Real-World Clinical Outcomes of Ujvira® (Trastuzumab Emtansine Biosimilar) in HER2-Positive Breast Cancer: A Retrospective Observational Study in Indian Patients

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Abstract: *Background*: HER2-positive breast cancer is an aggressive subtype requiring targeted therapies. Trastuzumabemtansine has shown efficacy in clinical trials but remains costly, limiting accessibility in low-resource settings. Ujvira®, a biosimilar of T-DM1, offers a more affordable alternative. This study evaluates its real-world efficacy and safety in Indian patients.

Methods: This is a retrospective analysis of HER2-positive breast cancer patients treated with Ujvira® between January 2022 and December 2023 at a tertiary care center in India. Primary endpoint was progression-free survival (PFS). Secondary endpoints included overall survival (OS), safety and clinical response per RECIST v1.1. Kaplan-Meier analysis was used for survival estimates; comparisons across lines of therapy were assessed using the log-rank test.

Results: The study included 23 patients (median age 51 years, range 35–72), with 74% having an ECOG performance status of 0–1. T-DM1 biosimilar was administered in a palliative setting to 20 patients and as adjuvant therapy to 3 patients. Among the palliative group, 45% had brain metastases at baseline, and treatment was given as second-line in 45%, third-line in 40%, and fourth-line or later in 15% of cases. Overall, 50% achieved a partial response, 35% had stable disease, and 15% showed disease progression. At a median follow-up of 15 months, 30% remained on treatment, 65% had progressed, and one patient was lost to follow-up. The median PFS was 9.6 months, and the median OS was 14 months. In the adjuvant setting, 2 of 3 patients completed 14 cycles, while one progressed with brain metastases after 9 cycles. The most common adverse events were thrombocytopenia, anemia, and transaminitis, with grade 3 events occurring in 26% and grade 4 events in 4% of patients.

Conclusion: Ujvira® showed efficacy comparable to innovator T-DM1 in terms of PFS, supporting its role in HER2-positive breast cancer management. However, shorter OS may reflect high brain metastases rates and limited access to post-progression therapies. The study's retrospective design, small sample size, and selection bias limit generalizability. Larger prospective studies are needed to validate findings.

Keywords: HER2-positive breast cancer, trastuzumabemtansine, T-DM1, Ujvira®, biosimilar, real-world study, progression-free survival, overall survival.

1. INTRODUCTION

HER2-positive breast cancer, which accounts for 15-20% of all breast cancers, is associated with an aggressive disease course and poor prognosis [1]. Trastuzumab, a humanized IgG1 monoclonal antibody, was the first targeted therapy approved in year 2000 for HER2-positive breast cancer, significantly improving survival. However, resistance to trastuzumab often develops, necessitating second-line therapies.[2]

Trastuzumabemtansine (T-DM1), an antibody-drug conjugate (ADC) combining trastuzumab with the cytotoxic agent emtansine, was developed to overcome this resistance [3-5]. T-DM1 targets HER2-positive cells, delivering chemotherapy directly to the tumor. In clinical trials, such as EMILIA and TH3RESA, T-DM1 demonstrated superior progression-free survival (PFS) and overall survival (OS) compared to other regimens, including lapatinib plus capecitabine [6-7]. T-DM1 is now the preferred third-line treatment for HER2-positive breast cancer.

Despite its efficacy, T-DM1's high cost limits accessibility, particularly in low-resource settings like India, where economic constraints often restrict access to advanced therapies. Biosimilars, such as Ujvira®, developed by Zydus Life sciences Ltd. and approved by the Drug Controller General of India (DCGI), offer a cost-effective alternative, potentially improving access to life-saving treatments while maintaining comparable efficacy and safety. Real-world data is critical for biosimilars, as it provides evidence of their performance in diverse patient populations and healthcare settings, complementing controlled clinical trial results and supporting their broader adoption. This study aims to evaluate the real-world efficacy and safety of Ujvira® in Indian patients with HER2-positive breast cancer.

