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A systematic review and extracted individual patient data meta-analysis of long-term outcomes in triple-negative breast cancer after a pathologic complete response: does the type of neoadjuvant therapy matter?

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Introduction: Neoadjuvant chemotherapy is the standard of care for stage IB-III triple-negative breast cancer (TNBC), with pathological complete response (pCR) strongly associated with survival. Although the escalation of neoadjuvant therapies with platinum and immune checkpoint inhibitors (ICI) improves pCR rates and long-term outcomes, patients with pCR in the control arms of pivotal trials also show favorable outcomes. Whether the type of neoadjuvant regimen leading to pCR impacts long-term survival differently is largely unknown. **Objective**: Correlate the type of neoadjuvancy performed for complete pathological response with the survival rate. **Methods:** A systematic review and meta-analysis was conducted, searching the databases PubMed, Embase, and Cochrane, and conference proceedings for phase II and III trials including early-stage patients with TNBC with pCR. A pooled analysis of Kaplan-Meier-derived individual patient data was performed for event-free survival and overall survival, with subgroup analyses by treatment regimens. **Results:** Of 2,830 identified publications, 18 trials (16 randomized and 2 single-arm) comprising 3,430 patients with TNBC and pCR were included. Neoadjuvant ICI with chemotherapy improved event-free survival (hazard ratio [HR] 0.67; 95% confidence interval [CI] 0.50–0.89; p<0.01) compared with chemotherapy-only regimens, with no significant overall survival difference for patients with pCR (HR 0.84; 95%CI 0.50–1.41; p=0.51). In contrast, event-free and overall survival were not significantly different regardless of platinum use (HR 0.55; 95%CI 0.20–1.50; p=0.24 and HR 0.33; 95%CI 0.09–1.22; p=0.10, respectively). Similarly, anthracycline-containing regimens showed comparable event-free survival to anthracycline-free regimens (HR 0.86; 95%CI 0.51–1.45; p=0.58). For patients with pCR after ICI therapy, the benefit of adjuvant ICI for event-free or overall survival was not statistically significant (HR 1.16; 95%CI 0.55–2.44; p=0.70 and HR 2.91; 95%CI 0.40–21.37; p=0.29, respectively). **Conclusion:** Neoadjuvant ICI-based regimens improved event-free survival in early-stage patients with TNBC with pCR. However, adjuvant ICI after pCR appears to offer no additional benefit, and event-free survival remains unaffected by neoadjuvant chemotherapy type (with or without platinum or anthracycline).

Keywords: meta-analysis; triple-negative breast cancer; pathologic complete response; immune checkpoint inhibitor; neoadjuvant treatment.