Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, April 14, 2026
5:00 PM – 6:00 PM ET

Faculty

Christine L Hann, MD, PhD
Jacob Sands, MD

Moderator

Neil Love, MD

RTP Year in Review 2026

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Christine L Hann, MD, PhD
Associate Professor of Oncology
Director, Small Cell Lung Cancer Therapeutics
Sidney Kimmel Comprehensive Cancer Center
Johns Hopkins University School of Medicine
Baltimore, Maryland

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Jacob Sands, MD
Associate Chief, Thoracic Oncology
Dana-Farber Cancer Institute
Assistant Professor
Harvard Medical School
Boston, Massachusetts

Commercial Support

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Dr Love — Disclosures

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Contracted Research	Amgen Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc

Dr Sands — Disclosures

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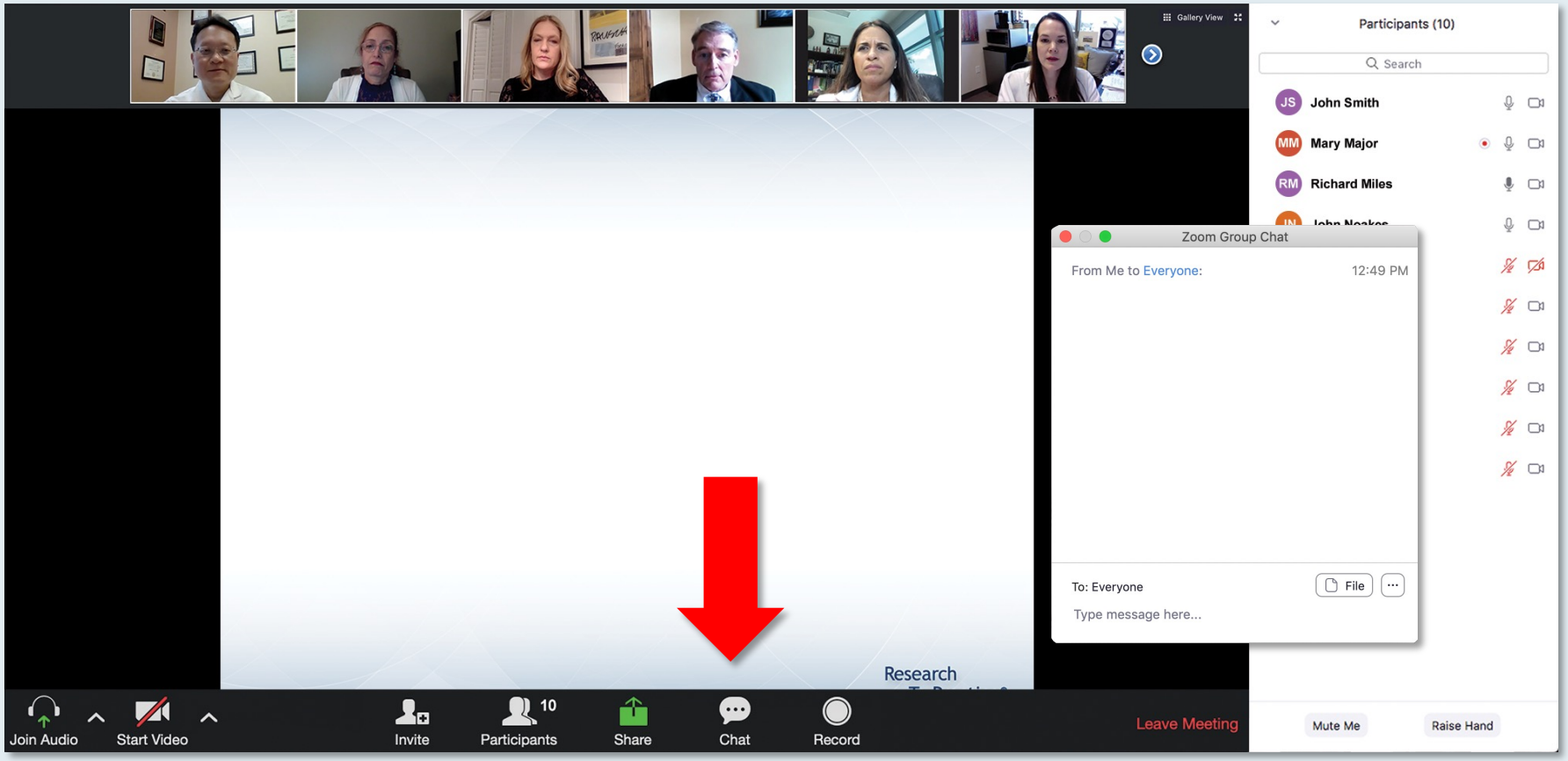

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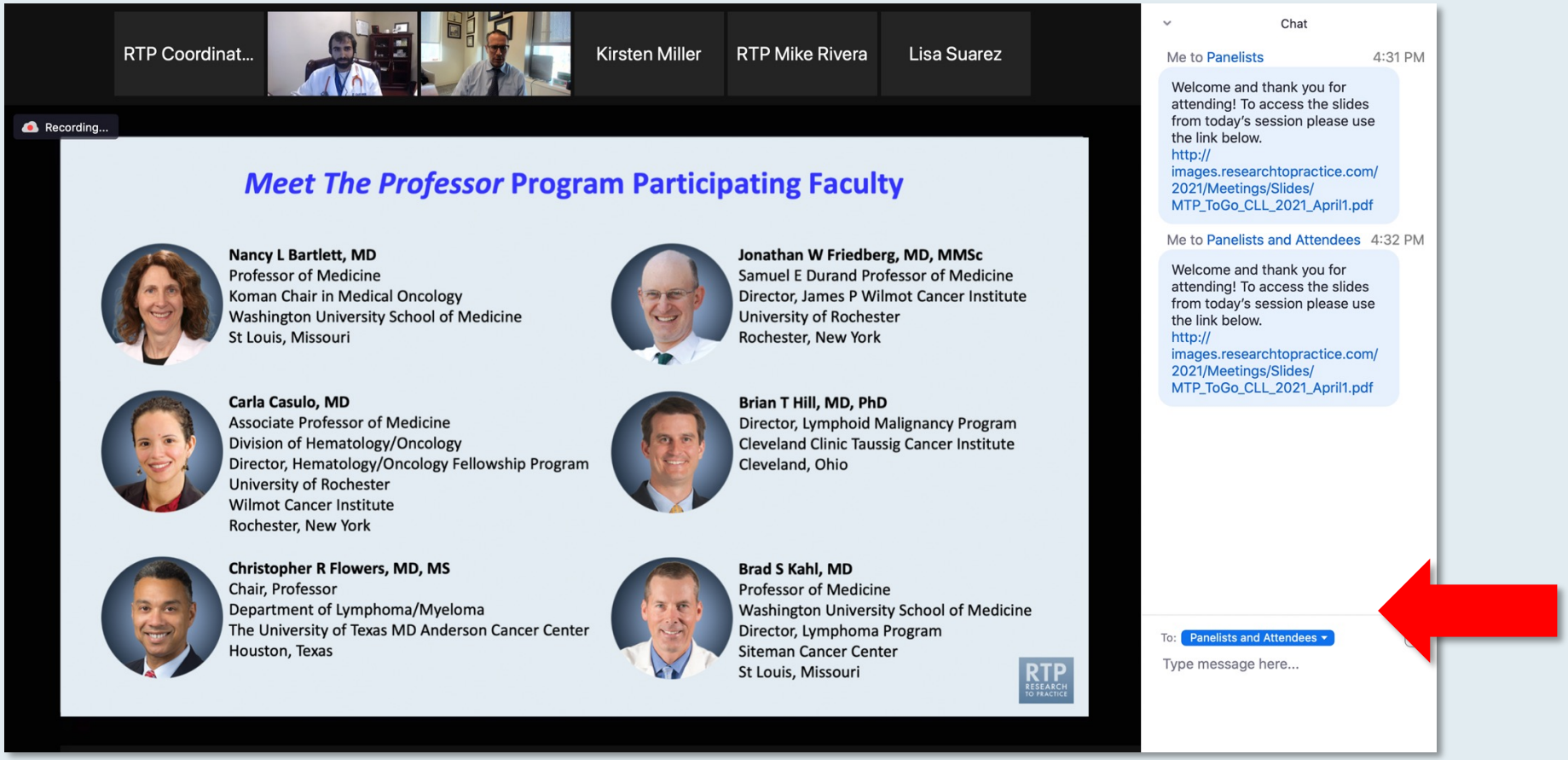

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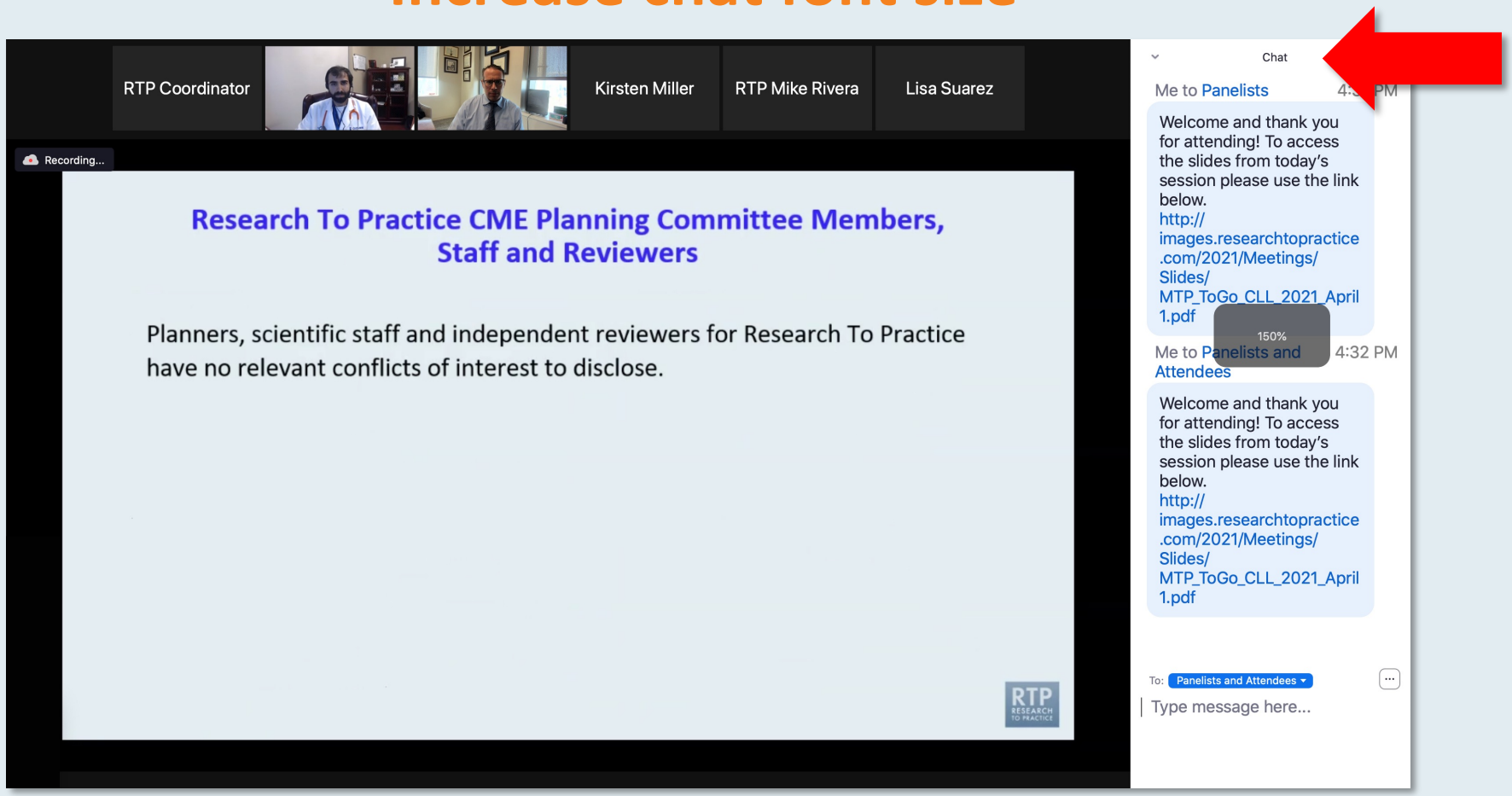

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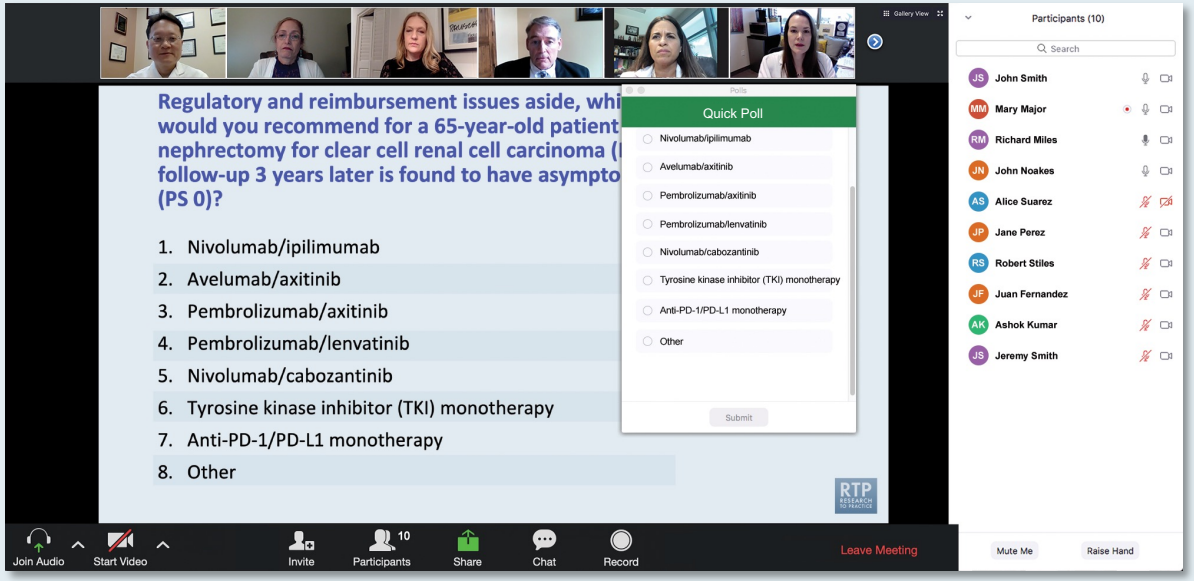

Extensive-Stage Small Cell Lung Cancer — Current Patterns of Care with First-Line and Maintenance Therapy

HOSSEIN BORGHAEI, MD
FOX CHASE CANCER CENTER

ANNE CHIANG, MD, PHD
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Developed in Partnership with Florida Cancer Specialists & Research Institute

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Friday, April 24, 2026

7:00 PM – 9:00 PM

Keynote Session: Diffuse Large B-Cell Lymphoma and Follicular Lymphoma

Manali Kamdar, MD, MBBS
Krish Patel, MD
Gilles Salles, MD, PhD

Fellows Welcome!

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John N Allan, MD
Adam Kittai, MD

8:50 AM – 9:40 AM

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MODULE 3: Paraneoplastic Syndromes – Lambert-Eaton Myasthenic Syndrome

MODULE 4: Bispecific T-Cell Engagers – Tarlatamab

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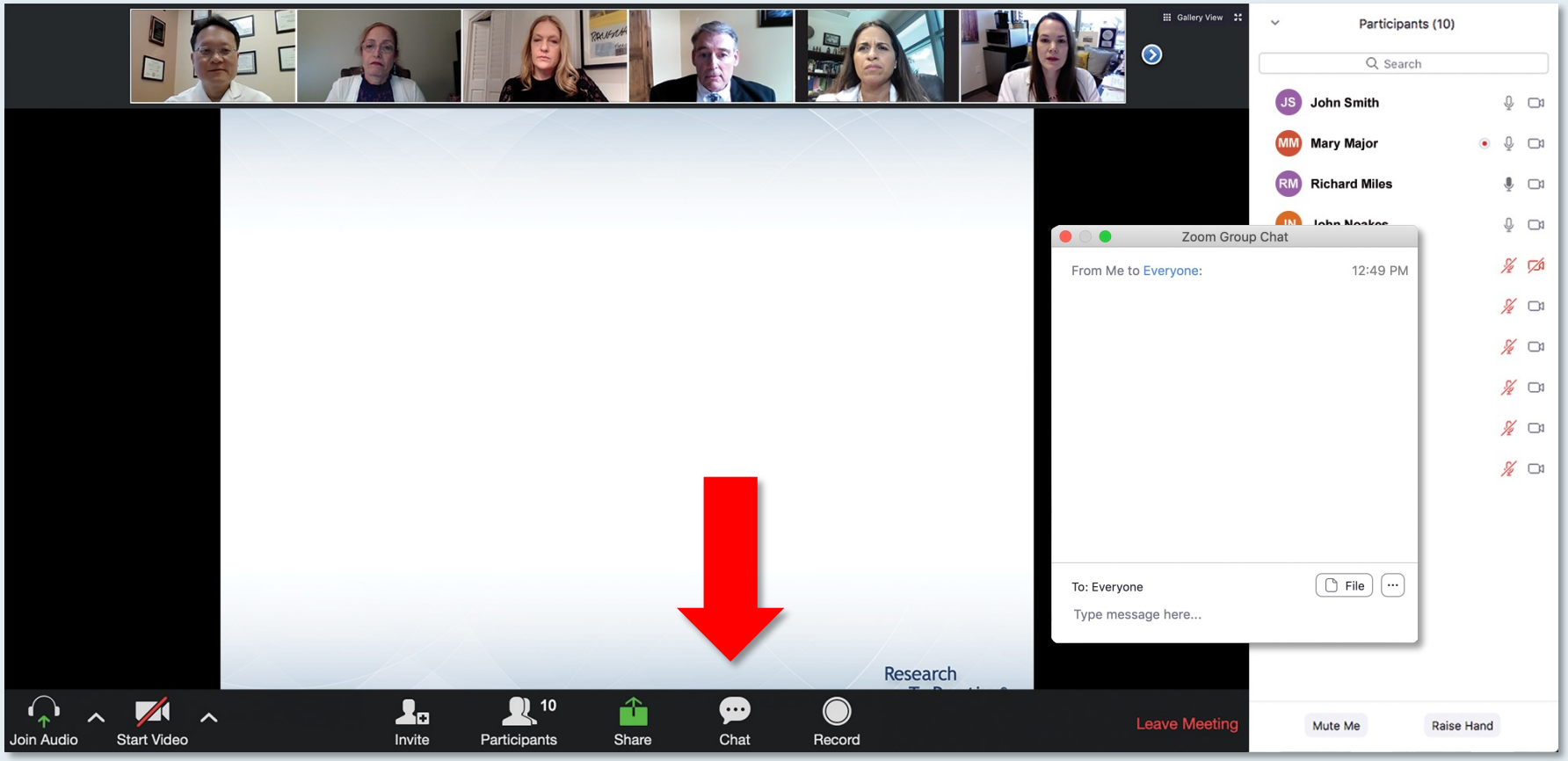

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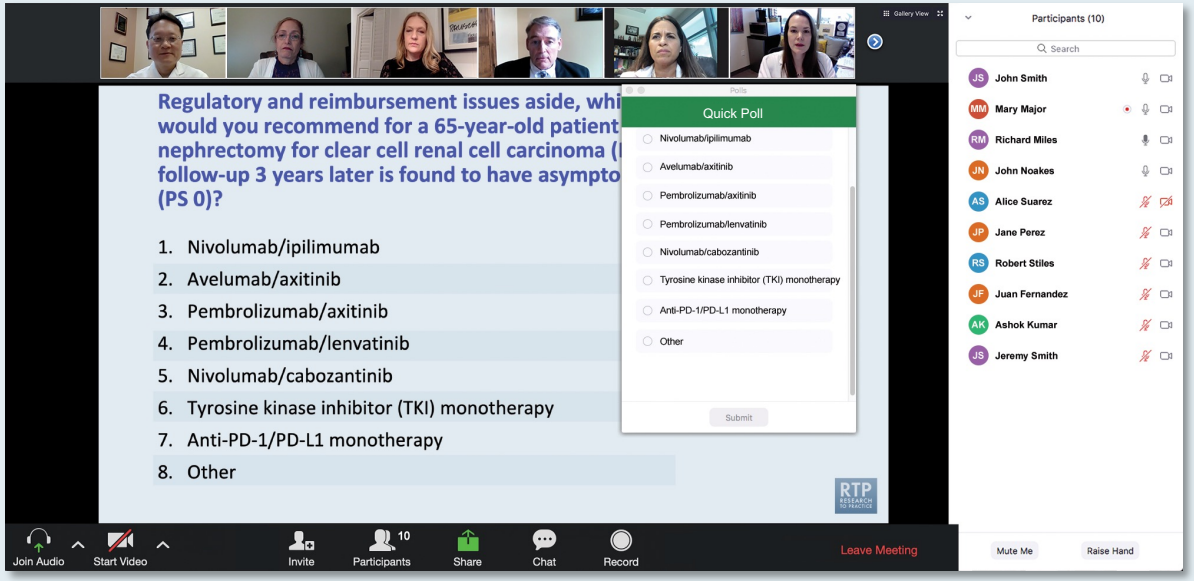

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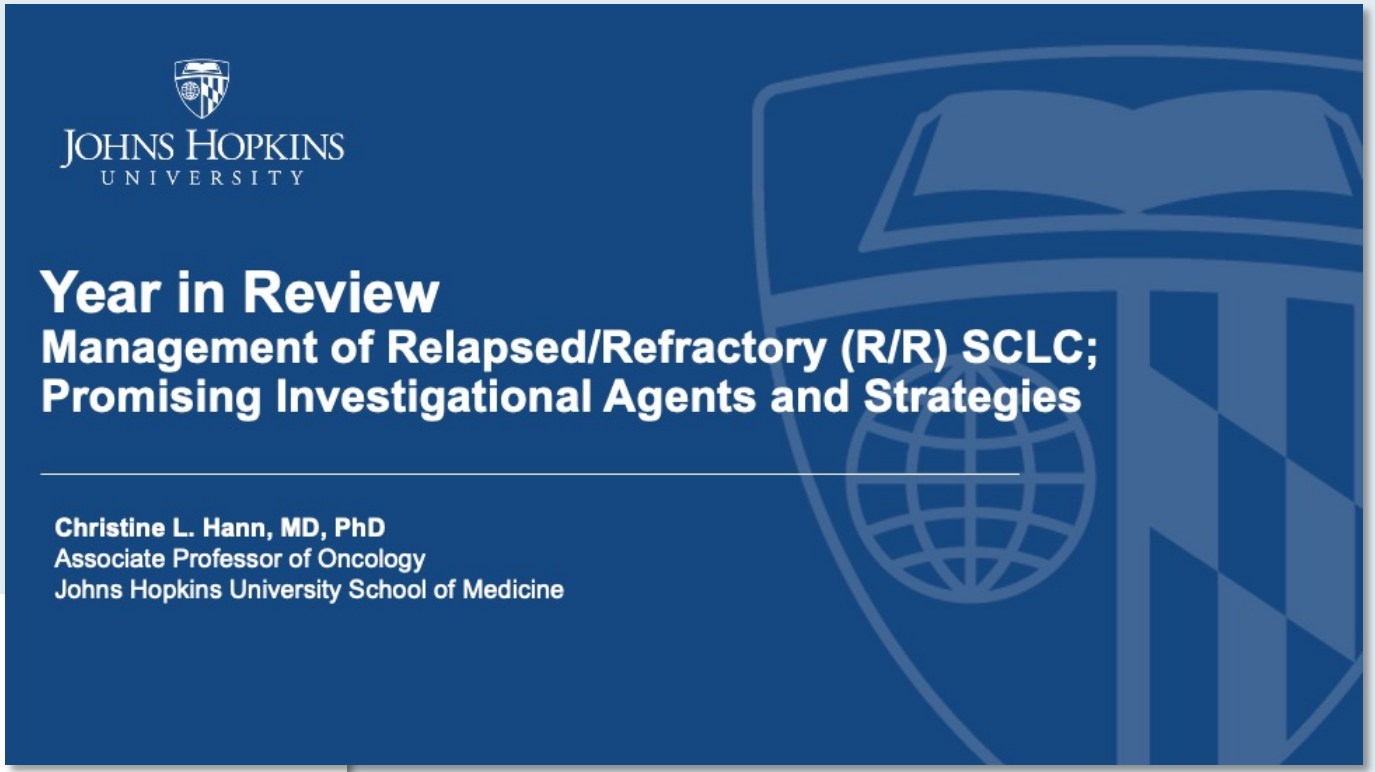

Year in Review SCLC 2025
Limited-Stage Small Cell Lung Cancer (LS-SCLC); First-Line and Maintenance Therapy for Extensive-Stage SCLC (ES-SCLC)

Jacob Sands, MD

Dana-Farber Cancer Institute

RTP Year in Review 2026

Key Datasets

Jacob Sands, MD

- Higgins KA et al. **Chemoradiation atezolizumab** in **limited-stage** small cell lung cancer: Results of **NRG Oncology/Alliance LU005**. *J Clin Oncol* 2025;44(8):630-40.
- Barbie DA et al. Clinical and molecular characteristics of **early progressors (EPs) and long-term progression-free survivors** (LTPs) from the **phase 3 ADRIATIC** trial of **consolidation durvalumab (D) vs placebo (P) after concurrent chemoradiotherapy (cCRT)** in **limited-stage** small-cell lung cancer (LS-SCLC). ASCO 2025;Abstract 8014.
- Reinmuth N et al. **Durvalumab plus platinum-etoposide** in **extensive-stage** small-cell lung cancer: **Outcomes in age, sex, and platinum subgroups** from the **phase 3 CASPIAN** Study. *Clin Lung Cancer* 2025;26(8):626-41.
- Paz-Ares L et al. 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. *Lancet* 2025;405(10495):2129-43.
- Paz-Ares L et al. **Patterns of disease progression (PD) and efficacy associated with tumour burden** from the phase III **IMforte** study of lurbinectedin (lurbi) + atezolizumab (atezo) as first-line (1L) maintenance treatment (tx) in ES-SCLC. ESMO 2025;Abstract 2762MO.

