Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive, advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: a randomized, phase 2, multicenter, open-label study (DESTINY-Gastric01)

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BACKGROUND
• Approximately 20% of gastric cancer patients have HER2-positive disease at presentation
• Although the overall response rate (ORR) of trastuzumab (Trastuzumab) in gastric and gastroesophageal junction (GEJ) cancer was higher in clinical trials than in registry studies after initial treatment failure with anthracyclines and taxanes, response rates of Trastuzumab are lower in patients with later-line settings
• Current treatments approved for later lines (irinotecan, taxanes, trifluridine/tipiracil, ramucirumab, and trastuzumab-emtansine) have limited efficacy

METHODS
Study Design and Population
• OS was estimated using the Kaplan-Meier method for all patients with available data, including the 24-week interim OS analysis and the 1-year OS analysis
• OS was the primary endpoint
• ECOG PS, Eastern Cooperative Oncology Group performance status; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; ICR, independent central review; IHC, immunohistochemistry; ISH, in situ hybridization; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan

RESULTS
Patients
• 126 Randomized: 63 T-DXd; 63 PC
• Of data cutoff in the T-DXd arm than in the PC arm (22.4% vs 4.8%)
• OS was a key secondary endpoint to be statistically evaluated hierarchically if the primary endpoint (OS) was not met
• Median duration of confirmed response was 11.3 months (95% CI, 5.6 months to not estimable) with T-DXd vs 1.6 months (95% CI, 0.0 months to 4.0 months) with PC

Efficacy
• 31% HR and corresponding 95% CI were estimated using Cox proportional hazards model stratified by region

Safety
• All serious adverse drug reactions (ADRs) and all deaths were considered serious adverse drug reactions

CONCLUSIONS
• The overall survival (OS) benefit was significant (HR for death, 0.47 [95% CI, 0.31-0.71]; P = .003)
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REFERENCES
• Web of Science, Scopus, Medline, and PubMed were searched for relevant articles

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