9-1-2022

1549TiP DeLLphi-303: Phase Ib first-line combination study of tarlatamab, a DLL3-targeting half-life extended bispecific T-cell engager (HLE BiTE®), with carboplatin, etoposide, and PD-L1 inhibition in extensive stage small cell lung cancer (ES-SCLC)

Shirish M. Gadgeel

J. Al-Mondhiry

M. J. Ahn

S. W. Kim

L. Paz-Ares

See next page for additional authors

Authors

Shirish M. Gadgeel, J. Al-Mondhiry, M. J. Ahn, S. W. Kim, L. Paz-Ares, H. Prenen, M. Boyer, J. G. Bustamanta Alvarez, B. Solomon, S. Huang, M. Minocha, M. Kistler, and N. Hashemi Sadraei

1549TiP DeLLphi-303: Phase Ib first-line combination study of tarlatamab, a DLL3-targeting half-life extended bispecific T-cell engager (HLE BiTE®), with carboplatin, etoposide, and PD-L1 inhibition in extensive stage small cell lung cancer (ES-SCLC)

S.M. Gadgeel[1], J. Al-Mondhiry[2], M-J. Ahn[3], S-W. Kim[4], L. Paz-Ares[5], H. Prenen[6], M. Boyer[7], J.G. Bustamante Alvarez[8], B. Solomon[9], S. Huang[10], M. Minocha[11], M. Kistler[12], N. Hashemi Sadraei[12]

[1]Oncology Department, Henry Ford Cancer Institute, Detroit, MI, USA; [2]Division of Oncology, University of Southern California, Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [3]Department of Hematology and Oncology, Samsung Medical Center Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [4]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [5]Medical Oncology Department - Edificio Maternidad, Hospital Universitario 12 de Octubre, CNIO-H120 Lung Cancer Unit, Ciberonc and Universidad Complutense, Madrid, Spain; [6]Oncology Department, UZA - University Hospital Antwerp, Edegem, Belgium; [7]Department of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [8]Medical Oncology Dept., West Virginia University, Morgantown, WV, USA; [9]Hematology and Oncology, Avera McKennan Hospital & University Health Center, Sioux Falls, SD, USA; [10]Biostatistics, Amgen Inc., Thousand Oaks, CA, USA; [11]Clinical Pharmacology, Amgen Inc., Thousand Oaks, CA, USA; [12]Research and Development, Amgen Inc., Thousand Oaks, CA, USA

Background: The inhibitory Notch ligand, delta-like ligand 3 (DLL3), is a compelling therapeutic target due to its aberrant expression on the cell surface in most small cell lung cancer (SCLC). Tarlatamab (AMG 757) is a half-life extended bispecific T-cell engager (HLE BiTE®) molecule designed to specifically bind DLL3 on target cancer cells and CD3 on T cells, resulting in T cell-dependent killing of tumor cells. Data from an ongoing first-in-human monotherapy study show acceptable safety with evidence of tarlatamab efficacy in patients with relapsed/refractory SCLC (NCT03319940). Adding programmed death ligand 1 (PD-L1) inhibitors to first-line platinum chemotherapy is the emerging standard-of-care (SOC) in ES-SCLC and preclinical data suggests increased antitumor activity of BiTE molecules when combined with PD-1/PD-L1 inhibition or chemotherapy.[1] These data support a clinical trial of tarlatamab combined with frontline carboplatin, etoposide, and PD-L1 inhibition in ES-SCLC.

Trial design: This is a phase 1b, multicenter, open-label study evaluating tarlatamab in combination with first-line SOC chemo-immunotherapy in subjects with ES-SCLC. Tarlatamab will be evaluated in two separate settings: A) In combination with carboplatin, etoposide, and a PD-L1 inhibitor followed by maintenance cycles of tarlatamab plus PD-L1 inhibitor, and B) In combination with PD-L1 inhibitor following SOC chemo-immunotherapy as a maintenance only approach. Key eligibility criteria include patients with histologically or cytologically confirmed ES-SCLC with no prior systemic treatment (except as specified in protocol) and ECOG performance status $\leq$1. The primary objective is to evaluate the safety, tolerability, and determine the recommended phase 2 dose and/or maximum tolerated dose of tarlatamab in combination with PD-L1 inhibition with or without chemotherapy. Secondary endpoints are objective response rate, duration of response, disease control, progression-free survival, overall survival, and pharmacokinetics. References Belmontes B, et al. *Sci. Transl. Med.* 2021;13:eabd1524.

