Breast

Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer

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N Engl J Med. 2022 Mar 24;386(12):1143-1154. doi: 10.1056/NEJMoa2115022.

BACKGROUND

Trastuzumab emtansine is the current standard treatment for patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer whose disease progresses after treatment with a combination of anti-HER2 antibodies and a taxane.

METHODS

We conducted a phase III, multicenter, open-label, randomised trial to compare the efficacy and safety of trastuzumab deruxtecan (a HER2 antibody-drug conjugate) with those of trastuzumab emtansine in patients with HER2-positive metastatic breast cancer previously treated with trastuzumab and a taxane. The primary end point was progression-free survival (as determined by blinded independent central review); secondary end points included overall survival, objective response, and safety.

RESULTS

Among 524 randomly assigned patients, the percentage of those who were alive without disease progression at 12 months was 75.8% (95% confidence interval [CI], 69.8 to 80.7) with trastuzumab deruxtecan and 34.1% (95% CI, 27.7 to 40.5) with trastuzumab emtansine (hazard ratio for progression or death from any cause, 0.28; 95% CI, 0.22 to 0.37; P<0.001). The percentage of patients who were alive at 12 months was 94.1% (95% CI, 90.3 to 96.4) with trastuzumab deruxtecan and 85.9% (95% CI, 80.9 to 89.7) with trastuzumab emtansine (hazard ratio for death, 0.55; 95% CI, 0.36 to 0.86; prespecified significance boundary not reached). An overall response (a complete or partial response) occurred in 79.7% (95% CI, 74.3 to 84.4) of the patients who received trastuzumab deruxtecan and in 34.2% (95% CI, 28.5 to 40.3) of those who received trastuzumab emtansine. The incidence of drug-related adverse events of any grade was 98.1% with trastuzumab deruxtecan and 86.6% with trastuzumab emtansine, and the incidence of drug-related adverse events of grade 3 or 4 was 45.1% and 39.8%, respectively. Adjudicated drug-related interstitial lung disease or pneumonitis occurred in 10.5% of the patients in the trastuzumab deruxtecan group and in 1.9% of those in the trastuzumab emtansine group; none of these events were of grade 4 or 5.

CONCLUSIONS

Among patients with HER2-positive metastatic breast cancer previously treated with trastuzumab and a taxane, the risk of disease progression or death was lower among those who received trastuzumab deruxtecan than among those who received trastuzumab emtansine. Treatment with trastuzumab deruxtecan was associated with interstitial lung disease and pneumonitis.