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Dense-breast study: dose-dense neoadjuvant chemotherapy in breast cancer: a network meta-analysis of efficacy and toxicity

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Objective: To evaluate the efficacy and toxicity of dose-dense versus standard anthracycline- and taxane-based neoadjuvant chemotherapy regimens in breast cancer through a systematic review and network meta-analysis. **Methods:** This Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)-compliant included seven randomized trials and high-quality observational studies comprising 2,670 patients with non-metastatic breast cancer. The primary endpoint was pathological complete response (pCR), and secondary endpoints included overall survival, disease-free survival, and grade 3–4 toxicities. Subgroup analyses were conducted across molecular subtypes and treatment characteristics. Treatment ranking was performed using surface under the cumulative ranking curve (SUCRA) analysis. **Results:** Dose-dense regimens significantly improved pCR rates compared to standard regimens (effect size: 0.87; 95% confidence interval 0.81–0.93), with an absolute pCR rate of 43.9%. Survival analyses showed a 15%–25% relative reduction in recurrence and mortality with dose-dense therapy. The most pronounced benefits were observed in human epidermal growth factor receptor-type 2 (HER2)-positive and triple-negative breast cancer subgroups, especially in high-risk, early-stage disease. However, dose-dense regimens were associated with increased toxicity, including grade 3–4 neutropenia (10%–24%) and anemia (up to 30%). SUCRA analysis ranked trastuzumab-based, platinum-containing, and combination regimens highest in efficacy, while standard anthracycline- and capecitabine-based regimens ranked lower. Subgroup and sensitivity analyses confirmed the robustness of these findings and emphasized the heterogeneity of benefits across tumor types and clinical risk factors. **Conclusion:** Dose-dense neoadjuvant chemotherapy regimens improved pCR, disease-free survival, and overall survival, particularly in HER2-positive and triple-negative breast cancer patients. However, their increased toxicity profile necessitates judicious patient selection and comprehensive supportive care. Future directions include integrating biomarkers, immune checkpoint inhibitors, and novel agents to enhance efficacy and personalize treatment. Dose-dense chemotherapy should be prioritized in high-risk subtypes where the therapeutic benefit outweighs the potential adverse effects.

Keywords: neoadjuvant therapy; triple-negative breast cancer; receptor, ErbB-2; pathologic complete response; network meta-analysis; survival; toxicity.