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Tarlatamab plus durvalumab (durva) vs durva as 1L maintenance (1LM) therapy following durva, platinum, and etoposide (1L durva + EP) in extensive-stage small cell lung cancer (ES-SCLC): Primary analysis of the phase 3 DeLLphi-305 trial

J. Sands¹, T. Yoshida², M-J. Ahn³, C. Gay⁴, M.H.H. Schuler⁵, H. Liu⁶, A. Sezer⁷, A. Bilici⁸, I. Korantzis⁹, S.M. Lim¹⁰, I. Okamoto¹¹, O. Juan-Vidal¹², Y. Chen¹³, G. Schvartsman¹⁴, A-M.C. Dingemans¹⁵, J. Clarke¹⁶, M. Marigil¹⁷, Y. Zhang¹⁸, B. Abidi¹⁹, M. Pérol²⁰

¹ Department of Thoracic Medical Oncology, Dana-Farber Cancer Institute, Boston, United States of America, ² Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan, ³ Department of Hematology and Oncology, Samsung Medical Center, Seoul, Republic of Korea, ⁴ Department of Thoracic/Head & Neck Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, United States of America, ⁵ Department of Medical Oncology, West German Cancer Center, University Hospital Essen, Essen, Germany, ⁶ Department of Medical Oncology, Jilin Cancer Hospital, Changchun, China, ⁷ Department of Medical Oncology, Medical Park Seyhan Hospital, Adana, Türkiye, ⁸ Department of Medical Oncology, Istanbul Medipol University, Bagcilar Medipol Mega Hospital, Istanbul, Türkiye, ⁹ Department of Oncology, Saint Luke's Hospital, Thessaloniki, Greece, ¹⁰ Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea, ¹¹ Department of Respiratory Medicine, Kyushu University Hospital, Fukuoka, Japan, ¹² Department of Medical Oncology, Hospital Universitario y Politécnico la Fe de Valencia, Valencia, Spain, ¹³ Department of Thoracic Oncology and Melanoma Research, Cancer and Hematology Centers of Western Michigan, Grand Rapids, United States of America, ¹⁴ Department of Medical Oncology, Hospital Israelita Albert Einstein, Sao Paulo, Brazil, ¹⁵ Department of Pulmonology, Erasmus MC Cancer Institute, University Medical Center, Rotterdam, Netherlands, ¹⁶ Department of Medicine, Duke Cancer Institute, Durham, United States of America, ¹⁷ Clinical Development, Amgen Inc., Thousand Oaks, United States of America, ¹⁸ Global Biostatistics, Amgen Inc., Thousand Oaks, United States of America, ¹⁹ Global Safety, Amgen Inc., Thousand Oaks, United States of America²⁰ Department of Medical Oncology, Léon Bérard Cancer Center, Lyon, France

Background

Adding tarlatamab to 1L ES-SCLC therapy showed encouraging efficacy in the phase 1b DeLLphi-303 study (NCT05361395). We report the primary analysis of the randomized phase 3 DeLLphi-305 trial evaluating tarlatamab + durva vs durva as 1LM therapy for ES-SCLC.

Methods

563 patients (pts) with ES-SCLC without progression after 1L durva + EP were randomized (1:1) to receive either tarlatamab + durva (n = 282) or durva (n = 281) until progression or unacceptable toxicity. Tarlatamab was given 1 mg IV cycle 1 day 1 (C1D1); 10 mg IV C1D8, C1D15, then 10 mg IV Q2W; durva was given 1500 mg IV Q4W. The primary endpoint was overall survival (OS) with key secondary endpoint progression-free survival (PFS) per investigator assessment, each measured from time of randomization. Additional secondary endpoints were objective response rate (ORR) and safety.

