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Tarlatamab in previously treated SCLC: Extended follow-up of overall survival from the phase 3 DeLLphi-304 trial

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Background

Tarlatamab, a DLL3-targeting bispecific T-cell engager (BiTE®) immunotherapy, demonstrated a 40% reduced risk of death and a favorable safety profile vs chemotherapy (CTx) in patients (pts) with small cell lung cancer (SCLC) after first-line (1L) platinum-based CTx. The initial publication was based on a median follow-up of only 11.2 months (mo). We now report long-term efficacy and safety data from DeLLphi-304.

Methods

Pts were randomized 1:1 to tarlatamab or CTx (topotecan, lurbinectedin or amrubicin). The primary endpoint was overall survival (OS); secondary endpoints included progression-free survival (PFS), disease control (DC), duration of response (DOR), and safety.

Results

With extended follow-up (median 23 mo), tarlatamab continued to show lower risk of death vs CTx (HR 0.62; 95% CI, 0.51–0.76), with longer OS (median 13.6 vs 8.4 mo). The reduced mortality risk was maintained across high-risk subgroups, including pts with baseline platinum-resistant disease and those with brain metastases (Table). Tarlatamab showed consistent benefit in PFS vs CTx (HR 0.69; 95% CI, 0.57–0.84; median 4.2 vs 3.2 mo). OS at 18 mo was higher with tarlatamab (42% vs 24%), as was 12-mo PFS (21% vs 6%), indicating sustained benefit. DOR was longer with tarlatamab vs CTx (Table), with more ongoing responses at 12 mo (42% vs 10% of responders), and a higher proportion with sustained (≥ 52 week) DC (24% vs 4%).

Grade ≥ 3 treatment-related adverse events (TRAEs; 28% vs 63%) and discontinuations due to TRAEs (3% vs 7%) were less frequent with tarlatamab vs CTx. Tarlatamab showed long-term tolerability with TRAEs decreasing over time and no new safety signals.Table: 38080

Long-term Efficacy Outcomes	Tarlatamab n = 254 CTx n = 255	
OS		
Median, mo	13.6 (11.9–15.8)	8.4 (7.2–10.2)
HR overall	0.62 (0.51–0.76)	
HR (subgroup): platinum-resistant disease [†]	0.65 (0.48–0.86)	
HR (subgroup): baseline brain metastases	0.52 (0.38–0.70)	
12-mo OS, %	56 (50–62)	39 (33–45)
18-mo OS, %	42 (36–48)	24 (19–29)
PFS*		

Long-term Efficacy Outcomes	Tarlatab n = 254 CTx n = 255	
Median, mo	4.2 (3.0–4.4)	3.2 (2.9–4.2)
HR overall	0.69 (0.57–0.84)	
12-mo PFS, %	21 (16–26)	6 (3–10)
DOR,* median, mo	7.1 (4.5–12.4)	5.5 (4.2–5.7)
DC Rate,* %	68 (62–74)	64 (58–70)
Sustained DC* (≥ 52 weeks), n (%)	62 (24)	11 (4)

*Per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 †Platinum-resistant: chemotherapy-free interval < 90 days Parentheses show 95% CI unless noted

Conclusions

With extended follow-up, tarlatab demonstrated a durable survival benefit with a manageable safety profile vs CTx, with no new safety signals, reinforcing its role as the standard of care treatment in pts with SCLC after 1L platinum-based CTx, including those with high-risk disease.

Clinical trial identification

NCT05740566.

Editorial acknowledgement

Medical writing support for the development of this abstract was provided by Kim H. Lew, PharmD, an employee of Amgen Inc.

Legal entity responsible for the study

Amgen Inc.

Funding

Amgen Inc.

