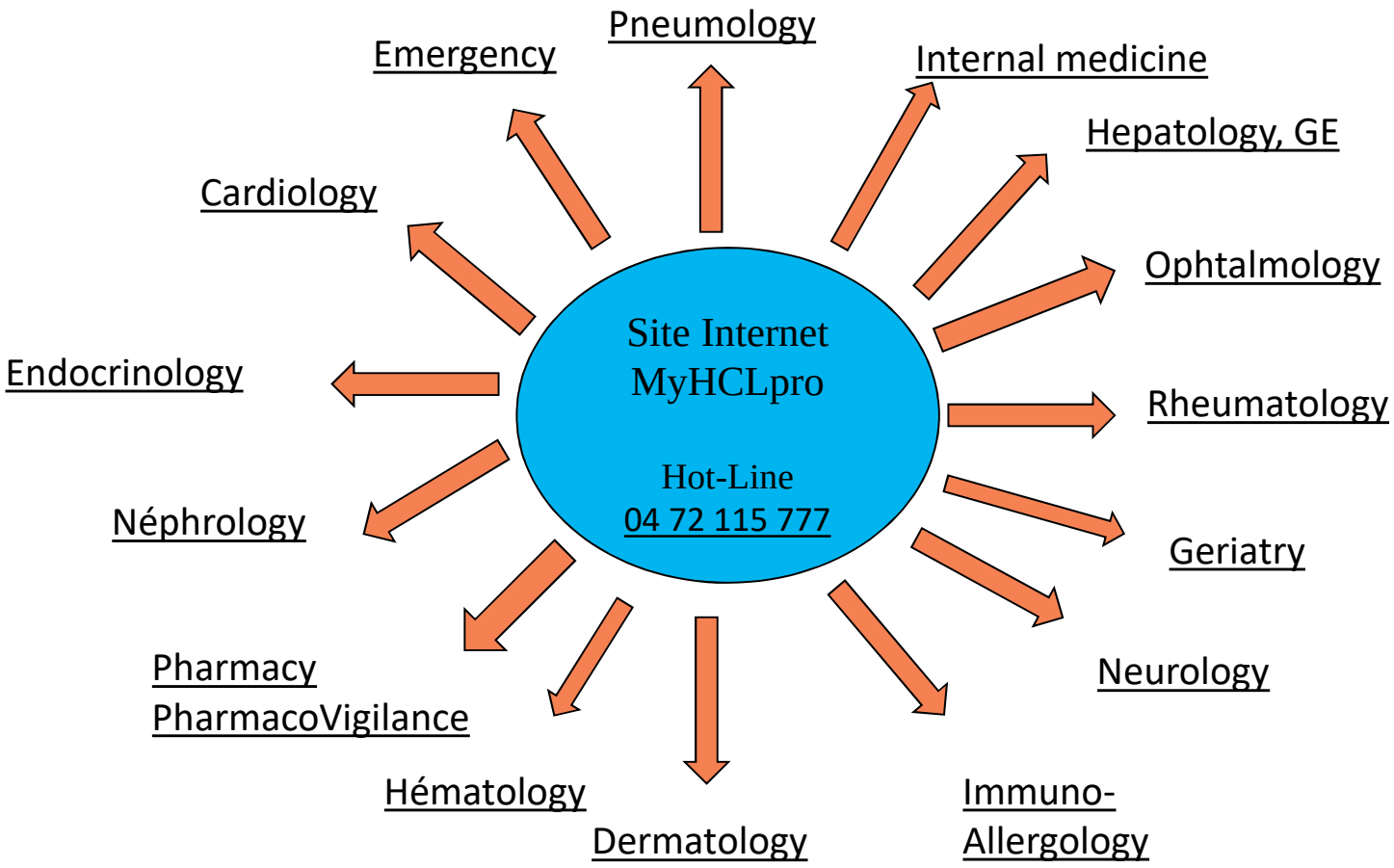


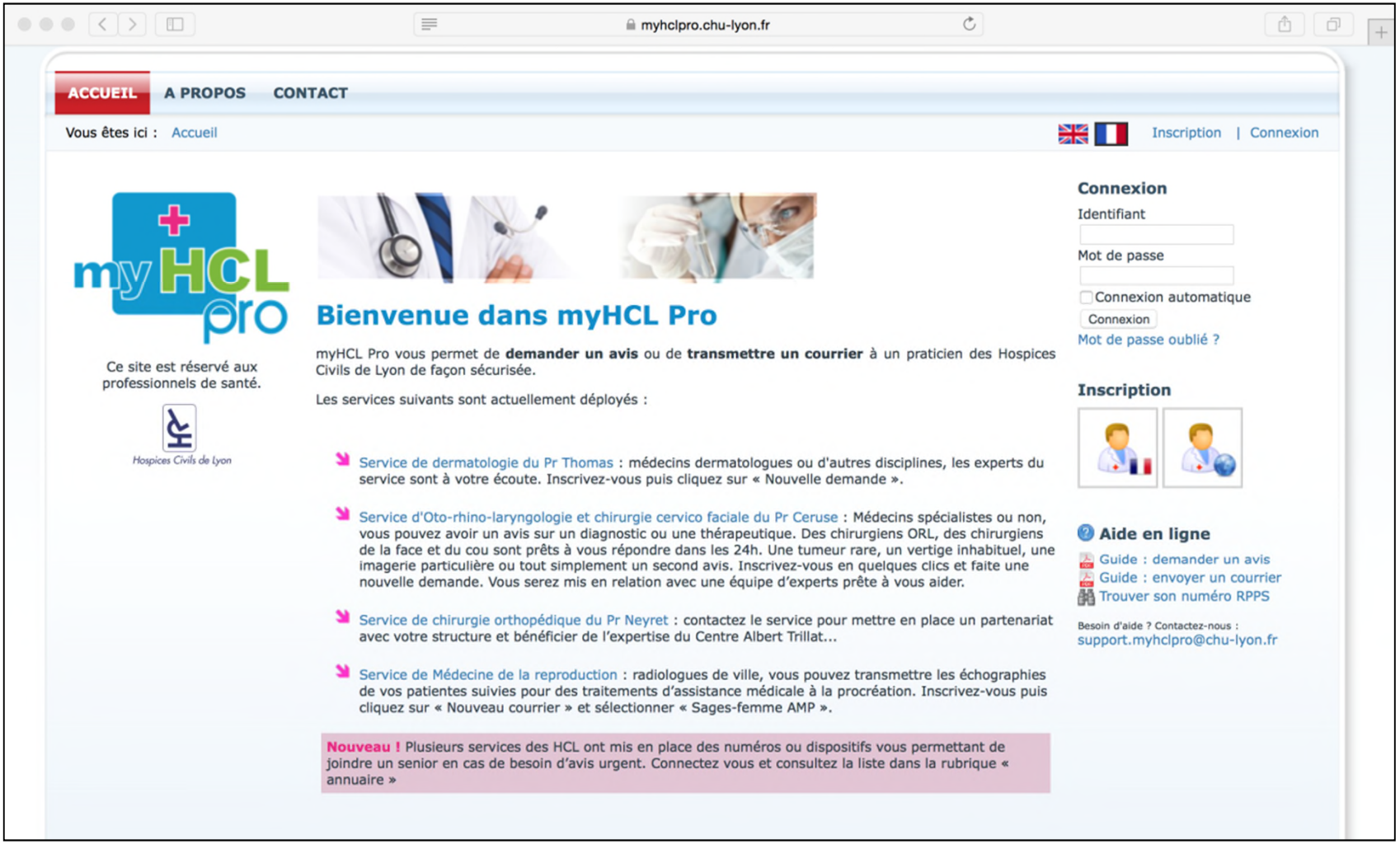
Figure 1. Organs Affected by Immune Checkpoint Blockade.
Immune checkpoint blockade can result in inflammation of any organ. Shown are the most common immune-related adverse events that clinicians encounter in patients treated with immune checkpoint blockade.

N ENGL J MED 378;2 NEJM.ORG JANUARY 11, 2018

Grades 3/4: 10% à plus de 50% associations

A network of experts (> 1000 patients treated)





A website dedicated to professionals and patients

ImmuCare self monitoring

Publications

Bottlaender et al. Journal for Immuno Therapy of Cancer (2017) 5:57
DOI 10.1186/s40425-017-0261-2

Journal for ImmunoTherapy of Cancer

CASE REPORT — Open Access

Acute interstitial nephritis after sequential ipilumumab - nivolumab therapy of metastatic melanoma

Lea Bottlaender[1,2], Anne-Laure Breton[1,2,3*], Louis de Laforcade[2,4], Frederique Dijoud[2,5], Luc Thomas[1,2,3] and Stephane Dalle[1,2,3]

Abstract

Background: The anti-Programmed Death receptor 1 (anti-PD-1) antibodies nivolumab and pembrolizumab are new treatments in metastatic melanoma. Immunotherapies are best known to be responsible for thrombotic microangiopathy. However, immune interstitial nephritis has been described in a patient treated by nivolumab and ipilimumab concomitantly, and three cases of granulomatous interstitial nephritis have been reported with ipilimumab monotherapy. We report herein a case of acute interstitial immune nephritis in a patient treated with nivolumab after ipilimumab for pulmonary metastatic melanoma.

