Practical Perspectives: Experts Review Actual Cases of Patients with Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 16, 2025
5:00 PM – 6:00 PM ET

Faculty

Stephen V Liu, MD
Charles Rudin, MD, PhD

Moderator

Neil Love, MD

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Faculty

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Associate Professor of Medicine
Georgetown University Hospital
Washington, DC

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Charles Rudin, MD, PhD
Deputy Director, MSK
Sylvia Hassenfeld Chair in Lung Cancer Research
Co-Director, Druckenmiller Center for
Lung Cancer Research
Memorial Sloan Kettering Cancer Center
Professor of Medicine
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New York, New York

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Dr Love — Disclosures

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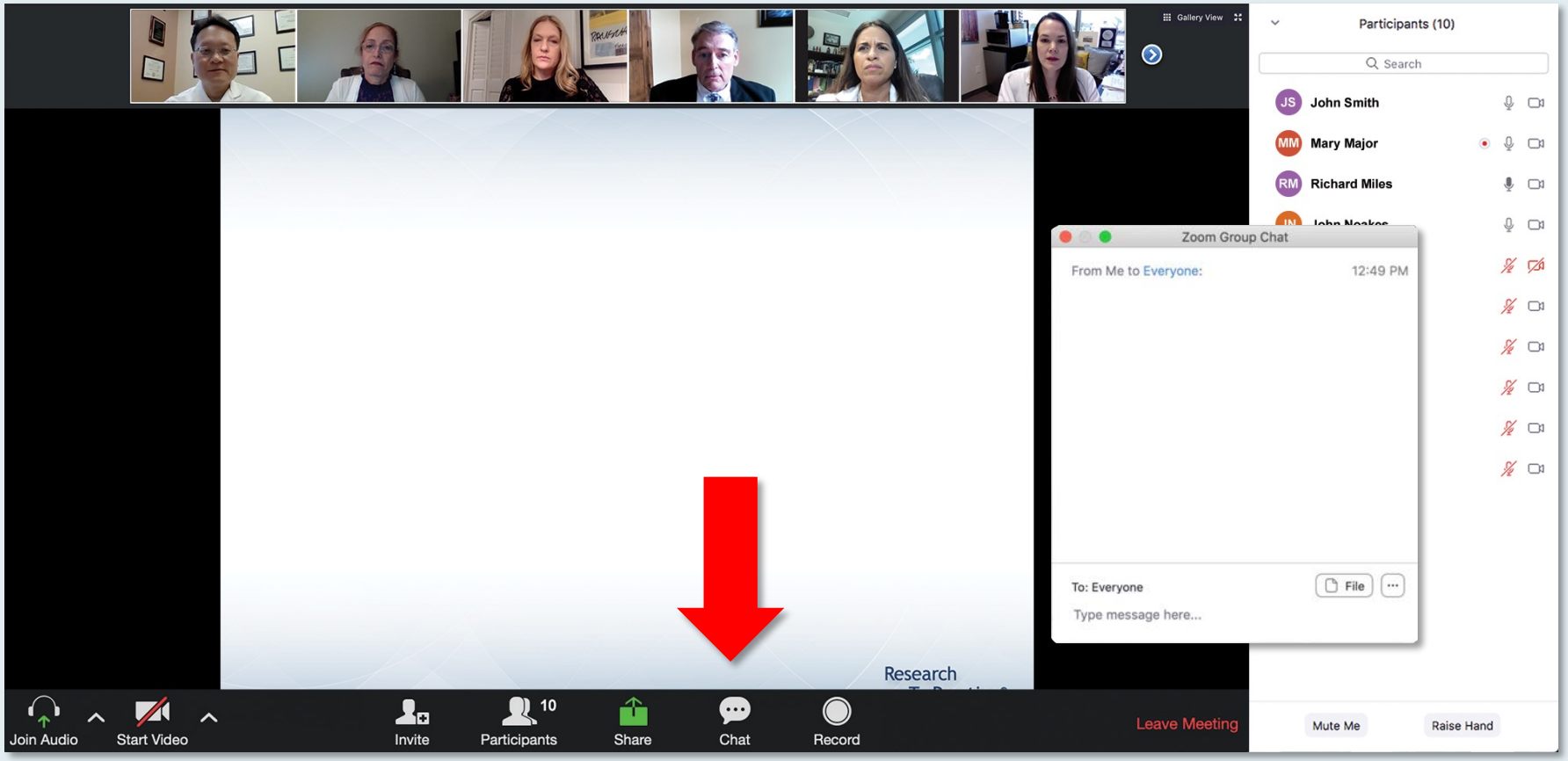

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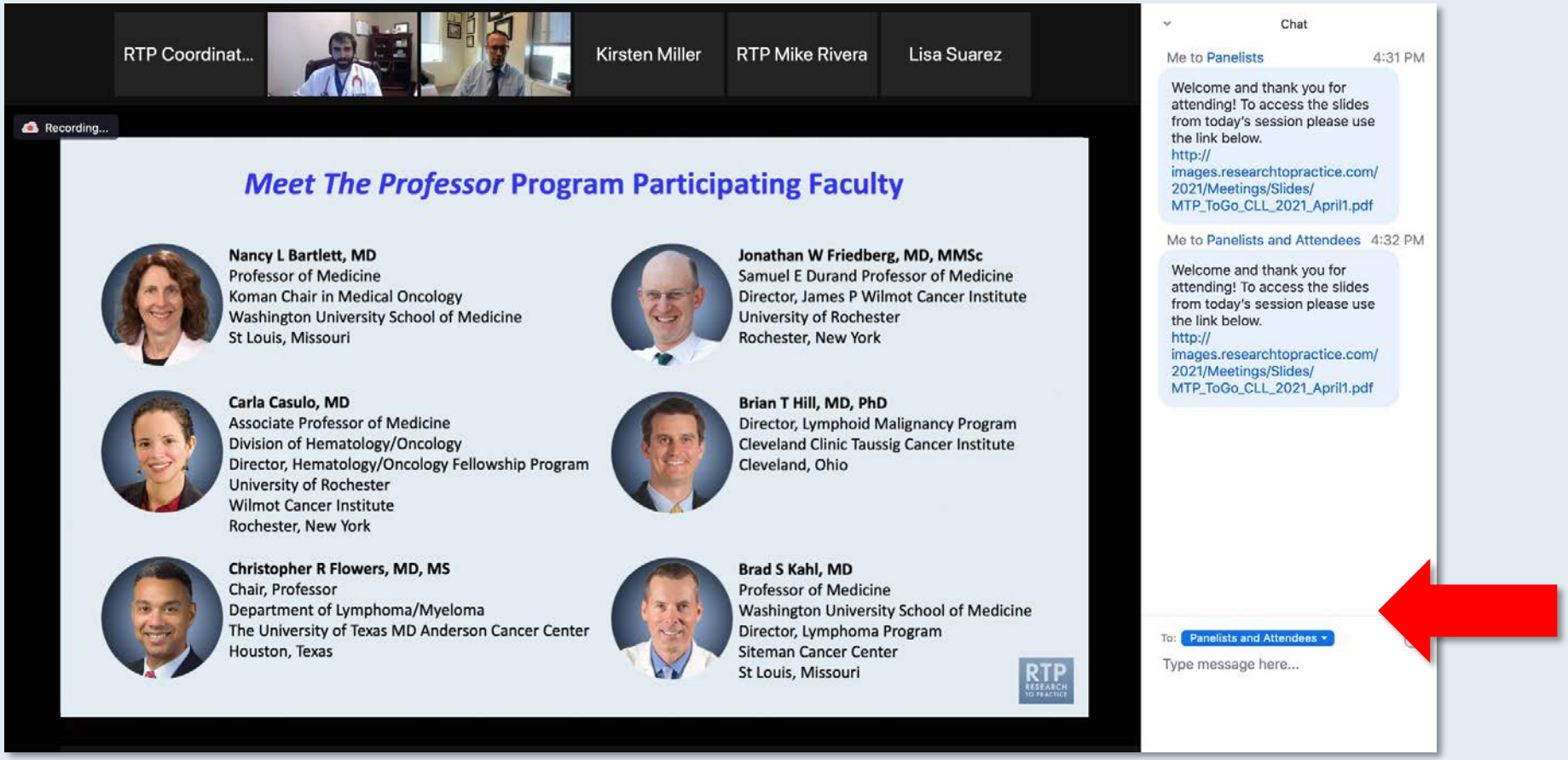

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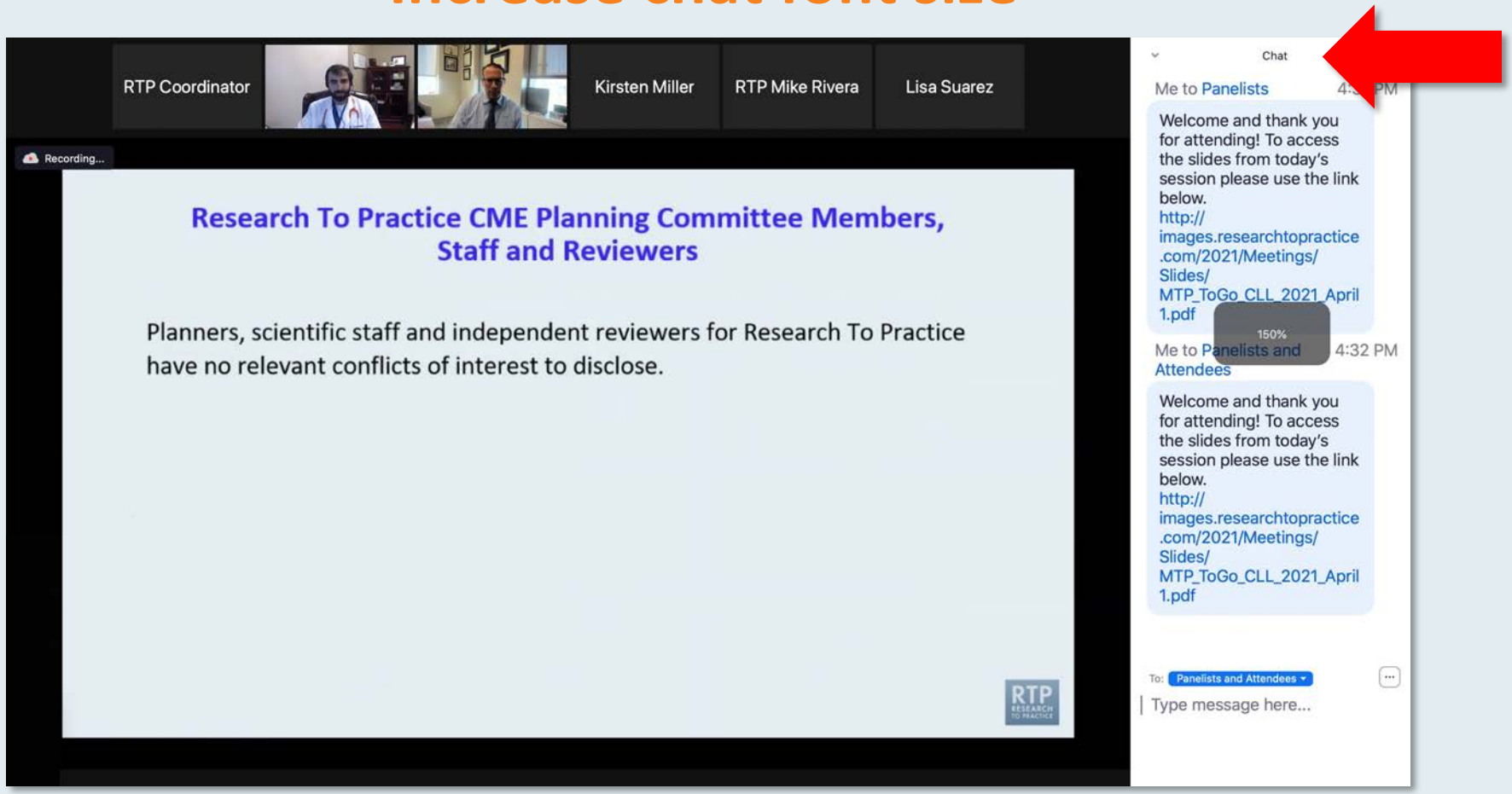

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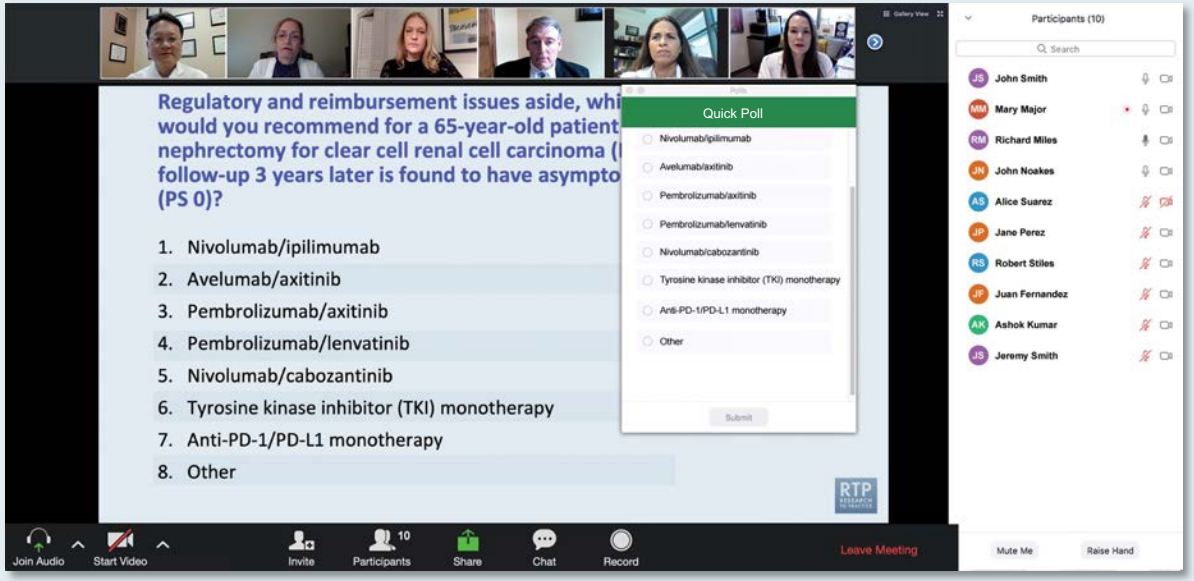

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The Implications of Recent Datasets for the Current and Future Management of Small Cell Lung Cancer — A 2024 World Conference on Lung Cancer Review

DR JACOB SANDS
DANA-FARBER CANCER INSTITUTE

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Inside the Issue: Managing Ocular Toxicities Associated with Antibody-Drug Conjugates and Other Cancer Therapies

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Neel Pasricha, MD
Tiffany A Richards, PhD, ANP-BC, AOCNP

Moderator

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Cancer Q&A: Addressing Common Questions Posed by Patients with Relapsed/Refractory Multiple Myeloma

A Webinar Series for Clinicians and Patients,
Developed in Partnership with Cancer*Care*®

Patients	Clinicians
Wednesday, July 23, 2025	**Thursday, August 7, 2025**
6:00 PM – 7:00 PM ET	**5:00 PM – 6:00 PM ET**

Faculty

Natalie S Callander, MD
Sagar Lonial, MD, FACP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Knowledge and Practice Gaps in the Community — Optimizing the Use of Oral Selective Estrogen Receptor Degraders for Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, July 29, 2025

5:00 PM – 6:00 PM ET

Faculty

Komal Jhaveri, MD, FACP

Virginia Kaklamani, MD, DSc

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Practical Perspectives: Experts Review
Actual Cases of Patients with Biliary Tract Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, August 6, 2025
5:00 PM – 6:00 PM ET

Faculty

Haley Ellis, MD
James J Harding, MD

Moderator

Neil Love, MD

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Selection and Sequencing of Therapy for Metastatic Triple-Negative Breast Cancer

A CME/MOC-Accredited Live Webinar

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Faculty

Ana C Garrido-Castro, MD
Professor Peter Schmid, FRCP, MD, PhD

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SOHO SYMPOSIUM SERIES

Two Exciting Events You Do Not Want to Miss

A 2-Part CME/MOC-, NCPD- and ACPE-Accredited Satellite Symposium Series During the Society of Hematologic Oncology 2025 Annual Meeting

Relapsed/Refractory Multiple Myeloma

Thursday, September 4, 2025

6:42 PM – 7:42 PM CT
(7:42 PM – 8:42 PM ET)

Follicular Lymphoma

Friday, September 5, 2025

11:47 AM – 12:47 PM CT
(12:47 PM – 1:47 PM ET)

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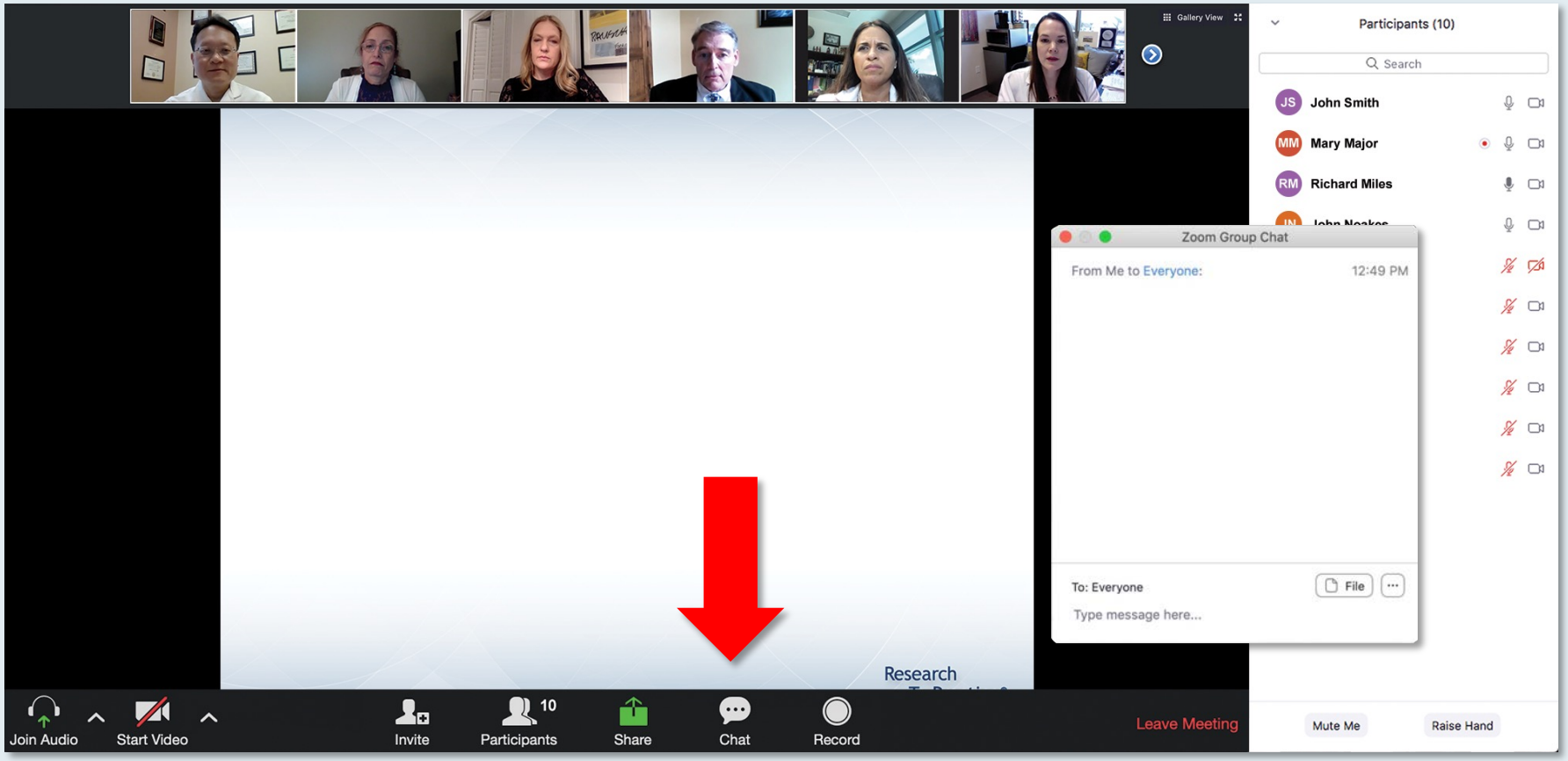

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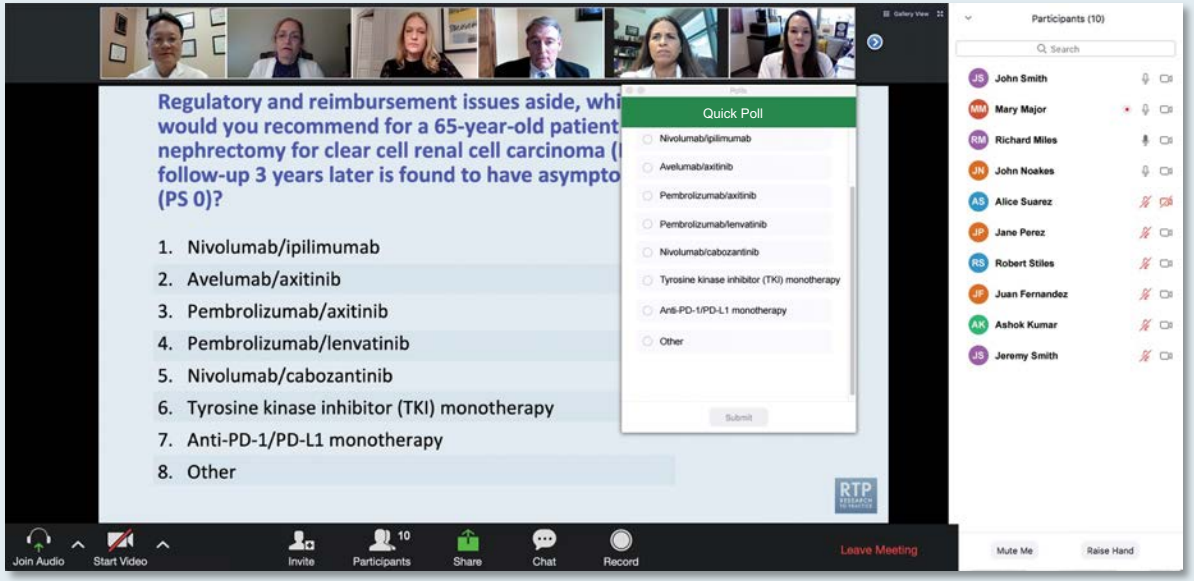

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Bethlehem, Pennsylvania

Estelamari Rodriguez, MD, MPH
Sylvester Comprehensive Cancer Center
Miami, Florida

Kimberly Ku, MD
Illinois CancerCare
Bloomington, Illinois

Priya Rudolph, MD, PhD
Georgia Cancer Specialists
Athens, Georgia

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Agenda

Case 1: Adjuvant Systemic Therapy?

