PROPOSAL STUDY

"PRRT: predictive factors associated with response to treatment in patients with neuroendocrine tumors."

Aim of the study

To validate all the parameters that have been demonstrated to predict the response to PRRT in large cohort of patients with GEP-NET and BP-NET.

Reference: Albertelli et al, PRRT: identikit of the perfect patient. REMD 2020. PMID: 32978685

Principal investigators:

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Associated investigators:

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Design of the study and methods

The study is designed as a retrospective multicenter study. Therefore, it is open to all centers that would like to contribute with their cohort of patients to this proposed study.

Primary endpoint: evaluation and comparison of the different proposed predictive markers of response to PRRT (primary tumor site, grading, tumor burden, FDG-PET, ^{68}Ga-PET).

Exploratory endpoint: toxicity and evaluation of potential parameters that could predict the toxicity to PRRT

Ethic Committee: University of Palermo (as a multicenter study). As soon we receive the confirmation of collaboration from the other centers, we will update the Ethic Committee.

Inclusion criteria

Patients with confirmed histological or cytological diagnosis of GEP-NET (pancreatic, gastric, duodenal, ileal, rectum-colon, appendix) or BP-NET (bronco-pulmonary) who received PRRT from 1/01/2010.

The histological/cytological diagnosis could be derived from the primary tumor or from a metastasis (synchronous or metachronous) and should be classified in accordance with the 2010 WHO classification *(Rindi et al, Nomenclature and classification of digestive neuroendocrine tumors. IARC: Lyons 2010)*. In case of a

diagnosis before 2010, a re-classification on primary or on metachronous metastases according to the WHO 2010 criteria is mandatory.

Age ≥18 yrs.

Mandatory clinical data before the start of PRRT:

- Age
- Sex
- date of diagnosis
- characteristics of the tumor (primary tumor site, endocrine secretion, sporadic or genetic, ki67-index and grading)
- lines of therapy received before PRRT
- tumor stage, site of metastases, rate of liver involvement (in case of liver metastases)
- characteristics of FDG-PET and/or ^{68}Ga-PET before the start of the PRRT

Mandatory data of the PRRT:

- Details of the PRRT (type, number of cycles, total dose)
- Presence of side effects (kidney failure, hematologic, bowel obstruction)

Mandatory data of response to PRRT:

- Details of response to PRRT after 3 and 6 months from the treatment, and, if available, also after 12 months, according to RECIST criteria and to the uptake of ^{68}Ga-PET and/or FDG-PET (laboratory markers are not mandatory)
- Details on survival: progression free survival after PRRT and overall survival

Exclusion criteria

Patients with pheochromocytoma, paraganglioma, medullary thyroid cancer, or other types of NETs that are not in the inclusion criteria.

Age <18 yrs.

Missing information within the mandatory data above described.

Project time frame:

Deadline for notification of intention to participate in the study: 25th July 2021

Deadline of the data collection: 25th September 2021

Expected submission: January 2022

Publication policy:

- Recipient scientists, who agree to provide data for this project, will be included as co-authors in the publications originating from this collaboration.
- The **number of authors *per* center and order of authorship depends on the relative contribution to the study.** The authorship policy is suggested based on the final number of patients that fulfill the inclusion criteria and that could be used for the final analysis, as follows:
    - Centers that include between 5 and 15 patients will be acknowledged with 1 author position.

    - Centers that include between 16 and 25 patients will be acknowledged with 2 author positions.
    - Centers that include between 25 and ≤ 40 patients will be acknowledged with 3 author positions.
    - Centers that include >40 patients will be acknowledged with 4 author positions.
- The target journal will be chosen based on the results.

Contact:

All researchers that are interested to participate to this proposal project please contact Manuela Albertelli (manuela.albertelli@unige.it) and Barbara Altieri (Altieri_B@ukw.de).

Sincerely,

Manuela Albertelli, Barbara Altieri and Antongiulio Faggiano