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Table 1: Characteristics of Patients Treated with TDM-1

Variables	Frequency (n=23)	Percentage
Age, median	51 (35-72)	
Age group		
<60 years	19	82.6%
≥61 years	4	14.3%
ECOG Performance status		
1	17	74.0%
2	5	22.0%
3	1	4.0%
ER/PR status at baseline		
Positive	8	34.8%
Negative	15	65.2%
Intent of treatment		
Adjuvant	3	13.0%
Palliative	20	87.0%
n=20 (palliative setting)		
Site of disease involvement		
Visceral	19	95.0%
Non-visceral	1	5.0%
Visceral Metastasis		
Lung	10	50.0%
Brain	9	45.0%
Liver	7	35.0%
Prior systemic therapy		
Anthracycline based	8	40.0%
Taxane	20	100.0%
Platinum	8	40.0%
Capecitabine	12	60.0%
Gemcitabine	3	15.0%
Endocrine therapy	7	35.0%
Prior anti-Her2 therapy		
Trastuzumab	20	100.0%
Pertuzumab	1	5.0%
Lapatinib	10	50.0%
Trastuzumab re-treatment	5	25.0%

2. MATERIALS AND METHODS

Study Design

This retrospective, single-centerobservational study was conducted at a tertiary care hospital in Visakhapatnam. It analyzed data from HER2-positive breast cancer patients who received the T-DM1 biosimilar from January 2022 and December 2023. Patient demographics, clinical characteristics, treatment history, and outcomes were collected from hospital records.

Study Population

This study included HER2-positive breast cancer patientswho received T-DM1 biosimilar as adjuvant or palliative therapy. Baseline demographics, cancer

stage, ER/PR status, HER2 IHC, and HER2 FISH (if IHC 2+) were documented. Patients were eligible regardless of prior use of trastuzumab or other HER2-targeted therapies or the presence of baseline visceral metastases, including central nervous system (CNS) involvement.

Outcomes

The primary endpoint was progression-free survival (PFS) in palliative therapy setting, measured from the initiation of T-DM1 biosimilar therapy until disease progression or death from any cause. Secondary endpoints included overall survival (OS), safety, and clinical response. OS was measured from the start of T-DM1 biosimilar treatment until death. Safety was evaluated based on the severity of adverse events (AEs), graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0. Clinical response was assessed using RECIST criteria version 1.1, categorizing patients as having complete response (CR), partial response (PR), progressive disease (PD), or stable disease (SD).

Statistical Analysis

Descriptive statistics were used to summarize patient demographics, treatment regimens, and outcomes. Kaplan-Meier survival curves with 95% confidence intervals (CIs) were used to estimate PFS and OS. Differences between groups were assessed using the log-rank test, with p-values <0.05 considered statistically significant.

3. RESULTS

A total of 23 breast cancer patients were analyzed, with a median age of 51 years (IQR: 45–58). At baseline, most patients were at stage III (52.1%), followed by stage IV (39.1%) and stage II (8.2%). The majority (n=20) received T-DM1 biosimilar in a palliative setting, while a smaller group (n=3) received it in an adjuvant setting. Among the palliative cohort, 95% (n=19) had visceral metastases, with the most

Table 2: Distribution of patients according to the line of therapy with palliative intent

Line of therapy	Initial line of target drug therapy for patients	
	Frequency	Percentage
2nd line	9	45.0%
3rd line	8	40.0%
4th line	2	10.0%
6th line	1	5.0%

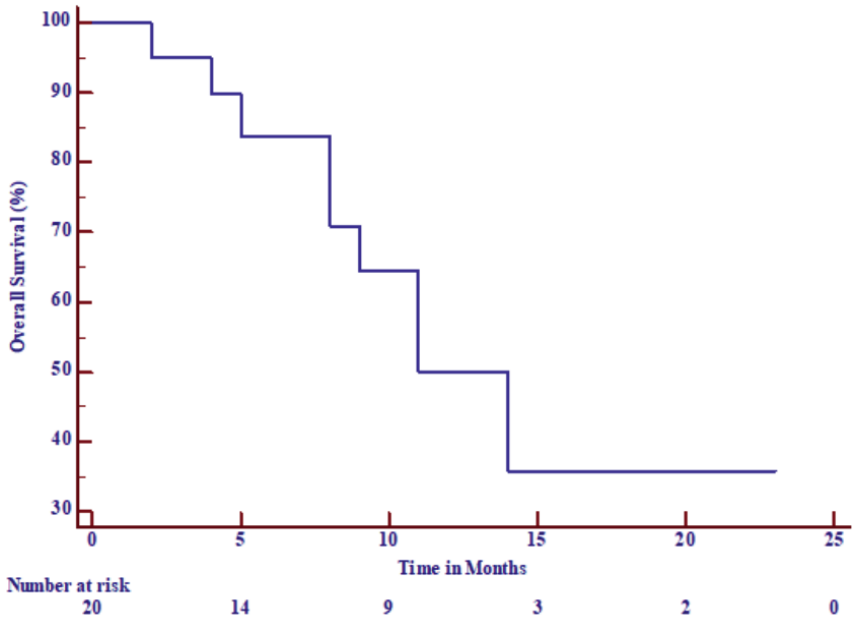

Figure 1: Overall survival of patients who were treated with T-DM1 in palliative setting (Median OS = 14 months).

common sites being the lung (50%), brain (45%), and liver (35%).