Case 2: Lambert-Eaton Syndrome and Other Paraneoplastic Syndromes

Case 3: Small Cell Transformation of EGFR-Mutant NSCLC

Case 4: Trilaciclib in Extensive-Stage Disease

Comments: ASCO and Other Recent Datasets (Part 1)

Case 5: Short DFI with Brain Mets After Chemo/RT/Durvalumab … Lurbinectedin?

Case 6: Tarlatamab After Rapid Disease Progression on Chemo/Atezolizumab

Case 7: ICANS on Tarlatamab with Brain Mets

Case 8: BiTE with Lurbinectedin on Protocol

Comments: ASCO and Other Recent Datasets (Part 2)

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Case Presentation: 73-year-old man with rheumatoid arthritis and angiosarcoma of the scalp is found to have a lung nodule and undergoes resection

Dr Estelamari Rodriguez (Miami, Florida)

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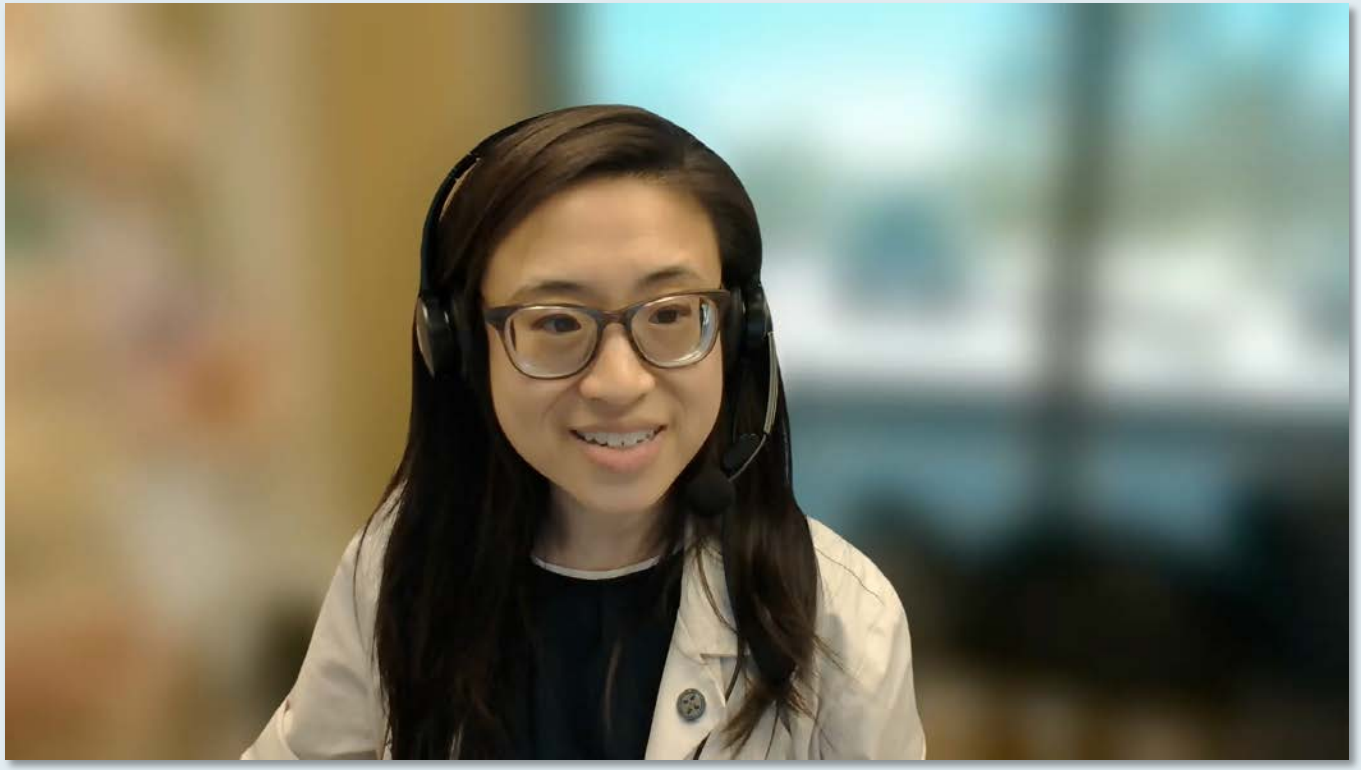
Case Presentation: 64-year-old woman who presents with limited-stage SCLC with Lambert-Eaton syndrome now has NED after chemoradiation but still with motor weakness



Dr Kimberly Ku (Bloomington, Illinois)

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Case Presentation: 50-year-old man with metastatic EGFR exon 19 del lung adenocarcinoma receives osimertinib with progression at 11 months and small cell transformation

Dr Estelamari Rodriguez (Miami, Florida)

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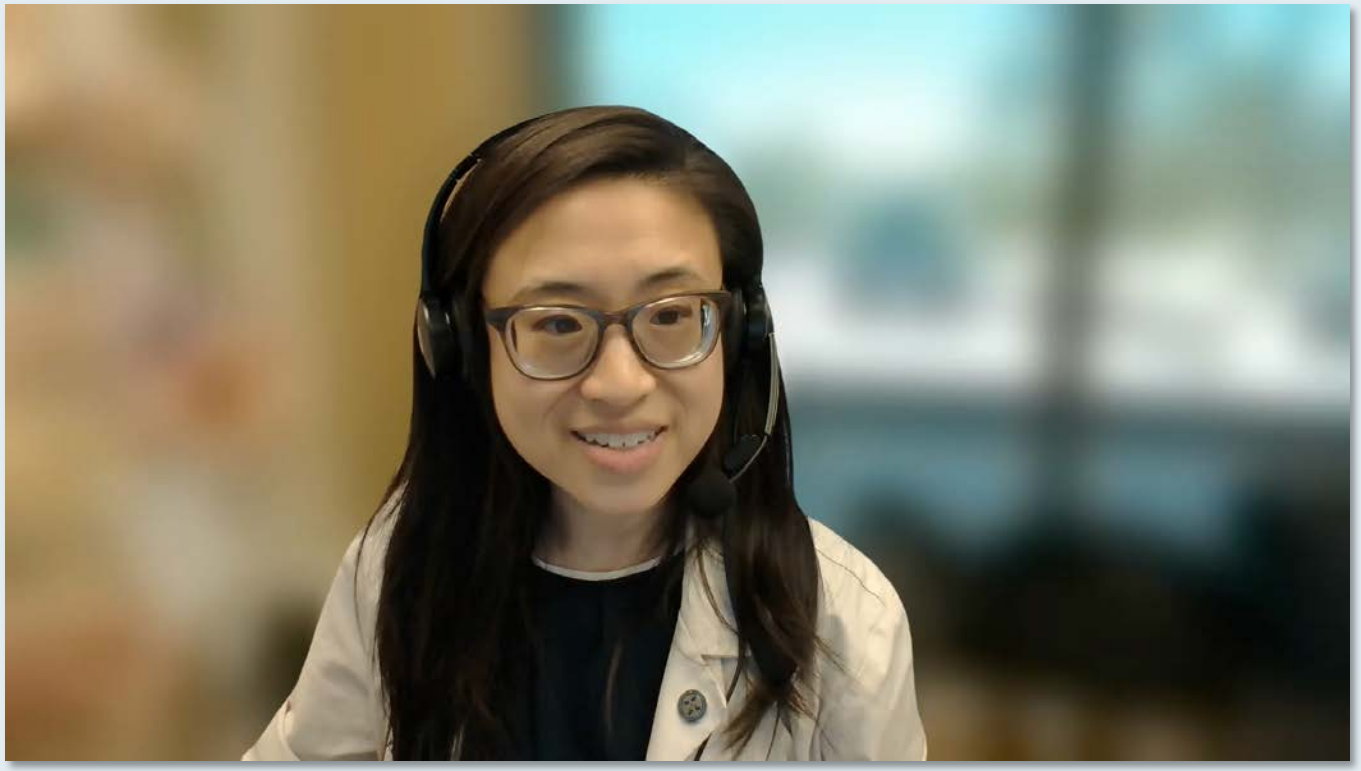
Case 8: BiTE with Lurbinectedin on Protocol

Comments: ASCO and Other Recent Datasets (Part 2)

Case Presentation: 66-year-old woman with ES-SCLC and brain metastases receives carboplatin/etoposide/atezolizumab and preemptive trilaciclib but develops Grade 3 neutropenia



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2025 ASCO ANNUAL MEETING

Abstract LBA8005

Randomized phase II trial investigating whether atezolizumab after chemoradiotherapy (CRT) prolongs survival in limited stage (LS) small cell lung cancer (SCLC)

Grønberg BH,[1,2*] Aanerud M,[3,4] Dumoulin DW,[5] Nyman J,[6] Schytte T,[7] Bjaanæs MM,[8] Neumann K,[9] Tsakonas G,[10] Kastelijn EA,[11] Helbekkmo N,[12] Langer SW,[13] Rothschild S,[14] Appenzeller C,[15] Stigt J,[16] McCulloch T,[17] Sorger H,[18,19] Sandvei MS,[1,2] Killingberg KT,[1,2] Frøseth TC,[2] and Halvorsen TO[1,2]

[1]Department of Clinical and Molecular Medicine, NTNU, Norwegian University of Science and Technology, Norway; [2]Department of Oncology, St. Olavs hospital, Trondheim University Hospital, Norway; [3]Department of Thoracic Medicine, Haukeland University Hospital, Norway; [4]Department of Clinical Science, University of Bergen, Norway; [5]Department of Pulmonology, Erasmus MC, Erasmus University Rotterdam, The Netherlands; [6]Department of Oncology, Sahlgrenska University Hospital, Sweden; [7]Department of Oncology, Odense University Hospital, Denmark; [8]Department of Oncology, Oslo University Hospital, Norway; [9]Department of Pulmonology, Akershus University Hospital, Norway; [10]Department of Oncology, Karolinska University Hospital, Sweden; [11]Department of Pulmonology, Sint Antonius Hospital, Utrecht/Nieuwegein, The Netherlands; [12]Department of Oncology, University Hospital of North Norway, Norway; [13]Department of Oncology, Rigshospitalet, University of Copenhagen, Denmark; [14]Department of Oncology, University Hospital of Basel, Switzerland; [15]Cantonal Hospital St. Gallen, Switzerland; [16]Dept of Respiratory Medicine, Isala Hospital, The Netherlands; [17]Department of Oncology, Aalborg University Hospital, Denmark; [18]Department of Medicine, Levanger Hospital, Norway; [19]Department of Circulation and Medical Imaging, NTNU, Norwegian University of Science and Technology, Norway

**bjorn.h.gronberg@ntnu.no*

Key Takeaway Point

In patients with LS SCLC, atezolizumab after chemoradiotherapy was tolerable, but did not improve progression free or overall survival

Grønberg BH et al. ASCO 2025;Abstract LBA8005.

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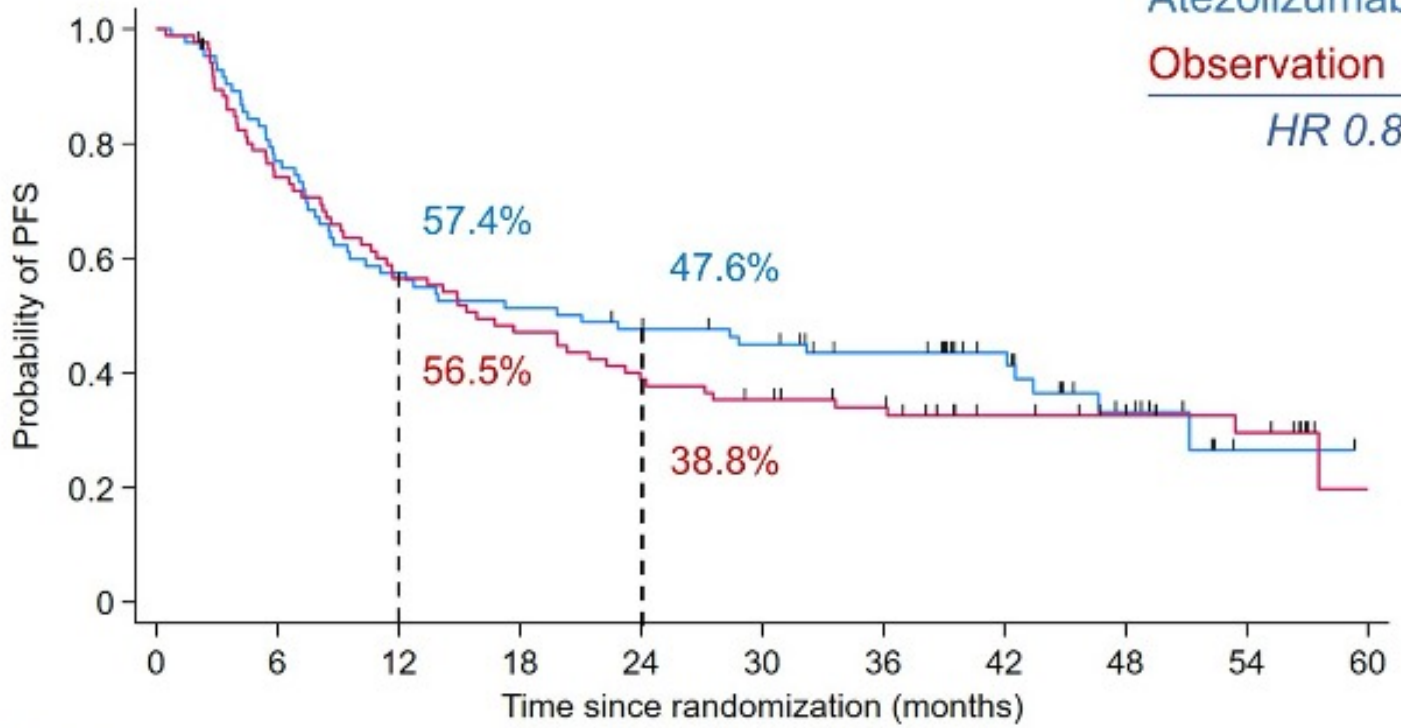
Progression-Free Survival (PFS) with Atezolizumab After Chemoradiation Therapy for LS-SCLC

	Median	95% CI
Atezolizumab	21.1 months	9.5 – 43.4
Observation	15.9 months	10.6 – 24.0

HR 0.89, 95% CI 0.61 – 1.30, p=0.55

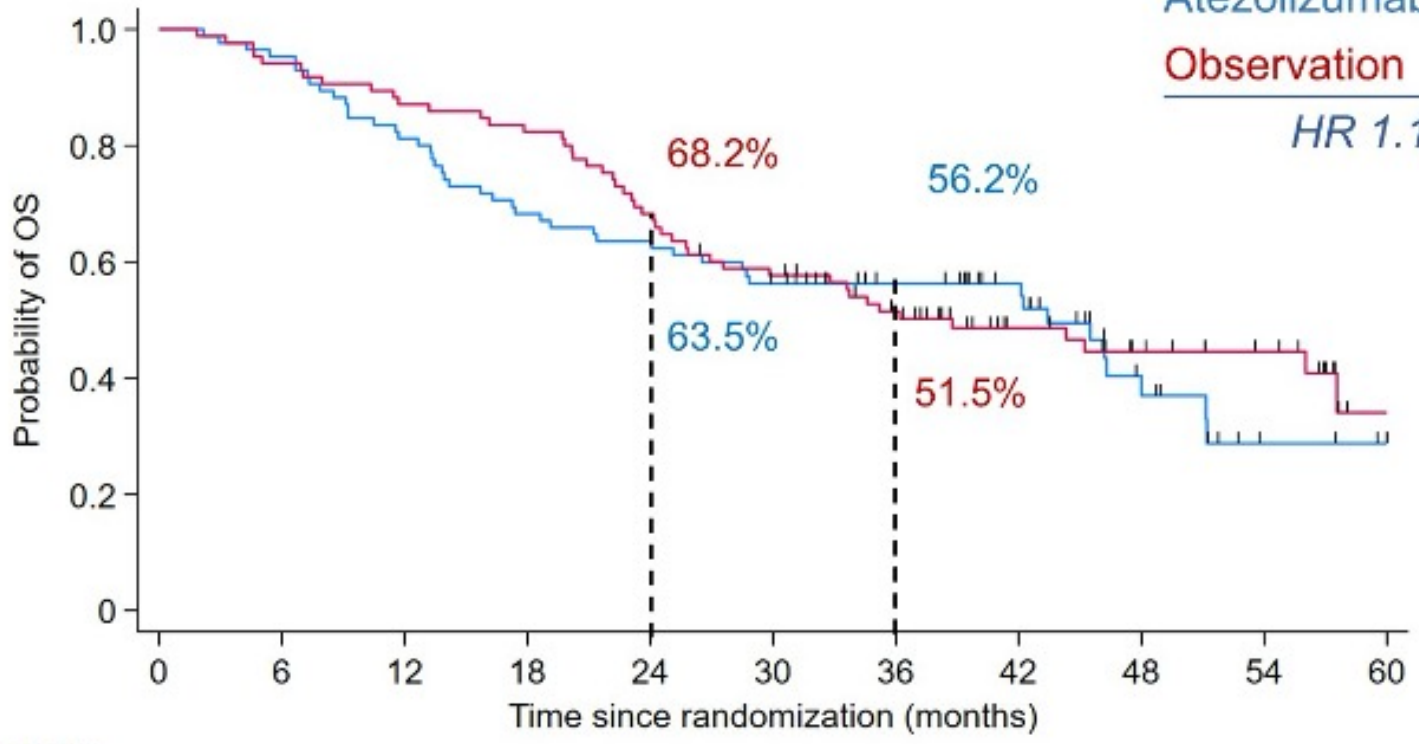


Grønberg BH et al. ASCO 2025;Abstract LBA8005.

