Integrating New Advances into Community Oncology Practice

A Multitumor Symposium Hosted in Conjunction with the American Oncology Network

CME/MOC, NCPD and ACPE Accredited

Saturday, August 22, 2026
9:00 AM – 2:20 PM CT

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Agenda

Module 1 — Chronic Lymphocytic Leukemia
Farrukh T Awan, MD, MS, MBA

Module 2 — Gastroesophageal Cancers
Samuel J Klempner, MD

Module 3 — Ovarian and Endometrial Cancer
Shannon N Westin, MD, MPH, FASCO, FACOG

Module 4 — Diffuse Large B-Cell Lymphoma
Ann LaCasce, MD, MMSc

Module 5 — Lung Cancer
Stephen V Liu, MD

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Diffuse Large B-Cell Lymphoma Faculty

Ann LaCasce, MD, MMSc
Associate Professor, Hematology and Medical Oncology
Program Director, Dana-Farber/MGB Fellowship in Hematology/Oncology
Dana-Farber Cancer Institute
Harvard Medical School
Boston, Massachusetts

MODERATOR

Stephen “Fred” Divers, MD
Chief Medical Officer
American Oncology Network
Board Executive
Community Oncology Alliance
Hot Springs, Arkansas

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Dr LaCasce — Disclosures

Advisory Committees	Caribou Biosciences Inc, Genmab US Inc, Kite, A Gilead Company
Consulting Agreements	Genmab US Inc, Pierre Fabre, Takeda Pharmaceuticals USA Inc

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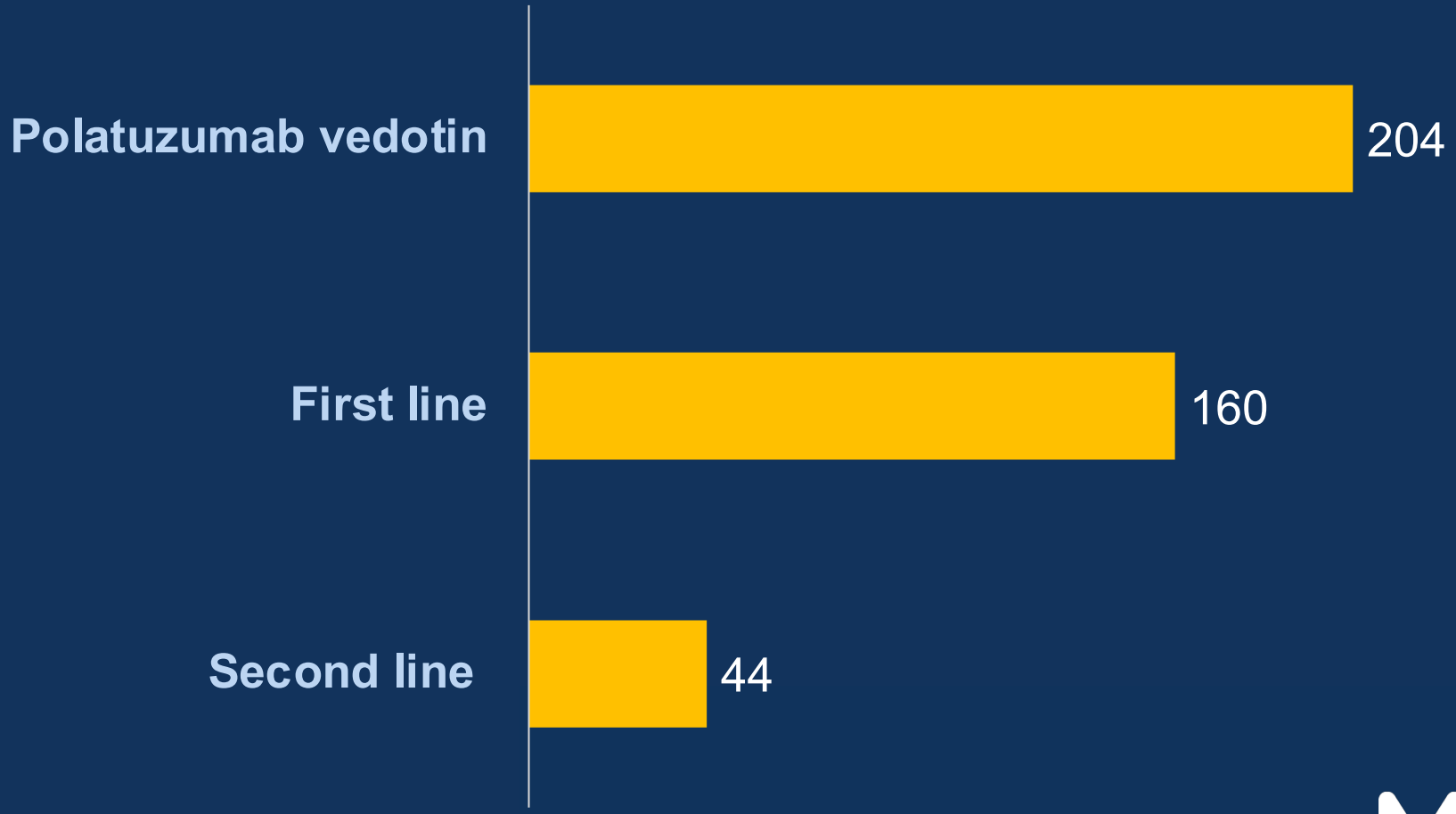
Dr Divers — Disclosures

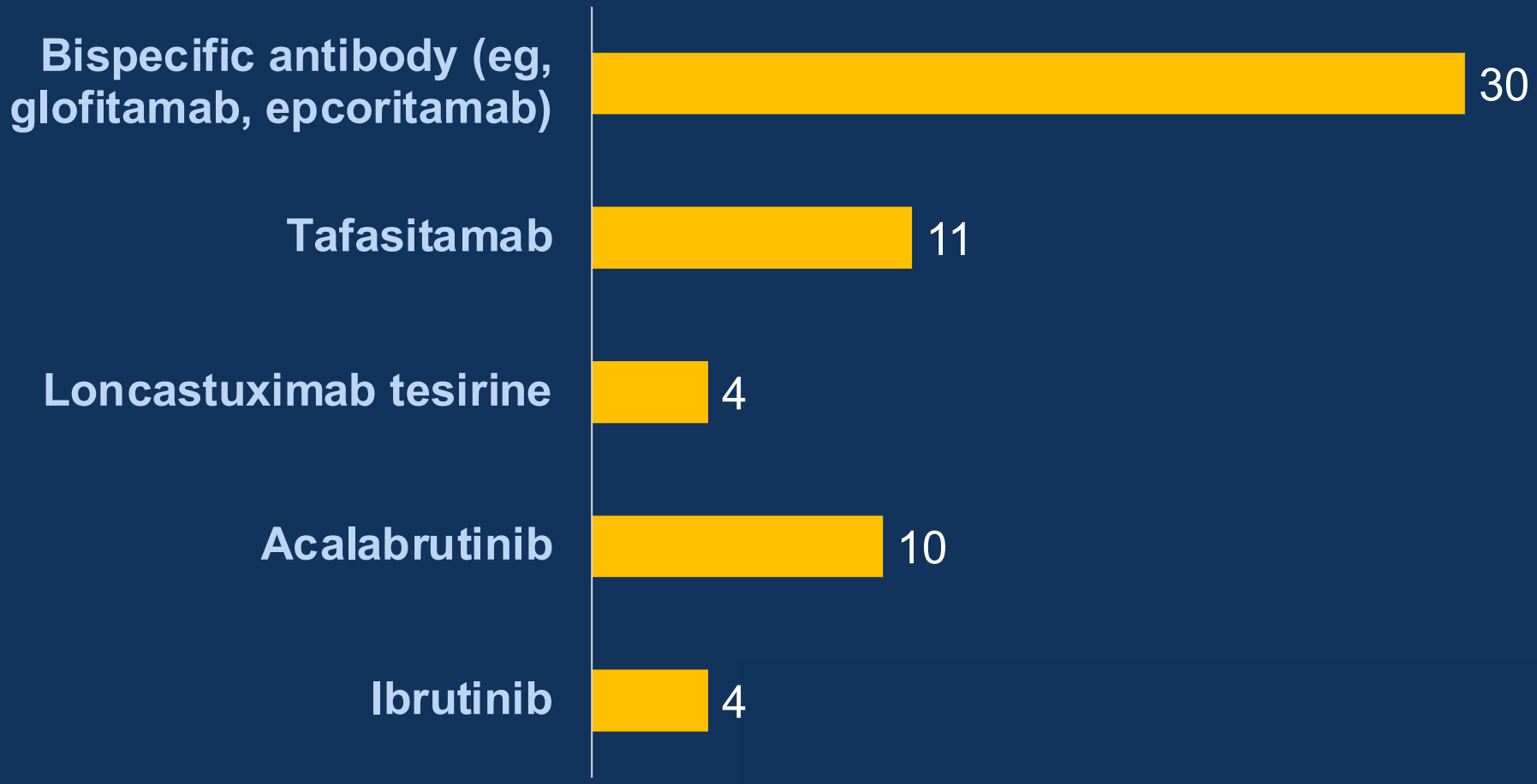
Advisory Committees	Daiichi Sankyo Inc

Snapshot of AON Practice
DLBCL

Snapshot of AON Practice
DLBCL — Polatuzumab vedotin



Snapshot of AON Practice
DLBCL — Other Treatments



Snapshot of AON Practice

DLBCL — CAR (Chimeric Antigen Receptor) T-Cell Therapy

Lisocabtagene maraleucel	0
Axicabtagene ciloleucel	0
Tisagenlecleucel	0

Agenda

Module 4 — Diffuse Large B-Cell Lymphoma: *Dr LaCasce*

- **First-Line Treatment**
- **Bispecific Antibodies and CAR T-Cell Therapy**

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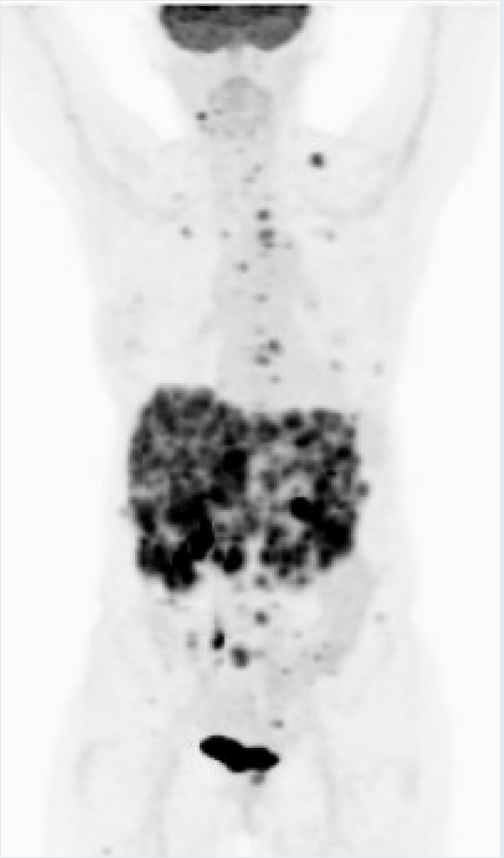
Case Presentation: Dr LaCasce

79-year-old woman who initially noted a neck node in 2025. She then developed shoulder and hip discomfort and was started on 20 mg of prednisone for presumed polymyalgia rheumatica. She then developed abnormal liver function tests and was found to have extensive abnormality within the liver on ultrasound and MRI leading to a biopsy which revealed diffuse large B-cell lymphoma, non-germinal center subtype with a Ki-67 fraction of 80%. PET scan revealed disease replacing much of the liver as well as FDG avid disease within multifocal bony sites as well as small volume nodes in the cervical and supraclavicular regions. IPI was a 4 with LDH 366. In February 2026, she initiated polatuzumab plus R CHP chemotherapy. After 3 cycles of treatment, she is in a metabolic complete remission and will complete her therapy next week.



Baseline PET

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Which first-line therapy would you generally recommend for an otherwise healthy patient with Stage IV activated B-cell (ABC)-type DLBCL with an IPI score of 3?

	65-year-old	80-year-old
 Dr Abramson	R-CHP + polatuzumab vedotin	Dose-reduced R-CHP + polatuzumab vedotin
 Dr Flowers	R-CHP + polatuzumab vedotin	R-CHP + polatuzumab vedotin
 Dr Kamdar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr LaCasce	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Matasar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Phillips	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Prof Salles	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Westin	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin

Which first-line therapy would you generally recommend for an otherwise healthy patient with Stage IV germinal center B-cell (GCB)-type diffuse large B-cell lymphoma (DLBCL) with an International Prognostic Index (IPI) score of 3?

	65-year-old	80-year-old
 Dr Abramson	R-CHP + polatuzumab vedotin	Dose-reduced R-CHP + polatuzumab vedotin
 Dr Flowers	R-CHP + polatuzumab vedotin	R-CHP + polatuzumab vedotin
 Dr Kamdar	R-CHP + polatuzumab vedotin	R-mini-CHOP
 Dr LaCasce	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Matasar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Phillips	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Prof Salles	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Westin	R-CHOP	R-mini-CHOP

R-CHP = rituximab/cyclophosphamide/doxorubicin/prednisone; R-mini-CHOP = rituximab/cyclophosphamide/doxorubicin/vincristine/prednisone (attenuated)

Cases and Discussion Questions

A 76-year-old very fit man presented with throat pain, trouble swallowing. Tonsil biopsy: DLBCL, GCB-type, Ki-67 50%. PET scan showed disease above and below the diaphragm, splenic involvement, IPI 2. Pola-R-CHP just started.

Sean Warsch, MD

How are you selecting patients with newly diagnosed DLBCL for treatment with polatuzumab vedotin/R-CHP?

Given that POLARIX was not powered to look at cell-of-origin subsets, what do you make of those data? Do you use cell of origin to determine who should receive polatuzumab vedotin/R-CHP? Are you using gene expression profiling assays or any other type of testing to aid in this decision?

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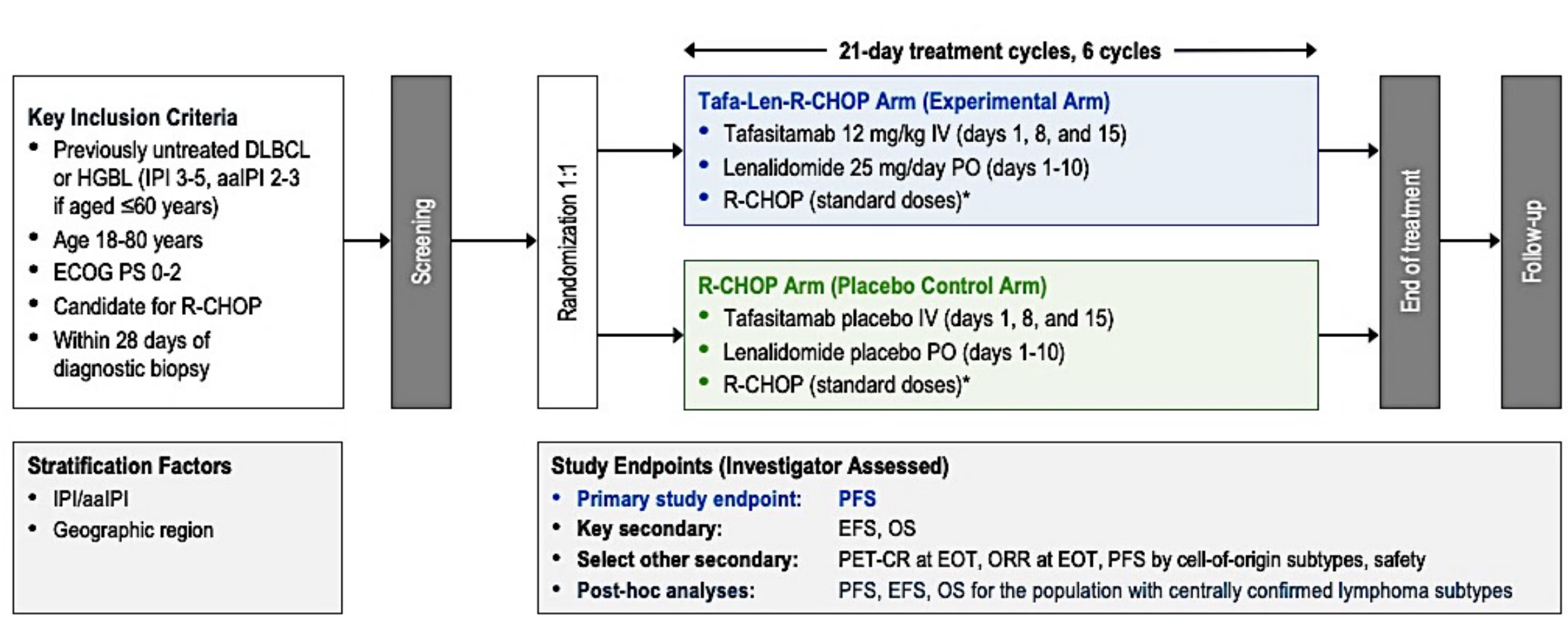
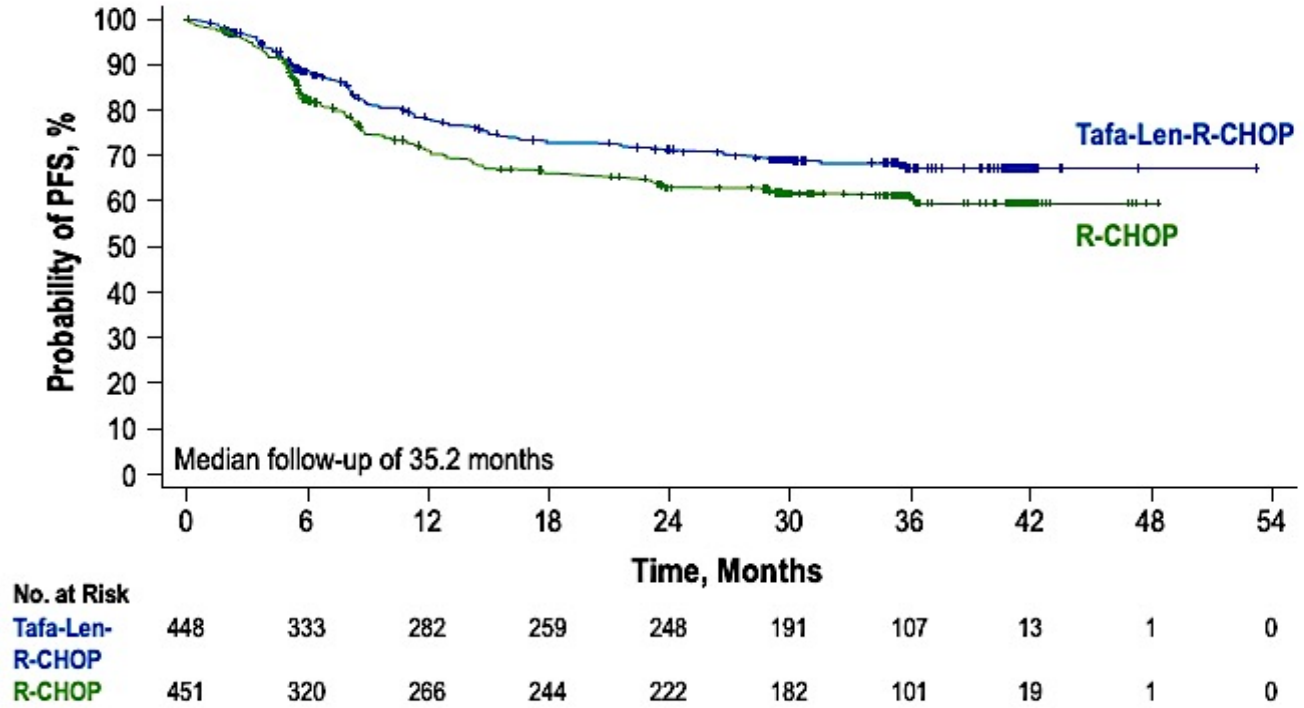
Phase III frontMIND Study Design



*Rituximab administered at 375 mg/m^2 IV (day 1); cyclophosphamide, doxorubicin, and vincristine administered IV (day 1); prednisone/prednisolone administered PO (days 1-5).
aaIPI, age-adjusted IPI; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; EOT, end of treatment; HGBL, high-grade B-cell lymphoma; HRQoL, health-related quality of life; IPI, International Prognostic Index; IV, intravenously; Len, lenalidomide; ORR, objective response rate; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; PO, orally; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

Lenz G et al. ASCO 2026;Abstract LBA7000; Lenz G et al. *Lancet* 2026 June 20;407(10547):2528-41.

Phase III frontMIND Primary Endpoint: Investigator-Assessed Progression-Free Survival



HR 0.75* (*P*=0.0194)
95% CI: 0.59, 0.96

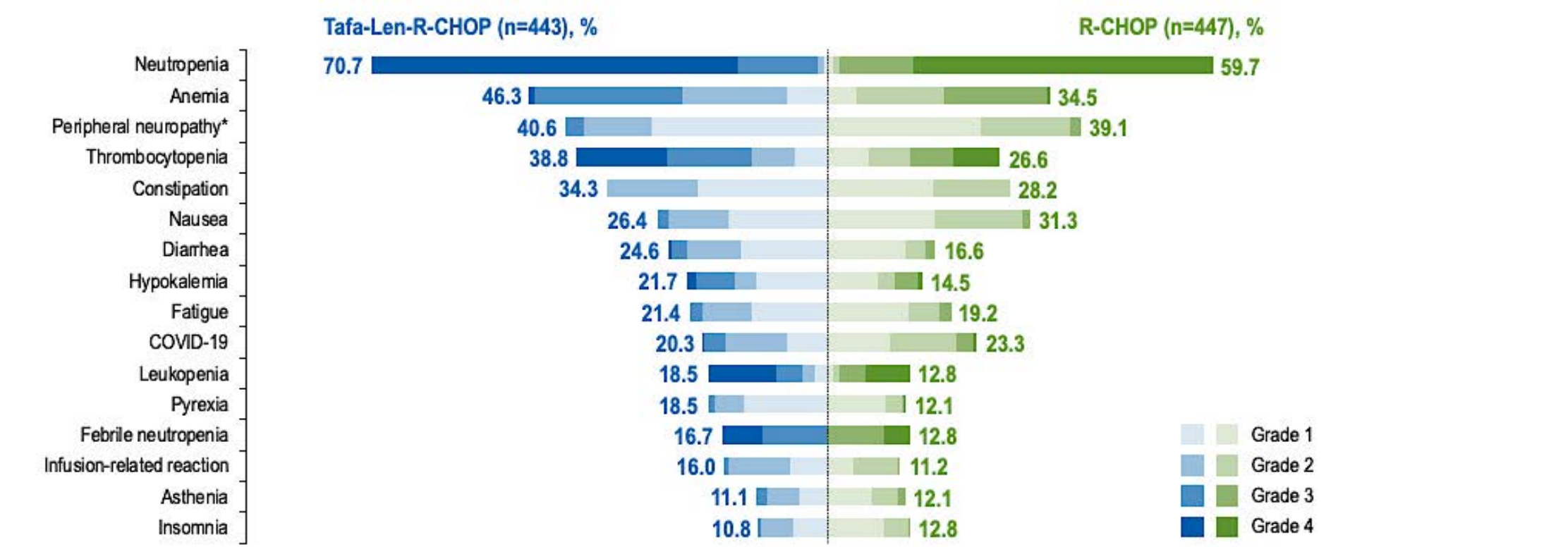
- A **25% reduction in risk of progression or death** demonstrated with Tafa-Len-R-CHOP vs R-CHOP
- **2-year PFS:** 71.1% with Tafa-Len-R-CHOP vs 62.9% with R-CHOP (Δ=**8.2%**)
- **3-year PFS:** 67.3% with Tafa-Len-R-CHOP vs 60.7% with R-CHOP (Δ=**6.6%**)

ITT population. *Calculated using a stratified Cox proportional hazards model.
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; Len, lenalidomide; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone or prednisolone; Tafa, tafasitamab.

In key prespecified subgroup analyses, there are trends toward PFS advantage with Tafa-Len-R-CHOP

Lenz G et al. ASCO 2026;Abstract LBA7000; Lenz G et al. *Lancet* 2026 June 20;407(10547):2528-41.

Phase III frontMIND: Most Frequent Treatment-Emergent Adverse Events



- **Most common** grade ≥3 adverse events were related to **cytopenias**
  - Rate of **serious febrile neutropenia:** 13.3% with Tafa-Len-R-CHOP and 9.8% with R-CHOP

Safety events with Tafa-Len-R-CHOP were manageable and did not affect the delivery of the R-CHOP backbone

Lenz G et al. ASCO 2026;Abstract LBA7000; Lenz G et al. *Lancet* 2026 June 20;407(10547):2528-41.

PHOENIX: A Phase III Trial of Ibrutinib in Combination with R-CHOP as First-Line Therapy for Non-GCB DLBCL

- N = 838 patients randomly assigned to ibrutinib with R-CHOP (n = 419) or placebo with R-CHOP (n = 419).
- Ibrutinib with R-CHOP did not improve EFS in the intent-to-treat (ITT) population (hazard ratio [HR] 0.934) or the activated B-cell (ABC) population (HR 0.949).
- For patients younger than 60, ibrutinib with R-CHOP improved EFS (HR 0.579), PFS (HR 0.556), and OS (HR 0.330) and slightly increased serious adverse events (35.7% vs 28.6%), but the proportion of patients receiving at least 6 cycles of R-CHOP was similar between the treatment arms (92.9% vs 93.0%).
- **Conclusions:**
  - The study did not meet its primary endpoint in the ITT or ABC population.
  - However, patients younger than 60 who received ibrutinib with R-CHOP had significantly improved PFS and OS compared to those receiving R-CHOP alone.

Younes A et al. *J Clin Oncol* 2019;37:1285-9.

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ACCEPT: A Phase Ib/II Study of Acalabrutinib in Combination with R-CHOP as First-Line Therapy for DLBCL

Clinical outcome	Cohort 1 R-CHOP + acalabrutinib 100 mg once daily (n = 7)			Cohort 2/Phase II R-CHOP + acalabrutinib 100 mg twice a day (n = 24)		
	ABC (n = 3)	GCB (n = 3)	Total (n = 6)	ABC (n = 12)	GCB (n = 9)	Total (n = 24)
Overall response, (n)	100% (2)	67.6% (2)	83.3% (5)	91.7% (11)	100% (9)	95.8% (23)
Complete response, (n)	100% (2)	33.3% (1)	66.7% (4)	75% (9)	100% (9)	83.3% (20)
Partial response, (n)	0%	33.3% (1)	16.7% (1)	16.7% (2)	0%	12.5% (3)
PFS at 24 months	80%			94.7%		
OS at 24 months	80%			95.7%		
EFS at 24 months	60%			90.2%		

ABC = activated B cell; GCB = germinal center B-cell like; OS = overall survival; EFS = event-free survival

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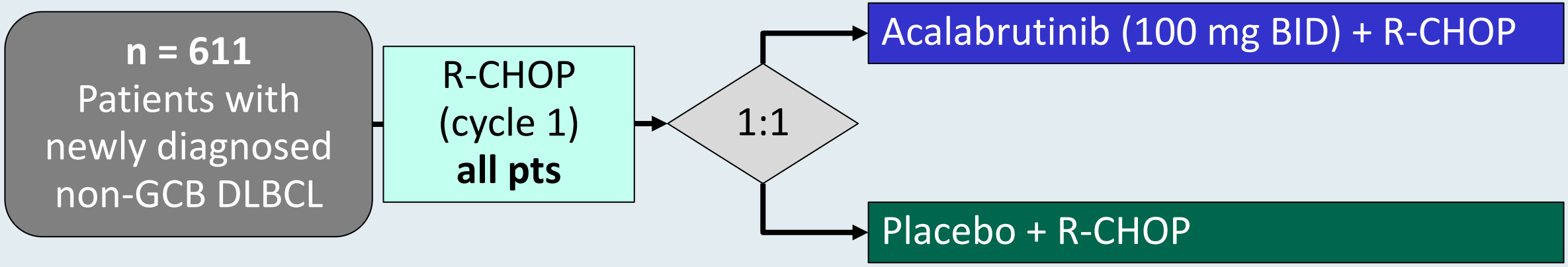
Davies AJ et al. *JCO Oncol Adv* 2026.

Phase III ESCALADE (ACE-LY-312) Study Design



All patients will receive primary prophylaxis with G-CSF accompanying all R-CHOP cycles.

Primary endpoint
PFS

Secondary endpoints
EFS, CR rate, OS, pharmacokinetics, safety

GCB = germinal center B-cell-like; G-CSF = granulocyte-colony stimulating factor; CR = complete response

Sehn LH et al. ASCO 2021;Abstract TPS7572.

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Cases and Discussion Questions

A 67-year-old man presents with Stage IV DLBCL involving bulky retroperitoneal adenopathy, spleen, and bone marrow. IPI is 4. FISH is negative for MYC/Bcl-2 rearrangements, but the tumor is double expressor by IHC. ECOG PS is 1 and cardiac function is normal.

Sunil Babu, MD

When are you employing CNS prophylaxis for DLBCL? Would you do so for this patient?

For which patients with newly diagnosed DLBCL do you envision using front-line tafasitamab/lenalidomide/R-CHOP?

What role, if any, do you foresee for BTK inhibitors in DLBCL?

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Module 4 — Diffuse Large B-Cell Lymphoma: *Dr LaCasce*

- **First-Line Treatment**
- **Bispecific Antibodies and CAR T-Cell Therapy**

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Cases and Discussion Questions

An 82-year-old gentleman received initial treatment with polatuzumab vedotin with dose-adjusted R-CHOP for Stage IV DLBCL with skin involvement. Achieved CR but had recurrence in less than 12 months. He received outpatient epcoritamab step-up dosing. CR, 3 PET scans have all been negative.

