# ASSOCIATION BETWEEN PROGRESSION FREE SURVIVAL AND OVERALL SURVIVAL IN WOMEN RECEIVING FIRST-LINE TREATMENT FOR METASTATIC BREAST CANCER: EVIDENCE FROM THE ESME REAL-WORLD DATABASE

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**Coordinating Investigator**
Carine Bellera

**Scientific responsive**
Coralie Courtinard

**Clinical Research Unit**

Simone MATHOULIN-PÉLISSIER, MD, PhD — Institut Bergonié, Bordeaux
*Head of the Unit*



**SPONSOR** **INSTITUT BERGONIÉ**

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| **Title of the study** | **ASSOCIATION BETWEEN PROGRESSION FREE SURVIVAL AND OVERALL SURVIVAL IN WOMEN RECEIVING FIRST-LINE TREATMENT FOR METASTATIC BREAST CANCER:**<br>**EVIDENCE FROM THE ESME REAL-WORLD DATABASE** |
| **Abbreviation of the trial** | **DATECAN-ESME** |
| **Sponsor Identification** | **Institut Bergonié, Comprehensive Cancer, Bordeaux** |
| **Coordinating Investigator** | Carine Bellera |
| **Scientific responsive** | Coralie COurtinard |
| **Number of investigational sites planned** | 18 |
| **Number of patients** | 20033 |
| **Duration of the study** | Retrospective study |
| **Medical conditions** | Metastatic breast cancer |
| **Rationale of the study** | Overall survival (OS) is the gold standard endpoint to assess treatment efficacy in cancer clinical trials.<br>In metastatic breast cancer (mBC), progression-free survival (PFS) is commonly used as an intermediate endpoint.<br>Evidence remains scarce regarding the degree of association between PFS and OS. Our study aimed to describe the individual-level association between real-world PFS (rwPFS) and OS according to first-line treatment in female patients with mBC managed in real-world setting for each BC subtype (defined by status for both hormone-receptor [HR] expression and HER2 protein expression/gene amplification). |
| **Objectives** | To estimate rwPFS, OS and association between rwPFS and OS according to first-line treatment in female patients with mBC managed in real-world setting for each BC subtype (defined by status for both hormone-receptor [HR] expression and HER2 protein expression/gene amplification). |
| **Study design** | Retrospective study<br>The Epidemio-Strategy and Medical Economic (ESME) Research Program is a French academic initiative supporting the centralization of structured and non- structured<br>data documented in the electronic health records (EHR) (clinical notes, pathology reports and radiology reports) of patients treated for malignant conditions in a unique secured web-based data platform available for researchers.<br>The ESME mBC data platform is an EHR-derived database that gathers exhaustive data on consecutive patients who initiated a L1 treatment for mBC between 01 January 2008 and 31 December 2017 in one of 18 French Comprehensive Cancer Centers (clinicaltrials.gov; NCT 03,275,311). Patients who only receive surgery of a breast-related metastatic lesion ae not eligible for selection into the ESME mBC database |
| **Randomization and Treatment groups** | Not applicable |
| **Eligibility criteria** | All female patients older than 18 years diagnosed with mBC (de novo disease or first metastatic recurrence) between January 1, 2008, and December 31, 2017, and who received a L1 systemic treatment such as chemotherapy, endocrine therapy or targeted |

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| | therapy, whatever the sequence (monotherapy or combination of therapies using distinct mechanisms of actions, i.e., polytherapy).<br><br>A treatment line is defined as all anti-cancer treatments received in the absence of tumor progression.<br><br>Patients without informative data for tumor subtype are excluded (e.g., status for both HR expression and HER2 expression/gene amplification).<br><br>Patients receiving radiation therapy or anti-resorptive drugs (e.g., bisphosphonates, denosumab) as unique treatment are not considered in the analysis.<br><br>Patients are excluded if a second breast cancer was diagnosed before the onset of metastatic disease in order to limit potential inconsistencies between both breast cancer tumor subtypes and the metastases. |
| **Treatment schedule and route of administration** | This is a retrospective study, based on clinical records. |
| **Endpoints** | rwPFS : time from initial diagnosis of mBC to the date of disease progression (regional recurrence, progression, appearance/occurrence of metastases and distant recurrence) or death (any cause), whichever came first.<br><br>OS : time from diagnosis of mBC to the date of death from any cause. |
| **Statistical analysis plan** | This is a retrospective study, based on clinical records.<br><br>Sample size : On April 14, 2020, the ESME mBC database included a total of 23,697 mBC subjects. Of those, 20,033 satisfy the eligibility criteria for our study population<br><br>Statistical Analysis Plan (SAP)<br><br>Baseline characteristics will be summarized using frequency and percentage for qualitative variables. Median and inter-quartile range will be reported for quantitative variables. We will report frequencies and proportions for variables with missing or not documented information. No statistical test will be performed for the descriptive analyses.<br><br>Median follow-up will be estimated using the reverse Kaplan–Meier Method. Survival data will be estimated using Kaplan–Meier method and we will report median survival times with their respective 95% confidence interval (95%CI). Data for patients without the events of interest will be censored at the date of last contact recorded in the database.<br><br>We will estimate the individual-level association between rwPFS and OS using a Spearman rank correlation coefficient expressed as a value between 0 (no association) and 1 (perfect association) with 95% CI. Copula models allow one to jointly model two time-to-event variables. We will use a reviewed copula-based approach that introduced an iterative multiple imputation method for the estimation of the correlation coefficient. The strength of the rwPFS/OS association will be ranged according to the estimated correlation coefficient as follows: 0–0.19 is considered as very weak, 0.2–0.39 as weak, 0.40–0.59 as moderate, 0.6–0.79 as strong, and 0.8–1 as very strong correlation. We will estimate and report individual rwPFS/OS associations according to mBC subtype and first-line mBC treatment.<br><br>Data will be analyzed using R software (v 3.6). |
| **IDMC** | **Not applicable** |