Results

With median (m) follow-up time of 15.9 and 16.1 months (mo), respectively, tarlatamab + durva significantly improved OS (HR: 0.42; 95% CI 0.32, 0.54; P < 0.001; mOS: 21.1 [95% CI, 20.8 to NE] vs 12.7 mo [95% CI, 11.2 to 14.8]). Tarlatamab + durva significantly improved PFS (HR: 0.34; 95% CI 0.28, 0.42; P < 0.001; mPFS: 7.4 vs 1.9 mo). ORR was 26.4% (95% CI 20.9%, 32.5%) for tarlatamab + durva and 4.1% (95% CI 2.0%, 7.4%) for durva (P < 0.001). Grade ≥ 3 TEAEs occurred in 46.8% (tarlatamab + durva) and 40.6% (durva) of pts. Cytokine release syndrome (CRS) and immune-effector cell-associated neurotoxicity syndrome (ICANS) occurred in 49.6% and 1.1% of tarlatamab + durva pts and were mostly low grade (Table).Table: LBA3

	Tarlatamab + durva (n = 282)	Durva (n = 281)
OS		
mOS, mo (95% CI)	21.1 (20.8, NE)	12.7 (11.2, 14.8)
HR (95% CI); P value	0.42 (0.32, 0.54); P < 0.001	
12 mo OS rate, % (95% CI)	79.4 (74.2, 83.7)	53.3 (47.3, 59.0)
Median follow-up, mo	15.9	16.1
PFS		
mPFS	7.4 (5.6, 9.1)	1.9 (1.9, 2.0)
HR (95% CI); P value	0.34 (0.28, 0.42); P < 0.001	

	Tarlatamab + durva (n = 282)	Durva (n = 281)
ORR, % (95% CI)	26.4 (20.9, 32.5)	4.1 (2.0, 7.4)
P value	P < 0.001	
TEAEs, n (%)	(n = 282)	(n = 278)
Any grade	281 (99.6)	258 (92.8)
Gr ≥ 3	132 (46.8)	113 (40.6)
CRS ^a , n (%)		
Any grade	140 (49.6)	4 (1.4)
Gr ≥ 3	1 (0.4)	0
ICANS ^a , n (%)		
Any grade	3 (1.1)	0
Gr ≥ 3	0	0

^aNo fatal events occurred. NE, not estimable; Gr, grade; TEAE, treatment-emergent adverse event.

Conclusions

Tarlatamab + durva significantly improved OS, PFS, and ORR in 1LM ES-SCLC. The overall incidence of adverse events was comparable between groups. CRS and ICANS events were primarily low grade and no fatal events occurred. These results establish tarlatamab + durva as a new standard of care 1LM therapy for ES-SCLC.

Clinical trial identification

NCT06211036.

