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Outcome of patritumab deruxtecan (HER3-DXd) in patients with HER2-positive metastatic breast cancer and CNS involvement previously treated with trastuzumab deruxtecan: A subanalysis of TUXEDO-3

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Disclosure Information

Rupert Bartsch

I have the following relevant financial relationships to disclose:

- Advisory Role: Astra-Zeneca, Daiichi-Sankyo, Eisai, Eli-Lilly, Gilead, Gruenenthal, MSD, Novartis, Pfizer, Pierre-Fabre, Roche, Stemline
- Honoraria: Amgen, Astra-Zeneca, BMS, Daichi-Sankyo, Eisai, Eli-Lilly, Gilead, Gruenenthal, MSD, MedMedia, Novartis, Pfizer, Pierre-Fabre, Roche, Stemline
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BACKGROUND

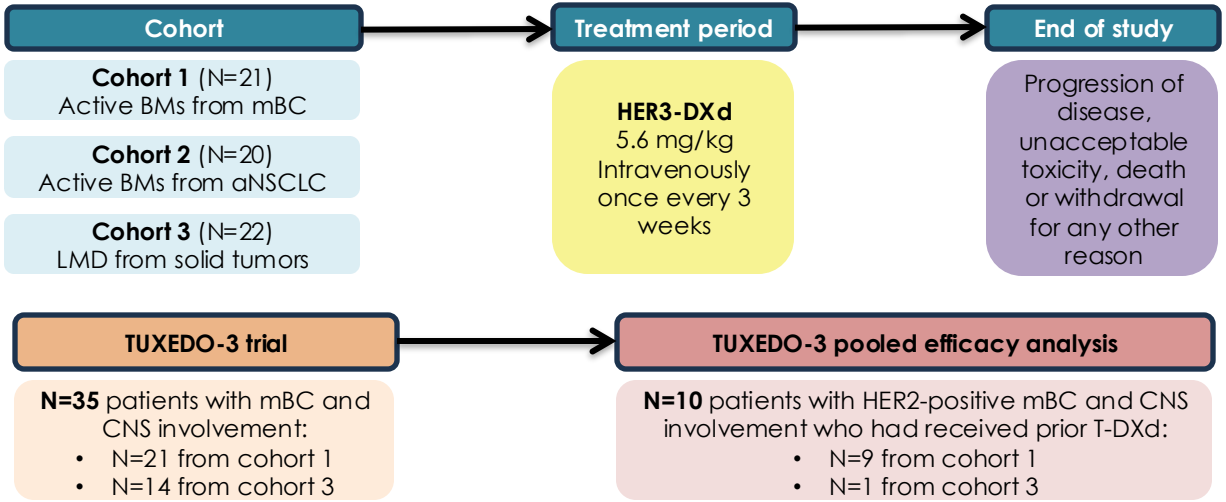
- TUXEDO-3 (NCT05865990) is an international, multicenter, multicohort, single-arm, phase II trial that showed central nervous system (CNS) activity of patritumab deruxtecan (HER3-DXd) in patients with metastatic breast cancer (mBC) and active BMs (cohort 1), advanced non-small cell lung cancer and active BMs (cohort 2), and leptomeningeal disease (LMD) from any solid tumors (cohort 3).

- The DESTINY-Breast12 trial demonstrated clinically meaningful activity of trastuzumab deruxtecan (T-DXd) in patients with HER2-positive BC BMs previously treated with trastuzumab emtansine (T-DM1). However, evidence remain scarce regarding optimal treatment strategies for patients progressing on T-DXd.

- We performed an unplanned *post-hoc*, descriptive, pooled efficacy analysis of TUXEDO-3 patients with HER2-positive mBC and CNS involvement who had received prior T-DXd

METHODS

- Patients with HER2-positive mBC with active BMs (cohort 1) or LMD (cohort 3) who had received T-DXd prior to start the TUXEDO-3 trial were eligible for this analysis.
- HER3-DXd (5.6 mg/kg) was intravenously administered in 21-day cycles until progression of disease, unacceptable toxicity, death or withdrawal for any other reason.
- This analysis evaluated progression-free survival (PFS) for bicompartmental, intracranial and extracranial lesions, and overall survival (OS).
- Survival estimates were analyzed using the Kaplan-Meier method and 95% CI.



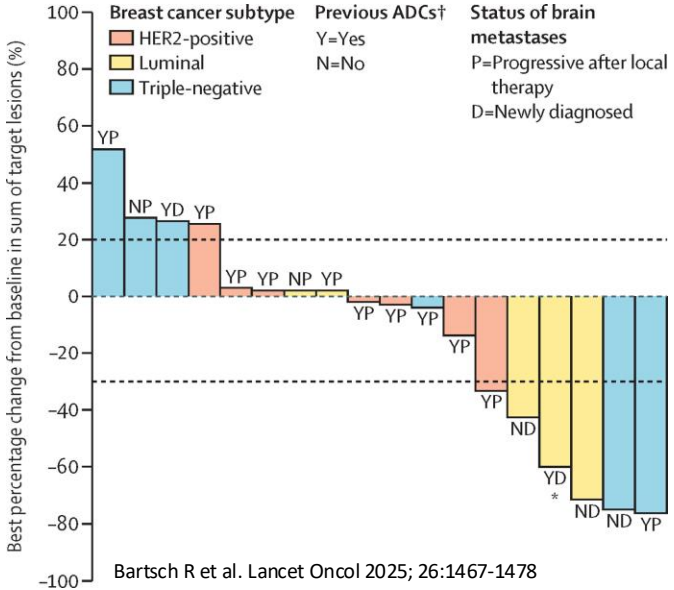
aNSCLC: Advanced non-small cell lung cancer
BMs: Brain metastases
CNS: Central nervous system
HER2: Human epidermal growth factor receptor 2
HER3-DXd: Patritumab deruxtecan
LMD: Leptomeningeal disease
mBC: Metastatic breast cancer
T-DXd: Trastuzumab deruxtecan

RESULTS (1)

- From 12 December 2023 to 2 July 2024, a total of 35 patients with mBC and CNS involvement (active BMs [N=21] and LMD [N=14]) were enrolled in the TUXEDO-3 study. Ten (28.6%) patients had HER2-positive mBC (9 with active BMs and 1 with LMD, who also had parenchymal BMs.

