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18F-FES PET-defined whole-body ER heterogeneity identifies endocrine responsiveness and predicts survival in ER+/HER2- metastatic breast cancer (MBC): Results of a prospective international clinical trial

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Background

ER+ MBC is defined by immunohistochemical ER expression in the primary tumor or metastatic lesions, overlooking spatial heterogeneity across disease sites. In this study, nested in the ET-FES trial, we used 18F-FES PET/CT to characterize whole-body ER heterogeneity and identify patients less likely to benefit from endocrine therapy (ET).

Methods

ET-FES is a prospective, international, phase II trial conducted within the JTC-2011 ERA-NET TRANSCAN program. ER+/HER2- MBC patients diagnosed between 04/2015 and 12/2020 were enrolled. At baseline, all patients underwent 18F-FES PET/CT and either 18F-FDG PET/CT or conventional CT and received first line ET as per protocol schedule. Patients were classified into 3 groups based on the proportion of 18F-FDG or CT-positive lesions and 18F-FES uptake, by visual analysis: A (100% concordant), B (partially concordant), C (100% discordant, no 18F-FES uptake). HR for progression/death was calculated comparing patients with concordant 18F-FES/18F-FDG/CT lesions (group A) with all the other patients (B+C).

Results

Among 147 patients enrolled in the ET-FES trial, 124 were eligible for this analysis. Of them, 92 (74.2%) were classified as group A, 22 (17.7%) as group B, and 10 (8.1%) as group C. After a median follow-up of 70.2 months (IQR 62.2–92.9), 100 patients (80.6%) experienced disease progression and 66 (53.2%) died. Median PFS was 18.1 months (95% CI, 11.3–25.3) in group A vs 11.7 (95% CI, 6.6–18.8) in groups B/C (HR 1.42; p=0.13). Median OS was 71.4 months in group A (95% CI, 50.7–88.4) vs 42.5 (95% CI, 25.4–73.7) in group B/C; 60-month OS rate was 59.6% in group A vs 40.9% in groups B/C (HR=1.79; 95% CI, 1.05–3.03, p=0.04).

Conclusions

These 5-year ET-FES results provide the first prospective evidence from a clinical trial that whole-body ER heterogeneity assessed by 18F-FES PET has a significant prognostic role in ER+/HER2- MBC treated with ET. Metastatic lesions lacking 18F-FES uptake despite detection by 18F-FDG-PET or CT may reflect biologically heterogeneous and less endocrine-responsive disease, supporting the role of combined functional imaging for treatment personalization.

Clinical trial identification

EudraCT 2013-000-287-29.

Legal entity responsible for the study

Legal entity responsible for the study: UPO - University of Piemonte Orientale, Italy.

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Disclosure

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