Trastuzumab Deruxtecan in HER2 Mutated Advanced NSCLC

Safety Results

DESTINY-Lung01

HER2-activating mutation cohort
Intent-to-treat population (N = 91)
Dose = 6.4 mg/kg

	n (%)
Any adverse event	91 (100)
Treatment-related adverse event	88 (97)
Adverse event leading to dose reduction	31 (34)
Adverse event leading to discontinuation of therapy	23 (25)

AEs in >20% of patients, n (%)					
	Any grade	Grades 1-2	Grade 3	Grade 4	Grade 5
Nausea	69 (75.8)	61 (67.1)	8 (8.8)	0	0
Fatigue	55 (60.4)	49 (53.9)	6 (6.6)	0	0
Vomiting	42 (46.2)	37 (40.7)	5 (5.5)	0	0
Alopecia	42 (46.2)	42 (46.2)	0	0	0
Diarrhea	37 (40.7)	34 (37.4)	2 (2.2)	1 (1.1)	0
Constipation	34 (37.4)	34 (37.4)	0	0	0
Anemia	33 (36.3)	23 (25.3)	10 (11.0)	0	0
Decreased appetite	32 (35.2)	32 (35.2)	0	0	0
Neutropenia	32 (35.2)	15 (16.5)	14 (15.4)	3 (3.3)	0
Leukopenia	21 (23.1)	17 (18.7)	4 (4.4)	0	0
Weight decreased	21 (23.1)	19 (20.9)	2 (2.2)	0	0
Pneumonitis	19 (20.9)	14 (15.4)	4 (4.4)	0	1 (1.1)

HER2, human epidermal growth factor receptor 2; AEs, adverse events.

Li BT et al. *N Engl J Med*. 2022;386:241-251.

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Safety Results: Interstitial Lung Disease (ILD)

DESTINY-Lung01

Adjudicated Drug-Related ILD	
	6.4 mg/kg (n = 91)
Any grade, n (%)	**24 (26.4)**
Grade 1	3 (3.3)
Grade 2	15 (16.5)
Grade 3	4 (4.4)
Grade 4	0
Grade 5	2 (2.2)
Median duration of disease, weeks (range)	43 (24-94)

Trastuzumab deruxtecan withdrawn in 16 patients and interrupted in 8 patients because of adjudicated ILD.

DESTINY-Lung02

Adjudicated Drug-Related ILD		
	5.4 mg/kg (n = 101)	**6.4 mg/kg (n = 50)**
Any grade, n (%)	**6 (5.9)**	**7 (14.0)**
Grade 1	3 (3.0)	1 (2.0)
Grade 2	2 (2.0)	6 (12.0)
Grade 3	1 (1.0)	0
Grade 4	0	0
Grade 5	0	0
Cases resolved, n (%)	3 (50.0)	1 (14.3)
Median time to onset of first adjudicated ILD, days (range)	67.5 (40-207)	41.0 (36-208)

HER2, human epidermal growth factor receptor 2.

Li BT et al. *N Engl J Med*. 2022;386:241-251; Goto K et al. Presented at ESMO 2022; Abstract LBA55.

Trastuzumab Deruxtecan in HER2 Mutated Advanced NSCLC

Management of Interstitial Lung Disease (ILD)

Interstitial lung disease/pneumonitis

Asymptomatic (grade 1)

Interrupt trastuzumab deruxtecan until resolved to Grade 0, then:

- If resolved ≤28 days from date of onset, maintain dose
- If resolved >28 days from date of onset, reduce dose one level
- Consider corticosteroid treatment as soon as ILD/pneumonitis suspected

Symptomatic (grade ≥2)

- Permanently discontinue trastuzumab deruxtecan
- Promptly initiate corticosteroid treatment as soon as ILD/pneumonitis suspected

Dose Reduction Schedule for NSCLC	
Recommended starting dose	5.4 mg/kg
First dose reduction	4.4 mg/kg
Second dose reduction	3.2 mg/kg
Requirement for further dose reduction	Discontinue treatment

Additional adverse events associated with dose reductions or treatment interruptions:
Neutropenia, febrile neutropenia, thrombocytopenia, left ventricular dysfunction

Additional adverse event associated with permanent discontinuation:
Patients with LVEF 40%-45% and absolute decrease from baseline 10%-20% who do not recover to within 10% from baseline after a 3-week treatment interruption

HER2, human epidermal growth factor receptor 2; LVEF, left ventricular ejection fraction.

ENHERTU (fam-trastuzumab deruxtecan-nxki). Prescribing information. Daiichi Sankyo, Inc.; Revised Nov 2022.