Key Datasets

Jacob Sands, MD (continued)

- Reck M et al. **Safety** of **lurbinectedin + atezolizumab** as **1L maintenance treatment** in ES-SCLC: Results from the phase 3 **IMforte** study. WCLC 2025;Abstract MA11.04.
- Paulson KG et al. Safety and activity of **tarlatamab in combination with a PD-L1 inhibitor as first-line maintenance** therapy after chemo-immunotherapy in patients with **extensive-stage** small-cell lung cancer **(DeLLphi-303)**: A multicentre, non-randomised, phase 1b study. *Lancet Oncol* 2025;26(10):1300-11.
- Peters S et al. **DAREON®-8: A phase I trial of first-line obrixtamig plus chemotherapy and atezolizumab** in **extensive-stage** small cell lung carcinoma (ES-SCLC). ESMO 2025;Abstract 2759MO.
- Heymach JV et al. Global **phase 2 randomized trial of BNT327 (pumitamig; PD-L1 x VEGF-A bsAb) + chemotherapy for 1L ES-SCLC**: Dose optimization analysis. WCLC 2025;Abstract OA13.02.

Key Datasets

Christine L Hann, MD, PhD

- Calles A et al. **Lurbinectedin plus pembrolizumab** in **relapsed** SCLC: The **phase I/II LUPER** study. *J Thorac Oncol* 2025;20(7):969-82.
- Mountzios G et al. **Tarlatamab** in small-cell lung cancer **after platinum-based chemotherapy**. *N Engl J Med* 2025;393(4):349-61.
- Schuler MH et al. **Detailed safety analysis** of **DeLLphi-304**: The first phase III study to evaluate **tarlatamab versus chemotherapy** for **previously treated** small cell lung cancer. ESMO 2025;Abstract LBA100.
- Wermke M et al. **Phase I dose-escalation results** for the delta-like ligand 3/CD3 IgG-like T-cell engager **obrixtamig (BI 764532)** in patients with **delta-like ligand 3+ small cell lung cancer or neuroendocrine carcinomas**. *J Clin Oncol* 2025; 43(27):3021-31.
- Beltran H et al. **Updated results** from a **phase I/II study** of **gocatamig** for **small cell lung cancer (SCLC) and other neuroendocrine cancers**. ESMO 2025;Abstract 2758MO.

Key Datasets

Christine L Hann, MD, PhD (continued)

- Rudin CM et al. **Ifinatamab deruxtecan** in patients with extensive-stage small cell lung cancer: Primary analysis of the phase II IDeate-Lung01 Trial. *J Clin Oncol* 2026;44(4):261-73.
- Simoes da Rocha PF et al. **Intracranial activity of ifinatamab deruxtecan (I-DXd)** in patients (pts) with extensive-stage (ES) small cell lung cancer (SCLC) and baseline (BL) brain metastases (BM): Primary analysis of IDeate-Lung01. ESMO 2025;Abstract 2760MO.
- Dowlati A et al. Phase 2 open-label study of **sacituzumab govitecan as second-line therapy** in patients with extensive-stage SCLC: Results from TROPiCS-03. *J Thorac Oncol* 2025;20(6):799-808.
- Owonikoko TK et al. Randomized phase II study of paclitaxel plus **alisertib versus paclitaxel** plus placebo as second-line therapy for SCLC: Primary and correlative biomarker analyses. *J Thorac Oncol* 2020;15(2):274-87.
- Owonikoko TK et al. **Alisertib** in patients with **extensive-stage** small-cell lung cancer: The **phase 2 ALISCA-Lung1** study. ASCO 2024;Abstract TPS8128.

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INTRODUCTION: Biopharmacology of SCLC – “Wildfire sparked in dry grass”

MODULE 1: Limited-Stage Disease

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Expert Second Opinion: Investigators Provide Perspectives on the Best-Practice Use of Immunotherapy for Endometrial Cancer

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Saturday, April 11, 2026

12:45 PM – 2:15 PM AST

Faculty

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Moderator

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Nicoletta Colombo, MD

Gottfried E Konecny, MD

Alexander B Olawaiye, MD

Moderator

Shannon N Westin, MD, MPH, FASCO, FACOG

RTP RESEARCH TO PRACTICE

Data + Perspectives: The Potential Role of TROP2- and CDH6-Directed Antibody-Drug Conjugates in Gynecologic Cancers

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Sunday, April 12, 2026

1:30 PM – 3:00 PM AST

Faculty

Ramez N Eskander, MD

Bradley J Monk, MD

Moderator

Kathleen N Moore, MD, MS

RTP RESEARCH TO PRACTICE

Expert Second Opinion: Investigators Provide Perspectives on the Management of HER2-Positive Gynecologic Cancers

An Independent CME Symposium During the SGO 2026 Annual Meeting on Women's Cancer®

Saturday, April 11, 2026

12:45 PM – 2:15 PM AST

Faculty

Joyce F Liu, MD, MPH

Brian M Slomovitz, MD

Moderator

David M O'Malley, MD

RTP RESEARCH TO PRACTICE

Year in Review:
Small Cell Lung Cancer

INTRODUCTION: Biopharmacology of SCLC – "Wildfire sparked in dry grass"

MODULE 1: Limited-Stage Disease

MODULE 2: Extensive-Stage Disease

MODULE 3: Paraneoplastic Syndromes – Lambert-Eaton Myasthenic Syndrome

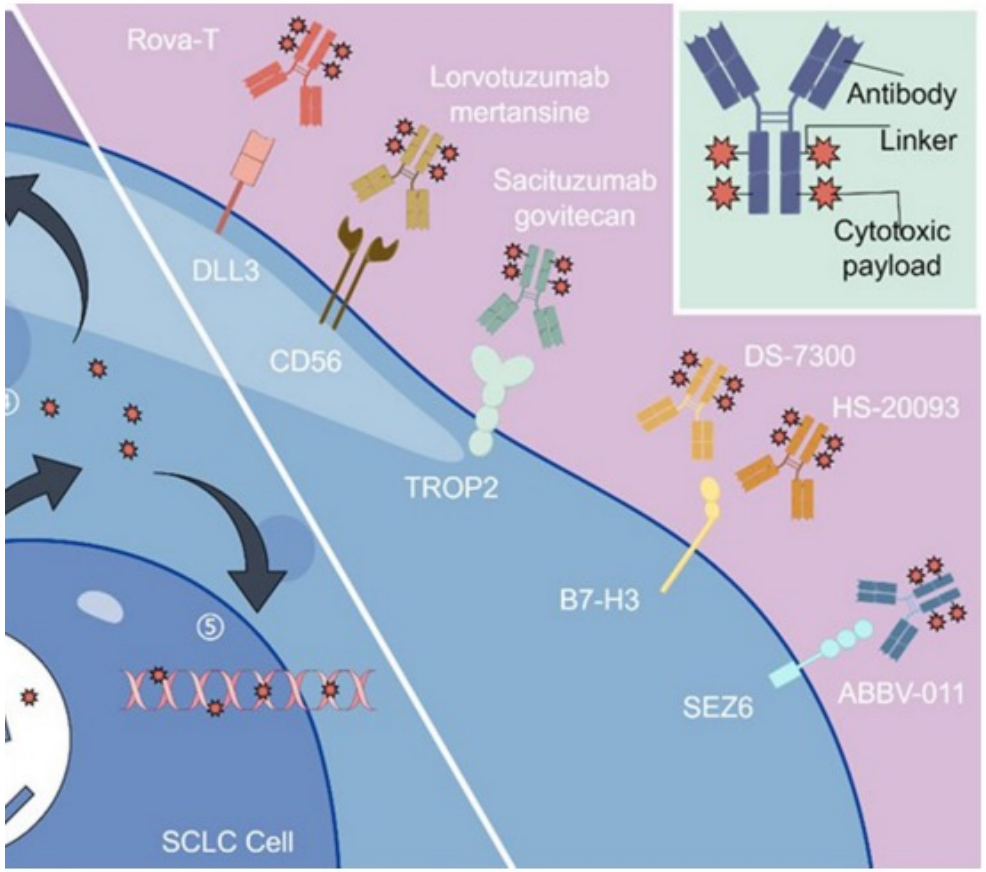
MODULE 4: Bispecific T-Cell Engagers – Tarlatamab

MODULE 5: Antibody-Drug Conjugates – Ifinatamab Deruxtecan

MODULE 6: Other Novel Agents – Alisertib, CAR T-Cell Therapy

RTP Year in Review 2026

SCLC cell surface targets under active clinical evaluation



B7-H3 (CD276)
- B7 family of immune checkpoint proteins
- inhibits T-cell activation and promotes immune evasion
- SCLC expression ~65%

DLL3 (Delta-like Ligand 3)
- Inhibitory TM ligand of the Notch pathway
- SCLC expression ~85%

SEZ6 *(Seizure Related 6 Homolog)*
- TM protein on surface of selected neuronal lineage cells
- Highly expressed in SCLC

TROP-2 *(trophoblast cell-surface antigen 2)*
- TM glycoprotein involved in cell signaling, proliferation, and migration
- SCLC expression low (~18%)

Bispecific EGFR/HER3-ADC: Izalontamab brengitecan (Iza-Bren)

Meng Y et al. *Discov Oncol*. 2024;15(1):327. Ajay A et al. *npj Precis Oncol*. 2025;9:1.

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RTP Year in Review 2026

Original Reports | Thoracic Oncology

Chemoradiation ± Atezolizumab in Limited-Stage Small Cell Lung Cancer: Results of NRG Oncology/Alliance LU005

Kristin A. Higgins, MD[1]; Chen Hu, PhD[2,3]; Helen J. Ross, MD[4]; Salma K. Jabbour, MD[5]; David E. Kozono, MD, PhD[6]; Taofeek K. Owonikoko, MD, PhD[7]; Timothy A. Ritter, PhD[8]; Terence M. Williams, MD, PhD[9]; James Welsh, MD[10]; Jeffry P. Simko, PhD, MD[11]; B Movsas, MD[12]; Canhua Xiao, PhD[13]; Kyoichi Kaira, MD, PhD[14]; Amit K. Gupta, MD[15]; Pranshu Mohindra, MD[16]; Elie G. Dib, MD[17]; Jeremy Brownstein, MD[18]; Stephen Chun, MD[10]; Charles S. Kuzma, MD[19]; Rupesh Kotecha, MD[20]; Adedayo A. Onitilo, MD[21]; Yuhchyau Chen, MD, PhD[22]; Thomas E. Stinchcombe, MD[23]; Xiaofei Wang, PhD[23]; Rebecca Paulus, BS[2,24]; and Jeffrey D. Bradley, MD[25]

DOI https://doi.org/10.1200/JCO-25-01569

J Clin Oncol 2026;44(8):630-40.

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]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]AstraZeneca, Waltham, MA, USA; [3]AstraZeneca, Gaithersburg, MD, USA; [4]Jilin Cancer Hospital, Changchun, China; [5]Sarah Cannon Research Institute, Nashville, TN, USA; [6]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [7]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department II of Thoracic Oncology, Peking University Cancer Hospital & Institute, Beijing, China; [8]Cancer & Hematology Centers of Western Michigan, Grand Rapids, MI, USA; [9]National Cancer Center Hospital East, Kashiwa, Japan; [10]Chungbuk National University Hospital, Cheongju, Republic of Korea; [11]The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, 450008, China; [12]Hospital Vall d'Hebron and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [13]Hospitals of the City of Cologne gGmbH, Cologne, Germany; [14]Istanbul University Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Istanbul, Türkiye; [15]Johns Hopkins University, Baltimore, MD, USA; [16]AstraZeneca, Mississauga, ON, Canada; [17]AstraZeneca, New York, NY, USA; [18]Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, the Netherlands

RTP Year in Review 2026

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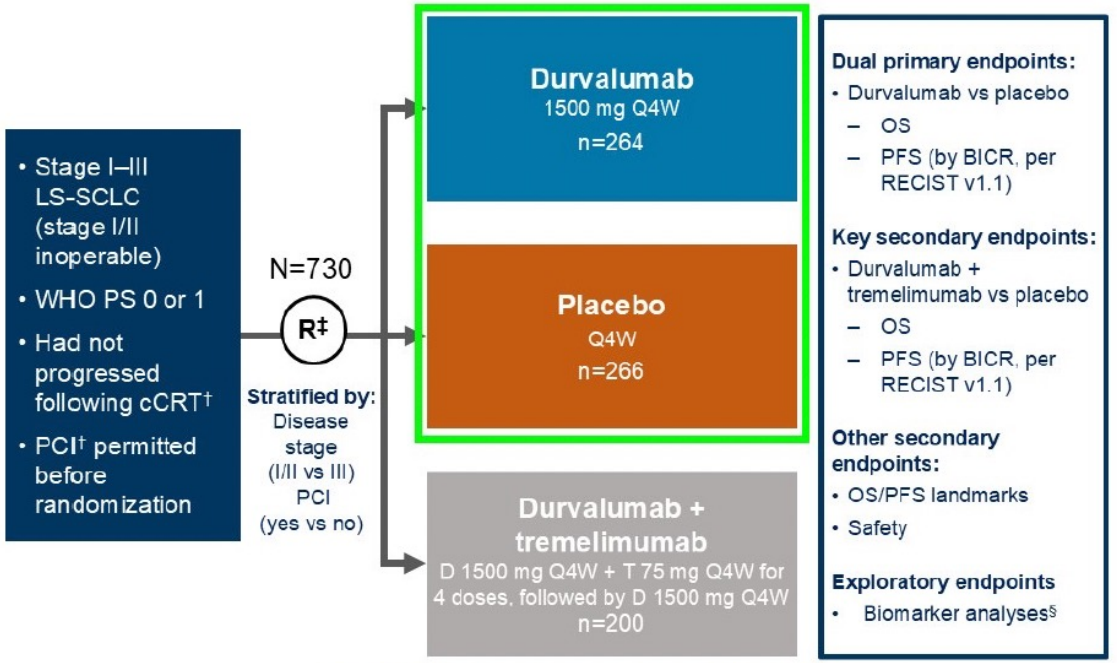
Background

- Consolidation durvalumab has become the new standard of care in patients with LS-SCLC and no progression after cCRT, based on the results of the ongoing ADRIATIC study
  - At the first planned interim analysis, durvalumab significantly improved the dual primary endpoints of OS and PFS vs placebo[1]
  - Durvalumab was well tolerated, with a manageable safety profile[1]
- Here we report post-hoc, exploratory analyses of clinical characteristics, patterns of progression, and associated immune-related biomarkers (CD8, MHC I, and PD-L1 by IHC; T-cell inflamed signature [TIS], *CD8A*, and STING pathway by RNA sequencing)* in:
  - Early progressors (EPs; patients with PFS <6 months)
  - Long-term progression-free survivors (LTPs; PFS or censored after >12 months)

Phase 3, randomized, double-blind, placebo-controlled, multicenter, international ADRIATIC study (NCT03703297)



Treatment until investigator-determined progression or intolerable toxicity, or for a **maximum of 24 months**

1. Cheng Y, et al. N Engl J Med 2024;391:1313–27
*In the biomarker-evaluable populations using pre-cCRT tumor samples collected at screening
†cCRT and PCI treatment, if received per local standard of care, must have been completed within 1–42 days prior to randomization
‡The first 600 patients were randomized in a 1:1:1 ratio to the three treatment arms; subsequent patients were randomized 1:1 to either durvalumab or placebo
§Not applicable for China

Barbie DA et al. ASCO 2025;Abstract 8014

ASCO Rapid Recommendations

Systemic Therapy for Small Cell Lung Cancer: ASCO Guideline Rapid Recommendation Update

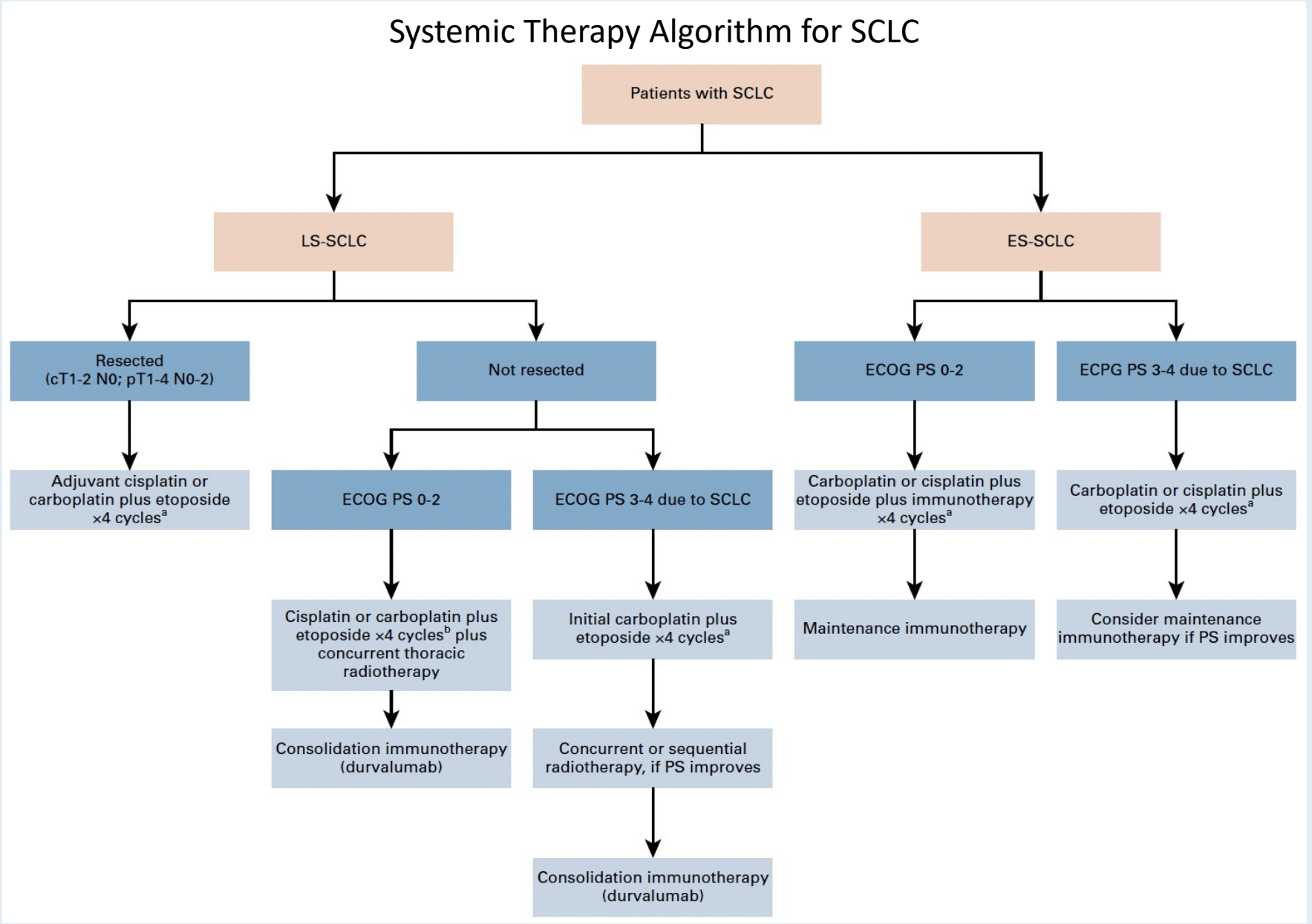
Gregory P. Kalemkerian, MD[1]; Humera Khurshid, MD[2]; and No sat Ismaila, MD[3]; for the Systemic Therapy for Small Cell Lung Cancer Guideline Expert Panel

DOI https://doi.org/10.1200/JCO-24-02245

ASCO Rapid Recommendation Updates highlight revisions to select ASCO guideline recommendations as a response to the emergence of new and practice-changing data. The rapid updates are supported by an evidence review and follow the guideline development processes outlined in the ASCO Guideline Methodology Manual. The goal of these articles is to disseminate updated recommendations, in a timely manner, to better inform health practitioners and the public on the best available cancer care options. Guidelines and updates are not intended to substitute for independent professional judgment of the treating clinician and do not account for individual variation among patients. See appendix for disclaimers and other important information (Appendix 1 and Appendix 2, online only).

J Clin Oncol 2025.;43:101-5.

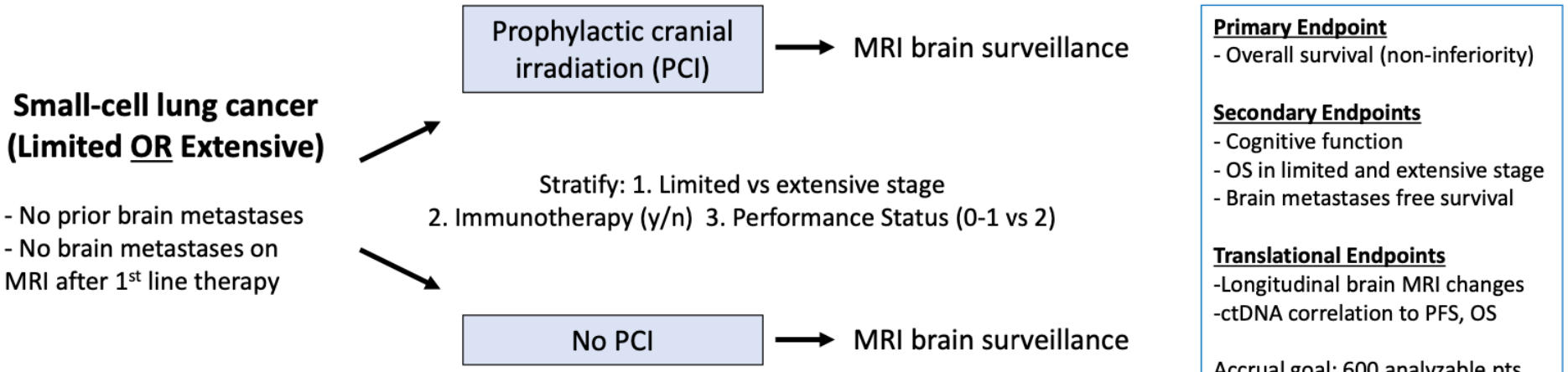
Systemic Therapy Algorithm for SCLC



Kalemkerian GP et al. *J Clin Oncol* 2025.;43:101-5.

Phase III MAVERICK (SWOG 1827) Study Design

MRI Brain Surveillance Alone Versus MRI Surveillance and Prophylactic Cranial Irradiation: A Randomized Phase III Trial in Small-Cell Lung Cancer



Primary Endpoint
- Overall survival (non-inferiority)

Secondary Endpoints
- Cognitive function
- OS in limited and extensive stage
- Brain metastases free survival

Translational Endpoints
-Longitudinal brain MRI changes
-ctDNA correlation to PFS, OS

Accrual goal: 600 analyzable pts

- MRI brain surveillance scheduled at 3, 6, 9, 12, 18, 24 months
- Hippocampal-avoidance PCI and WBRT are allowed
- Radiation therapy is recommended at the time of brain metastases (WBRT and SRS allowed)
- Patients managed with any/all NCCN-acknowledged first-line treatment strategies are eligible

PIs Chad Rusthoven and Paul Brown

Rusthoven C. www.swog.org. Accessed April 2026.

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RTP Year in Review 2026

ES SCLC: current landscape

Maintenance

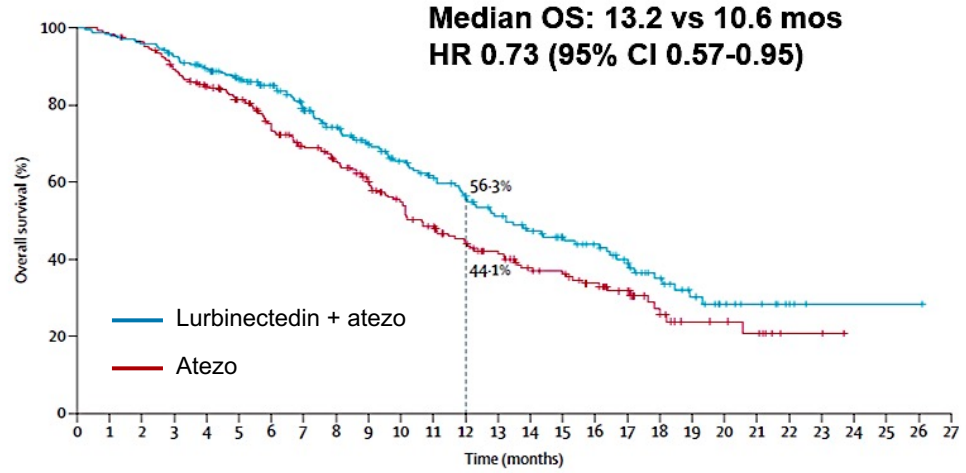
2nd Line

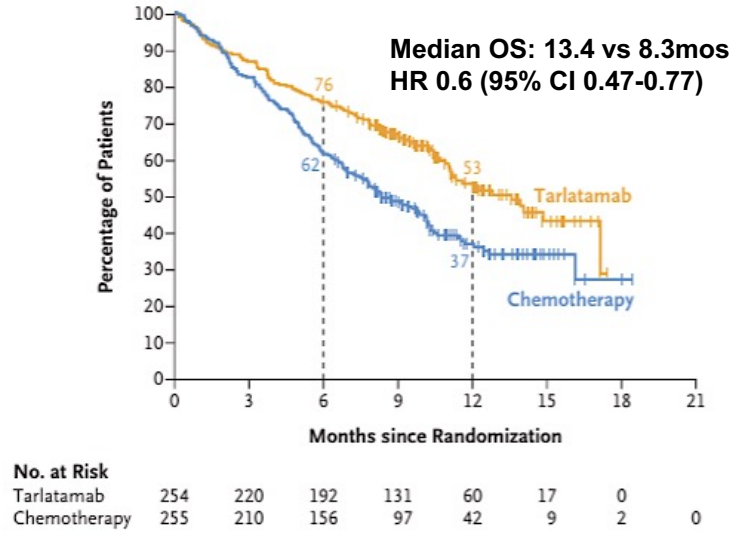
Chemo-ICB → ICB → Tarlatamab

Lurbinectedin

IMforte
improvement in mOS and mPFS
Approved May 2025

DeLLphi-301/304
improvement in mPFS, mOS
Full Approval Nov 2025



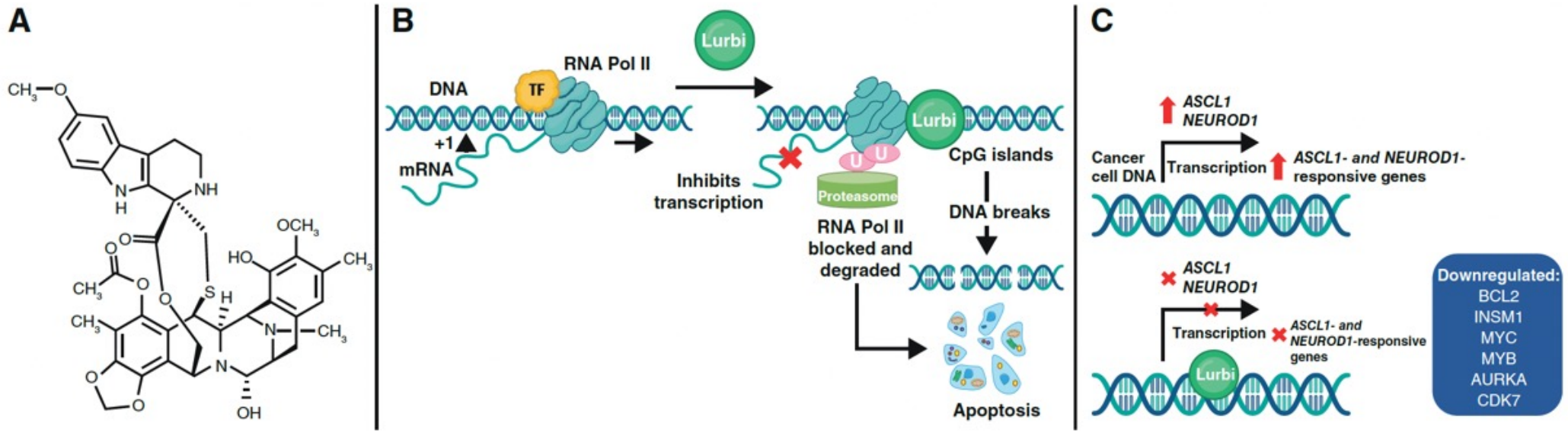


Paz-Ares L et al. *Lancet*. 2025;405(10495):2129-2143. Mountzios G et al. *N Engl J Med*. 2025 Jul 24;393(4):349-361.

LungenClinic GROSSHANSDORF

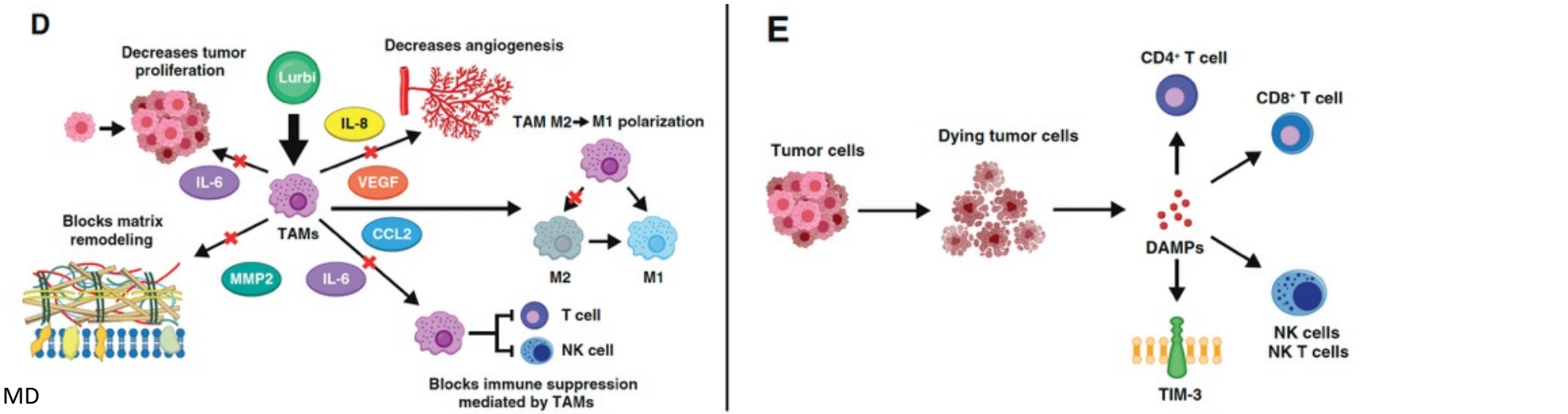
Lurbinectidin - Mode of Action

Calles A et al, Molecular Cancer Therapeutics 2025



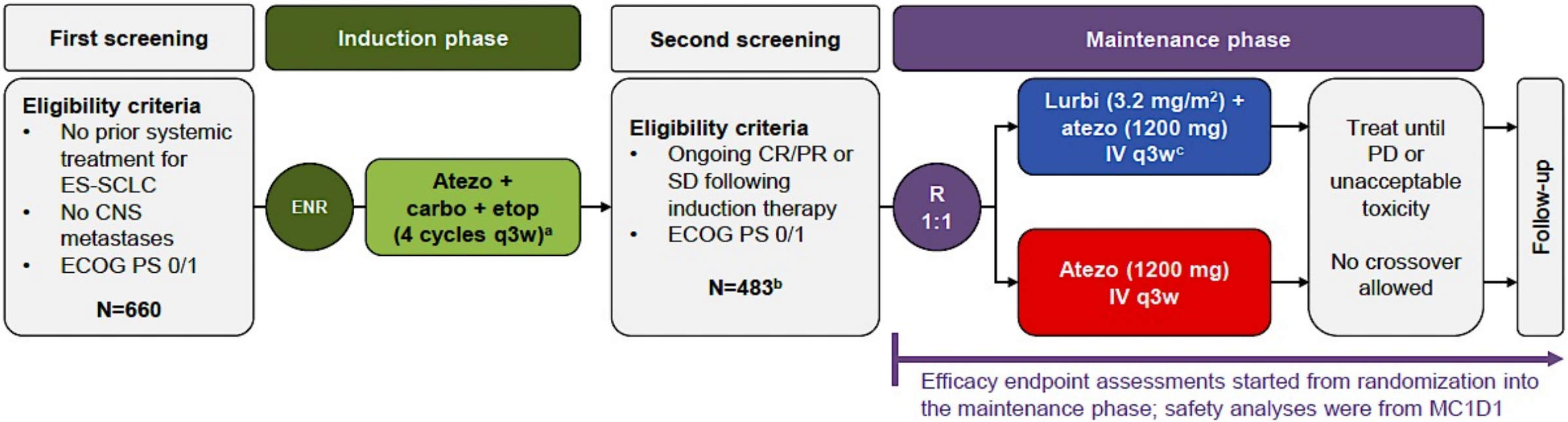
Effect on Microenvironment

Indirect Effect on Immunogenicity



Courtesy of Martin Reck, MD

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

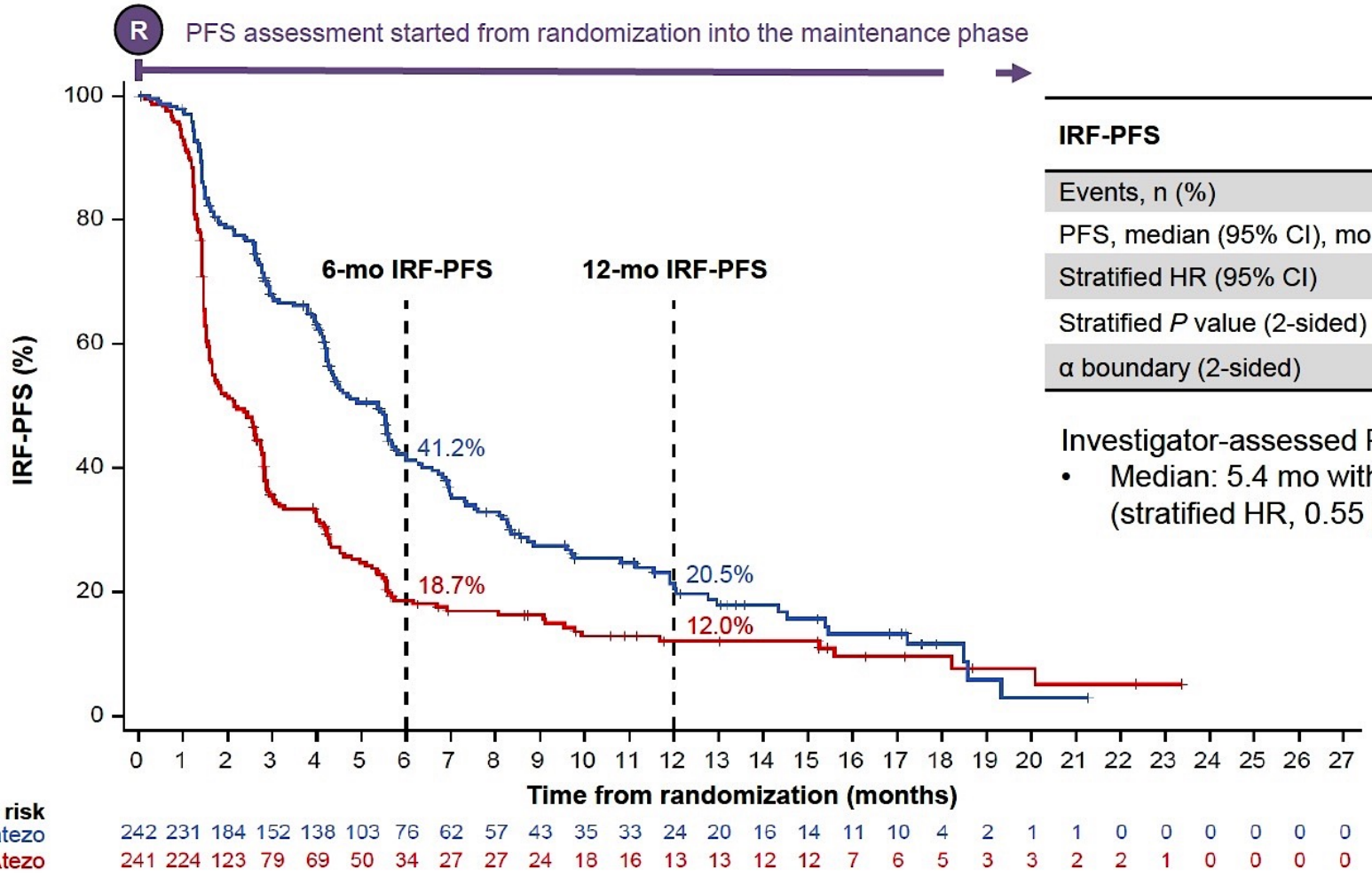
Secondary endpoints included
INV-PFS, ORR, DOR, and safety

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.

Paz-Ares et al. ASCO 2025;Abstract 8006

IMforte PFS



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	

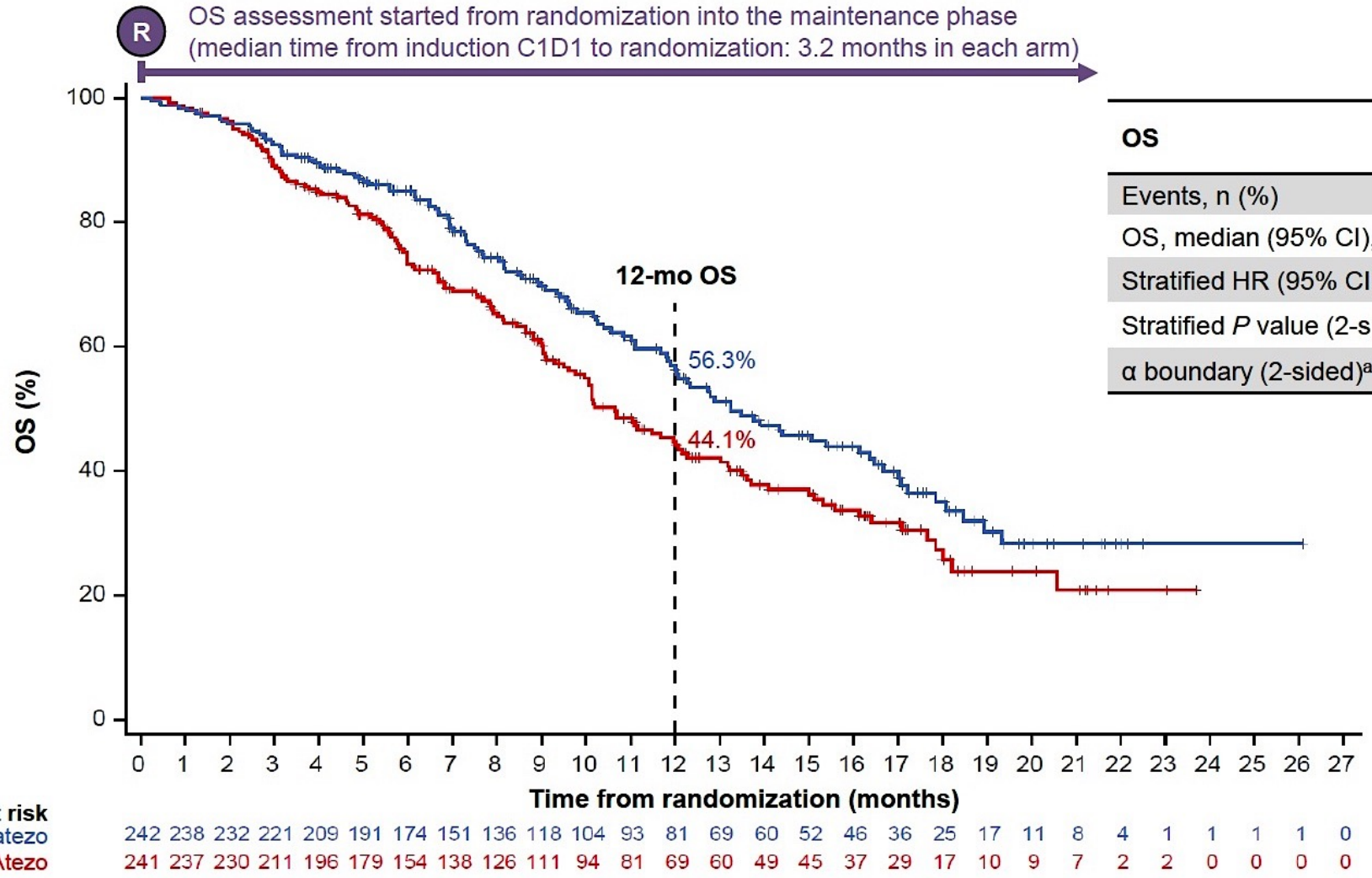
Investigator-assessed PFS was consistent with IRF-PFS

- 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 et al. ASCO 2025;Abstract 8006

IMforte OS



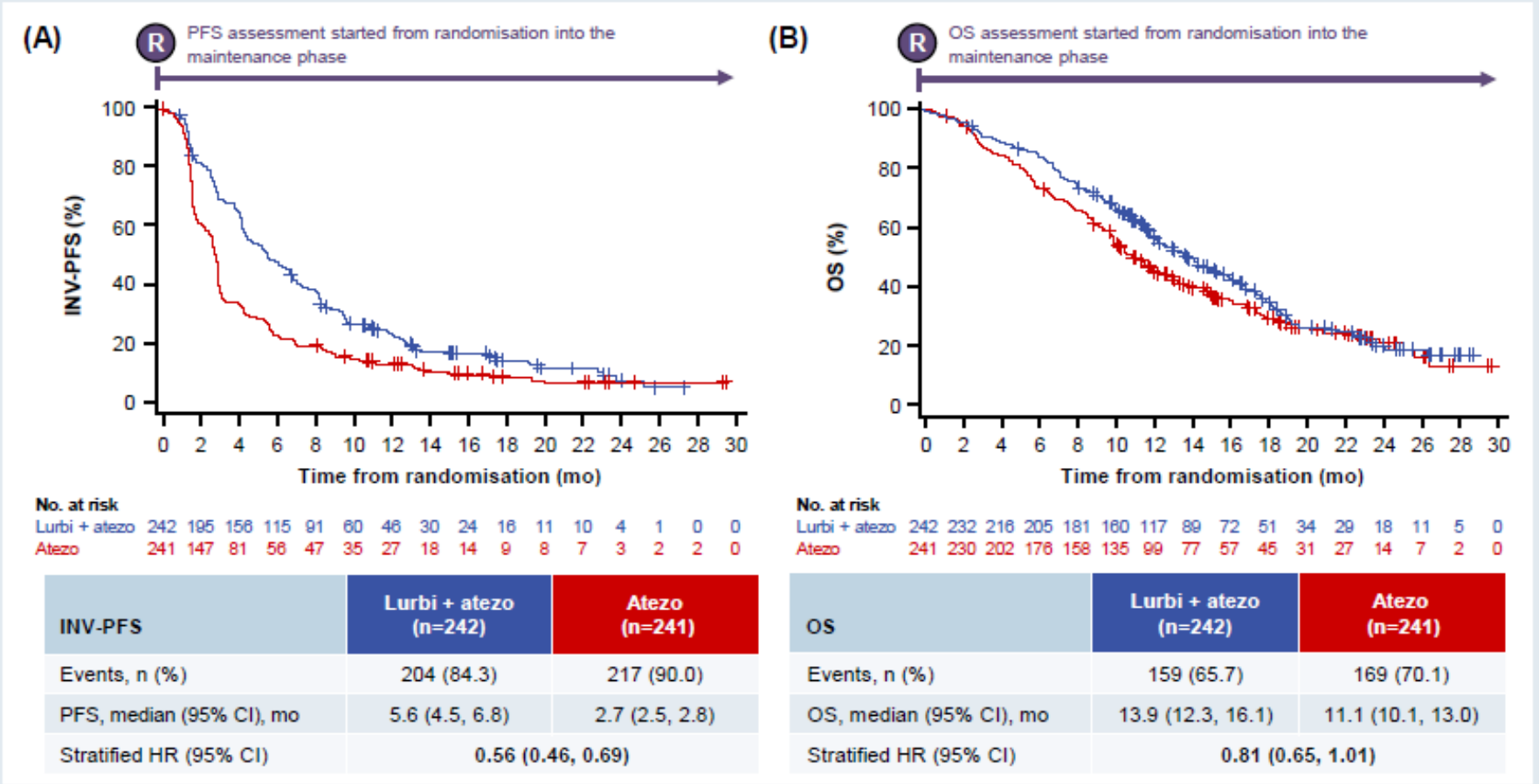
OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	113 (46.7)	136 (56.4)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	**0.73 (0.57, 0.95)**	
Stratified *P* value (2-sided)	0.0174	
α boundary (2-sided)[a]	0.0313	

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.

Paz-Ares et al. ASCO 2025;Abstract 8006

IMforte Updated Curves

Figure 3. Updated (A) INV-PFS and (B) OS[a] from randomisation into the maintenance phase



INV-PFS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	204 (84.3)	217 (90.0)
PFS, median (95% CI), mo	5.6 (4.5, 6.8)	2.7 (2.5, 2.8)
Stratified HR (95% CI)	**0.56 (0.46, 0.69)**	

OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	159 (65.7)	169 (70.1)
OS, median (95% CI), mo	13.9 (12.3, 16.1)	11.1 (10.1, 13.0)
Stratified HR (95% CI)	**0.81 (0.65, 1.01)**	

[a] The primary OS analysis was evaluated when 51.6% of patients had died in the study; updated exploratory OS analysis was evaluated when 67.9% of patients had died in the study.
CI, confidence interval; HR, hazard ratio; INV, investigator-assessed; mo, months; OS, overall survival; PFS, progression-free survival.

Paz-Ares et al. ESMO 2025

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RTP Year in Review 2026

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RTP Year in Review 2026

Summary

- **Tarlatamab receives full approval after platinum-based therapy**
  - Multiple other DLL3-TCEs under active development
  - Early data of tarlamatab in maintenance is extremely promising

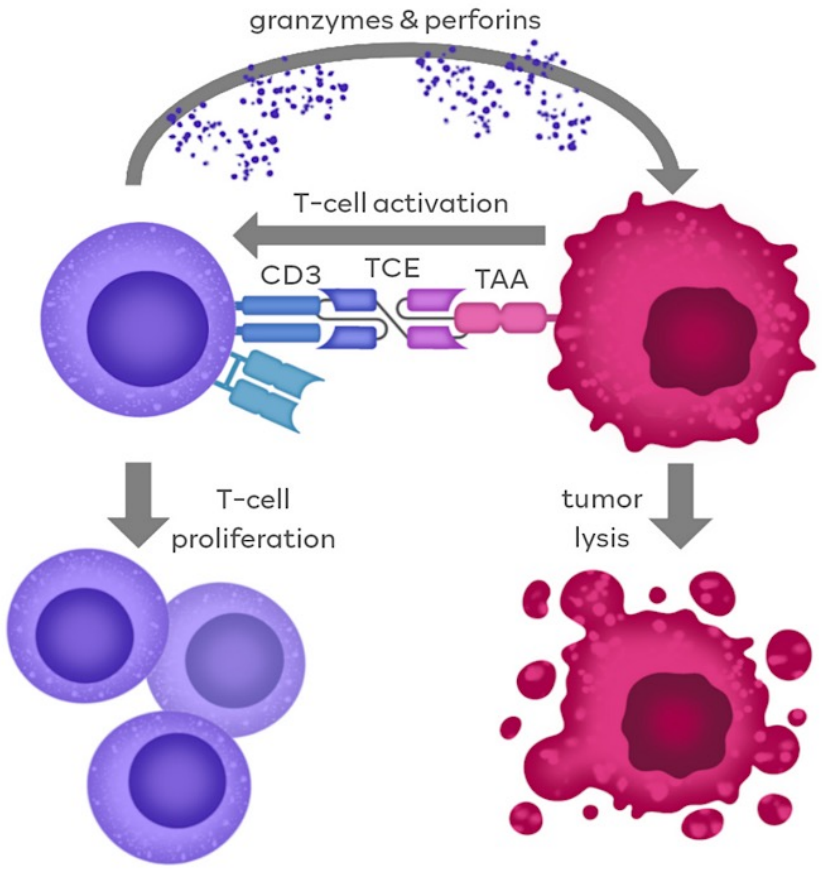
- **ADCs are emerging as a novel therapeutic in SCLC**
  - Early phase studies report response rates of > 50% without patient selection
  - Multiple Phase 3 RCT are being conducted in the relapsed setting
  - Multiple studies are ongoing to move ADCs earlier in therapy
  - Hematologic toxicities are expected given the Topo1i payload
  - ILD is a concern

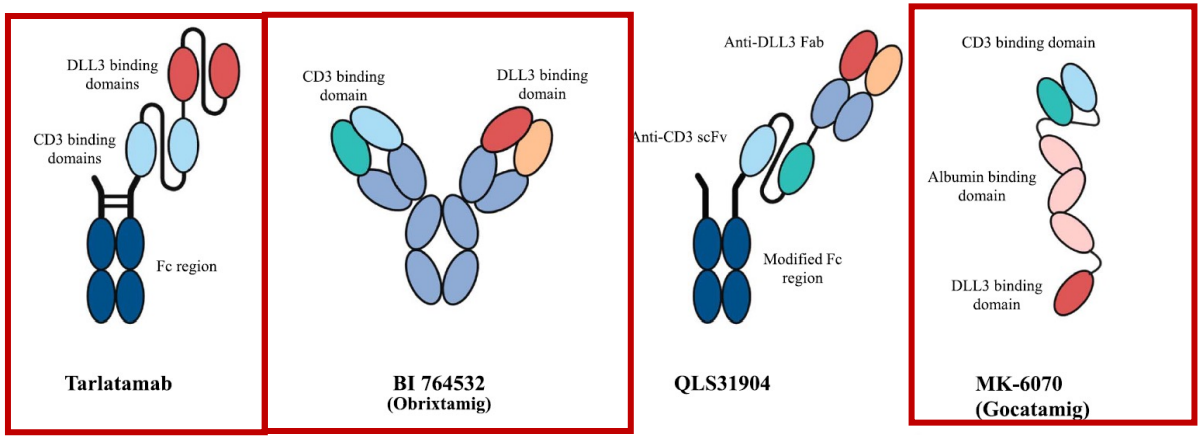
- **Biomarker development is needed to help triage patients**
  - ADC payloads are consistently Topo1 inhibitors, which may limit sequential ADCs

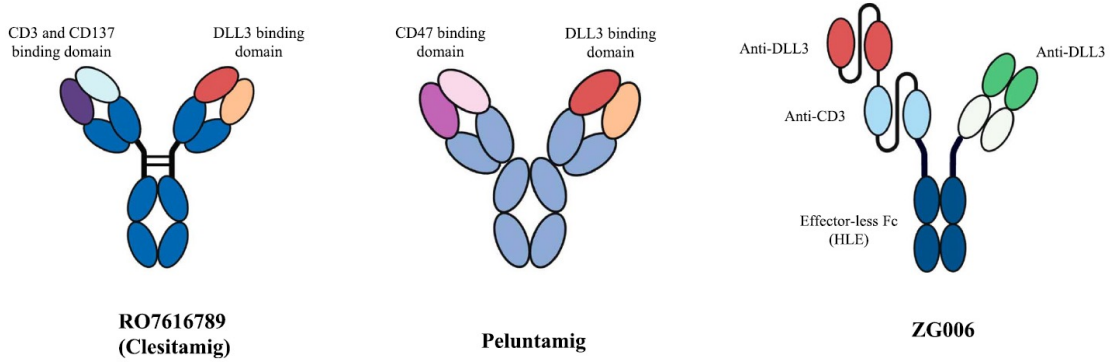
Courtesy of Christine L Hann, MD, PhD

DLL3-TCE

T-cell engagers in SCLC (and other DLL3+ tumors)





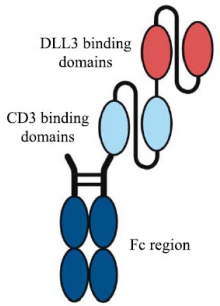


Aijaz A et al. Am Soc Clin Oncol Educ Book. 2025 Jun;45(3):e472794.
Cech P et al. Cancers (Basel). 2024 Apr 20;16(8):1580.

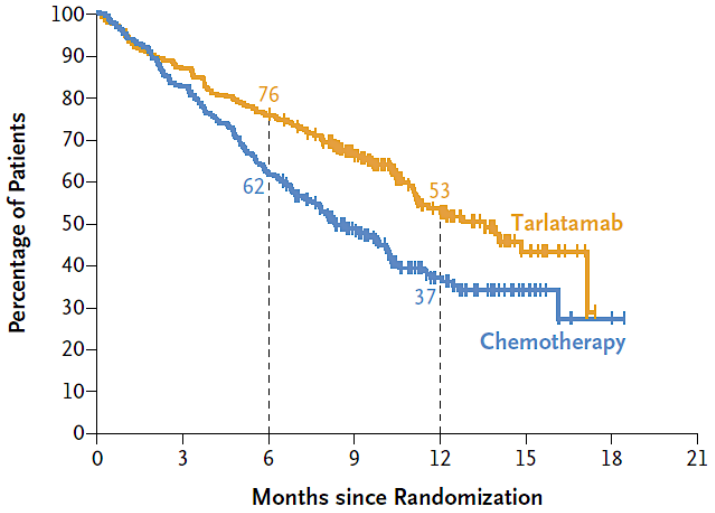
DLL3-TCE

DeLLphi-304: Tarlatamab vs TPC in SCLC after Platinum-Based Chemotherapy

- Relapsed SCLC after first-line therapy
  - N = 509, randomized to tarlatamab or TPC (topotecan, lurbinectedin, amrubicin)
- Primary EP: OS (13.6mos vs 8.3 mos)



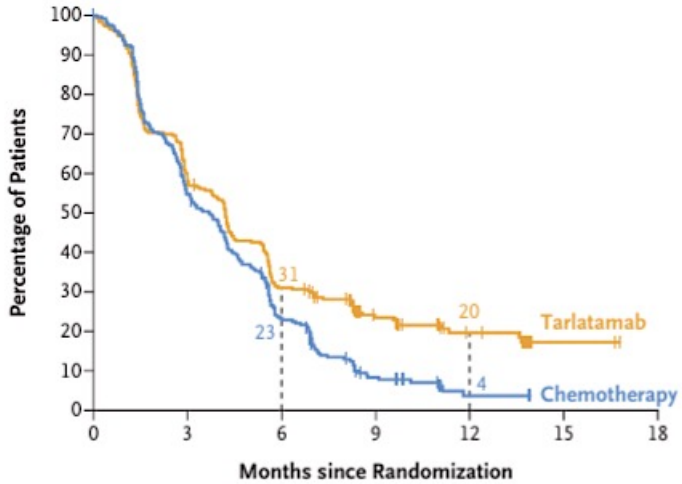
Tarlatamab



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



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

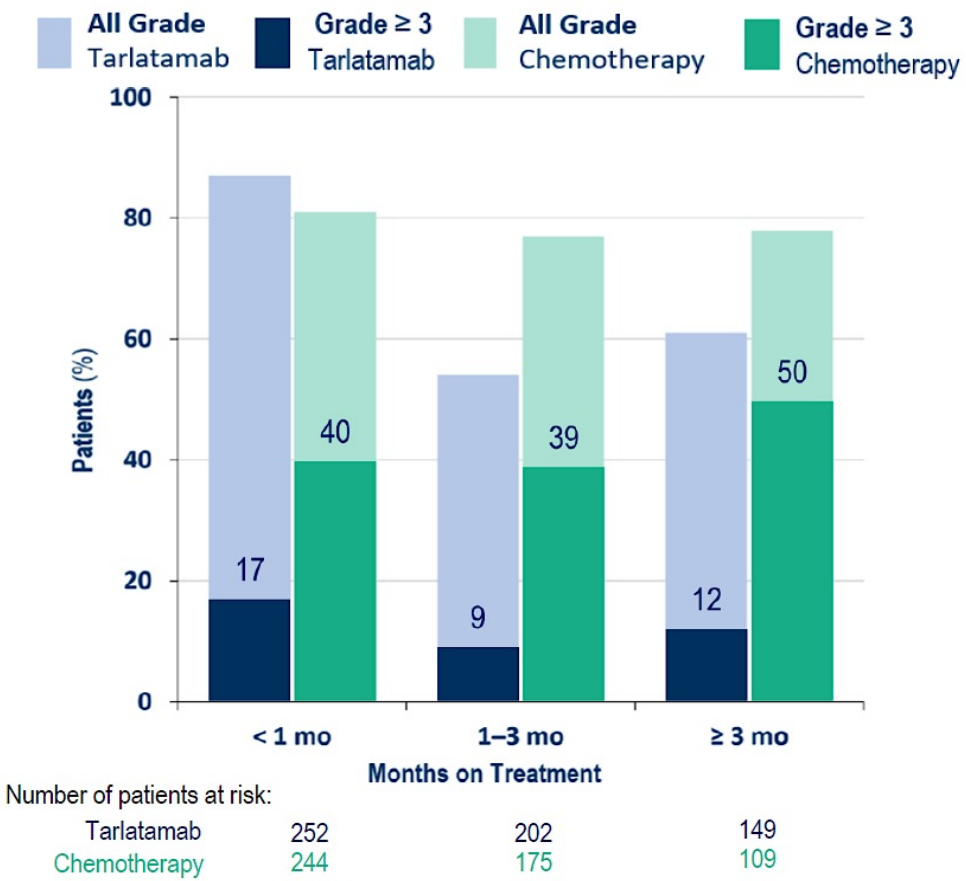
Estimated RMST for Progression-free Survival at 12 Months	
	mo
Tarlatamab (N=254)	5.3
Chemotherapy (N=255)	4.3

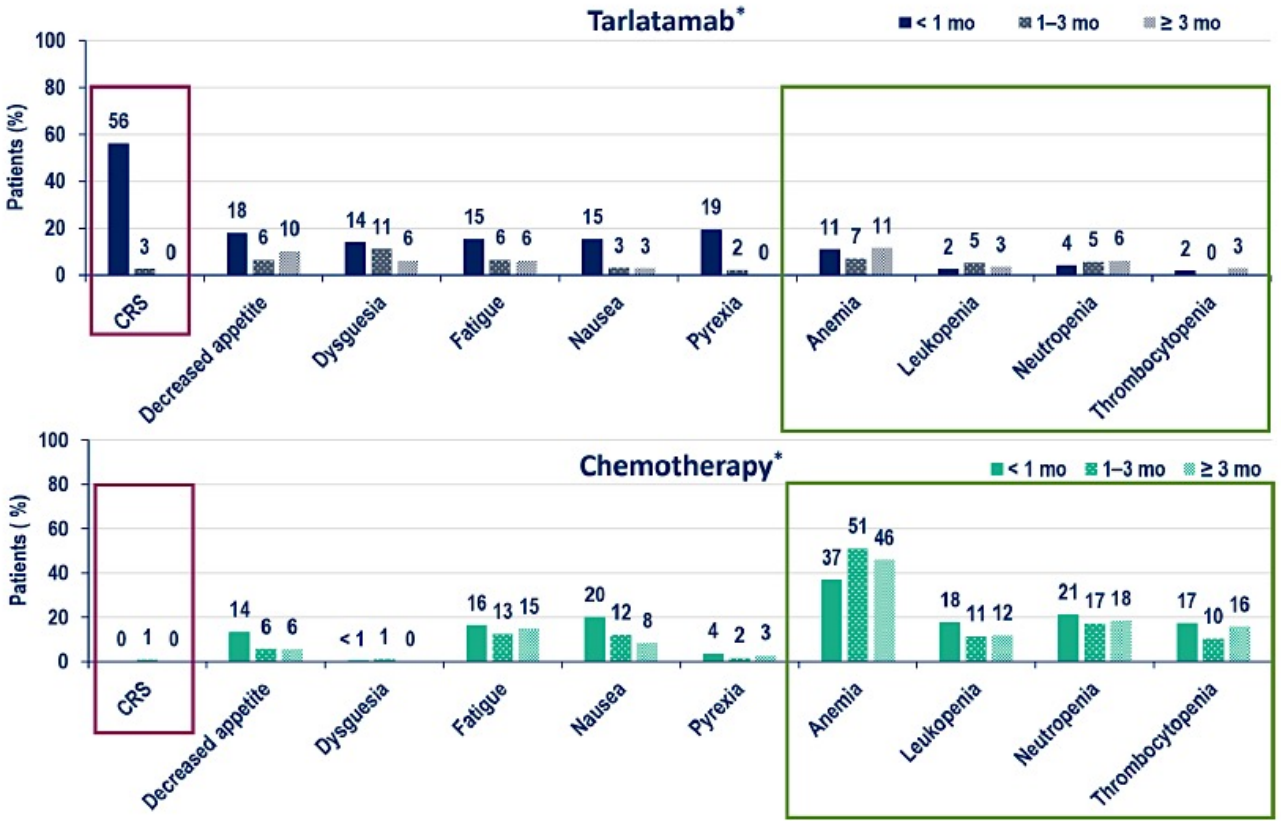
Piecewise weighted average hazard ratio for progression or death, 0.71 (95% CI, 0.59–0.86)
P=0.002, RMST for progression-free survival

Mountzios G et al. Tarlatamab in Small-Cell Lung Cancer after Platinum-Based Chemotherapy. N Engl J Med 2025;393(4):349-61.

DLL3-TCE

DeLLphi-304 Toxicities: tarlatamab vs chemotherapy





Schuler MH et al. Detailed safety analysis of DeLLphi-304: The first phase III study to evaluate tarlatamab versus chemotherapy for previously treated small cell lung cancer. ESMO 2025;Abstract LBA100.

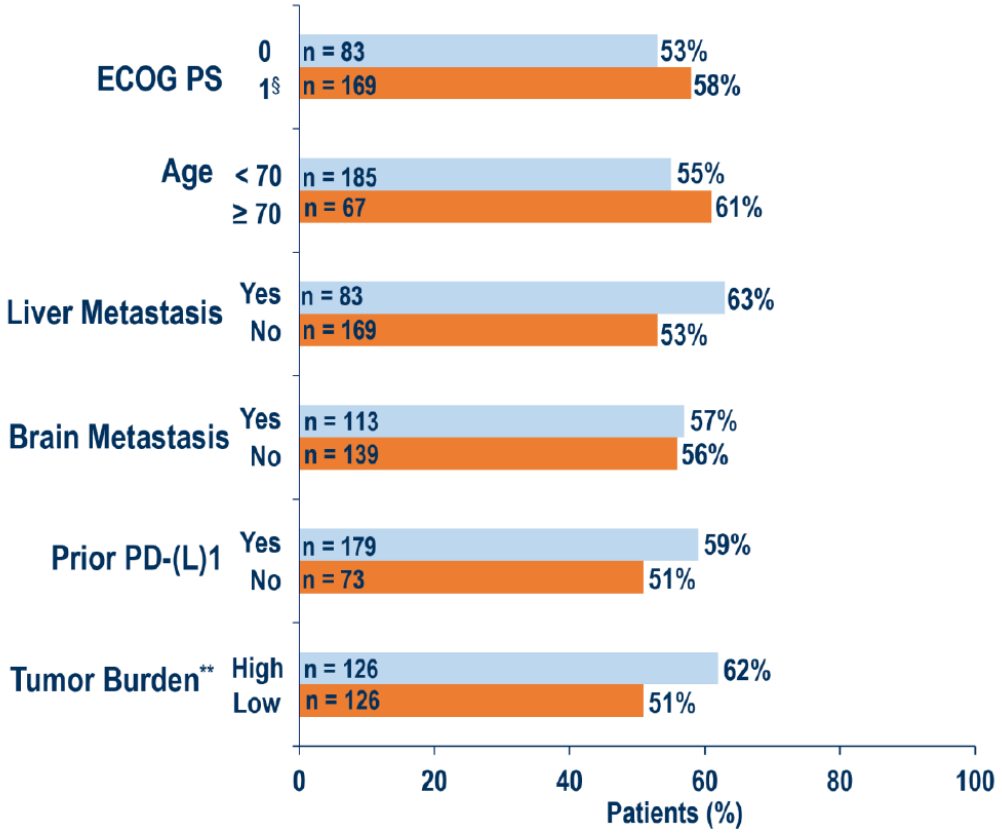
DLL3-TCE

DeLLphi-304 Tarlatamab: CRS timing and subgroup analysis

Treatment-related CRS During First Two Doses of Tarlatamab

Tarlatamab (n = 252)	Minimum Required Monitoring Duration	
	6–8 Hours (n = 43)	48 Hours (n = 209)
Treatment-related CRS (all grade), n (%)	16 (37)	125 (60)
Grade 1	12 (28)	94 (45)
Grade 2	4 (9)	28 (13)
Grade 3*	0	3 (1)
Leading to discontinuation	0	1 (0.5)
Utilization of any CRS intervention	9 (21)	45 (22)
Median time to intervention, hours	17	27
Hospitalization for any grade†	3 (7)	16 (8)
Patients with any resolved event‡, n/n' (%)	16/16 (100)	123/125 (98)

Descriptive Analysis of Treatment-related CRS Events



Schuler MH et al. Detailed safety analysis of DeLLphi-304: The first phase III study to evaluate tarlatamab versus chemotherapy for previously treated small cell lung cancer. ESMO 2025;Abstract LBA100.

2024 ASCO ANNUAL MEETING

DeLLphi 301

DeLLphi-301: Tarlatamab phase 2 trial in small cell lung cancer (SCLC)—Efficacy and safety analyzed by presence of brain metastases

Anne-Marie C. Dingemans,[1] Myung-Ju Ahn,[2] Fiona Blackhall,[3] Martin Reck,[4] Horst-Dieter Hummel,[5] Suresh S. Ramalingam,[6] Melissa L. Johnson,[7] Hiroaki Akamatsu,[8] Jürgen Wolf,[9] Jacob Sands,[10] Taofeek K.Owonikoko,[11] Hossein Borghaei,[12] Sujoy Mukherjee,[13] Shuang Huang,[13] Pablo Martinez,[13] Luis Paz-Ares[14]

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Patient Baseline Clinical Characteristics

Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 100)†	
	Yes (n = 23)	No (n = 77)
ECOG PS 0 / 1, n (%)	4 (17) / 19 (83)	22 (29) / 55 (71)
Median prior lines of therapy, n (range)	2 (2–5)	2 (1–6)
Prior anti-PD-(L)1 treatment, n (%)	19 (83)	55 (71)
DLL3 expression (> 0% of tumor cells), x/X (%)	21/22 (95)	59/61 (97)

Median follow-up period: 10.6 months‡

*Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383. †The intention-to-treat analysis set consists of all patients who were randomized and enrolled according to assigned treatment dose levels. ‡OS data yet to mature. **DLL3,** delta-like ligand 3; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PD-(L)1**, programmed cell death 1 protein/programmed cell death ligand-1 protein; **Q2W**, every 2 weeks.

Dingemans A-M C et al. ASCO 2024;Abstract 8015

Efficacy Summary

Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 100)†	
	Yes (n = 23)	No (n = 77)
ORR, % (95% CI)	52 (31–73)	38 (27–49)
Median DOR, months (range)	NE (3–12+)	NE (2–12+)
DOR probability at 12 months, KM estimate, % (95% CI)	55 (22–78)	50 (29–68)
Median PFS, months (95% CI)	6.7 (3–NE)	4.0 (3–6)
Median OS‡, months (95% CI)	14.3 (14–NE)	NE (9–NE)

Tarlatamab demonstrated durable response with promising survival regardless of the presence of treated, stable brain metastases at baseline

Data cutoff, June 27, 2023. Median follow-up: 10.6 months. *Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383. †The intention-to-treat analysis set consists of all patients who were randomized and enrolled according to assigned treatment dose levels. ‡OS data yet to mature. **CI,** confidence interval; **DOR**, duration of response; **KM**, Kaplan-Meier; **NE**, not estimable; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks.

Dingemans A-MC et al. ASCO 2024;Abstract 8015.

Treatment-Related Adverse Events (TRAEs)

Baseline brain metastases:	Tarlatamab 10 mg Q2W* (n = 99)†	
	Yes (n = 22)	No (n = 77)
TRAEs, n (%)	21 (95)	71 (92)
Grade ≥3	8 (36)	25 (32)
Fatal (grade 5)§	0	0
Leading to dose interruption and / or reduction of tarlatamab	3 (14)	11 (14)
Leading to discontinuation of tarlatamab	1 (5)	3 (4)
TRAEs of interest		
CRS‡	12 (55)	39 (51)
Grade ≥3	0	0
Leading to discontinuation of tarlatamab	0	0
ICANS and associated neurological events§	3 (14)	5 (6)
Grade ≥3	0	0
Leading to discontinuation of tarlatamab	0	1 (1)

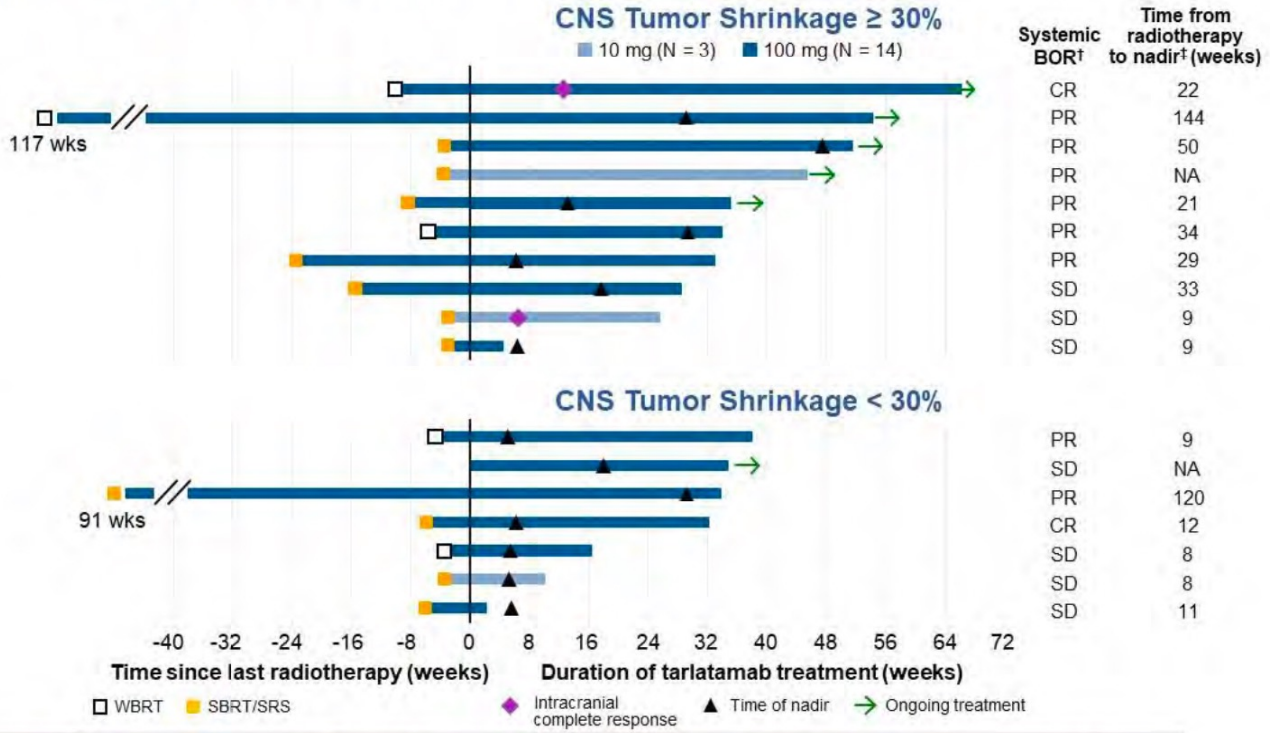
*Given as 1 mg on Day 1, followed by 10 mg on Days 8, 15, and Q2W thereafter. For 100 mg data, scan QR code or see https://meetings.asco.org/abstracts-presentations/232383. †The safety analysis includes all patients who received ≥ 1 dose of tarlatamab. One patient in the tarlatamab 10 mg group did not receive tarlatamab. Coded using MedDRA version 26.1. CRS and ICANS events were graded using American Society for Transplantation and Cellular Therapy 2019 Consensus Grading. ‡CRS based on AMQ narrow search. §ICANS and associated neurological events based on 61 selected preferred terms with AMQ broad search. §One patient (1%) in the tarlatamab 10 mg group died during part 3 from respiratory failure assessed by the investigator to be related to the trial treatment; contributing factors include baseline chronic obstructive pulmonary disease requiring supplemental oxygen, baseline compromised functional reserve, concurrent Grade 3 CRS and pneumonitis after cycle 1 day 1 treatment, and a decision against escalation to ICU-level care. This patient did not have brain metastases at baseline screening. **AMQ**, Amgen MedDRA query; **CRS**, cytokine release syndrome; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **MedDRA**, Medical Dictionary for Regulatory Activities; **Q2W**, every 2 weeks; **TRAE**, treatment-related adverse event.

Dingemans A-MC et al. ASCO 2024;Abstract 8015.

Intracranial Activity*

Tarlatamab 10 mg (n = 3) or 100 mg (n = 14) Q2W with baseline CNS lesion ≥ 10 mm

- **mRANO BM§ analyses (N = 17)**
  - CNS tumor shrinkage ≥ 30% in 10 of 17 patients (59%)
  - Intracranial disease control in 94% (16 of 17) patients (95% CI, 71.3–99.9)
  - Median duration of intracranial disease control was NE (range, 2.6–13.9+ months)
  - CNS disease progression per modified RANO-BM occurred in 3 of 17 patients (18%)



CNS tumor shrinkage was observed in patients with previously treated brain metastases

Dingemans A-MC et al. ASCO 2024;Abstract 8015.

Phase 1b study of tarlatamab with anti-PD-L1 as 1L maintenance for ES-SCLC: DeLLphi 303 Study[a]

DeLLphi 303

1L Chemo-IO

Platinum-etoposide + anti-PD-L1[c]

(4-6 cycles)

Enrollment

Key Inclusion Criteria

- ✓ No disease progression following 4–6 cycles of 1L chemo-IO
- ✓ ECOG PS 0 or 1
- ✓ Patients with treated and asymptomatic brain metastases were permitted
- ✓ No active autoimmune disease or disease requiring immunosuppressive therapy[d]

1L Maintenance[b]

Non-randomized[e]

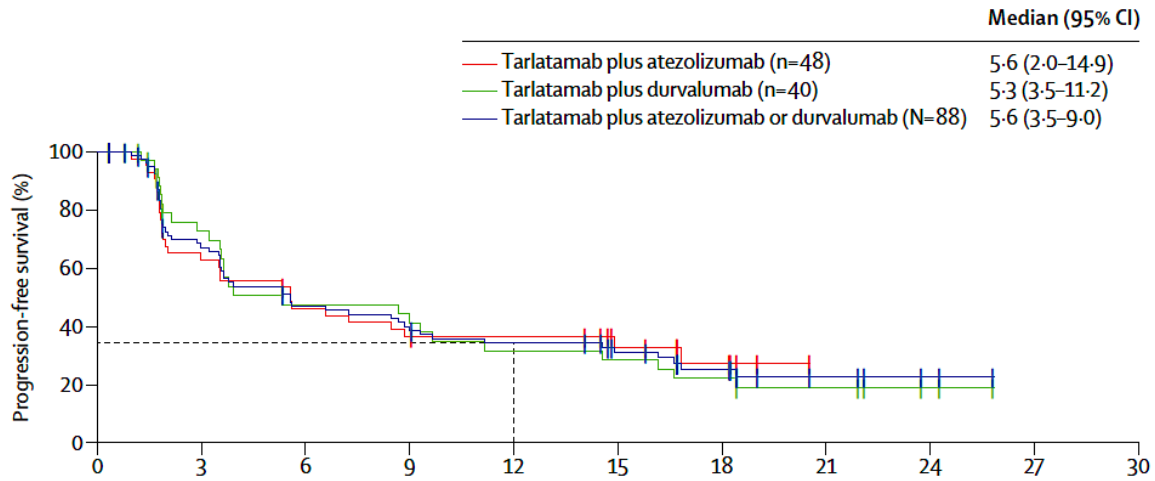
Switching to a different anti-PD-L1 than that received in 1L chemo-IO was permitted

Tarlatamab (10 mg IV Q2W) + Atezolizumab (1680 mg IV Q4W) n = 48

Tarlatamab (10 mg IV Q2W) + Durvalumab (1500 mg IV Q4W) n = 40

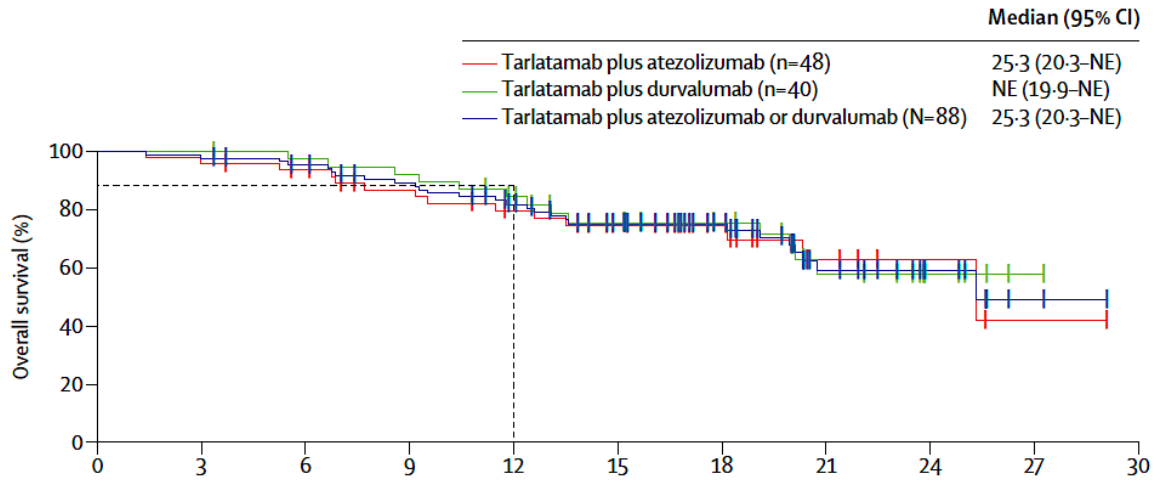
Primary Endpoints[f]: Dose-limiting toxicities[g], treatment-emergent and treatment-related adverse events
Secondary Endpoints[h]: Progression-free survival, overall survival, objective response rate, duration of response, and disease control

[a]Cohorts 5, 6, and 8; NCT05361395. [b]Maintenance therapy commenced within 8 weeks of the start of the last cycle of 1L chemo-IO. [c]Patients without access to 1L anti-PD-L1 were allowed. [d]Patients with active autoimmune disease requiring systemic treatment (except replacement therapy) within the past 2 years were excluded. [e]Patients were allocated to treatment arms in a non-randomized manner based on slot availability. [f]Also included vital signs, electrocardiograms, and clinical laboratory tests [g]Dose-limiting toxicities were assessed for cohort 5 only. [h]Also included serum concentrations of tarlatamab, quantification of biomarker expression, and incidence of anti-tarlatamab antibody formation. **1L:** first-line; **chemo-IO:** chemo-immunotherapy; **ECOG PS**: Eastern Cooperative Oncology Group performance status; **ES-SCLC:** extensive-stage small cell lung cancer; **IV:** intravenous; **PD-L1:** programmed death-ligand 1; **Q2W:** once every 2 weeks; **Q4W**: once every 4 weeks.



Number at risk (censored)											
Tarlatamab plus atezolizumab	48 (0)	27 (5)	19 (6)	15 (6)	14 (7)	9 (11)	5 (14)	0 (19)	·· (··)	·· (··)	·· (··)
Tarlatamab plus durvalumab	40 (0)	23 (8)	15 (8)	14 (8)	10 (8)	9 (8)	7 (8)	5 (9)	2 (12)	0 (14)	·· (··)
Tarlatamab plus atezolizumab or durvalumab	88 (0)	50 (13)	34 (14)	29 (14)	24 (15)	18 (19)	12 (22)	5 (28)	2 (31)	0 (33)	·· (··)

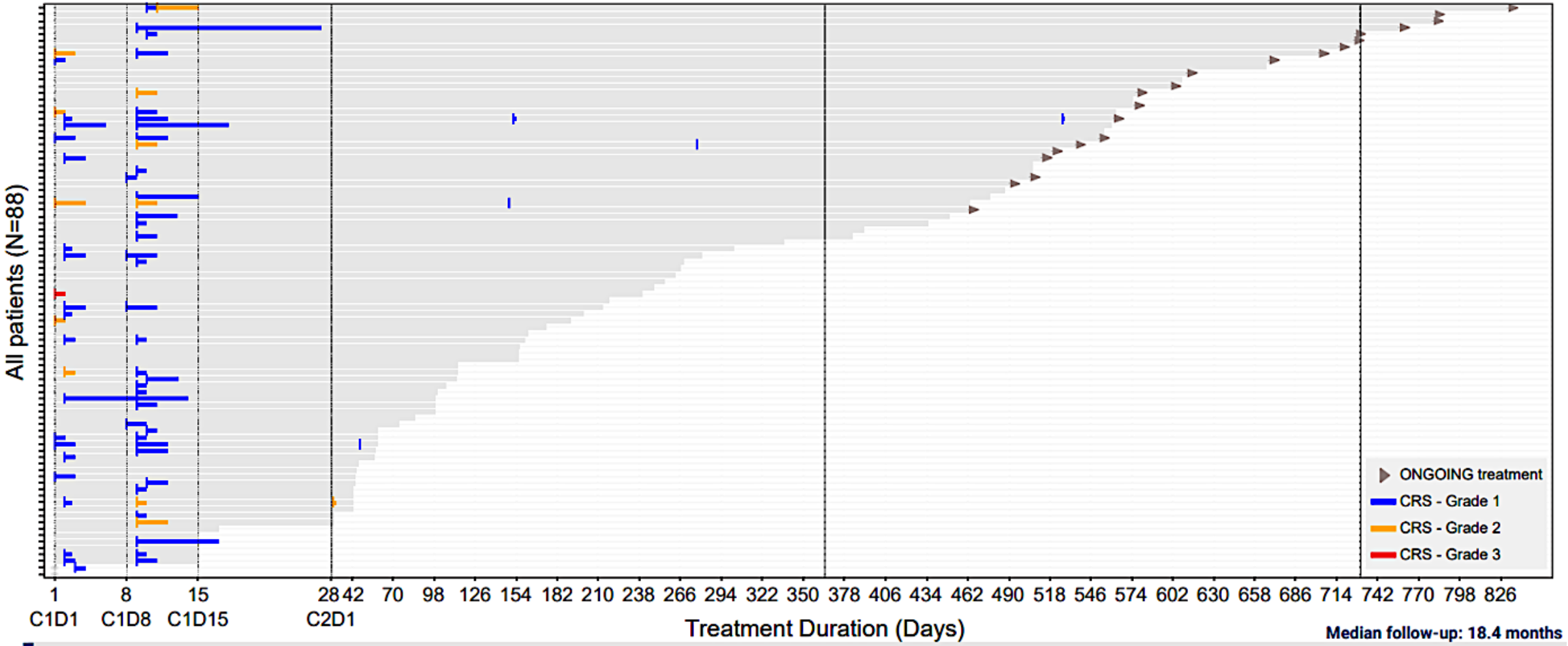
B



Number at risk (censored)											
Tarlatamab plus atezolizumab	48 (0)	46 (0)	43 (2)	37 (5)	32 (7)	26 (11)	16 (21)	6 (29)	3 (32)	1 (33)	0 (34)
Tarlatamab plus durvalumab	40 (0)	40 (0)	38 (1)	36 (1)	31 (3)	25 (6)	21 (10)	11 (16)	5 (22)	1 (26)	0 (27)
Tarlatamab plus atezolizumab or durvalumab	88 (0)	86 (0)	81 (3)	73 (6)	63 (10)	51 (17)	37 (31)	17 (45)	8 (54)	2 (59)	0 (61)

Paulson et al. Lancet Oncol. 2025

DeLLphi-303



CRS occurred in 49 (56%) of patients, with most events grade 1 (43%) or grade 2 (11%); all CRS events resolved.

Paulson et al. WCLC 2025

DLL3-TCE

Tarlatamab Studies

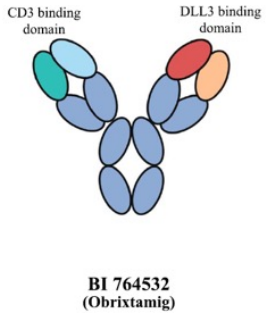
Trial number	Setting	Description	Phase	Estimated completion
NCT06117774	LS SCLC consolidation	Tarlatamab after chemoRT (DeLLphi-306)	Ph 3	03/31/30
NCT07005128	1st line	Tarlatamab, Durvalumab, Carboplatin, and Etoposide Versus Durvalumab, Carboplatin, and Etoposide in First-line ES SCLC (DeLLphi-312)	Ph3	01/04/29
NCT06211036	1st line maintenance	Tarlatamab and Durvalumab Versus Durvalumab Alone following Platinum, Etoposide and Durvalumab (DeLLphi-305)	Ph3	07/05/27
NCT06745323	Relapsed	Tarlatamab Dosing Regimens in Subjects With SCLC (DeLLphi-309)	Ph2	02/13/29
NCT06898957	Multiple	Tarlatamab in Combination With YL201 With or Without Anti-programmed Death Ligand 1 (PD-L1)	Ph1b	04/23/31
NCT06598306	Relapsed	Subcutaneous Tarlatamab in Participants With ES SCLC (DeLLphi-308)	Ph1b	01/02/27
NCT06957314		Hospital-at-Home for People Receiving Tarlatamab		4/23/28

Courtesy of Christine L Hann, MD, PhD

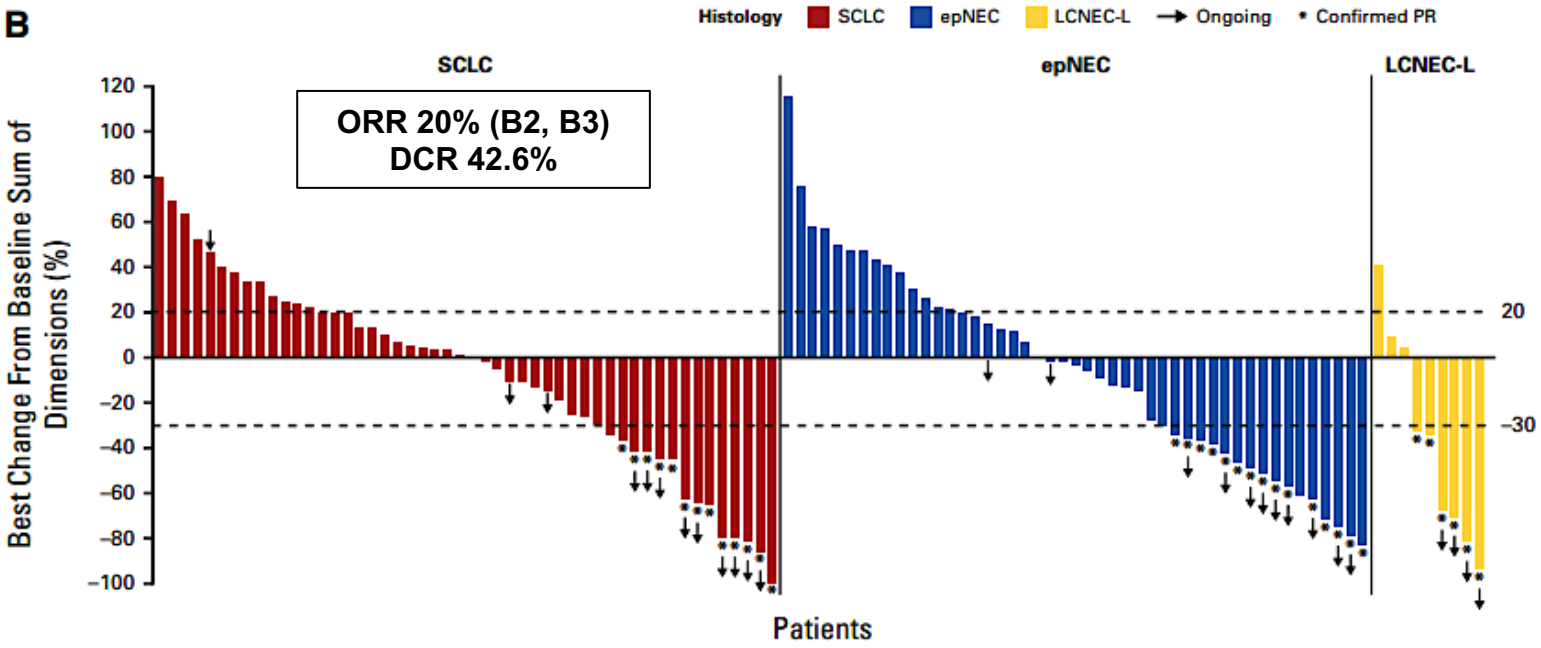
DLL3-TCE

Obrixtamig: Phase 1a dose-escalation

- Relapsed SCLC (n = 61), epNEC, LCNEC, DLL3+
- Doses: 4 dosing schedules: including 2 fixed doses (A, B1)
  - *B2) step-up dose qW x 2, target dose qW*
  - *B3) Step-up dose qW x 3, target dose qW x 3; then q3W*
- Primary EP: MTD



Obrixtamig is an IgG-like TCE, which allows for less frequent dosing



Summary

- B2/B3 - Step-up schedules moving forward
- Doses: 90qW; 1,080 q3W mg/kg
- MTD not reached
- CRS 57% (G3+ 3%)

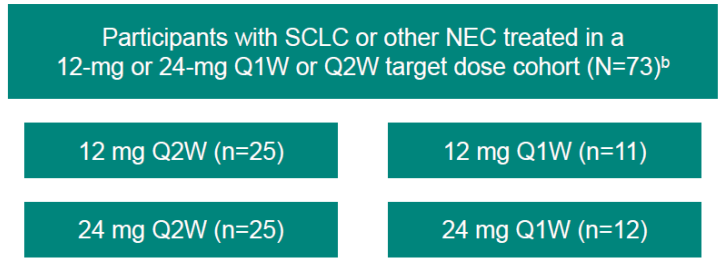
Studies

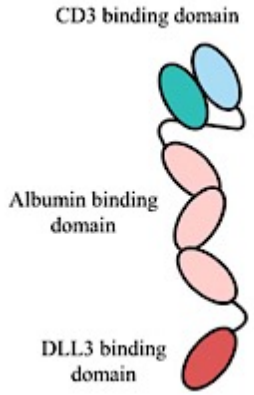
- + PD-1 in DLL3+ SCLC/NEC
- + PD-1 1st line in DLL3+ NEC
- Ph2 dose selection SCLC
- With Topotecan in SCLC
- 1st ES SCLC

Wermke M et al. Phase I Dose-Escalation Results for the Delta-Like Ligand 3/CD3 IgG-Like T-Cell Engager Obrixtamig (BI 764532) in Patients With Delta-Like Ligand 3+ Small Cell Lung Cancer or Neuroendocrine Carcinomas. J Clin Oncol 2025;43(27):3021-31.(NCT04429087)

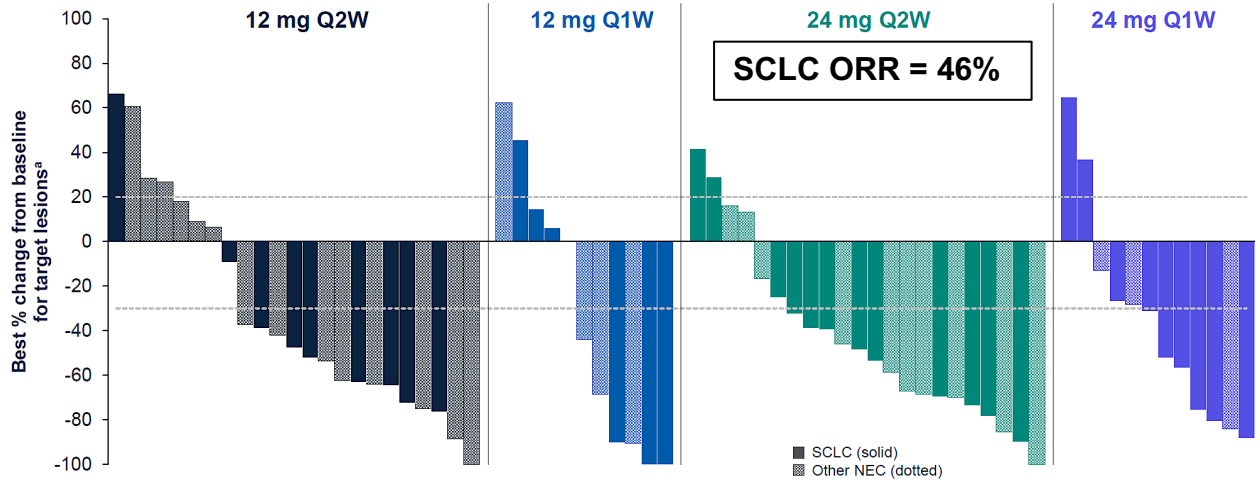
Gocatamig: Phase 1/2 Study for SCLC and other NEC

- Phase 1/2 study
  - with 4 dosing schedules: either 1 or 2 step-up dosing
- Relapsed SCLC or other NEC
- Primary EP: Safety/tolerability





DLL3-directed T-cell engager developed using the TriTAC®platform: small size (~50kDa), prolonged half-life (13.8 days)



Summary

- Monotherapy dose: 24mg q2W
- Toxicities manageable
  - no DLTs, CRS Gr1-2 (98%)

Study

- Phase 1b/2 of MK-6070 and I-DXd in Participants With Relapsed SCLC (NCT06780137)

Beltran H et al. Updated results from a phase I/II study of gocatamig for small cell lung cancer (SCLC) and other neuroendocrine cancers. ESMO 2025;Abstract 2758MO.

Year in Review:
Small Cell Lung Cancer

INTRODUCTION: Biopharmacology of SCLC – “Wildfire sparked in dry grass”

MODULE 1: Limited-Stage Disease

MODULE 2: Extensive-Stage Disease

MODULE 3: Paraneoplastic Syndromes – Lambert-Eaton Myasthenic Syndrome

MODULE 4: Bispecific T-Cell Engagers – Tarlatamab

MODULE 5: Antibody-Drug Conjugates – Ifinatamab Deruxtecan

MODULE 6: Other Novel Agents – Alisertib, CAR T-Cell Therapy

RTP Year in Review 2026

ADCs in SCLC: Summary & Challenges

Agent	Target	Payload	N	ORR	IC activity	Toxicities
IDXd (12 mg/kg)	B7-H3	Topo1i	137	48%	Y (38/58%)	ILD 12.3%
YL201	B7-H3	Topo1i	53	64%	Y (30%)	ILD 1.3%
HS-20093 (8 mg/kg)	B7-H3	Topo1i	26	61%	NR	ILD 1%
MHB088C (2mg/kg)	B7-H3	Topo1i	33	42%	NR	
SHR-4849/IDE849	DLL3	Topo1i	100	73%	Y (83.3%)	NR
ZL-1310	DLL3	Topo1i	89	47%	Y (33%)	ILD 10%
ABBV-706	SEZ6	Topo1i	80	58%	Y (57%)	ILD 9%
Sacituzumab Govitecan	TROP2	Topo1i	43	42%		
Iza-Bren	EGFR-HER3	Topo1i	58	48.1%	NR	Not reported

Conclusions

- Active agents!
- CNS activity reported

Challenges

- Toxicities (ILD)
- Lack of biomarkers
- Same payload

Courtesy of Christine L Hann, MD, PhD

Ifinatamab Deruxtecan Granted Priority Review in the US for Adult Patients with Previously Treated Extensive-Stage SCLC Who Experienced Disease Progression on or After Platinum-Based Chemotherapy

Press Release: April 13, 2026

"[On April 13, 2026, the manufacturer's] Biologics License Application (BLA) for ifinatamab deruxtecan (I-DXd) has been accepted and granted Priority Review by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy.

The BLA is based on results from the IDeate-Lung01 phase 2 trial, with support from the IDeate-PanTumor01 phase 1/2 trial. Results from the primary analysis of IDeate-Lung01 were presented at the 2025 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer (#WCLC25) and published in the Journal of Clinical Oncology. Ifinatamab deruxtecan also was previously granted Breakthrough Therapy Designation by the FDA in August 2025 for the treatment of adult patients with ES-SCLC with disease progression on or after platinum-based chemotherapy."

https://daiichisankyo.us/press-releases/-/article/ifinatamab-deruxtecan-granted-priority-review-in-the-us-for-adult-patients-with-previously-treated-extensive-stage-small-cell-lung-cancer-who-experienced-disease-progression-on-or-after-platinum-based-chemotherapy

Original Reports | Thoracic Oncology

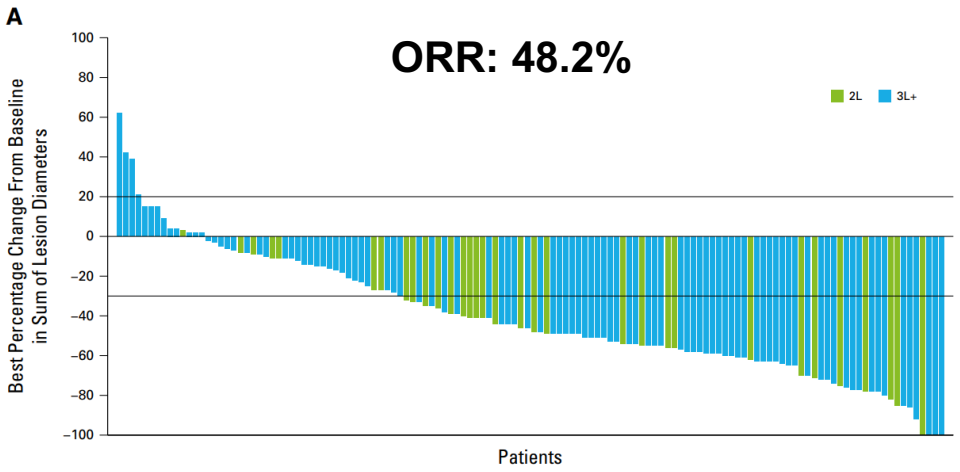
Ifinatamab Deruxtecan in Patients With Extensive-Stage Small Cell Lung Cancer: Primary Analysis of the Phase II IDeate-Lung01 Trial

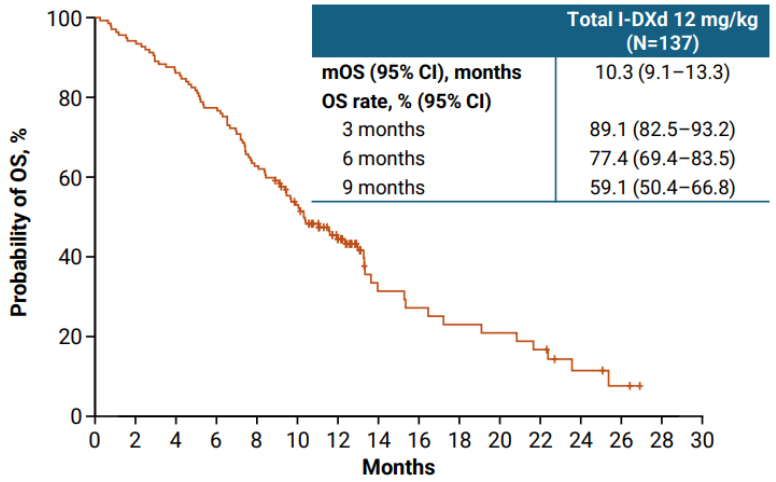
Charles M. Rudin, MD, PhD[1]; Melissa L. Johnson, MD[2]; Luis Paz-Ares, MD, PhD[3]; Makoto Nishio, MD, PhD[4]; Christine L. Hann, MD, PhD[5]; Nicolas Girard, MD, PhD[6]; Pedro Rocha, MD, PhD[7]; Hidetoshi Hayashi, MD, PhD[8]; Tetsuya Sakai, MD, PhD[9]; Yu Jung Kim, MD, PhD[10]; Haichuan Hu, MD, PhD[11]; Meng Qian, PhD[12]; Jasmeet Singh, MD, MPHA[12]; Juliette Godard, PharmD[13]; Mei Tang, MD, PhD[12]; and Myung-Ju Ahn, MD[14]

DOI https://doi.org/10.1200/JCO-25-02142

Ifinatamab Deruxtecan (IDXd)

- **IDeate-Lung01:** Phase 2 randomized study relapsed SCLC
  - Dose optimization: 8mg/kg vs 12 mg/kg q3W
  - dose expansion: 12 mg/kg (n= 137 at 12 mg/kg)
- Relapsed SCLC after platinum-based CT
  - Asymptomatic CNS disease
- 1 EP: ORR by BICR





	Total I-DXd 12 mg/kg (N=137)
mOS (95% CI), months	10.3 (9.1–13.3)
OS rate, % (95% CI)	
3 months	89.1 (82.5–93.2)
6 months	77.4 (69.4–83.5)
9 months	59.1 (50.4–66.8)

Activity

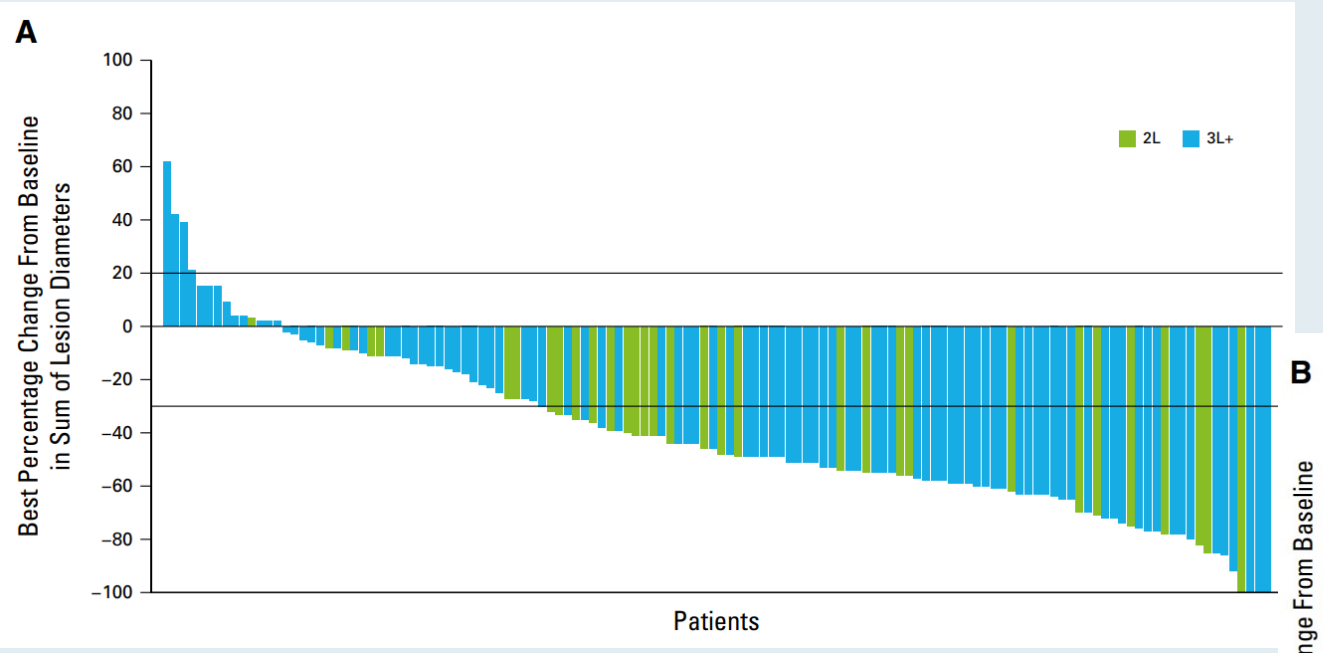
- ORR: 48.2% (56.3% 2L)
- mDOR 5.3 mos
- mPFS: 4.9 mos
- mOS: 10.3 mos
- IC responses observed in
  - 38.5% (prior RT)
  - 57.7% (no prior RT)
- Responses observed post-tarla

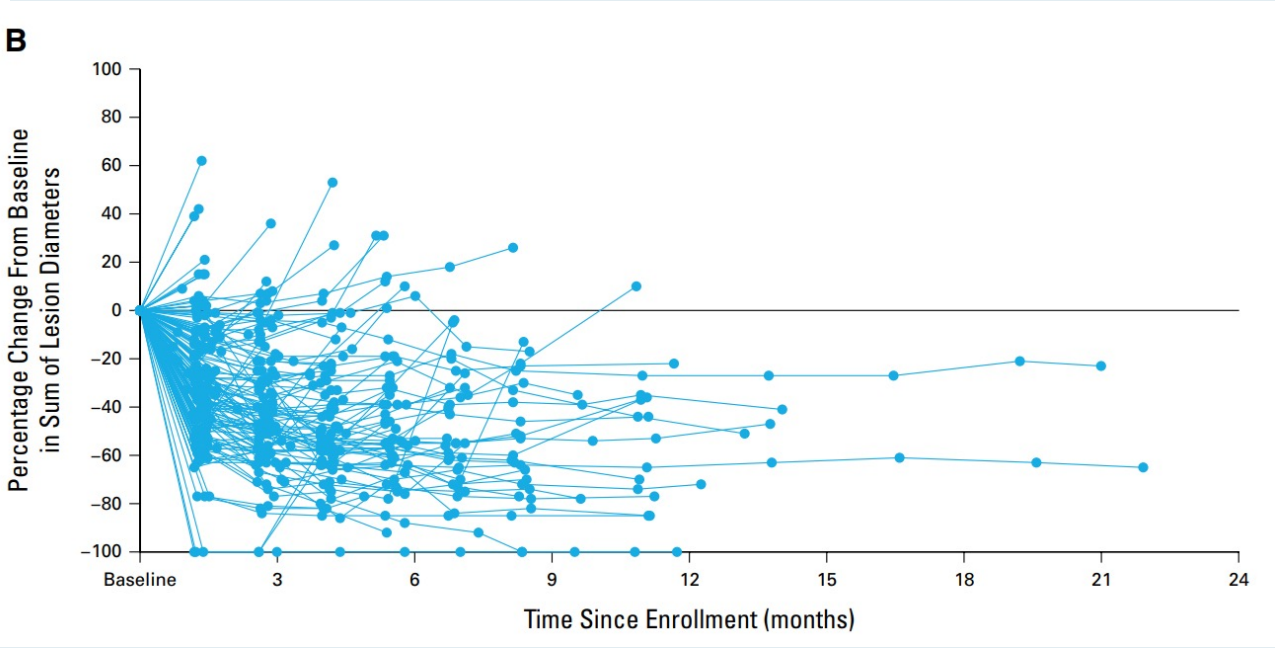
Toxicities

- 36.5% ≥ G3 TRAEs
  - Hematologic (≤14%)
  - GI (<10%)
- ILD-pneumonitis:
  - 12.4% (most G1/2)
  - 4.4% G3
  - 3 G5, 1 related

Ahn MJ et al. WCLC 2025. Abstract OAO6.03. Rudin CM et al. *J Clin Oncol*. 2025;JCO-25-02142. Rocha P et al. ESMO 2025. Abstract 2760MO.

Phase II Ideate-Lung01 Trial: Antitumor Activity of I-DXd





Rudin CM et al. *J Clin Oncol* 2026;44:261-273.

RTP Year in Review 2026

Phase II Ideate-Lung01 Trial: Confirmed Response by BICR

TABLE 2. Confirmed Response by BICR in Parts 1 and 2, and in the Total 12-mg/kg Group

	Part 1 (dose optimization)		Part 2 (extension)	Parts 1 and 2
End Point	8 mg/kg (n = 46)	12 mg/kg (n = 42)	12 mg/kg (n = 95)	Total 12 mg/kg (n = 137)
ORR, % (95% CI)	26.1 (14.3 to 41.1)	54.8 (38.7 to 70.2)	45.3 (35.0 to 55.8)	48.2 (39.6 to 56.9)
BOR, No. (%)				
CR	2 (4.3)	0	3 (3.2)	3 (2.2)
PR	10 (21.7)	23 (54.8)	40 (42.1)	63 (46.0)
SD	25 (54.3)	15 (35.7)	39 (41.1)	54 (39.4)
PD	5 (10.9)	2 (4.8)	8 (8.4)	10 (7.3)
Not evaluable	4 (8.7)	2 (4.8)	5 (5.3)	7 (5.1)
DCR, % (95% CI)	80.4 (66.1 to 90.6)	90.5 (77.4 to 97.3)	86.3 (77.7 to 92.5)	87.6 (80.9 to 92.6)
TTR, median (range), months	1.4 (1.3-2.6)	1.4 (1.0-8.1)	1.4 (1.2-3.9)	1.4 (1.0-8.1)
DOR, median (95% CI), months	7.9 (4.1 to NE)	4.2 (3.5 to 7.0)	5.6 (3.7 to 7.2)	5.3 (4.0 to 6.5)

Abbreviations: BICR, blinded independent central review; BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; TTR, time to response.

Rudin CM et al. *J Clin Oncol* 2026;44:261-273.

IDeate-Lung01: intracranial activity of IDXd

	With baseline BM (n=65)		Without baseline BM (n=72)
	Intracranial	Systemic	Systemic
cORR,[a] % (95% CI)	46.2% (33.7–59.0)	46.2% (33.7–59.0)	50.0% (38.0–62.0)
cBOR,[a] n (%)			
CR	20 (30.8%)	1 (1.5%)	2 (2.8%)
PR	10 (15.4%)	29 (44.6%)	34 (47.2%)
SD	29 (44.6%)	28 (43.1%)	26 (36.1%)
PD	1 (1.5%)	5 (7.7%)	5 (6.9%)
NE	5 (7.7%)[b]	2 (3.1%)[c]	5 (6.9%)[d]
cDCR,[a] % (95% CI)	90.8% (81.0–96.5)	89.2% (79.1–95.6)	86.1% (75.9–93.1)
DOR,[a] median (95% CI), months	6.2 (4.0–7.9)	4.3 (3.0–5.8)	5.9 (4.0–8.3)
TTR,[a] median (range), months	1.4 (0.9–8.5)	1.4 (1.0–8.1)	1.4 (1.2–4.0)
PFS,[a] median (95% CI), months	—	4.5 (4.0–5.4)	5.4 (4.2–6.7)
OS, median (95% CI), months	—	10.4 (7.9–15.3)	10.1 (8.4–13.3)

Simoes da Rocha PF et al. Intracranial activity of ifinatamab deruxtecan (I-DXd) in patients (pts) with extensive-stage (ES) small cell lung cancer (SCLC) and baseline (BL) brain metastases (BM): Primary analysis of IDeate-Lung01. ESMO 2025;Abstract 2760MO.

Phase II Ideate-Lung01 Trial: Adverse Events

Adverse Events	All Cause, No. (%)	Related to Treatment,[a] No. (%)
Any TEAE	135 (98.5)	123 (89.8)
Grade ≥3 TEAE	85 (62.0)	50 (36.5)
Serious TEAE	54 (39.4)	25 (18.2)
TEAE associated with dose interruption	2 (1.5)	2 (1.5)
TEAE associated with dose delay	49 (35.8)	35 (25.5)
TEAE associated with dose reduction	24 (17.5)	21 (15.3)
TEAE associated with treatment discontinuation	15 (10.9)	13 (9.5)
TEAE associated with death	16 (11.7)	6 (4.4)

TEAE = treatment-emergent adverse event

Rudin CM et al. *J Clin Oncol* 2026;44:261-273.

Phase II Ideate-Lung01 Trial: Adverse Events

TEAEs Reported in >10% of Patients in the Total 12-mg/kg Group at Any Grade or in >5% of Patients at Grade ≥3, Regardless of Relationship to Treatment	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Nausea	66 (48.2)	5 (3.6)	59 (43.1)	3 (2.2)
Anemia	62 (45.3)	19 (13.9)	47 (34.3)	14 (10.2)
Decreased appetite	53 (38.7)	5 (3.6)	45 (32.8)	2 (1.5)
Neutropenia[b]	52 (38.0)	23 (16.8)	47 (34.3)	19 (13.9)
Constipation	42 (30.7)	0	17 (12.4)	0
Lymphopenia[c]	38 (27.7)	22 (16.1)	27 (19.7)	17 (12.4)
Leukopenia[d]	37 (27.0)	7 (5.1)	32 (23.4)	5 (3.6)
Diarrhea	33 (24.1)	3 (2.2)	21 (15.3)	2 (1.5)
Asthenia	32 (23.4)	5 (3.6)	26 (19.0)	2 (1.5)
Thrombocytopenia[e]	29 (21.2)	10 (7.3)	26 (19.0)	8 (5.8)
Vomiting	27 (19.7)	3 (2.2)	16 (11.7)	1 (0.7)
Fatigue	27 (19.7)	3 (2.2)	22 (16.1)	3 (2.2)
Hyponatremia	24 (17.5)	5 (3.6)	3 (2.2)	0
Increased AST	23 (16.8)	1 (0.7)	13 (9.5)	1 (0.7)
Hypoalbuminemia	22 (16.1)	0	6 (4.4)	0
Increased ALT	21 (15.3)	0	12 (8.8)	0
Cough	17 (12.4)	0	2 (1.5)	0
Decreased weight	17 (12.4)	0	7 (5.1)	0
Hypokalemia	16 (11.7)	4 (2.9)	1 (0.7)	1 (0.7)
Dyspnea	14 (10.2)	1 (0.7)	2 (1.5)	1 (0.7)
Pyrexia	14 (10.2)	0	8 (5.8)	0
Headache	14 (10.2)	0	3 (2.2)	0

Rudin CM et al. *J Clin Oncol* 2026;44:261-273.

A phase 1b/2 study of gocatamig and ifinatamab deruxtecan for relapsed or refractory extensive-stage small cell lung cancer

P3.18.73

M. Johnson[1]; J. Bar[2]; J. C. Benitez Montañez[3]; C. Caglevic[4]; M. E. Gutierrez[5]; T. M. Kim[6]; N. Peled[7]; P. Rocha[8]; C. I. Rojas[9]; T. Shentzer Kutiel[10]; J.-M. Sun[11]; S. Vaidya[12]; Q. Liu[13]; A. Gramza[13]; J. Sands[14]

[1]SCRI Oncology Partners, Nashville, TN, USA; [2]Davidman Cancer Center, Shaba Medical Center, Ramat Gan, Israel; [3]Comité de Ética de la Investigación con Medicamentos Hospital Clínico San Carlos, Madrid, Spain; [4]Fundación Arturo López Pérez-Unidad de Investigación de Drogas Oncológicas, Santiago, Chile; [5]John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ, USA; [6]Seoul National University Hospital, Seoul, South Korea; [7]Shaare Zedek Medical Center, Jerusalem, Israel; [8]Vall d'Hebron University Hospital, Barcelona, Spain; [9]Bradford Hill Investigación Clínica, Santiago, Chile; [10]Rambam Health Care Campus, Haifa, Israel; [11]Samsung Medical Center, Seoul, South Korea; [12]Daiichi Sankyo, Basking Ridge, NJ, USA; [13]Merck & Co., Inc., Rahway, NJ, USA; [14]Dana-Farber Cancer Institute, Boston, MA, USA

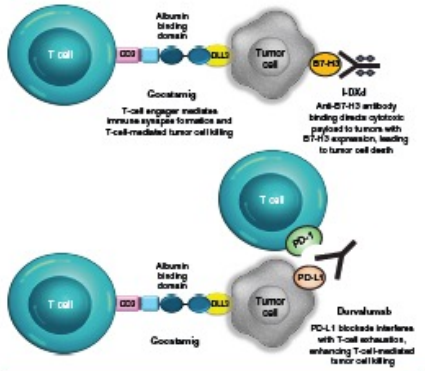
INTRODUCTION

- Delta-like ligand 3 (DLL3) and B7-H3 are two proteins highly expressed on the surface of small cell lung cancer (SCLC) cells[1,2]
- Gocatamig (MK-6070, HPN328) is a DLL3-directed T-cell engager developed using the TriTAC® platform[3] (**Figure 1**)
- Ifinatamab deruxtecan (I-DXd) is an antibody-drug conjugate (ADC) comprising a B7-H3 monoclonal antibody covalently linked to a topoisomerase I inhibitor[4] (**Figure 1**)
- Both gocatamig and I-DXd have shown encouraging antitumor activity and manageable safety profiles when administered as monotherapy in participants with extensive stage (ES)-SCLC relapsed or refractory to one or more prior lines of systemic chemotherapy[5,6]
- Durvalumab is a programmed death ligand 1 (PD-L1) inhibitor approved for use in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of ES-SCLC[7] (**Figure 1**)
- Because of their distinct mechanisms of action and minimally overlapping toxicities, combining gocatamig with an ADC or a checkpoint inhibitor may enhance efficacy without compromising tolerability
- We describe the ongoing phase 1b/2 study 6070-002 (NCT06780137) that is evaluating the combination of gocatamig with I-DXd or durvalumab, as well as gocatamig monotherapy and I-DXd monotherapy, for the treatment of relapsed or refractory ES-SCLC

Poster presented | Poster slides | Plain language summary

https://bit.ly/4ix0WHK | https://bit.ly/4CxW3qM | https://bit.ly/4mYJjB

Figure 1. Mechanisms of action of gocatamig, I-DXd, and durvalumab



OBJECTIVES

Primary

- Part 1: Evaluate the objective response rate (ORR), safety, and tolerability of gocatamig in combination with I-DXd or I-DXd alone
- Part 2: Evaluate the safety and tolerability of gocatamig monotherapy
- Part 3: Evaluate the safety and tolerability of gocatamig in combination with durvalumab

Secondary

- Part 1: Evaluate the duration of response (DOR) and progression-free survival (PFS), characterize the pharmacokinetic profile, and evaluate the immunogenicity of I-DXd alone or in combination with gocatamig
- Part 2: Evaluate the ORR, DOR, and PFS, characterize the pharmacokinetic profile, and evaluate the immunogenicity of gocatamig monotherapy
- Part 3: Evaluate the ORR, DOR, and PFS, characterize the pharmacokinetic profile, and evaluate the immunogenicity of gocatamig in combination with durvalumab

METHODS

Figure 2. The 6070-002 study design

2L, second-line; 2L+, second-line or later. [a]Bayesian optimal interval dosing.

- Gocatamig and I-DXd combination doses, the gocatamig monotherapy doses, and the gocatamig dose to be used in combination with durvalumab will depend on the results of the ongoing dual dose escalation and monotherapy cohorts of study 6070-001 (NCT04471727)
- Dose expansion in part 1 will depend on findings of the safety run-in period

Table 1. Key participant eligibility criteria

Inclusions
• Age 18 years or older
• Stage IV ES-SCLC (T any, N any, M1a/b/c) following:
– Part 1 safety run-in, Part 2, and Part 3: At least one prior line of platinum-based chemotherapy with or without PD-(L)1 inhibitors
– Part 1 dose-expansion: Only one prior line of platinum-based chemotherapy with or without PD-(L)1 inhibitors
• Measurable disease by RECIST 1.1 outside the CNS
• ECOG performance status 0 or 1
• Available tumor tissue sample
• Adequate organ function
Exclusions
• Pleural effusion, pericardial effusion, or ascites requiring drainage procedures
• History of pneumonitis or interstitial lung disease
• Clinically severe pulmonary compromise
• Active or history of autoimmune disease or immune deficiency
• Uncontrolled or significant (or history of significant) cardiovascular disease
• Unresolved grade ≥2 AEs (per NCI CTCAE 5.0) from prior anticancer therapy
• Last systemic anticancer treatment or other investigational agent/device within 3 weeks of scheduled dosing
• Severe, life-threatening immune-mediated AEs or IRRs with prior immune-oncology agents
• Radiotherapy within 2 weeks of study treatment (parts 1 and 2), or radiation to the lung within 6 months or the abdominal area within 4 weeks of study treatment (part 1)
• Prior treatment with a DLL3-targeted agent (except part 1 safety run-in period for the I-DXd monotherapy arm)
• Other malignancy within 3 years of screening (except basal cell or squamous cell carcinoma of the skin or carcinoma in situ)
• Prior treatment with B7-H3–targeted agents (part 1)
• Prior discontinuation of an ADC that consists of an exatecan derivative due to treatment-related toxicities (part 1)
• Untreated or symptomatic brain metastases or leptomeningeal disease

AE, adverse event; CNS, central nervous system; IRR, infusion-related reaction; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; RECIST, response evaluation criteria in solid tumors.

Assessments

- The incidence and causality of AEs, including serious AEs, will be collected from the time of treatment allocation through the last dose of study treatment and during the safety follow-up period
- Dose-limiting toxicities (DLTs; Table 2) will be assessed during the safety run-in period and graded using the NCI CTCAE v5.0 or the American Society for Transplant and Cellular Therapy (ASTCT) criteria
- ORR, DOR, and PFS will be assessed by the investigator per RECIST v1.1
- Pharmacokinetic and immunogenicity analyses for gocatamig alone or in combination with I-DXd or durvalumab will be performed

References

1. Owen DH, et al. *J Hematol Oncol.* 2019;12:61.
2. Dong P, et al. *Front Oncol.* 2019;8:264.
3. Austin RJ, et al. *Mol Cancer Ther.* 2021;20:109-120.
4. Yamato M, et al. *Mol Cancer Ther.* 2022;21(4):635-646.
5. Baltran H, et al. *J Clin Oncol.* 2024;42(16_suppl):8090.
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7. Imfinzi. Package insert. AstraZeneca. 2025.

Acknowledgments

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Contact Information

Contact Dr Melissa Johnson at melissajohnson@scri.com for questions or comments.

Table 2. Dose-limiting toxicities

Hematologic
• Grade 4 hematologic AE lasting ≥7 days
• Grade 4 thrombocytopenia of any duration
• Grade 3 thrombocytopenia associated with clinically significant bleeding
• Grade 3 or grade 4 febrile neutropenia
Nonhematologic
• Any grade ≥3 nonhematologic AE is considered a DLT, except
– Grade 3 fatigue lasting ≤7 days
– Grade 3 diarrhea, nausea, or vomiting lasting <72 hours
– Grade 3 diarrhea, nausea, or vomiting lasting >72 hours but <120 hours without use of antiemetics or antidiarrheals per standard of care
– Grade 3 rash without use of corticosteroids or anti-inflammatory agents per standard of care
– Grade 3 or 4 events of increased or decreased blood pressure if associated with symptoms of CRS/IRR and resolve in concordance with CRS symptom resolution and do not result in additional safety events
– Grade 3 or 4 nonhematologic laboratory that is asymptomatic and/or rapidly reversible (returned to baseline or to grade ≤1 within 7 days) unless identified as clinically relevant by the investigator
• Drug-induced liver injury, defined as serum chemistry values and clinical presentation with the following features:
– ALT or AST ≥3 × ULN
– Total bilirubin ≥2 × ULN
– Alkaline phosphatase <2 × ULN
– No other cause for abnormalities, such as viral hepatitis A, B, or C, preexisting or acute liver disease, or another drug capable of causing the observed injury
• Grade ≥2 interstitial lung disease or pneumonitis
• Grade 5 toxicity

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRS, cytokine release syndrome; ULN, upper limit of normal.

Statistical analyses

- The safety analysis population will consist of all participants who received at least one dose of study treatment
- The efficacy analysis population for will consist of all participants with a baseline scan who received at least one dose of study treatment
- The per-protocol population for pharmacokinetic and immunogenicity analyses will consist of the subset of participants who complied with the protocol sufficiently to ensure that their data are likely to show the effects of treatment

Current status

- Recruitment is currently ongoing at sites worldwide in Australia, Chile, China, Israel, Japan, South Korea, Spain, Türkiye, and the United States
- Enrollment is estimated to be approximately 138 participants across all treatment arms

A Phase 1b/2 Study of Gocatamig and Ifinatamab Deruxtecan for Relapsed or Refractory Extensive-Stage Small Cell Lung Cancer

M. Johnson[1]; J. Bar[2]; J. C. Benítez Montañez[3]; C. Caglevic[4]; M. E. Gutierrez[5]; T. M. Kim[6]; N. Peled[7]; P. Rocha[8]; C. I. Rojas[9]; T. Shentzer Kutiel[10]; J.-M. Sun[11]; S. Vaidya[12]; Q. Liu[13]; A. Gramza[13]; J. Sands[14]

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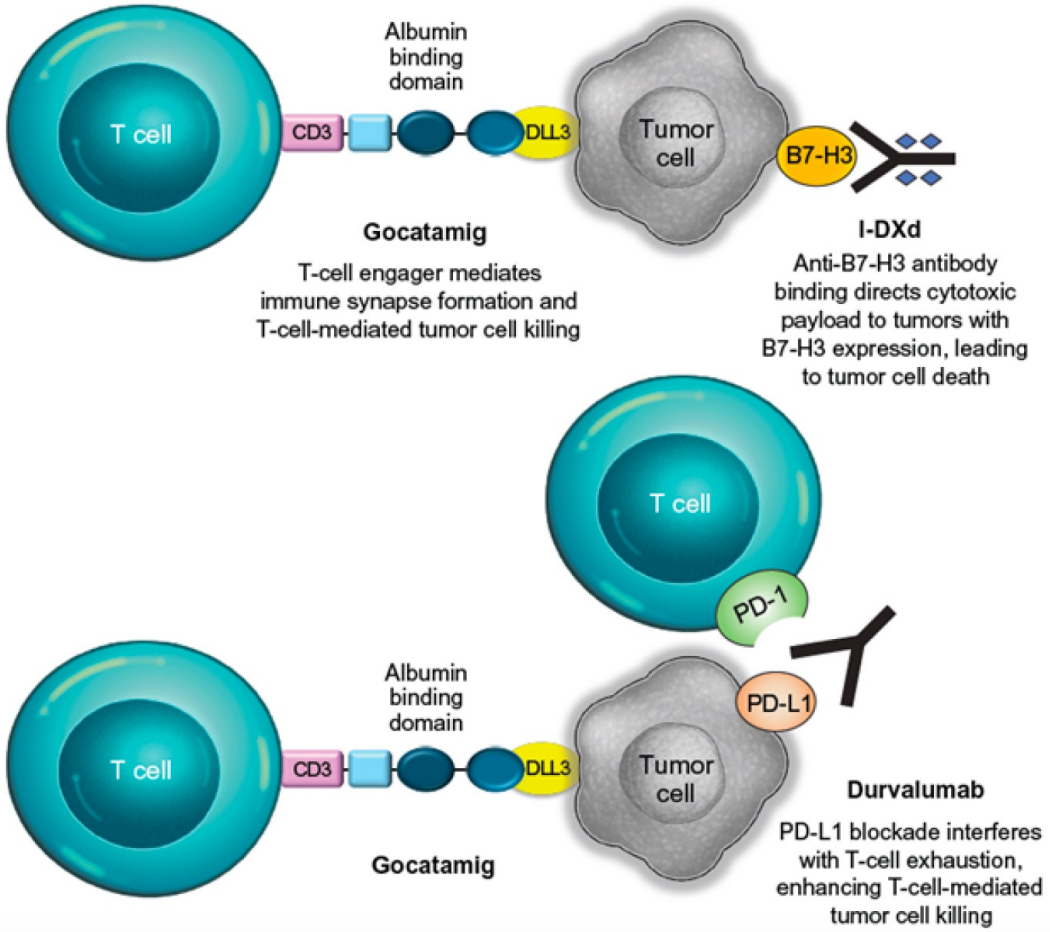
WCLC 2025;Abstract P3.18.73.

Mechanisms of Action of Gocatamig, I-DXd, and Durvalumab



Multiple B7-H3 ADCs are under development

	IDXd	YL-201	MHB-088C	HS20093/ GSK 5764227
Payload	Topo-1 inhibitor (exatecan-derivative)	Novel Topo-1 inhibitor	Topo-1 inhibitor (“SuperTopo1”) payload	Topo-1 inhibitor (exatecan-derivative)
DAR	4	8	4	4
Linker	Tetrapeptide-based cleavable linker	Protease-cleavable linker	Cleavable linker	Cleavable maleimide tetrapeptide linker
Trial reported	Phase 2 (n = 137)	Phase 1	Phase 1	Phase 1
Doses	12 mg/kg for phase 3	2.0 or 2.4 mg/kg	1.6-2.4 mg/kg	8 vs 10 mg/kg
Setting	Relapsed	Relapsed	Relapsed	Relapsed

Courtesy of Christine L Hann, MD, PhD

B7-H3 Targeted ADCs: summary

	IDXd	YL-201	MHB-088C	HS20093/ GSK 5764227
Payload	Topo-1 inhibitor (exatecan-derivative)	Novel Topo-1 inhibitor	Topo-1 inhibitor ("SuperTopo1") payload	Topo-1 inhibitor (exatecan-derivative)
DAR	4	8	4	4
Linker	Tetrapeptide-based cleavable linker	Protease-cleavable linker	Cleavable linker	Cleavable maleimide tetrapeptide linker
Trial reported	Phase 2 (n = 137)	Phase 1	Phase 1	Phase 1
Doses	12 mg/kg for phase 3	2.0 or 2.4 mg/kg	1.6-2.4 mg/kg	8 vs 10 mg/kg
Setting	Relapsed	Relapsed	Relapsed	Relapsed
ORR	48.2%	~64%	42.4%%	~61% (8 mg/kg)
mPFS	4.9 mos	5.7–7.6 mos		5.9–7.3 mo
Intracranial activity (ORR/DCR)	Y	Y		
Toxicities	Hematologic ILD/pneumonitis (12.4%)	Hematologic ILD rare (1.3%)	Hematologic ILD NR	Hematologic ILD Rare

Courtesy of Christine L Hann, MD, PhD

Ongoing B7-H3 ADC studies in SCLC

Phase/NCT	N	Arms	Endpoints	Dates
Phase 3 NCT06203210	540	IDXd vs TPC (lurbi, topo, AMR) (IDeate-Lung02)	1. ORR, OS 2. ORR, PFS	Start: 5/21/24 Primary comp: 4/30/27 Active, not recruiting
Phase 1/2 NCT06362252	123	I-DXd + Atezolizumab +/- Carboplatin as 1st line induction or maintenance (IDeate-Lung03)	1. DLT, TRAEs 2. PFS, ORR, DCR, CBR, TTR	Start: 7/22/24 Primary comp: 9/30/26
Phase 1/2 NCT04471727	232	Gocatamig, +/- atezo or +/- IDXd in DLL3+ tumors	1. AEs/PKs 2. ORR, BOR	Start: 12/14/20 Primary comp: 11/3/27
Phase 1 NCT06898957	200	YL201 + tarlatamab +/- PD-L1	1. DLTs, TEAEs 2. ORR, DOR, TTR, OS, PK	Start: 5/16/25 Primary comp: 4/23/31
R Phase 3 NCT06612151	300	YL201 vs topotecan in relapsed SCLC	1. OS 2. PFS, ORR, DoR	Start: 12/17/24 Primary comp: 12/1/27
Phase 3 NCT07099898	300	GSK5764227 (HS20093) vs topotecan in relapsed SCLC	1. ORR, OS 2. ORR, PFS, DOR, DCR, AEs, Brain PFS/DOR/OS	Start: 8/11/25 Primary comp: 9/2/26
Phase 3 NCT06954246 (China)	450	MHB088C vs TPC	1. OS 2. ORR, PFS, DOR, DCR, AEs, PK	Start: 6/4/25 Primary comp: 5/27

Courtesy of Christine L Hann, MD, PhD

DLL3 ADC

SHR-4849/IDE849 Studies

Phase/NCT	N	Study	Endpoints	Dates
Phase 1 NCT06443489* (SHR-4849/China only)	80	SHR-4849 in Patients With Advanced Solid Tumors	1. Safety, efficacy, and pharmacokinetics	Start: 6/26/24 Primary comp: 12/26
Phase 2 NCT07028281 (SHR-4849/China only)	120	SHR-4849 + Other Antitumor Drugs in Patients With Malignant Solid Tumors (PD-L1, CTLA-4, anti-VEGF, carboplatin, cisplatin)	1. DLT, AE/SAE, ORR 2. ORR, DOR, PFS, OS	Start: 5/12/25 Primary comp: 12/26
Phase 1/2 NCT07174583	208	IDE849 in Subjects With SCLC, High-Grade NEC, or Other DLL3-Expressing Tumors	1. DLT, TRAEs, ORR, DOR 2. DCR, PFS, OS, PK	Start: 10/14/25 Primary comp: 5/29
Phase 1 NCT06179069	112	ZL-1310 monotherapy, in combination with atezolizumab or atezo/carboplatin	Safety, efficacy, and pharmacokinetics	Start: 1/23/24 Primary comp: 5/30/27
Phase 1b/2 NCT06885281	86	Selected solid tumors	TRAE, SAE, antitumor activity	Start: 5/12/25 Primary comp: 12/26
Phase 3 NCT07218146	480	ZL-1310 compared to investigator's choice therapy (topotecan, lurbinectedin or amrubicin); prior tarla permitted	ORR by BICR, OS	Start: 11/30/25 Primary comp: 6/30/28

Courtesy of Christine L Hann, MD, PhD

SEZ6 and TROP2 ADC Studies

Phase/NCT	N	Arms	Endpoints	Dates
R Phase 2 NCT07155174	180	1st line ABBV-706/Atezo vs EP/atezo (SOC)	1. AEs, PFS 2. ORR, DOR, DC, OS	Start: 11/25/25 Primary comp: 9/31
R Phase 3 NCT07365241	531	ABBV-706 vs TPC in relapsed SCLC	1. ORR, OS 2. PFS, DoR	Start 4/14/26 Primary comp: 9/30
Phase 1/2 NCT04826341	120	Sacituzumab Govitecan Plus Berzosertib in SCLC, EP SCC, HR-deficient cancers resistant to PARP Inhibitors	Phase 1: MTD Phase 2: ORR	Start: 9/20/21 Primary comp: 3/1/26
Phase 3 NCT06801834	695	Sacituzumab Govitecan Versus SOC in Participants With Previously Treated SCLC (EVOKE-SCLC-04) Comparators: topo/AMR	1. ORR, OS 2. PFS, DOR	Start: 4/4/25 Primary comp: 10/29

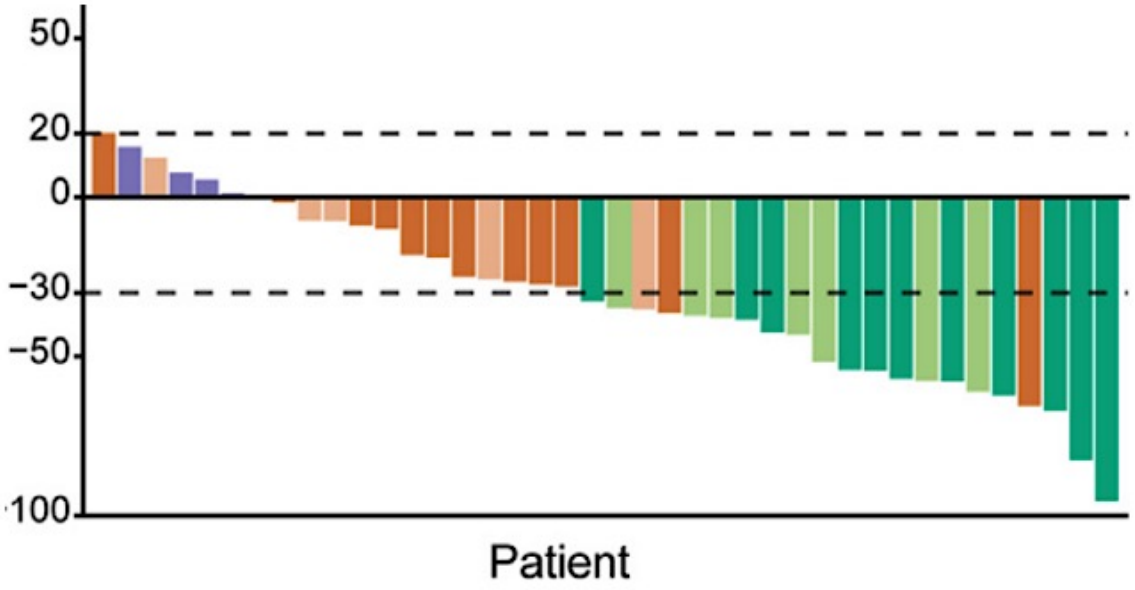
Courtesy of Christine L Hann, MD, PhD

Sacituzumab Govitecan

TROPICS-3 (NCT03964727)

- Phase 2 basket study including 43 with relapsed SCLC
- ES SCLC with progression after platinum-based CT
  - No CNS disease
- Primary EP: ORR

- **ORR 41.9%**



Activity

- ORR: 41.9% (N = 43)
- DCR 83.7%
- DOR 4.7 mo
- mPFS:4.4 mos
- mOS:13.6

Toxicities

- 74.4% had ≥ G3 TRAEs
  - Neutropenia (44%)
  - GI 9%
- SAE: 37.2%
- ILD NR

Dowlati et al, JTO Vol. 20 No. 6: 799–808

Year in Review:
Small Cell Lung Cancer

INTRODUCTION: Biopharmacology of SCLC – “Wildfire sparked in dry grass”

MODULE 1: Limited-Stage Disease

MODULE 2: Extensive-Stage Disease

MODULE 3: Paraneoplastic Syndromes – Lambert-Eaton Myasthenic Syndrome

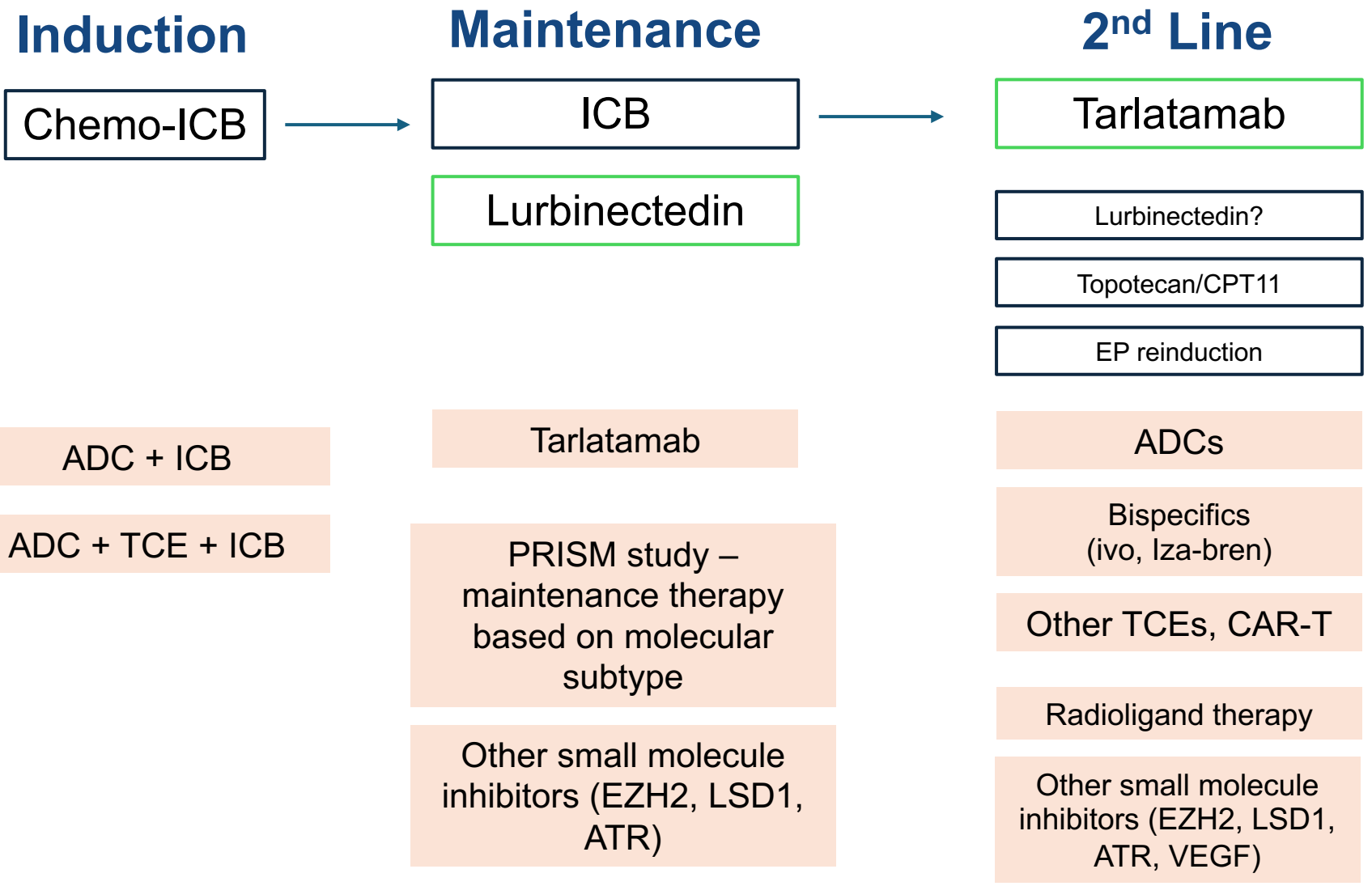
MODULE 4: Bispecific T-Cell Engagers – Tarlatamab

MODULE 5: Antibody-Drug Conjugates – Ifinatamab Deruxtecan

MODULE 6: Other Novel Agents – Alisertib, CAR T-Cell Therapy

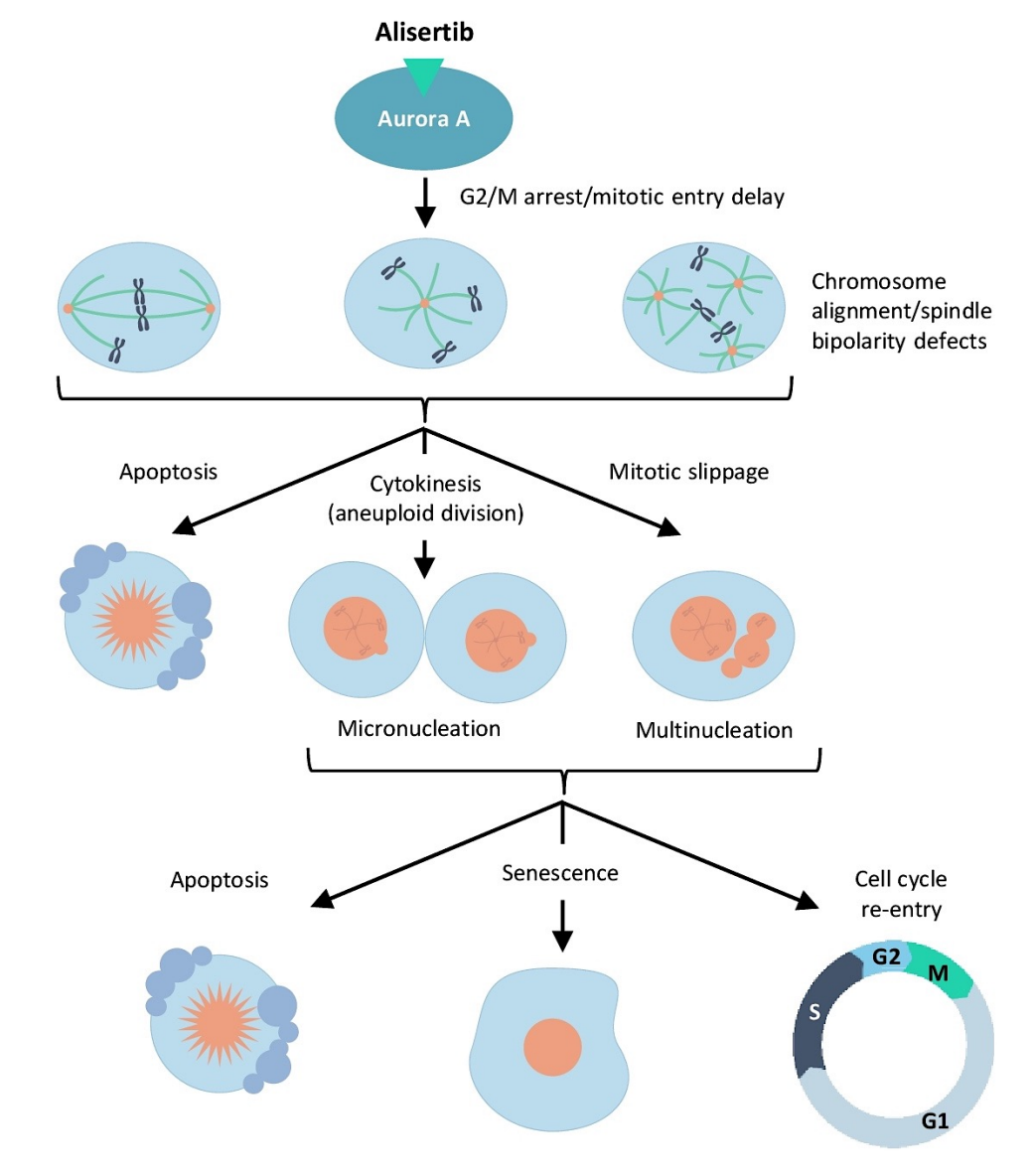
RTP Year in Review 2026

ES SCLC – the future?



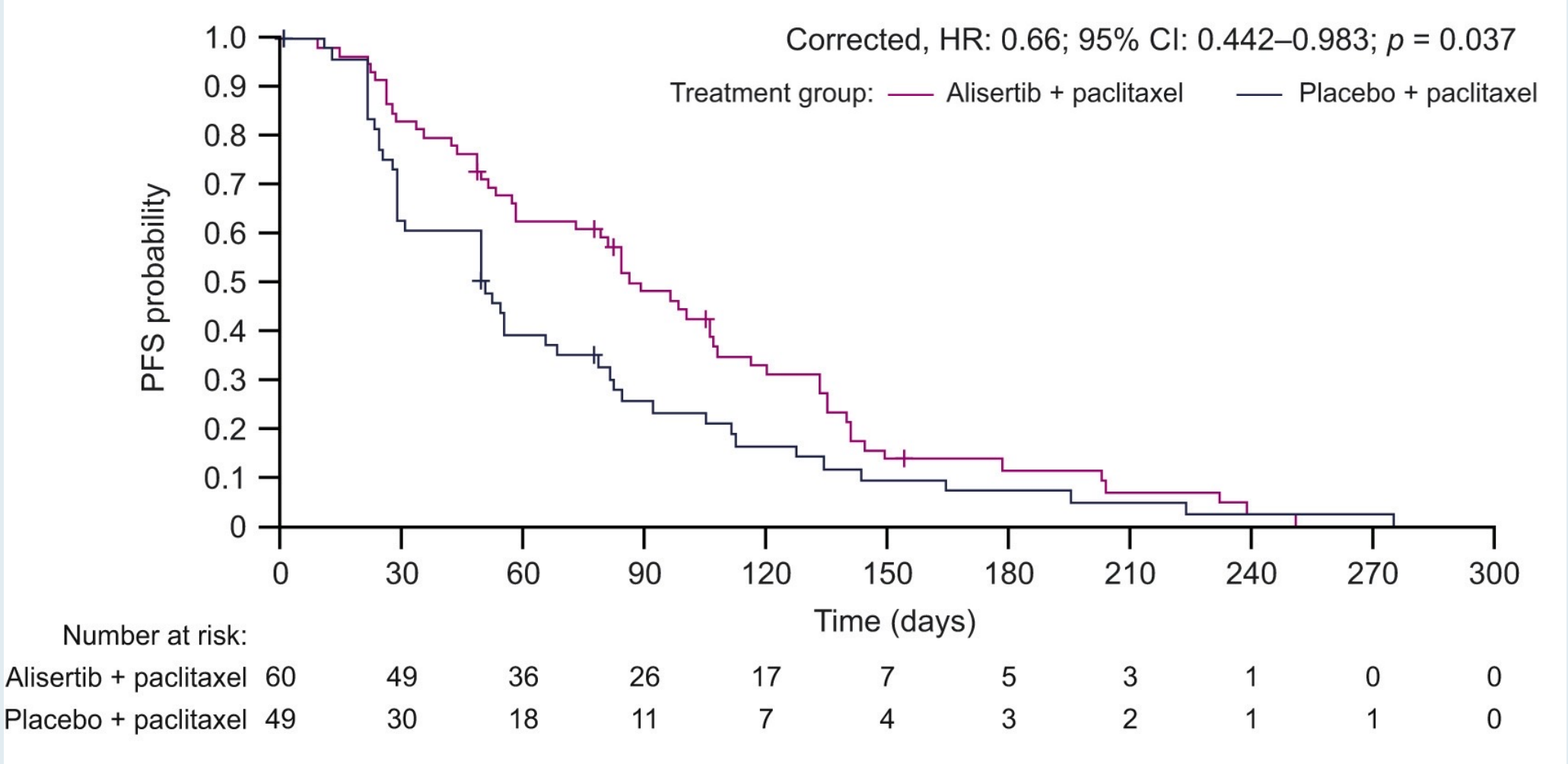
Courtesy of Christine L Hann, MD, PhD

Alisertib, a Small-Molecule Aurora Kinase A (AURKA) Inhibitor



Owonikoko TK et al. ASCO 2024;Abstract TPS8128.

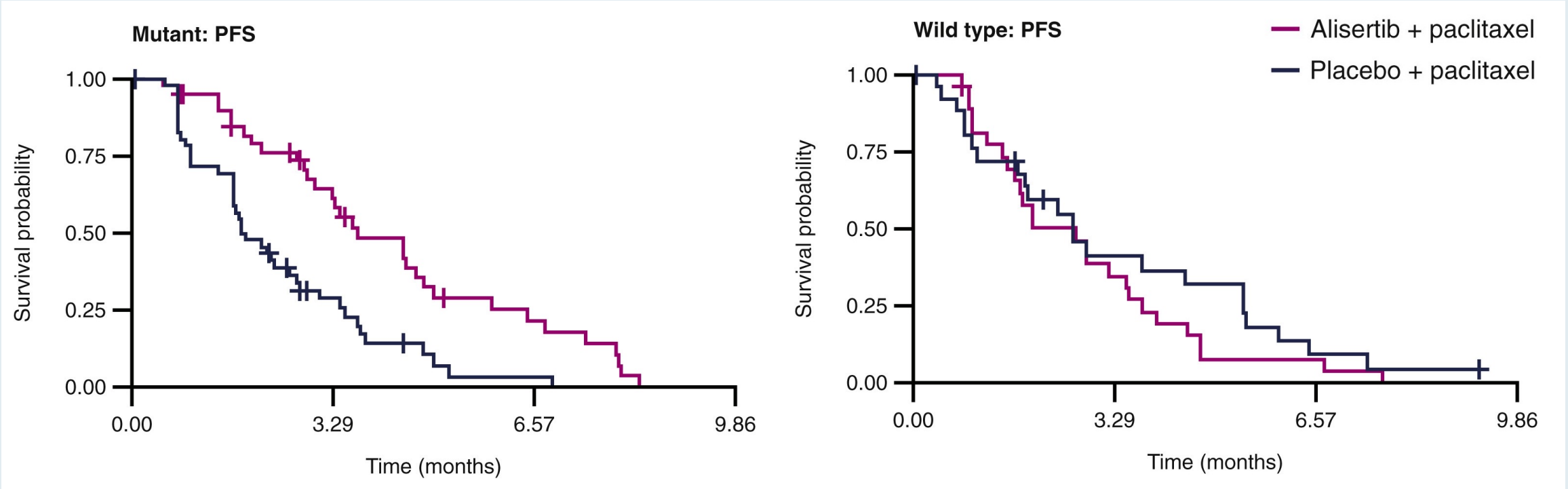
Phase II C14018 Trial of Alisertib with Paclitaxel: Progression-Free Survival (PFS) for Patients with Resistant or Refractory Disease Relapse



Owonikoko TK et al. *J Thorac Oncol* 2020 February;15(2):274-87.

RTP RESEARCH TO PRACTICE

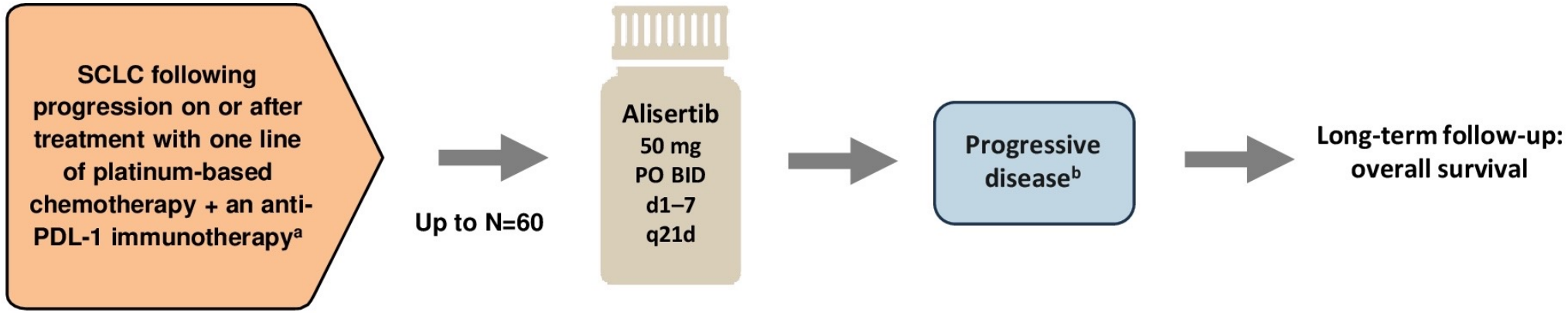
Phase II C14018: Alisertib with Paclitaxel — PFS for Patients with and without Cell Cycle Gene Mutations



	Mutant		Wild type	
	n	Median, months	n	Median, months
Alisertib + paclitaxel	40	3.68	28	2.63
Placebo + paclitaxel	47	1.80	25	2.60
HR (95% CI)	0.395 (0.239–0.654)		1.31 (0.736–2.33)	
***p*-value**	0.0003		0.359	

Owonikoko TK et al. *J Thorac Oncol* 2020 February;15(2):274-87.

Phase II ALISCA-Lung1 Study Design



[a]Up to one additional systemic anti-cancer therapy for SCLC is allowed, for a total of up to two prior lines of therapy.
[b]Other reasons for discontinuation: death, radiologic evidence of disease; unacceptable toxicity; patient withdrawal of consent; other specified treatment withdrawal criterion.
Primary prophylaxis with G-CSF following last dose of alisertib of each 21-day cycle and continuing through subsequent cycles.
BID, twice daily; d, day; PO, oral; q, every; SCLC, small-cell lung cancer.

Study objectives and endpoints

Primary

- Determine whether any biomarker correlates with alisertib response by investigator-assessed ORR, DOR, DCR, PFS according to RECIST v1.1, and OS within biomarker-defined subgroups from retrospectively evaluated patient samples

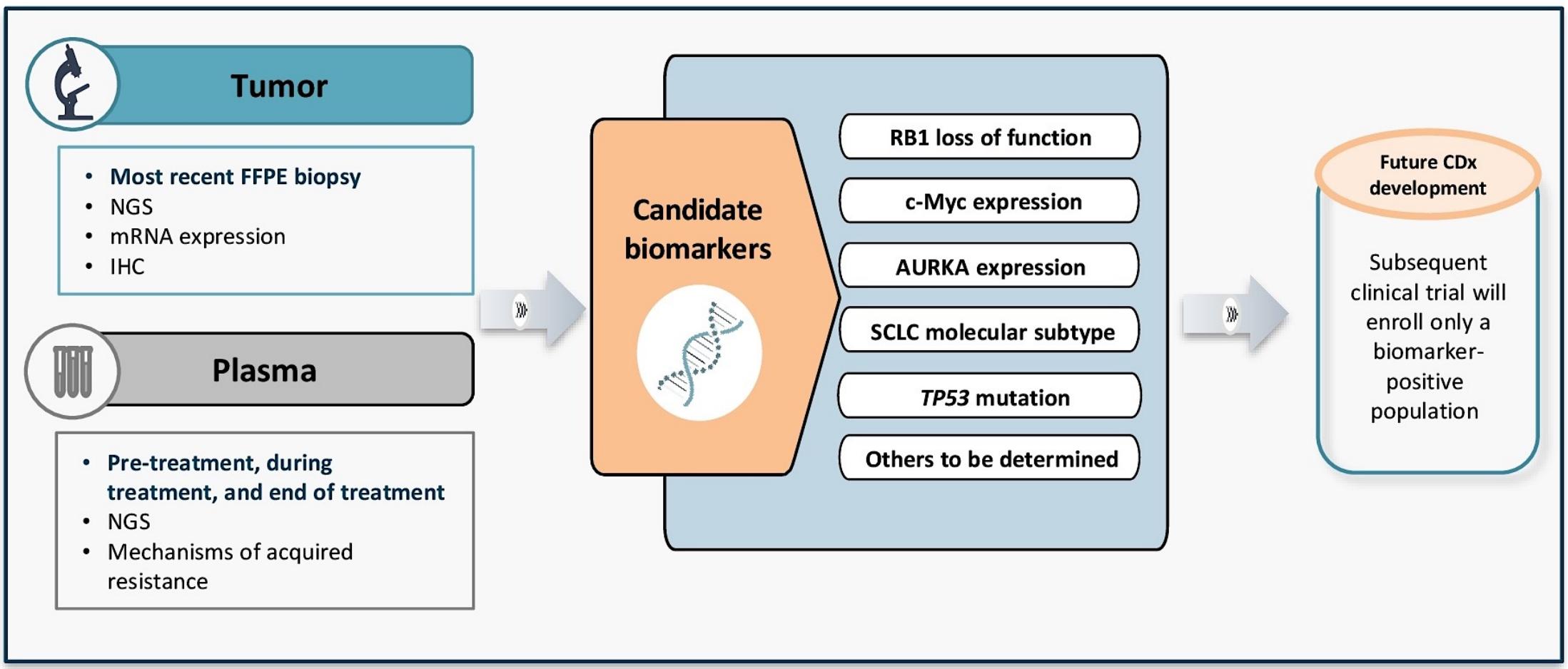
Secondary

- Determine investigator-assessed efficacy (ORR, DOR, DCR, and PFS) according to RECIST v1.1
- Determine OS outcomes
- Determine the safety profile of alisertib (AE and SAEs per NCI CTCAE v 5.0)
- Update the population PK profile of alisertib

AE, adverse event; DCR, disease-control rate; DOR, duration of response; G-CSF, granulocyte colony stimulating factor; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; RECIST, Response Evaluation Criteria in Solid Tumours; SAE, serious adverse event.

