Real-world patient characteristics and treatment patterns associated with tucatinib therapy in patients with HER2-positive metastatic breast cancer

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Objective

The objective of this study was to describe patient characteristics, treatment patterns, and clinical outcomes for tucatinib-based treatment in the real-world setting both overall and immediately following fam-trastuzumab deruxtecan (T-DXd).

Conclusions

These data support the evidence for durable effectiveness of tucatinib-based treatment in patients with human epidermal growth factor receptor 2 (HER2)–positive metastatic breast cancer (MBC) with and without brain metastases and across multiple lines of therapy.

Real-world time to next treatment (rwTTNT, as a proxy for progression-free survival [PFS][1]) with tucatinib-based treatment was slightly longer in patients treated in second-line (2L) or third-line (3L) compared with the overall population.

Response to tucatinib-based treatment was observed in the post-T-DXd setting.

Almost half of patients continued to receive tucatinib-based treatment at 12 months, suggesting durable tolerability and effectiveness of treatment.

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Background

- Tucatinib is an oral HER2-targeted therapy approved by the United States Food and Drug Administration in April 2020 for use in combination with trastuzumab and capecitabine for patients with previously treated HER2-positive MBC.[2]
- In the pivotal phase 2, randomized, placebo-controlled HER2CLIMB trial, addition of tucatinib to trastuzumab and capecitabine conferred a statistically significant and clinically meaningful improvement in median overall survival (OS; 21.9 [18.3–31.0] months) and PFS (7.8 [7.5–9.6] months) with median duration of therapy 7.3 months.[3]
  - In HER2CLIMB 48% of patients had active or stable brain metastases.[3]
- Due to the rapidly evolving treatment landscape, the impact of tucatinib-based therapy following other emerging treatments, such as T-DXd, is unknown.

Methods

- This retrospective study included patients in the Komodo Health Sentinel database (closed administrative health claims data in the US) diagnosed with MBC between Jan 1, 2017, and Sep 3, 2022, and initiating tucatinib-based treatment following its approval in April 2020.
- Patients were required to have 6 months continuous enrollment prior to the metastatic diagnosis date. Baseline demographic and clinical characteristics were described for the time period prior to initiating tucatinib-based treatment.
- Key outcomes measured from initiation of tucatinib-based treatment were rwTTNT (as a proxy for PFS[3]), real-world time to discontinuation (rwTTD), and persistence (proportion continuing treatment at prespecified timepoints for patients with sufficient continuous enrollment); for the overall population and for patients receiving tucatinib-based treatment immediately after T-DXd.
- Time-to-event analyses were conducted using the Kaplan–Meier method to account for censoring.

Results

Patient characteristics

- 528 patients received tucatinib-based treatment and met all inclusion criteria (**Table 1**).
- Overall, 400 patients (76%) had preexisting brain metastases prior to initiating tucatinib-based treatment and had broadly similar characteristics to those without brain metastases.
- Among patients receiving tucatinib-based treatment immediately following T-DXd (n=61):
  - 22 (36%) had de novo metastatic breast cancer at diagnosis.
  - 36 (59%) had brain metastases.
  - Median (IQR) prior lines of therapy was 3 (3–4).
  - Median (IQR) time from metastatic diagnosis to tucatinib-based treatment initiation was 32 (22–40) months.
  - Median (IQR) duration of follow-up was 5.7 (2.5–11.6) months.
- A higher proportion of patients without brain metastases received T-DXd as a prior treatment (21% vs 10% with brain metastases).

Treatment patterns

- Of the 528 patients in the analysis, 57 (11%), 164 (31%), 154 (29%), and 153 (29%) received tucatinib-based treatment in first-line (1L), 2L, 3L and 4L or later (4L+), respectively.
- Of patients with brain metastases (n=400; 76%), 43 (75% of all 1L-treated patients), 138 (84%), 111 (72%), and 108 (71%) received tucatinib-based treatment in 1L, 2L, 3L, and 4L+, respectively.

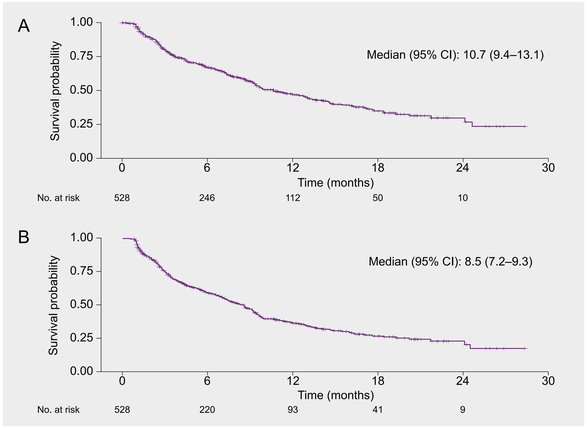
Table 1. Baseline characteristics for patients with HER2-positive MBC receiving tucatinib-based treatment in the Komodo Health Sentinel database

