Comparative efficacy of antibody drug conjugates (ADCs) in male versus female breast cancer across the spectrum of HER2 expression

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BACKGROUND

- ADCs have transformed breast cancer therapy, outperforming standard chemotherapy.
- Yet, **data in male breast cancer (MBC) are limited**, with management mostly extrapolated from female breast cancer (FBC) studies
- We compared survival outcomes between male and female patients treated with ADCs across HER2 expression levels.

METHODS

- A total of **2,954 patients (34 males, 2,920 females)** treated with trastuzumab deruxtecan (T-DXd), trastuzumab emtansine (T-DM1), or sacituzumab govitecan (SG) were included.
- Triple-negative cases were excluded due to rarity in men and the worse prognosis of triple-negative breast cancer, so that the cohorts would be more homogeneous without overrepresentation of triple-negative breast cancer in females. .
- HER2 status was defined as: null (IHC 0%), ultra-low (IHC 0 with faint 1–10%), low (IHC 1+ or 2+/CISH–), and positive (IHC 3+ or 2+/CISH+).
- Real world median overall survival (OS) was derived from insurance claims and calculated from the start of first ADC to last contact using Kaplan–Meier.
- Statistical significance was assessed using chi-square and Mann-Whitney U.

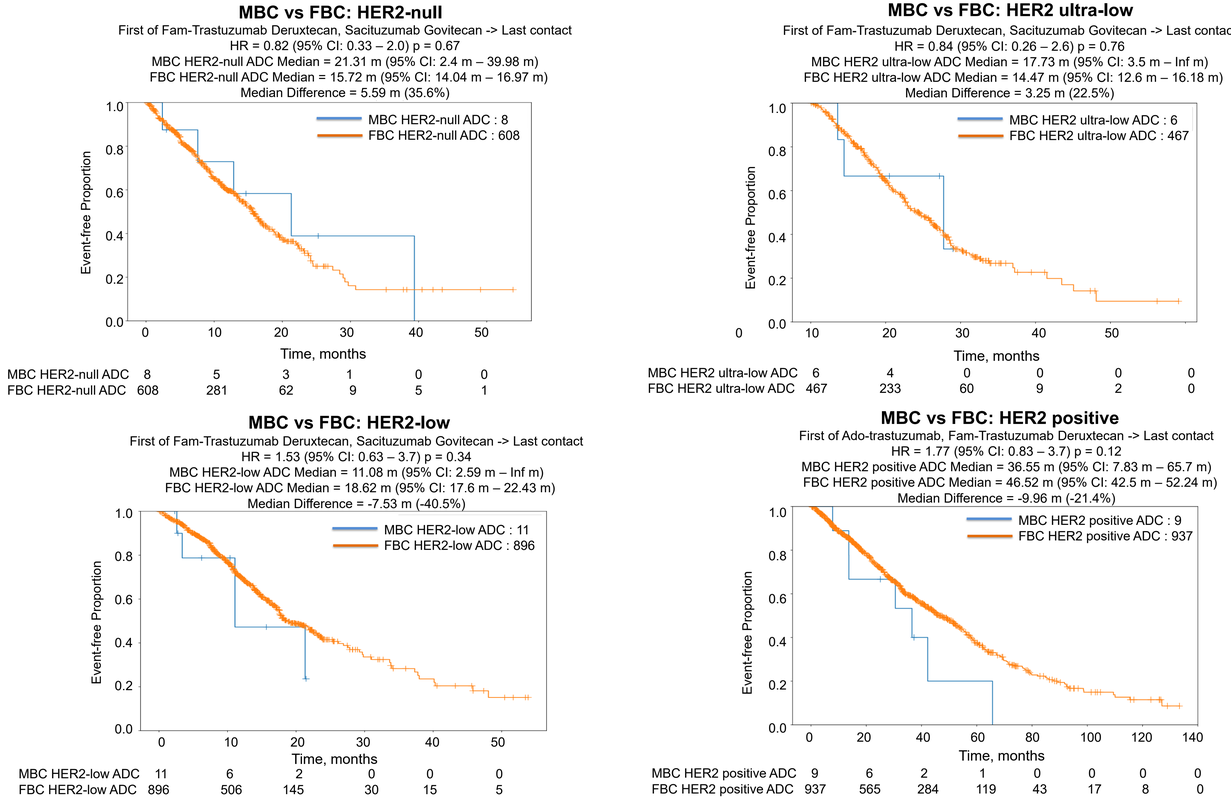
RESULTS

Table 1. Patients' demographic information: MBC vs FBC received ADC

Variables	HER2-null		HER2 ultra-low		HER2-low		HER2-positive	
Sex	Male	Female	Male	Female	Male	Female	Male	Female
Count (N)	8	612	6	467	11	903	9	938
Median age [range]	56 [38 - 64]	57.5 [25 - 89]	62.5 [40 - 70]	57.5 [29 - >89]	62.5 [44 - 80]	62.5 [22 - 88]	57.5 [29 - 85]	55.5 [20 - >89]
ER status (IHC)								
Positive	100% (8/8)	100% (609/609)	100% (6/6)	100% (467/467)	100% (11/11)	100% (902/902)	66.67% (6/9)	52.61% (493/937)
Negative	0% (0/8)	0% (0/609)	0% (0/6)	0% (0/467)	0% (0/11)	0% (0/902)	33.33% (3/9)	47.39% (444/937)
Race (count, N)								
White	100% (5/5)	76.63% (364/475)	60% (3/5)	72.7% (261/359)	62.5% (5/8)	75.48% (545/722)	62.5% (5/8)	71.39% (509/713)
Black	0% (0/5)	16.84% (80/475)	40% (2/5)	17.83% (64/359)	37.5% (3/8)	15.1% (109/722)	25% (2/8)	18.37% (131/713)
Asian or Pacific Islander	0% (0/5)	2.95% (14/475)	0% (0/5)	5.29% (19/359)	0% (0/8)	5.96% (43/722)	12.5% (1/8)	5.47% (39/713)