Overall Survival (OS) with Atezolizumab After Chemoradiation Therapy for LS-SCLC

	Median	95% CI
Atezolizumab	43.4 months	25.1 – 51.2
Observation	38.8 months	25.8 – 57.6

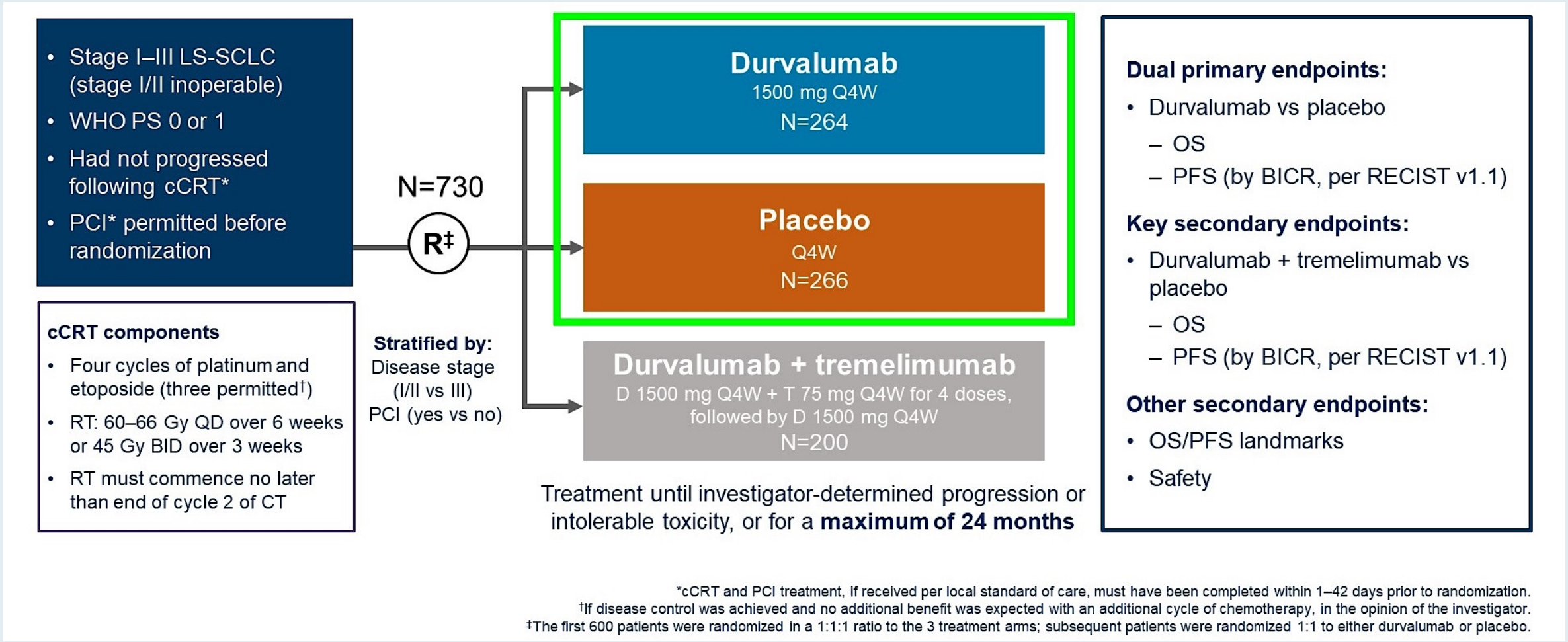
HR 1.14, 95% CI 0.76 – 1.71, p=0.53



Grønberg BH et al. ASCO 2025;Abstract LBA8005.

RTP RESEARCH TO PRACTICE

Phase III ADRIATIC Study Design

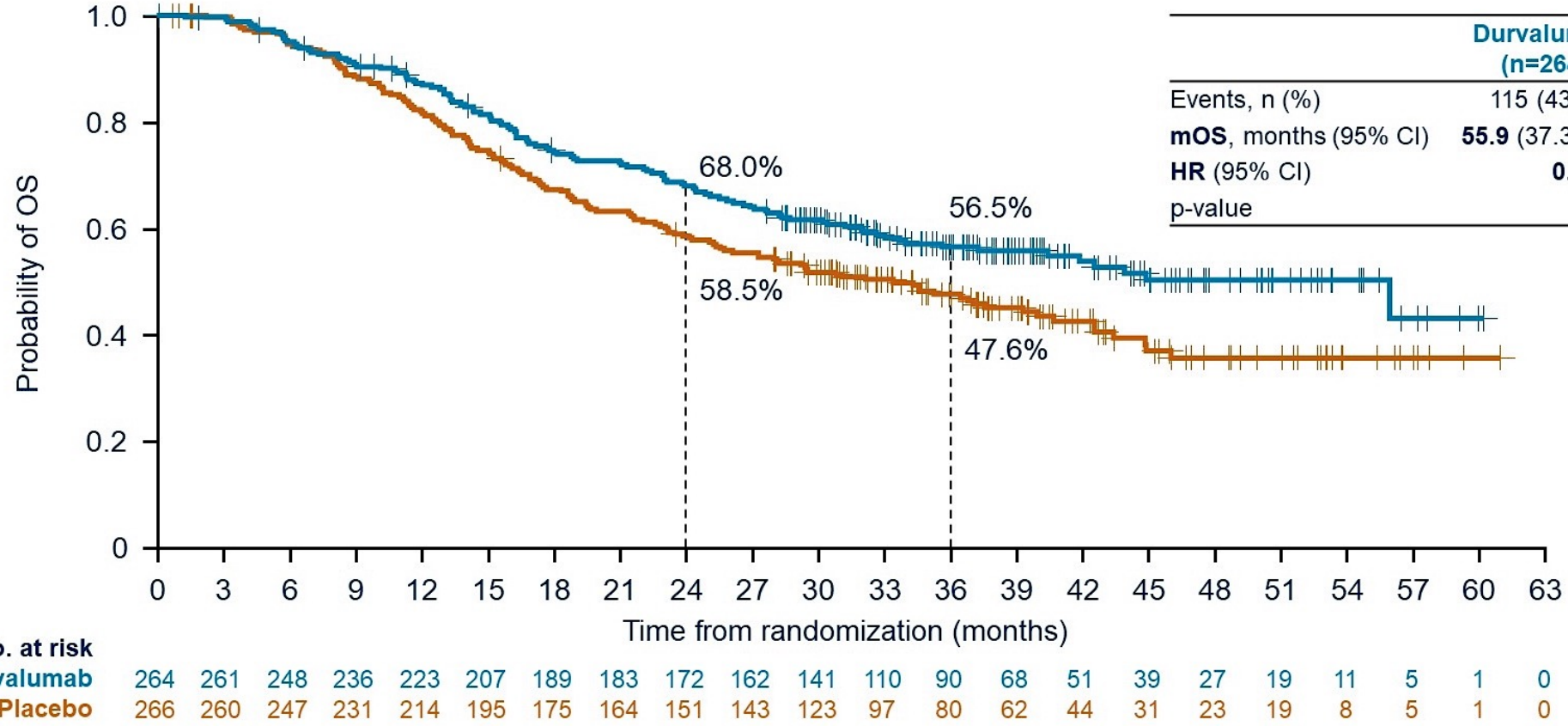


cCRT = concurrent platinum-based chemoradiation therapy; PCI = prophylactic cranial irradiation

Spigel DR et al. ASCO 2024;Abstract LBA5. Cheng Y et al. *N Engl J Med* 2024;391(14):1313-27.

ADRIATIC: Overall Survival

- Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

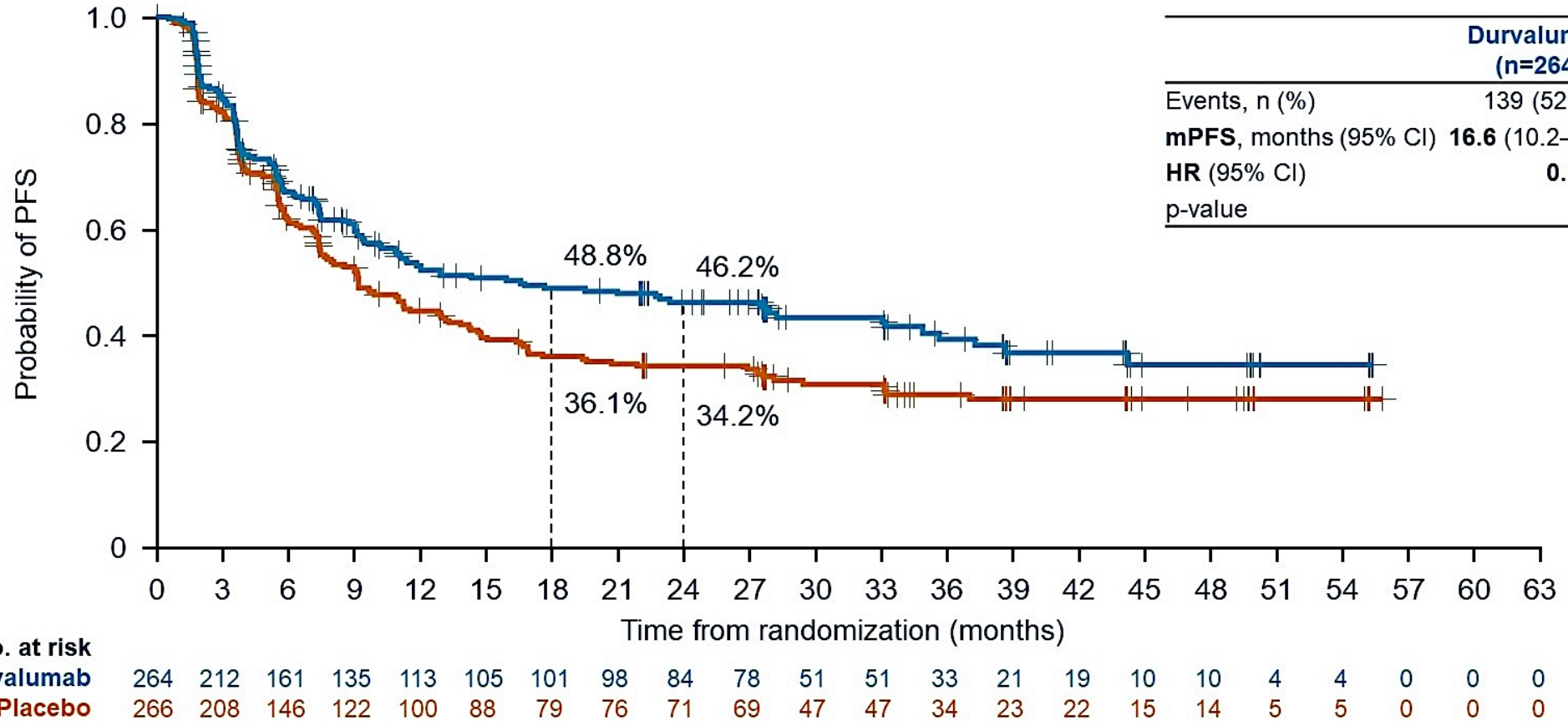
No. at risk																					
Durvalumab	264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0
Placebo	266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0

OS was analyzed using a stratified log-rank test adjusted for receipt of PCI (yes vs no). The significance level for testing OS at this interim analysis was 0.01679 (2-sided) at the overall 4.5% level, allowing for strong alpha control across interim and final analysis timepoints.

Spigel DR et al. ASCO 2024;Abstract LBA5. Cheng Y et al. *N Engl J Med* 2024;391(14):1313-27.

ADRIATIC: Progression-Free Survival

- Median duration of follow up in censored patients: 27.6 months (range 0.0–55.8)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

No. at risk																						
Durvalumab	264	212	161	135	113	105	101	98	84	78	51	51	33	21	19	10	10	4	4	0	0	0
Placebo	266	208	146	122	100	88	79	76	71	69	47	47	34	23	22	15	14	5	5	0	0	0

*By BICR per RECIST v1.1.

PFS was analyzed using a stratified log-rank test adjusted for disease stage (I/II vs III) and receipt of PCI (yes vs no). The significance level for testing PFS at this interim analysis was 0.00184 (2-sided) at the 0.5% level, and 0.02805 (2-sided) at the overall 5% level. Statistical significance for PFS was achieved through the recycling multiple testing procedure framework and testing at the 5% (2-sided) alpha level (adjusted for an interim and final analysis).

Spigel DR et al. ASCO 2024;Abstract LBA5. Cheng Y et al. *N Engl J Med* 2024;391(14):1313-27.

2025 ASCO ANNUAL MEETING

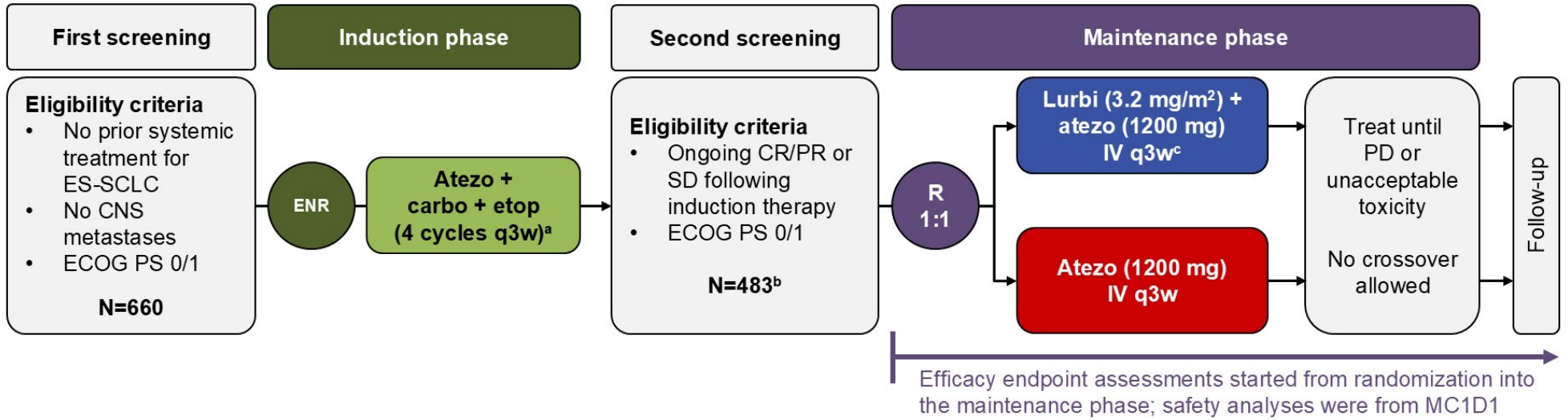
Abstract 8006

Lurbinectedin + atezolizumab as first-line maintenance treatment in patients with extensive-stage small cell lung cancer: Primary results of the Phase 3 IMforte trial

Luis Paz-Ares,[1] Hossein Borghaei,[2] Stephen V. Liu,[3] Solange Peters,[4] Roy S. Herbst,[5] Katarzyna Stencel,[6] Margarita Majem,[7] Grzegorz Czyżewicz,[8] Reyes Bernabé Caro,[9] Ki Hyeong Lee,[10] Melissa L. Johnson,[11] Nuri Karadurmuş,[12] Christian Grohé,[13] Vaikunth Cuchelkar,[14] Vilma Graupner,[15] Monika Kaul,[14] Ya-Chen Lin,[14] Debasis Chakrabarti,[16] Kamalnayan Bhatt,[16] Martin Reck[17]

[1]Hospital Universitario 12 de Octubre, H12O-CNIO Lung Cancer Unit, Universidad Complutense and Ciberonc, Madrid, Spain; [2]Fox Chase Cancer Center, Philadelphia, PA, USA; [3]Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; [4]University Hospital CHUV, Lausanne, Switzerland; [5]Yale School of Medicine, New Haven, CT, USA; [6]Wielkopolska Center of Pulmonology and Thoracic Surgery of Eugenia and Janusz Zeyland, Poznan, Poland; [7]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [8]The John Paul II Specialist Hospital, Kraków, Poland; [9]Hospital Universitario Virgen del Rocío, Seville, Spain; [10]Chungbuk National University Hospital, Cheongju, South Korea; [11]Tennessee Oncology, Sarah Cannon Research Institute, Nashville, TN, USA; [12]University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Türkiye; [13]Klinik für Pneumologie, Evangelische Lungenklinik Berlin, Berlin, Germany; [14]Genentech Inc, South San Francisco, CA, USA; [15]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]Jazz Pharmaceuticals plc, Dublin, Ireland; [17]Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany

IMforte Study Design



Stratification factors for randomization
- ECOG PS (0/1)
- LDH (≤ULN/>ULN)
- Presence of liver metastases (Y/N) at induction BL
- Prior receipt of PCI (Y/N)

Primary endpoints
IRF-PFS and OS

Secondary endpoints included
INV-PFS, ORR, DOR, and safety

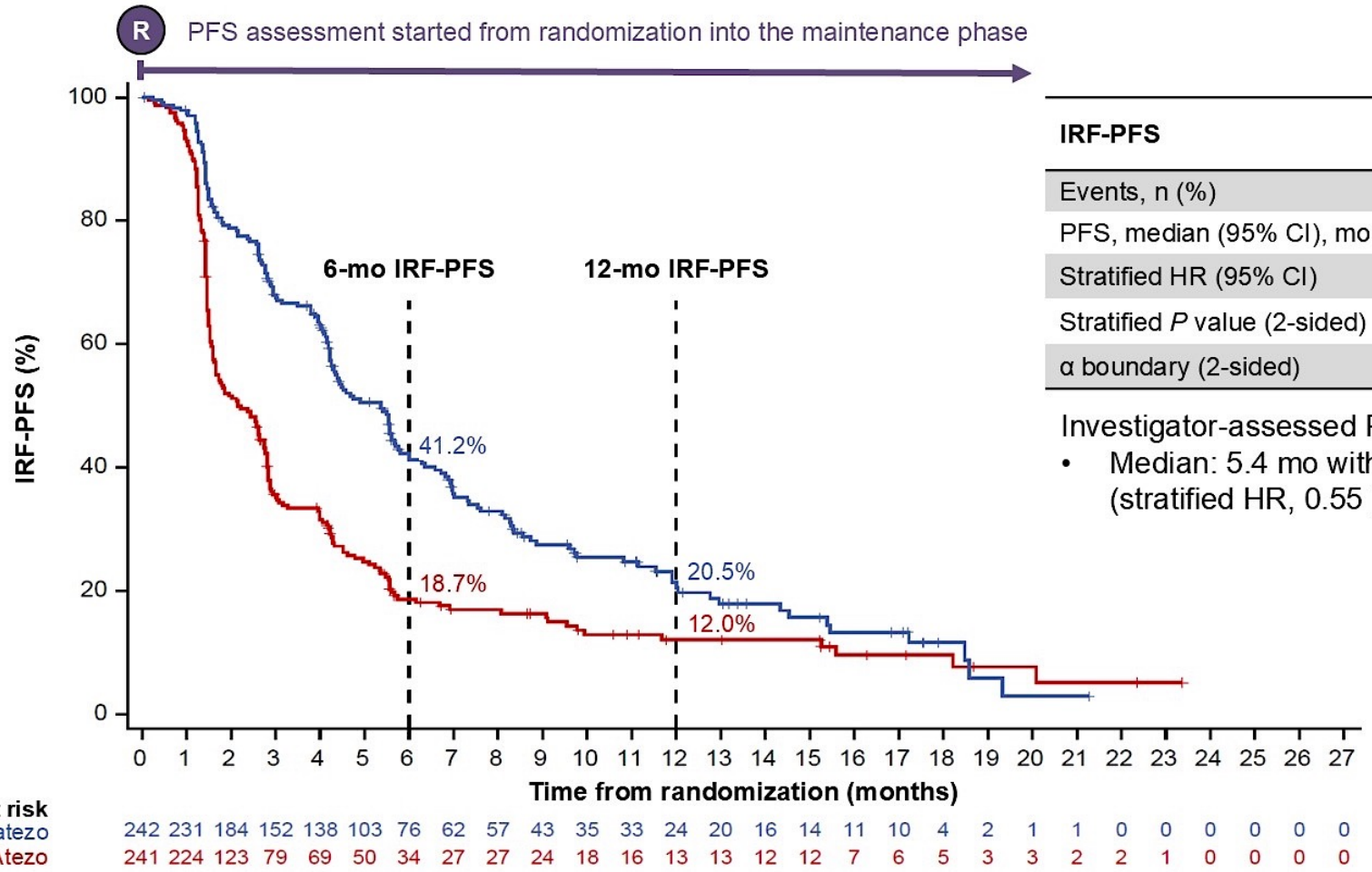
Last patient randomized: April 30, 2024
Clinical cutoff: July 29, 2024

ClinicalTrials.gov ID: NCT05091567.
[a] Administered per standard dose. [b] 73% of patients continued from induction to maintenance. [c] With **prophylactic granulocyte colony-stimulating factor** and anti-emetics.
atezo, atezolizumab; BL, baseline; carbo, carboplatin; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; ENR, enrollment; etop, etoposide; INV-PFS, investigator-assessed PFS; IRF-PFS, independent review facility-assessed PFS; IV, intravenously; LDH, lactate dehydrogenase; lurbi, lurbinectedin; MC1D1, maintenance Cycle 1 Day 1; PCI, prophylactic cranial irradiation; q3w, every 3 weeks; R, randomization; ULN, upper limit of normal; Y/N, yes/no.

