RIC-MEL:
Network for Research and Clinical Investigation on Melanoma

OVERVIEW

AT A GLANCE

> Onco-dermatology: Melanoma
> All patients with melanoma
> Coordinated by Prof. B. DRENO and Prof. C. LEBBE
> Nantes University Hospital sponsorship
> Funded by CeNGEPS and industrial partners
> Key words: Cancer - Melanoma - Database - Epidemiology - Translational research - Clinical trials

KEY FACTS & FIGURES

> Status: on-going, inclusion started in March 2012
> No completion date is defined
> Around 2,000 enrolled expected patients per year
> 14,316 patients included on December 17th, 2015
> Follow-up from inclusion until death
> National multcentric cohort:
41 General Hospitals, 6 centers de lutte contre le cancer (Cancer Centers) and 1 Hôpital d’Instruction des Armées (Army Hospital)

Aims of the RIC-Mel network are to promote translational research, to optimize the achievements of clinical trials and to support basic research. Aim of the RIC-Mel database is to give a permanently updated mapping of melanoma treated in France with the key information needed for any research projects.

Positioning

The RIC-Mel database is linked to the clinico-biologicoc-radiological database MELBASE dedicated to metastatic melanoma stage IV and unresectable stage III (setting-up by Saint-Louis hospital, Paris. Coordinated by Prof. C. LEBBE and Prof. B. DRENO)

> To date, the RIC-Mel cohort is the only one in France to take the census of the active file of melanoma patients
> Currently, four partnerships with pharmaceutical companies are on-going
> The RIC-Mel database aims to be opened to academic and new industrial patnerships
RIC-Mel’s leadership team brings together renown clinicians and researchers who have been committed in the field of melanoma since 25 years.

**Prof. Brigitte DRENO, Dermatology – Coordinator**
Chairman of the Department of Dermatology at Nantes hospital

- Research areas with significant contribution:
  - Skin cancers: Melanoma (immunotherapy), Basal cell carcinoma, Cutaneous lymphoma
  - Dermatological disorders: Actinic keratosis, Acne and related disorders, Dermocosmetics

- Expertise:
  - Expert for national and European Agencies: European Medicines Agency (EMEA), French National Agency for Medicines and Health Products Safety (ANSM), French National Cancer Institute (INCa), Evaluation Agency for Research and Higher education (AERES)

- Memberships:
  - National: French Society of Dermatology (SFD), French College of Teachers in Dermatology
  - International: European Society of Dermatology (EADV), European Society for Dermatological Research (ESDR), European Academy of Dermatological Oncology (EADO), International Society for Cutaneous Lymphoma (ISCL), Foreign member of the Canadian Society of Dermatology, Member of the Skin Cancer Foundation, Treasurer of the International League of National Dermatology (ILDS)

- International Editorial Board:
  - 2015: Journal of the European Academy of Dermatology and Venereology
  - 2009: International Journal of Clinical Dermatology and International Immunotherapy
  - 2006: European Journal of Cancer Prevention

**Prof. Célèste LEBBE, Dermatology – Coordinator**
Head of the Skin Cancer Unit in the Department of Dermatology at Saint-Louis Hospital (Paris)

- Coordination of clinical research on melanoma in Saint-Louis Hospital, Paris

- Coordination of a platform of melanoma experimental models in Inserm unit U976

- Board member:
  - French Society of Dermatology (SFD)
  - European Society for Dermatological Research (ESDR)
  - European Academy of Dermatological Oncology (EADO) (on board)
  - EORTC
  - SCOPE

- Coordination of 1 other network in melanoma:
  - National network: MELBASE, dedicated to metastatic melanoma stage IV and unresectable stage III

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**SCIENTIFIC NETWORK & MANAGEMENT**

The RIC-Mel constitutes the **French national database of the Skin Cancerology Group** (GCC)

