

ID: IB2019-METABONE

Patterns of Care and Outcomes in Patients With Metastatic Bone Tumors (METABONE)

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INCLUSION

- Patients age > 12 year old at initial diagnosis
- Histology of Ewing's sarcoma type, osteosarcoma, chondrosarcoma
- Diagnostic of primary event between 2008 and 2018
- Diagnostic of unresectable locoregional disease where palliative treatment is indicated, or metastatic disease
- Treatment and monitoring made in one of the GSF-GETO centers, with follow up data on treatment received available.

OBJECTIFS

I. OBJECTIVES AND ENDPOINTS

The primary objective of the METABONE study is to give a retrospective descriptive analysis of clinico-biological profiles, patterns of care and modalities of treatment of patients with unresectable locally advanced and/or metastatic malignant bone tumors in a real-life national setting.

The primary endpoint is description of initial and local/metastatic relapse events management of adult patients with the diagnosis of Ewing's sarcoma, osteosarcoma, chondrosarcoma, made in one of the centers of the RESOS network between 2008 and 2018, in terms of therapeutic strategies including chemotherapy, surgery, radiotherapy, interventional radiology.

Secondary endpoints

- Description of systemic treatments received in the palliative setting in terms of **PFS** (progression free survival) and **TNT** (Time to next treatment)
- **Overall survival** from unresectable locally advanced and/or metastatic stage
- Identification of **factors associated with PFS and TNT** for molecules used in the unresectable locally advanced and metastatic setting
- Identification of **prognostic factors for overall survival** (OS) in the unresectable locally advanced and/ metastatic setting

II. METHODS

PATIENTS

We estimate the population size in the database of about 2800 patient cases.

We seek to include 800 patients to be screened in the present study.

We aim to get about 400 to 500 informative patients with unresectable locally advanced or metastatic disease.

VARIABLES

Variables collected will be those of the **CONTICABONE DICTIONNARY**

Descriptive data

Centers, number of patients per center

Initial patients characteristics at diagnostic: Age at diagnosis, gender, PS at diagnosis, previous history of specific disease (Li Fraumeni, Multiple Exostosis)

Tumor characteristics at diagnostic : location, side, size, multifocality, LR spread and type, stage N M, histology, grade, previous radiation area,

Initial treatment: surgery, type of surgery, margins, tumor spillage, residual cellularity, neo/adjuvant systemic treatment indication (start and stop date, type), radiation therapy, other treatment (cryotherapy, radiofrequency, embolisation), clinical trial inclusion

Metastatic relapse/event characteristics: PS, location of first metastasis, number of sites

Treatment of metastatic event: systemic treatment (PS molecule used, start and stop date, best RECIST response, date of progression, clinical trial), locoregional treatment (surgery, radiotherapy, cryotherapy, radiofrequency, embolisation), clinical trial.

Dates: Birth, initial diagnostic, surgery of primary, local relapse, metastatic relapse, start of each chemo line, date of progression for each chemo line, last contact, death

Samples: Molecular cytogenetics : method (RT PCR, FISH), transcript (FOR EWING SARCOMA ONLY)

Survival data

Median follow up

Progression free survival (PFS): PFS defined as the time from the systemic treatment onset to progression or death due to any cause, whichever comes first. When neither death nor progression is observed, PFS is censored at the date of last patient contact.

Time to next treatment (TNT): TNT defined as the time from the systemic treatment onset to the next treatment or death due to any cause, whichever comes first. When neither death nor new systemic therapy is observed, TNT is censored at the date of last patient contact.

Overall survival (OS): OS is defined as the interval between the diagnosis of first tumor event and the time of death. OS in the unresectable locally advanced setting is defined as the interval between the diagnosis of unresectable locally advanced setting (at diagnosis or relapse) and the time of death. OS in the metastatic setting is defined as the interval between the diagnosis of metastatic disease (at diagnosis or relapse) and the time of death. When death is not observed, OS is censored at the date of last patient contact.

STATISTICS

Statistical analysis of the baseline demographics and clinical outcomes will be based on all data available up to the cut-off date of August 31, 2021.

Descriptive statistics will be used to show the distribution of variables in the population.

The variables included in the univariate and multivariate analyses are the descriptive data including:

- type of chemotherapy used (poly vs mono, class of chemo: TKI, Ifosfamide, other)
- locoregional treatment of metastasis,
- inclusion in a clinical trial in first line,
- at least one inclusion in a clinical trial during metastatic stage,
- use of off-label drug at least once during metastatic stage

Multivariate logistic regression models will be used to identify biological and clinical factors associated with the type of treatment received after 1st line: in second, third, 4th line, and with the probability of survival 5 years after the diagnosis of metastases.

Follow-up times will be described as median values based on the inverse Kaplan–Meier estimator.

Prognostic factors of TNT for each line (1st, second, Third) and OS will be identified using Cox proportional hazard models.

The correlation between TNT and OS will be evaluated at each of the four first-lines of metastatic chemotherapy by a Spearman rank correlation coefficient and expressed as a value between 0 (no association) and 1 (perfect association). We will use a reviewed copula-based approach that introduces an iterative multiple imputation method for the estimation of the correlation coefficient. The data will be analyzed using the SAS v9.3 and R v3.3 software packages.