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## LBA45

# Primary data from DESTINY-Lung01: A phase II trial of trastuzumab deruxtecan (T-DXd) in patients (Pts) with HER2-mutated (HER2m) metastatic non-small cell lung cancer (NSCLC)

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### Background

*HER2* mutations occur in ⊠3% of NSCLC; there are no HER2-targeted therapies approved for pts with NSCLC, representing a high unmet need. DESTINY-Lung01 (NCT03505710) assessed the efficacy and safety of T-DXd, a HER2 antibody-drug conjugate, in pts with *HER2*m NSCLC.

### Methods

In a multicenter, 2-cohort phase 2 trial, pts with *HER2m* NSCLC refractory to standard treatment received T-DXd 6.4 mg/kg. Primary endpoint was ORR per RECIST v1.1 by independent central review (ICR). Secondary endpoints include duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety. Exploratory biomarkers of HER2 alterations were analyzed.

### Results

Ninety-one pts with *HER2m* NSCLC were enrolled (data cutoff, May 3, 2021). Median follow-up was 13.1 mo. Median age was 60 years. 93.4% of pts had a *HER2* kinase domain mutation; 36.3% had asymptomatic central nervous system (CNS) metastasis not requiring ongoing treatment. Median number of prior cancer therapies was 2 (range, 0-7), including platinum-based therapy (94.5%) and PD-1/PD-L1 therapy (65.9%). Centrally confirmed ORR was 54.9% (95% CI, 44.2-65.4). Efficacy was consistent across subgroups, including pts previously treated with a HER2 TKI or with CNS metastasis. Treatment-related adverse events (TRAEs) occurred in 96.7% pts. Adjudicated drug-related interstitial lung disease (ILD) occurred in 24 pts (3 grade 1, 15 grade 2, 4 grade 3, 2 grade 5). Additional biomarker analyses showed responses across different *HER2*m subtypes, as well as in pts with no detectable HER2 expression or *HER2* gene amplification.Table: LBA45

Efficacy and safety of T-DXd in pts with *HER*2m NSCLC

| | N = 91 |
|---|---|
| Efficacy | |
| Confirmed ORR by ICR, n (%) | 50 (54.9) 95% CI, 44.2-65.4 |
| Complete response | 1 (1.1) |
| Partial response | 49 (53.8) |
| Stable disease | 34 (37.4) |
| Progressive disease | 3 (3.3) |
| Nonevaluable | 4 (4.4) |
| Disease control rate, n (%) 95% CI | 84 (92.3) 84.8-96.9 |
| Median DOR, mo 95% CI | 9.3 5.7-14.7 |
| Median PFS, mo 95% CI | 8.2 6.0-11.9 |

| | N = 91 |
|---|---|
| Median OS, mo 95% CI | 17.8 13.8-22.1 |
| Safety, n (%) | |
| Any TRAE / ILD | 88 (96.7)/24 (26.4) |
| TRAE/ILD grade ≥3 | 42 (46.2)/6 (6.6) |
| TRAE/ILD associated with dose discontinuation | 23 (25.3)/16 (17.6) |
| TRAE/ILD associated with dose reduction | 31 (34.1)/0 |
| TRAE/ILD associated with dose interruption | 29 (31.9)/8 (8.8) |
| Serious TRAE | 18 (19.8) |

## Conclusions

T-DXd demonstrated robust and durable activity in pts with previously treated *HER2*m NSCLC, with a manageable safety profile consistent with previous studies. This study provides compelling evidence of positive benefit/risk balance for T-DXd and supports its establishment as a potential new treatment standard for this population.

## Clinical trial identification

NCT03505710.


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## Legal entity responsible for the study

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## Disclosure

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