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Prof. Céleste LEBBE

Professor of Dermatology, Head of the Skin Cancer Unit in the Department of Dermatology, 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 U976

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 **multicentric 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-biologico-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 partnerships

LEADERSHIP

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
- > Dermatology: Actinic keratosis, Acne and related disorders, Dermocosmetics

Expertise:

- > Expert for national and European Agencies: European Medicines Agency (EMA), 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), American Academy of Dermatology (AAD), 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

Publications:

- > 556 publications; h-index: 42

Coordination of 2 others networks in melanoma:

- > Regional network: BioRderm (since 2007)
- > Local network: CRESIP (since 2011)

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

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, setting-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
- > **Pr Célèste LEBBE**, Saint Louis Hospital (AP-HP)
- > **Dr Didier CUISSOL**, 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 GRANDEL-BROCARD**, CHU de Nancy
- > **Dr Idalie JENNESSEAU**, 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)

DESIGN, METHODOLOGY & TIMELINE



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 & BIOBANK CONTENTS

DATABASE

PART I - Mandatory						
Identity	Initials	Birth date			Gender	
Primary tumor	Date of surgery	Type of melanoma	Breslow	Mitotic index	Ulceration	Regression
	Sentinel lymph node surgery		Date		Results	
	Lymph node removal		Number of invaded lymph node		Extracapsular extension	
AJCC Stage at inclusion and evolution	Date of diagnosis		Details		For stage III only : if inoperable or not	
Mutations	Type		Presence	Date	Comments	
Antigens	Type		Presence	Date	Comments	
Treatment	Type		Name	Nature (adjuvant/curative)	Dates	
Death	Yes/No			Date		

PART II - Optional					
Family history	Genetic investigation				
Metastases	Type	Date of diagnostic	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

Phase IV Product approval
Phase III
Phase II
Phase I
Pre-clinical
Proof of concept

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

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

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

BIBLIOGRAPHY & COMMUNICATIONS

Congress and events

- > 45TH annual ESDR meeting (09/2015)
- > Journées dermatologiques de Paris (12/2014)
- > 10TH EADO Congress (05/2014)
- > 7^e Journées du Cancéropôle Grand Ouest (04/2013)
- > 6^e Forum Scientifique de Pharmaco-épidémiologie (06/2013)
- > 3^e Journée Interrégionale du GIRCI Grand Ouest (06/2013)

Publications

- > Review cases of discordant mutational statute
M. Saint-Jean *et al.*, **Is a Single BRAF Wild-Type Test Sufficient to Exclude Melanoma Patients from Vemurafenib Therapy?** *Journal of Investigative Dermatology* (2014, vol.134, 1468-1470)
- > 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]