CR = complete response; PR = partial response; SD = stable disease; PD = disease progression

Paz-Ares L et al. ASCO 2025;Abstract 8006. Paz-Ares L et al. *Lancet* 2025;405(10495):2129-43.

IMforte: Independent Review Facility-Assessed Progression-Free Survival (IRF-PFS) from Randomization into Maintenance Phase



IRF-PFS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	174 (71.9)	202 (83.8)
PFS, median (95% CI), mo	5.4 (4.2, 5.8)	2.1 (1.6, 2.7)
Stratified HR (95% CI)	**0.54 (0.43, 0.67)**	
Stratified *P* value (2-sided)	<0.0001	
α boundary (2-sided)	0.001	

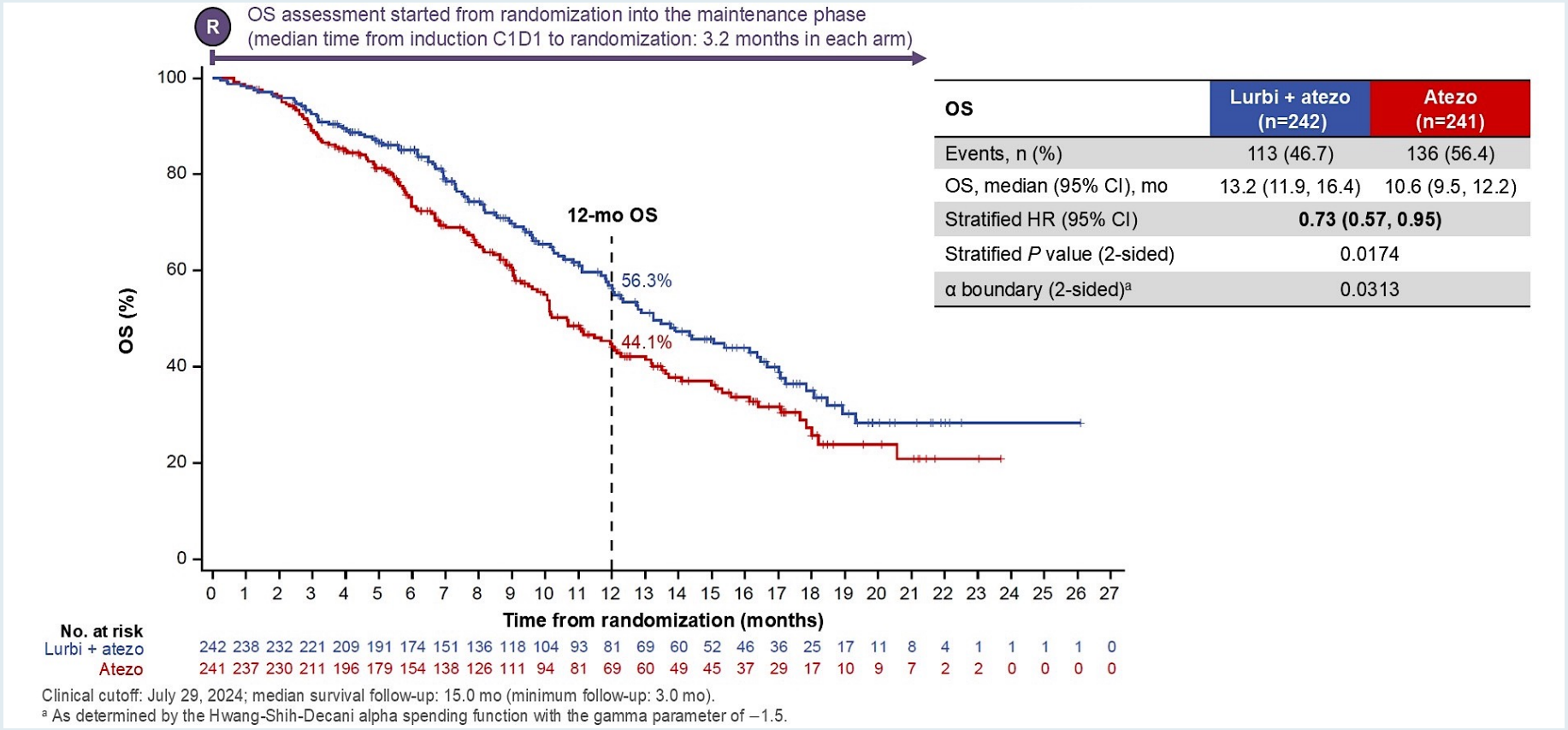
Investigator-assessed PFS was consistent with IRF-PFS

- Median: 5.4 mo with lurbi + atezo and 2.7 mo with atezo (stratified HR, 0.55 [95% CI: 0.45, 0.68])

Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).
CI, confidence interval; HR, hazard ratio.

Paz-Ares L et al. ASCO 2025;Abstract 8006. Paz-Ares L et al. *Lancet* 2025;405(10495):2129-43.

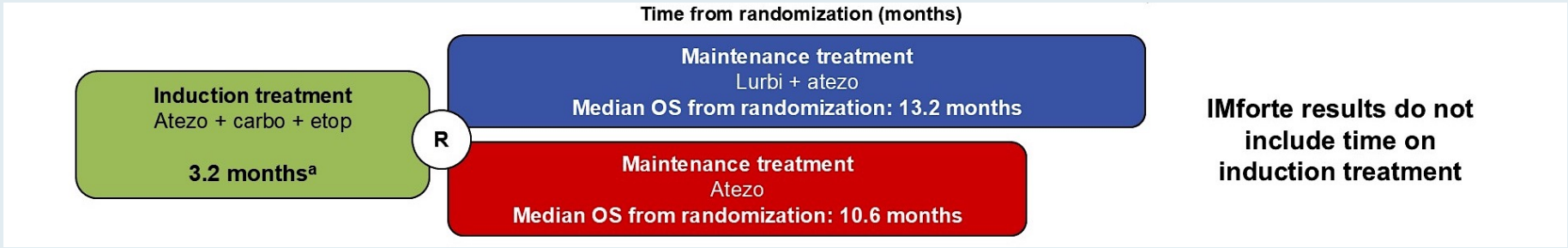
IMforte: Overall Survival (OS) from Randomization into Maintenance Phase



OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	113 (46.7)	136 (56.4)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	**0.73 (0.57, 0.95)**	
Stratified *P* value (2-sided)	0.0174	
α boundary (2-sided)[a]	0.0313	

Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).

[a] As determined by the Hwang-Shih-Decani alpha spending function with the gamma parameter of –1.5.

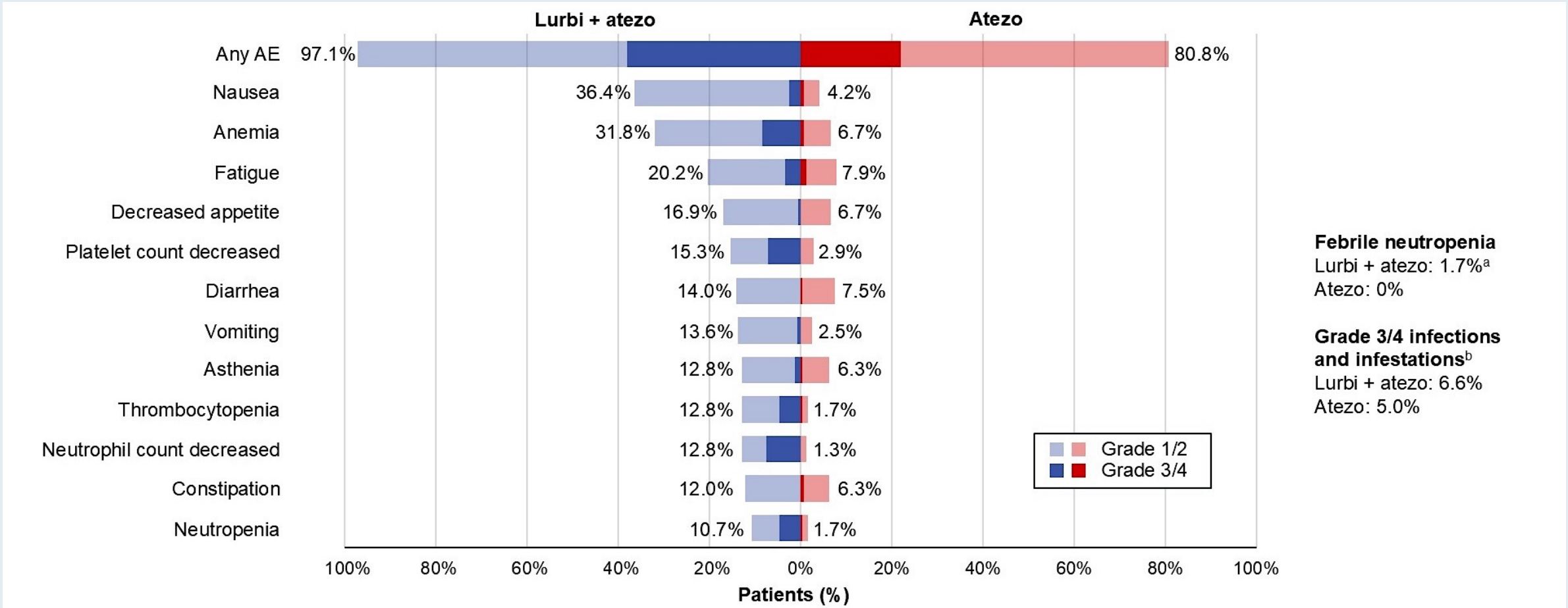


IMforte results do not include time on induction treatment

Paz-Ares L et al. ASCO 2025;Abstract 8006. Paz-Ares L et al. *Lancet* 2025;405(10495):2129-43.

RTP RESEARCH TO PRACTICE

IMforte: All-Cause Adverse Events (AEs) with Incidence ≥10% in Either Arm



Clinical cutoff: July 29, 2024. Percentage labels represent all-grade AEs, including Grade 5 AEs. Grade 5 AEs occurred in 12 (5.0%) patients in the lurbi + atezo arm and 6 (2.5%) patients in the atezo arm.
[a] Includes 1 Grade 5 AE. [b] Grade 5 infections: lurbi + atezo arm (n=6 [2.5%]): COVID-19 pneumonia, pneumonia, pneumonia viral, sepsis, septic shock, and vascular device infection (n=1 each); atezo arm (n=4 [1.7%]): pneumonia (n=2), abscess intestinal, and sepsis (n=1 each).

Paz-Ares L et al. ASCO 2025;Abstract 8006. Paz-Ares L et al. *Lancet* 2025;405(10495):2129-43.

Lancet 2025;405(10495):2129-43

Efficacy and safety of first-line maintenance therapy with lurbinectedin plus atezolizumab in extensive-stage small-cell lung cancer (IMforte): a randomised, multicentre, open-label, phase 3 trial

*Luis Paz-Ares, Hossein Borghaei, Stephen V Liu, Solange Peters, Roy S Herbst, Katarzyna Stencel, Margarita Majem, Mehmet Ali Nahit Şendur, Grzegorz Czyżewicz, Reyes Bernabé Caro, Ki Hyeong Lee, Melissa L Johnson, Nuri Karadurmuş, Christian Grohé, Sofia Baka, Tibor Csőszi, Jin Seok Ahn, Raffaele Califano, Tsung-Ying Yang, Yasemin Kemal, Marcus Ballinger, Vaikunth Cuchelkar, Vilma Graupner, Ya-Chen Lin, Debasis Chakrabarti, Kamalnayan Bhatt, George Cai, Robert Iannone, Martin Reck, for the IMforte investigators**

2025 ASCO ANNUAL MEETING

Abstract LBA8008

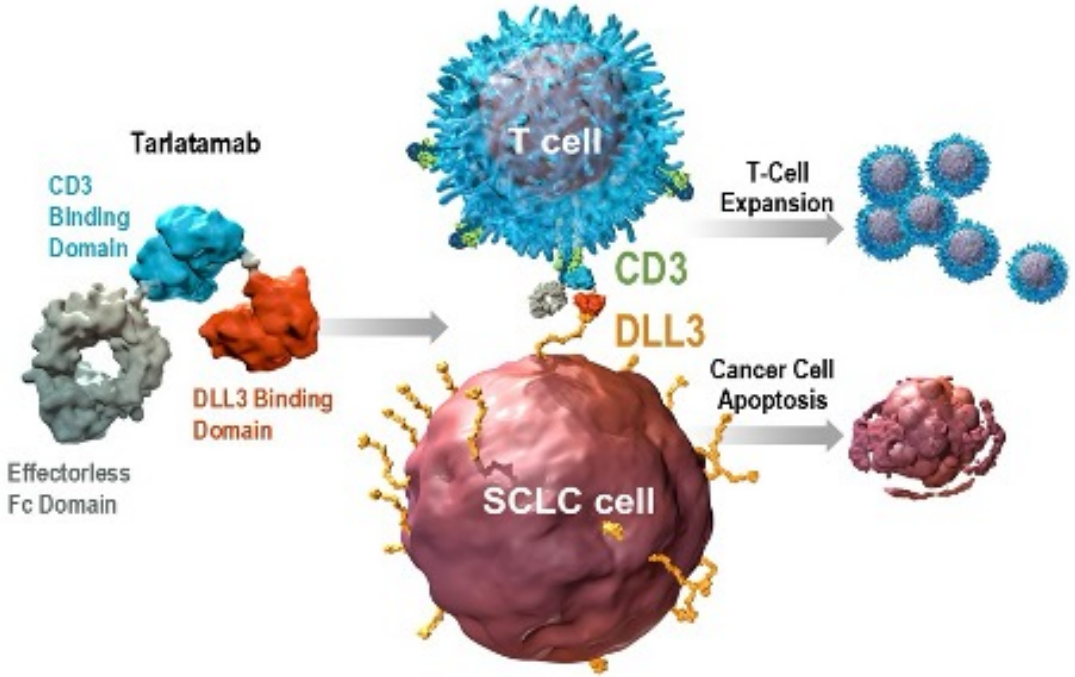
Tarlatamab versus chemotherapy as second-line treatment for small cell lung cancer (SCLC): primary analysis of the phase 3 DeLLphi-304 study

Charles M. Rudin, Giannis S. Mountzios, Longhua Sun, Byoung Chul Cho, Umut Demirci, Sofia Baka, Mahmut Gumus, Antonio Lugini, Tudor-Eliade Ciuleanu, Myung-Ju Ahn, Pedro Rocha, Bo Zhu, Fiona Blackhall, Tatsuya Yoshida, Taofeek K. Owonikoko, Luis Paz-Ares, Shuang Huang, Diana Gauto, Gonzalo Recondo, Martin Schuler

Speaker: **Charles M. Rudin, MD, PhD,** Fiona and Stanley Druckenmiller Center for Lung Cancer Research, Memorial Sloan Kettering Cancer Center, New York, USA.

DeLLphi-304 Background

- Tarlatamab is a bispecific T-cell engager immunotherapy that directs cytotoxic T cells to DLL3-expressing SCLC cells resulting in tumor cell lysis[1]
- Tarlatamab demonstrated durable anticancer efficacy in patients with previously treated SCLC[2,3]
- Survival with current 2L chemotherapy options is modest and is also associated with substantial hematological toxicity[4–6]
- The DeLLphi-304 study was conducted to assess whether tarlatamab could improve survival for patients with SCLC whose disease had progressed or recurred following one line of platinum-based chemotherapy[7]



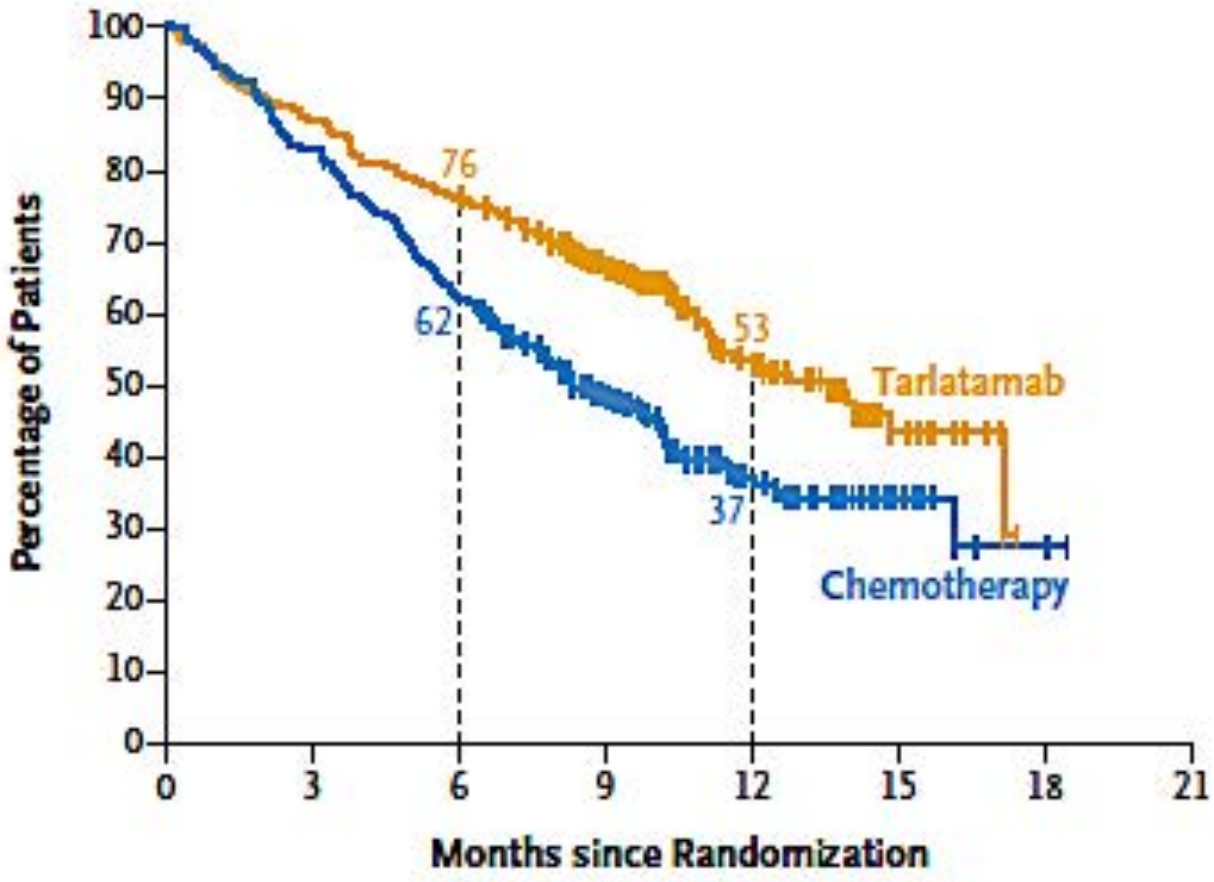
We present results from the first planned interim analysis of the phase 3 DeLLphi-304 trial comparing tarlatamab to chemotherapy for 2L treatment of SCLC

2L, second-line; **CD3,** cluster of differentiation 3; **DLL3,** delta-like ligand 3; **Fc,** fragment crystallizable region; **SCLC,** small cell lung cancer.

Rudin CM et al. ASCO 2025;Abstract LBA8008.