Other	0% (0/5)	3.58% (17/475)	0% (0/5)	4.18% (15/359)	0% (0/8)	3.46% (25/722)	0% (0/8)	4.77% (34/713)
Ethnicity (count, N)								
Not Hispanic or Latino	83.33% (5/6)	90.78% (453/499)	100% (6/6)	91.83% (337/367)	100% (8/8)	89.92% (660/734)	100% (6/6)	90.11% (74874/748)
Hispanic or Latino	16.67% (1/6)	9.22% (46/499)	0% (0/6)	8.17% (30/367)	0% (0/8)	10.08% (74/734)	0% (0/6)	9.89% (74/748)
Tumor site (count, N)								
Primary	100% (8/8)	25.65% (157/612)	33.33% (2/6)	25.7% (120/467)	9.09% (1/11)	26.47% (239/903)	0% (0/6)	30.17% (283/938)
Metastatic	0% (0/8)	74.35% (455/612)	66.67% (4/6)	70.3% (347/467)	90.91% (10/11)	73.54% (664/903)	100% (6/6)	69.83% (655/938)
Drugs (count, N)								
Fam-Trastuzumab Deruxtecan	75% (6/8)	56.05% (343/612)	83.33% (5/6)	79.23% (370/467)	81.82% (9/11)	91.25% (824/903)	55.56% (5/9)	58% (544/938)
Sacituzumab Govitecan	37.5% (3/8)	61.27% (375/612)	66.67% (4/6)	43.25% (202/467)	36.36% (4/11)	30.01% (271/903)	0% (0/9)	1.92% (18/938)
Ado-trastuzumab emtansine	25% (2/8)	2.78% (17/612)	0% (0/6)	7.07% (33/467)	18.18% (2/11)	9.75% (88/903)	66.67% (6/9)	69.62% (653/938)

- Race and ethnicity data is self reported
- TNBC patients and ER negative patients were removed from FBC HER2-null, ultra-low and low patients to balance with MBC

Figure 2. Survival of MBC vs FBC patient treated with ADC



T-DXd or SG were taken for HER2-null, ultra-low and low patients and, T-DXd or T-DM1 were taken for HER2-positive patients. Median survival from treatment initiation with either T-DXd or SG in the HER2-null cohort was 21.31 months (m) in males vs 15.72 m in females (HR 0.82, p=0.67); in the HER2-ultra low was 17.73 m in males vs 14.47 m in females (HR 0.84, p=0.76); in the HER2-low was 11.08 m in males vs 18.62 m in females (HR 1.53, p=0.34). Median survival from treatment initiation with either T-DXd or T-DM1 in the HER2-positive was 36.55 m in males vs 46.52 m in females (HR 1.77, p=0.12).

CONCLUSIONS

Survival with ADCs was similar between males and females across all HER2 levels. **Males with HER2-positive disease trended toward shorter OS, consistent with prior MaBC data**. Despite small cohorts and no HR-stratification for the limited sample, this is the first analysis of ADC outcomes in men across the HER2 spectrum.