Stephen "Fred" Divers, MD

When in the treatment course are you generally administering bispecific antibodies to patients with DLBCL, and how does this vary based on treatment history, patient age/fitness, etc?

Do you adhere to the recommended logistical requirements of the approved bispecifics to the letter? Do you offer treatment breaks to patients who are experiencing a prolonged CR with epcoritamab?

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Cases and Discussion Questions

A 74-year-old woman with DLBCL relapses 10 months after first-line therapy. She receives salvage treatment and autologous transplant but progresses again 9 months later. She has mild renal impairment and is not considered an ideal candidate for CAR T because of frailty and limited caregiver support.

Sunil Babu, MD

Would you favor a CD20 x CD3 bispecific in this setting, and how do you choose between them based on efficacy, CRS risk, treatment duration and convenience?

What are your thoughts on recent data combining antibody-drug conjugates and bispecific antibodies for DLBCL? Are you employing any of these regimens, and if so, for when and for whom? What do you make of the emerging data with epcoritamab/lenalidomide? When can you see yourself using that combination?

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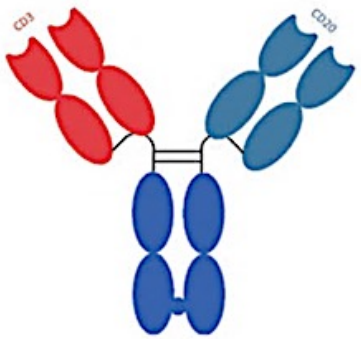
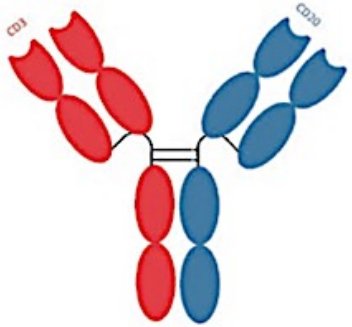
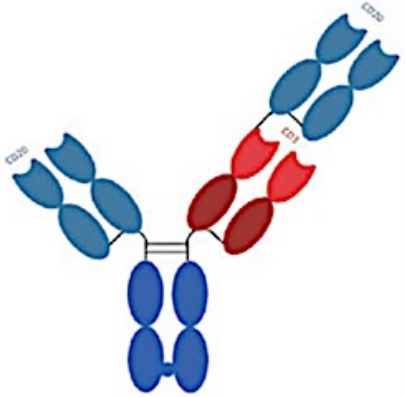
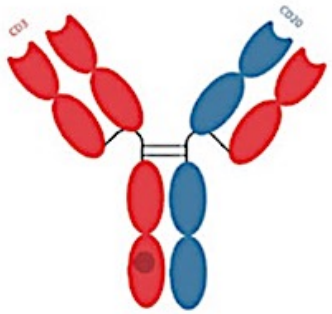
Bispecific Antibodies for DLBCL

MOSUNETUZUMAB	EPCORITAMAB	GLOFITAMAB	ODRONEXTAMAB
CD3xCD20	CD3xCD20	CD3x$(CD20)_2$	CD3xCD20
			
• Monovalent CD3 and monovalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and monovalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and bivalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and monovalent CD20 binding • Fully human IgG4-based antibody

Brijs J et al. *Belg J Hematol* 2023;14(2):67-72.

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Glofitamab for Relapsed/Refractory DLBCL Study: Efficacy (IRC and Investigator Assessed)

Clinical outcome	IRC assessment	Investigator assessment
Complete response, % (n)	39% (61)	37% (58)
Median duration of complete response, mo	Not reached	19.8
Objective response, % (n)	52% (80)	57% (89)
Median duration of objective response, mo	18.4	10.4
Median PFS, mo	4.9	3.8
Median OS, mo	—	11.5

Dickinson MJ et al. *N Engl J Med* 2022 December 15;387(24):2220-31.

IRC = independent review committee

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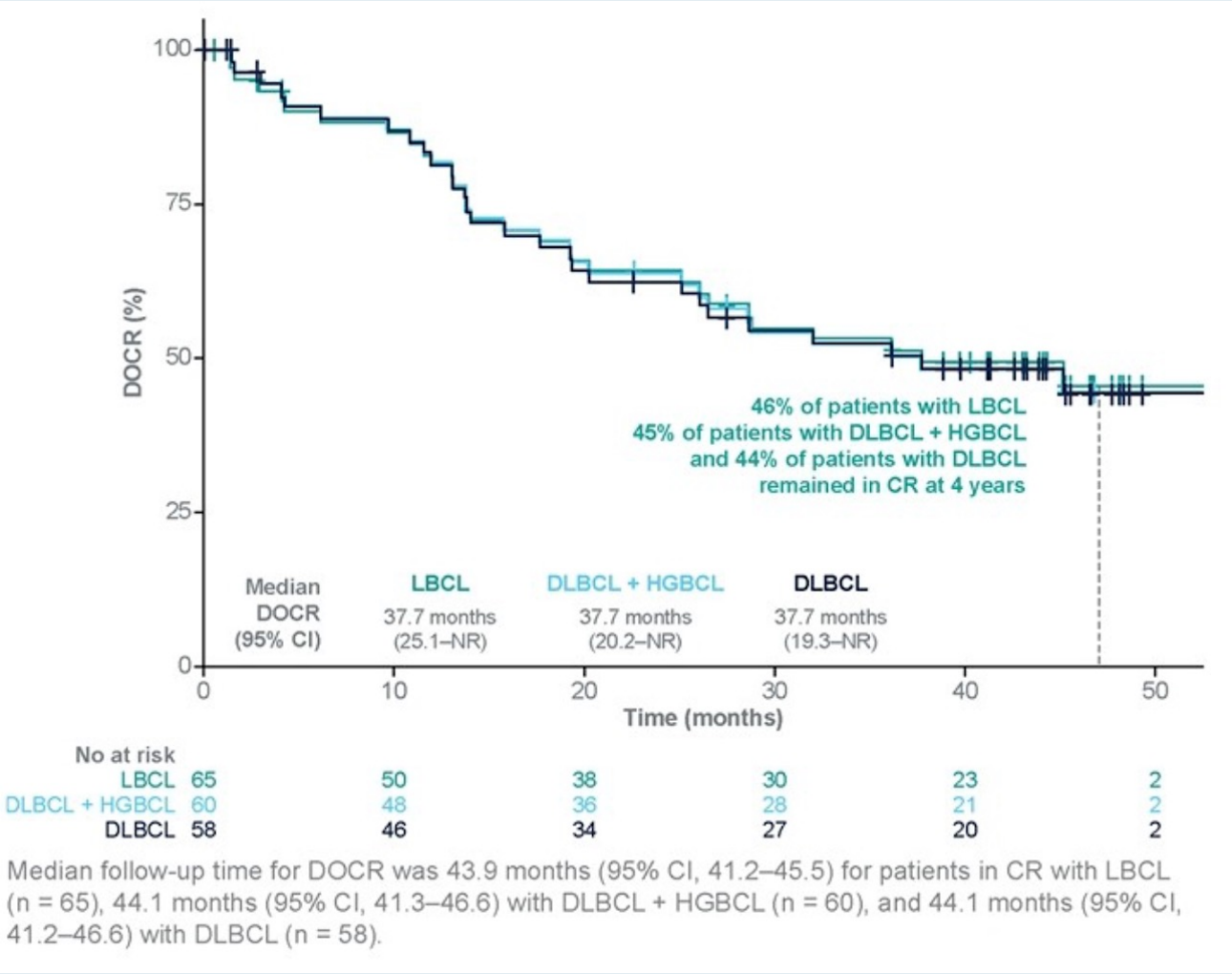
Phase II EPCORE NHL-1 Trial Long-Term Follow-Up: Responses



Median follow-up time for DOCR was 43.9 months (95% CI, 41.2–45.5) for patients in CR with LBCL (n = 65), 44.1 months (95% CI, 41.3–46.6) with DLBCL + HGBCL (n = 60), and 44.1 months (95% CI, 41.2–46.6) with DLBCL (n = 58).

	LBCL (N = 157)	DLBCL + HGBCL (n = 148)	DLBCL (n = 139)
ORR,[a] n (%)	92 (59)	85 (57)	80 (58)
CR	65 (41)	60 (41)	58 (42)
PR	27 (17)	25 (17)	22 (16)
Median DOR,[b] months (95% CI)	20.8 (13.0–32.0)	20.8 (13.0–32.0)	21.7 (13.4–32.0)
48-month estimate, %	34	33	34

[a]Based on investigator assessment using Lugano criteria.[5] [b]Median follow-up time for DOR was 44.3 months (95% CI, 43.0–47.7) for patients in response with LBCL (n = 92), 46.2 months (95% CI, 43.0–48.1) with DLBCL + HGBCL (n = 85), and 45.3 months (95% CI, 43.0–48.2) with DLBCL (n = 80).

LBCL = large B-cell lymphoma; HGBCL = high-grade B-cell lymphoma;
ORR = overall response rate; PR = partial response; DOR = duration of response

Thieblemont C et al. EHA 2026;Abstract PF977.

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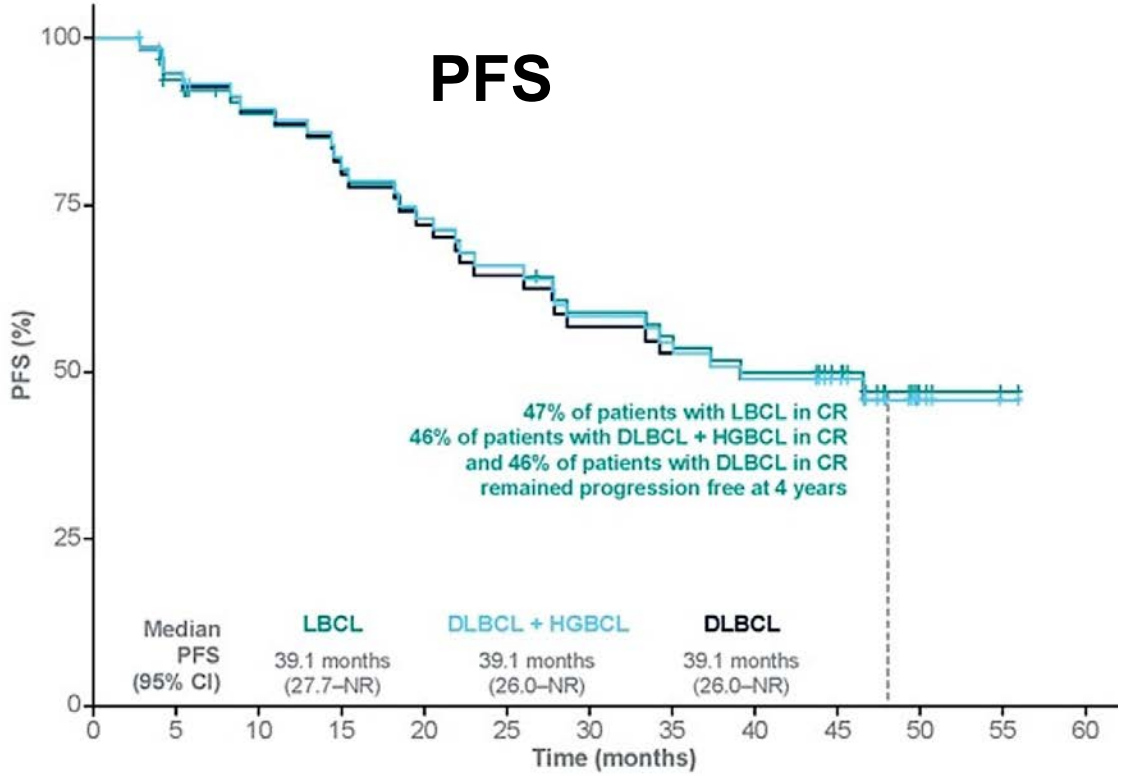
Phase II EPCORE NHL-1 Long-Term Follow-Up: Survival

PFS

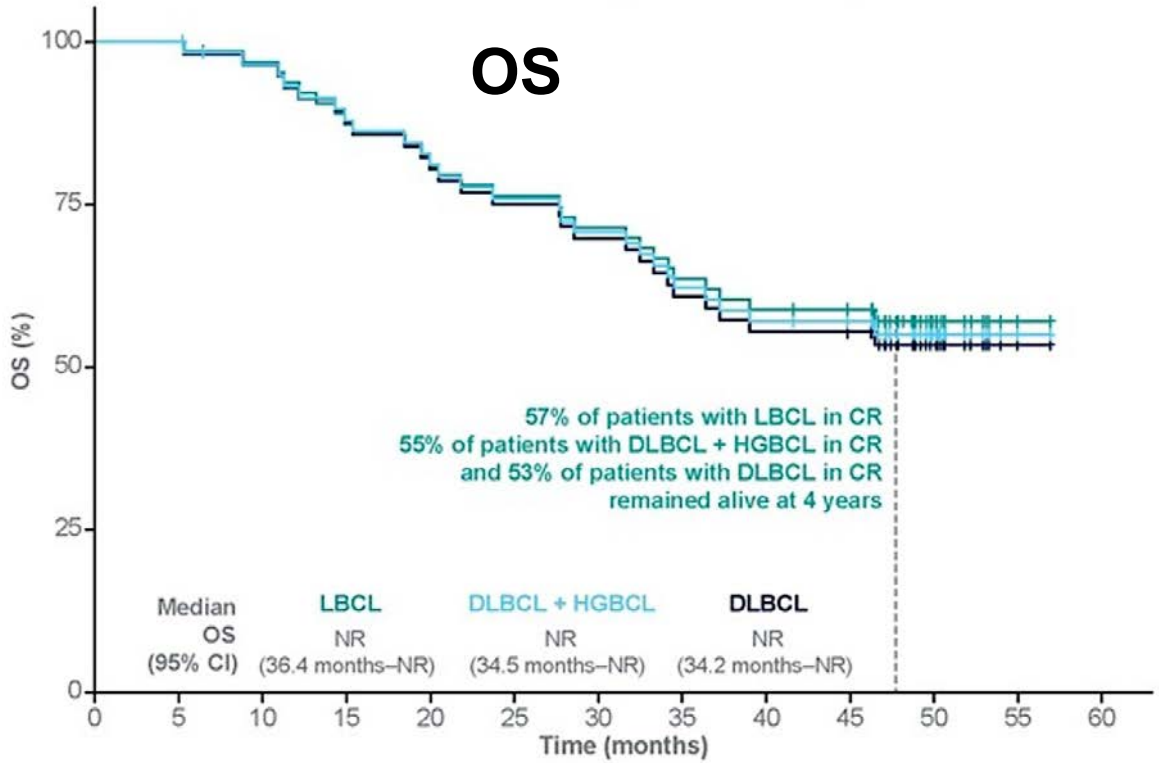


No at risk

LBCL	65	58	51	46	42	38	33	30	28	20	5	1	0
DLBCL + HGBCL	60	54	49	44	40	36	31	28	26	19	5	1	0
DLBCL	58	52	47	42	38	34	29	27	25	18	5	1	0

Median follow-up time for PFS was 46.6 months (95% CI, 44.2–49.3) for patients in CR with LBCL (n = 65), 47.4 months (95% CI, 44.2–49.5) with DLBCL + HGBCL (n = 60), and 46.7 months (95% CI, 44.2–49.7) with DLBCL (n = 58).

OS



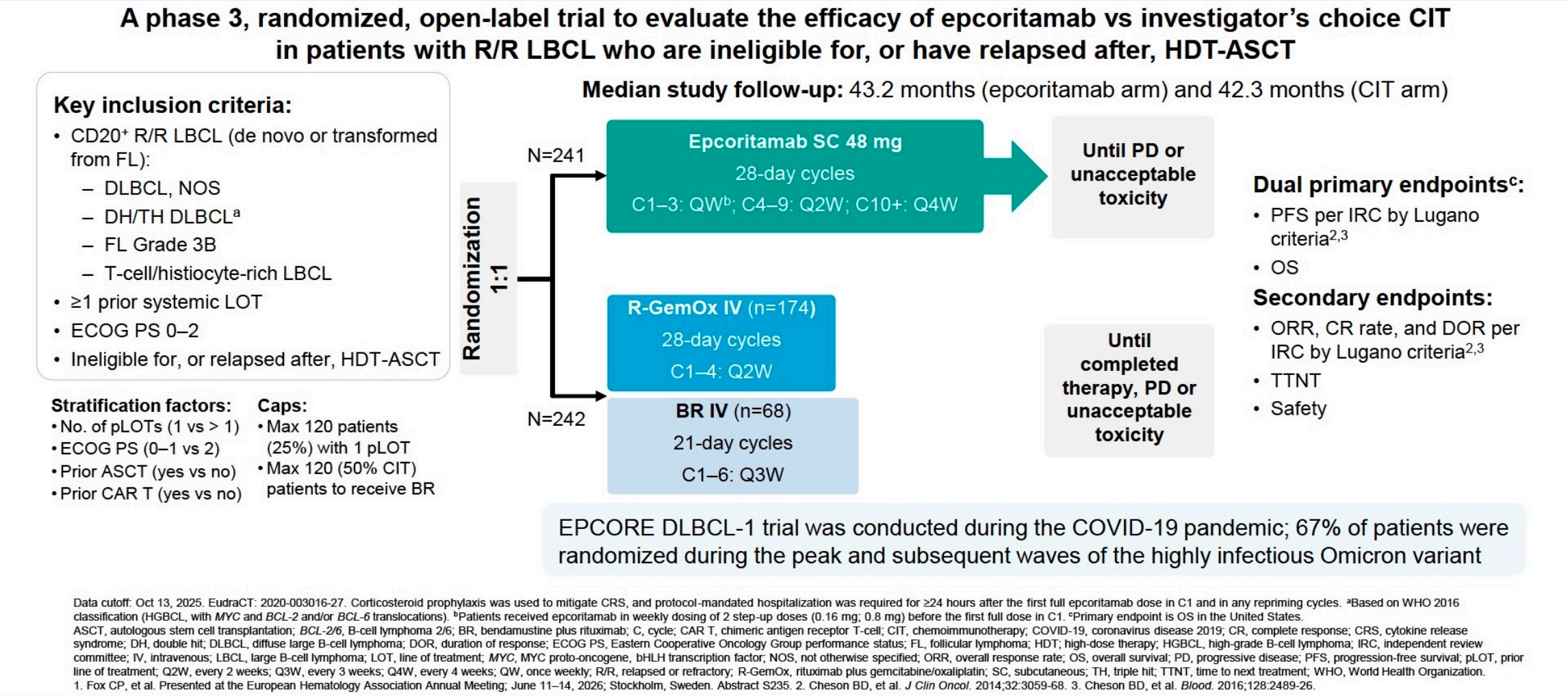
No at risk

LBCL	65	65	61	55	52	48	45	40	37	35	15	1	0
DLBCL + HGBCL	60	60	56	51	48	44	41	36	33	31	15	1	0
DLBCL	58	58	54	49	46	42	39	34	31	30	15	1	0

Median follow-up time for OS was 49.5 months (95% CI, 48.2–50.4) for patients in CR with LBCL (n = 65), 49.8 months (95% CI, 47.9–50.6) with DLBCL + HGBCL (n = 60), and 49.8 months (95% CI, 47.9–50.6) with DLBCL (n = 58).

Thieblemont C et al. EHA 2026;Abstract PF977.

EPCORE DLBCL-1: A Phase III Trial of Epcoritamab versus Investigator's Choice Chemoimmunotherapy (CIT) for R/R LBCL



Data cutoff: Oct 13, 2025. EudraCT: 2020-003016-27. Corticosteroid prophylaxis was used to mitigate CRS, and protocol-mandated hospitalization was required for ≥24 hours after the first full epcoritamab dose in C1 and in any repriming cycles. [a]Based on WHO 2016 classification (HGBCL, with *MYC* and *BCL-2* and/or *BCL-6* translocations). [b]Patients received epcoritamab in weekly dosing of 2 step-up doses (0.16 mg; 0.8 mg) before the first full dose in C1. [c]Primary endpoint is OS in the United States.
ASCT, autologous stem cell transplantation; *BCL-2/6*, B-cell lymphoma 2/6; BR, bendamustine plus rituximab; C, cycle; CAR T, chimeric antigen receptor T-cell; CIT, chemoimmunotherapy; COVID-19, coronavirus disease 2019; CR, complete response; CRS, cytokine release syndrome; DH, double hit; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; HDT; high-dose therapy; HGBCL, high-grade B-cell lymphoma; IRC, independent review committee; IV, intravenous; LBCL, large B-cell lymphoma; LOT, line of treatment; *MYC*, MYC proto-oncogene, bHLH transcription factor; NOS, not otherwise specified; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; pLOT, prior line of treatment; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; QW, once weekly; R/R, relapsed or refractory; R-GemOx, rituximab plus gemcitabine/oxaliplatin; SC, subcutaneous; TH, triple hit; TTNT, time to next treatment; WHO, World Health Organization.
1. Fox CP, et al. Presented at the European Hematology Association Annual Meeting; June 11–14, 2026; Stockholm, Sweden. Abstract S235. 2. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-68. 3. Cheson BD, et al. *Blood*. 2016;128:2489-26.

Fox CP et al. EHA 2026;Abstract S235.

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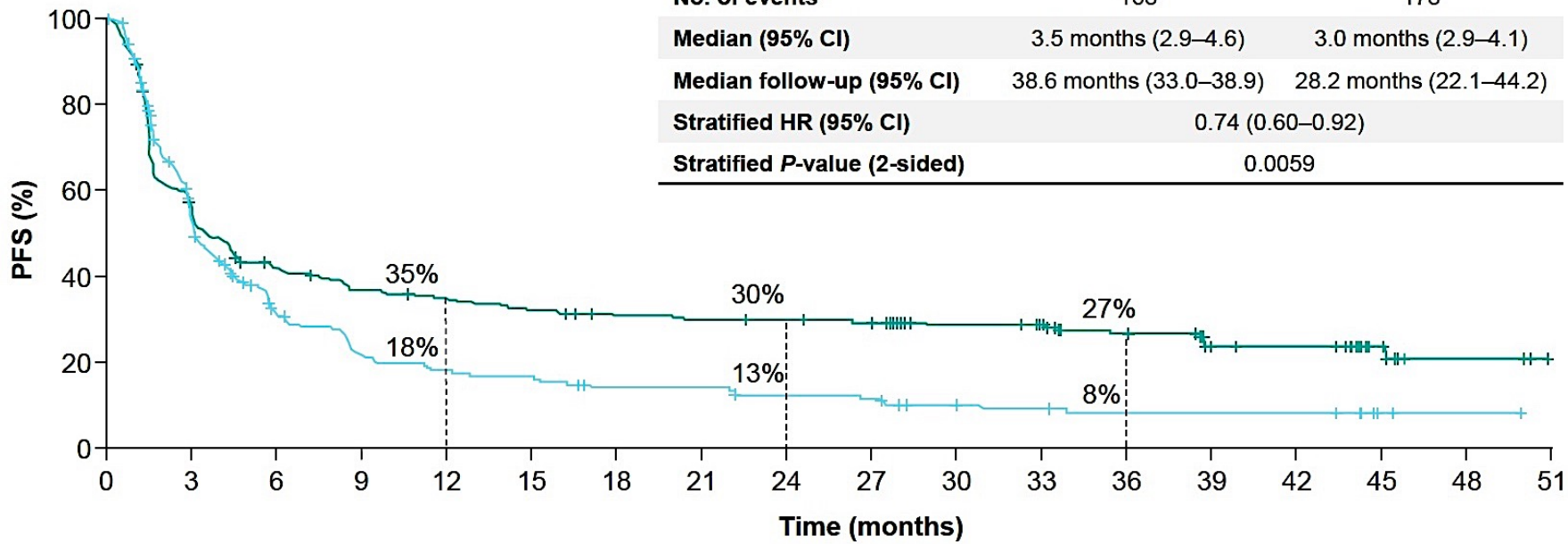
EPCORE DLBCL-1: Efficacy Summary

	Epcoritamab	CIT
No. of events	168	178
Median (95% CI)	3.5 months (2.9–4.6)	3.0 months (2.9–4.1)
Median follow-up (95% CI)	38.6 months (33.0–38.9)	28.2 months (22.1–44.2)
Stratified HR (95% CI)	0.74 (0.60–0.92)	
Stratified *P*-value (2-sided)	0.0059	



Data cutoff: Oct 13, 2025. PFS in the ITT population without censoring for subsequent anti-cancer therapy. Percentages are Kaplan–Meier estimates. HR (epcoritamab vs CIT) is based on stratified Cox regression model with treatment as the sole explanatory variable.
CI, confidence interval; CIT, chemoimmunotherapy; HR, hazard ratio; ITT, intent-to-treat; PFS, progression-free survival.
Fox CP, et al. Presented at the European Hematology Association Annual Meeting; June 11–14, 2026; Stockholm, Sweden. Abstract S235.

- Epcoritamab resulted in clinically meaningful improvement in CR, DOR and duration of complete response
- OS was not significantly different; confounded by COVID-19 mortality and higher use of effective subsequent treatments in the CIT arm

Fox CP et al. EHA 2026;Abstract S235.

EPCORE DLBCL-1: Most Common Treatment-Emergent Adverse Events

	Epcoritamab (N=236)	CIT (N=237)	Epcoritamab (N=236)	CIT (N=237)
	n (%)	n (%)	EAER[a]	EAER[a]
CRS[b]	124 (53)	NA	NA	NA
COVID-19[c]	88 (37)	28 (12)	4.8	3.9
Neutropenia[d]	84 (36)	109 (46)	6.4	30.1
Pyrexia	62 (26)	30 (13)	3.1	4.4
Anemia	61 (26)	84 (35)	2.6	15.6
Injection-site reactions[e]	51 (22)	NA	NA	NA
Diarrhea	47 (20)	30 (13)	2.1	4.3
Thrombocytopenia[f]	42 (18)	125 (53)	1.9	28.3
Nausea	32 (14)	74 (31)	1.4	11.3

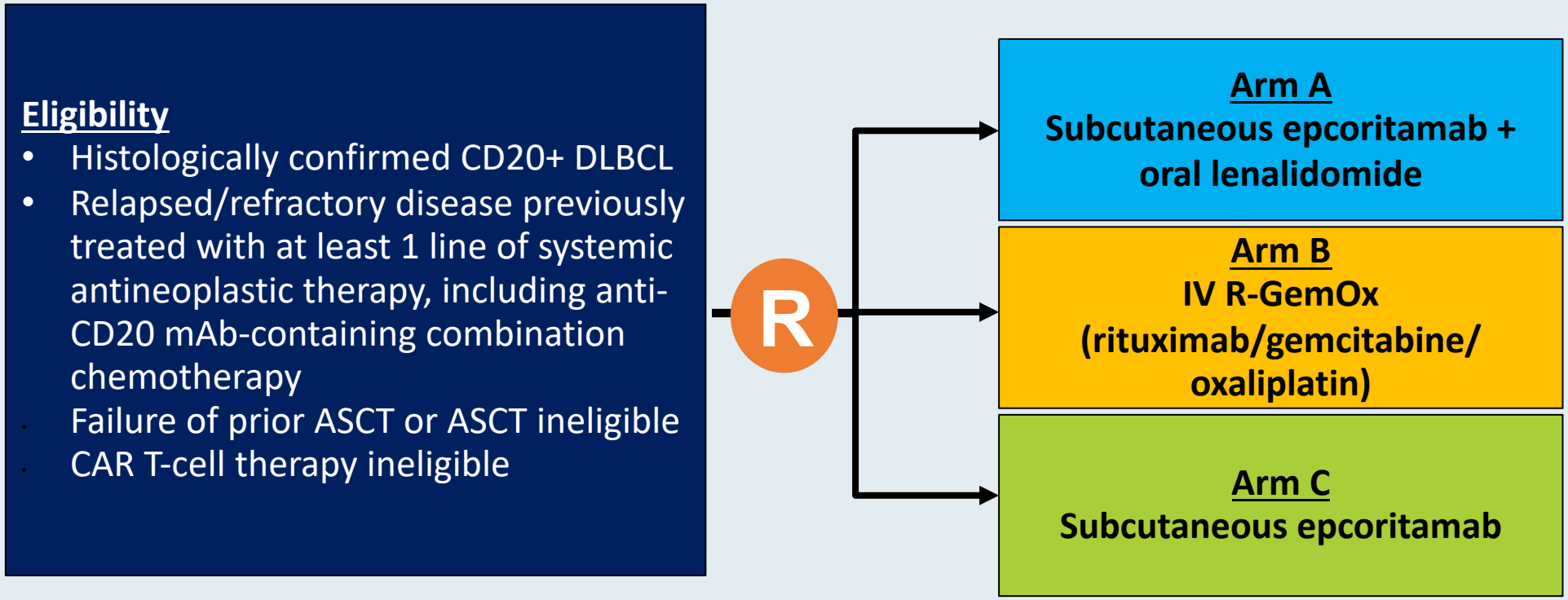
- Higher rates of Grade 3–4 infections (30% vs 12%) were reported in the epcoritamab vs the CIT arm, with Grade 3–4 infection EAERs of 4.3 vs 4.9, respectively
- Febrile neutropenia was reported in 2% of patients in the epcoritamab arm and 5% in the CIT arm; EAERs were 0.2 vs 1.7, respectively
- ICANS events were reported in 9 patients (Grade 1–2 in 7; Grade 3–4 in 2) in the epcoritamab arm

Data cutoff: Oct 13, 2025. [a]EAER equals the number of events*100/patient-months of exposure. [b]Most CRS events were Grade 1–2 (117/124 [94%]), with the remaining 7/124 (6%) Grade 3. [c]Includes preferred terms COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [d]Includes preferred terms neutropenia and neutrophil count decreased. [e]Includes preferred terms injection-site reaction, injection-site reaction erythema, injection-site reaction pain, injection-site reaction pruritus, injection-site reaction rash, injection-site reaction inflammation, injection-site reaction swelling. [f]Includes preferred terms platelet count decreased and thrombocytopenia.
CIT, chemoimmunotherapy; COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome; EAER, exposure-adjusted event rate; ICANS, immune effector cell-associated neurotoxicity syndrome; NA, not applicable; TEAE, treatment-emergent adverse event.
Fox CP, et al. Presented at the European Hematology Association Annual Meeting; June 11–14, 2026; Stockholm, Sweden. Abstract S235.

