San Antonio Breast Cancer Symposium - December 6-10, 2022

Real World Data for Trastuzumab Deruxtecan in HER2-Positive Metastatic Breast Cancer Patients with Brain Metastases

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BACKGROUND

Trastuzumab deruxtecan (T-DXd) improves outcomes in HER2-positive (HER2+) metastatic breast cancer (MBC) patients, including patients with previously treated stable brain metastases (BMs).

Approximately 10% of patients with HER2+ MBC present with BMs at initial diagnosis and up to 20% go on to develop BMs.[1]

Multiple HER2-directed agents are available for use in the treatment of HER2+ MBC. Single-agent fam-trastuzumab deruxtecan-nxki (T-DXd) and tucatinib in combination with trastuzumab and capecitabine have both demonstrated efficacy in HER2+ MBC patients with BMs.[2,3] However, the appropriate sequencing of HER2-targeted therapy for patients with HER2+ BMs is unknown.

METHODS

- Retrospective cross-sectional study of T-DXd prior authorization (PA) approvals by OncoHealth for HER2+ MBC.
- Data source: OncoHealth RWD including medical records, utilization management, and claims from 1/17/20 to 6/21/22.
- Imaging reports of CNS metastases prior to and while on T-DXd were reviewed.
- Reported CNS real-world overall response rate (rwORR) per RECIST 1.1, real-world disease-control rate (rwDCR).

OBJECTIVES

- Describe the characteristics of HER2+ MBC patients with BMs prior to T-DXd use.
- Analyze duration on treatments and sequencing of T-DXd in relation to tucatinib.

Table 1: Patient Characteristics

Patient Characteristics	T-DXd in patients with BMs (n=41) N(%)	T-DXd in patients without BMs (n=105) N(%)
Age <60 Age ≥60	23 (56) 18 (44)	38 (36) 67 (64)
Hormone status HR+ HR-	 33 (80) 8 (20)	 72 (69) 33 (31)
No. of HER2-targeted prior lines of therapy 0 1 2 3 >3	 1 (2) 7 (17) 15 (37) 6 (15) 11 (27)	 7 (7) 24 (23) 39 (37) 17 (16) 12 (11)
Visceral disease	41 (100)	82 (78)
De novo MBC	24 (59)	42 (40)

Table 2: Treatment Profile of T-DXd Patients with BMs

Characteristic	T-DXd patients with BMs (n=41) N(%)
Brain Mets Symptomatic Asymptomatic N/A	 22 (54) 6 (15) 13 (31)
Treated BMs Untreated BMs	37 (90) 4 (10)
Prior treatment of BMs SRS WBRT Craniotomy RT unspecified	 22 (54) 14 (34) 8 (20) 4 (10)
Median time from prior RT/Craniotomy to T-DXd (days)	252 (0-972)
Systemic treatment Tucatinib prior to T-DXd Tucatinib after T-DXd No exposure to Tucatinib	 9 (22) 6 (15) 26 (63)

RESULTS

- BMs were identified in 28% (41/146) patients with HER2+ MBC prior to initiating T-DXd. (Table 1)
- Among the 41 patients with BMs, 56% were < 60 years of age, 80% were HR+.
- De novo MBC was seen in 59% of patients and 27% had > 3 lines of prior therapies.
- Median number of prior MBC therapies was 2 (range: 0-8). 78% (32/41) did not receive tucatinib-based therapy prior to T-DXd.
- Tucatinib-based therapy was the most common subsequent line of therapy after T-DXd in patients with further therapy (6/8). (Table 2)
- 19 of 41 (46%) had symptomatic BMs.
- Prior local therapies for the BMs included craniotomy in 19.5% and brain radiotherapy in 87.8% prior to T-DXd. (Table 2)
- Limitations include that this observational study shows associations, not causation. Also, data were focused on T-DXd PAs. Data on tucatinib-based therapy without subsequent T-DXd was not evaluated.

Table 3: Real-World Endpoints in T-DXd Patients with BMs

Results	T-DXd patients with BMs (n=41) N(%)
CNS Response CR PR SD NA	 2 (5) 7 (17) 12 (29) 14 (34)
Disease Control Rate (rwDCR) (CR + PR + SD)	19 (46)
Median Duration on Tucatinib before T-DXd (days)	281.5 (20-526)
Median duration on T-DXd before Tucatinib (days)	436 (155, 564)

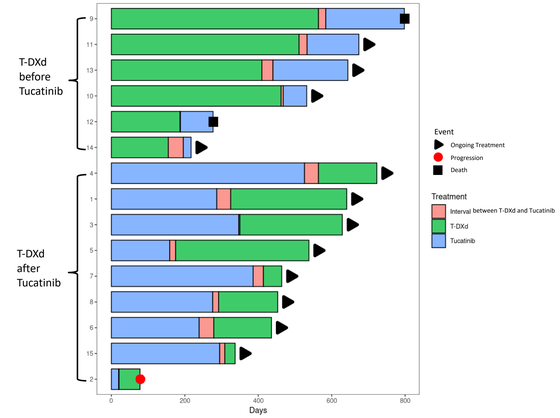
DISCUSSION

DESTINY-Breast03 included patients with clinically stable, previously treated BMs. Among 114 patients with stable BMs, the hazard ratio for disease progression or death was 0.38, favoring T-DXd (95% CI 0.23-0.64).[4] In HER2CLIMB among patients with BMs, the tucatinib arm experienced improved median OS (21.6 vs 12.5 months; HR 0.60, 95% CI 0.44-0.81) and CNS PFS (9.9 versus 4.2 months; HR 0.32, 95% CI 0.22-0.48).[5,6] However, it is unclear the appropriate sequencing of these two drugs in patients with BMs.

Patients who started with tucatinib were on that treatment for a median duration of 281.5 days (range 20-526). Patients who started with T-DXd were on that treatment for a median duration of 436 days (range 155-564). In this study we found physicians chose T-DXd prior to tucatinib for symptomatic brain metastases (20/22).

These findings are important as it provides clinically meaningful data on disease control and appropriate sequencing of these two agents that have activity on intracranial and leptomeningeal disease. We also found the majority of patients had > 3-month interval from recent BM treatment (radiation or surgery) and CNS disease control after initiation of T-DXd was attributable to the systemic therapy.

Figure 1. Sequence and Duration of T-DXd and Tucatinib in HER2+ MBC Patients with Brain Metastases



CONCLUSION

- In the real world, patients with symptomatic, progressing BMs are more likely to receive T-DXd prior to tucatinib-based therapy, with longer duration of stability and treatment, implying ***improved disease management in the T-DXd-to-tucatinib sequence***.
- Appropriate sequencing of available treatments with activity on BMs such as T-DXd and tucatinib-based therapy needs to be further studied.
- We will evaluate outcomes data with longer follow-up and further report the impact of T-DXd in HER2+ MBC patients with BMs, including which sequencing strategy leads to better outcomes.

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