The RIC-Mel database is **interconnected with MELBASE** (clinico-biologico-radiological database dedicated to metastatic melanoma stage IV and unresectable stage III, setup-up by Saint-Louis Hospital, Paris. Coordinated by Prof. C. LEBBE and Prof. B. DRENO)

The RIC-Mel governance is **organized on the basis of two instances**:

**Steering Committee:** deciding authority
- Prof. Brigitte DRENO, CHU de Nantes
- Dr Célèste LEBBE, Saint Louis Hospital (AP-HP)
- Dr Didier CUPISSOL, CLCC Val d’Aurelle Paul Lamarque, Montpellier
- Dr Bernard GUILLOT, CHRU de Montpellier
- Dr Lionel LARUE, CNRS UMR 3347 / Inserm U1021
- Prof. Marie-Thérèse LECCIA, CHU de Grenoble
- Dr Florence VRIGNAUD, CIC Biothérapies, CHU de Nantes

**Scientific Council:** evaluation of scientific projects
- Dr Florence GRANEL-BROCARD, CHU de Nancy
- Dr Idalie JENNESSEAX, Groupement Hospitalier du Havre
- Prof. Catherine LOK, CHU d’Amiens
- Dr Caroline ROBERT, Institut de Cancérologie Gustave Roussy
- Prof. Philippe MODIANO, Groupement des Hôpitaux de l’Institut Catholique de Lille
- Prof. Florent GRANGE, CHU de Reims
- Dr Thomas JOUARY, CH de Pau
- Dr Nicolas MEYER, CHU de Toulouse
- Prof. Luc THOMAS, Hospices Civils de Lyon
PROJECT DESCRIPTION

SCIENTIFIC OBJECTIVES

Main objectives
> To promote phase I/II clinical trials in the field of melanoma in France
> To give a permanently updated mapping of melanoma treated in France with the key information needed for any research projects

Secondary objectives
> To promote translational research, to optimize the achievements of clinical trials and to support basic research
> To federate clinical centers of dermatology and oncology as well as network related to melanoma around a common database
> To be a privileged interlocutor for industrial partners

Ultimate goal
> To be an interlocutor of quality for national and European authorities as well as industrial partners in order to ensure an international legibility to any French research on melanoma

INNOVATIVE SCIENTIFIC FEATURES

RIC-Mel is unique as a national database regarding all melanoma patients
RIC-Mel is recognized and validated by the French Society of Dermatology (SFD), the Skin Cancerology Group (GCC) and the health authorities as the single point of entry when requesting the access of data upon melanoma patients for translational/clinical research projects

METHODOLOGY QUALITY

The updated database can be accessible by RIC-Mel at any given moment and each center has an exclusive access for its own data
All patients included in the database agreed to participate and data are treated confidentially
The database has been approved by French Health Authorities, both ethically (CCTIRS) and confidentially for data (CNIL)
Data related to biological samples are collected for patients who have signed a consent form specific to each participating center
Quality management system based on ISO 9001 standards (in progress)
Recruitment objectives: Around 2,000 enrolled expected patients per year

Sites: 48 participating centers: 41 General Hospitals, 6 centres de lutte contre le cancer (Cancer Centers) and 1 Hôpital d’Instruction des Armées (Army Hospital)

Inclusion criteria: All melanoma patients followed in participating centers and agreed to participated
Patients must be alive at the time of inclusion in the database

INCLUSION COLLECTION
Database:
Part I (mandatory): Identity, Primary tumor, AJCC stage, Mutations, Antigens, Treatments
Part II (optional): Family history of melanoma, Metastases, HLA type, Sample collection, Doses, Global response and Adverse events (grade 3 & 4) for Curative and Investigational treatments

FOLLOW-UP: ACCORDING TO DISEASE PROGRESSION
Database:
Part I (mandatory): AJCC Stage evolution, New treatment lines, Death…
Part II (optional): Metastases, Sample collection, Doses, Global response and Adverse events (grade 3 & 4) for Curative and Investigational treatments
### DATABASE

