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Real-World Outcomes of Trastuzumab Deruxtecan with or without Endocrine Therapy in HER2-Low, Hormone Receptor-Positive Metastatic Breast Cancer: A Propensity-Matched Analysis

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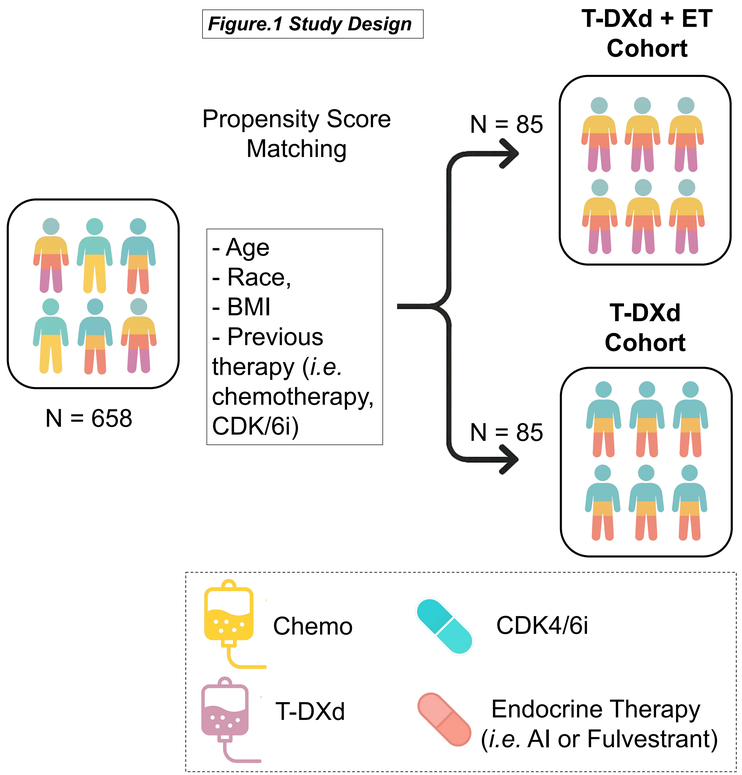
Background

Combination therapy involving anastrozole or fulvestrant with fam-trastuzumab deruxtecan-nxki (T-DXd) has demonstrated promising antitumour activity in chemotherapy-naïve, HER2-low, hormone receptor–positive (HR+) metastatic breast cancer (mBC) patients, as evidenced by the phase 1b DESTINY-Breast08 trial (NCT04556773). Although this regimen is not currently established as a standard of care, it is being utilized in several oncology centers.
However, real-world evidence supporting this strategy remains limited

Methods

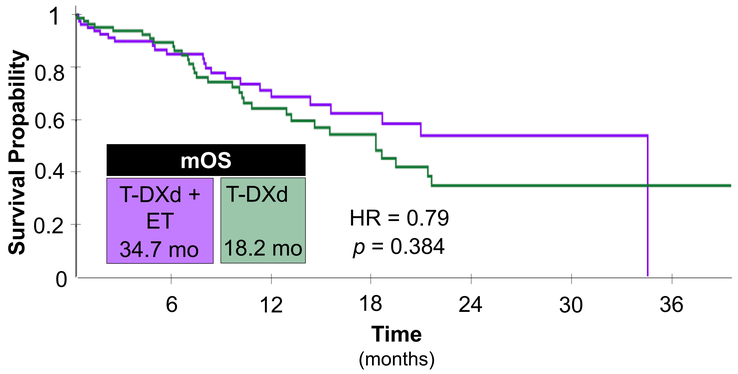
Applying the TriNetX Global Collaborative Network, we retrospectively identified two cohorts comprising 658 mBC patients, stratified by receipt of T-DXd monotherapy or T-DXd in combination with endocrine therapy (ET). Propensity score matching (1:1) was performed to balance the cohorts (T-DXd plus ET, n=85; T-DXd alone, n=85) for age, race, and body mass index, all of whom had prior exposure to CDK4/6 inhibitors and chemotherapy (*Figure.1*). Hazard ratios (HRs) were calculated to compare overall survival (OS) between groups

Figure.1 Study Design



Results

Following matching, the median age was 57.3 years (±13.9) in the T-DXd plus ET group and 56.7 years (±14.1) in the T-DXd monotherapy group. Median follow-up was 87.9 months for the combination cohort and 46.1 months for the monotherapy cohort. The combination group demonstrated a trend towards improved overall survival compared to T-DXd alone (HR=0.79; 95% CI, 0.465–1.344; p=0.384), although statistical significance was not achieved.



Conclusions

This represents the first large-scale real-world cohort analysis evaluating the addition of endocrine therapy to T-DXd in patients with HER2-low, HR+ mBC. While these preliminary findings suggest a potential survival benefit with the combination approach, the limited follow-up duration preclude definitive conclusions. Further prospective studies are warranted to elucidate the clinical utility of combining T-DXd with ET in this patient population. Our research aims to perform ongoing follow-up of these patients to generate more robust data, thereby further clarifying the clinical benefit of combining T-DXd with ET in this population.

Acknowledge

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