Clinical trial identification: NCT05361395.

Editorial acknowledgement: Medical writing support for this poster was provided by Eugene Gillespie, PhD, of Amgen, Inc.

Legal entity responsible for the study: Amgen Inc.

Funding: Amgen Inc.

Disclosure: S.M. Gadgeel: Financial Interests, Personal, Advisory Board: AstraZeneca, Amgen, Genentech/Roche, Bristol Myers Squibb, Pfizer, Novartis, Blueprint, Daiichii; Financial Interests, Personal, Other, Data Safety Monitoring Board: AstraZeneca. M. Ahn: Financial Interests, Personal, Advisory Role: AstraZeneca, Lilly, Takeda, Merck, MSD, Amgen, Yuhan, Daiichi-Sankyo, Roche, Pfizer, Arcus, Alpha-pharmaceuticals; Financial Interests, Personal, Invited Speaker: AstraZeneca, Lilly, Takeda, Merck, MSD, Amgen, Yuhan, Daiichi-Sankyo, Roche, Pfizer. S-W. Kim: Financial Interests, Personal, Invited Speaker: Boehringer Ingelheim, Amgen; Financial Interests, Personal, Yuhan. Financial Interests, Personal, Amgen, AstraZeneca, Boehringer Ingelheim, Janssen, Lilly, Norvasc, Takeda, Yuhan. L. Paz-Ares: Financial Interests, Personal, Advisory Board: Roche, MSD, Merck Serono, BMS, AZ, Lilly, Pfizer, PharmaMar, Bayer, Amgen, Janssen, GSK, Novartis, Takeda, Sanofi, Mirati; Financial Interests, Personal, Other, Board member: Genomica, Altum sequencing; Financial Interests, Personal, Invited Speaker: Altum sequencing, Amgen; Financial Interests, Institutional, Invited Speaker: Daiichi Sankyo, AstraZeneca, Merck Sharp & Dohme Corp, BMS, Janssen-cilag international NV, NOvartis, Roche, Sanofi, Tesaro, Alkermes, Lilly, Takeda, Pfizer, PharmaMar. H. Prenen: Financial Interests, Institutional, Advisory Board: Amgen, Roche, AstraZeneca; Financial Interests, Institutional, Invited Speaker: Bayer, Ipsen, Sanofi. M. Boyer: Financial Interests, Personal, Invited Speaker: AstraZeneca, Merck Sharpe & Dohme; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Institutional, Invited Speaker: AstraZeneca, Merck Sharpe & Dohme, Amgen, Janssen, Eli Lilly, EARLI, Immugene, Dizal; Non-Financial Interests, Leadership Role: Thoracic Oncology Group Australasia. B. Solomon: Financial Interests, Personal, Advisory Board: AstraZeneca, Bayer; Financial Interests, Institutional, Invited Speaker: Daiichi-Sankyo, Iovance, GSK, Mirati, ImmunityBio, AstraZeneca, Amgen; Non-Financial Interests, Member: ASCO, AACR, ESMO. S. Huang: Financial Interests, Personal, Full or part-time Employment: Amgen; Financial Interests, Personal, Stocks/Shares: Amgen. M. Minocha: Financial Interests, Personal, Full or part-time Employment: Amgen; Financial Interests, Personal, Stocks/Shares: Amgen. M. Kistler: Financial Interests, Personal, Full or part-time Employment: Amgen; Financial Interests, Personal, Stocks/Shares: Amgen. N. Hashemi Sadraei: Financial Interests, Personal, Full or part-time Employment: Amgen; Financial Interests, Personal, Stocks/Shares: Amgen. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.07.1643