Fox CP et al. EHA 2026;Abstract S235.

Phase III EPCORE DLBCL-4 Study Design

Trial identifier: NCT06508658 (closed)



Primary endpoint (Arm A vs Arm B): Progression-free survival

Secondary endpoints (Arm A vs Arm B): Complete response, overall survival, minimal residual disease negativity rate

www.clinicaltrials.gov. Accessed August 2026.

RTP RESEARCH TO PRACTICE

Positive Phase III Results Announced for Epcoritamab with Lenalidomide for Patients with Relapsed or Refractory DLBCL

Press Release: June 29, 2026

"[The manufacturer] today announced topline results from the **Phase 3 EPCORE DLBCL-4 trial** evaluating the combination of epcoritamab, a T-cell engaging bispecific antibody, and lenalidomide, compared to rituximab plus gemcitabine plus oxaliplatin (R-GemOx) in adult patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) who received at least one prior line of therapy**. Based on topline results from the prespecified primary analysis, the trial met its primary endpoint, demonstrating statistically significant and clinically meaningful improvement in progression-free survival (PFS).** The risk of disease progression and death was reduced by 60% (HR 0.40 [95% CI 0.30, 0.55]; *p*-value <0.0001) and 56% (HR 0.44 [95% CI 0.33, 0.60]; *p*-value <0.0001), based on different censoring rules in the US and outside the US, respectively.

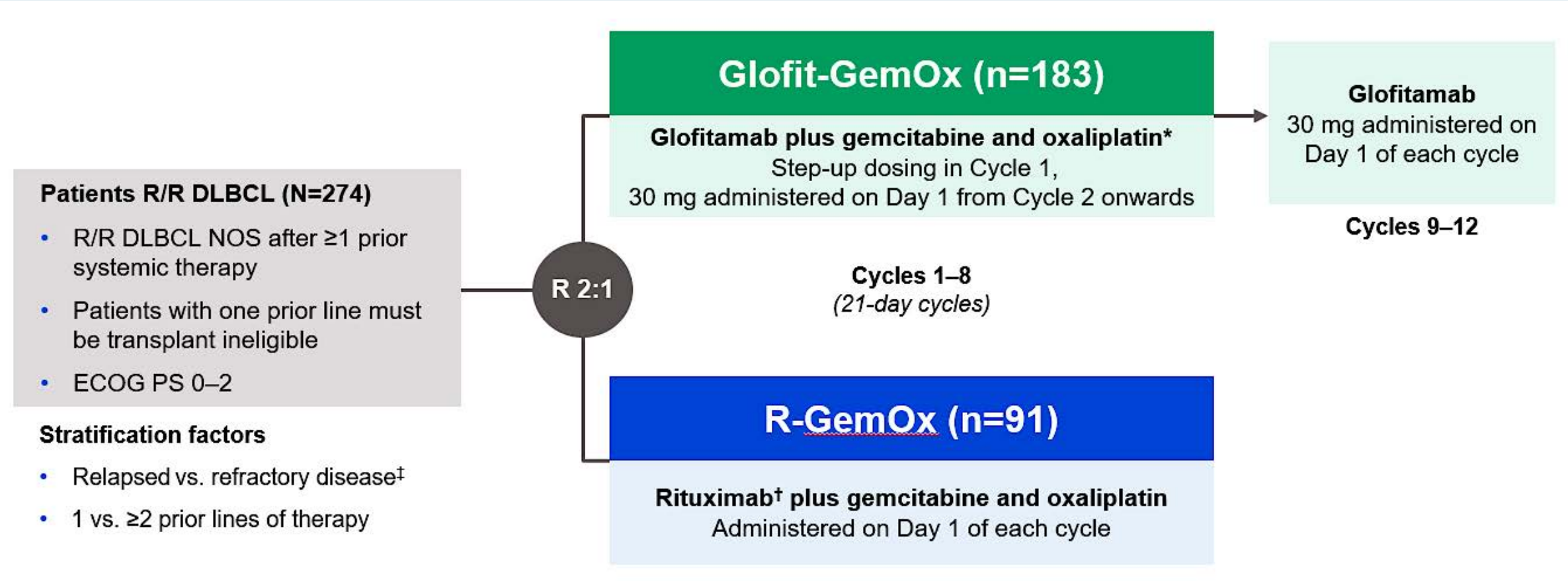
The safety profile of epcoritamab when administered in combination with lenalidomide was consistent with the known safety profiles of the individual agents (epcoritamab and lenalidomide).

Data will be submitted for presentation at a future medical meeting."

https://news.abbvie.com/2026-06-29-AbbVie-Announces-Positive-Phase-3-Results-for-Epcoritamab-Plus-Lenalidomide-in-Patients-with-Relapsed-or-Refractory-Diffuse-Large-B-Cell-Lymphoma

RTP RESEARCH TO PRACTICE

Phase III STARGLO Study Design



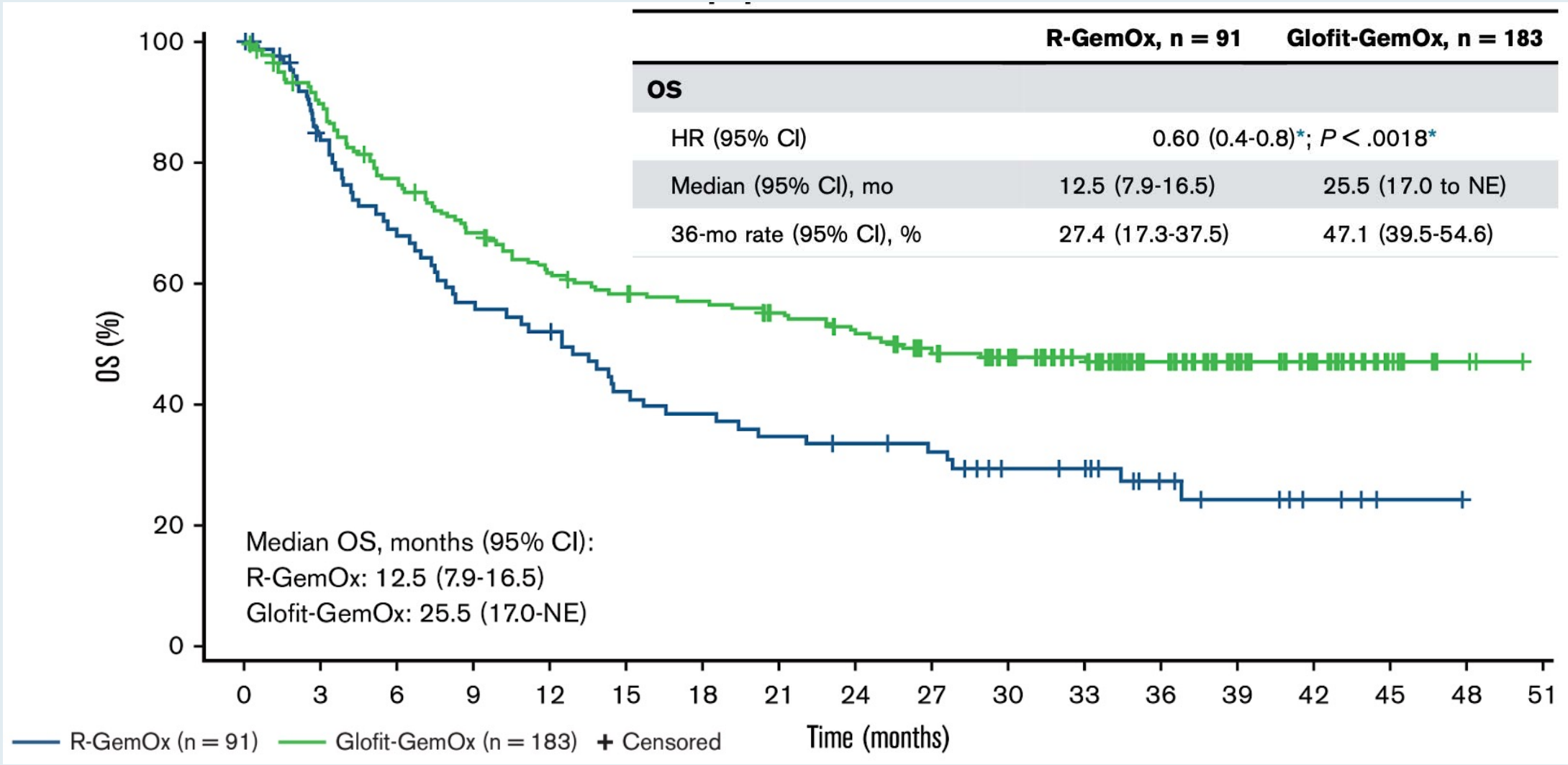
Primary endpoint:
Overall survival

Secondary endpoints:
Progression-free survival, objective response rate, DoR

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

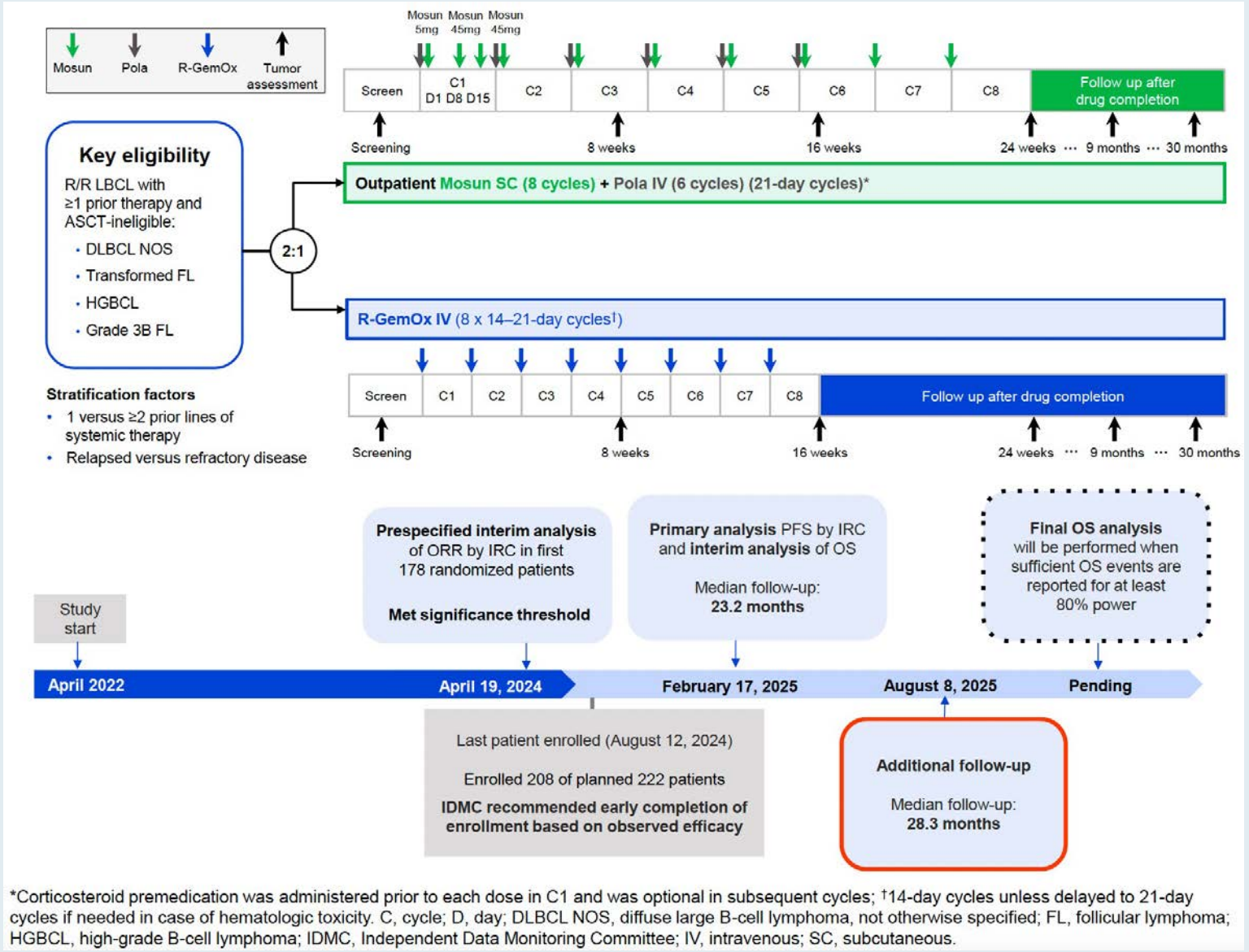
Phase III STARGLO 3-Year Follow-Up: OS (Primary Endpoint)

	R-GemOx, n = 91	Glofit-GemOx, n = 183
OS		
HR (95% CI)	0.60 (0.4-0.8)*; $P < .0018$*	
Median (95% CI), mo	12.5 (7.9-16.5)	25.5 (17.0 to NE)
36-mo rate (95% CI), %	27.4 (17.3-37.5)	47.1 (39.5-54.6)



Abramson JS et al. *Blood Adv* 2026 August 11;10(15):5367-77.

Phase III SUNMO Study Design

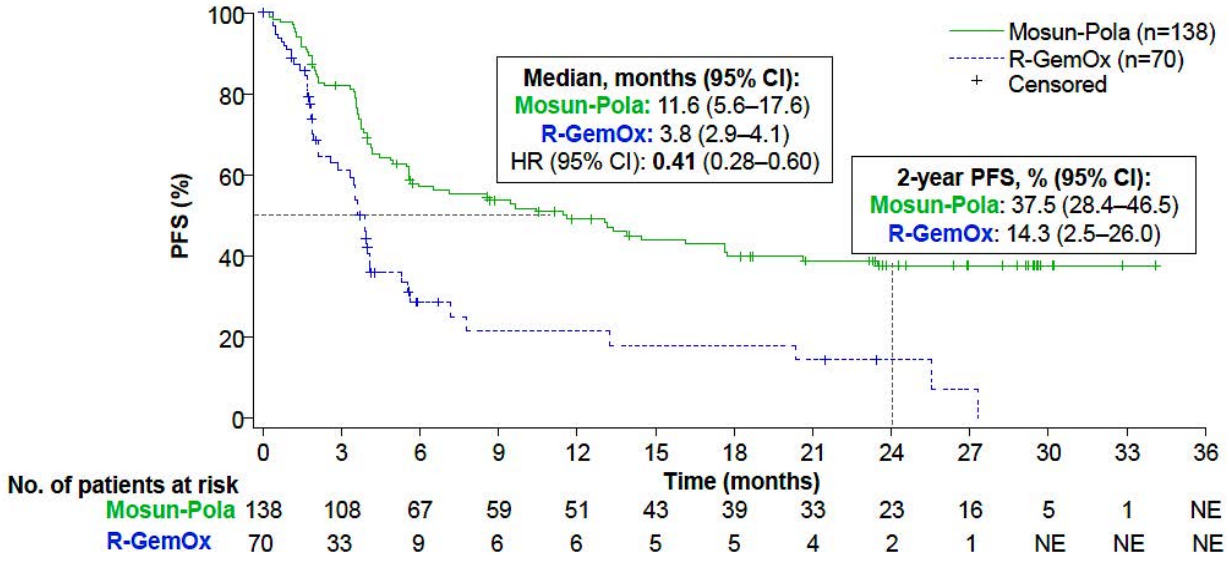


*Corticosteroid premedication was administered prior to each dose in C1 and was optional in subsequent cycles; †14-day cycles unless delayed to 21-day cycles if needed in case of hematologic toxicity. C, cycle; D, day; DLBCL NOS, diffuse large B-cell lymphoma, not otherwise specified; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; IDMC, Independent Data Monitoring Committee; IV, intravenous; SC, subcutaneous.

Budde LE et al. EHA 2026;Abstract PF968.

RTP RESEARCH TO PRACTICE

Phase III SUNMO: PFS, ORR (Dual Primary Endpoints)



% (95% CI), unless otherwise stated	Mosun-Pola (n=138)	R-GemOx (n=70)
ORR	70.3% (61.9–77.8)	40.0% (28.5–52.4)
CR	51.4% (42.8–60.0)	24.3% (14.8–36.0)
DOR		
Median, months	18.8 (11.5–NE)	6.0 (3.7–23.9)
2-year rate	47.9% (37.0–58.8)	15.4% (0.0–39.8)
DOCR		
Median, months	NR	18.3 (3.9–NE)
2-year rate	62.5% (50.1–74.9)	22.0% (0.0–56.2)

PFS is censored at earliest of NALT or two or more missing tumor assessments, whichever occurred first.
NALT, new anti-lymphoma therapy; NE, not evaluable; NR, not reached.

ORR = objective response rate

Budde LE et al. EHA 2026;Abstract PF968.

RTP RESEARCH TO PRACTICE

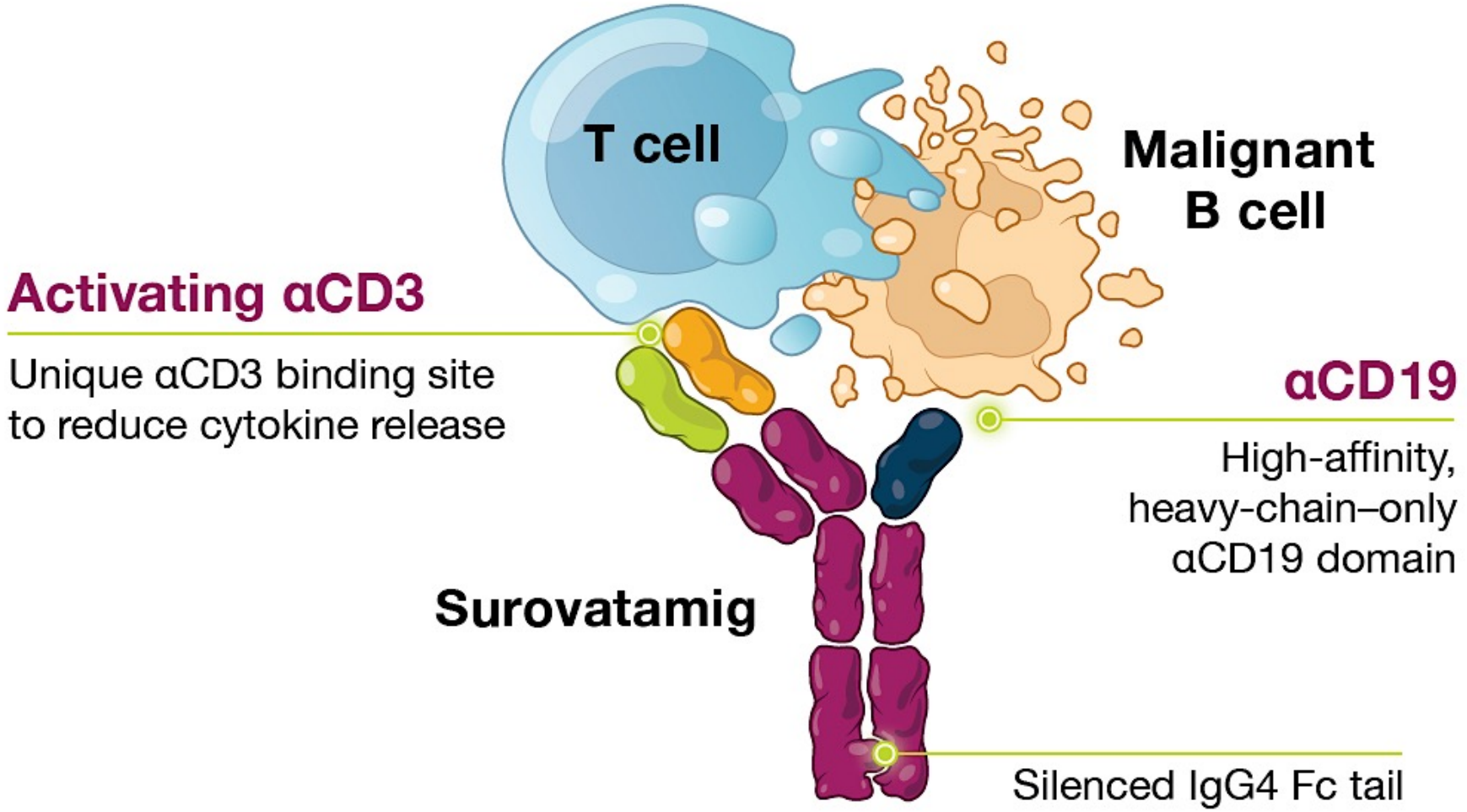
Select Ongoing Trials of Epcoritamab and Glofitamab for Newly Diagnosed DLBCL

Trial identifier	Phase	Treatment arms	Primary completion date
EPCORE DLBCL-2 (NCT05578976)	III	• Epcoritamab + R-CHOP followed by epcoritamab • R-CHOP followed by rituximab	June 2027
SKYGLO (NCT06047080)	III	• Glofitamab + pola-R-CHP • Pola-R-CHP	October 2027

www.clinicaltrials.gov. Accessed August 2026.

RTP RESEARCH TO PRACTICE

Surovatamig (AZD0486): A CD19 x CD3 Bispecific T-Cell Engager



Cheah C et al. ASH 2025;Abstract 3747.

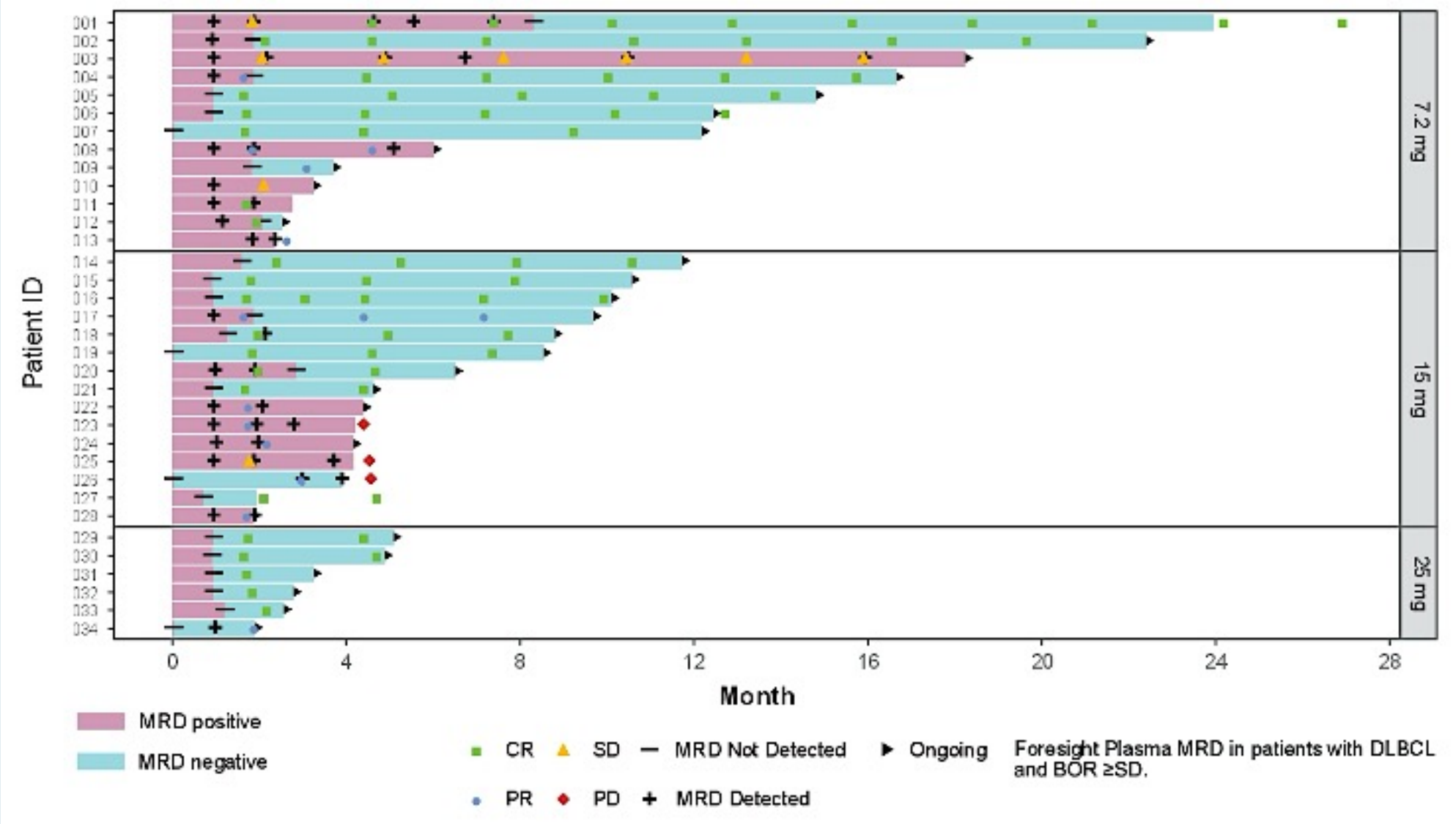
Phase I Surovatamig Study: Responses by Target Dose (≥7.2 mg)

	Overall (N=58)			CAR-T Naive (n=31)			CAR-T Exposed (n=27)		
	n	ORR	CR rate	n	ORR	CR rate	n	ORR	CR rate
7.2 mg	24	46%	33%	9	67%	44%	15	33%	27%
15 mg	26	62%	39%	16	75%	38%	10	40%	40%
25 mg	8	75%	63%	6	83%	67%	2	50%	50%

Kim TM et al. ASCO 2025;Abstract 7046.

RTP RESEARCH TO PRACTICE

Phase I Surovatamig Study: MRD in Plasma by Target Dose (≥7.2 mg)



MRD = minimal residual disease

Kim TM et al. ASCO 2025;Abstract 7046.

RTP RESEARCH TO PRACTICE

Phase I Surovatamig Study: Safety

Most common AEs (≥15%)	Any grade	Grade 3	Grade 4
CRS	42 (49)	0	0
Infections and infestations[b]	39 (45)	10 (12)	1 (1)
Neutropenia	29 (34)	9 (10)	15 (17)
Constipation	21 (24)	0	0
Anemia	20 (23)	14 (16)	0
Fatigue	20 (23)	3 (3)	0
ICANS	17 (20)	5 (6)	0
Hypogammaglobulinemia	16 (19)	0	0
Nausea	16 (19)	1 (1)	0
Diarrhea	14 (16)	0	0
Pyrexia	13 (15)	0	0

Values are n (%).
[a]All patients eventually received TD.
[b]Grouped by system organ class. One grade 5 event reported (pneumonia). COVID-19 infections reported in 9 (10%) patients (n=3 grade 1; n=6 grade 2).

AEs = adverse events; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

AZD0486 2SUD cohort (n=70), n (%)	Grade 1	Grade 2	Grade 3	Grade ≥4	Total
CRS	30 (43)	4 (6)	0	0	34 (49)
ICANS	4 (6)	6 (9)	4 (6)	0	14 (20)

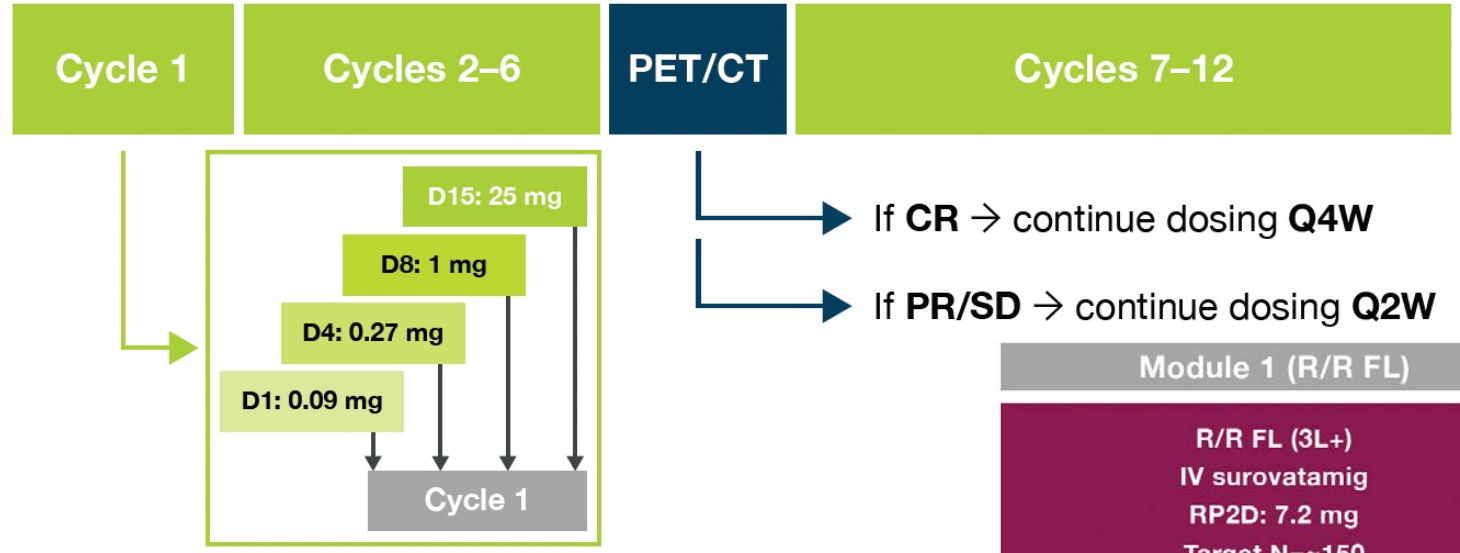
Kim TM et al. ASCO 2025;Abstract 7046.

