

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)

B.T. Li¹, E.F.F. Smit², Y. Goto³, K. Nakagawa⁴, H. Udagawa⁵, J. Mazieres⁶, M. Nagasaka⁷, L. Bazhenova⁸, A.N. Saltos⁹, E. Felip¹⁰, J.M. Pacheco¹¹, M. Pérol¹², L. Paz-Ares¹³, K. Saxena¹⁴, R. Shiga¹⁴, Y. Cheng¹⁵, S. Acharyya¹⁶, J. Shahidi¹⁴, D. Planchard¹⁷, P.A. Jänne¹⁸

¹ Medicine, Memorial Sloan Kettering Cancer Center, Weill Cornell Medicine, New York, NY, USA, ² Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands, ³ Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan, ⁴ Medical Oncology, Kindai University Hospital, Osaka, Japan, ⁵ Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan, ⁶ Thoracic Oncology, Centre Hospitalier Universitaire, Toulouse, France, ⁷ Oncology, Karmanos Cancer Institute, Detroit, MI, USA, ⁸ Medicine, University of California San Diego Moores Cancer Center, La Jolla, CA, USA, ⁹ Thoracic Oncology, Moffitt Cancer Center, Tampa, FL, USA, ¹⁰ Oncology, Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain, ¹¹ Internal Medicine, University of Colorado, Aurora, CO, USA, ¹² Medical Oncology, Centre Léon Bérard, Lyon, France, ¹³ Oncology, Hospital Universitario 12 de Octubre, CNIO-H12o Lung Cancer Unit, Complutense University and CNIO, Madrid, Spain, ¹⁴ Global Oncology R&D, Daiichi Sankyo, Basking Ridge, NJ, USA, ¹⁵ Clinical Safety and Pharmacovigilance, Daiichi Sankyo, Basking Ridge, NJ, USA, ¹⁶ Biostatistics and Data Management, Daiichi Sankyo, Basking Ridge, NJ, USA, ¹⁷ Medical Oncology, Gustave Roussy, Villejuif, France ¹⁸ Medical Oncology, Dana-Farber Cancer Institute and the Belfer Center for Applied Cancer Science, Boston, MA, USA

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 *HER2m* 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 *HER2m* 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 *HER2m* 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.

Editorial acknowledgement

Under the guidance of authors, medical writing and editorial support was provided by Cindy M. Rigby, PhD, and Charlene Rivera, PhD, of ApotheCom and was funded by Daiichi Sankyo, Inc.

Legal entity responsible for the study

Daiichi Sankyo, Inc., and AstraZeneca.

Funding

Daiichi Sankyo, Inc. and AstraZeneca.

