2021 ESMO congress

LBA49

Efficacy of datopotamab deruxtecan (Dato-DXd) in patients (pts) with advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC) and actionable genomic alterations (AGAs): Preliminary results from the phase I TROPION-PanTumor01 study

E.B. Garon[1], M.L. Johnson[2], A.E. Lisberg[3], A. Spira[4], N. Yamamoto[5], R.S. Heist[6], J.M. Sands[7], K. Yoh[8], F. Meric-Bernstam[9], S. Kitazono[10], J. Greenberg[11], F. Kobayashi[12], Y. Kawasaki[12], L. Jukofsky[11], K. Nakamura[11], T. Shimizu[5]

[1] David Geffen School of Medicine at UCLA, Los Angeles, CA, USA, [2] Sarah Cannon Research Institute, Tennessee Oncology, PLLC/OneOncology, Nashville, TN, USA, [3] UCLA Jonsson Comprehensive Cancer Center, Santa Monica, CA, USA, [4] Virginia Cancer Specialists, Fairfax, VA, USA, [5] Department of Experimental Therapeutics, National Cancer Center Hospital, Tokyo, Japan, [6] Massachusetts General Hospital, Boston, MA, USA, [7] Dana-Farber Cancer Institute, Boston, MA, USA, [8] National Cancer Center Hospital East, Chiba, Japan, [9] The University of Texas, MD Anderson Cancer Center, Houston, TX, USA, [10] The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan, [11] Daiichi Sankyo, Basking Ridge, NJ, USA[12] Daiichi Sankyo Co., Ltd., Tokyo, Japan

Background

Pts with adv/met NSCLC with AGAs derive limited benefit from existing treatments once tyrosine kinase inhibitors (TKIs) and platinum chemotherapies fail. Dato-DXd is an antibody-drug conjugate comprising a TROP2-directed monoclonal antibody conjugated to a potent topoisomerase I inhibitor via a stable tetrapeptide-based cleavable linker. Dato-DXd showed encouraging antitumor activity in the phase 1 TROPION-PanTumor01 trial in heavily pretreated pts with adv/met NSCLC treated with 4, 6, and 8 mg/kg. Here, we report results from this trial for pts with NSCLC with AGAs.

Methods

TROPION-PanTumor01 (NCT03401385) is an ongoing multicenter, open-label, dose-expansion study evaluating Dato-DXd in solid tumors, including NSCLC in 210 pts. It is assessing safety, pharmacokinetics, antitumor activity, and biomarkers in pts who progressed after standard treatment or had no standard treatment available and had measurable disease. Stable/treated brain metastases were permitted. Pts were not selected based on TROP2 expression or AGA status.

Results

34 pts had adv/met NSCLC with AGAs (8 at 4 mg/kg, 10 at 6 mg/kg, and 16 at 8 mg/kg). Median age was 62 years; 56% were women and 44% were men. Investigator-reported AGAs were *EGFR* (n=29), *ALK* (n=3), and *ROS1* and *RET* (both n=1). 82% of pts received ≥3 prior regimens and 85% prior TKI; 69% of pts with *EGFR* mutations had prior osimertinib. Median duration on study was 13 months. Confirmed ORR by BICR across doses was 35% (95% CI, 19.7-53.5). Median DOR was 9.5 months (95% CI, 3.3-NE). Most common any-grade AEs were nausea (62%) and stomatitis (56%); hematologic toxicities were infrequent. There was 1 incidence of treatment-related adjudicated interstitial lung disease, a grade 5 event at 8 mg/kg.

Conclusions

Antitumor activity and safety in adv/met NSCLC pts with AGAs are encouraging. The ongoing phase 2 TROPION-Lung05 trial (NCT04484142) is assessing Dato-DXd at 6 mg/kg in adv/met NSCLC with AGAs after targeted therapies and platinum chemotherapy.

Clinical trial identification

NCT03401385.

Editorial acknowledgement

Medical writing support was provided by Christine Zink, MD, of SciMentum, Inc, a Nucleus Holdings Ltd company, and was funded by Daiichi Sankyo, Inc. Editorial support was provided in accordance with Good Publication Practice guidelines.

Legal entity responsible for the study

Daiichi Sankyo, Inc.

Funding

Daiichi Sankyo, Inc.

