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CTC characterization with the DETECT CTC score predicts therapy response in triple-positive aBC: Translational results of the phase III DETECT V study

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Background

Circulating tumor cells (CTCs) are established prognostic biomarkers in advanced breast cancer (aBC); however, their clinical utility remains limited by modest predictive performance, which may be enhanced through phenotypic profiling.

Methods

DETECT V is a randomized phase III trial comparing endocrine therapy versus chemotherapy, each combined with dual HER2-targeted therapy, in patients with triple-positive aBC. CTCs were characterized by dual HER2 and estrogen receptor (ER) staining using CellSearch. Based on Paoletti et al., we developed the DETECT CTC score (range, 0–11; low risk, 0–2; high risk, 3–11) from the median CTC count per 7.5 mL of blood and HER2/ER staining intensity (0–3+). A median CTC count of <5 was assigned a score of 0. Patients with missing HER2 and/or ER intensity data were excluded.

Results

In this exploratory translational analysis, the baseline DETECT CTC score was available for 168 patients. High-risk patients (n=32) were older and had poorer ECOG performance status than low-risk patients (n=136). No significant differences were observed in histological subtype or metastasis-free interval. Detect CTC high risk patients had a significantly shorter progression-free survival (PFS) compared to CTC low risk patients (15.4 vs. 20.6 months, p=0.021), whereas CTC enumeration alone (≥ 5 CTCs vs. <5/7.5 mL) was not significantly associated with PFS (p = 0.082). Within the DETECT low-risk group, the addition of ribociclib significantly improved PFS (p<0.001) and overall survival (OS; p=0.005). OS was significantly shorter both for patients with ≥ 5 vs. <5 CTCs at baseline and for patients with a high vs. low DETECT CTC score (both p<0.001).

Conclusions

Incorporating ER and HER2 expression on CTCs enables pretreatment risk stratification and may support therapeutic decision-making, an issue of growing importance in the evolving HER2-targeted treatment landscape. Given its prognostic and predictive potential, this approach warrants further validation in prospective studies.

Clinical trial identification

NCT02344472.

Legal entity responsible for the study

University Hospital Ulm.

Funding

Roche Pharma AG Novartis Pharmaceuticals Eisai GmbH Celgene Corporation.

Disclosure

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