RTP RESEARCH TO PRACTICE

DeLLphi-304 Primary Endpoint: Overall Survival



No. at Risk							
Tarlatamab	254	220	192	131	60	17	0
Chemotherapy	255	210	156	97	42	9	2	0

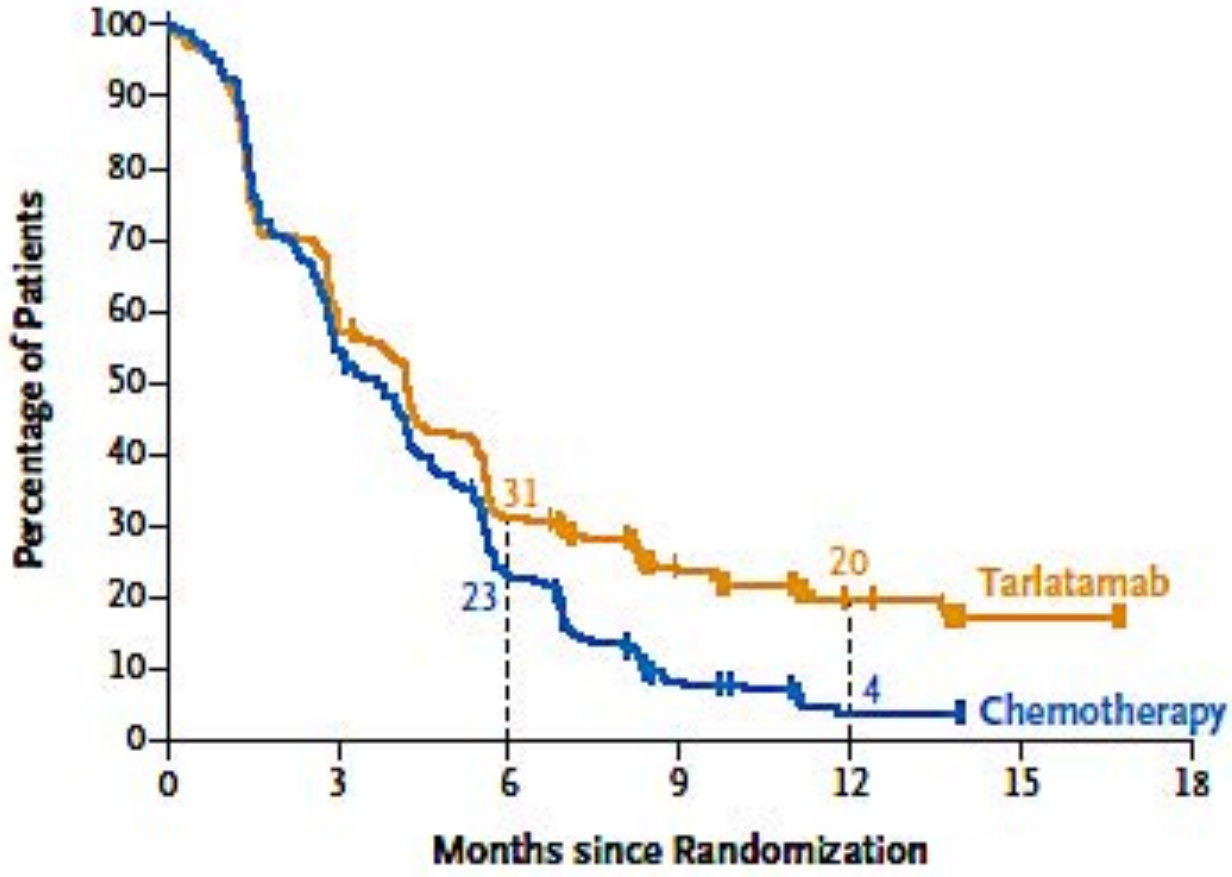
	Median Overall Survival (95% CI)
	mo
Tarlatamab (N=254)	13.6 (11.1–NR)
Chemotherapy (N=255)	8.3 (7.0–10.2)

Stratified hazard ratio for death, 0.60 (95% CI, 0.47–0.77)
P<0.001

Rudin CM et al. ASCO 2025;Abstract LBA8008; Mountzios G et al. *N Engl J Med* Jun 2 2025;[Online ahead of print].

RTP RESEARCH TO PRACTICE

DeLLphi-304: Progression-Free Survival



No. at Risk							
Tarlatamab	254	147	78	37	18	2	0
Chemotherapy	255	137	56	15	3	0	

Estimated RMST for Progression-free Survival at 12 Months

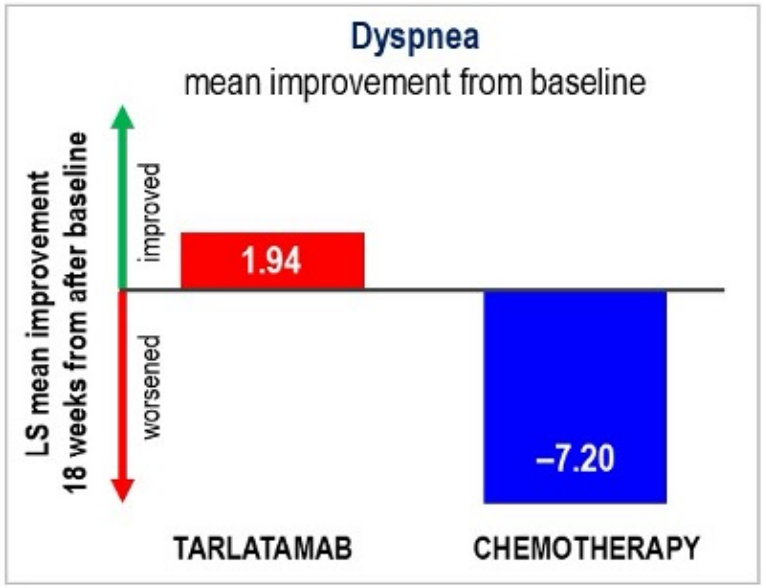
	mo
Tarlatamab (N=254)	5.3
Chemotherapy (N=255)	4.3

Piecewise weighted average hazard ratio for progression or death, 0.71 (95% CI, 0.59–0.86)
P=0.002, RMST for progression-free survival

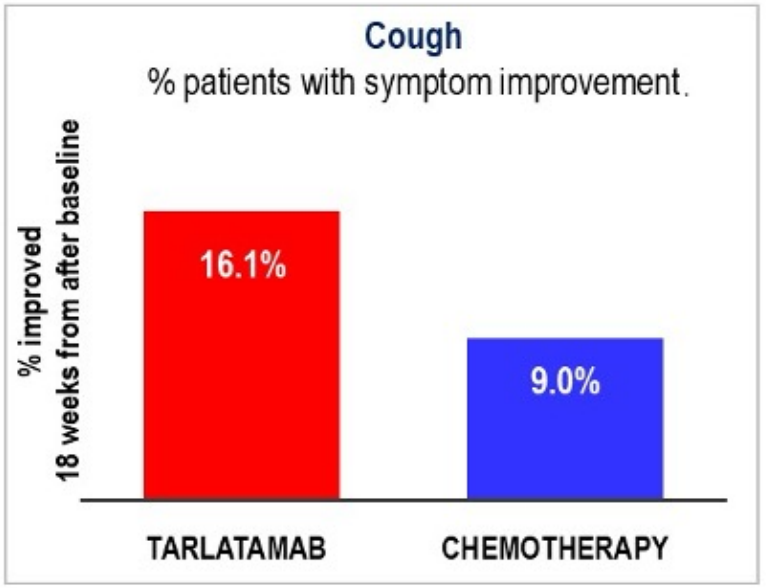
RMST = restricted mean survival time

Rudin CM et al. ASCO 2025;Abstract LBA8008; Mountzios G et al. *N Engl J Med* Jun 2 2025;[Online ahead of print].

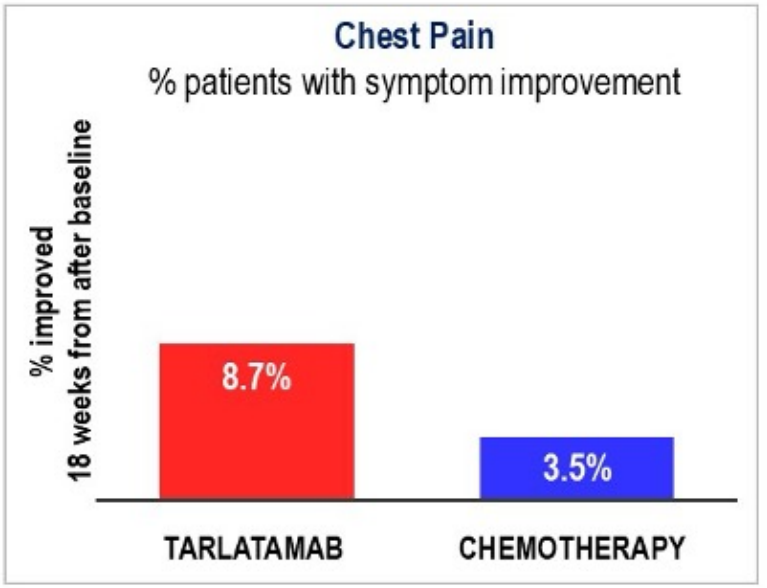
DeLLphi-304: Symptom Change from Baseline



LS mean difference = -9.14*
95% CI (-12.64, -5.64)
***p* < 0.001**



Odds ratio = 2.04*
95% CI (1.17, 3.55)
***p* = 0.012**



Odds ratio = 1.84*
95% CI (0.89, 3.81)
***p* = 0.1**
(Did not meet statistical significance)

The mean difference in the change after 18 weeks in the physical functioning score (10.35 points [95% CI: 6.00 to 14.69]) and the global health status score (8.93 points [95% CI: 5.04 to 12.83]) trended in favor of tarlatamab. *Similar results were observed when the sensitivity analyses were carried out incorporating a more conservative estimand (i.e., treatment policy strategy) for change from baseline after 18 weeks in **dyspnea** (mean difference, -6.19; [95% CI, -8.88 to -3.49]), **cough** (odds ratio, 1.48 [95% CI, 1.08 to 2.02]), **chest pain** (odds ratio, 1.21 [95% CI, 0.80 to 1.82]).

Rudin CM et al. ASCO 2025;Abstract LBA8008.

RTP RESEARCH TO PRACTICE

DeLLphi-304: Tarlatamab Safety Profile

	Tarlatamab (n = 252)*	Chemotherapy (n = 244)*
Median duration of treatment, months, (range)	4.2 (< 1–17)	2.5 (< 1–15)
All grade, TEAEs, n (%)	249 (99)	243 (100)
All grade, TRAEs n (%)	235 (93)	223 (91)
Grade ≥ 3 TRAEs, n (%)	67 (27)	152 (62)
Serious TRAEs, n (%)	70 (28)	75 (31)
TRAEs leading to dose interruption and/or dose reduction, n (%)	48 (19)	134 (55)
TRAEs leading to discontinuation, n (%)	7 (3)	15 (6)
Treatment-related grade 5 events†, n (%)	1 (0.4)	4 (2)

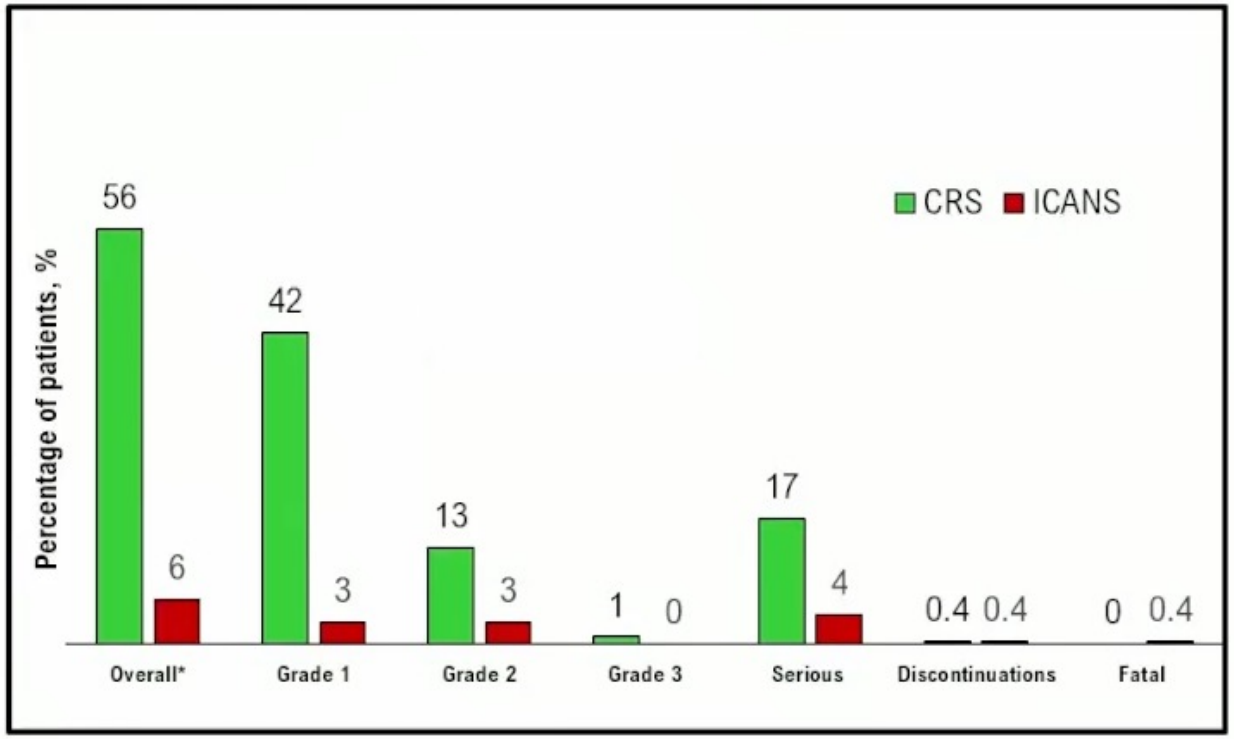
*Safety analysis set (all patients who received at least one dose of study treatment). †The single grade 5 TRAE observed with tarlatamab was attributed to ICANS in the setting of progressive neurological decline concurrent with persistent fever, hypoxemia, and hypotension. Grade 5 TRAEs observed with chemotherapy were attributed to general physical health deterioration (n = 1), pneumonia (n = 1), respiratory tract infection (n = 1), and tumor lysis syndrome (n = 1).

ICANS, immune effector cell-associated neurotoxicity syndrome; **TEAE,** treatment-emergent adverse event; **TRAE,** treatment-related adverse event.

Rudin CM et al. ASCO 2025;Abstract LBA8008.

DeLLphi-304: CRS and ICANS Events

Treatment-emergent CRS and ICANS with tarlatamab



CRS with first two infusions

Tarlatamab (N = 252)	Minimum required monitoring duration: 6 - 8 Hours (n = 43)	Minimum required monitoring duration: 48 Hours (n = 209)
Treatment emergent CRS, n (%)*	16 (37)	125 (60)
Grade 1	12 (28)	94 (45)
Grade 2	4 (9)	28 (13)
Grade 3	0 (0)	3 (1)
Serious adverse events	3 (7)	39 (19)
Leading to discontinuation of IP	0 (0)	1 (0.5)
Median time to intervention from last tarlatamab dose (hours)	17	27

*Grade 4 CRS or ICANS events were not observed. A single grade 5 treatment-related adverse event observed with tarlatamab was attributed to ICANS in the setting of progressive neurological decline concurrent with persistent fever, hypoxemia, and hypotension.

CRS, cytokine release syndrome; **ICANS,** immune effector cell-associated neurotoxicity syndrome; **IP**, investigational product.

Rudin CM et al. ASCO 2025;Abstract LBA8008.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tarlatamab in Small-Cell Lung Cancer after Platinum-Based Chemotherapy

Giannis Mountzios, M.D., Ph.D.,[1] Longhua Sun, M.D.,[2]
Byoung Chul Cho, M.D., Ph.D.,[3] Umut Demirci, M.D., Ph.D.,[4]
Sofia Baka, M.D., Ph.D.,[5] Mahmut Gümüş, M.D.,[6] Antonio Lugini, M.D.,[7]
Bo Zhu, M.D., Ph.D.,[8] Yan Yu, M.D.,[9] Ippokratis Korantzis, M.D., Ph.D.,[10]
Ji-Youn Han, M.D., Ph.D.,[11] Tudor-Eliade Ciuleanu, M.D., Ph.D.,[12]
Myung-Ju Ahn, M.D., Ph.D.,[13] Pedro Rocha, M.D., Ph.D.,[14]
Julien Mazières, M.D., Ph.D.,[15] Sally C.M. Lau, M.D., M.P.H.,[16]
Martin Schuler, M.D.,[17,18] Fiona Blackhall, M.D., Ph.D.,[19]
Tatsuya Yoshida, M.D., Ph.D.,[20] Taofeek K. Owonikoko, M.D., Ph.D.,[21]
Luis Paz-Ares, M.D., Ph.D.,[22] Tony Jiang, Ph.D.,[23] Ali Hamidi, M.D.,[23]
Diana Gauto, M.D.,[23] Gonzalo Recondo, M.D., Ph.D.,[23]
and Charles M. Rudin, M.D., Ph.D.,[24] for the DeLLphi-304 Investigators*

June 2, 2025;[Online ahead of print]

2025 ASCO ANNUAL MEETING

Breaking New Ground in Small Cell Lung Cancer: BiTE, TriTE and Chemoimmunotherapy

Abstracts LBA8008 (DeLLphi-304), 8006 (IMforte), and 8007 (ZG006)

Catherine B. Meador, MD PhD

Center for Thoracic Cancers, Massachusetts General Hospital

Harvard Medical School, Boston, MA, USA

Meador CB et al. ASCO 2025;Discussant.

IMforte: Conclusions and Practice Implications

- OS improved by adding lurbinectedin to 1L chemo+ICI in ES-SCLC in patients without progression after chemo
- However…. toxicity is not trivial
- Practice-changing data, but patient selection for this regimen will be key
  - Better biomarkers?[1]
  - SCLC subtypes?[2]
  - Role of ctDNA?[3]

[1]Chakraborty et al., Clin Cancer Res 2023; Kundu et al., Transl Lung Cancer Res 2021
[2] Gay et al., Cancer Cell 2021; Rudin et al., J Thorac Oncol 2023
[3] Sivapalan et al., Clin Cancer Res 2023; Valenza et al., Ann Oncol 2025

ICI = immune checkpoint inhibitor

Meador CB et al. ASCO 2025;Discussant.

RTP RESEARCH TO PRACTICE

Evolving Management Strategies for Cytokine Release Syndrome (CRS)

1. Learn from the (years of) experience of our malignant hematology colleagues – established monitoring protocols and resources
2. Explore alternative care settings during CRS risk window:
   - Home hospital → ☐ NCT06957314 Recruiting New
     A Study of **Hospital**-at-**Home** for People Receiving Tarlatamab
   - Outpatient (with medical equipment, 24/7 caregivers, and education)
3. Establish better predictive biomarkers – understand which patients are at highest risk for grade 2+ CRS

Meador CB et al. ASCO 2025;Discussant.

RTP RESEARCH TO PRACTICE

DeLLphi-304: Conclusions and Practice Implications

- **Tarlatamab is now the standard of care for second-line therapy in ES-SCLC.**
- **Further work is needed to optimize administration of tarlatamab**
  - **Inpatient CRS monitoring is currently recommended, but multiple trials and real-world datasets suggest it can be safely limited to C1D1 and C1D8.**
  - **Implementation of novel monitoring strategies may improve access**

Meador CB et al. ASCO 2025;Discussant.

The Road Ahead: Tarlatamab

Is earlier tarlatamab better (e.g. first-line ES-SCLC, or LS-SCLC)?

DeLLphi trial #	Phase	Indication	Design	Recruiting?	Trial ID
303	1b	1L ES-SCLC	Tarlatamab + standard therapy	N	NCT05037847
305	3	1L ES-SCLC maintenance	Tarlatamab + durva vs. durva alone	Y	NCT06502977
306	3	LS-SCLC post-chemoRT	Tarlatamab vs. placebo	Y	NCT06117774
310	1b	1L ES-SCLC maintenance	Tarlatamab + YL201 + atezo or durva	Y	NCT06898957

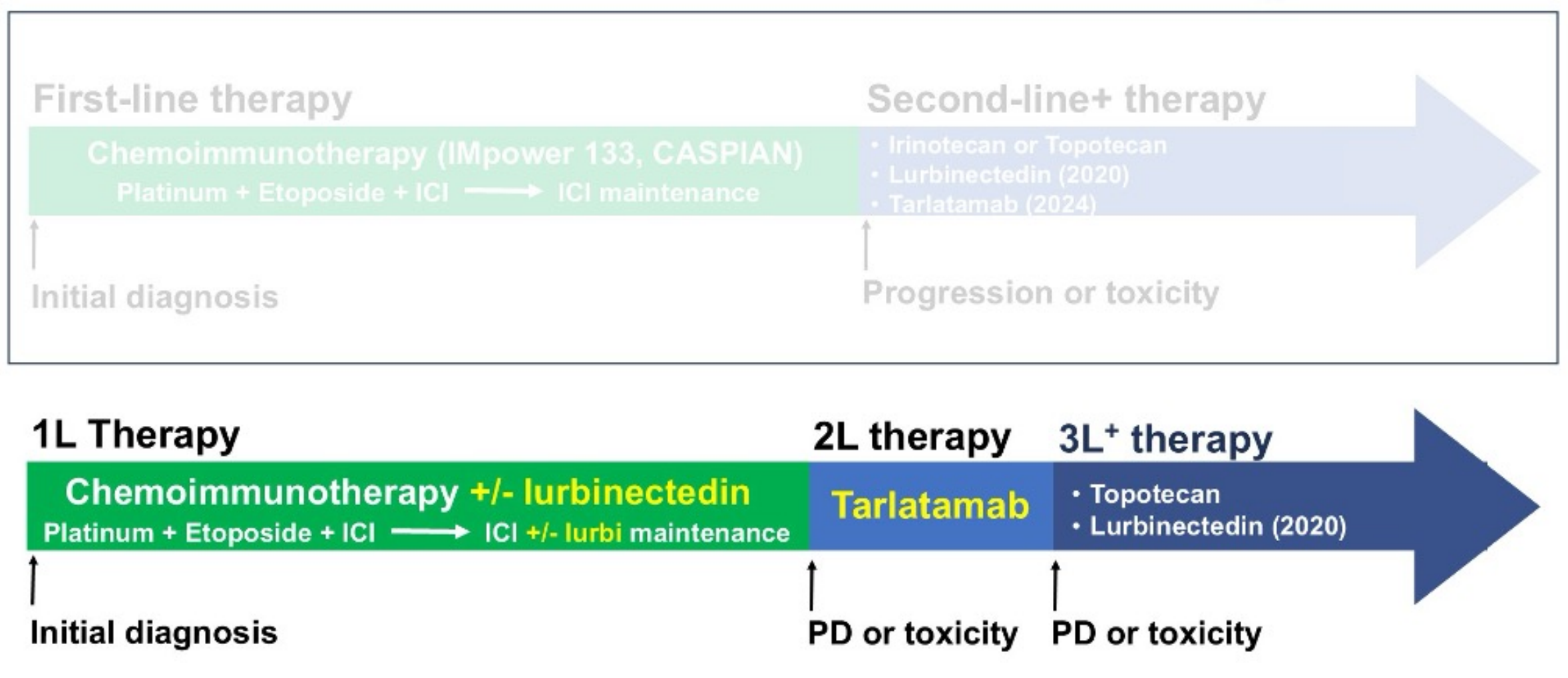
Is tarlatamab more effective in combination?