Disclosure

E.B. Garon: Financial Interests, Personal, Advisory Role: ABL Bio; Boehringer Ingelheim; Bristol Myers Squibb; Dracen; Eisai; EMD Serono; GlaxoSmithKline; Merck; Novartis; Sanofi; Shionogi; Xilio Therapeutics; Financial Interests, Institutional, Research Grant: AstraZeneca; Bristol Myers Squibb; Dynavax Technologies; EMD Serono; Genentech; Iovance Biotherapeutics; Lilly; Merck; Mirati Therapeutics; Neon Therapeutics; Novartis. M.L. Johnson: Financial Interests, Institutional, Research Grant: AbbVie, Acerta, Adaptimmune, Amgen, Apexigen, Arcus Biosciences, Array, Artios Pharma, AstraZeneca, Atreca, BeiGene, BerGenBio, Boehringer Ingelheim, Calithera, Checkpoint Therapeutics, Corvus, Curis, CytomX, Daiichi Sankyo, Dracen, Dynavax, Lilly, EMD Se; Financial Interests, Institutional, Advisory Role: AbbVie, Achilles Therapeutics, Amgen, AstraZeneca, Atreca, Boehringer Ingelheim, Bristol Myers Squibb, Calithera, Checkpoint Therapeutics, Daiichi Sankyo, Editas Medicine, Eisai, EMD Serono, G1 Therapeutics, Genentech/Roche, GlaxoSmithKline, Gritstone Onc; Financial Interests, Personal, Other, Consulting-Spouse: Astellas and Otsuka Pharmaceuticals. A.E. Lisberg: Financial Interests, Personal, Other, Employment (Immediate Family Member): Boston Scientific; Financial Interests, Personal, Stocks/Shares: Boston Scientific; Financial Interests, Personal, Invited Speaker, Honoraria: AstraZeneca, Bristol Myers Squibb, Leica Biosystems, Jazz Pharmaceuticals, Novocure, Pfizer, MorphoSys; Financial Interests, Personal, Advisory Role: AstraZeneca, Bristol Myers Squibb, Leica Biosystems, Jazz Pharmaceuticals, Novocure, Pfizer, MorphoSys; Financial Interests, Institutional, Research Grant: Daiichi Sankyo, Calithera Biosciences, AstraZeneca, Dracen Pharmaceuticals, WindMIL. A. Spira: Financial Interests, Personal, Stocks/Shares, Stock and Other Ownership Interests: Lilly; Financial Interests, Personal, Invited Speaker, Honoraria: Amgen; AstraZeneca/MedImmune; Bayer; Bristol Myers Squibb; CytomX Therapeutics; Janssen Oncology; Merck; Novartis; Takeda; Financial Interests, Institutional, Advisory Role: Amgen; Array BioPharma; AstraZeneca/MedImmune; Bristol Myers Squibb; Merck; Financial Interests, Personal, Advisory Role: Gritstone Oncology; Incyte; Jazz Pharmaceuticals; Mirati Therapeutics; Novartis; Financial Interests, Institutional, Research Grant: AbbVie; ADC Therapeutics; ADC Therapeutics; Amgen; Arch Therapeutics; Astellas Pharma; Astex Pharmaceuticals; AstraZeneca; Boehringer Ingelheim; Bristol Myers Squibb; CytomX Therapeutics; Daiichi Sankyo; Gritstone Oncology; Ignyta; Incyte; Janssen Oncolog. N. Yamamoto: Financial Interests, Personal, Invited Speaker, Honoraria: AstraZeneca; Chugai Pharma; Daiichi Sankyo/UCB Japan; Lilly Japan; Ono Pharmaceutical; Pfizer; Sysmex; Financial Interests, Personal, Advisory Role: Boehringer Ingelheim; Chugai Pharma; CMIC; Eisai; Otsuka; Takeda; Financial Interests, Institutional, Advisory Role: AbbVie; Astellas Pharma; Bayer; Boehringer Ingelheim; Bristol Myers Squibb; Chugai Pharma; Daiichi Sankyo; Eisai; GlaxoSmithKline; Janssen; Kyowa Hakko Kirin; Lilly Japan; Merck Serono; MSD; Novartis; Ono Pharmaceutical; Pfizer; Sumitomo Dainippon; Taiho; Financial Interests, Personal, Advisory Role: Chiome Bioscience; Otsuka. R.S. Heist: Financial Interests, Personal, Invited Speaker, Honoraria: Chugai/Roche; Financial Interests, Personal, Advisory Role: Apollomics; Boehringer Ingelheim; Daichii Sankyo; Daichii Sankyo; EMD Serono/Merck; EMD