Case presentation: Interstitial nephritis was diagnosed after acute kidney injury following three cycles and was confirmed by kidney biopsy. Kidney injury responded rapidly to prednisolone, which was then gradually reduced. As a follow-up computed tomography scan indicated mixed response, with minimal size progression of a pulmonary nodule, but a significant reduction in the size of the other nodules, nivolumab was reintroduced after renal function improvement. Low-dose corticosteroids were first maintained during nivolumab treatment and subsequently discontinued. Only one month after prednisolone discontinuation, creatinine levels increased. A second kidney biopsy confirmed relapse of acute interstitial nephritis.

Conclusions: To our knowledge, this is the first case of nivolumab-induced acute interstitial immune nephritis. This case highlights that anti-PD-1 immunotherapy may be continued when renal function is adequate, and this requires close interaction between dermatologists and nephrologists. This adverse effect should be made known to prescribers as nivolumab is associated with significant improvement of survival in metastatic melanoma and may be used in many different types of cancer.

Keywords: Pd-1, Melanoma, Acute kidney injury, Acute interstitial immune nephritis, Immunotherapy

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Immune-checkpoint inhibitors associated with interstitial lung disease in cancer patients

Myriam Delaunay[1], Jacques Cadranel[2], Amélie Lusque[3], Nicolas Meyer[4], Valérie Gounaut[5], Denis Moro-Sibilot[6], Jean-Marie Michot[7], Judith Raimbourg[8], Nicolas Girard[9], Florian Guisier[10], David Planchard[11], Anne-Cécile Metivier[12], Pascale Tomasini[13], Eric Dansin[14], Maurice Pérol[15], Marion Campana[16], Oliver Gautschi[17], Martin Früh[18], Jean-David Fumet[19], Clarisse Audigier-Valette[20], Sébastien Couraud[21], Stéphane Dalle[22], Marie-Thérèse Leccia[23], Marion Jaffro[24], Samia Collot[24], Grégoire Prévot[1], Julie Milia[1] and Julien Mazieres[1]

@ERSpublications
Awareness of clinical/radiological presentation of immunotherapy-related pneumonitis is crucial to ensure a diagnosis http://ow.ly/eIMF30bgolf

Cite this article as: Delaunay M, Cadranel J, Lusque A, *et al.* Immune-checkpoint inhibitors associated with interstitial lung disease in cancer patients. *Eur Respir J* 2017; 50: 1700050 [https://doi.org/10.1183/13993003.00050-2017].

ABSTRACT Immunotherapy is becoming a standard of care for many cancers. Immune-checkpoint inhibitors (ICI) can generate immune-related adverse events. Interstitial lung disease (ILD) has been identified as a rare but potentially severe event.

Between December 2015 and April 2016, we conducted a retrospective study in centres experienced in ICI use. We report the main features of ICI–ILD with a focus on clinical presentation, radiological patterns and therapeutic strategies.

We identified 64 (3.5%) out of 1826 cancer patients with ICI–ILD. Patients mainly received programmed cell death-1 inhibitors. ILD usually occurred in males, and former or current smokers, with a median age of 59 years. We observed 65.6% grade 2/3 severity, 9.4% grade 4 severity and 9.4% fatal ILD. The median (range) time from initiation of immunotherapy to ILD was 2.3 (0.2–27.4) months. Onset tended to occur earlier in lung cancer *versus* melanoma: median 2.1 and 5.2 months, respectively ($p=0.02$). Ground-glass opacities (81.3%) were the predominant lesions, followed by consolidations (53.1%). Organising pneumonia (23.4%) and hypersensitivity pneumonitis (15.6%) were the most common patterns. Overall survival at 6 months was 58.1% (95% CI 37.7–73.8%).

ICI–ILD often occurs early and displays suggestive radiological features. As there is no clearly identified risk factor, oncologists need to diagnose and adequately treat this adverse event.

This article has supplementary material available from erj.ersjournals.com

Received: Jan 10 2017 | Accepted after revision: April 20 2017

Conflict of interest: Disclosures can be found alongside this article at erj.ersjournals.com

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THERE IS A LONG WAY HOWEVER…

- Various collaborations with the CCC, a common vision of cancer care, but policies are not common (is it desirable ?)
- A lack of visibility : some self-inhibition
- No proper budget or employees : benevolance and precarity
- The « glass ceiling » : those who decide are not experts, the experts cannot decide
  - The French technocratic/bureaucratic approach
  - Too many strata of governance

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THANK YOU FOR YOUR ATTENTION