RTP RESEARCH TO PRACTICE

Ongoing Phase II SOUNDTRACK-B Study

Module 2

Study Design (N=~120)



1 cycle = 28 days.
IV surovatamig at 25 mg on D1, D15 (C2–6); on D1 only (C7–12) if CR; if PR/SD, on D1, D15 from C7–12.

Module 1 (R/R FL)	Module 2 (R/R LBCL)
R/R FL (3L+) IV surovatamig RP2D: 7.2 mg Target N=~150 Finite treatment: up to 24 cycles (each 28 days)[a]	R/R LBCL (3L+) IV surovatamig RP2D: 25 mg Target N=~120 Finite treatment: up to 12 cycles (each 28 days)[a]

[a]Or until disease progression or unacceptable toxicity.

Treatment Schedule

- IV surovatamig administered with SUD in cycle 1; target dose is given Q2W
- Module 1: triple SUD (**Figure 2**); module 2: triple SUD (**Figure 3**)
- In both modules, patients whose disease achieves CR and who have received at least 6 cycles of treatment will receive surovatamig Q4W on day 1 of subsequent cycles

Study Endpoints

- Primary: ORR
- Select secondary: DOR, CR rate, MRD-negative CR rate, safety

Cheah C et al. ASH 2025;Abstract 3747.

Ongoing Phase III SOUNDTRACK-D2 Study

Estimated primary completion date: 10 Jun 2030

n = 420 (est.)
Elderly or unfit patients with newly diagnosed LBCL

R

Surovatamig (RP3D) + R-mini-CHOP*

*** Patients will receive 2 cycles of R-mini-CHOP prior to experimental treatment**

R-mini-CHOP x 6 cycles

Primary endpoints
Safety, RP3D, PFS (Lugano 2014 criteria)

Secondary endpoints
Safety run-in: ORR, CR, DoR, DoCR, PFS, OS
Phase III: PFS2, TFST, Safety, PROs

Experimental safety run-in:

Surovatamig (RP2D) + R-mini-CHOP*

*** Patients will receive 2 cycles of R-mini-CHOP prior to experimental treatment**

RP3D = recommended Phase III dose; ORR = overall response rate; CR = complete response; DoCR = duration of complete response; PFS2 = time from randomization to second disease progression or death; TFST = time to subsequent therapy or death; PROs = patient-reported outcomes; RP2D = recommended Phase II dose

www.clinicaltrials.gov. NCT07215585. Accessed August 2026.

RTP RESEARCH TO PRACTICE

Based on the published literature and your clinical experience, would you like to have access to surovatamig for your patients with R/R DLBCL today?

 Dr Abramson	Yes, for patients with CD20-negative disease
 Dr Flowers	Yes, as part of second-line combinations prior to CAR T; third-line+ relapse
 Dr Kamdar	Yes, for CAR T-ineligible pts in the second-line setting
 Dr LaCasce	Yes, for patients who are ineligible for CD19 CAR T
 Dr Matasar	No
 Dr Phillips	Yes, after CAR T-cell therapy
 Prof Salles	Yes, for patients with PD on CD3 x CD20 combinations or monotherapy, and for those with CD20-negative disease
 Dr Westin	Yes, for patients with CD20 loss and non-CAR T eligible

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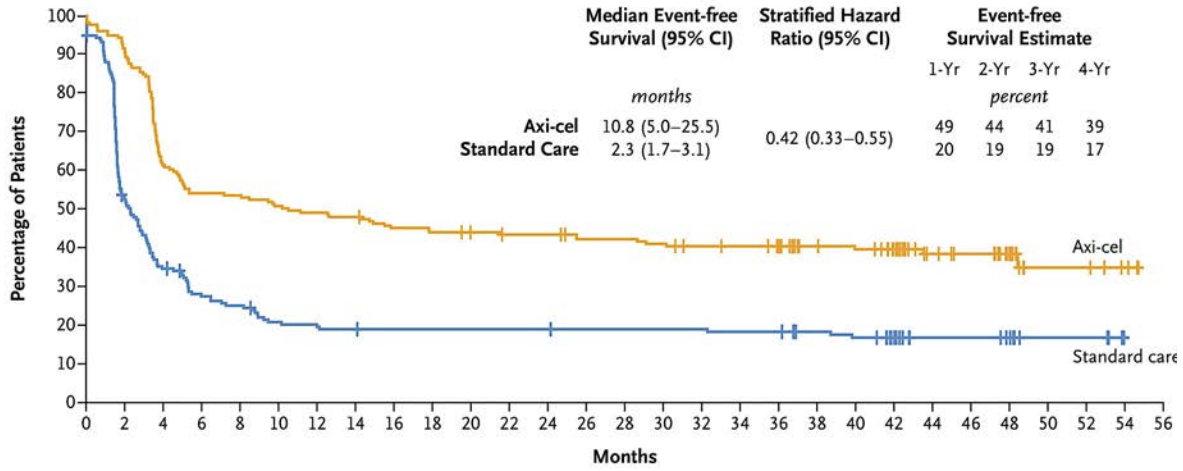
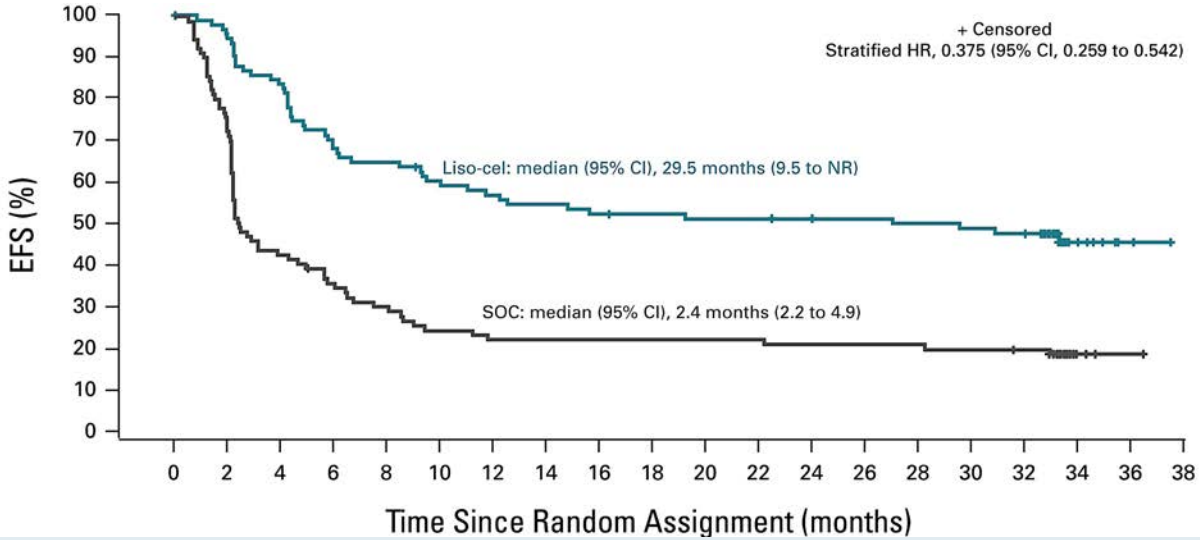
If surovatamig were granted regulatory approval, would you employ a CD20 x CD3 bispecific antibody and surovatamig in sequence for the same patient with R/R DLBCL?

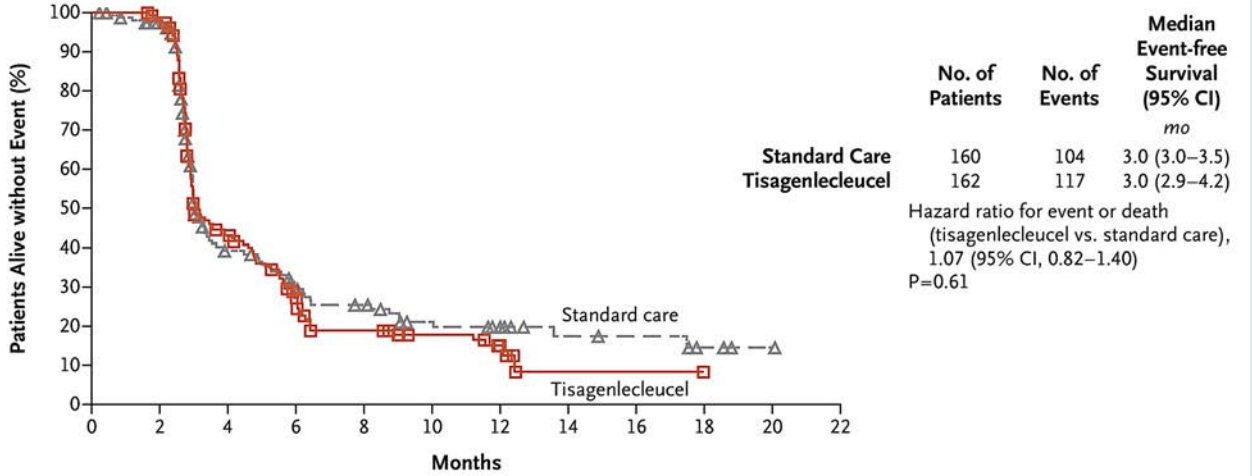
 Dr Abramson	Yes
 Dr Flowers	Yes
 Dr Kamdar	Yes
 Dr LaCasce	Maybe
 Dr Matasar	Yes
 Dr Phillips	Yes
 Prof Salles	Yes
 Dr Westin	Yes

RTP RESEARCH TO PRACTICE

Long-Term EFS with CD19-Directed CAR T-Cell Therapy for DLBCL







mEFS (mo)	CAR-T Tx (95% CI)	SC (95% CI)	HR (95% CI)
BELINDA (tisa-cel)	3.0 (2.9-4.2)	3.0 (3.0-3.5)	1.07 (0.82-1.40)
TRANSFORM (liso-cel)	29.5 (9.5-NR)	2.4 (2.2-4.9)	0.375 (0.259-0.542)
ZUMA-7 (axi-cel)	10.8 (5.0-25.5)	2.3 (1.7-3.1)	0.42 (0.33-0.55)

EFS = event-free survival; CAR = chimeric antigen receptor;
SC = standard care

Westin JR et al. *N Engl J Med* 2023 July 13;389(2):148-57.
Kamdar M et al. *Clin Oncol* 2025 August 20;43(24):2671-78.
Bishop MR et al. *N Engl J Med* 2022 February 17;386(7):629-39.

RTP RESEARCH TO PRACTICE

Case Presentation: Dr LaCasce

88-year-old male who was initially diagnosed with diffuse large B-cell lymphoma, germinal center subtype involving the bilateral neck and right axilla in August 2024, IPI 2. He was initially treated with R mini-CHOP, 75% dose. Interim PET after 3 cycles showed improvement, but following the last cycle of therapy, he developed a rapidly progressive left orbital lesion. Given the concern for impending visual loss, he received radiotherapy to a total dose of 1400 cGy. He then initiated glofitamab, plus gemcitabine and oxaliplatin. He completed all 12 cycles of therapy and achieved an early metabolic complete remission. Unfortunately, on restaging after completion of treatment, he developed a new right sided pleural-based lesion and rapidly developed a large effusion. Pleural fluid confirmed disease that was both CD19 and CD20 negative.

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Cases and Discussion Questions

A 58-year-old man with primary refractory DLBCL progresses during first-line therapy. He has rapidly enlarging abdominal adenopathy but remains ECOG 1 with preserved organ function.

Sunil Babu, MD

Would you proceed directly toward second-line CAR T, and how do you approach bridging therapy in a patient with rapidly progressive disease while awaiting collection and infusion?

How do you choose between axicabtagene ciloleucel and lisocabtagene maraleucel in this scenario? In your experience, does either of these products have substantially better responses than the other in the second line? What about survival outcomes?

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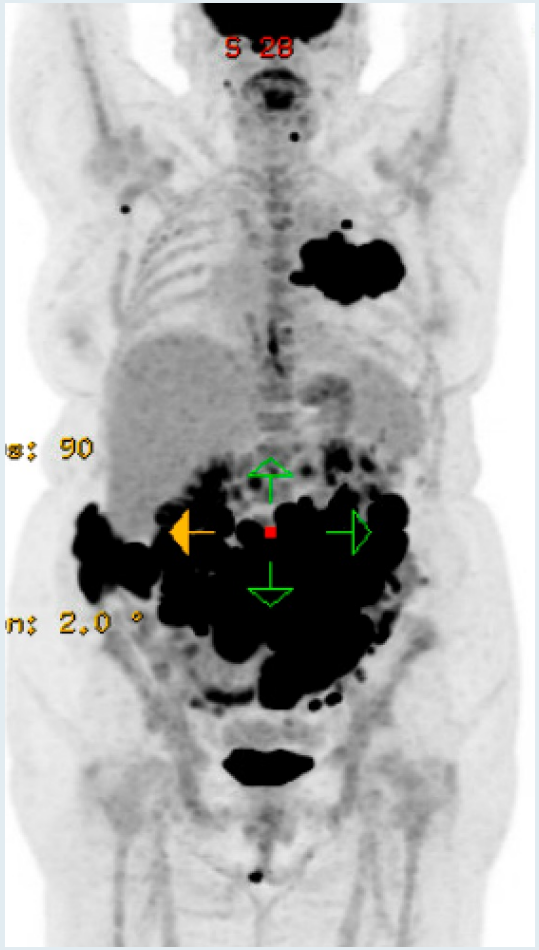
Case Presentation: Dr LaCasce

67-year-old Jehovah's Witness initially presented with neck adenopathy. She eventually underwent an excisional lymph node biopsy in October of 2023 which revealed diffuse large B-cell lymphoma, germinal center subtype in a background of follicular lymphoma. She had a BCL6 arrangement without MYC or Bcl-2 rearrangements. She had stage III disease with adenopathy above and below the diaphragm. Her IPI was a 3. She received 6 cycles of R-CHOP completed in February 2024. She presented in late 2025 with abdominal symptoms and was found to have extensive disease recurrence in the abdomen involving the small bowel, lymph nodes and with a large left-sided lung mass. Biopsy confirmed CD10 positive diffuse large B-cell lymphoma. She was treated with 1 cycle of polatuzumab, R gem ox followed by T-cell pheresis. She was then admitted to the hospital for rapid glofitamab ramp-up. Prior to CAR-T cell therapy she had a dramatic response by CT scans. She subsequently received liso-cel and had no CRS or neurologic toxicity. Her day 30 PET scan shows a metabolic complete remission.



January 2026

RTP RESEARCH TO PRACTICE

Up Next …

Dr Stephen V Liu discusses
the management of lung cancer

RTP
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TO PRACTICE

Integrating New Advances into Community Oncology Practice

A Multitumor Symposium Hosted in Conjunction with the American Oncology Network

CME/MOC, NCPD and ACPE Accredited

Saturday, August 22, 2026
9:00 AM – 2:20 PM CT

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RESEARCH TO PRACTICE

Agenda

Module 1 — Chronic Lymphocytic Leukemia
Farrukh T Awan, MD, MS, MBA

Module 2 — Gastroesophageal Cancers
Samuel J Klempner, MD

Module 3 — Ovarian and Endometrial Cancer
Shannon N Westin, MD, MPH, FASCO, FACOG

Module 4 — Diffuse Large B-Cell Lymphoma
Ann LaCasce, MD, MMSc

Module 5 — Lung Cancer
Stephen V Liu, MD

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MODERATOR
Stephen “Fred” Divers, MD
Chief Medical Officer
American Oncology Network
Board Executive
Community Oncology Alliance
Hot Springs, Arkansas

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Dr Liu — Disclosures

Consulting Agreements	AbbVie Inc, Amgen Inc, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Daiichi Sankyo Inc, Ellipses Pharma, Genentech, a member of the Roche Group, Gilead Sciences Inc, GSK, Jazz Pharmaceuticals Inc, Johnson & Johnson, Merck, Merus, Natera, Novartis, Nuvalent, OSE Immunotherapeutics, Pfizer Inc, PharmaMar, Regeneron Pharmaceuticals Inc, Revolution Medicines Inc, Rigel Pharmaceuticals Inc, SystImmune Inc, Takeda Pharmaceuticals USA Inc, Yuhan Corporation
Contracted Research	AbbVie Inc, Alkermes, Amgen Inc, AstraZeneca Pharmaceuticals LP, Avenzo Therapeutics, BioNTech SE, Cogent Biosciences, Duality Biologics, Ellipses Pharma, Genentech, a member of the Roche Group, Gilead Sciences Inc, Henlius, MediLink Therapeutics, Merck, Merus, Nuvalent, Nuvation Bio Inc, OSE Immunotherapeutics, Puma Biotechnology Inc, Synthekine, SystImmune Inc

RTP
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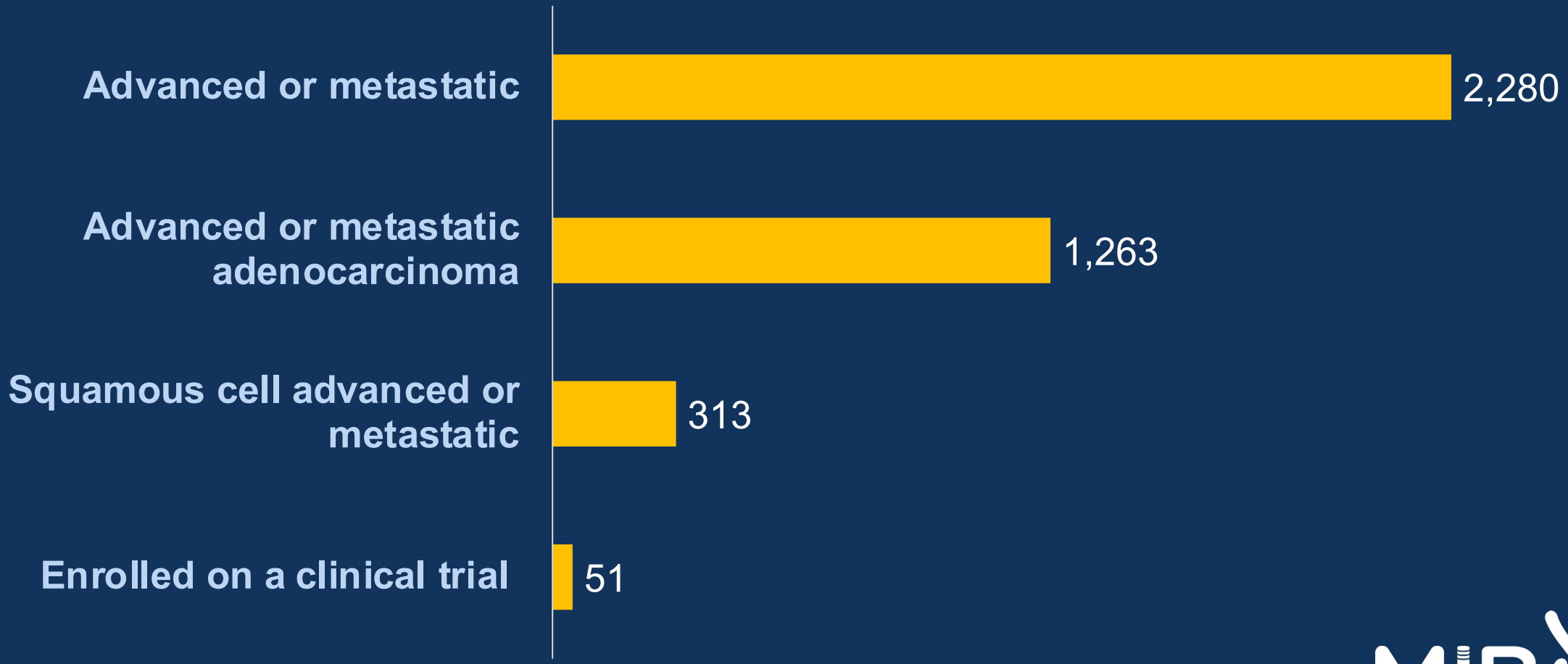
TO PRACTICE

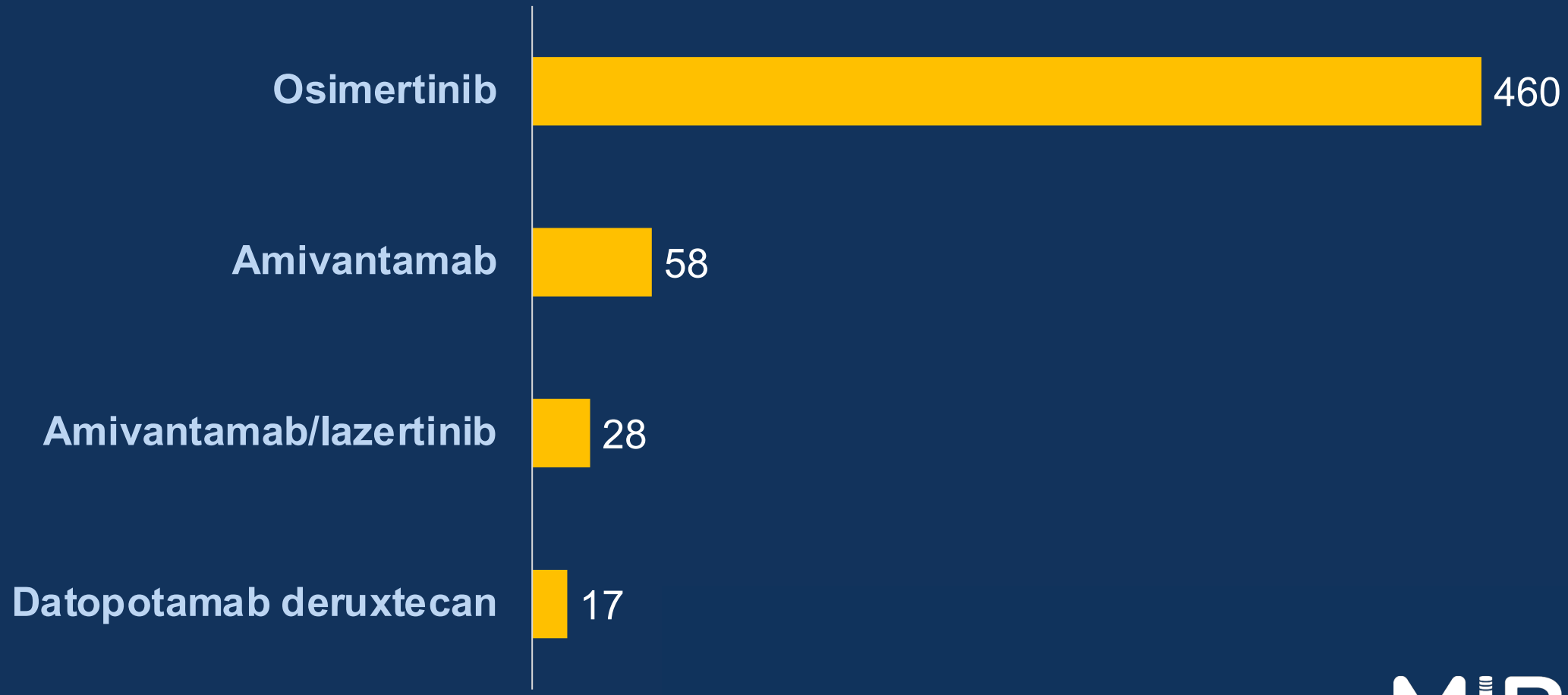
Dr Divers — Disclosures

Advisory Committees	Daiichi Sankyo Inc

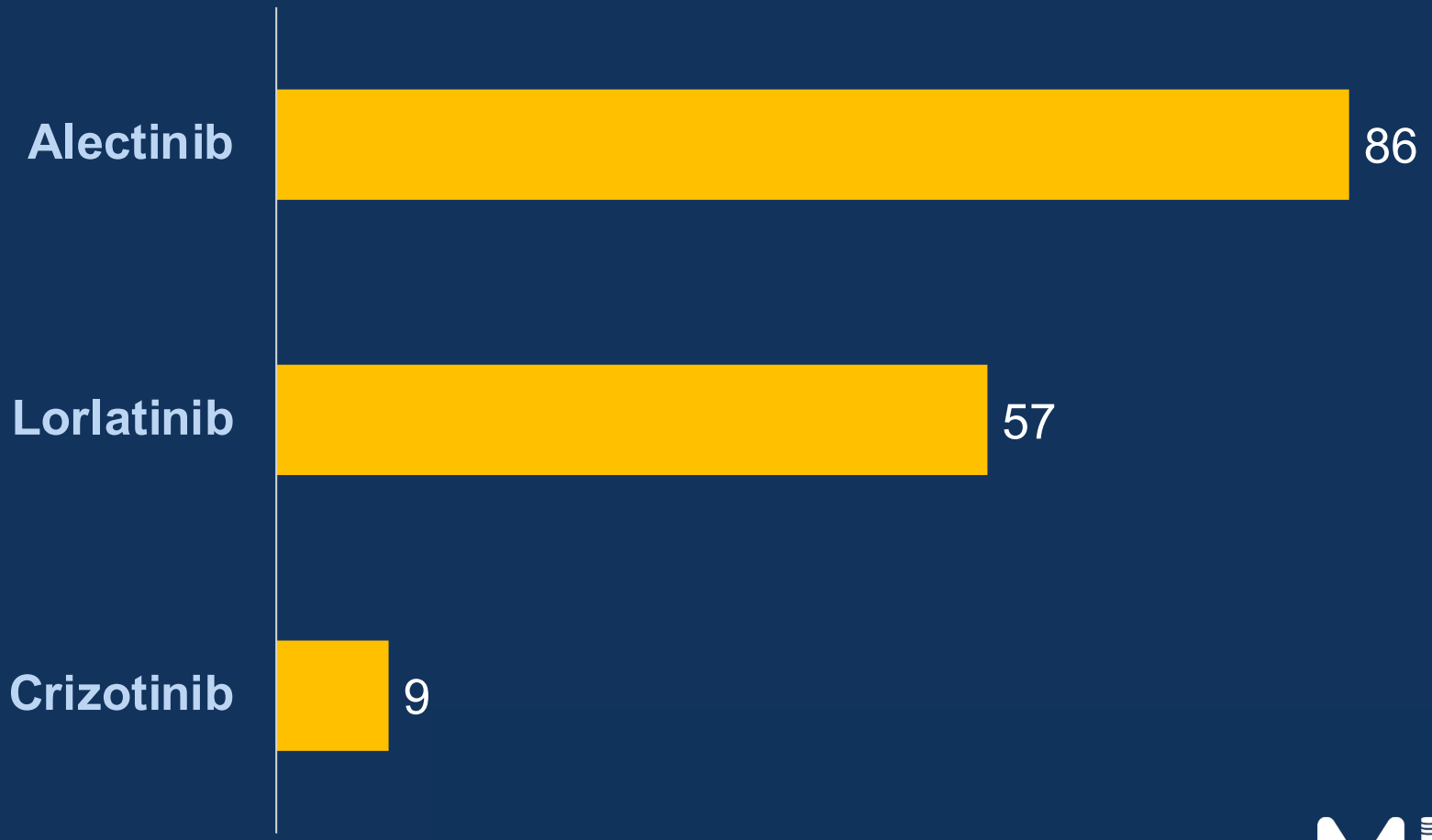
Snapshot of AON Practice
Non-Small Cell Lung Cancer



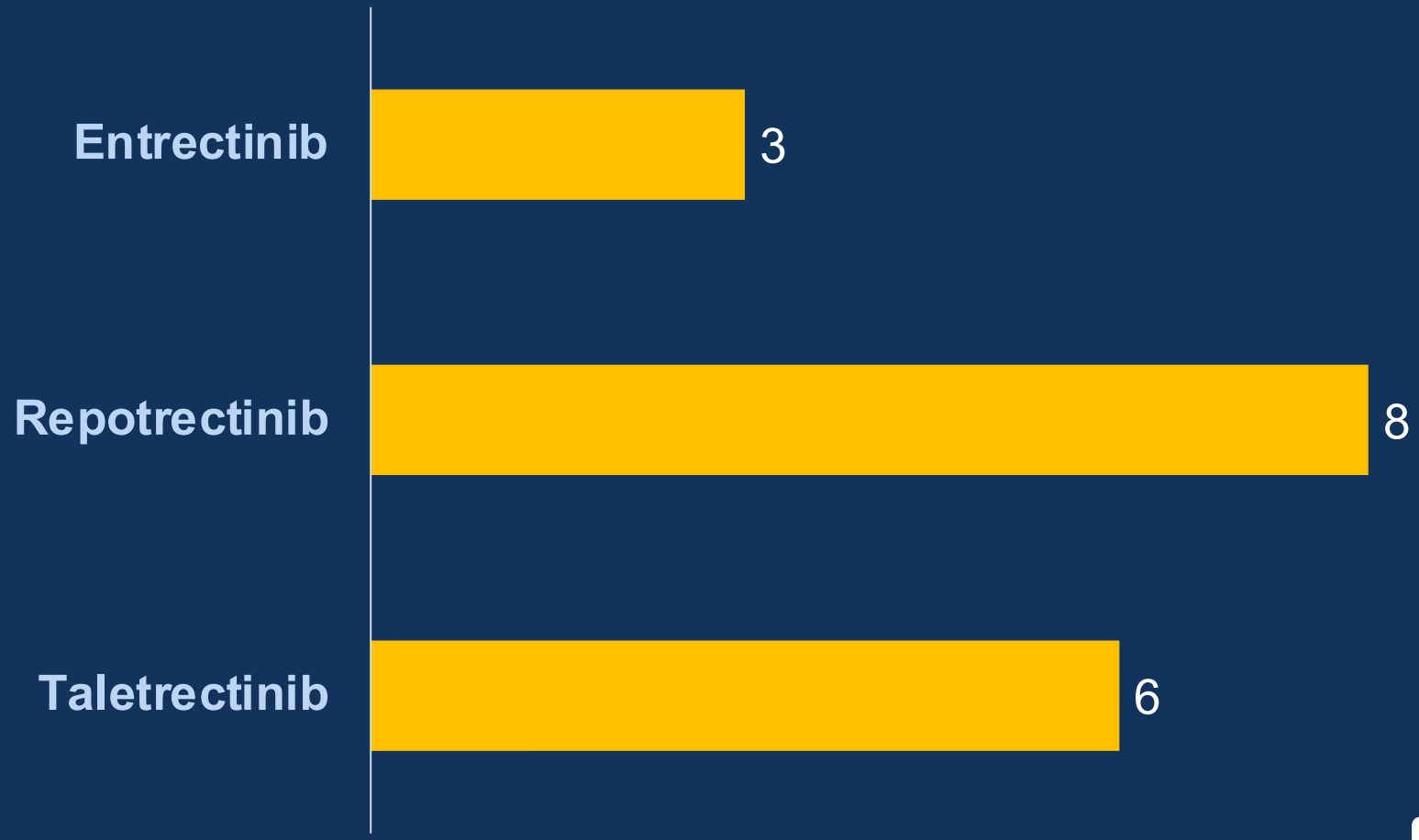
Snapshot of AON Practice
NSCLC with EGFR Mutation



