Neoadjuvant antibody-drug conjugates for early-stage breast cancer: a systematic review and meta-analysis

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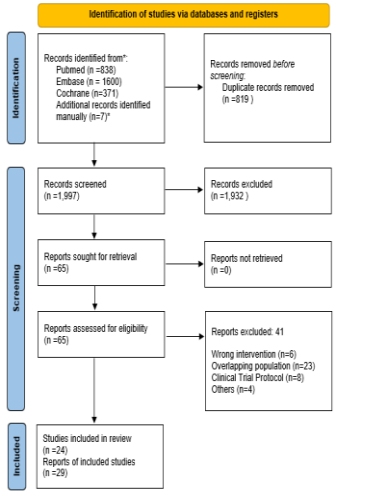
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Background

Pathologic complete response (pCR) is a key endpoint of neoadjuvant therapy in early-stage breast cancer (EBC), associated with improved survival in triple-negative and HER2-positive subtypes. Antibody–drug conjugates (ADCs), established in metastatic disease, are now showing promise in the neoadjuvant setting.

Methods

We systematically searched for studies of EBC patients treated with neoadjuvant ADCs, alone or in combination. Studies of adjuvant therapy, metastatic disease, or those without disaggregated ADC data were excluded. Meta-analyses used a random-effects model, with heterogeneity assessed via I² and Cochran's Q test.



*Additional records identified manually were Mafalda Oliveira 2025 (presented at SABCS 2024); Abelman 2025, Zhenzhen Liu 2025, Lin-Xiaoxi Ma 2025, Xiaoxiao Liu 2025, Junjie Li 2025; (abstracts presented at ASCO 2025), and DESTINY-Breast 11 (presented at ESMO 2025).

Figure 1. Prisma flow diagram of study screening and selection.

Results

24 studies with 2,363 patients were included. Most were phase II trials, and two were phase III. Nine ADCs targeting HER2, TROP2, HER3, or LIV1 with six payload types were identified. The pooled pCR rate was 38.34% (95% CI, 29.36-47.72), highest in HER2+/HR– , 65.06%, followed by HER2+/HR+ 47.53%, HER2–/HR not specified, 45.52%, HER2+/HR not specified 43.84%, TNBC 29.37%, and HER2–/HR+ 2.94% (p<0.0001). By target, pCR was 43.93% for HER2, 41.41% for TROP2, 16.57% for LIV-1 and 3% for HER3 (p<0.0001). Frequent all-grade adverse events included nausea (54.52%), diarrhea (48.24%), alopecia (39.11%), ALT elevation (30.88%), AST elevation (34.78%), neutropenia (29.53%), vomiting (25.95%), anemia (24.85%), thrombocytopenia (17.46%), and ILD (1.37%). Grade ≥3 events occurred in 25.06%.

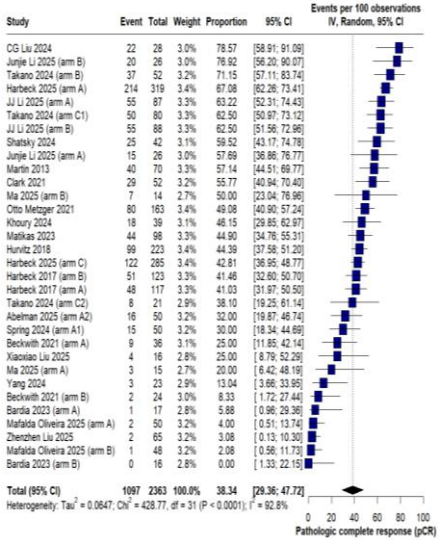


Figure 2. Meta-analysis of proportions for the outcome overall pathologic complete response (pCR).

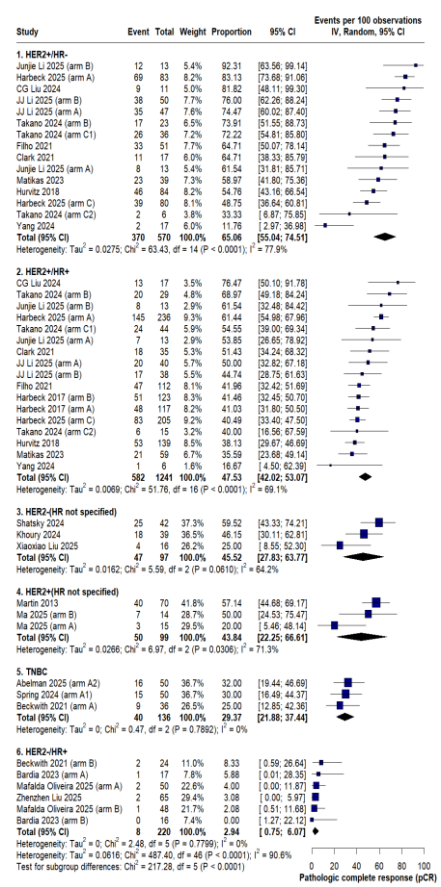


Figure 3. Subgroup analysis of pathologic complete response (pCR) according to histological subtype.

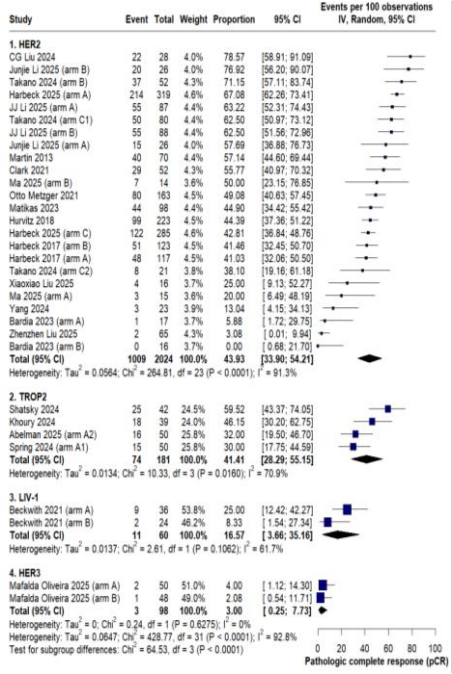


Figure 4. Subgroup analysis of pathologic complete response (pCR) according to antibody-drug conjugate target.

Conclusions

Neoadjuvant ADCs yield clinically meaningful pCR rates in EBC, with the greatest benefit in HER2-positive disease. These results support further studies exploring their use as a neoadjuvant strategy in selected patients and underscore the need for biomarker-guided treatment to optimize efficacy and safety.

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