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Incidence of interstitial lung disease and cardiotoxicity with trastuzumab deruxtecan in breast cancer patients: A systematic review and single-arm meta-analysis

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Objective: We performed a systematic review and meta-analysis to assess the incidence and severity of those adverse events (AEs) in metastatic breast cancer (mBC) patients treated with trastuzumab deruxtecan (T-DXd). **Methodology:** We comprehensively searched PubMed, Cochrane, and Scopus databases for randomized clinical trials (RCTs) and observational cohort studies, including mBC patients with HER2-low or -positive expression who have received at least one dose of T-DXd. The DESTINY-Breast02 study was also included after its presentation at the SABCS 2022. Our meta-analysis followed the Cochrane Reviews and PRISMA statement guidelines. The statistical analysis was performed using the R software, and the results are presented as pooled analysis in forest plots. **Results:** We included nine studies: three phase III RCTs, three phase II and two phase I non-RCTs, and one retrospective cohort comprising 1,443 patients with a mean follow-up of 14.9 months. The median age of our population ranged from 53 to 59 years. Most were non-Asian (40.5%) and presented with hormone-receptor-positive mBC (66.8%). In a pooled analysis, the incidence of ILD was 13.0% (179 patients; 95%CI 11.0–13.0). Patients enrolled in phase III clinical trials had an ILD rate of 12.0%, while the observational cohort reported a numerically higher rate of 18.0%. Most ILD cases, 84.9% (152 patients), were mild (grade 1 or 2). Grade 3 or 4 AEs were reported in 13 (7.3%) patients, and grade 5 in 14 (7.8%) patients. We assessed cardiotoxicity by the reduction of left ventricular ejection fraction (LVEF) compared with baseline measures. Decreased LVEF was seen in 3.6% (95%CI 3.0–5.0%), and most patients were asymptomatic. A total of 11 patients developed prolonged QT interval, and four had left ventricular dysfunction and cardiac failure. **Conclusion:** Our meta-analysis reinforces the importance of close vigilance for pulmonary and cardiac toxicities in mBC patients on treatment with T-DXd. Early detection and management by a multidisciplinary team following the most recent guidelines may improve patient outcomes.

Keywords: breast cancer; interstitial lung disease; cardiotoxicity.