Decoding the immune landscape of metastatic breast cancer via liquid biopsy

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Abstract

Background and objective: Metastatic breast cancer (mBC) remains largely incurable, despite advances in personalized therapies. Dysregulation of the immune system plays a critical role in disease progression. This study aims to assess circulating immune cells with circulating tumor cells (CTCs) and their correlation with clinical outcome to identify circulating biomarkers for prognosis in mBC patients.

Methods: Blood samples were collected from 60 mBC patients (ClinicalTrials.gov NCT04025541) and 21 healthy donors. This cohort showed heterogeneity with different molecular subtypes: 50 patients hormone receptor (HR)+/ HER2- (83.3%), 5 patients HR+/HER2+ (8.3%), 3 patients had HR-/ HER2+ (5.0%), and 2 patients triple-negative (3.3%). Blood was used for CTC detection using the FDA-cleared CellSearch® system. Peripheral blood mononuclear cells were subjected to multi-parametric flow cytometry to characterize all immune cell subsets.

Results: 44 patients were under hormone therapy (73%) in association with CD4/6 inhibitors. 32 patients (53.3%) had progression during follow-up (median 22.5 months-95% CI [21-24]). CTCs were detected in 58.3% of mBC patients, with the number of CTCs ranging from 1-962. Immune profiling revealed a higher proportion of regulatory T cells (Tregs) in mBC ($p<0.001$), particularly in CTC(+) cases ($p=0.025$), alongside increased immune checkpoint expression ($p<0.001$). Notably, mBC patients exhibited altered B cell ($p=0.018$), NK cell ($p<0.001$), with elevated TIGIT on NK cells ($p=0.005$) and a shift toward pro-tumor macrophages ($p=0.046$). CTCs ($p=0.026$) and Treg+/PD1+ ($p=0.007$) expression correlated with poor progression-free survival.

Conclusion: This study emphasizes the critical role of liquid biopsy in monitoring immune alterations and disease progression in mBC. The analysis revealed significant immune dysregulation, including increased Tregs, upregulated immune checkpoint markers, and altered NK cell and macrophage profiles, which contribute to immune evasion and metastasis. Notably, CTCs and Treg+/PD1+ expression correlated with poor progression-free survival in mBC patients. These findings highlight liquid biopsy as a valuable non-invasive tool for monitoring immune responses and identifying prognostic tumor-derived and tumor-induced circulating biomarkers. Insights gained may guide targeted therapies to restore immune function and improve treatment outcomes in mBC patients.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.