DeLLphi trial #	Phase	Indication	Design	Recruiting?	Trial ID
302	1b	2L+ SCLC	Tarlatamab + anti-PD-1 therapy	Y	NCT04184050
305	3	1L ES-SCLC maintenance	Tarlatamab + durva vs. durva alone	Y	NCT06502977
310	1b	2L SCLC	Tarlatamab + YL201	Y	NCT06898957
		1L ES-SCLC maintenance	Tarlatamab + YL201 + atezo or durva		

Meador CB et al. ASCO 2025;Discussant.

RTP RESEARCH TO PRACTICE

ES-SCLC: Current Treatment Landscape



Meador CB et al. ASCO 2025;Discussant.

2025 ASCO ANNUAL MEETING

Abstract 8007

A Phase 2 Dose Optimization Study of Alveltamig (ZG006), a DLL3/DLL3/CD3 Trispecific T Cell Engager, as Monotherapy in Patients with Refractory Small Cell Lung Cancer

Xinghao Ai, Yan Yu, Tongmei Zhang, Tienan Yi, Mingjun Li, Wenxiu Yao, Liang Han, Longhua Sun, Anwen Liu, Qi Mei, Guang Han, Zhen Zhang, Yinyin Li, Lu Li, Li Zheng, Yong Fang, Yongzhong Luo, Jason Jisheng Wu, Shun Lu

Shanghai Chest Hospital, Shanghai, China; The Affiliated Tumor Hospital of Harbin Medical University, Harbin, China; Beijing Chest Hospital,Capital Medical University, Beijing, China;Department of Oncology,Xiangyang Central Hospital,Affiliated hospital of Hubei University of Arts and Science,Xiangyang, China; Department of Medical Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; Sichuan Cancer Hospital, Chengdu, China; Xuzhou Central Hospital, Xuzhou, China; Department of Respiratory Medicine, The First Affiliated Hospital of Nanchang University, Nanchang, China; The Second Affiliated Hospital of Nanchang University, Nanchang, China; Medical Oncology Department, Shanxi Bethune Hospital, Taiyuan, China; Hubei Cancer Hospital, Tongji Medical College,Huazhong University of Science and Technology, Wuhan, China; Nanyang First People's Hospital, Nanyang, China; Department of Oncology, Shenyang Chest Hospital, Shenyang,China; West China Hospital, Sichuan University, Chengdu, China; Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China; Hunan Cancer Hospital, Changsha, China; Suzhou Zelgen Biopharmaceuticals Co., Ltd., Suzhou, China; Department of Medical Oncology, Shanghai Chest Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Key Takeaway Points

Robust Antitumor Efficacy

Alveltamig (ZG006) demonstrated robust antitumor activity in refractory SCLC in both 10 mg and 30 mg dose groups, with an ORR at 62.5% and 58.3% and DCR at 70.8% and 66.7%, respectively, highlighting its therapeutic potential

Manageable Safety Profile

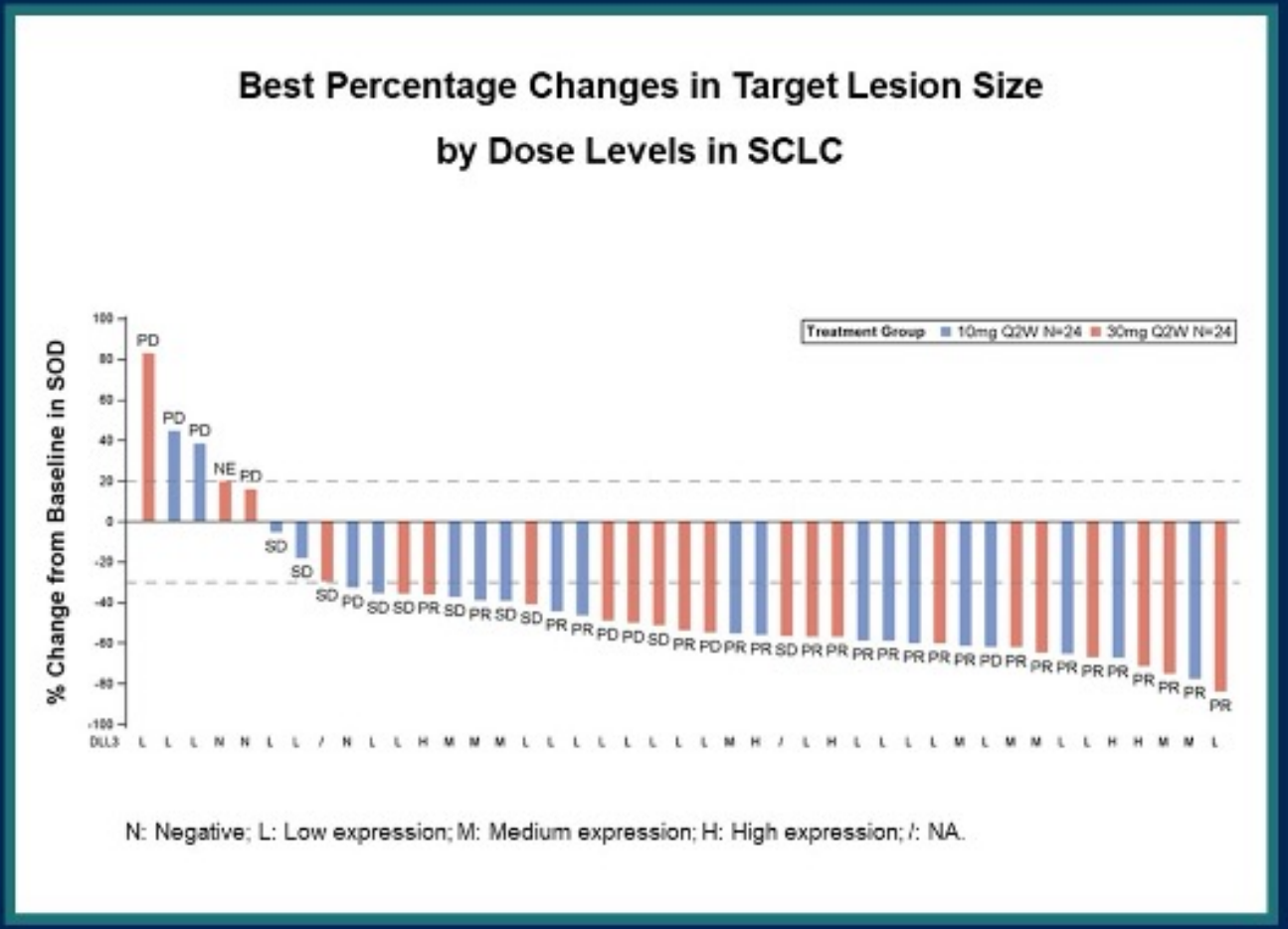
Alveltamig (ZG006) was generally well tolerated and treatment-related adverse events (TRAEs) were comparable and manageable in both groups; CRS, with majority being grade 1 or 2, occurred mainly in the first two dosing cycles and recovered rapidly after symptomatic treatment

Ai X et al. ASCO 2025;Abstract 8007.

RTP RESEARCH TO PRACTICE

Alveltamig Antitumor Activity as Assessed by IRC

	10 mg Q2W (N=24)	30 mg Q2W (N=24)
BOR		
CR, n (%)	0	0
PR, n (%)	15 (62.5)	14 (58.3)
SD, n (%)	2 (8.3)	2 (8.3)
PD, n (%)	6 (25.0)	6 (25.0)
NE, n (%)	1 (4.2)	2 (8.3)
ORR*, n (%) **95% CI**	15 (62.5) (40.6, 81.2)	14 (58.3) (36.6, 77.9)
DCR*, n (%) **95% CI**	17 (70.8) (48.9, 87.4)	16 (66.7) (44.7, 84.4)



CR: Complete Response; PR: Partial Response; SD: Stable Disease; PD: Progressive Disease; BOR: Best Overall Response; *: Non-confirmed

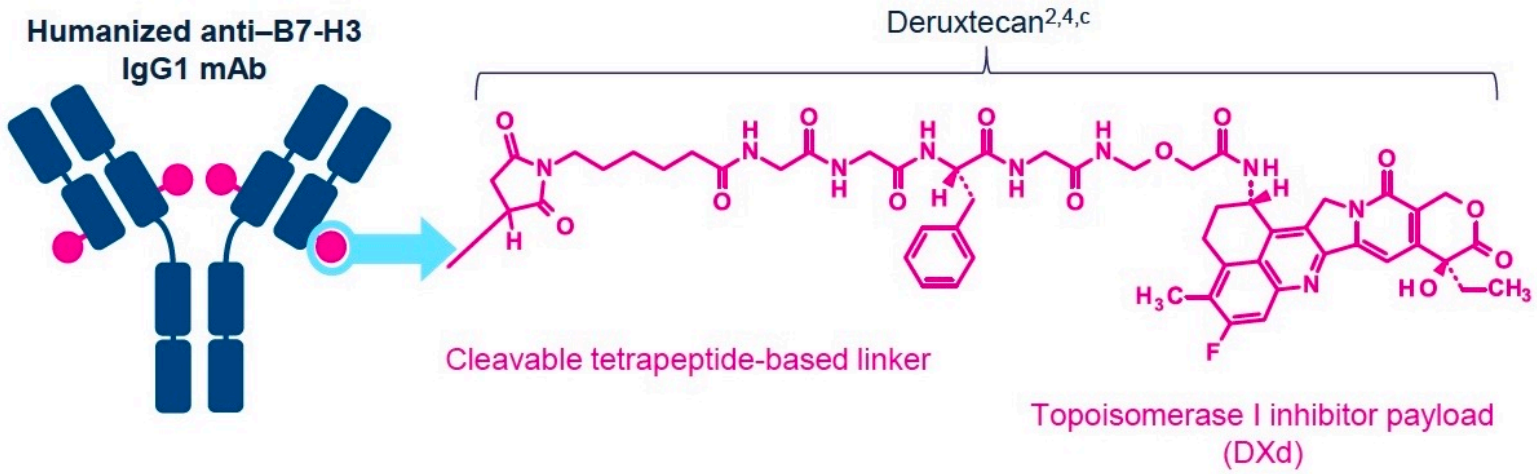
ORR = objective response rate

Ai X et al. ASCO 2025;Abstract 8007.

Ifinatamab Deruxtecan (I-DXd)

I-DXd is a B7-H3 (CD276)–directed ADC with 3 components[1–4]:

- A humanized anti–B7-H3 IgG1 mAb
- A tetrapeptide-based cleavable linker that covalently bonds antibody and payload
- A topoisomerase I inhibitor payload (an exatecan derivative, DXd)



The **mAb** directs the DXd ADC to the tumor cell.

1. Optimized drug-to-antibody ratio ≈4[4,a,b]

The **linker** binds the mAb to the payload.

2. Plasma-stable linker-payload[4,a]
3. Tumor-selective cleavable linker[4,a]

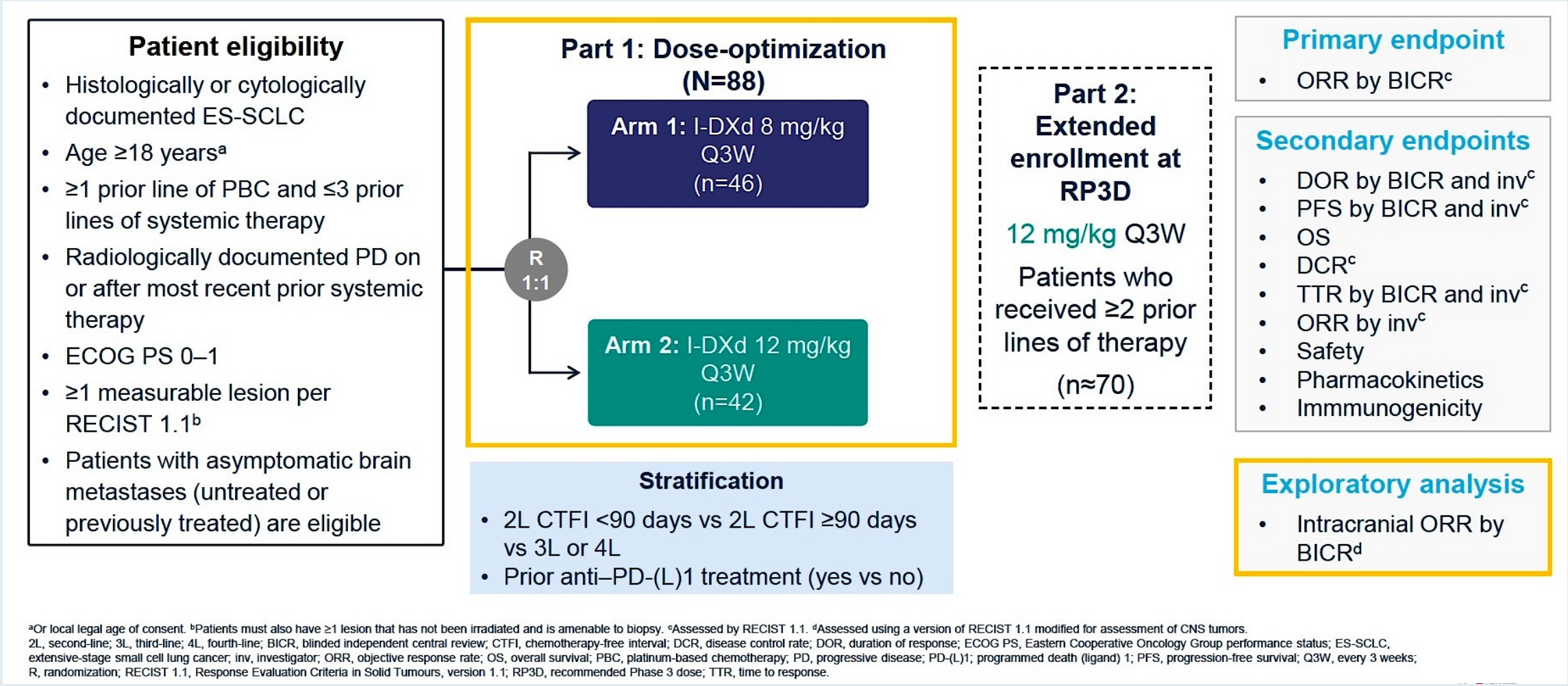
The **payload** induces cell death when delivered to the tumor.

4. Topoisomerase I inhibitor[2,4,a]
5. High potency[4,a]
6. Short systemic half-life[4,a,b]
7. Bystander antitumor effect[2,5,a]

[a]The clinical relevance of these features is under investigation. [b]Based on animal data. [c]Refers to the linker and payload.
ADC, antibody–drug conjugate; B7-H3, B7 homolog 3; CD276, cluster of differentiation 276; IgG1, immunoglobulin G1; mAb, monoclonal antibody.
1. Okajima D, et al. *Mol Cancer Ther*. 2021;20:2329–2340. 2. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67:173–185. 3. Ogitani Y, et al. *Clin Cancer Res*. 2016;22:5097–5108. 4. Yamato M, et al. *Mol Cancer Ther*. 2022;21:635–646.
5. Ogitani Y, et al. *Cancer Sci*. 2016;107:1039–1046.

Hayashi H et al. Japanese Society of Medical Oncology (JSMO) 2025;Abstract O12-4.

Phase II IDeate-Lung01 Study Design



[a]Or local legal age of consent. [b]Patients must also have ≥1 lesion that has not been irradiated and is amenable to biopsy. [c]Assessed by RECIST 1.1. [d]Assessed using a version of RECIST 1.1 modified for assessment of CNS tumors.
2L, second-line; 3L, third-line; 4L, fourth-line; BICR, blinded independent central review; CTFI, chemotherapy-free interval; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; inv, investigator; ORR, objective response rate; OS, overall survival; PBC, platinum-based chemotherapy; PD, progressive disease; PD-(L)1; programmed death (ligand) 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; RP3D, recommended Phase 3 dose; TTR, time to response.

Hayashi H et al. JSMO 2025;Abstract O12-4.

IDeate-Lung01: Baseline Characteristics

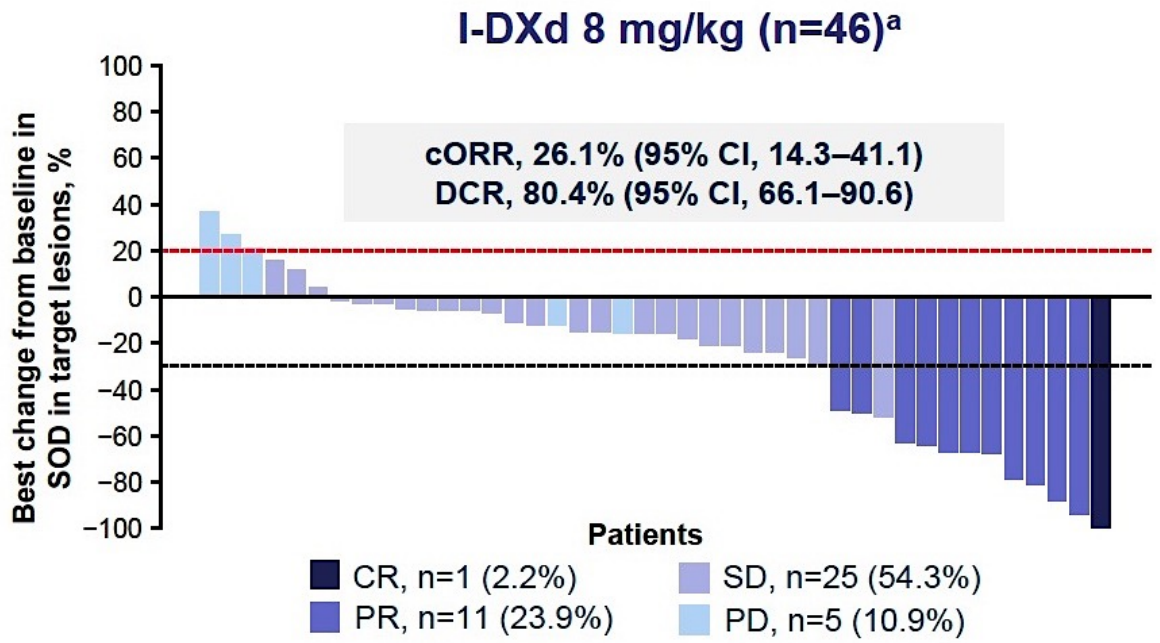
	I-DXd 8 mg/kg n=46	I-DXd 12 mg/kg n=42	Total N=88
Age, median (range), years	64 (42–85)	64 (34–79)	64 (34–85)
Male, n (%)	30 (65.2)	33 (78.6)	63 (71.6)
ECOG PS, n (%)			
0	13 (28.3)	6 (14.3)	19 (21.6)
1	33 (71.7)	36 (85.7)	69 (78.4)
ES-SCLC at diagnosis, n (%)	32 (69.6)[a]	35 (83.3)	67 (76.1)
ES-SCLC at study entry, n (%)	46 (100)	42 (100)	88 (100)
Patients with brain metastases at baseline, n (%)	19 (41.3)	18 (42.9)	37 (42.0)
Subset of patients with brain target lesions at baseline, n (%)	6 (13.0)	10 (23.8)	16 (18.2)
Number of prior lines of systemic therapy, n (%)			
1	13 (28.3)	12 (28.6)	25 (28.4)
2	22 (47.8)	22 (52.4)	44 (50.0)
3	11 (23.9)	8 (19.0)	19 (21.6)
Chemotherapy-free interval,[b] n (%)			
<90 days	22 (47.8)	23 (54.8)	45 (51.1)
≥90 days	22 (47.8)	19 (45.2)	41 (46.6)
Select prior anticancer therapy received, n (%)			
Lurbinectedin	11 (23.9)	3 (7.1)	14 (15.9)
Irinotecan or topotecan	14 (30.4)	17 (40.5)	31 (35.2)
Tarlatamab	4 (8.7)	2 (4.8)	6 (6.8)
Amrubicin	3 (6.5)	3 (7.1)	6 (6.8)
Received prior anti–PD-(L)1 therapy,[c] n (%)	35 (76.1)	32 (76.2)	67 (76.1)

