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1075 – Translating phase III trials into real-world practice: evaluation of pathologic complete response in HER2-positive breast cancer and the potential impact of antibody–drug conjugates in the neoadjuvant setting

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Introduction: Neoadjuvant therapy is a cornerstone in the management of early and locally advanced human epidermal growth factor receptor 2 (HER2)-positive breast cancer. Pathologic complete response (pCR) is a robust surrogate endpoint associated with improved prognosis and guides adjuvant treatment decisions. Dual HER2 blockade with trastuzumab and pertuzumab combined with chemotherapy has become the standard of care, yielding high pCR rates. However, lower sensitivity in estrogen receptor-positive (ER+) tumors suggests relevant biological heterogeneity. Antibody–drug conjugates, such as trastuzumab deruxtecan (T-DXd), have demonstrated high antitumor activity; data from DESTINY-Breast11 (DB-11) indicate increased pCR rates in the neoadjuvant setting. Translating these findings into clinical practice is essential to validate their real-world impact.

Methods: This retrospective study included patients with HER2-positive breast cancer treated with chemotherapy and dual anti-HER2 blockade at a cancer center between 2015 and 2024. pCR was evaluated according to ER status, chemotherapy regimen, and eligibility for DB-11.

Results: A total of 175 patients were included (median age: 44 years; stage I: 6.3%, stage II: 59.4%, and stage III: 34.3%; ER+: 69.1%; node-positive: 56.0%). The overall pCR rate was 61.1%, reaching 81.5% in ER– and 52.1% in ER+ tumors, with no differences across chemotherapy regimens. Among 116 patients eligible for DB-11, pCR was 58.6% (78.9% in ER–; 48.7% in ER+). These results were comparable to the control arm of DB-11 (56.3%; 67.1% in ER–; 52.3% in ER+).

Conclusion: Real-world findings reproduced the DB-11 control arm, reinforcing the study's external validity. The absolute increase in pCR with T-DXd (≈11%) suggests a potential clinical benefit regardless of ER status, despite response heterogeneity. These data support the rational incorporation of antibody–drug conjugates in the neoadjuvant setting and highlight the importance of translating phase III evidence into clinical practice to optimize oncologic outcomes. Cost-effectiveness analyses are ongoing.

Ethics: Research Ethics Committee Approval (CAAE 21308019.9.0000.5432).

Keywords: breast neoplasms; HER2; neoadjuvant therapy; molecular targeted therapy; pathologic complete response.