In the palliative group, T-DM1 biosimilar was administered as a 2nd-line treatment in 45% of patients and as a 3rd-line treatment in 40% (Table **2**). Overall, 50% achieved PR, 35% had SD, and 15% experienced PD. The median OS was 14 months, with no significant difference between those receiving TDM-1 as 2nd-line (15 months) vs ≥3rd-line therapy (16 months) (HR = 0.51, 95% CI: 0.11 to 2.37) (not statistically significant, p = 0.39) (Figure **1** and **2**). Similarly, the median PFS was 9.6 months, with no statistically significant difference between second-line and later-line settings (HR = 0.58, 95% CI: 0.10 to 3.49, p = 0.57) (Figure **3** and **4**).

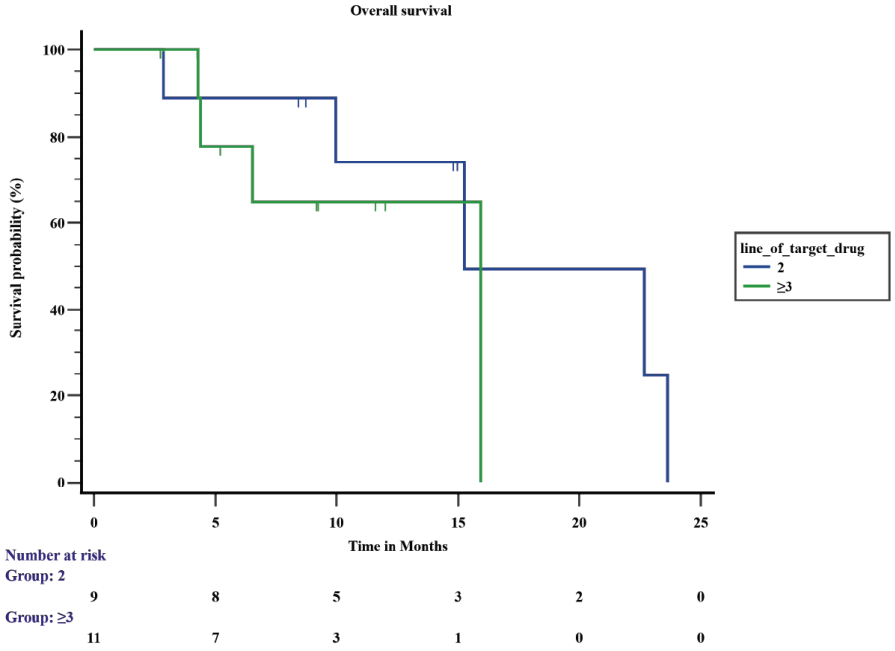

Figure 2: OS of patients who were treated with T-DM1 in 2nd line (n=9) vs≥3rd-line therapy (n=11).

Median OS for 2nd line of treatment = 15 months.
Median OS for ≥3 line of treatment = 16 months.
Logrank test = 0.74; p = 0.39.

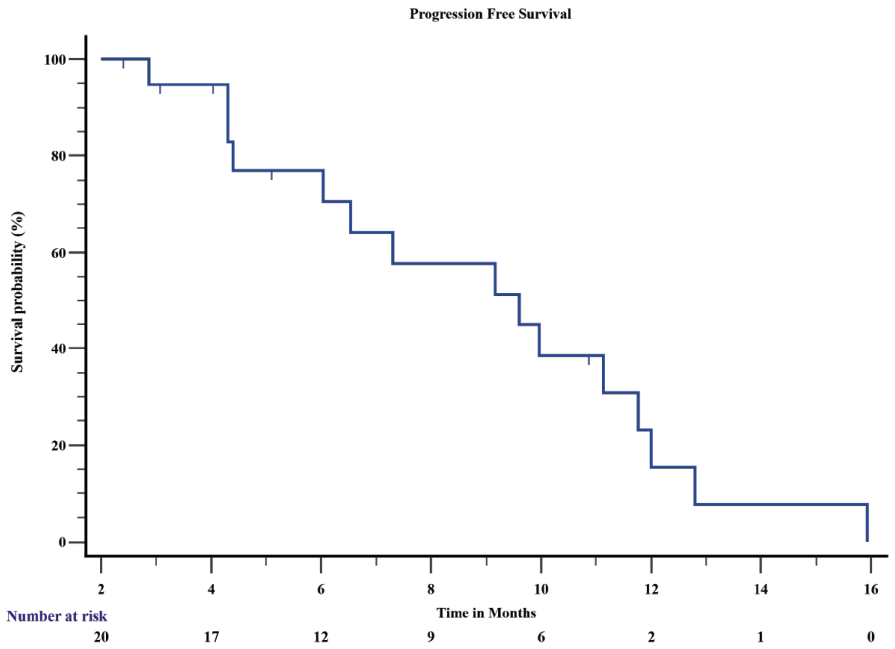

Figure 3: Progression free survival of patients who were treated with T-DM1 in palliative setting (Median PFS = 9.6 months).