Snapshot of AON Practice
NSCLC with ALK Rearrangement

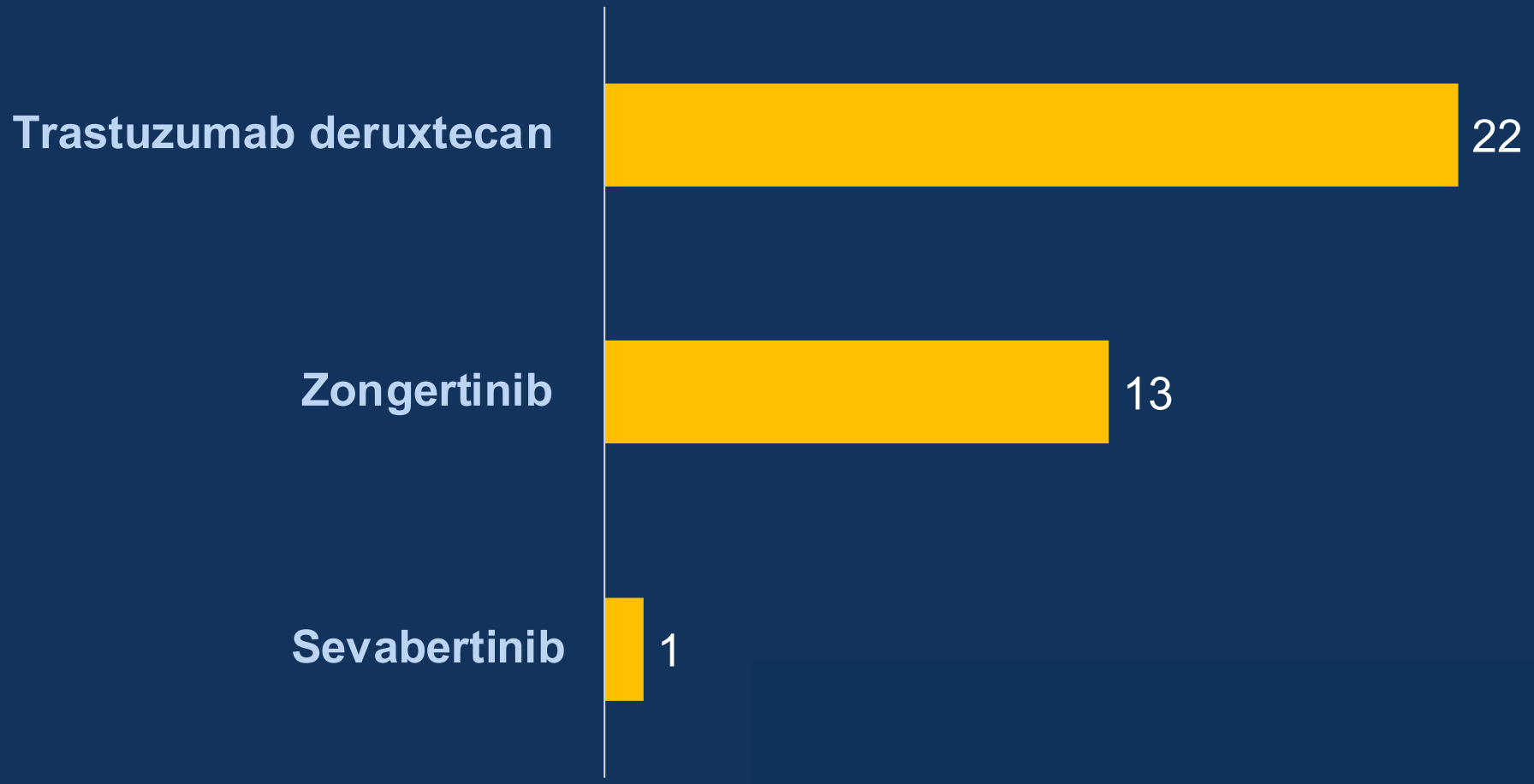


Snapshot of AON Practice
NSCLC with ROS1 Rearrangement

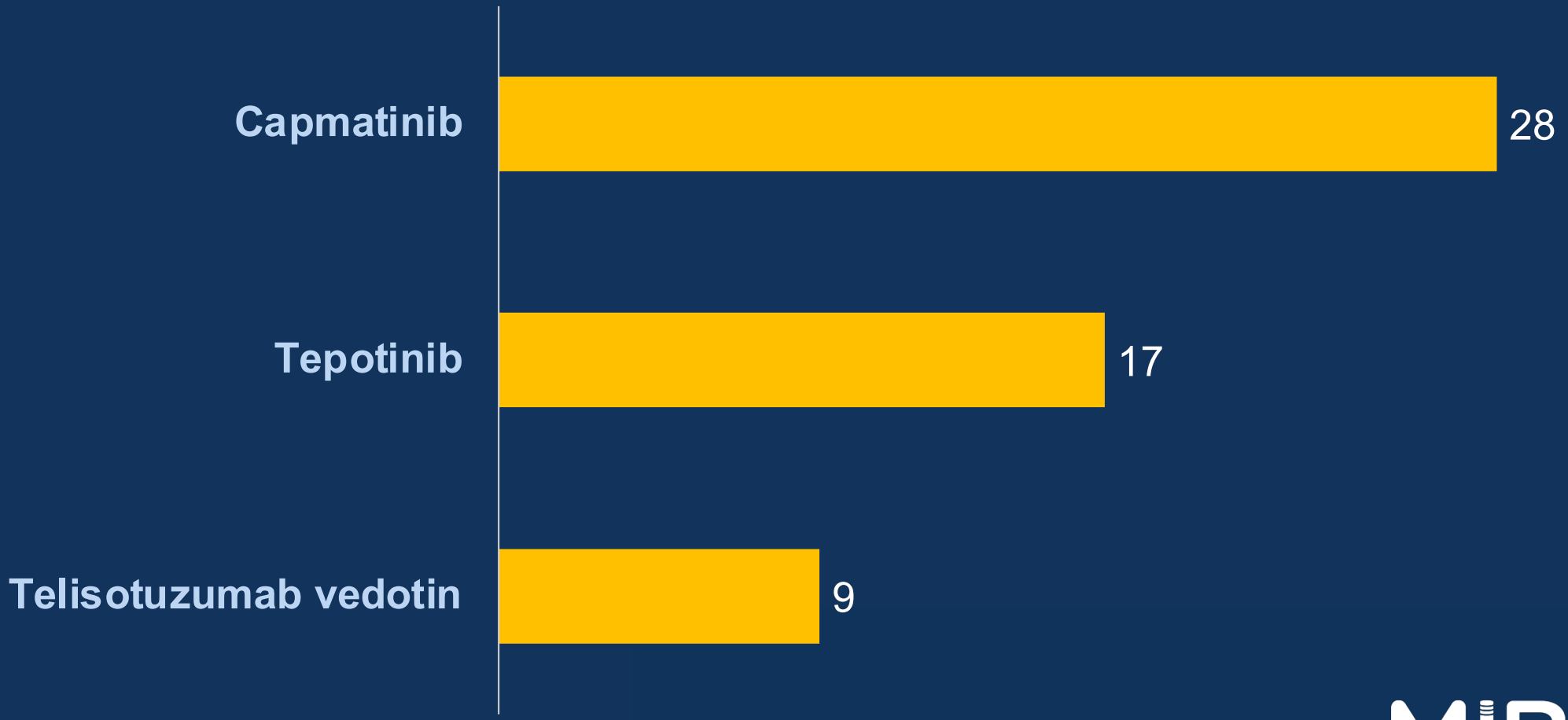


Snapshot of AON Practice
NSCLC with KRAS Mutation

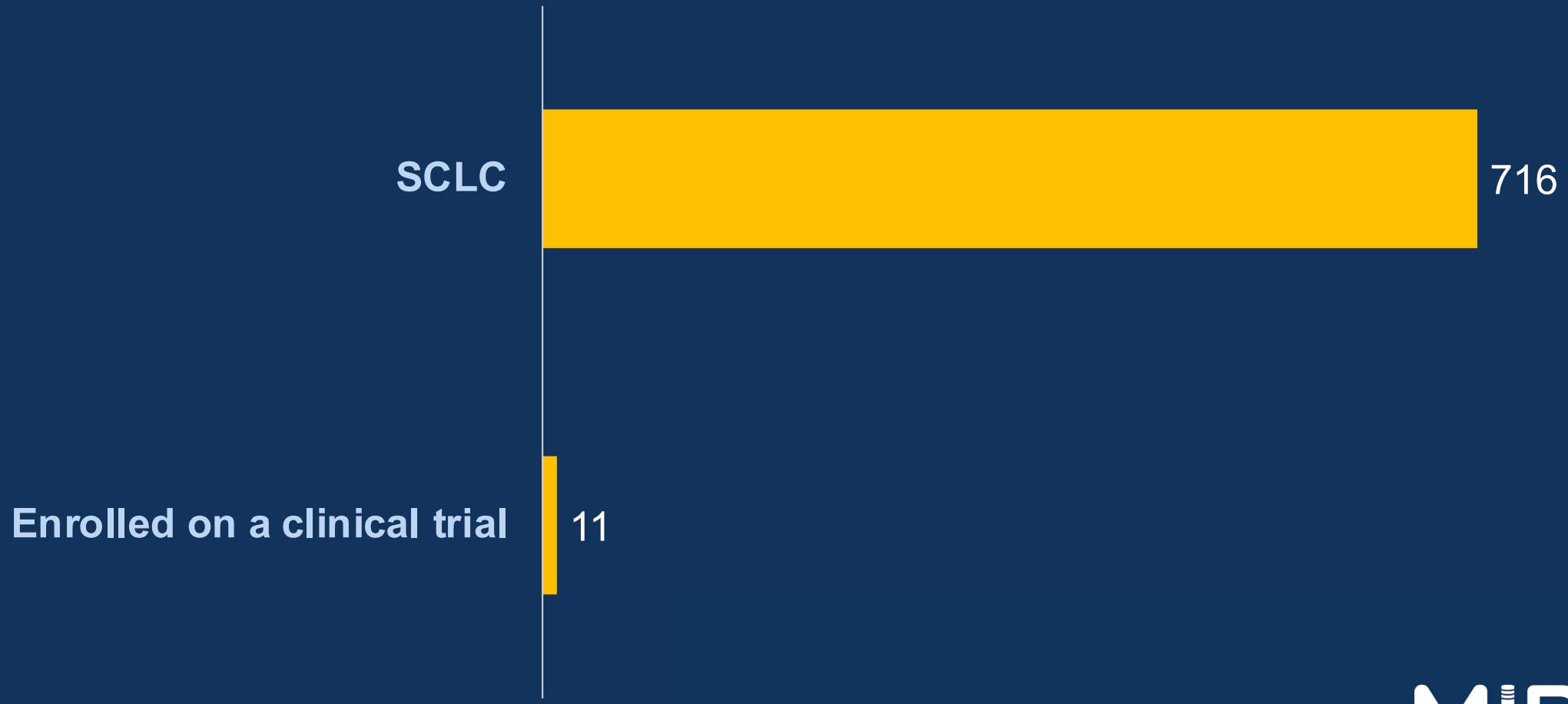
Snapshot of AON Practice
NSCLC with HER2 Alterations



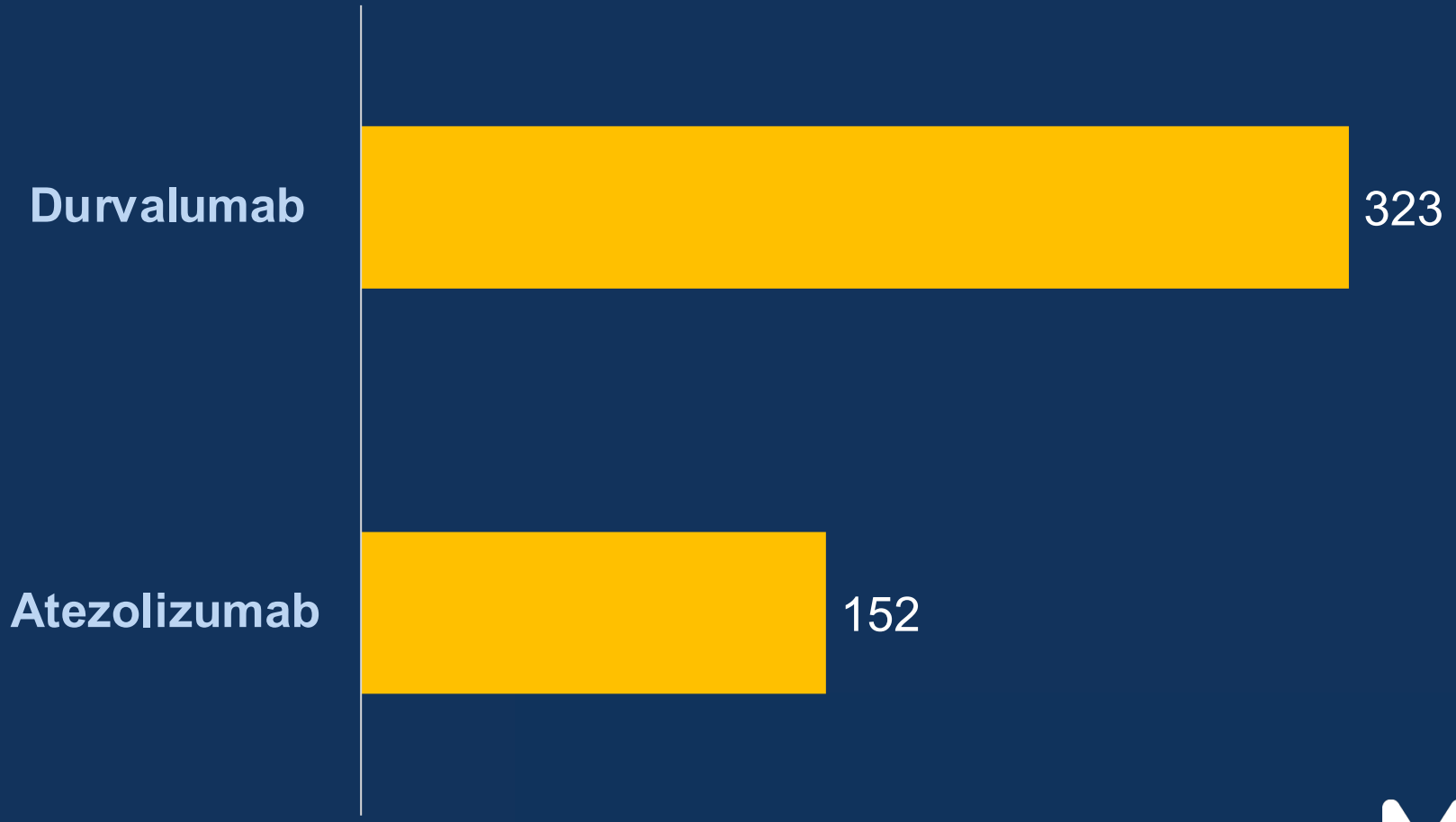
Snapshot of AON Practice
NSCLC with MET Alterations



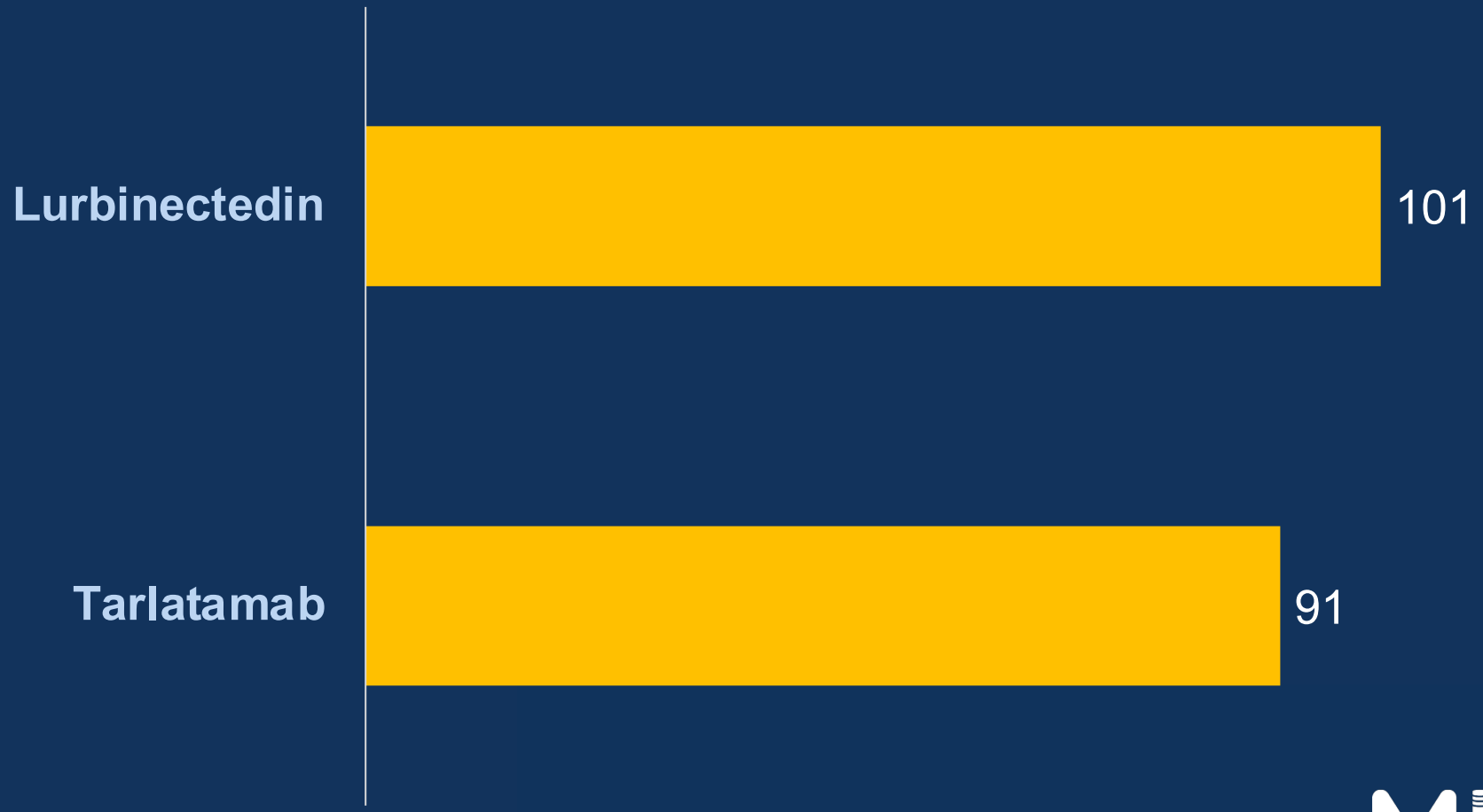
Snapshot of AON Practice
Small Cell Lung Cancer (SCLC)



Snapshot of AON Practice
SCLC — Immunotherapy



Snapshot of AON Practice
SCLC — Other Treatments



Agenda

Module 5 — Lung Cancer: *Dr Liu*

- **EGFR Mutations**
- **HER2 Alterations**
- **ALK Fusions**
- **Available and Investigational Immunotherapies**
- **Small Cell Lung Cancer**

RTP RESEARCH TO PRACTICE

Cases and Discussion Questions

74-year-old woman with a PMH of breast cancer is diagnosed with EGFR exon 21 L858R-mutant metastatic NSCLC. S/p first-line carboplatin/pemetrexed/ osimertinib. Currently receiving Dato-DXd and doing well.

Stephen "Fred" Divers, MD

How do you select first-line treatment for EGFR-mutant metastatic NSCLC?

How do you select second- and later-line treatment for EGFR-mutant metastatic NSCLC, and how does that vary based on the specific first-line therapy received? How does the duration of response to up-front therapy affect your decision?

RTP RESEARCH TO PRACTICE

Cases and Discussion Questions (Continued)

Where in the treatment sequence are you most likely to employ datopotamab deruxtecan (Dato-DXd) for patients with EGFR-mutated NSCLC? Are you comfortable using it for patients with uncommon EGFR mutations?

In your experience, how does the global tolerability of Dato-DXd compare to that of traditional chemotherapy? Is it better tolerated or about the same?

What prophylactic measures do you recommend for your patients who are about to start treatment with Dato-DXd to reduce the risk of side effects?

RTP
RESEARCH
TO PRACTICE

Cases and Discussion Questions (Continued)

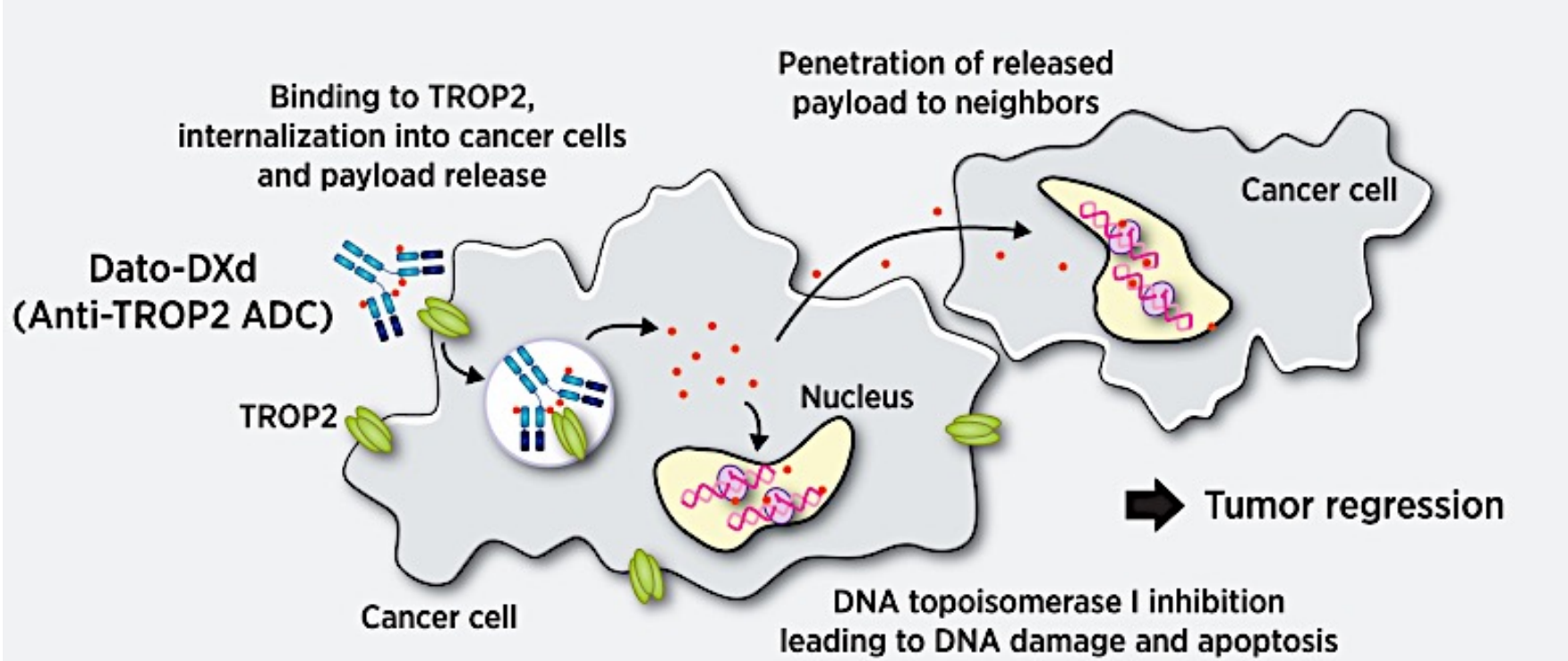
Do you always rebiopsy after disease progression on first-line osimertinib with or without chemotherapy? How often do you encounter patients with MET overexpression or amplification in this scenario?

How do you envision osimertinib/savolitinib fitting in relative to other available therapies for these patients?

RTP
RESEARCH
TO PRACTICE

TROP2-Targeting Antibody-Drug Conjugates (ADCs) for Non-Small Cell Lung Cancer (NSCLC)

TROP2 is an intracellular calcium-signaling transducer that is overexpressed in epithelial cancers, including NSCLC.

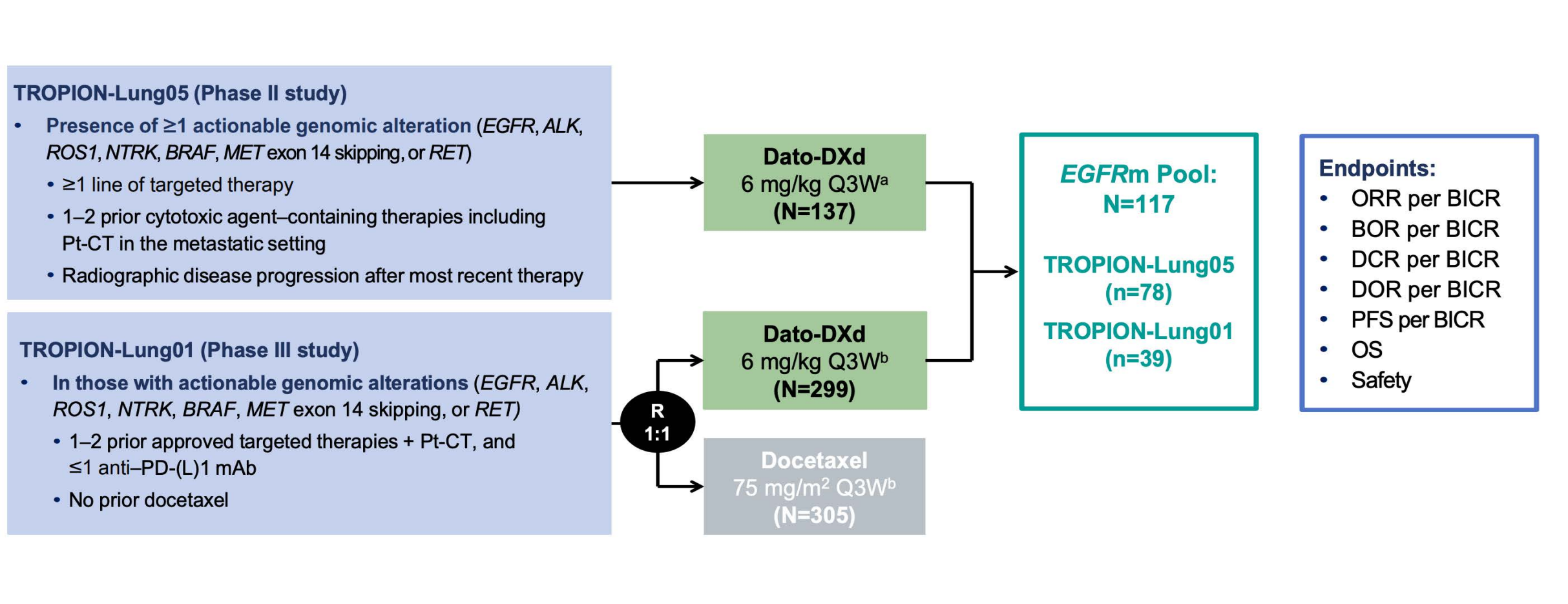


Datopotamab deruxtecan (Dato-DXd) showed potent antitumor activity against TROP2-expressing tumors by efficient payload delivery into tumors

Kuo P et al. *PLoS One* 2025;20(4):e0321555. Okajima D et al. *Mol Cancer Ther* 2021;20(12):2329-40.

RTP RESEARCH TO PRACTICE

Datopotamab Deruxtecan (Dato-DXd) for EGFR-Mutated NSCLC: Pooled Analysis from the TROPION-Lung01 and TROPION-Lung05 Studies



Pt-CT = platinum chemotherapy; ORR = objective response rate; BICR = blinded independent central review; BOR = best overall response; DCR = disease control rate; DOR = duration of response; PFS = progression-free survival; OS = overall survival

Ahn MJ et al. ESMO Asia 2024;Abstract LBA7. Ahn MJ et al. *J Thorac Oncol* 2025;20(11):1669-82.

RTP RESEARCH TO PRACTICE

Pooled Analysis from TROPION-Lung01 and TROPION-Lung05: Efficacy

Response	*EGFR*m Pool (N=117)	Prior Osimertinib (N=96)
Confirmed ORR,[a] n (%) [95% CI]	50 (**42.7**) [33.6–52.2]	43 (**44.8**) [34.6–55.3]
BOR, n (%) CR PR SD Non-CR/Non-PD PD NE	 5 (**4.3**) 45 (**38.5**) 48 (41.0) 3 (2.6) 12 (10.3) 4 (3.4)	 4 (**4.2**) 39 (**40.6**) 37 (38.5) 2 (2.1) 10 (10.4) 4 (4.2)
Median DOR, months (95% CI)	**7.0** (4.2–9.8)	**6.9** (4.2–9.8)
DCR,[b] n (%) [95% CI]	101 (**86.3**) [78.7–92.0]	82 (**85.4**) [76.7–91.8]
Median PFS, months (95% CI)	**5.8** (5.4–8.2)	**5.7** (5.4–7.9)
Median OS, months (95% CI)	**15.6** (13.1–19.0)	**14.7** (13.0–18.3)

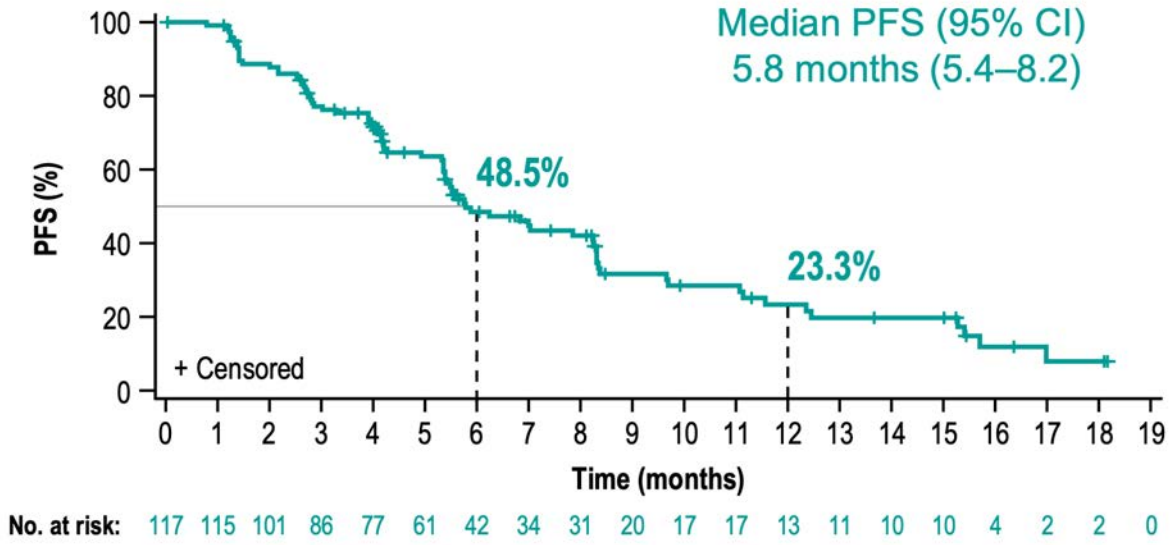
CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; NE = not evaluable

Ahn MJ et al. ESMO Asia 2024;Abstract LBA7. Ahn MJ et al. *J Thorac Oncol* 2025;20(11):1669-82.

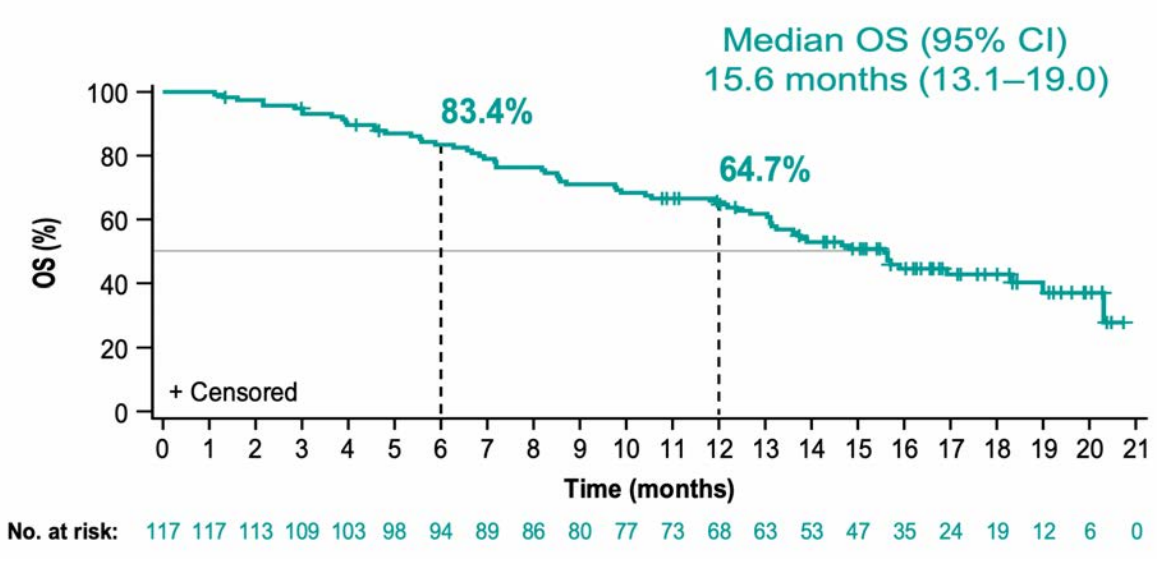
RTP RESEARCH TO PRACTICE

Pooled Analysis from TROPION-Lung01 and TROPION-Lung05: Efficacy

PFS



OS



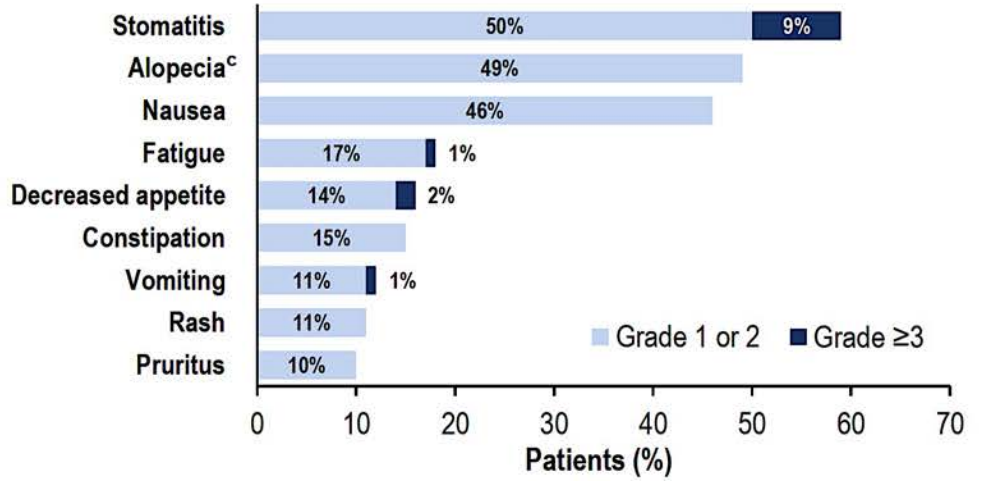
Ahn MJ et al. ESMO Asia 2024;Abstract LBA7; Ahn MJ et al. *J Thorac Oncol* 2025;20(11):1669-82.

RTP RESEARCH TO PRACTICE

Pooled Analysis from TROPION-Lung01 and TROPION-Lung05: Safety

	*EGFR*m Pool (N=117)
TRAEs, n (%)	111 (95)
Grade ≥3	27 (23)
Associated with dose reduction	26 (22)
Associated with dose delay	27 (23)
Associated with treatment discontinuation	6 (5)
Associated with death	0 (0)
Serious TRAEs	9 (8)
AESIs[a], n (%)	
Stomatitis/oral mucositis	81 (69)
Grade 3[b]	11 (9)
Ocular surface events	38 (32)
Grade 3[b]	3 (3)
Adjudicated drug-related ILD	5 (4)
Grade 3[b]	1 (1)

TRAEs Occurring in ≥10% of EGFRm Pool (N=117)



- Median Dato-DXd treatment duration: **6.1 months**

- Overall safety profile consistent with TROPION-Lung01 and 05
- No grade 4 or 5 adjudicated drug-related ILD
- Ocular surface events[a] were primarily dry eye (12%), vision blurred and keratitis (each 7%)
- No TRAEs associated with death

[a]AESIs listed are treatment emergent and include all preferred terms that define the medical concept. Some patients may have had >1 event. [b]No grade 4 or 5 events occurred. [c]Includes an event incorrectly reported as grade 3 per CTCAE grades.
AESI, adverse event of special interest; CTCAE, Common Terminology Criteria for Adverse Events; Dato-DXd, datopotamab deruxtecan; *EGFR*m, *EGFR* mutated; ILD, interstitial lung disease; TRAE, treatment-related adverse event.

Ahn MJ et al. ESMO Asia 2024;Abstract LBA7; Ahn MJ et al. *J Thorac Oncol* 2025;20(11):1669-82.

RTP RESEARCH TO PRACTICE

Select Ongoing Phase III Trials of TROP2-Targeted ADCs for NSCLC

Trial identifier	N	Setting	Treatment arms	Key endpoints	Estimated completion date
TROPION-Lung14 (NCT06350097)	582	1L EGFR-mutated NSCLC	Dato-DXd + osimertinib versus osimertinib	PFS, OS	2031-08-29
TROPION-Lung15 (NCT06417814)	744	2L EGFR-mutated NSCLC (progressed on prior osimertinib)	Dato-DXd + osimertinib versus Dato-DXd versus chemotherapy	PFS, OS	2028-09-27
TROPION-Lung07 (NCT05555732)	1,170	1L nonsquamous NSCLC (w/o AGA, PD-L1 <50%)	Dato-DXd + pembrolizumab + platinum versus Dato-DXd + pembrolizumab versus pembrolizumab + pemetrexed + platinum	PFS, OS	2031-05-11
TROPION-Lung08 (NCT05215340)	740	1L NSCLC (w/o AGA, PD-L1 ≥50%)	Dato-DXd + pembrolizumab versus pembrolizumab	PFS, OS	2032-03-04

1L = first-line; AGA = actionable genomic alterations

RTP RESEARCH TO PRACTICE

Select Ongoing Phase III Trials of TROP2-Targeted ADCs for NSCLC

Trial identifier	N	Setting	Treatment arms	Key endpoints	Estimated completion date
AVANZAR (NCT05687266)	1,350	1L nonsquamous NSCLC (w/o AGA)	Dato-DXd + durvalumab + carboplatin versus pembrolizumab + chemotherapy	PFS, OS	2027-11-01
TROPION-Lung10 (NCT06357533)	675	1L nonsquamous NSCLC (w/o AGA, PD-L1 ≥50%)	Dato-DXd + rilvegostomig versus rilvegostomig versus pembrolizumab	PFS, OS	2029-12-28
TROPION-Lung17 (NCT07291037)	400	2L TROP2 NMR-positive nonsquamous NSCLC	Dato-DXd versus docetaxel	PFS, OS	2029-01-29

2L = second-line; NMR = normalized membrane ratio

RTP RESEARCH TO PRACTICE

Phase III SAFFRON Trial: Savolitinib and Osimertinib versus Chemotherapy for EGFR-Mutant NSCLC with MET Overexpression or Amplification After Treatment with Osimertinib

- Locally advanced or metastatic NSCLC
- EGFRm (Ex19del/L858R) and/or T790M, and MET overexpression and/or amplification
- Disease progression on first- or second-line treatment with osimertinib
- No prior chemotherapy in the metastatic setting allowed
- ECOG PS 0-1

N = 324

1:1

Savolitinib (300 mg BID) + **osimertinib** (80 mg QD)

Pemetrexed (500 mg/m^2) + **carboplatin** (AUC5) or **cisplatin** (75 mg/m^2), Q3W x 4 cycles → **maintenance pemetrexed** (500 mg/m^2), Q3W

Primary endpoint:
PFS by blinded independent central review

Key secondary endpoints:
OS (overall population and for patients with MET overexpression), PFS for patients with MET overexpression, ORR, DoR, pharmacokinetics, and safety

Stratification factors: line of therapy (second/third line), baseline brain metastases (yes/no) and race (Asian/non-Asian)

Lu S et al. WCLC 2022;Abstract EP08.02; www.clinicaltrials.gov. NCT05261399. Accessed August 2026.

RTP RESEARCH TO PRACTICE

Osimertinib and Savolitinib Demonstrated Statistically Significant and Clinically Meaningful Improvements in PFS and OS for MET-Driven EGFR-Mutated Lung Cancer After Disease Progression on Osimertinib

Press Release: August 17, 2026

"Positive high-level results from the SAFFRON Phase III trial showed osimertinib plus savolitinib demonstrated a statistically significant and clinically meaningful improvement in both progression-free survival (PFS) and overall survival (OS) versus doublet platinum-based chemotherapy in patients with epidermal growth factor receptor-mutated (EGFRm) non-small cell lung cancer (NSCLC). Patients in the trial had tumours with high levels of MET overexpression or amplification and had progressed on prior treatment with osimertinib.

The safety profile for osimertinib plus savolitinib was consistent with the known profiles of each medicine, and there were no new safety findings."

https://www.astrazeneca.com/media-centre/press-releases/2026/tagrisso-orpathys-improved-pfs-os-egfrm-lung.html.

RTP RESEARCH TO PRACTICE

Cases and Discussion Questions

66-year-old man with no history of tobacco use who presented with several weeks of cough and dyspnea is diagnosed with metastatic NSCLC with an EGFR exon 20 insertion mutation and PD-L1 TPS 0%. Minimal disease burden and symptoms. Brain MRI is negative.

Jennifer Yanucci, MD

How do you currently think through selection/sequencing of therapies for NSCLC with exon 20 insertion mutations, and how might this change in the near future? If amivantamab/chemotherapy, sunvozertinib monotherapy and zipalertinib/chemotherapy were all available as first-line therapy, how would you choose among them?

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Cases and Discussion Questions (Continued)

If this patient received first-line amivantamab/chemotherapy and experienced disease progression, what would be your preferred second-line therapy? What would it be if you had access to both sunvozertinib and zipalertinib in the relapsed setting?

How do amivantamab, sunvozertinib and zipalertinib differ in terms of tolerability profile? What are the most common AEs with each one?

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WU-KONG1B Trial: Sunvozertinib for Platinum-Pretreated NSCLC with EGFR Exon 20 Insertion Mutations

Tumor Response	200 mg-Rand (n = 85)	300 mg-Rand (n = 89)	300 mg-All (n = 107)
Objective response rate, No. (%)	39 (45.9)	42 (47.2)	49 (45.8)
97.5% CI[a]	33.6 to 58.5	35.1 to 59.5	34.8 to 57.0
P[b]	<.0001	<.0001	<.0001
Disease control rate, No. (%)	76 (89.4)	82 (92.1)	95 (88.8)
97.5% CI[a]	79.6 to 95.6	83.3 to 97.2	80.1 to 94.6
Best overall response, No. (%)			
Complete response	5 (5.9)	3 (3.4)	3 (2.8)
Partial response	34 (40.0)	39 (43.8)	46 (43.0)
Stable disease	37 (43.5)	40 (44.9)	46 (43.0)
Progressive disease	6 (7.1)	5 (5.6)	8 (7.5)
Not evaluable	3 (3.5)	2 (2.2)	4 (3.7)

NOTE. Tumor assessment followed RECIST 1.1.

Abbreviations: IRC, independent review committee; ORR, objective response rate.

[a]Based on the Clopper-Pearson exact CI method for a single binomial proportion.

[b]The one-sided *P* value against a null hypothesis of ORR ≤17% was calculated based on Simon's two-stage method for the 300 mg-all group, and the binomial exact test was used for other treatment groups.

Yang JC et al. *J Clin Oncol* 2025;43(29):3198-208.

RTP RESEARCH TO PRACTICE

WU-KONG1B: Safety

The Most Common (≥30%) Treatment-Related Adverse Events

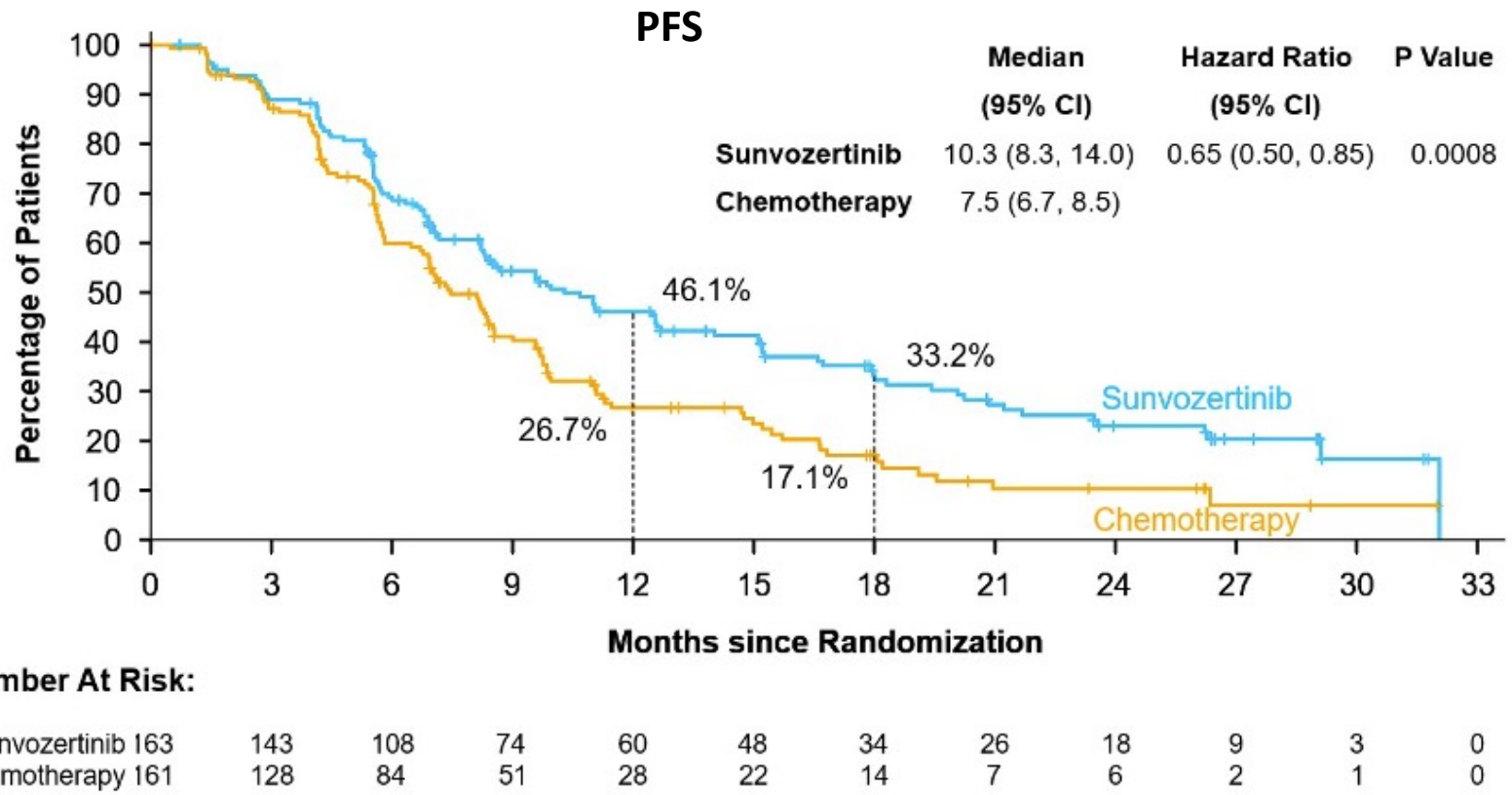
	200 mg-Rand (n = 91), No. (%)		300 mg-All (n = 111), No. (%)	
Preferred Term	All Grades	Grade ≥3	All Grades	Grade ≥3
Patients with any treatment-related TEAE	86 (94.5)	37 (40.7)	108 (97.3)	62 (58.6)
Diarrhea	62 (68.1)	2 (2.2)	92 (82.9)	20 (18.0)
Blood creatine phosphokinase increased	32 (35.2)	6 (6.6)	58 (52.3)	14 (12.6)
Rash	37 (40.7)	4 (4.4)	53 (47.7)	5 (4.5)
Decreased appetite	39 (42.9)	0 (0.0)	34 (30.6)	4 (3.6)
Anemia	28 (30.8)	4 (4.4)	42 (37.8)	7 (6.3)
Nausea	25 (27.5)	2 (2.2)	44 (39.6)	2 (1.8)
Vomiting	26 (28.6)	0 (0.0)	41 (36.9)	1 (0.9)
Paronychia	24 (26.4)	0 (0.0)	42 (37.8)	1 (0.9)

Abbreviation: TEAE, treatment-emergent adverse event.

Yang JC et al. *J Clin Oncol* 2025;43(29):3198-208.

RTP RESEARCH TO PRACTICE

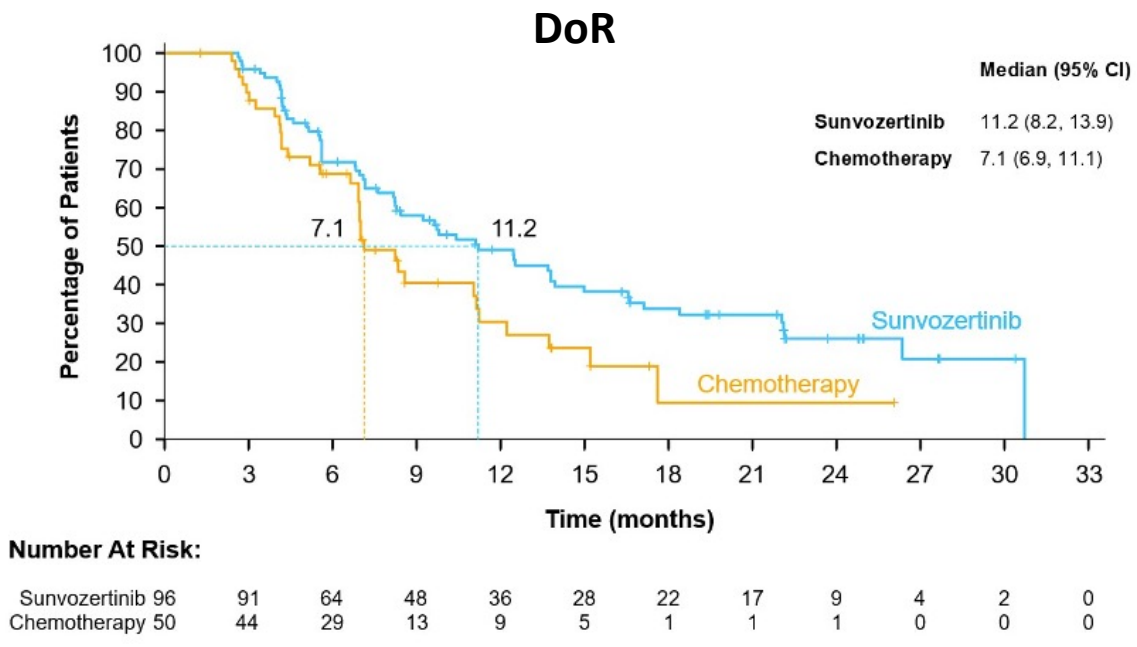
WU-KONG28 Trial: First-Line Sunvozertinib versus Platinum-Based Chemotherapy for NSCLC with EGFR Exon 20 Insertion Mutations

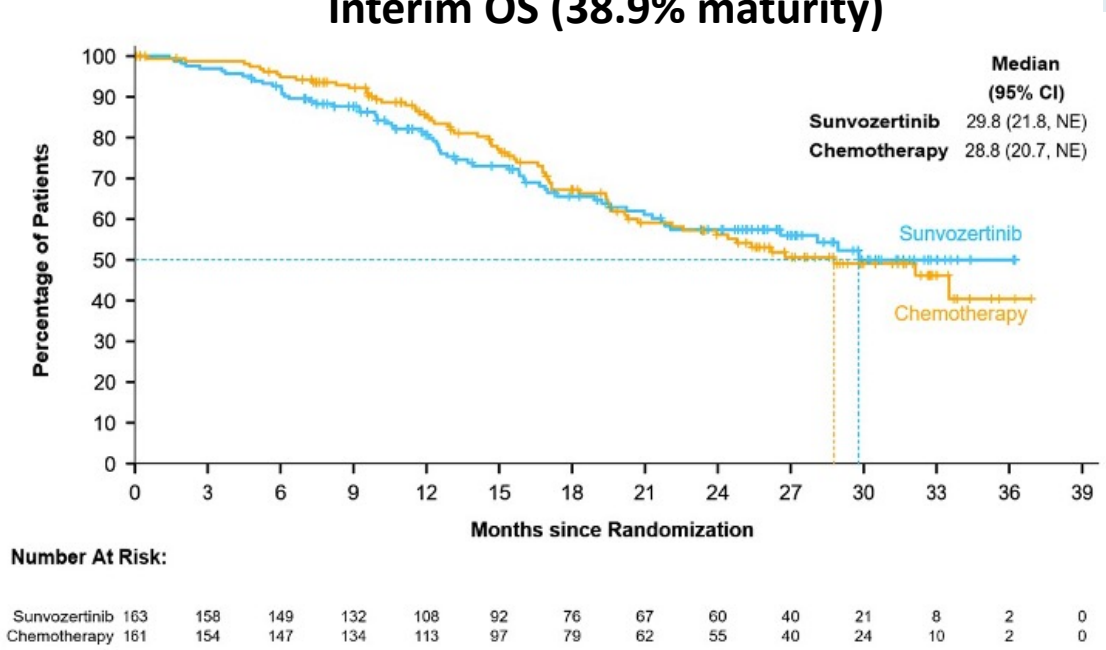


Median follow-up time: 24.0 months in the sunvozertinib arm and 18.0 months in the chemotherapy arm.

Heymach JV et al. ASCO 2026;Abstract LBA8500. Zhou C et al. *N Engl J Med* 2026;[Online ahead of print].

WU-KONG28: DOR and OS





Median follow-up time: 22.1 months in the sunvozertinib arm and 13.8 months in the chemotherapy arm.

Median follow-up time: 26.1 months in the sunvozertinib arm and 26.7 months in the chemotherapy arm.

Heymach JV et al. ASCO 2026;Abstract LBA8500. Zhou C et al. *N Engl J Med* 2026;[Online ahead of print].

REZILIENT1 Study: Zipalertinib for NSCLC with EGFR Exon 20 Insertion Mutations in Patients Who Received Prior Platinum-Based Chemotherapy with or without Amivantamab

Outcome	Primary efficacy population (N=176)	Platinum-based chemotherapy without ex20ins-targeted therapy (n=125)	Prior amivantamab ± other ex20ins-target therapy (n=51)[a]
BOR, No. (%)[b]			
CR	1 (1)	0	1 (2)
PR	61 (35)	50 (40)	11 (22)
Unconfirmed PR[c]	7 (4)	6 (5)	1 (2)
SD	88 (50)	55 (44)	33 (65)
PD	11 (6)	8 (6)	3 (6)
Not evaluable[d]	8 (5)	6 (5)	0
Confirmed ORR, No. (%) [95% CI][e]	62 (35) [28–43]	50 (40) [31–49]	12 (24) [13–38]
DCR, No. (%) [95% CI][f]	157 (89) [84–93]	111 (89) [82–94]	46 (90) [79–97]
CBR, No. (%) [95% CI][g]	113 (64) [57–71]	85 (68) [59–76]	28 (55) [40–69]
Median time to response, days (range)	44 (31–295)	44 (39–232)	44 (39–232)
Median DOR, months (95% CI)	8.8 (8.3–12.7)	8.8 (8.3–12.7)	8.5 (4.2–14.8)

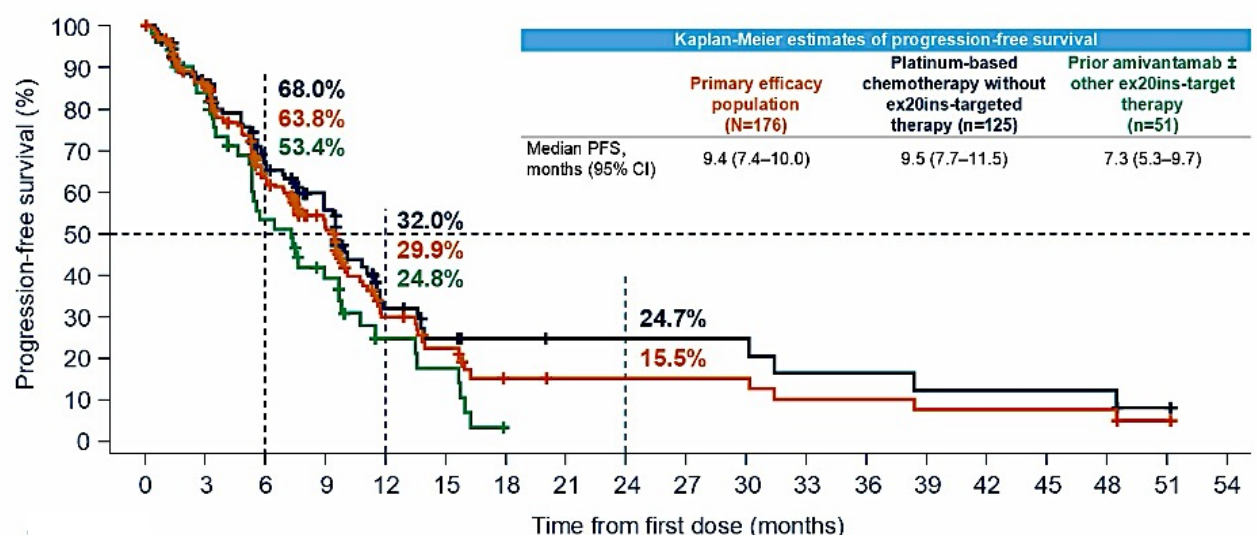
Patients were evaluable for response if they had received at least one dose of zipalertinib and had at least one post-dose tumor assessment or had discontinued prior to the first efficacy assessment due to clinical disease progression or toxicity. [a]Including 30 patients who received prior amivantamab without and 21 patients with other ex20ins-targeted therapy. [b]Response confirmed ≥4 weeks after response first noted. [c]Patients had PR but confirmatory scan had not yet been performed. [d]No post-baseline imaging. [e]Proportion of patients with confirmed CR or PR. [f]Proportion of patients with CR, PR, or SD. [g]Proportion of patients with CR, PR, or with SD lasting ≥24 weeks.
BOR, best overall response; CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; ex20ins, exon 20 insertions; ICR, independent central review; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Yu HA et al. ASCO 2025;Abstract 8503. Piotrowska Z et al. *J Clin Oncol* 43(21):2387-97.

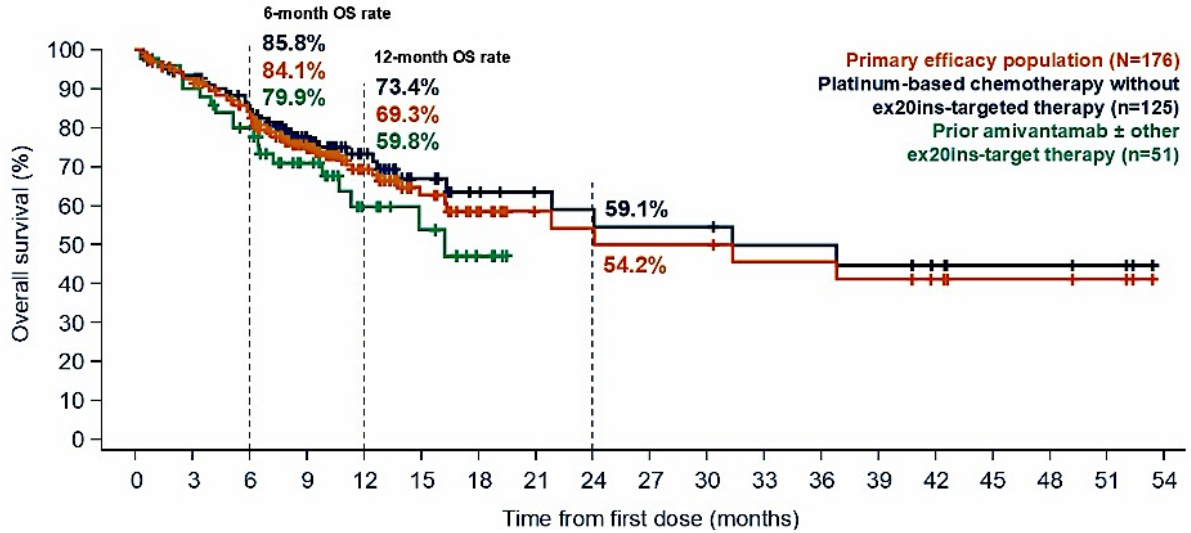
RTP RESEARCH TO PRACTICE

REZILIENT1: PFS and OS

PFS



OS



Yu HA et al. ASCO 2025;Abstract 8503. Piotrowska Z et al. *J Clin Oncol* 43(21):2387-97.

Zipalertinib and Chemotherapy Meets Primary Endpoint of PFS in a Planned Interim Analysis of the Phase III REZILIENT3 Trial for Untreated NSCLC with EGFR Exon 20 Insertion Mutations

Press Release: August 12, 2026

"The REZILIENT3 trial, a global Phase 3 clinical trial evaluating the combination of zipalertinib and platinum-based chemotherapy compared with chemotherapy alone in the first-line treatment of adult patients with previously untreated, locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR) exon 20 insertion (ex20ins) mutations, met its primary endpoint of progression-free survival (PFS) at a planned interim analysis.

In this analysis, the study demonstrated a statistically significant and clinically meaningful improvement in PFS in the zipalertinib containing arm. Observed safety for the zipalertinib containing arm was manageable. Based on these data, the Independent Data Monitoring Committee recommended unblinding the study. The trial will continue to monitor efficacy and safety."

https://www.taihooncology.com/us/news/zipalertinib-plus-chemotherapy-meets-primary-endpoint-of-progression-free-survival-in-planned-interim-analysis-of-phase-3-rezilient3-trial-in-first-line-egfr-exon-20-insertion-mutation-non-small-cell-lung-cancer/

RTP RESEARCH TO PRACTICE

Agenda

Module 5 — Lung Cancer: *Dr Liu*

- **EGFR Mutations**
- **HER2 Alterations**
- **ALK Fusions**
- **Available and Investigational Immunotherapies**
- **Small Cell Lung Cancer**

RTP RESEARCH TO PRACTICE

Cases and Discussion Questions

76-year-old “Senior Olympics athlete” with metastatic NSCLC with a HER2 TKD mutation. Received initial therapy with carboplatin, pemetrexed and pembrolizumab, then T-DXd with response followed by progression. Started on zongertinib with significant diarrhea and rash, 30% to 40% reduction in disease volume.

Stephen “Fred” Divers, MD

What is the optimal first-line therapy for patients with metastatic NSCLC and a HER2 TKD mutation? If zongertinib, sevabertinib and trastuzumab deruxtecan (T-DXd) were all equally accessible in the front-line setting — which it looks like they may soon be — how would you choose among them?

RTP
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Cases and Discussion Questions (Continued)

How would you indirectly compare the tolerability of zongertinib, sevabertinib and T-DXd? What are the most common toxicities with these agents?

What is the optimal second-line therapy for patients with HER2 TKD mutations and disease progression on first-line zongertinib? What second-line therapy would you choose after disease progression on first-line T-DXd or sevabertinib, assuming those agents move into the front-line setting?

Would you be comfortable using T-DXd for a patient with a history of interstitial lung disease, perhaps from prior thoracic radiation therapy?

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TO PRACTICE

Cases and Discussion Questions (Continued)

How do you sequence T-DXd for patients with metastatic NSCLC and HER2 overexpression (IHC 3+)?

Would you employ T-DXd for a patient with HER2 IHC 2+ or IHC 1+ disease?

How common is co-occurring HER2 mutation and HER2 overexpression? What do you do in these cases?

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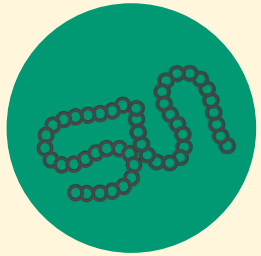
TO PRACTICE

Targeting HER2 in NSCLC

Activating ERBB2 Mutations

TKD-activating mutations:
TKIs including zongertinib for any line and sevabertinib approved for ≥2L

Activating mutations:
T-DXd approved for ≥2L setting



HER2 Overexpression (IHC 3+)

T-DXd approved for patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment (tumor agnostic)

ERBB2 Amplification

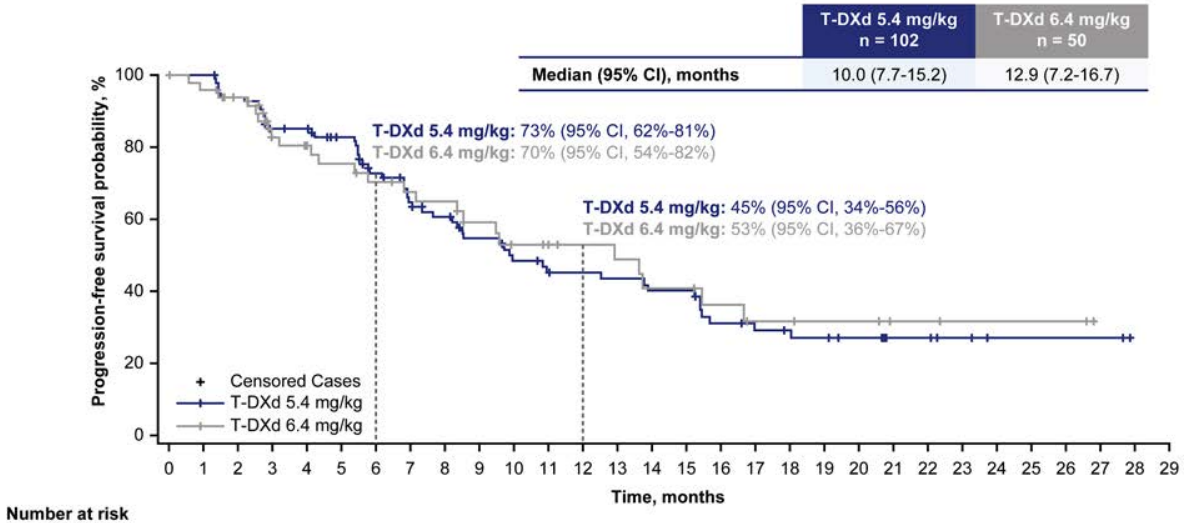
No approved therapies specifically for ERBB2 amplification

TKI = tyrosine kinase inhibitor

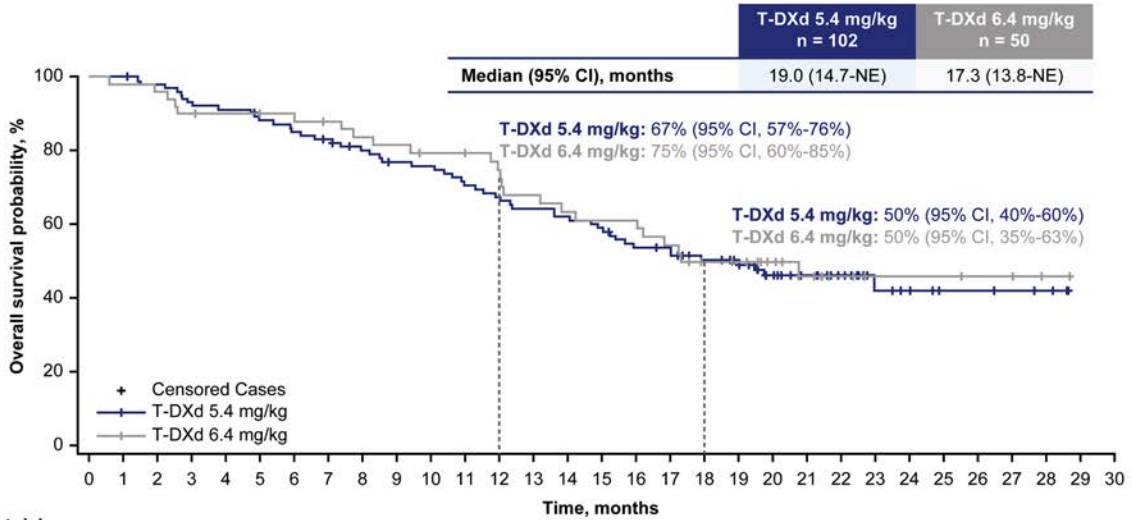
RTP RESEARCH TO PRACTICE

DESTINY-Lung02 Study: Trastuzumab Deruxtecan for HER2-Mutated NSCLC in the Second Line and Beyond

PFS



OS



Jänne PA et al. *J Thorac Oncol* 2025;20(12):1814-28.

Adjudicated Drug-Related Interstitial Lung Disease (ILD)

Adjudicated Drug-Related ILD Variable	T-DXd 5.4 mg/kg n = 101[b]	T-DXd 6.4 mg/kg n = 50[b]
Any grade, n (%)	15 (14.9)	16 (32.0)
Grade 1	4 (4.0)	3 (6.0)
Grade 2	9 (8.9)	11 (22.0)
Grade 3	1 (1.0)	1 (2.0)
Grade 4	0	0
Grade 5	1 (1.0)[c]	1 (2.0)[c]
Grade ≥3	2 (2.0)	2 (4.0)
Outcome of ILD events,[d,e] n/N (%)		
Fatal	1/15 (6.7)	1/16 (6.3)
Not recovered/not resolved	3/15 (20.0)	6/16 (37.5)
Recovering/resolving	1/15 (6.7)	0
Recovered/resolved with sequelae	0	1/16 (6.3)
Recovered/resolved	10/15 (66.7)	8/16 (50.0)
Treatment of ILD,[e,f] n/N (%)		
Steroids[g]	12/15 (80.0)	13/16 (81.3)
Antibiotics	7/15 (46.7)	5/16 (31.8)
Steroids and antibiotics	6/15 (40.0)	4/16 (25.0)

Jänne PA et al. *J Thorac Oncol* 2025;20(12):1814-28.

RTP RESEARCH TO PRACTICE

Trastuzumab Deruxtecan Demonstrated Statistically Significant and Clinically Meaningful Improvement in PFS as First-Line Treatment for HER2-Mutant Advanced NSCLC in the DESTINY-Lung04 Phase III Trial

Press Release: August 17, 2026

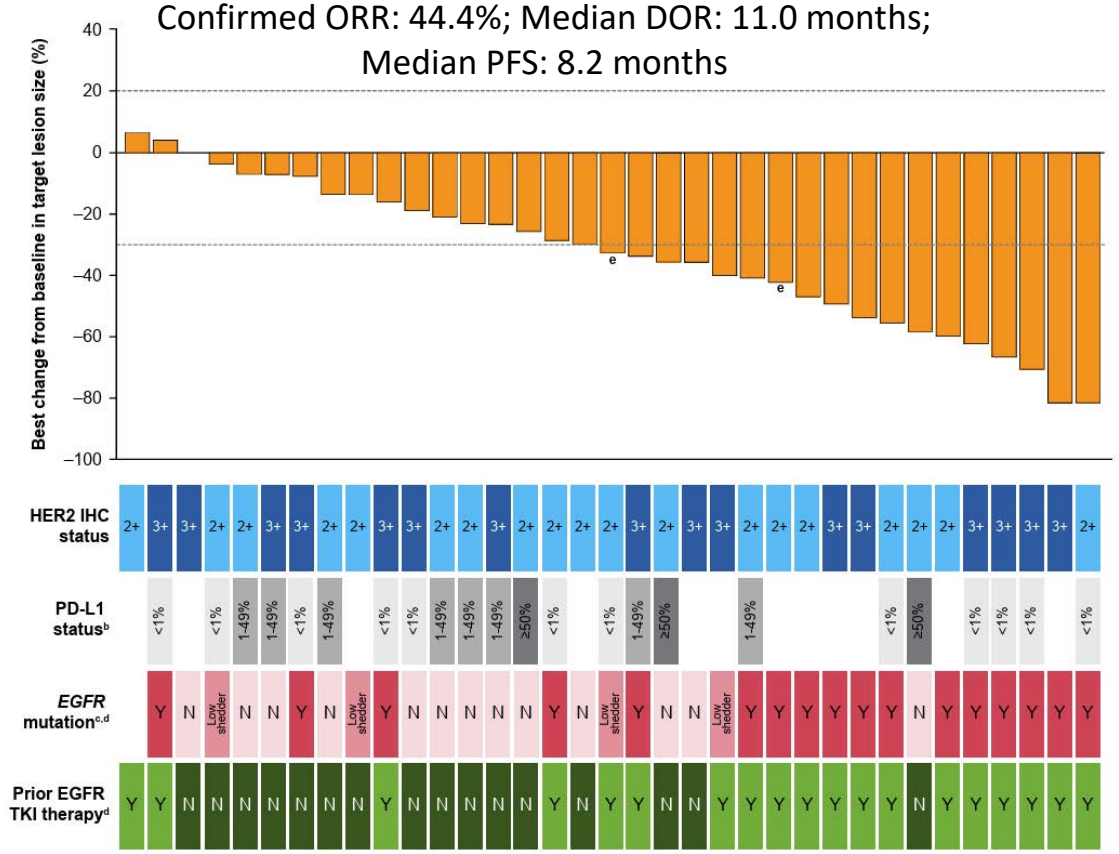
"Positive high-level results from the DESTINY-Lung04 Phase III trial showed trastuzumab deruxtecan demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) versus global standard of care (platinum-pemetrexed doublet chemotherapy plus pembrolizumab) as 1st-line treatment of patients with unresectable, locally advanced or metastatic HER2-mutant non-squamous non-small cell lung cancer (NSCLC).

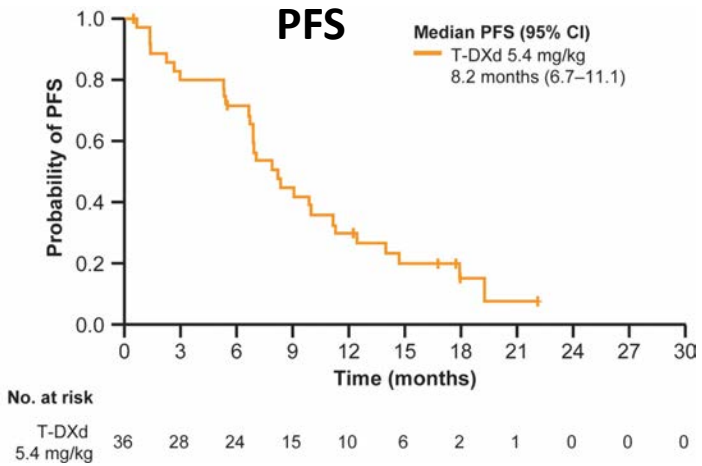
The safety profile of trastuzumab deruxtecan observed in DESTINY-Lung04 was generally consistent with its known profile, with no new safety concerns identified."

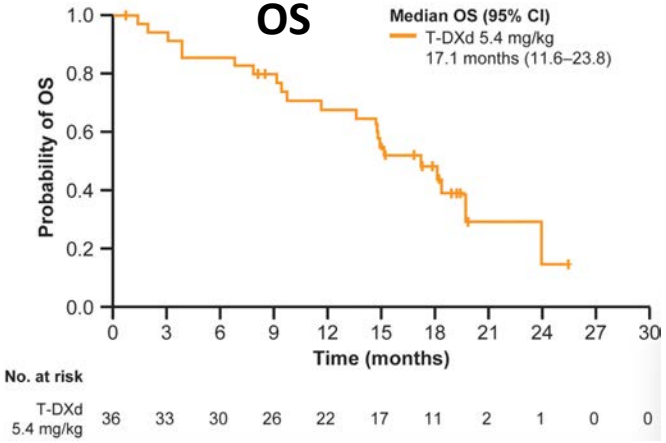
https://www.astrazeneca.com/media-centre/press-releases/2026/enhertu-improved-pfs-in-1l-her2m-lung-cancer.html.

RTP RESEARCH TO PRACTICE

DESTINY-Lung03 Study: T-DXd for HER2-Overexpressing NSCLC





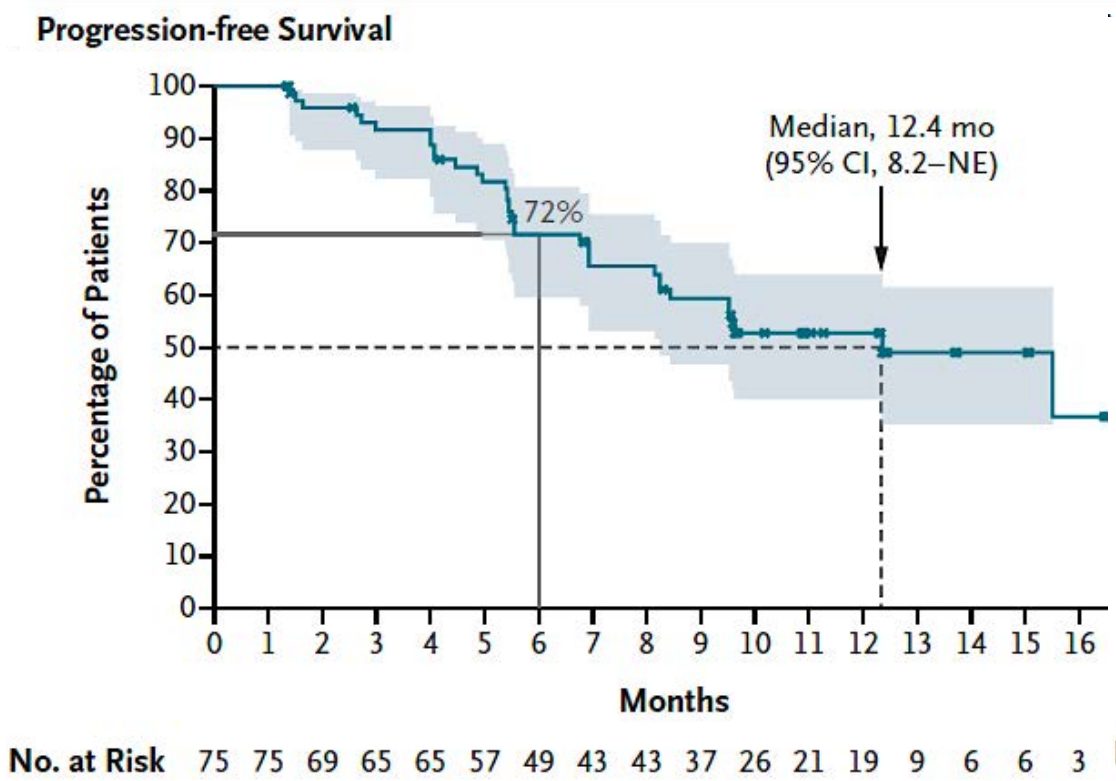


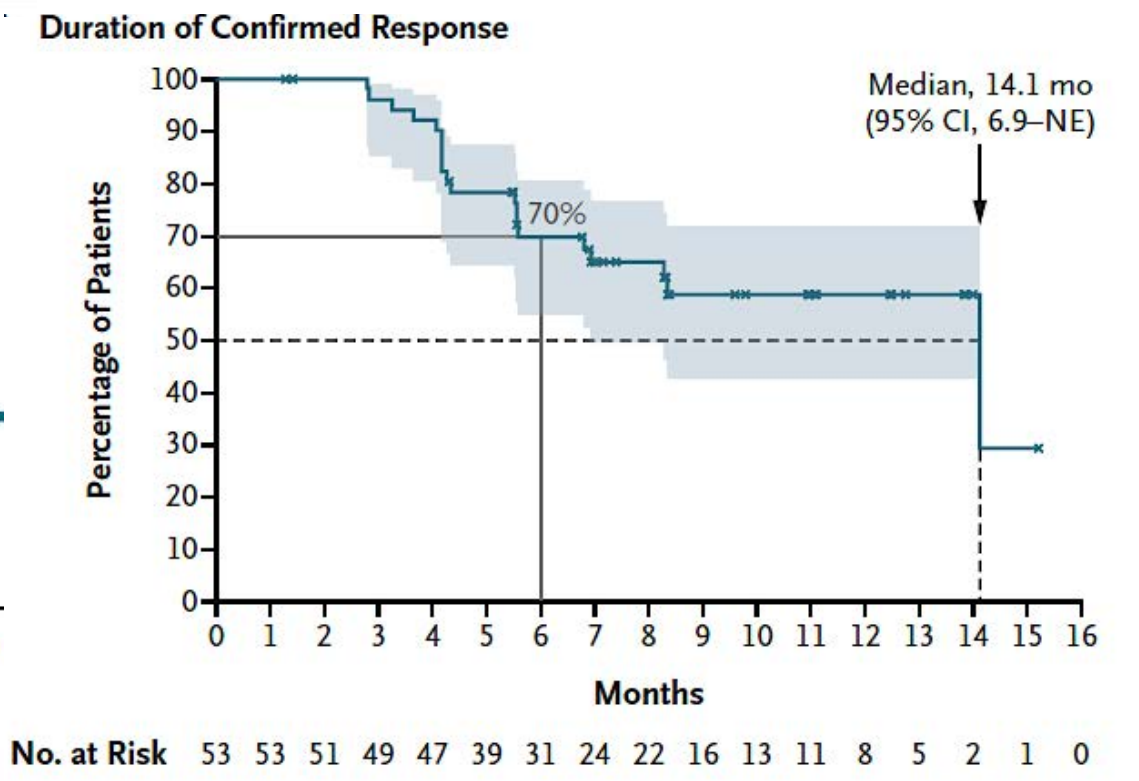
ORR = objective response rate

Planchard D et al. *J Thorac Oncol* 2026;21(5):103541.

Beamion LUNG-1 Study: Zongertinib for Previously Treated HER2-Mutated NSCLC

Zongertinib: HER2-specific, EGFR-sparing TKI



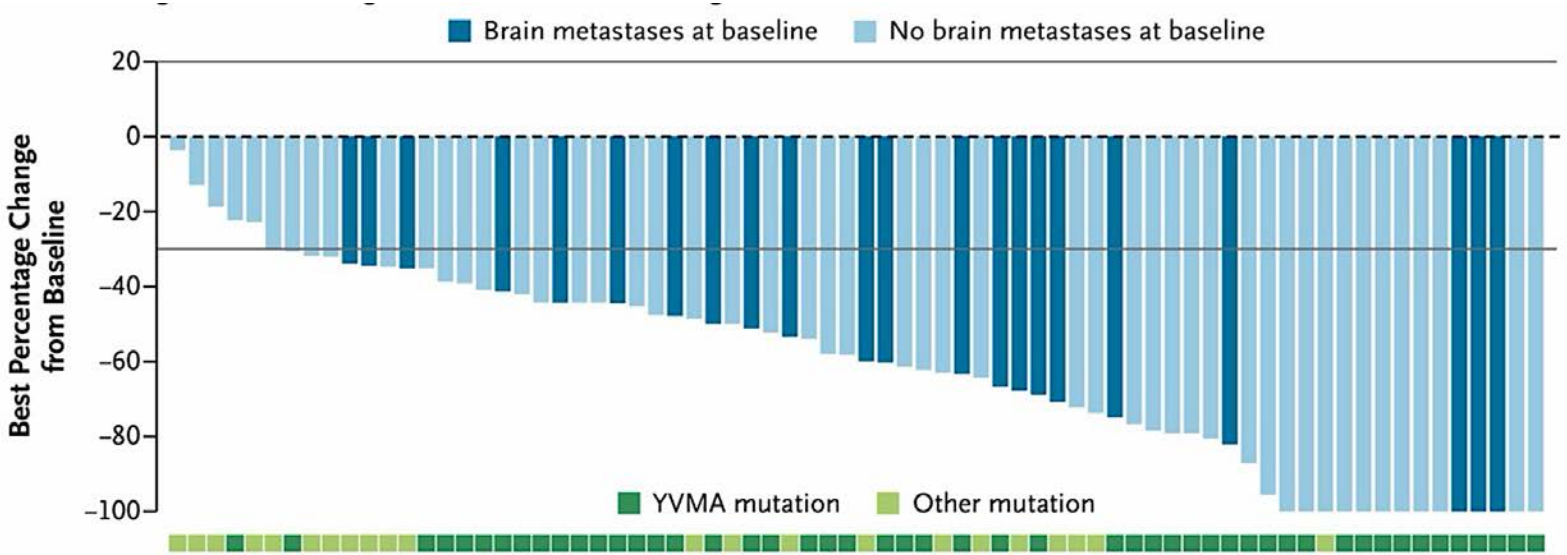


Heymach JV et al. *N Engl J Med* 2025;392:2321-33.

RTP RESEARCH TO PRACTICE

Beamion LUNG-1: Zongertinib for Treatment-Naïve HER2-Mutated NSCLC

Confirmed response by BICR (RECIST v1.1)	Cohort 2: Treatment-naïve patients N = 74
ORR	**76%**
CR, n (%)	8 (11)
PR, n (%)	48 (65)
DCR	**96%**
SD, n (%)	15 (20)
PD, n (%)	1 (1)*



- Median time to objective response was 1.4 months (95% CI, 1.1 to 6.9)

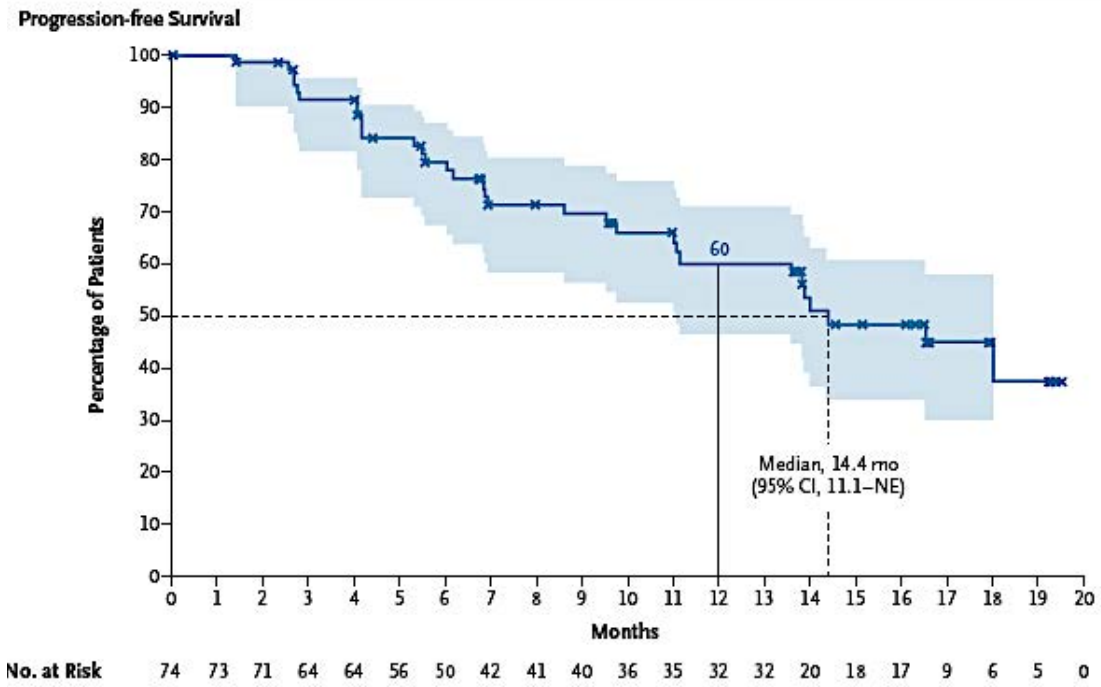
ORR = objective response rate

Heymach JV et al. *N Engl J Med* 2026;394(17):1675-84. Heymach JV et al. ELCC 2026;Abstract 6MO.