Characteristic	Overall (N=528)
Age (years), median (range)	54 (46–60)
De novo at diagnosis, n (%)	243 (46)
Sites of metastasis at metastatic diagnosis date,[a] n (%)	
Brain	370 (70)
Bone	352 (67)
Lung	218 (41)
Liver	246 (47)
Time to tucatinib-based treatment initiation[b] (months), median (IQR)	19 (9–32)
Follow-up (months), median (IQR)	9 (4–17)
Prior lines of therapy, median (IQR)	2 (1–3)
Prior treatments for metastatic disease,[a] n (%)	
Fam-trastuzumab deruxtecan (T-DXd)	68 (13)
Trastuzumab-DM1 (T-DM1)	231 (44)
Trastuzumab	425 (80)
Pertuzumab	378 (72)

[a]Not mutually exclusive. [b]Time from metastatic diagnosis to tucatinib-based treatment initiation.
HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer.

- In 2L, tucatinib-based treatment was most commonly received following trastuzumab- and pertuzumab-based treatment.
- In 3L, tucatinib-based treatment was most commonly received following T-DM1–based treatment and prior to T-DXd–based treatment.
- Most patients (n=377; 71%) received tucatinib in combination with trastuzumab and capecitabine.
- 151 patients did not receive the full triplet regimen: 75 (14%) received tucatinib and capecitabine without trastuzumab; 52 (10%) received tucatinib and trastuzumab without capecitabine; 19 (4%) received tucatinib monotherapy; and 5 (1%) received other anticancer therapies alongside tucatinib.

Figure 1. Kaplan–Meier curve for (A) rwTTNT and (B) rwTTD among patients with HER2-positive MBC receiving tucatinib-based treatment in the Komodo Health Sentinel database



HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; rwTTD, real-world time to discontinuation; rwTTNT, real-world time to next treatment.

Table 2. rwTTNT and rwTTD for patients with HER2-positive MBC receiving tucatinib-based treatment in the Komodo Health Sentinel database

Effectiveness outcome	Overall (N=528)	2L + 3L (n=318)	Following T-DXd (n=61)
rwTTNT (months), median (95% CI)	10.7 (9.4–13.1)	11.5 (9.6–14.4)	7.5 (5.0–13.3)
Patients alive who had not started subsequent treatment, % (95% CI)			
6 months	67.5 (63.2–72.0)	72.2 (67.2–77.6)	53.7 (40.0–71.4)
12 months	47.0 (42.0–52.6)	54.7 (48.7–61.5)	29.6 (16.8–52.2)
rwTTD (months), median (95% CI)	8.5 (7.2–9.3)	9.1 (7.7–9.9)	7.3 (3.2–9.5)

2L, second-line; 3L, third-line; HER2, human epidermal growth factor receptor 2; MBC; metastatic breast cancer; rwTTD, real-world time to discontinuation; rwTTNT, real-world time to next treatment; T-DXd, fam-trastuzumab deruxtecan.

- 61 (12%) patients received tucatinib-based treatment immediately following T-DXd (12 patients received tucatinib-based treatment in 2L/3L, and 49 in 4L+; median 4L). Median (IQR) duration of T-DXd therapy prior to tucatinib-based treatment was 5.3 (2.1–8.3) months.

rwTTNT and rwTTD

- Median (IQR) follow-up from tucatinib-based treatment initiation was 9 (4–17) months.
- Overall median rwTTNT was 10.7 months (**Figure 1A**) and slightly longer in patients receiving tucatinib-based treatment in 2L or 3L (11.5 months; **Table 2**).
- Overall median rwTTD was 8.5 months (**Figure 1B**) and also slightly longer in patients receiving tucatinib-based treatment in 2L or 3L (9.1 months; **Table 2**).
- rwTTNT and rwTTD for patients receiving tucatinib-based treatment following T-DXd (median 4L of therapy) were 7.5 (5.0–13.3) months and 7.3 (3.2–9.5) months, respectively.
- Persistence at 12 months was 46% overall, 49% in 2L or 3L, and 40% following T-DXd (**Figure 2**).

Figure 2. Persistence for patients with HER2-positive MBC receiving tucatinib-based treatment in the Komodo Health Sentinel database

Persistence is the proportion of patients with follow-up and still on therapy at each timepoint. Figure shows median line of therapy in which patients received tucatinib-based treatment and the percentage of patients with brain metastases prior to initiating tucatinib-based treatment.
2L, second-line; 3L, third-line; 4L, fourth-line; HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; NA, not assessed due to insufficient number of patients; T-DXd, fam-trastuzumab deruxtecan.

Limitations

- These analyses are unadjusted and purely descriptive in nature. No adjustment was made for confounding factors.
- Further stratification of cohorts by both line of therapy and brain metastases would have resulted in sample sizes too small for meaningful analyses.
- Findings may not be generalizable to patient populations not represented in the Komodo Health Sentinel database.