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Disclosure

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Pharmaceutical, Daiichi Sankyo, MSD, Pfizer, Taiho Pharmaceutical, Novartis; Financial Interests, Institutional, Local PI: Chugai Pharmaceutical, Boehringer Ingelheim, AstraZeneca, Bristol-Myers Squibb, Daiichi Sankyo, GSK, MSD, Taiho Pharmaceutical, Novartis. O. Juan-Vidal: Financial Interests, Personal, Advisory Board: Amgen Inc. , AstraZeneca, Bristol-Myers Squibb, Janssen, Pierre Fabre, Roche/Genentech; Financial Interests, Personal, Invited Speaker: Amgen Inc., Bristol-Myers Squibb, Johnson and Johnson, Lilly, Pfizer, Pierre Fabre, Roche/Genentech; Financial Interests, Personal, Other, Travel expenses: MSD, Roche/Genentech; Non-Financial Interests, Institutional, Funding: AstraZeneca. Y. Chen: Financial Interests, Personal, Advisory Board: AstraZeneca , Bristol-Myers Squibb; Financial Interests, Personal, Other, speaker faculty: AstraZeneca , Bristol-Myers Squibb, Amgen Inc. , Pfizer , Jazz Pharmaceuticals, Daiichi Sankyo; Financial Interests, Institutional, Local PI: AstraZeneca , Merck, Ipsen, Bristol-Myers Squibb, Amgen Inc., Helsinn, EMD/Serono, Lilly, Daiichi Sankyo; Financial Interests, Institutional, Coordinating PI: Moderna. G. Schvartsman: Financial Interests, Personal, Advisory Board: AstraZeneca, Pfizer, Resolute science, Daiichi Sankyo; Financial Interests, Personal, Invited Speaker: Merck, Amgen, Bristol-Myers Squibb International; Financial Interests, Research Grant: Bristol-Myers Squibb International; Financial Interests, Coordinating PI: Amgen, Astr. A.C. Dingemans: Financial Interests, Institutional, Advisory Board: Roche, Amgen, Bayer, AstraZeneca, Boehringer Ingelheim, Johnson & Johnson, Mirati, Boehringer Ingelheim, Pfizer, MSD; Financial Interests, Institutional, Other, IDMC: Roche; Financial Interests, Institutional, Invited Speaker: Eli Lilly, BeOne, Johnson and Johnson; Financial Interests, Institutional, Research Grant: Amgen; Financial Interests, Institutional, Local PI: Lilly, Amgen, Daiichi Sankyo, JNJ, Mirati, Bayer, Merus, Revolution Medicine; Financial Interests, Institutional, Coordinating PI: Roche; Financial Interests, Institutional, Steering Committee Member: Roche, Eli Lilly, Amgen, Boehringer Ingelheim; Non-Financial Interests, Other, Chair Scientific Chair Council EORTC: EORTC; Non-Financial Interests, Member: IASLC, ASCO, AACR, ERS; Non-Financial Interests, Leadership Role: EORTC. J. Clarke: Financial Interests, Personal, Advisory Board: BMS, Synthekine, Merck, Genentech, Daiichi Sankyo; Financial Interests, Personal, Other, DSMB: Biothera, Pharmacosmos; Financial Interests, Personal, Other, Speaking and advisory: Boehringer Ingelheim; Financial Interests, Institutional, Research Grant: BMS, Lilly, Genentech, Immuneering, Amgen, AstraZeneca, Abel Zeta; Financial Interests, Research Grant: Grid Therapeutics. M. Marigil: Financial Interests, Personal, Full or part-time Employment: Amgen Inc. ; Financial Interests, Personal, Stocks/Shares: Amgen Inc. Y. Zhang: Financial Interests, Personal, Full or part-time Employment, I am Senior Manager, biostatistics in Amgen: Amgen; Financial Interests, Personal, Stocks/Shares, I have stocks from Amgen: Amgen. B. Abidi: Financial Interests, Personal, Full or part-time Employment: Amgen Inc. ; Financial Interests, Personal, Stocks/Shares: Amgen Inc. M. Pérol: Financial Interests, Personal, Advisory Board, Advisory board: AbbVie, Amgen, ANHEART THERAPEUTICS, AstraZeneca, BMS, Daiichi Sankyo, ESAI, Ipsen, JANSSEN, Lilly, MSD, Novartis, NOVOCURE, Pfizer, Roche, Sanofi, Takeda; Financial Interests, Personal, Invited Speaker, Symposium: AstraZeneca, BMS, ILLUMINA, MEDSCAPE, MSD, Pfizer, Roche, Takeda; Financial Interests, Personal, Advisory Board, Expert Testimony: AstraZeneca; Financial Interests, Personal, Advisory Board: Regeneron, Pierre Fabre, Nuvation Bio; Financial Interests, Personal, Invited Speaker: Pierre Fabre, Amgen, Novocure, Ipsen, Johnson and Johnson; Financial Interests, Steering Committee Member, Steering Committee member: Lilly; Financial Interests, Institutional, Local PI, Local PI: AbbVie, Amgen, Anheart Therapeutics, Apollomics, Arrivent Biopharma, AstraZeneca, Bayer, Boehringer Ingelheim, Daiichi Sankyo, INNATE PHARMA, Roche; Financial Interests, Institutional, Research Grant, Resarch grant: AstraZeneca, Boehringer Ingelheim, Roche, Takeda; Financial Interests, Personal, Trial Chair, Trial Chair: Anheart Therapeutics; Financial Interests, Personal, Other, IDMC Chair: PharmaMar; Financial Interests, Personal, Steering Committee Member, Steering Committee Member: Roche; Financial Interests, Personal, Steering Committee Member, IDMC Chair: Sophiagenetics; Financial Interests, Personal, Other, DMSB: Roche; Financial Interests, Personal, Steering Committee Member, Steering Committee member: Nuvation Bio; Financial Interests, Trial Chair, DeLLphi-305: Amgen; Financial Interests, Steering Committee Member: Daiichi Sankyo; Financial Interests, Institutional, Local PI: ArriVent BioPharma, Taiho Oncology; Other, Other, Travel support: AstraZeneca, MSD, Pfizer, Amgen. 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