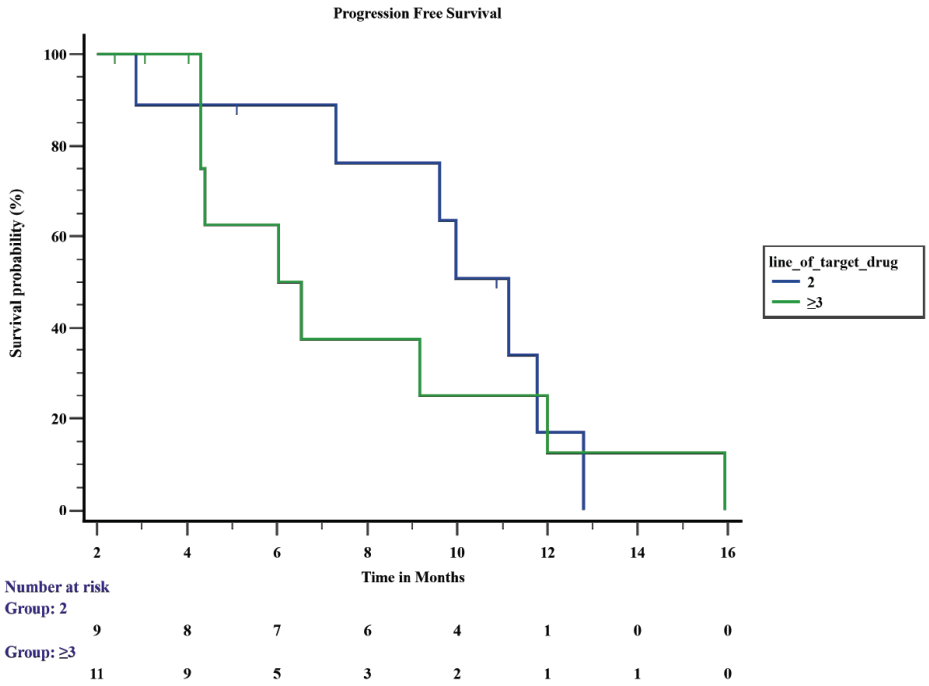

Figure 4: PFS of patients who were treated with T-DM1 in 2nd line (n=9) vs≥3rd-line therapy (n=11).

Median PFS for 2nd line of treatment = 11 months.
Median PFS for ≥3 line of treatment = 6 months.
Logrank test = 0.33; p = 0.57.

In the adjuvant setting, two of three patients completed 14 cycles of T-DM1, while one experienced disease progression with brain metastases after nine cycles.

Safety analysis revealed that 30.4% of patients experienced grade 3 or higher adverse events, with thrombocytopenia (21.7%), anemia (8.6%), and transaminitis (4.3%) being the most common severe toxicities (Table **3**).

At a median follow-up duration of 15 months, 30% of patients remained on T-DM1 biosimilar, 65% experienced disease progression, and one patient was lost to follow-up.

4. DISCUSSION

This real-world study provides valuable insights into the effectiveness and safety of Ujvira®in HER2-positive breast cancer, particularly in the second-line setting in

Table 3: Adverse events

Adverse events	Events of any grade	Events of Grade 3 or above
Any event	22 (95.6%)	7 (30.4%)
Specific events		
Anemia	14 (60.8%)	2 (8.7%)
Thrombocytopenia	14 (60.8%)	5 (21.7%)
Transaminitis	14 (60.8%)	1 (4.3%)
Hyperbilirubinemia	2 (8.7%)	0
Hyperkalemia	1 (4.3%)	0
Hyponatremia	1 (4.3%)	0
Liver dysfunction	1 (4.3%)	0
Myalgia	2 (8.7%)	0
Neutropenia	1 (4.3%)	0
LV Dysfunction	1 (4.3%)	0