Disclosure

B.T. Li: Non-Financial Interests, Personal, Advisory Role: Daiichi Sankyo, AstraZeneca, Amgen, Genentech, Boehringer Ingelheim, Lilly; Financial Interests, Institutional, Research Grant: Amgen, Genentech, AstraZeneca, Daiichi Sankyo, Lilly, Illumina, GRAIL, Guardant Health, Hengrui Therapeutics, MORE Health and Bolt Biotherapeutics; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Resolution Bioscience, MORE Health, and Jiangsu Hengrui Medicine; Financial Interests, Personal, Licensing Fees: Karger Publishers, Shanghai Jiao Tong University Press (intellectual property as book author). E.F.F. Smit: Financial Interests, Institutional, Advisory Role: AstraZeneca, Bristol Myers Squibb, Bayer, Cellgene, DSI, Eli Lilly, MSD, Merck, Novartis, Pfizer, Takeda, Regeneron, Roche Genentech, Roche Diagnostics; Financial Interests, Institutional, Research Grant: AstraZeneca, Bristol Myers Squibb, Merck, MSD, Roche Genentech. Y. Goto: Financial Interests, Personal, Invited Speaker: AstraZeneca, MSD, Ono Pharmaceutical, Taiho, Chugai, Novartis, Eli Lilly, Pfizer, Daiichi Sankyo, Bristol Myers Squibb, Merck, Thermo Fischer, Boehringer Ingelheim; Financial Interests, Personal, Advisory Board: Eli Lilly, AstraZeneca, Chugai, Taiho, Boehringer Ingelheim, Ono Pharmaceutical, Bristol Myers Squibb, Pfizer, MSD, Novartis, Daiichi Sankyo, Illumina, Guardant Health Inc.; Non-Financial Interests, Institutional, Research Grant: AbbVie, Eli Lilly, Bristol Myers Squibb, DaiichiSankyo, Preferred Network; Financial Interests, Personal and Institutional, Research Grant: Pfizer, Chugai, Novartis, . K. Nakagawa: Financial Interests, Personal, Other, Honoraria: Astellas Pharma Inc./Takeda Pharmaceutical Co.,Ltd./NANZANDO Co.,Ltd./AstraZeneca K.K./Chugai Pharmaceutical Co.,Ltd./Roche Diagnostics K.K./MSD K.K./Eli Lilly Japan K.K./Nippon Kayaku Co., Ltd./Ono Pharmaceutical Co.,Ltd./Merck Biopharma Co., Ltd./Bayer Y; Financial Interests, Personal, Advisory Role: Astellas Pharma Inc./Takeda Pharmaceutical Co.,Ltd./Eli Lilly Japan K.K./Pfizer Japan Inc./KYORIN Pharmaceutical Co., Ltd./Ono Pharmaceutical Co.,Ltd.; Financial Interests, Institutional, Research Grant: MSD K.K./AstraZeneca K.K./Pfizer Japan Inc./ICON Japan K.K./Astellas Pharma Inc./Bayer Yakuhin, Ltd/Takeda Pharmaceutical Co.,Ltd./Novartis Pharma K.K./Otsuka Pharmaceutical Co., Ltd./Eli Lilly Japan K.K./EPS International Co.,Ltd./Bayer Yakuhin, Ltd/Bri. J. Mazieres: Financial Interests, Personal, Other, Honoraria: Roche, BMS, MSD, AstraZeneca, Takeda, Daiichi Sankyo; Financial Interests, Institutional, Research Grant: Roche, Pierre Fabre, AstraZeneca. M. Nagasaka: Financial Interests, Personal, Advisory Role: AstraZeneca, Caris, Daiichi Sankyo, Takeda, Novartis, EMD Serono, JNJ, Pfizer; Financial Interests, Personal, Speaker's Bureau: Blueprint Medicines; Financial Interests, Personal, Other, Travel expenses: An Heart Therapeutics. L. Bazhenova: Financial Interests, Institutional, Other, Honoraria: AstraZeneca, Takeda; Financial Interests, Personal, Advisory Role: Neuvogen, Janssen, Daiichi Sankyo, Boehringer Ingelheim, Merck, Regeneron, Bristol Myers Squibb, Novartis; Financial Interests, Institutional, Research Grant: Beyondspring. A.N. Saltos: Financial Interests, Personal, Other, Honoraria: MJH Life Sciences; Financial Interests, Institutional, Research Grant: Novartis, Daiichi Sankyo, Lilly, Mersana, Genmab, AstraZeneca, Turning Point Therapeutics. E. Felip: Financial Interests, Personal, Advisory Board: Amgen, AstraZeneca, Bayer, Beigene, Boehringer-Ingelheim, BMS, Eli Lilly, F. Hoffman-La Roche, Glaxo Smith Kline, Janssen, Medical Trends, Merck Sharp and Dohme, Merck Serono, Peptomyc, Pfizer, Puma, Regeneron, Sanofi, Syneos Health, Takeda; Financial Interests, Personal, Speaker's Bureau:

Amgen, AstraZeneca, BMS, Eli Lilly, F. Hoffmann-La Roche, Janssen, Medscape, Merck Sharp and Dohme, Merck Serono, Peervoice, Pfizer, Springer, Touch Medical. J.M. Pacheco: Financial Interests, Institutional, Other, Honoraria: Takeda, Genentech; Financial Interests, Personal, Advisory Role: AstraZeneca, Blueprint Medicines, Gerson Lehrman Group, Hengrui Pharmaceuticals, Jazz Pharmaceuticals, Novartis, Pfizer, Takeda, Research America; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Daiichi Sankyo, AstraZeneca, Novartis, Pfizer, Takeda; Financial Interests, Institutional, Research Grant: Pfizer. M. Pérol: Financial Interests, Personal, Other, Honoraria: Roche, Genentech, Eli Lilly, Pfizer, Boehringer-Ingelheim, Clovis Oncology, Merck Sharp & Dome, Bristol Myers Squibb, Novartis, Pierre Fabre, AstraZeneca, Takeda, Sanofi, GlaxoSmithKline, Gritstone; Financial Interests, Personal, Advisory Role: Roche, Genentech, Eli Lilly, Pfizer, Boehringer-Ingelheim, Clovis Oncology, Merck Sharp & Dome, Bristol Myers Squibb, Novartis, Pierre Fabre, AstraZeneca, Takeda, Sanofi, GlaxoSmithKline, Gritstone; Financial Interests, Personal, Speaker's Bureau: Roche, AstraZeneca; Financial Interests, Institutional, Research Grant: Roche, AstraZeneca, Boehringer-Ingelheim, Takeda, Chugai; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Roche, Genentech, Eli Lilly, Pfizer, Boehringer-Ingelheim, Merck Sharp & Dome, Bristol Myers Squibb, AstraZeneca, Takeda. L. Paz-Ares: Financial Interests, Personal, Speaker's Bureau: Roche, MSD, Merck Serono, BMS, AstraZeneca, Lilly, Pfizer, Pharmamar, Bayer, AbbVie, Amgen, Janssen, GSK, Novartis, Ipsen, Boehringer, Takeda, Sanofi, Blueprint, Mirati; Financial Interests, Institutional, Research Grant: BMS, AstraZeneca, Pharmamar. K. Saxena: Financial Interests, Personal, Other, Full/Part-time employment: Daiichi Sankyo, Inc. R. Shiga: Financial Interests, Personal, Other, Full/Part-time employment: Daiichi Sankyo, Inc. Y. Cheng: Financial Interests, Personal, Other, Full/Part-time employment: Daiichi Sankyo, Inc. J. Shahidi: Financial Interests, Personal, Other, Full/Part-time employment: Daiichi Sankyo, Inc. D. Planchard: Financial Interests, Personal, Other, Honoraria: AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Merck, Novartis, Pfizer, prIME Oncology, Peer CME, Roche, Samsung; Financial Interests, Institutional, Other, Honoraria: AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Eli Lilly, Merck, Novartis, Pfizer, Roche, Medimmun, Sanofi-Aventis, Taiho Pharma, Novocure, Daiichi Sankyo; Financial Interests, Personal, Advisory Role: AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly, Merck, Novartis, Pfizer, prIME Oncology, Peer CME, Roche, Samsung; Financial Interests, Personal, Other, Travel expenses: AstraZeneca, Roche, Novartis, prIME Oncology, Pfizer. P.A. Jänne: Financial Interests, Personal, Advisory Role: Pfizer, Boehringer Ingelheim, AstraZeneca, Merrimack, Chugai Pharma, Roche/Genentech, LOXO, Mirati Therapeutics, Araxes Pharma, Ignyta, Lilly, Takeda, Novartis, Biocartis, Voronoi Health Analytics, SFJ Pharmaceuticals Group, Sanofi, Biocartis, Daiichi San; Financial Interests, Personal, Stocks/Shares: Gatekeeper Pharmaceuticals, LOXO; Financial Interests, Personal, Research Grant: AstraZeneca, Astellas Pharma, Daiichi Sankyo, Lilly, Boehringer Ingelheim, Puma Biotechnology, Takeda, Revolution Medicines; Financial Interests, Personal, Royalties: I am a co-inventor of DFCl owned patent on EGFR mutations licensed to Lab Corp. I receive post-marketing royalties from this invention. All other authors have declared no conflicts of interest.

© *European Society for Medical Oncology*