1550TiP Phase II, multicenter, randomized, open-label study of DS-7300 in patients (pts) with pre-treated extensive-stage small cell lung cancer (ES-SCLC)

L. Paz-Ares[1], M.L. Johnson[2], N. Girard[3], C.L. Hann[4], M-J. Ahn[5], M. Nishio[6], J. Godard[7], A. Laadem[8], N. Yoshizuka[9], M. Qian[10], B. Cheng[11], C.M. Rudin[12]

[1]Medical Oncology Department - Edificio Maternidad, Hospital Universitario 12 de Octubre, Madrid, Spain; [2]Lung Cancer Research, Sarah Cannon Research Institute-Cancer Centre, Nashville, TN, USA; [3]Thorax Institute, Institut Curie, Paris, France; [4]Oncology Department, Johns Hopkins University School of Medicine, Baltimore, MA, USA; [5]Hematology-Oncology Department, Samsung Medical Center (SMC) - Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [6]Department of Thoracic Medical Oncology, The Cancer Institute Hospital of JFCR, Koto-ku, Japan; [7]Clinical Science, Daiichi Sankyo, Inc., Rueil-Malmaison, France; [8]Clinical Development, Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [9]Global Oncology R&D, Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [10]Biostatistics & Data Management, Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [11]CSPV, Daiichi Sankyo Inc., Basking Ridge, NJ, USA; [12]Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Background: ES-SCLC is highly aggressive and despite high response rates to first-line therapy, disease progression often occurs within 6 months. There are limited later-line therapeutic options for relapsed SCLC, indicating a significant unmet need for treatment with durable benefit in second line and beyond. B7 homolog 3 protein (B7-H3), a type 1 transmembrane protein in the B7 family, is overexpressed in many cancers, including SCLC, and correlated with poor prognosis. DS-7300 is a novel, antibody drug conjugate comprising a humanized anti-B7-H3 immunoglobulin G1 monoclonal antibody and potent topoisomerase I inhibitor payload (exatecan derivative, DXd) covalently linked by a stable tetrapeptide-based cleavable linker. DS-7300 (4.8-16.0 mg/kg) demonstrated promising clinical activity in an ongoing phase 1/2 first-in-human study, with 7/9 evaluable, heavily pretreated pts with SCLC achieving a response as of Jan 22, 2022. This study (NCT05280470) will define the recommended phase 2 dose and prospectively investigate efficacy of DS-7300 in ES-SCLC.

Trial design: This global, multicenter, phase 2 study will include pts with ES-SCLC who received 1 to 3 prior lines of therapy. Eighty pts will be randomized 1:1 (8 mg/kg or 12 mg/kg) and treated with DS-7300 intravenously on day 1 of each 21-day cycle until unacceptable toxicity, progressive disease, or consent withdrawal; an additional ~60 pts may be enrolled at the recommended phase 2 dose after study steering committee consultation. The primary endpoint is objective response rate (ORR) assessed by blinded independent central review (BICR) per Response Evaluation Criteria in Solid Tumours (RECIST) v1.1. Secondary endpoints are progression-free survival, duration of response, disease control rate, and time to response assessed by the investigator and BICR based on RECIST v1.1; overall survival; ORR by investigator assessment based on RECIST v1.1; treatment-emergent adverse events and other safety parameters; plasma pharmacokinetic parameters for DS-7300, total anti-B7-H3, and DXd; and antidrug antibodies. Exposure-response and biomarkers analyses are exploratory endpoints. Estimated study completion is Jun 2024.

Clinical trial identification: NCT05280470.

Editorial acknowledgement: Medical writing support was provided by Meredith Rogers, MS, CMPP (The Lockwood Group, Stamford, CT, USA).

Legal entity responsible for the study: Daiichi Sankyo, Inc.

Funding: Daiichi Sankyo, Inc.