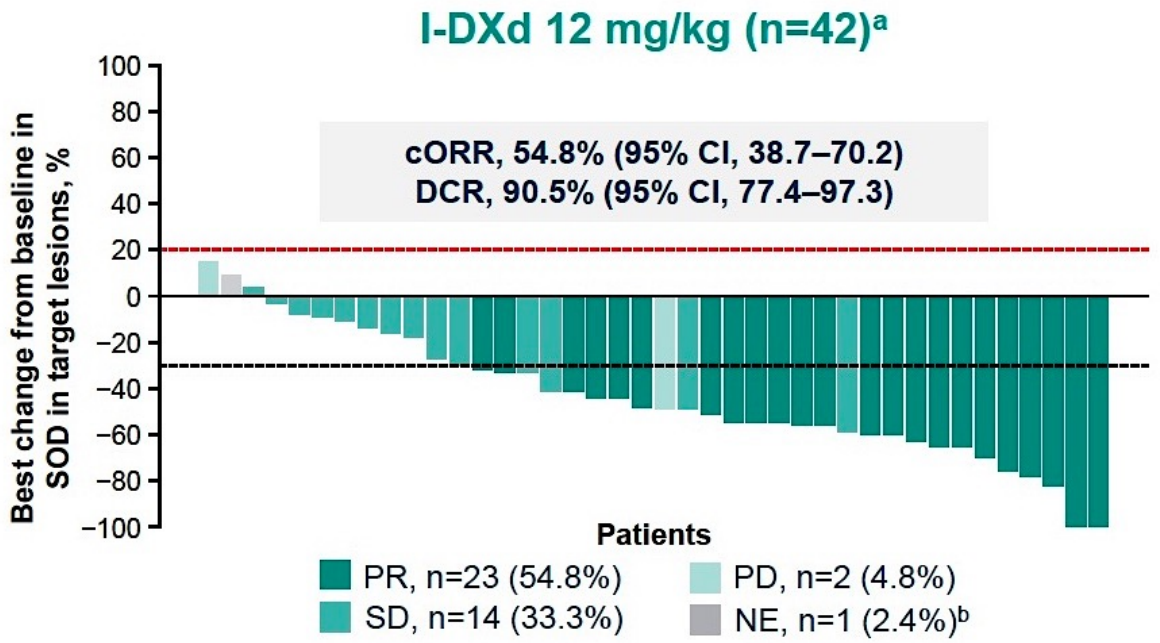
- Median treatment duration: **8 mg/kg**, 3.5 months (range, 0.03–13.9); **12 mg/kg**, 4.7 months (range, 0.03–15.2)
- Median follow-up: **8 mg/kg**, 14.6 months (range, 0.6–17.0); **12 mg/kg**, 15.3 months (range, 0.8–20.3)

Data cutoff: April 25, 2024.
[a]One patient had missing data. [b]Two patients had missing data in the 8-mg/kg cohort. [c]Three patients (8 mg/kg, n=2; 12 mg/kg, n=1) were previously treated in a blinded randomized clinical trial; information regarding patients' prior anti–PD-(L)1 therapy was not available.
ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; PD-(L)1; programmed death (ligand) 1.

Hayashi H et al. JSMO 2025;Abstract O12-4.

IDeate-Lung01: Responses





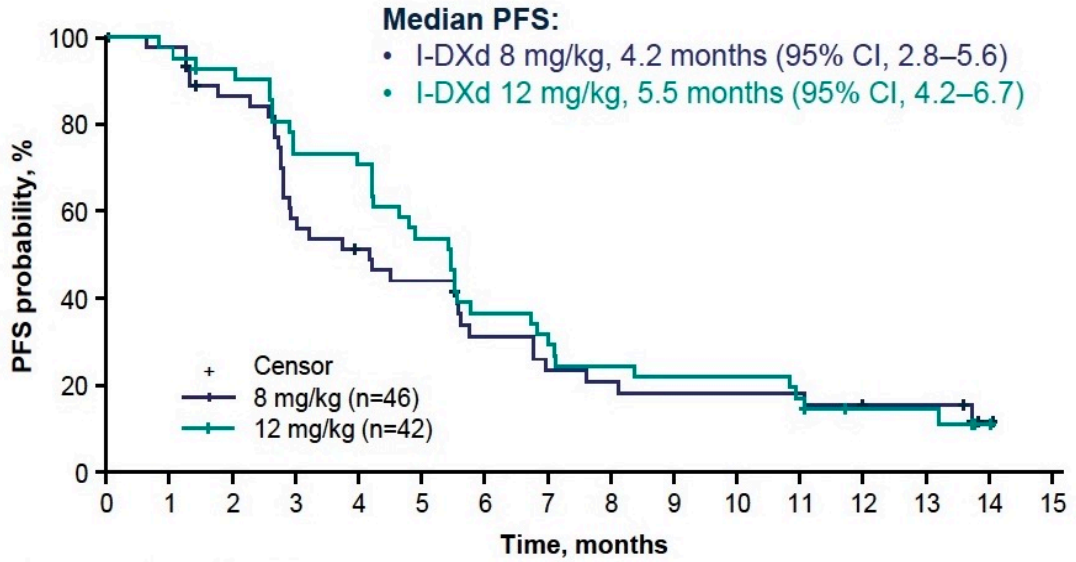
Data cutoff: April 25, 2024. Median follow-up for the 8-mg/kg and 12-mg/kg cohorts was 14.6 (range, 0.6–17.0) months and 15.3 (range, 0.8–20.3) months, respectively.
[a]Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan were included in the waterfall plot: in the I-DXd 8-mg/kg cohort (n=42), 2 patients died and 2 patients withdrew consent before the Week 6 assessment; in the 12-mg/kg cohort (n=40), 1 patient died before the Week 6 assessment, and 1 patient did not have target lesions at baseline. [b]This patient has a BOR of NE because the only post-baseline tumor scan was conducted outside the designated time window; the timepoint response was SD.
BICR, blinded independent central review; BOR, best overall response; CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; DCR, disease control rate; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SOD, sum of diameters.

Hayashi H et al. JSMO 2025;Abstract O12-4.

RTP RESEARCH TO PRACTICE

IDeate-Lung01: Survival

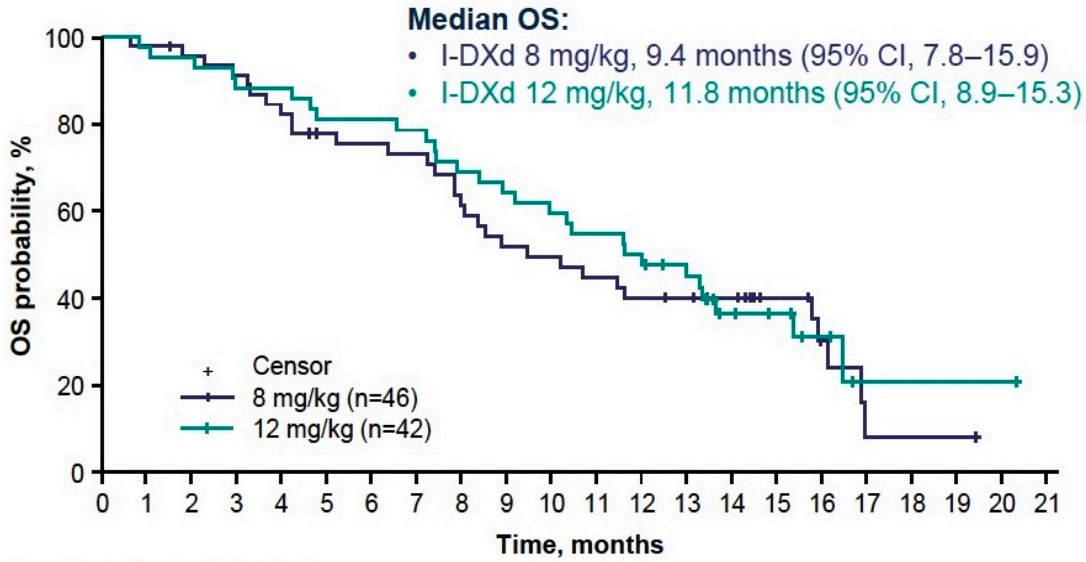
PFS



Number of patients still at risk

8 mg/kg	46	44	37	25	21	18	12	9	8	7	7	7	5	5	1	0
12 mg/kg	42	41	38	30	29	22	15	12	10	9	9	7	4	4	1	0

OS



Number of patients still at risk

8 mg/kg	46	45	43	41	37	33	32	31	26	22	21	19	17	16	14	9	5	1	1	1	0	0
12 mg/kg	42	41	40	37	37	34	34	33	29	27	25	23	20	17	10	8	5	1	1	1	1	0

Data cutoff: April 25, 2024. Median follow-up for the 8-mg/kg and 12-mg/kg cohorts was 14.6 (range, 0.6–17.0) months and 15.3 (range, 0.8–20.3) months, respectively.
CI, confidence interval; OS, overall survival; PFS, progression-free survival.

Hayashi H et al. JSMO 2025;Abstract O12-4.

RTP RESEARCH TO PRACTICE

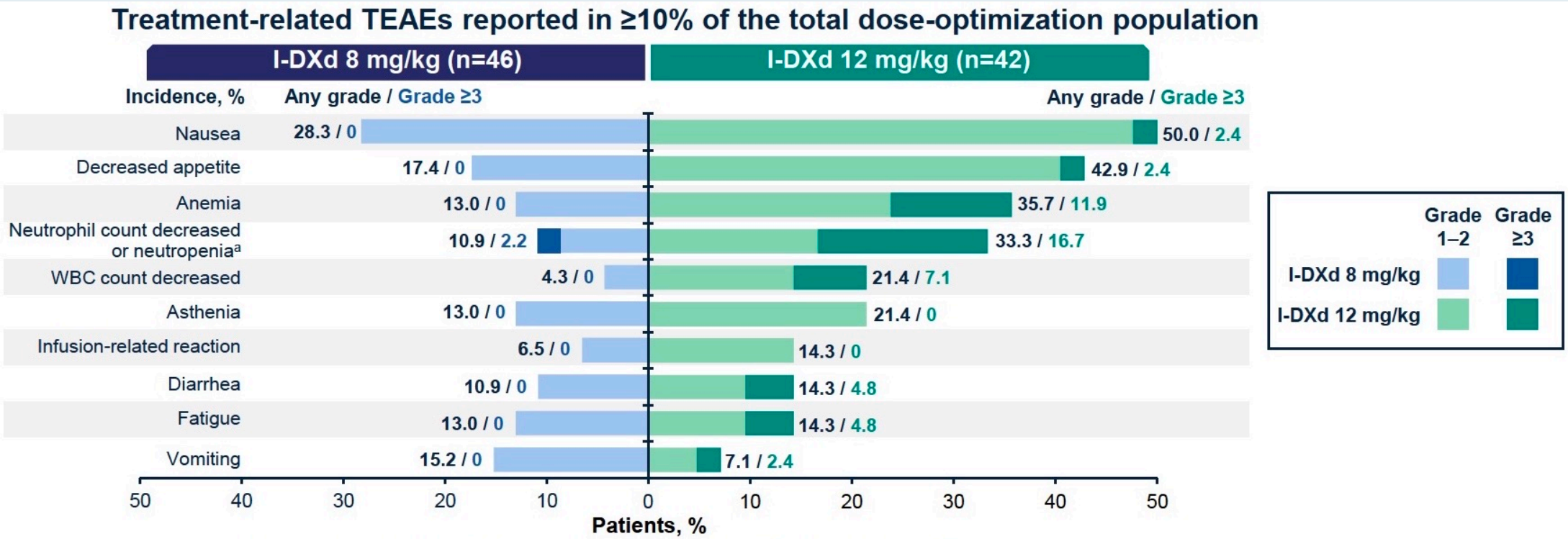
IDeate-Lung01: Intracranial Activity of I-DXd

	Patients with brain metastases at baseline		Subset of patients with brain target lesions	
	8 mg/kg (n=19)	12 mg/kg (n=18)	8 mg/kg (n=6)	12 mg/kg (n=10)
CNS efficacy				
CNS confirmed ORR,[a] % (95% CI)	36.8 (16.3–61.6)	38.9 (17.3–64.3)	66.7 (22.3–95.7)	50.0 (18.7–81.3)
CNS confirmed BOR,[a] n (%)				
CR	5 (26.3)	4 (22.2)	2 (33.3)	2 (20.0)
PR	2 (10.5)[b]	3 (16.7)[b]	2 (33.3)	3 (30.0)
SD or non-CR/non-PD[c]	8 (42.1)	10 (55.6)	2 (33.3)	5 (50.0)
PD	1 (5.3)	0	0	0
Not evaluable	3 (15.8)	1 (5.6)	0	0
CNS confirmed DCR,[a,d] % (95% CI)	78.9 (54.4–93.9)	94.4 (72.7–99.9)	100 (54.1–100.0)	100 (69.2–100.0)
CNS DOR, median (95% CI),[a] months	4.3 (3.3–NE)	7.4 (3.0–NE)	3.9 (3.3–NE)	6.5 (3.0–NE)
CNS TTR, median (range),[a] months	1.4 (1.2–1.5)	1.2 (0.9–2.8)	1.3 (1.2–1.4)	1.2 (0.9–2.8)
Systemic efficacy				
Systemic confirmed ORR,[e] % (95% CI)	26.3 (9.1–51.2)	61.1 (35.7–82.7)	16.7 (0.4–64.1)	60.0 (26.2–87.8)
Concordance between systemic and CNS objective response,[f] %	78.9	77.8	NR	NR

Data cutoff: April 25, 2024.
[a]Assessed by BICR, using a version of RECIST 1.1 modified for assessment of CNS tumors. [b]All patients with PR had target lesions at baseline. [c]Only patients without baseline brain target lesions could have response classified as "non-CR/non-PD." [d]CR + PR + SD + non-CR/non-PD. [e]By BICR per RECIST 1.1. [f]Percentage of patients with both CNS and systemic objective response, and with neither CNS nor systemic objective response.
BICR, blinded independent central review; BOR, best overall response; CI, confidence interval; CNS, central nervous system; CR, complete response; DCR, disease control rate; DOR, duration of response; NE, not estimable; NR, not reported; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; SD, stable disease; TTR, time to response.

Hayashi H et al. JSMO 2025;Abstract O12-4.

IDeate-Lung01: Adverse Events

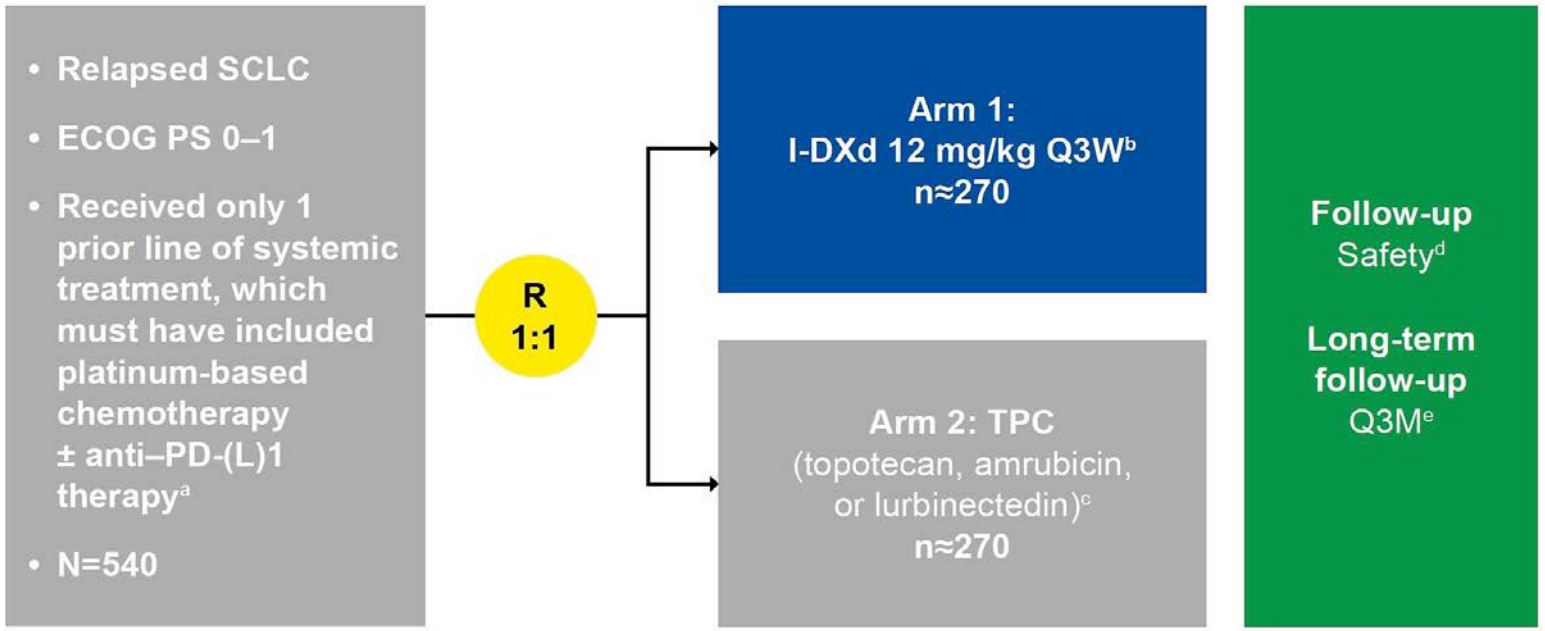


- ILD/pneumonitis adjudicated as treatment-related[b] was reported in:
  - Four (8.7%) of 46 patients in the **8-mg/kg** cohort (Grade 2, n=3; Grade 5, n=1)
  - Five (11.9%) of 42 patients in the **12-mg/kg** cohort (Grade 1, n=1; Grade 2, n=3; Grade 3, n=1)

Data cutoff: April 25, 2024. The median follow-up for 8-mg/kg and 12-mg/kg cohorts was 14.6 months (range, 0.6–17.0) and 15.3 months (range, 0.8–20.3) respectively.
[a]TEAEs associated with preferred terms neutrophil count decreased and neutropenia have been combined; no patients in either cohort were reported to have febrile neutropenia. [b]No ILD events are pending adjudication at the time of data cutoff.
ILD, interstitial lung disease; TEAE, treatment-emergent adverse event; WBC, white blood cell.

Hayashi H et al. JSMO 2025;Abstract O12-4.

Phase III IDeate-Lung02 Study



Stratification

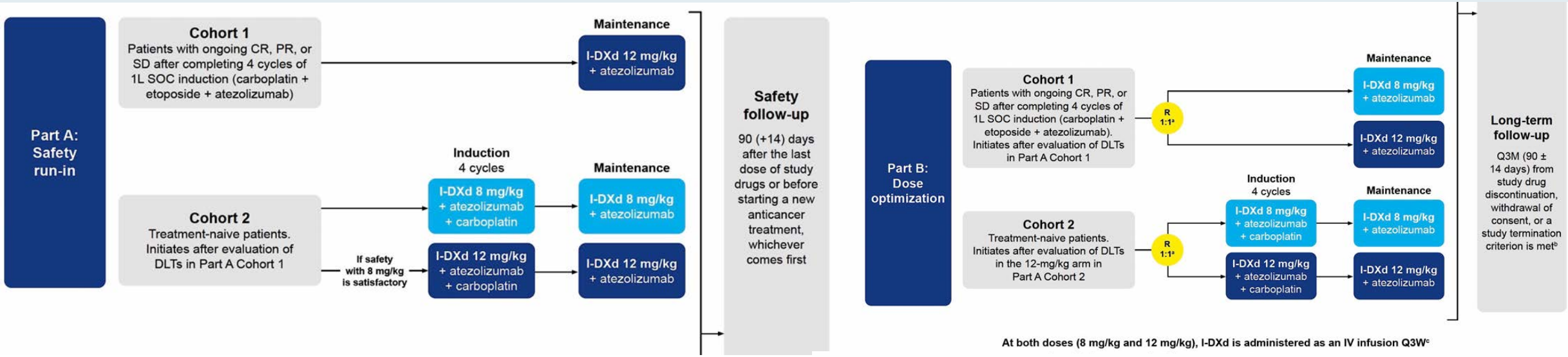
CTFI following 1L therapy (<90 vs ≥90 days)
TPC (topotecan vs amrubicin vs lurbinectedin)
Treatment with prior PD-(L)1 inhibitors (yes vs no)
Presence or history of asymptomatic brain metastases (yes vs no)

Primary endpoints: ORR, OS
Secondary endpoints: ORR, PFS, DOR, DCR, TTR, PROs, Safety, Immunogenicity, Pharmacokinetics, Relationship between B7-H3 expression and outcomes

[a]≥80% of patients are expected to have received prior anti–PD-(L)1 therapy. [b]Until PD, unacceptable toxicity, loss to follow-up, consent withdrawal, death, or other reason. [c]Comparator treatments will only be utilized in countries where they are approved in second and subsequent LoTs for patients with SCLC who progressed on or after platinum-based therapy; ≥70% of patients in the comparator group will receive topotecan. [d]Safety follow-up visit will occur 40 days (+7 days) after the last dose. [e]Long-term follow-up will occur to assess survival; assess tumor progression until PD for patients discontinuing for reasons other than PD; and to collect information on further anticancer treatments, Q3M (90 ±14 days) from study-drug discontinuation (end of treatment), withdrawal of consent, or from when a study-termination criterion is met.