Disclosure

C.M. Rudin: Financial Interests, Personal, Advisory Board, Consulting re: oncology drug development: Amgen, AstraZeneca, Daiichii Sankyo, Hoffmann-La Roche, Novartis, Jazz Pharmaceuticals; Financial Interests, Personal, Advisory Board, SAB member: Auron, Earli, DISCO; Financial Interests, Personal, Advisory Board, Licensing fees and royalties for DLL3-directed therapies: Memorial Sloan Kettering; Financial Interests, Institutional, Local PI: Merck; Financial Interests, Institutional, Coordinating PI: Daiichii Sankyo. M. Ahn: Financial Interests, Personal, Advisory Board: AstraZeneca, Takeda, MSD, Yuhan, Amgen, Janssen, Bristol Myers Squibb, Roche, Daiichi Sankyo, Merck, VORONOL, Genexin, Boehringer Ingelheim, AIMED BIO. M.H.H. Schuler: Financial Interests, Personal, Invited Speaker: Amgen, Bristol-Myers Squibb, Janssen, Roche, GSK, MSD, Lilly; Financial Interests, Personal, Advisory Board: Amgen, AstraZeneca, Bristol-Myers Squibb, GSK, Janssen, Novartis, Roche, Sanofi, MSD, Regeneron, Lilly, Gilead; Financial Interests, Institutional, Research Grant: Bristol-Myers Squibb, Janssen; Non-Financial Interests, , Principal Investigator, Member, Study Steering Board: Janssen; Non-Financial Interests, , Principal Investigator, Member, Study Steering Committee: Amgen. F. Blackhall: Financial Interests, Personal, Other, IDMC Chair: AstraZeneca; Financial Interests, Personal, Advisory Board, Small cell Advisory Board: Amgen; Financial Interests, Personal, Member of Board of Directors, Director of Division of Research and Innovation: The Christie NHS Foundation Trust; Financial Interests, Institutional, Coordinating PI, Institutional payment for clinical trial activities: Amgen, Pfizer; Financial Interests, Institutional, Coordinating PI, Payment for clinical trial activities: Mirati; Financial Interests, Institutional, Coordinating PI, Clinical trial activities: BMS; Financial Interests, Institutional, Funding, Real world evidence research programme: Roche; Financial Interests, Institutional, Research Grant, Translational research: Boehringer Ingelheim; Financial Interests, Institutional, Coordinating PI, DAREON trial SCLC: Boehringer Ingelheim; Non-Financial Interests, , Leadership Role, Medical Lead Cancer Cluster NIHR Biomedical research centre: The University of Manchester. G. Mountzios: Financial Interests, Personal, Advisory Board: ROCHE, BMS, TAKEDA, Janssen, Sanofi; Financial Interests, Personal, Invited Speaker: MSD, ASTRAZENECA, PFIZER, NOVARTIS, AMGEN; Financial Interests, Institutional, Local PI: MSD; Financial Interests, Personal, Local PI: AstraZeneca, Roche, Novartis, Lilly, GSK, Amgen, Gilead Pharmaceuticals, BMS, Boehringer Ingelheim; Financial Interests, , Trial Chair: AstraZeeca; Financial Interests, Personal, Steering Committee Member: Amgen; Non-Financial Interests, , Officer, Member of the Educational Publications Working GroupMember of the Lung Cancer Faculty: ESMO. T. Yoshida: Financial Interests, Personal, Advisory Board: Pfizer, MSD, Amgen, Boehringer Ingelheim; Financial Interests, Personal, Invited Speaker: Astrazeneca, Chugai pharmaceutical, Pfizer, Takeda, Lilly, Ono pharmaceutical, Novartis, Daiichi sankyo, MSD, BMS, Amgen; Financial Interests, Institutional, Local PI: Astrazeneca, Novartis, Amgen, Daiichi sankyo, BMS, MSD, Ono pharmaceutical, Chugai pharmaceutical, AbbVie, Astellas, Boehringer Ingelheim, Nuvalent. B.C. Cho: Financial Interests, Personal, Advisory Board: Cyrus therapeutics, J INTS Bio, KANAPH Therapeutic Inc; Financial Interests, Personal, Other, Consulting role: Amgen,

