Project outline and justification for data/sample request

1. Investigators

1.1. Recipient Scientist, coordinator of the proposed project

Eric BAUDIN

1.2. Status of the Recipient Scientist

Service de Médecine Nucléaire et de Cancérologie Endocrinienne
Institut Gustave-Roussy
114, rue Édouard-Vaillant, 94805 Villejuif, France
Phone: 33-142-114-211

1.3. Associated Investigators

Segolene HESCOT
Isabelle BORGET (statistics)
Rossella LIBE (coordinator of the French network)

2. Project

2.1. Name of Project

MAPP-Prono: Malignant pheochromocytoma and paraganglioma : pronostic markers of overall survival of metastatic PP

2.2. Scientific context

Pheochromocytoma and paraganglioma are defined as malignant by the occurrence of metastases i.e. of chromaffin tissue in non chromaffin organs. Malignant pheochromocytoma and paraganglioma (MPP) are characterized by their heterogeneity concerning primary site, genetic predisposition, hormonal secretion and finally metastatic organs. Furthermore their natural history remains unknown. We recently studied progression free survival (PFS) of therapy-naïve MPP in a French cohort and demonstrated that half of patients have stable disease at one year without any therapeutic intervention and have prolonged overall survival (OS). On the other hand, progressive patients can be diagnosed early, usually on the first imaging work-up at 3 months. Heterogeneity concerning survival is described in the literature ranging from 40 to 77% at five year from the time of metastasis diagnosis. In addition, progression free survival ranged from 4 to 36 months in therapeutic trials. Finally, we previously reported that the presence or absence of SDHB mutation was associated with distinct median survival of 42 or 244 months. However, no prognostic marker of MPP OS has been definitely validated. Our aim is to determine prognostic markers of survival in a large European cohort of MPP.

2.3. Aim

<u>Primary objective:</u>

To look for prognostic markers of overall survival of MPP

Overall survival is defined by time from diagnosis of MPP (first thorax-abdomen or head and neck CT or PET FDG) to death by any cause.

<u>Secondary objectives:</u>

To describe MPP

To determine specific survival

To determine the role of the delay between initial diagnosis and first treatment of MPP
To determine the role of the type and delay of first of MPP therapy

2.4. Methods

Inclusion criteria

-Confirmed diagnosis of MPP (including pheochromocytoma, abdominal, thoracic or head and neck paraganglioma) by the presence of distant metastasis between 1998 and 2010

-Initial full characterization at time of metastasis performed within 4 months.

Exclusion criteria

-Benign pheochromocytoma and paraganglioma

-Absence of thoracic-abdomen-pelvic CT scan (PET FDG is not mandatory but advocated) (characteristics of these patients will be reviewed)

Capture within a databasis linked to Ensat databasis

Requested clinical annotations

Data collection

1-Initial characterization a T0 defined by the time of first CT or PET with metastatic disease:

-Gender
-Age at the time of metastasis,
-Genetic status according to recent recommendations
-Location and size the primary
-Presence of hormone- or tumor-related symptoms
-Levels of chromogranine A and or metanephrines and methoxytyramine
- Biological assessment
-Presence or absence of necrosis, of veinous invasion, the mitotic count and Ki67 at pathology of the primary
-Delay between initial diagnosis and diagnosis of metastasis
-Metastatic sites categorized as: bone, lymph nodes, lung, primary site and liver

2-Morphologic work-up including neck, thoracic and abdomen computed tomography (CT) and/or magnetic resonance imaging (MRI) scans will be recorded as well as scintigraphic means used for staging.

3-Treatments: time and type of first therapy

4-Time and cause of death: related or not to MPP

5-Status at last follow-up

2.5. Requested samples (type, justification of sample size)

none

2.6. Expected results

Identification of prognostic markers of overall survival in MPP

2.7. Projected time frame

Deadline for data acquisition :
2014 09 30
Deadline for data analysis
2014 12 31
Expected manuscript submission:
2015 03 31
Targeted Journals (depending on outcome): open to discussion
Journal of Clinical Oncology
JCEM
Endocrine related cancer…

3. Publication policy

1. Recipient scientist formally agrees with the provider(s) - at the time of the request or soon after the provider(s) have accepted the collaboration - the(ir) presence (if any) as co-authors in the publications originating from the collaboration.
2. Number of authors per centre and order of authorships are specified as follows:
   1-3 co-authors per centre depending on patient numbers provided as follows:
   Centers with more than 10% of patients will have two authors, more than 20% 3 authors….
   Order:
   1. Segolene Hescot
   2. 1st center
   3. 2nd center
   4. 3rd center…..
   Before the last: Isabelle Borget
   Last: Eric Baudin
3. The authors agree to acknowledge ENS@T contribution: "This project has been supported by the European Network for the Study of Adrenal Tumors (ENS@T).

4. Conditions of data usage

1. The Recipient scientist will use the data for research purposes only.

2. The data will be used by the Recipient scientist solely in connection with the Research Project as outlined above.

3. The Recipient scientist shall use the data in compliance with all applicable laws and government regulations of the Recipient's country.

4. The Recipient Scientist shall not release the data to any person other than the personnel under the Recipient Scientist's direct supervision.

5. When the Research Project is completed, a detailed description of the use of the data will be made available to the appropriate ENS@T Working Group

6. In the event that a journal publication or scientific article is published based on use of the data, the Recipient Scientist will send a copy of such publication, or the publication cite, promptly after it becomes available to the Recipient, to the appropriate ENS@T Working Group

Date Signature