Hayashi H et al. JSMO 2025;Abstract P93-5.

Phase Ib/II IDeate-Lung03 Study



Primary endpoints: Safety (DLTs [Part A] and TEAEs [Parts A and B])
Secondary endpoints: PFS, ORR, DCR, DOR, CBR, TTR, Best percentage change in sum of diameters of measurable tumors, OS, Pharmacokinetics, Immunogenicity

[a]Randomization stratified by lactate dehydrogenase (≤ULN vs ULN) and ECOG performance status (0 vs 1), as determined at induction baseline. [b]Long-term follow-up will occur to assess survival and tumor progression until PD for patients who discontinue treatment for reasons other than PD, and to collect information on further anticancer treatments. [c]Atezolizumab is administered as an IV infusion Q3W at a dose of 1,200 mg; carboplatin is administered as an IV infusion Q3W, AUC 5; etoposide is administered as an IV infusion Q3W on Day 1 to Day 3 at a dose of 100 mg/m^2.

Hayashi H et al. JSMO 2025;Abstract P93-6.

Agenda

Case 1: Adjuvant Systemic Therapy?

Case 2: Lambert-Eaton Syndrome and Other Paraneoplastic Syndromes

Case 3: Small Cell Transformation of EGFR-Mutant NSCLC

Case 4: Trilaciclib in Extensive-Stage Disease

Comments: ASCO and Other Recent Datasets (Part 1)

Case 5: Short DFI with Brain Mets After Chemo/RT/Durvalumab … Lurbinectedin?

Case 6: Tarlatamab After Rapid Disease Progression on Chemo/Atezolizumab

Case 7: ICANS on Tarlatamab with Brain Mets

Case 8: BiTE with Lurbinectedin on Protocol

Comments: ASCO and Other Recent Datasets (Part 2)

Case Presentation: 85-year-old man with mild dementia and LS-SCLC receives cisplatin/etoposide with RT and maintenance durvalumab but then develops worsening confusion and is found to have multiple bilateral brain metastases

Dr Priya Rudolph (Athens, Georgia)

RTP RESEARCH TO PRACTICE

Agenda

Case 1: Adjuvant Systemic Therapy?

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Comments: ASCO and Other Recent Datasets (Part 2)

Case Presentation: 59-year-old man with ES-SCLC and rapid PD after 4 cycles of first-line carboplatin/etoposide/ atezolizumab receives tarlatamab

Dr Ranju Gupta (Bethlehem, Pennsylvania)

RTP
RESEARCH
TO PRACTICE

Agenda

Case 1: Adjuvant Systemic Therapy?

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Comments: ASCO and Other Recent Datasets (Part 2)

RTP RESEARCH TO PRACTICE

Case Presentation: 66-year-old woman with ES-SCLC receives carboplatin/etoposide with atezolizumab and RT followed by maintenance atezolizumab followed on relapse by lurbinectinin followed on relapse by tarlatamab

Dr Estelamari Rodriguez (Miami, Florida)

RTP RESEARCH TO PRACTICE

Agenda

Case 1: Adjuvant Systemic Therapy?

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Case 8: BiTE with Lurbinectedin on Protocol

Comments: ASCO and Other Recent Datasets (Part 2)

Case Presentation: 66-year-old woman with LS-SCLC receives chemoradiation and durvalumab consolidation followed on relapse by entry on a trial of a BiTE with lurbinectedin

Dr Estelamari Rodriguez (Miami, Florida)

RTP
RESEARCH
TO PRACTICE

Agenda

Case 1: Adjuvant Systemic Therapy?

Case 2: Lambert-Eaton Syndrome and Other Paraneoplastic Syndromes

Case 3: Small Cell Transformation of EGFR-Mutant NSCLC

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Comments: ASCO and Other Recent Datasets (Part 2)

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RESEARCH
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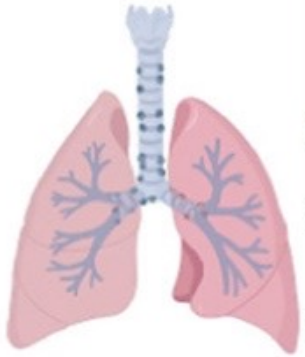
Relapsed SCLC: The Phase I/II LUPER Study

RELAPSED SCLC PATIENTS



- Progressing to first-line platinum-based chemotherapy
- ECOG PS 0-1
- No prior immunotherapy
- Asymptomatic CNS metastasis

GOAL: To evaluate the efficacy and safety of lurbinectedin combined with pembrolizumab in patients with relapsed SCLC, aiming to prevent early disease progression and achieve durable responses

TRIAL OVERVIEW

Phase I
Dose Escalation (3+3 design)

N = 3-6 patients per dose

Lurbinectedin 2.4 mg/m² (starting dose) + Pembrolizumab 200 mg

ENDPOINTS

PRIMARY	SECONDARY
• RP2D and MTD of lurbinectedin combined with pembrolizumab	• Safety as per NCI-CTCAE 5.0 • Preliminary efficacy by RECIST 1.1

Phase II
Dose Expansion

N ≈ 30 patients

Lurbinectedin RP2D + Pembrolizumab 200 mg

ENDPOINTS

PRIMARY	SECONDARY
• ORR as per RECIST 1.1	• Safety as per NCI-CTCAE 5.0 • CBR, DoR, PFS, and OS • PK and PGx

Calles A et al. *J Thorac Onc* 2025;20(7)969-82.

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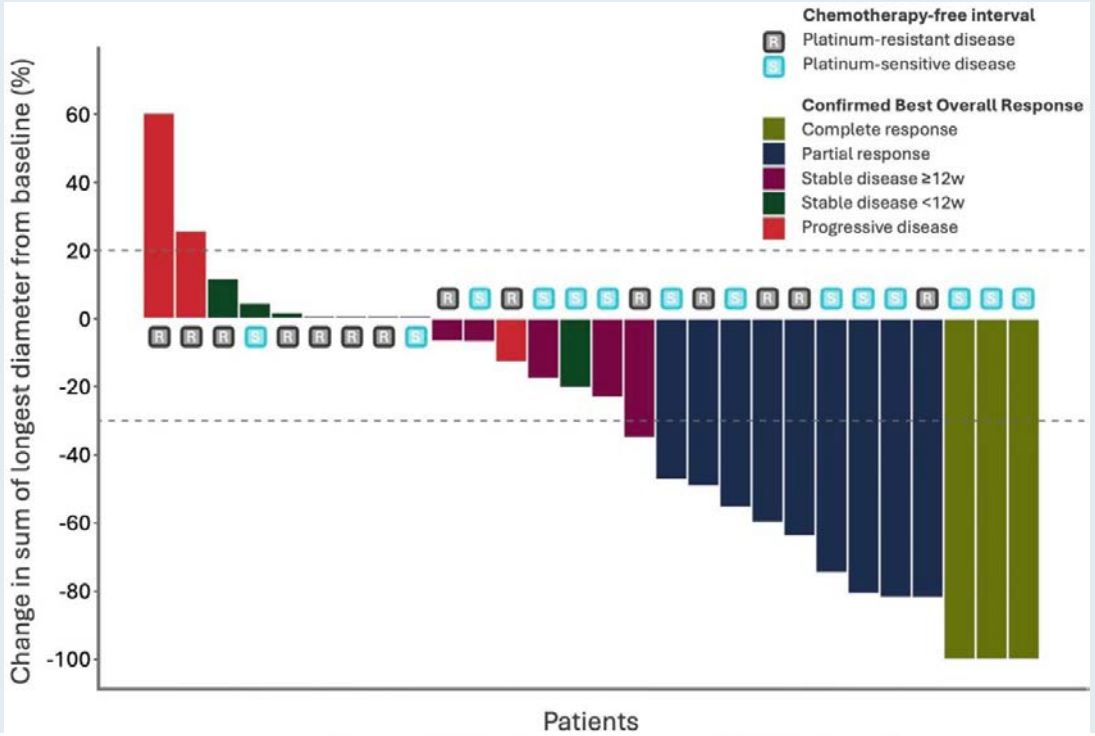
LUPER: Responses



Tumor Response, n (%)	Platinum-Resistant (N = 14)	Platinum-Sensitive (N = 14)	Overall (N = 28)
Unconfirmed ORR			
No	9 (64.3)	6 (42.9)	15 (53.6)
Yes	5 (35.7)	8 (57.1)	13 (46.4)
95% CI	(12.8; 64.9)	(28.9; 82.3)	(27.5; 66.1)
Confirmed ORR			
No	10 (71.4)	6 (42.9)	16 (57.1)
Yes	4 (28.6)	8 (57.1)	12 (42.9)
95% CI	(8.4-58.1)	(28.9-82.3)	(24.5-62.8)

n (%): number of participants (percentage on the basis of N).
N: number of patients.
[a]Response evaluation is missing for four patients who died before the tumor assessment.

ORR = objective response rate

Calles A et al. *J Thorac Onc* 2025;20(7)969-82.

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Relapsed SCLC: The Phase III LAGOON Trial

- Relapsed SCLC
- One prior platinum containing regimen
- CTFI ≥30 days
- ECOG 0-2
- Adequate hematological, renal, and liver function

Randomization 1:1:1
705 patients

- Lurbinectedin 3.2 mg/m² IV D1 q3w
- Lurbinectedin 2.0 mg/m² IV D1 + Irinotecan 75 mg/m² IV D1, 8 q3w + GCSF
- **Institutional choice chemotherapy**
  Topotecan 2.3 mg/m² oral or 1.5 mg/m² IV D1-5 q3w
  Irinotecan IV 350 mg/m² D1q3w

Stratified by:
- CTFI
- Prior PD-L1/PD-1
- LDH
- CNS involvement
- Investigator's preference of the control Arm

Treatment until progression by RECIST 1.1

Screening up to 28D | **Treatment period** | **Follow-up period**

Primary endpoint: Overall survival
Secondary: PFS, ORR, DoR, Safety, PRO

CTFI = chemotherapy-free interval

Besse B et al. ASCO 2023;Abstract TPS8613.

2025 ASCO ANNUAL MEETING

Abstract 8013

Safety and efficacy of lurbinectedin plus atezolizumab as second-line treatment for advanced small-cell lung cancer: Results of the 2SMALL phase 1/2 study (Abstract 8013)

Santiago Ponce Aix[1], Alejandro Navarro[2], Maria Eugenia Olmedo García[3], Laura Mezquita[4], Margarita Majem[5], David Vicente[6], Reyes Bernabé[7], Alba Moratiel Pellitero[8], Manuel Cobo[9], Javier De Castro[10], Silverio Ros[11], Marta Lopez Brea[12], Rosario G. Campelo[13], Javier Baena[1], Helena Bote[1], Mercedes Herrera[1], Pedro Rocha[2], Jon Zugazagoitia[1], Enriqueta Felip[2], Luis Paz-Ares[1]

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This study has been sponsored by Fundación OncoSur

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PRESENTED BY: Santiago Ponce Aix MD

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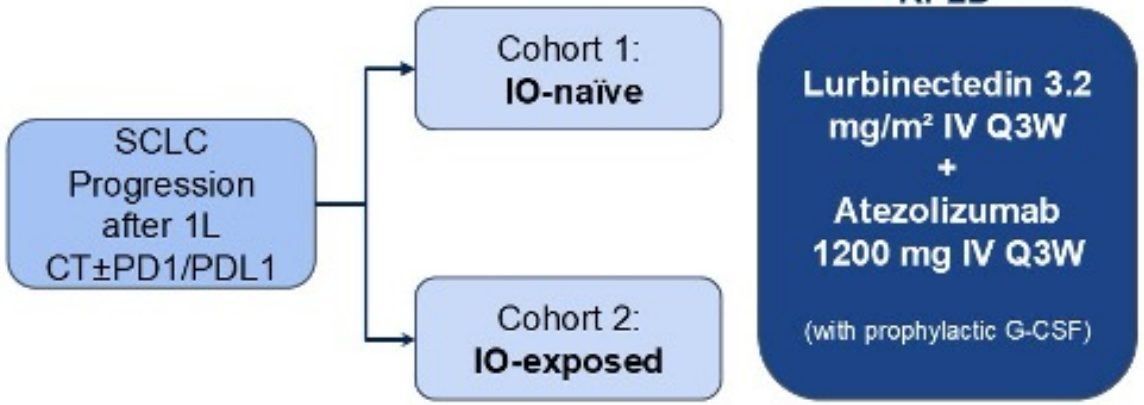
2SMALL Phase II Trial Design

Non-randomized, open-label phase II study of lurbinectedin plus atezolizumab as second-line therapy for advanced SCLC (NCT04253145)

Key Eligibility Criteria:
- Age ≥ 18 years
- Histologically/cytologically confirmed advanced SCLC
- Progression to 1L platinum based CT ± PD1/PDL1
- CTFI ≥30 days
- Measurable disease
- ECOG PS (0/1)
- Brain metastasis allowed if treated and asymptomatic



Primary endpoints
- Safety
- ORR (per RECIST v1.1)

Secondary endpoints
- Duration of response (DoR)
- Clinical benefit (CB) CR, PR, SD ≥3 mo)
- PFS
- OS
- Others: PK, PGt and PGx

Phase II included two predefined groups based on platinum sensitivity: platinum-sensitive (CTFI ≥90 days) and platinum-resistant (CTFI 30 to <90 days). Patients with platinum-refractory disease (CTFI <30 days) were excluded.

Sample size (~160) based on ORR as primary endpoint; power 80%, α=0.05.

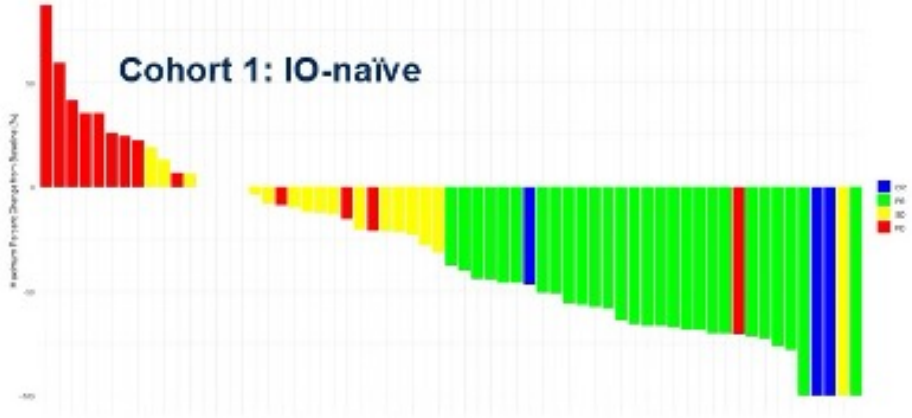
ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenously; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PGt, pharmacogenetics; PGx, pharmacogenomics; PK, pharmacokinetics; q3w, every 3 weeks.

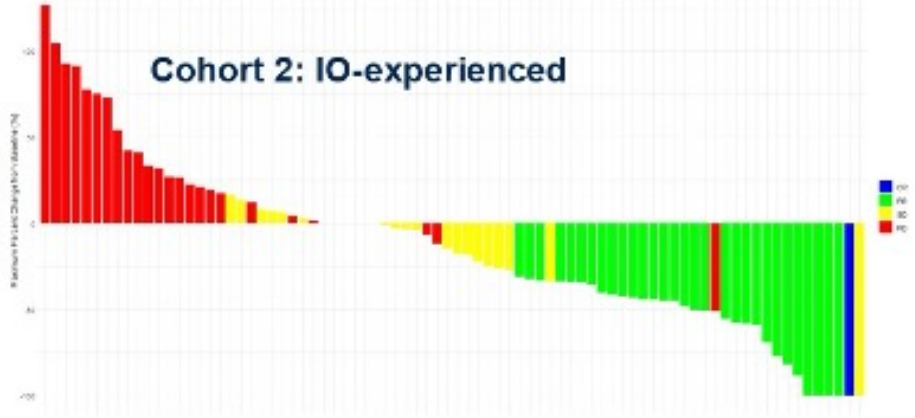
Data cutoff: May 31, 2024

Aix SP et al. ASCO 2025;Abstract 8013.

2SMALL: Efficacy

	Cohort 1 IO-naïve (n=68)	Cohort 2 IO-experienced (n= 83)	TOTAL n=151	Platinum - sensitive CTFI ≥90 days (n=92)	Platinum - resistant CTFI 30 to <90 days (n=59)
ORR n, % (95% CI)	30, 44.1% (32.3 - 56.6%)	31, 37.3% (27.2 - 48.7%)	61, 40.4% (32.6 - 48.7%)	40, 43.5% (33.3 - 54.2%)	21, 35.6% (23.9% - 49.2%)
DoR, mo, median (95% CI)	5.6 (3.9 - 7.5)	3.97 (3 - 4.4)	4.1 (3.3 - 5.6)	4.4 (3.3 - 7.0)	4.07 (2.9 - 6.0)
DCR (%)	51 (75%)	56 (67.5%)	107 (70.9%)	66 (71.7%)	41 (69.5%)





IO = immunotherapy; CTFI = chemotherapy-free interval; ORR = objective response rate; DoR = duration of response; DCR = disease control rate

Aix SP et al. ASCO 2025;Abstract 8013.

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Updated Analysis from NEJ045A Study: Safety and Efficacy of Durvalumab plus Carboplatin and Etoposide for Previously Untreated Extensive-Stage Small-Cell Lung Cancer Patients with a Poor Performance Status

Asao T et al.

ASCO 2025;Abstract 8557 (Poster).

Abstract 8014

2025 ASCO ANNUAL MEETING

Clinical and molecular characteristics of early progressors and long-term progression-free survivors from the phase 3 ADRIATIC trial of consolidation durvalumab versus placebo after concurrent chemoradiotherapy in limited-stage small-cell lung cancer

David A. Barbie,[1] Mingchao Xie,[2] Maria A.S. Broggi,[3] Ying Cheng,[4] David R. Spigel,[5] Byoung Chul Cho,[6] Jian Fang,[7] Yuanbin Chen,[8] Yoshitaka Zenke,[9] Ki Hyeong Lee,[10] Qiming Wang,[11] Alejandro Navarro,[12] Eva Lotte Buchmeier,[13] Mustafa Özgüroğlu,[14] Christine L. Hann,[15] Jocelyn Chen,[16] Victoria Lai,[17] Yashaswi Shrestha,[3] Suresh Senan[18]

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Multi-omic Analysis and Overall Survival Update of Phase II TRIDENT Study: Durvalumab plus Olaparib in Extensive-Stage Small-Cell Lung Cancer (ES-SCLC)

Zhao Y et al.

ASCO 2025;Abstract 8101 (Poster).

Implementation of Tarlatamab Treatment for Small Cell Lung Cancer Using an Outpatient Care Program

Carlisle JW et al.

ASCO 2025;Abstract 8106 (Poster).

Inside the Issue: Managing Ocular Toxicities Associated with Antibody-Drug Conjugates and Other Cancer Therapies

A CME/MOC-Accredited Live Webinar

Thursday, July 17, 2025
5:00 PM – 6:00 PM ET

Faculty

Rebecca A Dent, MD, MSc
Hans Lee, MD
Neel Pasricha, MD
Tiffany A Richards, PhD, ANP-BC, AOCNP

Moderator

Neil Love, MD

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