ArriVent, AstraZeneca, BMS, Boehringer-Ingelheim, CJ Bioscience, Cyrus therapeutics, GSK, Glied, Johnson & Johnson, MSD, Yuhan, Regeneron; Financial Interests, Personal, Invited Speaker: ASCO, AstraZeneca, Guardant, Roche, ESMO, IASLC, Korean Cancer Association, Korean Society of Medical Oncology, Korean Society of Thyroid-Head and Neck Surgery, Korean Cancer Study Group, Novartis, MSD, The Chinese Thoracic Oncology Society, Pfizer, Zailab; Financial Interests, Personal, Member of Board of Directors: J INTS BIO; Financial Interests, Personal, Full or part-time Employment: Yonsei University Health System; Financial Interests, Personal, Stocks/Shares: KANAPH Therapeutic Inc, J INTS BIO; Financial Interests, Personal, Royalties, PDX, PDO, PDC Licensing Contract – not patent: Champions Oncology, Crown Bioscience, Imagen, PearlRiver Bio GmbH; Financial Interests, Institutional, Research Grant: CJ bioscience, Cyrus, Johnson & Johnson, MSD, Dong-A ST, Yuhan, ImmuneOncia, JINTSbio, Ligachem bioscience; Other, , Other, Founder: DAAN Biotherapeutics. S. Arulananda: Financial Interests, Personal, Invited Speaker: Merck-Sharpe & Dohme, AstraZeneca, Roche – Genentech, Bristol-Myers Squibb, Merck Serono, Takeda, Amgen, Boehringer-Ingelheim, Pfizer, Medison; Financial Interests, Personal, Advisory Board: Roche, BeOne, Amgen, Bayer, AstraZeneca, Merck-Sharpe & Dohme, Johnson & Johnson, Bristol-Myers Squibb, Medison, Race Oncology, Daiichi-Sankyo, Merck Serono, Boehringer-Ingelheim; Non-Financial Interests, , Leadership Role: TOGA. P.E. Lammers: Financial Interests, Personal, Advisory Board: Amgen, Daiichii Sankyo, AstraZeneca, Menarini-Stemline, Merck, Novartis; Financial Interests, Personal, Invited Speaker: AstraZeneca, Amgen. S.R. Punekar: Financial Interests, Personal, Advisory Board: Revolution Medicine, Regeneron Pharmaceuticals, Cogent Therapeutics; Financial Interests, Institutional, Local PI, Clinical Trial PI: Revolution Medicine, Simcere Pharmaceuticals, Astellas Pharmaceuticals, Constellation, A2Bio, Vitrac; Financial Interests, Institutional, Local PI, Clinical Tria PI: Neogene, Affini-T, Prelude, Tango; Financial Interests, Personal, Local PI, Travel Support: Revolution Medicine; Financial Interests, Institutional, Local PI: Synthekine, Amgen, AstraZeneca, Clasp Therapeutics, Bioncotech Therapeutics; Financial Interests, Personal, Other, Royalties for Book: elselvier; Non-Financial Interests, , Principal Investigator, Clinical Trial PI: Revolution Medicine, A2Bio, Simcere, Constellation, Vitrac, Astellas Pharmaceuticals, Neogene; Non-Financial Interests, , Principal Investigator, Clinical Tria PI: Affini-T, Prelude, Tango; Non-Financial Interests, , Principal Investigator: Amgen. P.F. Simoes da Rocha: Financial Interests, Personal, Advisory Board: Daiichii Sankyo, IGES pharma, Boehringer Ingelheim; Financial Interests, Personal, Invited Speaker: AstraZeneca, Amgen, Daiichii Sankyo, ThermoFisher; Other, , Other, Congress and travel: MSD, BMS, AstraZeneca, Kyowa Kirin, Roche, PharmaMar, Lilly. J. Mazieres: Financial Interests, Personal, Advisory Board: ROCHE, ASTRAZENECA, MERCK, BMS, TAKEDA, DAIICHI, PIERRE FABRE, AMGEN; Financial Interests, Personal, Invited Speaker: ROCHE, ASTRAZENECA, PIERRE FABRE; Financial Interests, Institutional, Research Grant: ROCHE, PIERRE FABRE; Financial Interests, Institutional, Funding: BMS. M. Gumus: Financial Interests, Institutional, Invited Speaker: Pfizer, Gen Pharmaceuticals, Novartis, Bayer, AstraZeneca; Financial Interests, Institutional, Advisory Board: Amgen, Roche, BMS, AstraZeneca, MSD, Roche, Erkim Drug, Turkey; Financial Interests, Institutional, Coordinating PI: Amgen; Financial Interests, Institutional, Local PI: Jounce Therapeutics. S. Huang: Financial Interests, Personal, Full or part-time Employment: Amgen; Financial Interests, Personal, Stocks/Shares: Amgen. A. Hamidi: Financial Interests, Personal, Full or part-time Employment: Amgen; Financial Interests, Personal, Stocks/Shares: Amgen. U. Patil: Financial Interests, Personal, Full or part-time Employment: Amgen; Financial Interests, Personal, Stocks/Shares: Amgen. All other authors have declared no conflicts of interest.