- At data cutoff (6 September 2025), no patients remained on treatment and one continued in follow-up.

Characteristics	*n*=10
Median age (range), years	54.5 (35.0-75-0)
Median follow-up (range), months	8.1 (2.0-15.2)
Median treatment duration (range), months	3.2 (0.0-10.3)
Previous treatment lines for aBC, range	4 (2-7)
Prior T-DXd, n (%)	10 (100)
Prior tucatinib, n (%)	6 (60)
Prior T-DM1, n (%)	3 (30)
T-DXd as last treatment line prior to HER3-DXd	3 (30)
Median time from last T-DXd (range), months	12.4 (0.5-26.7)



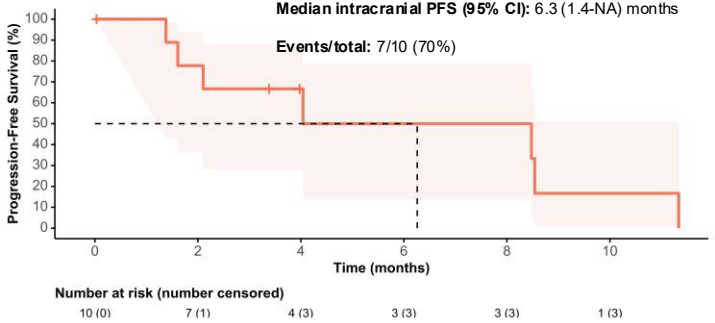
TUXEDO-3 cohort 1: Intracranial Response Rate (RANO-BM) in patients with post-baseline cMRT

Bartsch R et al. Lancet Oncol 2025; 26:1467-1478

RESULTS (2)

- Median PFS was 6.3 months for intracranial lesions as per RANO-BM criteria (Figure A), and 11.3 months for extracranial lesions (Figure B) and 6.3 months for bicompartmental lesions (Figure C) as per RECIST v.1.1. Median OS was 8.1 months (Figure D).

A



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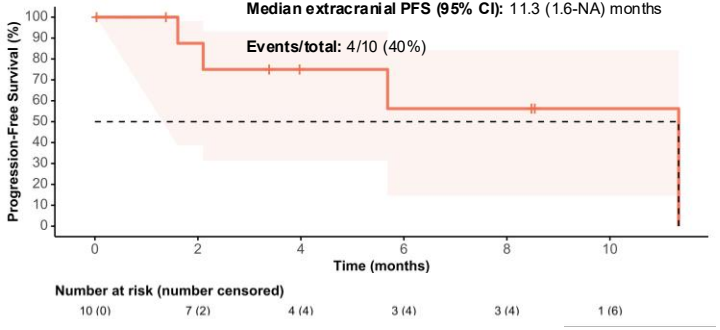

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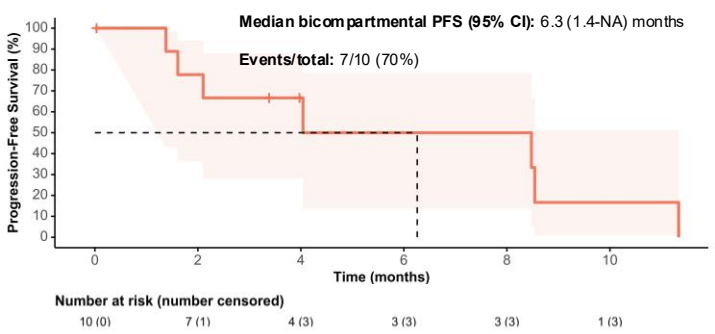

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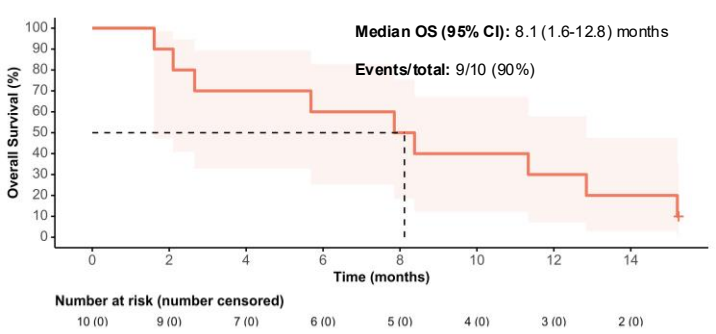

CI: Confidence interval

NA: Not achieved

OS: Overall survival

PFS: Progression-free survival

CONCLUSIONS

- HER3-DXd showed promising PFS and OS in patients with HER2-positive mBC and active BMs/LMD who had been previously treated with T-DXd.

- Despite the small sample size, these findings suggest a potential strategy for sequential ADC treatment in a patient population with no established standard of care.

- With a median PFS exceeding 6 months, further investigation of HER3-DXd in patients with CNS involvement progressing on T-DXd is warranted.

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