Disclosure: L. Paz-Ares: Financial Interests, Personal, Advisory Board, Speaker fees: Roche, MSD, BMS, AZ, Lilly, PharmaMar, BeiGene, Daiichii, Medscape, PER; Financial Interests, Personal, Advisory Board: Merck Serono, Pfizer, Bayer, Amgen, Janssen, GSK, Novartis, Takeda, Sanofi, Mirati; Financial Interests, Personal, Other, Board member: Genomica, Altum sequencing; Financial Interests, Institutional, Invited Speaker: Daiichi Sankyo, AstraZeneca, Merck Sharp & Dohme corp, BMS, Janssen-cilag international NV, NOvartis, Roche, Sanofi, Tesaro, Alkermes, Lilly, Takeda, Pfizer, PharmaMar; Financial Interests, Personal, Invited Speaker: Amgen; Financial Interests, Other, Member: AACR, ASCO, ESMO; Financial Interests, Other, Foundation Board Member: AECC; Financial Interests, Other, President ASEICA (Spanish Association of Cancer Research): ASEICA; Financial Interests, Other, Foundation president: ONCOSUR; Financial Interests, Other, member: Small Lung Cancer Group. M.L. Johnson: Financial Interests, Institutional, Research Grant, Paid to Institution: AbbVie, Acerta, Adaptimmune, Amgen, Apexigen, Arcus Biosciences, Array BioPharma, Artios Pharma, AstraZeneca, Atreca, BeiGene, BerGenBio, BioAtla, Boehringer Ingelheim, Calithera Biosciences, Checkpoint Therapeutics, Corvus Pharmaceuticals, Curis, CytomX, Daiichi Sankyo, Dracen Pharmaceuticals, Dynavax, Lilly, Elicio Therapeutics, EMD Serono, Erasca, Exelixis, Fate Therapeutics, Genentech/Roche, Genmab, Genocea Biosciences, GlaxoSmithKline, Gritstone Oncology, Gaurdant Health, Harpoon, Helsinn Healthcare SA, Hengrui Therapeutics, Hutchinson MediPharma, IDEAYA Biosciences, IGM Biosciences, Immunocore, Incyte, Janssen, Jounce Therapeutics, Kadmon Pharmaceuticals, Loxo Oncology, Memorial Sloan Kettering, Merck , Merus, Mirati Therapeutics , NeoImmune Tech, Neovia Oncology, Novartis, Numab Therapeutics, Nuvalent, OncoMed Pharmaceuticals , Pfizer, PMV Pharmaceuticals, RasCal Therapeutics, Regeneron Pharmaceuticals, Relay Therapeutics, Revolution Medicines, Ribon Therapeutics, Rubius Therapeutics, Sanofi, Seven and Eight Biopharmaceuticals/Birdie Biopharmaceuticals, Shattuck Labs, Silicon Therapeutics, Stem CentRx, Syndax Pharmaceuticals, Takeda Pharmaceuticals, Tarveda, TCR2 Therapeutics, Tempest Therapeutics, Tizona Therapeutics, Tmunity Therapeutics, Turning Point Therapeutics, University of Michigan, Vyriad, WindMIL, Y-mAbs Therapeutics; Financial Interests, Institutional, Other, Consulting/Paid to Institution: AbbVie, Amgen, Astellas, AstraZeneca, Axelia Oncology, Black Diamond, Boehringer Ingelheim, Bristol-Myers Squibb, Calithera Biosciences, Checkpoint Therapeutics, Daiichi Sanyko, EcoR1, Editas Medicine, Esai , EMD Serono, G1 Therapeutics, Genentech/Roche, Genmab; Financial Interests, Institutional, : Genocea Biosciences. N. Girard: Financial Interests, Personal, Invited Speaker: AstraZeneca, BMS, MSD, Roche, Pfizer, Mirati, Amgen, Novartis, Sanofi; Financial Interests, Personal, Advisory Board: AstraZeneca, BMS, MSD, Roche, Pfizer, Janssen, Boehringer, Novartis, Sanofi, AbbVie, Amgen, Lilly, Grunenthal, Takeda, Owkin; Financial Interests, Institutional, Research Grant, Local: Roche, Sivan, Janssen; Financial Interests, Institutional, Funding: BMS; Non-Financial Interests, Officer, International Thymic Malignancy Interest Group, President: ITMIG; Other, Family member is an employee: AstraZeneca. C.L. Hann: