Concurrent Trastuzumab Deruxtecan and Radiation Therapy in HER2-positive and HER2-low Metastatic Breast Cancer: Assessing the efficacy

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BACKGROUND

In the recent **DESTINY-Breast** clinical trials, the addition of trastuzumab deruxtecan, a HER2-targeted therapy, has shown significant promise in treating HER2-positive metastatic breast cancer. Trastuzumab deruxtecan has also been found to improve progression-free survival (PFS) and overall survival (OS) compared with standard therapies in HER2-low expressing breast cancer.1 However, the efficacy and safety of combining trastuzumab deruxtecan (T-DXd) with radiation therapy (RT) remains uncertain, leading many oncologists to consider suspending trastuzumab deruxtecan during radiotherapy.

OBJECTIVES

The combination in patients with HER2-positive and HER2-low metastatic breast cancer (MBC) of Concurrent Trastuzumab Deruxtecan (T-DXd) and Radiation Therapy (RT) is not enough studied.

METHODS

We conducted a retrospective study including patients treated between November 2020 and Junuary 2024. Patients with HER2-positive and HER2-low MBC who received concurrent T-DXd and RT were identified. Data on patient demographics, treatment regimens, radiation doses, toxicity profiles, efficacy, and treatment discontinuations were collected. The toxicities were graded using CTCAE V5.0.

RESULTS

Population of 33 patients with HER2-positive and HER2-low MBC who underwent concurrent T-DXd and RT, were studied. The median follow-up (FU) was 14 months. There were 39.4 partial remissions and 9.4 attained complete remission. In addition, 39.4% experienced stable disease, and 12.1% faced disease progression necessitating a change in therapy. Safety assessment revealed that acute toxicities were mainly associated with systemic treatment. Survival analysis showed 11 deaths (33.3%) during the FU period, with a median overall survival of 26 months and median progression-free survival of 12 months.

RESULTS

Figure 1. Summary of Responding Metastatic Sites

Case	Metastatic site	RT technique	Dose (Gy)/Fx	CTV volume (cc)	PTV volume (cc)	Response
1	Right chest wall	VMAT	40.05/15	183.7	200.1	Complete remission
2	Right chest wall	VMAT	40.05/15	538.1	569.7	Complete remission
3	Left chest wall and left lymph nodes (L2-L4, IP, IMN)	VMAT	50/25	337.3	521.5	Complete remission
4	WBI + left frontal lesion	• *WBI* :VMAT • *Frontal lesion* : SRT	• *WBI*: 30/10 • *Frontal lesion*: 27/3	• *WBI*: 370.8 • *Frontal lesion*: 3.6	• *WBI*: 1605.6 • *Frontal lesion*: 5.7	Partial remission
5	Left femur	3D	30/10	282.6	545.2	Partial remission
6	Right acetabulum	VMAT	20/5	136.6	277.8	Partial remission
7	Femur and brain lesions (left temporal, basifrontal and parietal)	• *Femur* : 3D • *Brain lesions* : SRT	• *Femur*: 20/5 • *Brain lesions*: 9/3 • *Left temporal lesion*: 30/5	• *Femur*: 477.8 • *Brain lesions*: (Parietal: 1, Basifrontal: 0.4) • *Left temporal lesion*: 2.4	• *Femur*: 900.6 • *Brain lesions*: (Parietal: 1.7, Basifrontal: 0.8) • *Left temporal lesion*: 3.9	Partial remission
8	Vertebrae T7-T10 + left hip and femur	3D	30/10	Not specified	Not specified	Partial remission
9	Adrenal gland	SBRT	46/5	51.9	110.5	Partial remission
10	Vertebrae L4-L5 and left acetabulum	VMAT	20/5	• *L4-L5*: 46.7 • *Left Acetabulum*: 114.8	• *L4-L5*: 270.1 • *Left Acetabulum*: 239.9	Partial remission
11	Vertebrae T7-T9	VMAT	20/5	111.3	204.7	Partial remission
12	Vertebrae T5-T8 and T10-L1	VMAT	20/5	• *T5-T8*: 102.7 • *T10-L1*: 210.6	• *T5-T8*: 198.5 • *T10-L1*: 340.6	Partial remission
13	Vertebrae C2, T6 and right Humerus	VMAT	• *C2 and T6*: 20/5 • *Right Humerus*: 8/1	• *C2*: 69.1 • *T6*:102 • *Right Humerus*: 85.9	• *C2*: 140.4 • *T6*:204.5 • *Right Humerus*:174.9	Partial remission
14	Vertebrae L4-L5	VMAT	20/5	52.2	72.7	Partial remission
15	VertebraeT12-L1 and SI	VMAT	20/5	• *T12-L1*: 118 • *SI*: 182.6	• *T12-L1*: 221 • *SI*: 327.8	Partial remission
16	Vertebrae T5	VMAT	20/5	66.9	117.4	Partial remission

Figure 2. Patient's characteristics

Total, N (%)	33 (100)
Sex, n (%)	
Male	1 (3.03)
Female	32 (96.9)
Age, y	Median: 58.5 Range: 35-80
Histology, n (%)	
Ductal carcinoma	28 (84.8)
Lobular carcinoma	3 (9.09)
Others	2 (6.06)
HER2 status, n (%)	
0: 2	2 (6.06)
1+: 9	9 (27.2)
2+: 9	9 (27.2)
3+:12	12 (36.3)
Equivoque: 1	1 (3.03)
Hormone receptor expression (HR), n (%)	
HR+	25 (75.7)
HR−	8 (24.2)
Previous line of chemotherapy before T-DXd, n (%)	
Yes	33 (100)
No	0 (0)
Site of metastases, n (%)	
Bone	23 (63.6)
Brain	13 (27.2)
Chest wall	4 (12.1)
Nodal	2 (6.06)
Adrenal gland	1 (3.03)

CONCLUSION

The combination of T-DXd with RT demonstrates promising efficacy with a manageable safety profile. Further studies are warranted to fully elucidate the potential synergistic effects of this treatment regimen and its impact on patient outcome.

REFERENCES

Bouziane J, Loap P, Allali S, Escalup L, Pierga JY, Kirova Y. Concurrent Trastuzumab Deruxtecan and Radiation Therapy in HER2-positive and HER2-low Metastatic Breast Cancer: Assessing the Efficacy. Am J Clin Oncol. 2025 Jul 16. doi: 10.1097/COC.0000000000001237. Epub ahead of print. PMID: 40667835.

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