Owonikoko TK et al. ASCO 2024;Abstract TPS8128.

Phase II ALISCA-Lung1: Planned Biomarker Analysis



CDx, companion diagnostics; FFPE, formalin-fixed paraffin-embedded; IHC, immunohistochemistry; NGS, next-generation screening.

Owonikoko TK et al. ASCO 2024;Abstract TPS8128.

ALISCA-Lung2 Trial: Dose Escalation with Alisertib for SCLC

Pathologically confirmed SCLC with prior treatment of one platinum-based chemotherapy and an anti-PD-1/PD-L1 immunotherapy.

Up to one additional systemic anti-cancer therapy for SCLC is allowed, for up to 2 prior treatment regimens.

~10 Patients per cohort

Cohort 1
***Alisertib 30 mg BID** + Paclitaxel

Cohort 2
***Alisertib 40 mg BID** + Paclitaxel

Cohort 3
***Alisertib 50 mg BID** + Paclitaxel

Cohort 4
***Alisertib 60 mg BID** + Paclitaxel

Cohort 5
Alisertib 70 mg BID + Paclitaxel

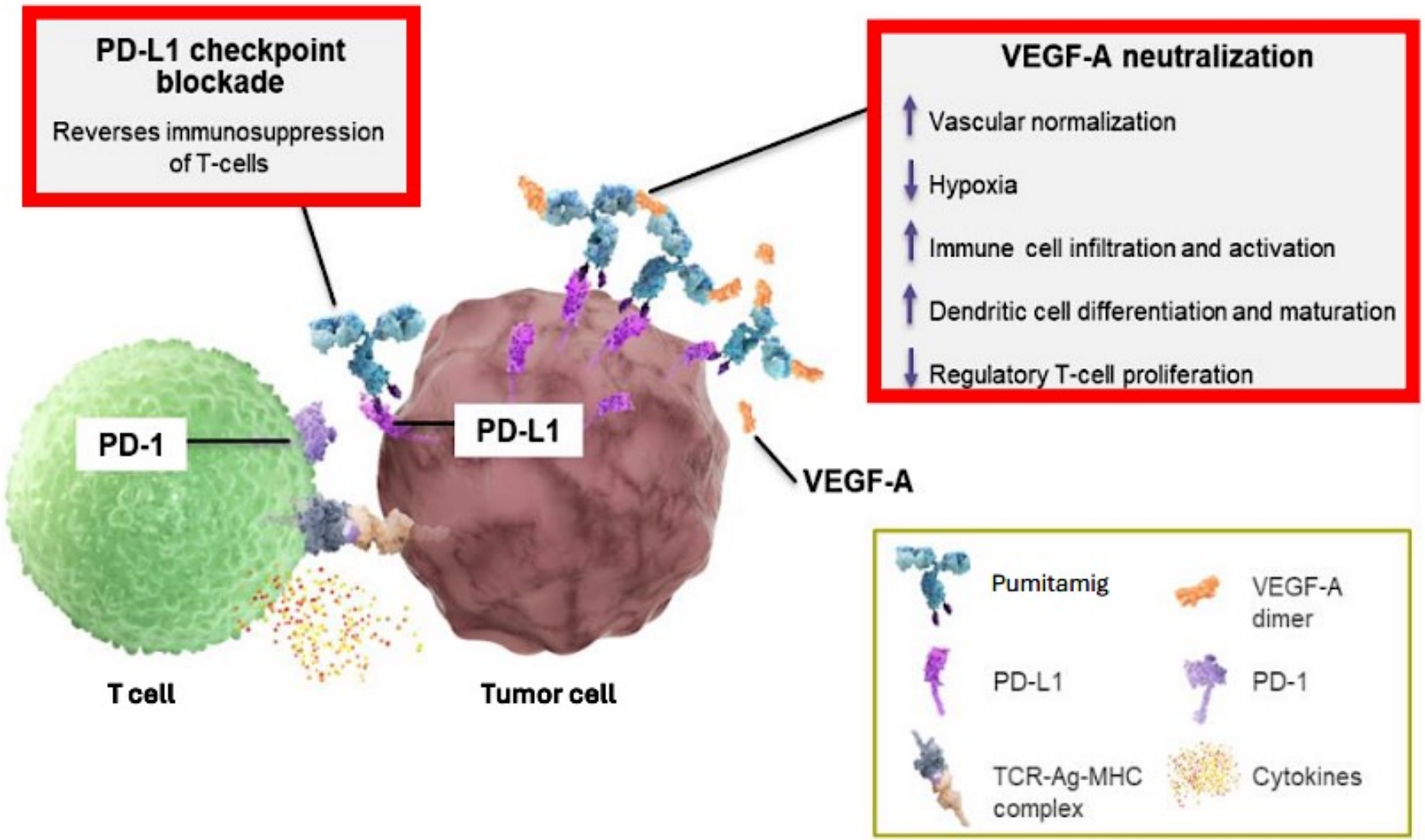
Primary Endpoint: Treatment-Related Adverse Events
Secondary Endpoints: ORR, DoR, DCR, PFS, OS

ORR = objective response rate; DoR = duration of response;
DCR = disease control rate; PFS = progression-free survival;
OS = overall survival; BID = twice a day

***Alisertib dose may be increased by 10 mg BID in the following cohort if 3 or fewer patients experience an event during cycle 1.**

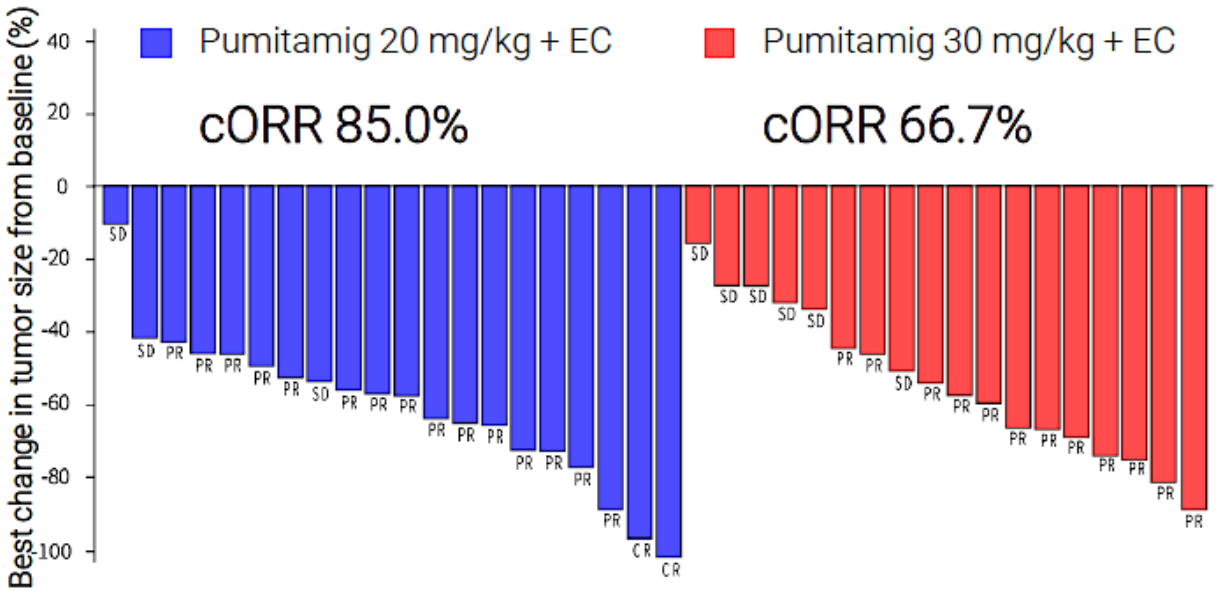
www.clinicaltrials.gov. NCT07465757. Accessed April 2026.

Pumitamig (BNT327) MOA



Heymach et al. WCLC 2025

Tumor response



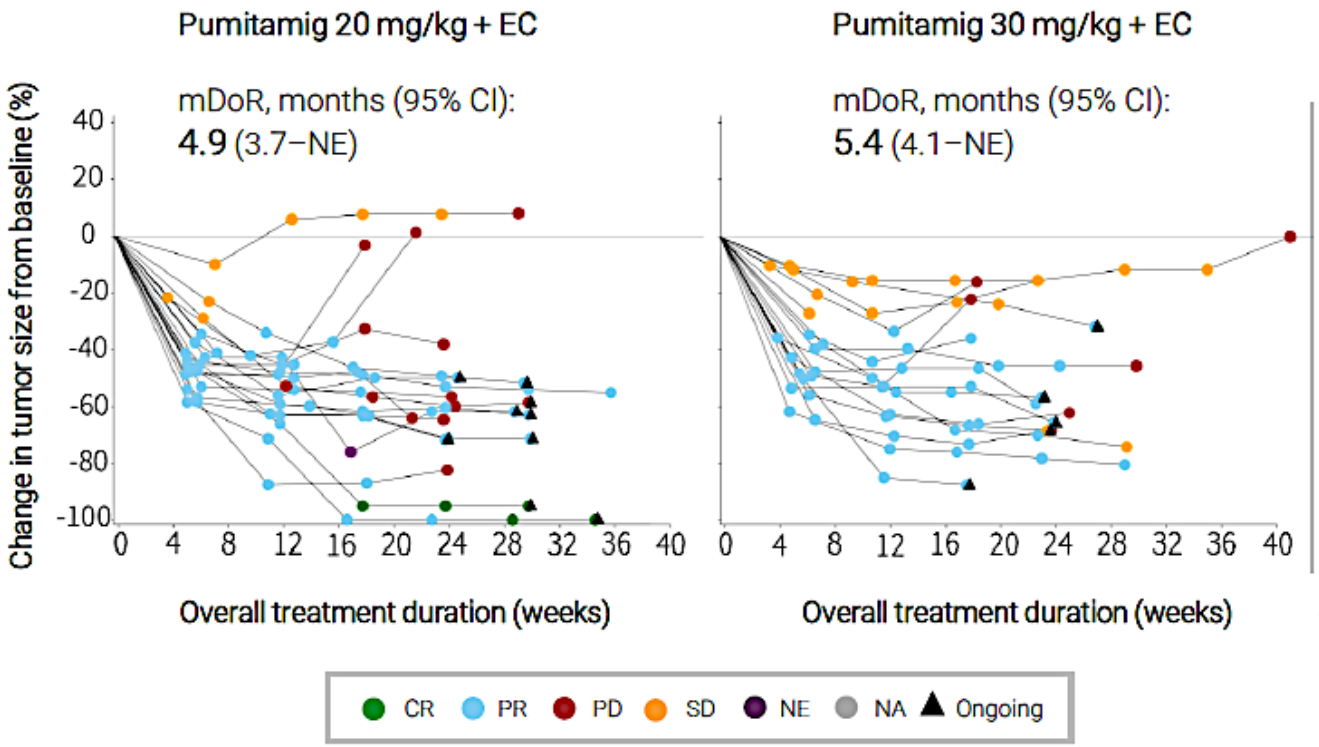
	All (N=43)	Pumitamig 20 mg/kg + EC (N=22)	Pumitamig 30 mg/kg + EC (N=21)
Evaluable patients, n	38	20	18
BOR*, n			
CR	2	2	0
PR	27	15	12
SD	9	3	6
PD	0	0	0
Primary endpoints			
uORR*, % (95% CI)	86.8 (71.9–95.6)	90.0 (68.3–98.8)	83.3 (58.6–96.4)
cORR*, % (95% CI)	76.3 (59.8–88.6)	85.0 (62.1–96.8)	66.7 (41.0–86.7)
Best % change in tumor size*, mean (std dev)	−56.7(20.5)	−60.0 (20.6)	−53.1 (20.5)
Early tumor shrinkage†, % (95% CI)	89.5 (75.2–97.1)	90.0 (68.3–98.8)	88.9 (65.3–98.6)
Secondary endpoint			
DCR*, % (95% CI)	100 (90.7–100)	100 (83.2–100)	100 (81.5–100)

Encouraging antitumor activity observed with both dose levels of pumitamig

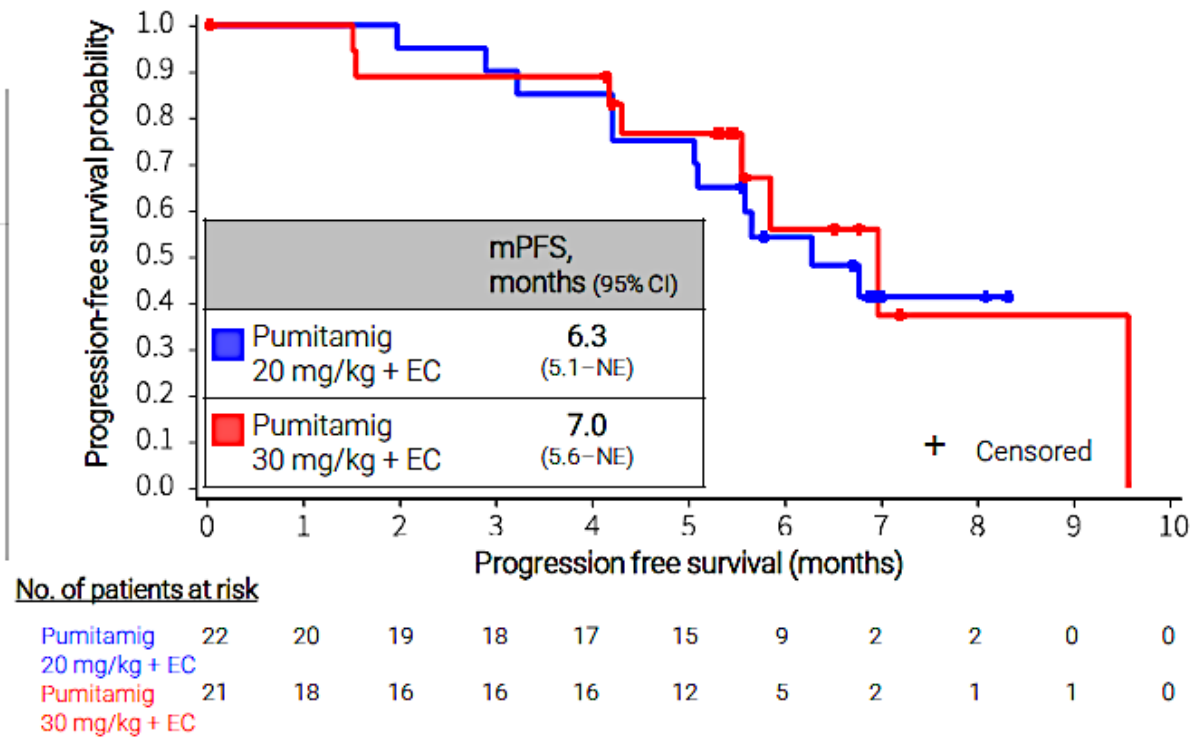
Heymach et al. WCLC 2025

Duration of response and progression-free survival

- mDoR in months (95% CI): **4.9** (4.2–NE) overall.



- mPFS in months (95% CI): **6.8** (5.6–NE) overall.



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Pumitamig-related TEAEs (occurring in ≥5% of overall population)

Patients, n (%)	All (N=43)		Pumitamig 20 mg/kg + EC (N=22)		Pumitamig 30 mg/kg + EC (N=21)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any	18 (41.9)	6 (14.0)	9 (40.9)	1 (4.5)	9 (42.9)	5 (23.8)
Nausea	4 (9.3)	0	4 (18.2)	0	0	0
Fatigue	4 (9.3)	0	3 (13.6)	0	1 (4.8)	0
Constipation	3 (7.0)	0	2 (9.1)	0	1 (4.8)	0
Hypertension	3 (7.0)	2 (4.7)	1 (4.5)	0	2 (9.5)	2 (9.5)
Epistaxis	2 (4.7)	0	1 (4.5)	0	1 (4.8)	0
Hemoptysis	2 (4.7)	1 (2.3)	1 (4.5)	1 (4.5)	1 (4.8)	0
Decreased platelet count	2 (4.7)	1 (2.3)	1 (4.5)	0	1 (4.8)	1 (4.8)
Alopecia	2 (4.7)	0	1 (4.5)	0	1 (4.8)	0
Proteinuria	2 (4.7)	1 (2.3)	0	0	2 (9.5)	1 (4.8)

- Pumitamig-related Grade ≥3 AEs were reported in:

  1 patient with 20 mg/kg
  - Hemoptysis (n=1)

  5 patients with 30 mg/kg
  - Hypertension (n=2)
  - Decreased platelet count (n=1)
  - Proteinuria (n=1)
  - Pulmonary embolism (n=1)

Heymach et al. WCLC 2025

Abstract no. 8104

Safety, tolerability, and preliminary efficacy results from an ongoing Phase 1 study of LB2102, a dnTGFBR2-armored DLL3-targeted autologous CAR-T cell therapy, in patients with relapsed or refractory SCLC or LCNEC

Jacob Sands MD[1]; Alberto Chiappori MD[2]; Ben Creelan MD[2]; Paul Schwarzenberger MD[3]; Mythili Koneru MD PhD[3]; Sahista Vahora PharmD[3]; Christian Davis MS[3]; Da Xu PhD[3]; Chuan Wang PhD[3]; Reinhold Munker MD[4]; Zhonglin Hao MD PhD[4]; and Adam J. Schoenfeld MD[5]

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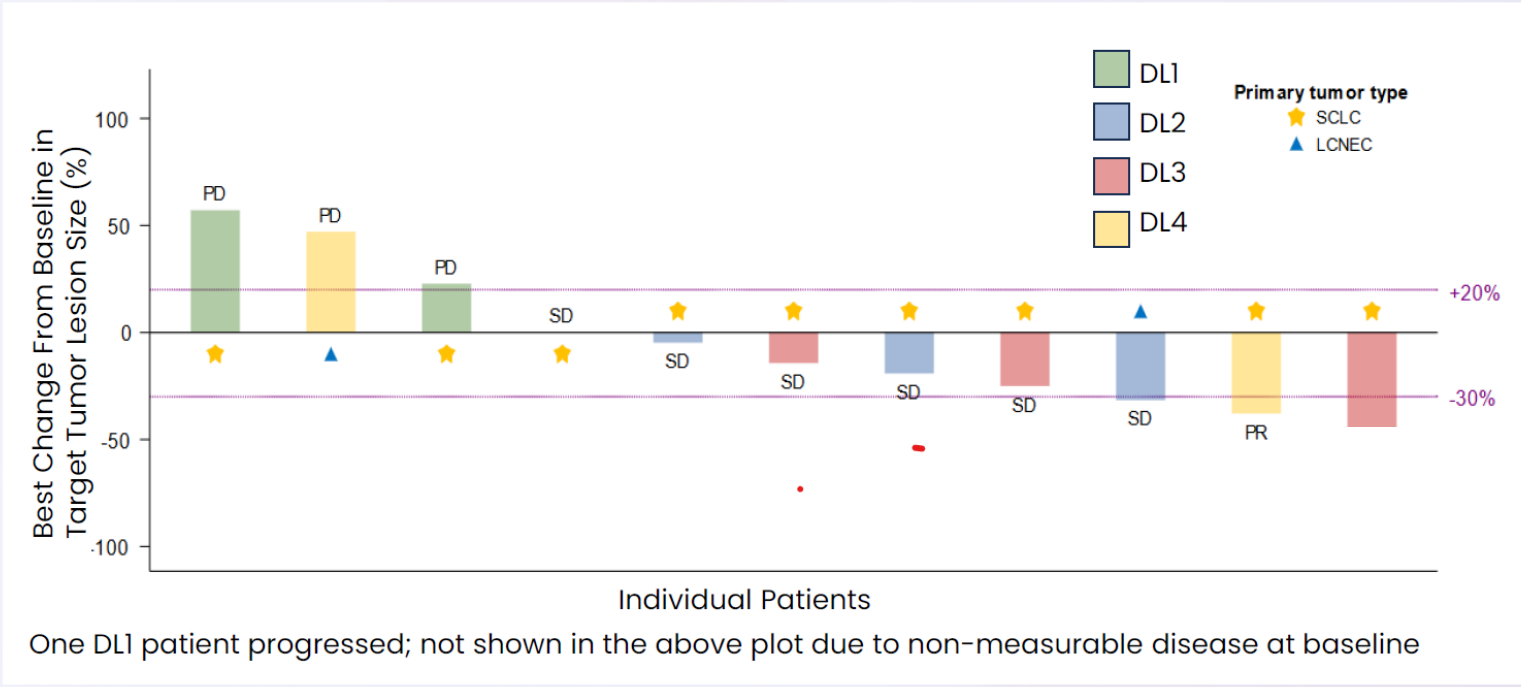
[1]Dana Farber Cancer Institute, Boston, MA; [2]Moffitt Cancer Center, Tampa, FL; [3]Legend Biotech USA Inc, Somerset, NJ; [4]Markey Cancer Center, Lexington, KY; [5]Memorial Sloan Kettering Cancer Center, New York City, NY

ClinicalTrials.gov no: NCT05680922

Phase I Study of LB2102: Efficacy Outcomes

Figure 2. Best Percent Change from Baseline in Target Lesion



One DL1 patient progressed; not shown in the above plot due to non-measurable disease at baseline

Sands J et al. *J Clin Oncol* 2025;43:8104

Phase I Study of LB2102: Efficacy Outcomes

Table 4. Patient Best Responses to LB2102

	DL1: 0.3x10^6 CAR+ T cells/kg [N=3] n (%)	DL2: 1.0x10^6 CAR+ T cells/kg [N=3] n (%)	DL3: 2.0x10^6 CAR+ T cells/kg [N=3] n (%)	DL4: 4.0x 10^6 CAR+ T cells/kg [N=3] n (%)	Overall [N=12] n (%)
Best Response (per RECIST 1.1 criteria) [a]					
CR	0	0	0	0	**0**
PR [b]	0	0	1 (33.3)	1 (33.3)	**2 (16.7)**
SD	0	3 (100)	2 (66.7)	1 (33.3)	**6 (50.0)**
Progressive disease (PD)	3 (100)	0	0	1 (33.3)	**4 (33.3)**
Disease control rate (SD+PR+CR)	0	3 (100)	3 (100)	2 (66.7)	**8 (66.7)**

[a] 1 patient had non-measurable disease at baseline on DL1

[b] 1 patient who achieved a PR with 70% tumor shrinkage also showed **no tumor metabolic activity on PET/CT**

Sands J et al. *J Clin Oncol* 2025;43:8104

Phase I Study of LB2102: Treatment-Emergent Adverse Events

	DL1: 0.3 x 10^6 CAR+ T cells/kg [N=3] n (%)	DL2: 1.0 × 10^6 CAR+ T cells/kg [N=3] n (%)	DL3: 2.0 × 10^6 CAR+ T cells/kg [N=3] n (%)	DL4: 4.0 × 10^6 CAR+ T cells/kg [N=3] n (%)	Overall [N=12] n (%)
Any TEAE [a]	3 (100)	3 (100)	3 (100)	3 (100)	**12 (100)**
Grade 1	0	0	0	1 (33.3)	**1 (8.3)**
Grade 2	3 (100)	0	0	1 (33.3)	**4 (33.3)**
Grade 3	0	1 (33.3)	2 (66.7)	0	**3 (25.0)**
Grade 4	0	2 (66.7)	1 (33.3)	1 (33.3)	**4 (33.3)**
Grade 5	0	0	0	0	**0**
Any Serious TEAE	1 (33.3)	1 (33.3)	1 (33.3)	2 (66.7)	**5 (41.7)**
Related to LB2102	0	0	0	1 (33.3)	**1 (8.3)**
Any AESI	0	0	0	0	**0**
Any DLT	0	0	0	0	**0**
Any TEAE Leading to follow-up discontinuation	0	0	0	0	**0**

[a] The number of patients with at least 1 TEAE is summarized at their maximum severity grade.
AESIs in this trial are CRS Grade ≥ 3, any-grade neurotoxicity, infection Grade ≥ 4, or new primary malignancy.

AESI = adverse event of special interest

Sands J et al. *J Clin Oncol* 2025;43:8104

Consensus or Controversy? Clinical Investigators Discuss and Debate Current Approaches to First- and Second-Line Therapy for HR-Positive Metastatic Breast Cancer

CME/MOC-Accredited Live Webinar

Wednesday, April 15, 2026

5:00 PM – 6:00 PM ET

Faculty

Sara A Hurvitz, MD, FACP

Virginia Kaklamani, MD, DSc

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP Year in Review 2026