Serono/Merck; Novartis; Tarveda Therapeutic; Financial Interests, Institutional, Research Grant: AbbVie; Agios; Celgene; Corvus Pharmaceuticals; Daiichi Sankyo; Debiopharm Group; Exelixis; Incyte; Lilly; Millennium; Mirati Therapeutics; Novartis; Peregrine Pharmaceuticals; Pfizer; Roche; Turning Point Therapeutics. J.M. Sands: Financial Interests, Personal, Advisory Role: AstraZeneca; AstraZeneca; Blueprint Medicines; Boehringer Ingelheim; Daiichi Sankyo/UCB Japan; Foundation Medicine; Guardant Health; Jazz Pharmaceuticals; Lilly; Medtronic; Medtronic; PharmaMar; Takeda Travel, Accommodations, Expenses - AstraZeneca. K. Yoh: Financial Interests, Personal, Invited Speaker, Honoraria: AstraZeneca; Boehringer Ingelheim; Bristol Myers Squibb Japan; Chugai Pharma; Janssen; Kirin Pharmaceuticals; Lilly Japan; Novartis; Taiho Pharmaceutical; Financial Interests, Personal, Advisory Role: Chugai Pharma; Financial Interests, Institutional, Research Grant: AstraZeneca; Bayer; Bristol Myers Squibb; Chugai Pharma; Daiichi Sankyo; Lilly Japan; MSD; Novartis; Ono Pharmaceutical; Pfizer; Taiho Pharmaceutical; Takeda. F. Meric-Bernstam: Financial Interests, Personal, Full or part-time Employment: MD Anderson Cancer Center; Financial Interests, Personal, Invited Speaker, Honoraria: Mayo Clinic; Rutgers Cancer Institute of New Jersey; Financial Interests, Personal, Advisory Role: Aduro Biotech; Alkermes; Debiopharm Group; eFFECTOR Therapeutics; Genentech; IBM Watson Health; Immunomedics; Inflection Biosciences; Jackson Laboratory for Genomic Medicine; Kolon Life Sciences; Mersana; Origimed; PACT Pharma; Parexel International; Pfiz; Financial Interests, Institutional, Research Grant: AbbVie; Aileron Therapeutics; AstraZeneca; Bayer;; Calithera Biosciences; Curis; CytomX Therapeutics; Daiichi Sankyo; Debiopharm Group; eFFECTOR Therapeutics; Genentech; GlaxoSmithKline; Guardant Health; Jounce Therapeutics; Millennium; Novartis; Pfizer; Financial Interests, Personal, Research Grant: Boehringer Ingelheim; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Beth Israel Deaconess Medical Center; Taiho Pharmaceutical. J. Greenberg: Financial Interests, Personal, Full or part-time Employment: Daiichi Sankyo; Financial Interests, Personal, Stocks/Shares: Daiichi Sankyo. F. Kobayashi: Financial Interests, Personal, Full or part-time Employment: Daiichi Sankyo. Y. Kawasaki: Financial Interests, Personal, Full or part-time Employment: Daiichi Sankyo Co., LTD. L. Jukofsky: Financial Interests, Personal, Full or part-time Employment: Daiichi Sankyo, Inc. K. Nakamura: Financial Interests, Personal, Full or part-time Employment: Daiichi Sankyo, Inc. T. Shimizu: Financial Interests, Personal, Advisory Role: Daiichi Sankyo; Financial Interests, Personal, Research Grant: Daiichi Sankyo; Financial Interests, Institutional, Research Grant: Novartis, AbbVie, Daiichi Sankyo, Takeda Oncology, Eli Lilly, Loxo Oncology, Bristol Myers Squibb, Eisai, Pfizer, AstraZeneca, Incyte, Symbio Pharmaceuticals, Chordia Therapeutics, 3D-Medicine, Five Prime, PharmaMar, Astellas; Financial Interests, Personal, Invited Speaker, Honoraria: Daiichi Sankyo, AbbVie, Taiho, Eisai, MSD, Takeda Oncology, Amgen; Financial Interests, Personal, Other, Support for attending meetings and travel: The Consortium on Harmonization of Institutional Requirements for Clinical Research (CHAIR) Joint Scientific Committee Review Member and External IRB Member of Phase 1 Trials in Hong Kong, HKSAR, China. All other authors have declared no conflicts of interest.