developing nations, where access to newer HER2-targeted therapies is often limited. The EMILIA trial established T-DM1 as the standard second-line therapy, demonstrating a median PFS of 9.6 months and an OS of 30.9 months [6]. In our study, T-DM1 biosimilar showed a comparable median PFS of 11 months but a shorter OS of 15 months, likely due to a higher incidence of brain metastases (45%), variability in real-world treatment sequencing, and restricted availability of novel agents such as trastuzumabderuxtecan (T-DXd) and tucatinib, which have superior CNS activity but remain financially inaccessible in many developing nations [6-8]. The TH3RESA trial, which evaluated T-DM1 in more heavily pretreated patients, reported a median PFS of 6.2 months and an OS of 22.7 months [7]. Our study observed a PFS of 6 months in third-line or later settings, but with a shorter OS of 16 months, possibly reflecting disparities in post-progression performance status and treatment options. In the adjuvant setting, the KATHERINE trial demonstrated a significant improvement in invasive disease-free survival (iDFS) with T-DM1 (HR = 0.50, $p < 0.001$), but in our study, only three patients received T-DM1, limiting meaningful comparisons [10]. Regarding safety, the toxicity profile of T-DM1 biosimilar was comparable to that of innovator T-DM1 in similar clinical trials, with grade ≥3 AEs occurring in 30.4% of patients, primarily thrombocytopenia (21.7%), anemia (8.6%), and transaminitis (4.3%), which is slightly lower than the rates reported in EMILIA (41%) and TH3RESA (47.1%) [11-13].

A key limitation of this study is the small sample size (n=23), which may restrict the generalizability of the findings and the ability to draw robust conclusions, particularly in the adjuvant setting. Additionally, comparisons with the EMILIA, TH3RESA, and KATHERINE trials should be interpreted cautiously, as these are non-randomized, historical comparisons that may be influenced by differences in patient populations, treatment settings, and access to subsequent therapies [6-7,10].

The availability of Ujvira® has the potential to significantly impact treatment equity in India by providing a cost-effective alternative to innovator T-DM1 and other novel HER2-targeted therapies. As a biosimilar, Ujvira® offers a more affordable option for patients progressing on trastuzumab and taxane-based therapies, addressing financial barriers in resource-limited settings where access to expensive agents like T-DXd and tucatinib is often unattainable. By improving access to effective second-line treatment, Ujvira® could reduce disparities in care and enhance outcomes for HER2-positive breast cancer patients in India.

Treatment sequencing in real-world settings often differs from clinical trials due to variations in resource availability, patient performance status, and physician preferences [14]. Unlike the controlled settings of trials like EMILIA and TH3RESA, real-world patients may receive heterogeneous prior treatments or face delays in accessing subsequent therapies, particularly in developing nations [6-7]. These factors, combined with the high prevalence of brain metastases and limited CNS-directed options, contribute to the observed differences in OS and highlight the need for tailored treatment strategies in resource-constrained environments.

These findings reinforce the role of Ujvira® as an effective and safe second-line option for HER2-positive breast cancer in settings with restricted access to newer agents. However, the shorter OS underscores the challenges of managing advanced disease in resource-limited environments, emphasizing the urgent need for affordable CNS-directed therapies and improved post-progression treatment options. Future studies with larger cohorts and longer follow-up are essential to optimize treatment sequencing, explore cost-effective strategies, and enhance CNS disease management in these settings.

5. CONCLUSION

In this retrospective study, the T-DM1 biosimilar, Ujvira®, showed PFS outcomes similar to those reported for innovator T-DM1 in historical clinical trials, indicating its potential role in treating HER2-positive breast cancer. However, shorter OS was observed, possibly due to a higher incidence of CNS metastases and limited access to subsequent therapies. These findings are constrained by the study's small sample size, retrospective design, and non-randomized comparison, limiting their generalizability. While Ujvira® may serve as a cost-effective option in resource-limited settings, such as India, larger prospective studies are needed to validate these findings and clarify its role in treatment sequencing and long-term outcomes.

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CONFLICT OF INTEREST

The authors declare that there is no potential conflict of interest.

AUTHOR CONTRIBUTION

Each author has made substantial contributions to the conception, data acquisition, analysis, design, and interpretation of the study. We have also reviewed and approved the final version of the manuscript for submission.

ETHICAL STATEMENT

Ethical review and approval were waived for this study by the institution due to its retrospective nature. The authors are accountable for all aspects of the work, including data access, integrity, and analytical accuracy.

INFORMED CONSENT STATEMENT

Written informed consent was not required from patients due to the retrospective nature of the study, and patient data was retrieved from the Medical Records Department (MRD) after obtaining necessary permissions.

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