#### PART I - Mandatory

<table>
<thead>
<tr>
<th>Identity</th>
<th>Initials</th>
<th>Birth date</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumor</td>
<td>Date of surgery</td>
<td>Type of melanoma</td>
<td>Breslow</td>
</tr>
<tr>
<td></td>
<td>Sentinel lymph node surgery</td>
<td>Date</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lymph node removal</td>
<td>Number of invaded lymph node</td>
<td>Extracapsular extension</td>
</tr>
<tr>
<td>AJCC Stage at inclusion and evolution</td>
<td>Date of diagnosis</td>
<td>Details</td>
<td>For stage III only: if inoperable or not</td>
</tr>
<tr>
<td>Mutations</td>
<td>Type</td>
<td>Presence</td>
<td>Date</td>
</tr>
<tr>
<td>Antigens</td>
<td>Type</td>
<td>Presence</td>
<td>Date</td>
</tr>
<tr>
<td>Treatment</td>
<td>Type</td>
<td>Name</td>
<td>Nature (adjuvant/curative)</td>
</tr>
<tr>
<td>Death</td>
<td>Yes/No</td>
<td>Date</td>
<td></td>
</tr>
</tbody>
</table>

#### PART II - Optional

| Family history | Genetic investigation |
| Metastases | Type | Date of diagnosis | Presence |
| HLA type | A | B |
| Sample collection | Type (skin, blood, metastases...) | Storage condition | Date |
| | Comments | Storage location |
| Curative and investigational treatments | Dosage | Response |
| Adverse events (grade 3 and 4) | Type | Grade | Action on treatment | Other action | Outcome |

### ACCESS MODALITIES TO ANY REQUEST FOR DATA ANALYSIS

- Submission of a scientific project to the Scientific Council of the RIC-Mel network, containing the rational and the objective(s) of the study as well as a description of the data analysis.
- In case of the project is approved by the Scientific Council, a collaboration agreement is established with the Nantes Hospital, in respect of its coordinating center of the RIC-Mel network status.
- Extraction and results of the data analysis from the national active list of patients with melanoma are transmitted via as aggregated data file.
**RESEARCH COLLABORATION OPPORTUNITIES**

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**Translational research**

- Identification of biomarkers for the development of diagnostic or prognostic tests for melanoma cancers based on the correlation of biological and clinical data.

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**Clinical development**

- Optimization of clinical studies (timing, measures and scales, sub population characterization, design...)
- Support clinical enrollment
- Epidemiological studies to identify the melanoma patients population in France
- Epidemiological studies to support market access

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**Outcomes research**

- Pharmaco-epidemiological studies: drug safety, “real-world” use, effectiveness, practices patterns, acceptance, risk/benefit, risk management
- Pharmaco-economic cost/benefit studies; Health economic outcomes
- Comparative studies to assess product efficiency
- Post-marketing studies

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**BIBLIOGRAPHY & COMMUNICATIONS**

### Congress and events

- 45th annual ESDR meeting (09/2015)
- Journées dermatologiques de Paris (12/2014)
- 10th EADO Congress (05/2014)
- 7th Journées du Cancérolopôle Grand Ouest (04/2013)
- 6th Forum Scientifique de Pharmaco-épidémiologie (06/2013)
- 3rd Journée Intermédionale du GIRCI Grand Ouest (06/2013)

### Publications

- Review cases of discordant mutational statute
- Review cases of skin toxicities induced by vemurafenib:
  - L. Peuvrel et al., Profile of Vemurafenib-induced severe skin toxicities, Journal of the European Academy of Dermatology and Venereology [Epub ahead of print]
- Clinical data extractions for correlation with biological results:
  - A. Knol et al., Clinical significance of BRAF mutation status in circulating tumor DNA of metastatic melanoma patients at baseline, Experimental Dermatology [Submitted]