Real-world incidence and management of trastuzumab deruxtecan-associated interstitial lung disease

J. Hundal[1], N. Rehman[2], A. Abushamma[3], S. Haddad[2], M. Velimirovic[1], W. Wei[1], B. Honnekeri[2], X. Chen[1], M. Smith[1], M. Kruse[1], A. Ali[1]

[1]Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, [2]Internal Medicine, Cleveland Clinic, Cleveland, OH, [3]Internal Medicine, Cleveland Clinic, Akron, OH

Introduction

- Trastuzumab deruxtecan (T-DXd) is a HER2-directed antibody–drug conjugate with proven efficacy in HER2-positive, HER2-low, and HR+/HER2 ultra-low metastatic breast cancer (MBC) [1-3]
- Interstitial lung disease (ILD)/pneumonitis remains a serious treatment-related toxicity and can be fatal.
- Real-world data describing incidence, clinical course, and management patterns of T-DXd–associated ILD are limited, particularly outside clinical trials

Objective: To evaluate the real-world incidence, clinical course, and management of T-DXd–associated ILD in patients with metastatic breast cancer

Methods

- **Design:** Retrospective study
- **Population:** Patients with metastatic breast cancer treated with T-DXd between Dec 2019–Dec 2023.
- Data Collected: Demographics, tumor subtype, prior therapies, T-DXd line of therapy, outcomes, and ILD events.
- **Primary Endpoint:** Incidence of pneumonitis/ILD confirmed by clinical + radiographic assessment.
- **Analysis:** Descriptive statistics for baseline characteristics, ILD grading, management, and outcomes.

Results

Table 1: Patient Characteristics*

Characteristic	Category	Total No (N, %)	ILD Suspected (N, %)	ILD Confirmed (N, %)
Sex	Male	1 (1.3%)	1 (100%)	0 (0%)
	Female	75 (98.7%)	3 (4.6%)	7 (10.8%)
Race	White	66 (86.8%)	3 (4.6%)	7 (10.6%)
	Asian	1 (1.3%)	0 (0%)	0 (0%)
	Black or African American	5 (6.6%)	1 (20%)	0 (0%)
	Multiracial/Multicultural	4 (5.3%)	0 (0%)	0 (0%)
De Novo or Recurrent Metastatic Cancer	De Novo	39 (51.3%)	1 (2.6%)	2 (5.1%)
	Recurrent	5 (6.6%)	0 (0%)	1 (20%)
Receptor Status	ER+PR+	40 (52.6%)	0 (0%)	4 (10%)
	ER-PR-	18 (23.7%)	2 (11.1%)	2 (11.1%)
	Others	18 (23.7%)	2 (11.1%)	1 (5.6%)

Table 2: Management of ILD in Patients Treated with T-DXd

Presentation	Neo-adjuvant Therapy	Radiation	Toxicity Grade	Management	Steroid Duration (days)	Time to Resolution (days)	Prior Treatment with CDK4/6 inhibitor	HER2 status (IHC)	T-Dxd Line of Therapy	Prior T-DxD Cycles	Bronchoscopy
Recurrent	N/A	Gamma Knife	2	Prednisone	28	N/A	Palbociclib	2+	3rd	29	No
DeNovo	Herceptin Taxol	Spine	2	Prednisone	0	N/A	None	3+	3rd	16	No
Recurrent	Cyclophosphamide, doxorubicin, THP, trastuzumab pertuzumab	Gamma Knife	3	Prednisone	109	N/A	N/A	3+	3rd	1	No
De Novo	Trastuzumab Pertuzumab	No	3	Prednisone	106	64	None	3+	5th	2	No
De Novo	Letrozole	Gamma Knife	3	Prednisone	43	N/A	Ribociclib	2+	4th	6	Yes
Recurrent	N/A	No	5	Prednisone	23	20	N/A	3+	1st	18	No

*Percentages do not add up to a total of 100 due to missing data

Conclusion

- In this real-world cohort of patients with metastatic breast cancer treated with T-DXd, the incidence of all-grade ILD (7.9%) was lower than that reported in DESTINY trials (10–17.4%).
- Rate of Grade ≥3 ILD (5.2%) was higher than DESTINY trial rates (2.4–2.7%), and one ILD-related death occurred.
- None of the six confirmed ILD cases underwent bronchoscopy prior to initiating steroids, indicating variability in diagnostic practices.
- These findings highlight the importance of routine screening, early recognition of pulmonary symptoms, and individualized management strategies.
- The limited use of bronchoscopy underscores the need for greater integration of pulmonary medicine in the evaluation of suspected ILD

Future Directions

- Establish standardized pathways for early detection and multidisciplinary management
- Identify clinical and radiographic predictors to better stratify ILD risk prior to therapy

References

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