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1193 – Molecular subtype conversion in recurrent breast cancer: a systematic review and clinical implications

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Introduction: Breast cancer intrinsic subtypes, defined by estrogen receptor (ER), progesterone receptor (PR), HER2 status, and proliferation indices, are pivotal to prognostication and treatment selection. Increasing evidence demonstrates clinically meaningful discordance between primary and recurrent or metastatic disease. A systematic review was performed to synthesize the magnitude, patterns, and implications of molecular subtype conversion in breast cancer recurrence.

Methods: A systematic literature search was conducted through the PubMed, Scopus, and Web of Science databases for studies published between 2010 and 2025. Eligible studies reported paired biomarker data (ER, PR, HER2, and/or Ki-67) from primary and recurrent/metastatic tumors. Data extraction focused on rates and direction of receptor discordance, subtype conversion, and associated clinical outcomes. Findings were synthesized qualitatively, emphasizing consistency across heterogeneous cohorts.

Results: Biomarker discordance was consistently observed across studies, with reported rates of 10%–40% for ER, 20%–50% for PR, and 5%–20% for HER2. Loss of hormone receptor expression predominated, whereas HER2 status demonstrated bidirectional conversion. These shifts frequently resulted in transition from luminal subtypes to more aggressive phenotypes, including HER2-enriched and triple-negative disease. Subtype conversion was associated with inferior survival outcomes and led to clinically significant modifications in systemic therapy in a substantial proportion of patients.

Conclusion: Molecular subtype conversion in recurrent breast cancer is a prevalent and prognostically relevant phenomenon with direct therapeutic implications. Routine re-biopsy of recurrent or metastatic lesions should be strongly considered to guide the individualized treatment of patients. Future prospective studies are warranted to elucidate the biological mechanisms driving receptor plasticity and to define its impact on long-term outcomes.

Ethics: Public data – Literature review.

Keywords: mutation; molecular subtype; prognostic factors.