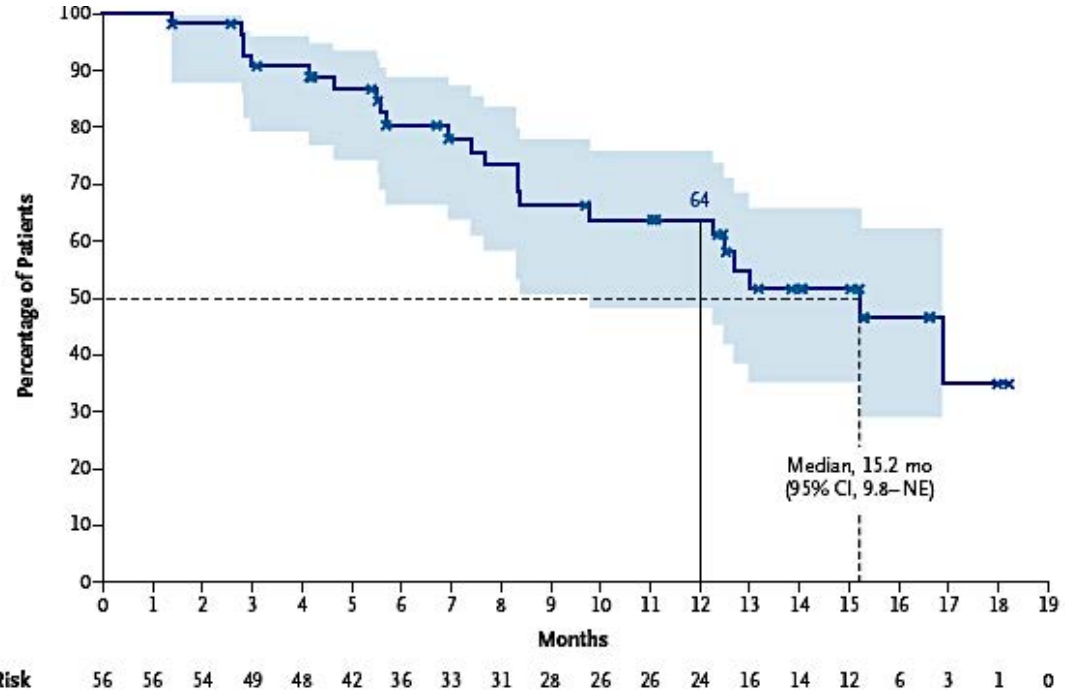
RTP RESEARCH TO PRACTICE

Beamion LUNG-1: Zongertinib for Treatment-Naïve HER2-Mutated NSCLC (Continued)

PFS



DoR

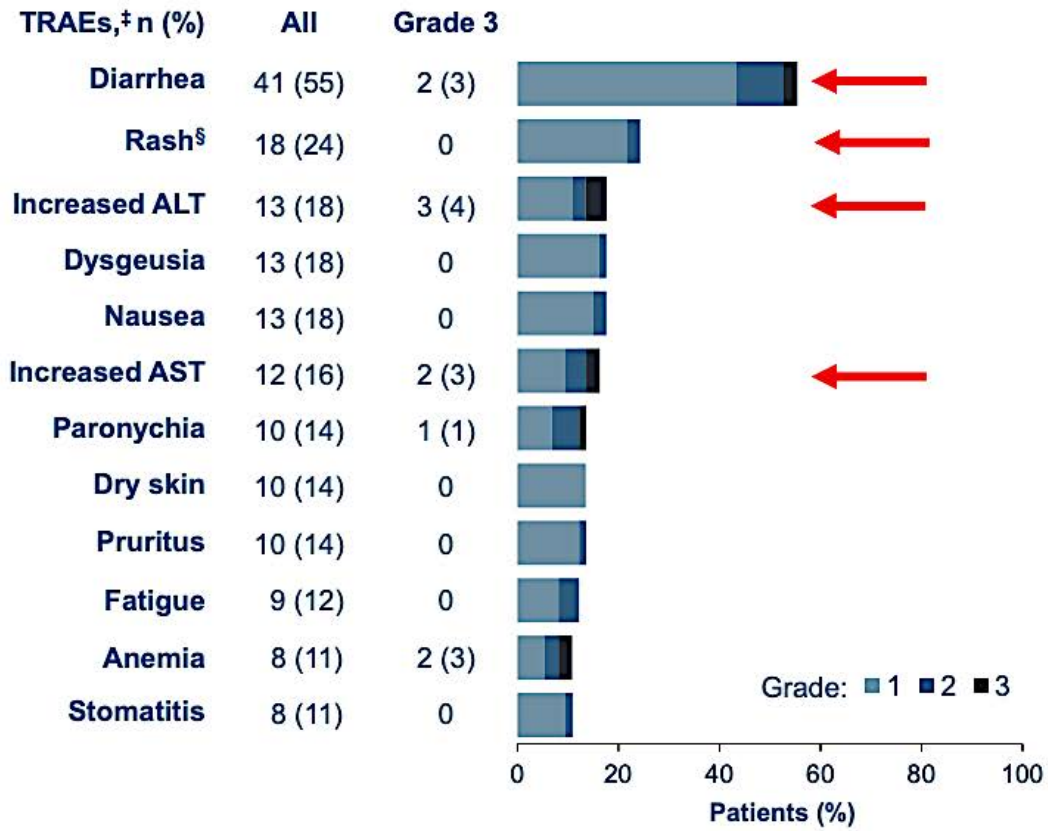


Heymach JV et al. *N Engl J Med* 2026;394(17):1675-84. Heymach JV et al. ELCC 2026;Abstract 6MO.

RTP RESEARCH TO PRACTICE

Zongertinib for Treatment-Naïve HER2-Mutated NSCLC: Safety Profile

- Zongertinib had a manageable safety profile in treatment-naïve patients (Cohort 2): TRAEs were reported in 67 (91%) patients, with grade ≥3 TRAEs in 14 (19%) patients
  - Most common grade ≥3 TRAE was increased ALT
  - Low rates of grade ≥3 diarrhea and rash
  - AEs leading to dose reduction occurred in 12 (16%) patients*
  - AEs leading to discontinuation occurred in 7 (9%) patients†



Median duration of treatment: 14.0 months (range, 0–21.0); two cases (3%) of ILD/pneumonitis were reported (both grade 2); there was one grade 4 TRAE (decreased neutrophil count) and no grade 5 TRAEs; The safety profile of patients with active brain metastases (cohort 4) consistent with the overall Beamion LUNG-1 patient population. *AEs leading to dose reduction were: increased ALT, increased AST (both n = 3), diarrhea, decreased ejection fraction (both n = 2), anemia, increased blood bilirubin, hypertransaminasemia, lower GI hemorrhage, peripheral neuropathy, paronychia and vomiting (all n = 1); †AEs leading to dose discontinuation were: decreased ejection fraction (n = 2), increased ALT, anemia, increased AST, diarrhea, pericardial effusion and pneumonitis (all n = 1); ‡TRAEs as assessed by the investigator that occurred in ≥10% of patients are shown; §grouped term

Heymach JV et al. *N Engl J Med* 2026;394(17):1675-84. Heymach JV et al. ELCC 2026;Abstract 6MO.

RTP RESEARCH TO PRACTICE

SOHO-01 Trial Cohorts D, F: Sevabertinib for Treatment-Naïve and Previously Treated HER2-Mutated NSCLC

Sevabertinib: Reversible TKI

Cohort D: Patients previously treated with systemic therapy but naïve to HER2 ex20ins-targeted therapy

Cohort F: Patients naïve to systemic treatment for locally advanced or metastatic disease

	Cohort D			Cohort F		
	Treated patients with non-squamous histology and *HER2* TKD mutation (*n*=70)	Treated patients with non-squamous histology and *HER2* YVMA mutation (*n*=49)	All treated patients (*n*=81)	Treated patients with non-squamous histology and *HER2* TKD mutation (*n*=69)	Treated patients with non-squamous histology and *HER2* YVMA mutation (*n*=55)	All treated patients (*n*=73)
ORR, % (95% CI)[a]	73 (61, 83)	78 (63, 88)	67 (55, 77)	75 (64, 85)	75 (61, 85)	75 (64, 85)
DCR, % (95% CI)[b]	84 (74, 92)	88 (75, 95)	81 (71, 89)	90 (80, 96)	89 (78, 96)	89 (80, 95)
mDoR, months (95% CI)	9.5 (6.3, 13.5)[c]	9.5 (6.3, 15.0)[d]	9.5 (6.3, 13.5)[e]	15.1 (8.8, NE[f])[c]	15.1 (8.8, NE[f])[d]	12.2 (8.8, NE[f])[e]
mPFS, months (95% CI)	9.6 (6.9, 14.5)	12.2 (6.9, 16.5)	8.3 (6.9, 12.3)	13.5 (10.0, NE[f])	16.4 (9.9, NE[f])	13.5 (10.0, NE[f])

[a]Patients with confirmed CR or PR; [b]Patients with confirmed CR or PR or stable disease for ⩾12 weeks; [c]Subset of patients with confirmed CR or PR (Cohort D, *n*=51; Cohort F, *n*=52); [d]Subset of patients with confirmed CR or PR (Cohort D, *n*=38; Cohort F, *n*=41); [e]Subset of patients with confirmed CR or PR (Cohort D, *n*=54; Cohort F, *n*=55); [f]Value cannot be estimated
CI, confidence interval; CR, complete response; DCR, disease control rate; mDoR, median duration of response; mPFS, median progression-free survival; NE, not estimable; PR, partial response

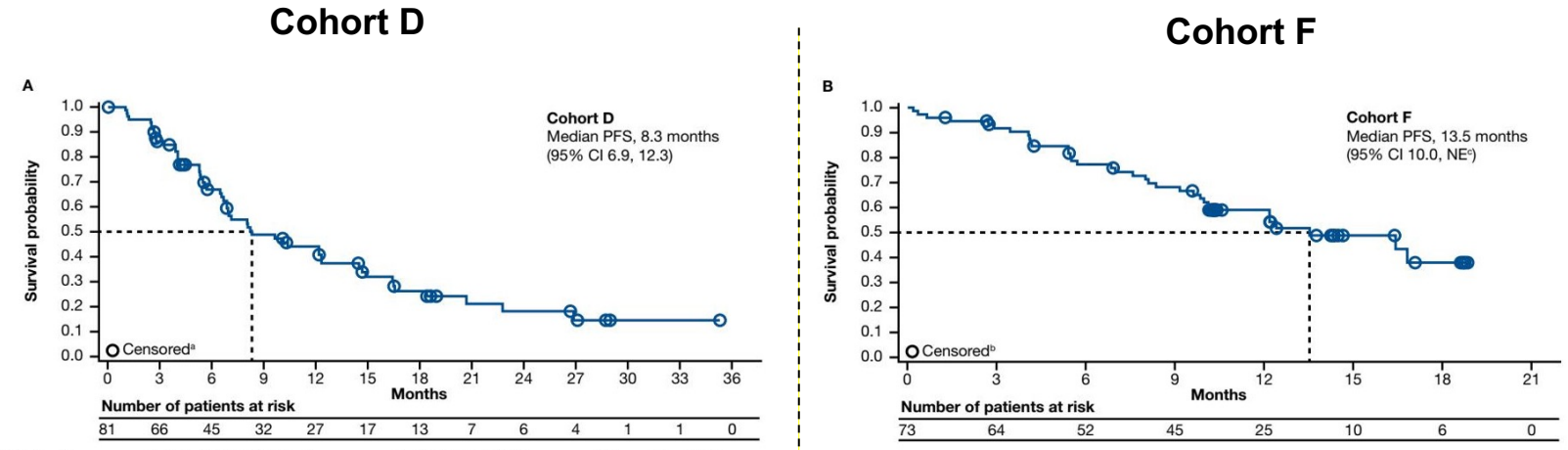
ORR = overall response rate

Loong HH et al. ASCO 2026;Abstract 8622.

RTP RESEARCH TO PRACTICE

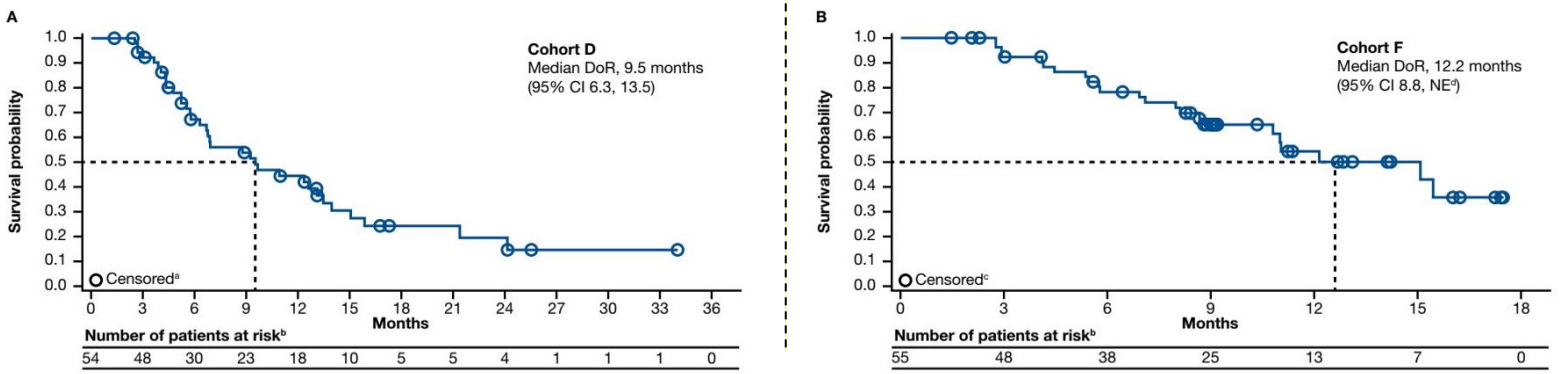
SOHO-01 Cohorts D, F: Sevabertinib for Treatment-Naïve and Previously Treated HER2-Mutated NSCLC

PFS



[a]Patients censored: 27 (33%); [b]Patients censored: 39 (53%); [c]Value cannot be estimated
NE, not estimable

DoR



[a]Patients censored: 19 (35%); [b]Patients with confirmed CR or PR; [c]Patients censored: 35 (58%); [d]Value cannot be estimated
NE, not estimable

Loong HH et al. ASCO 2026;Abstract 8622.

RTP RESEARCH TO PRACTICE

Select Ongoing Phase III Trials of HER2-Targeted Therapy for NSCLC

Trial identifier	N	Setting	Treatment arms	Key endpoints	Estimated completion date
DESTINY-Lung06 (NCT06899126)	686	1L HER2-overexpressing, PD-L1 TPS <50% NSCLC	T-DXd + pembrolizumab versus pembrolizumab + chemotherapy	PFS, OS	2032-11-24
Beamion LUNG-2 (NCT06151574)	428	1L nonsquamous NSCLC with HER2 TKD mutations	Zongertinib versus standard Tx	PFS, OS	2028-01-28
Beamion LUNG-3 (NCT07195695)	400	Adjuvant; Resectable, Stage II-IIIB HER2-mutated NSCLC	Zongertinib versus standard Tx	DFS, OS	2036-09-02
SOHO-02 (NCT06452277)	444	1L HER2-mutated NSCLC	Sevabertinib versus standard Tx	PFS, OS	2029-06-27

TPS = tumor proportion score

RTP RESEARCH TO PRACTICE

Agenda

Module 5 — Lung Cancer: *Dr Liu*

- **EGFR Mutations**
- **HER2 Alterations**
- **ALK Fusions**
- **Available and Investigational Immunotherapies**
- **Small Cell Lung Cancer**

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TO PRACTICE

Cases and Discussion Questions

45-year-old never smoker presents with metastatic lung adenocarcinoma and multiple asymptomatic brain metastases, the largest measuring 1.2 cm. NGS demonstrates an EML4-ALK fusion. ECOG PS is 0.

Sunil Babu, MD

In general, what is your preferred first-line treatment for metastatic NSCLC with an ALK fusion?

Which ALK inhibitor would you choose in the first line for this patient with baseline CNS disease?

When can highly CNS-active systemic therapy allow you to defer brain radiation?

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TO PRACTICE

Cases and Discussion Questions

I have a patient right now who has Stage III unresectable disease, is getting chemoradiation and has an ALK gene rearrangement.

Brian P Mulherin, MD

In patients with unresectable locally advanced NSCLC, for which actionable genomic alterations do you (or would you like to) recommend targeted treatment rather than durvalumab consolidation after chemoradiation therapy?

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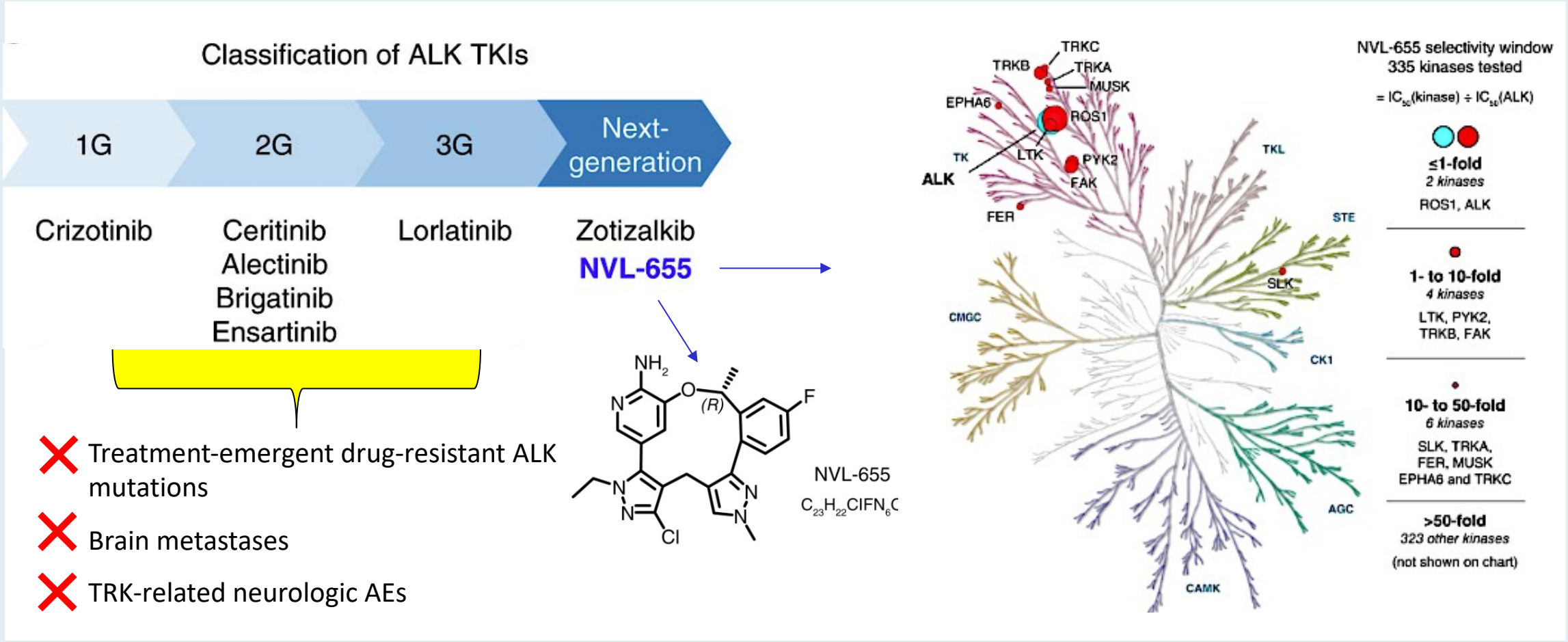
Targeting ALK in NSCLC



Lin J et al. *Cancer Discov* 2024;14(12):2367-86.

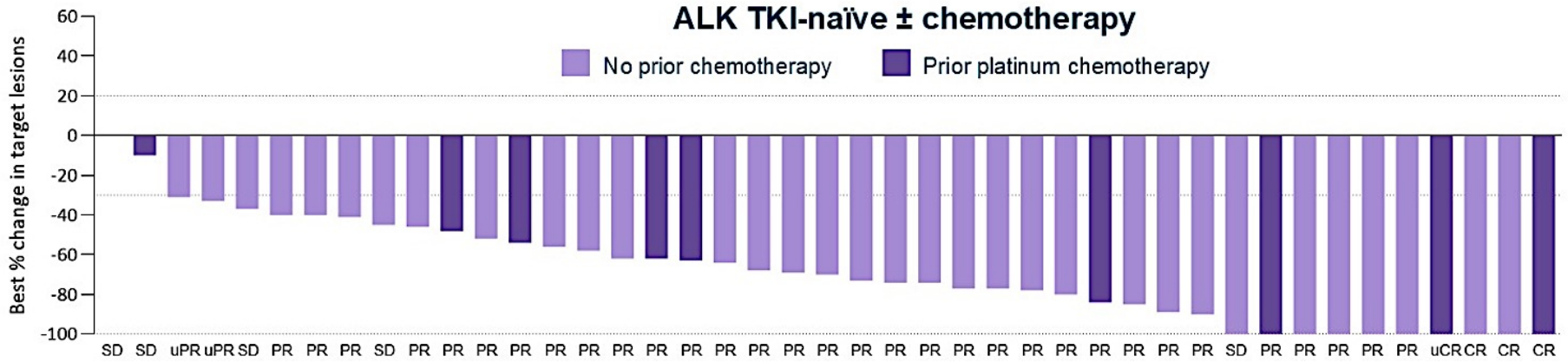
ALKOVE-1: Efficacy of Neladalkib for ALK TKI-Naïve Disease

ALK TKI-naïve, BICR	Response-evaluable N = 44
ORR, % (n/N)	**86%** (38/44) [a]
CR, % (n/N)	9% (4/44) [b]
% DOR ≥ 12 months [95% CI] [c]	**91%** [70, 98]
DOR range	1.7+ to 14.8+ months

[a] Includes 2 single-timepoint PR pending confirmation for ongoing patients. [b] Includes 1 single-timepoint CR pending confirmation in ongoing patient with prior confirmed PR. [c] Analyses of DOR based on Kaplan-Meier estimates.

ALK TKI-naïve, BICR	CNS Response-evaluable N = 9
IC-ORR, % (n/N)	**78%** (7/9)
IC-CR, % (n/N)	44% (4/9) [d]
IC-DOR	**No CNS progression events among intracranial responders**
IC-DOR range	3.1+ to 7.0+ months

[d] Includes 1 single-timepoint IC-CR pending confirmation in ongoing patient with prior confirmed IC-PR.



BICR, blinded independent central review; **CI**, confidence interval; **CNS**, central nervous system; **CR**, complete response; **DOR**, duration of response; **ORR**, objective response rate; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease; **TKI**, tyrosine kinase inhibitor.

Lin JJ et al. ASCO 2026;Abstract 8503.

RTP RESEARCH TO PRACTICE

Agenda

Module 5 — Lung Cancer: *Dr Liu*

- **EGFR Mutations**
- **HER2 Alterations**
- **ALK Fusions**
- **Available and Investigational Immunotherapies**
- **Small Cell Lung Cancer**

RTP RESEARCH TO PRACTICE

Cases and Discussion Questions

69 y/o woman who presented with SOB, anorexia with a 20-lb weight loss and cough. Imaging showed a 3.4-cm RUL nodule, bulky ipsilateral hilar and mediastinal LAD, 3 liver metastases, a right adrenal metastasis, innumerable bone metastases and 2 asymptomatic cerebellar metastases. Bx confirmed squamous cell carcinoma of the lung, PD-L1 TPS 20%. Tissue- and blood-based NGS showed no actionable genomic alterations. ECOG PS 1.

Brian P Mulherin, MD

If this patient were to ask you the chances that she would be alive and free of progressive disease with first-line pembrolizumab/chemotherapy after 1 year, how would you respond? What about after 3 years? 5 years?

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Cases and Discussion Questions (Continued)

Do you believe immune checkpoint bispecific antibodies will replace anti-PD-1/PD-L1 antibodies as first-line treatment? Which immune checkpoint bispecific antibodies (PD-1 x VEGF, PD-1 x TIGIT), if any, are you particularly enthusiastic about?

This patient has been researching and says, "I've read about a drug that's approved in China and is more effective than what I can currently receive. Will this be available here anytime soon? If it were, would you recommend it?" How would you respond?

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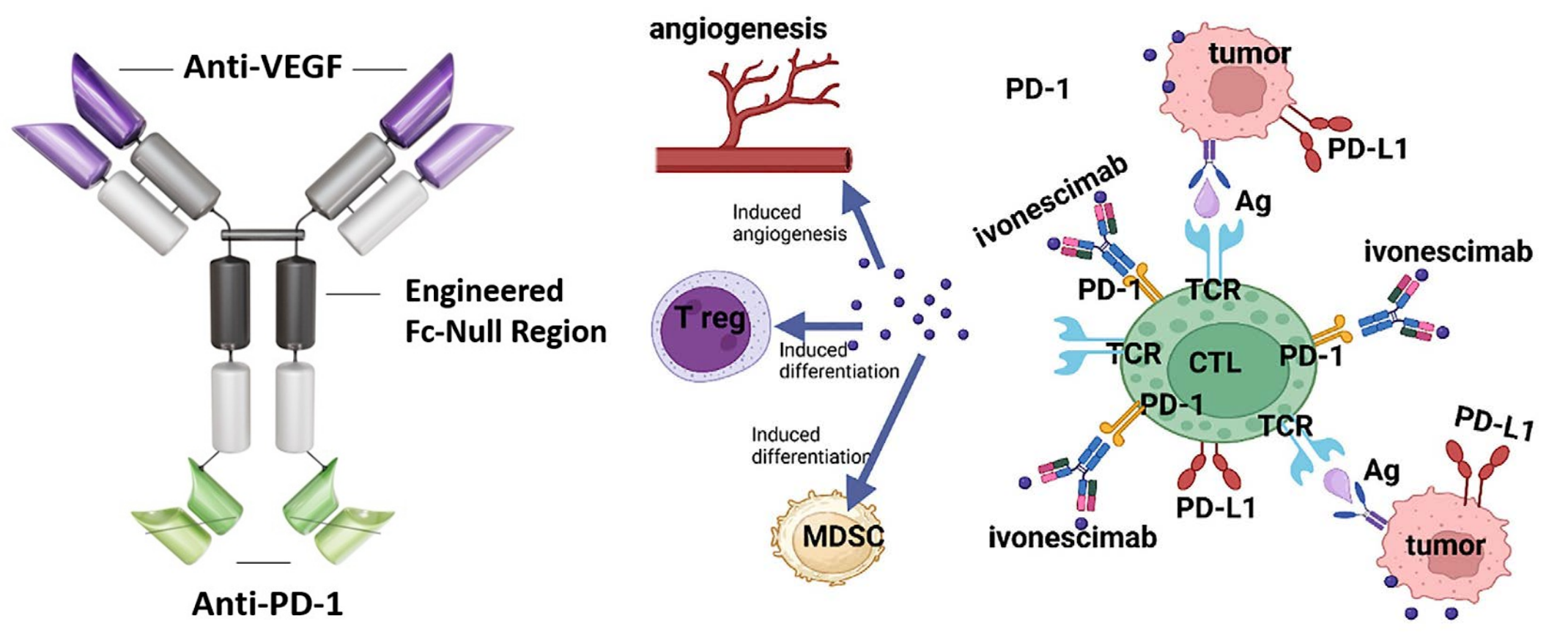
Ivonescimab: PD-1 x VEGF Bispecific Antibody



Zhang L et al. ASCO 2024;Abstract 8508.

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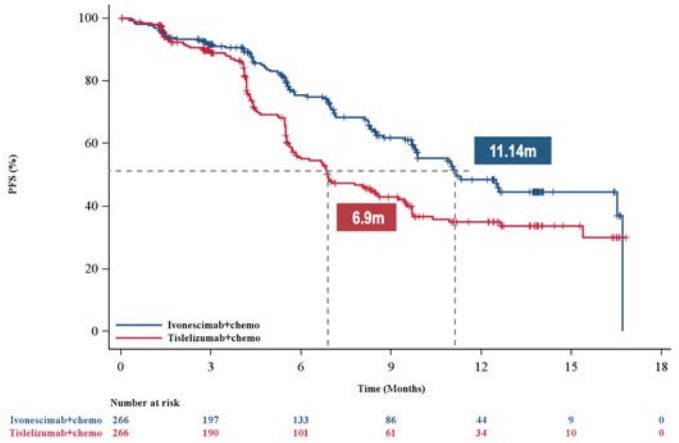
TO PRACTICE

HARMONi-6 Trial: First-Line Ivonescimab with Chemotherapy versus Tislelizumab with Chemotherapy for Squamous NSCLC

PFS

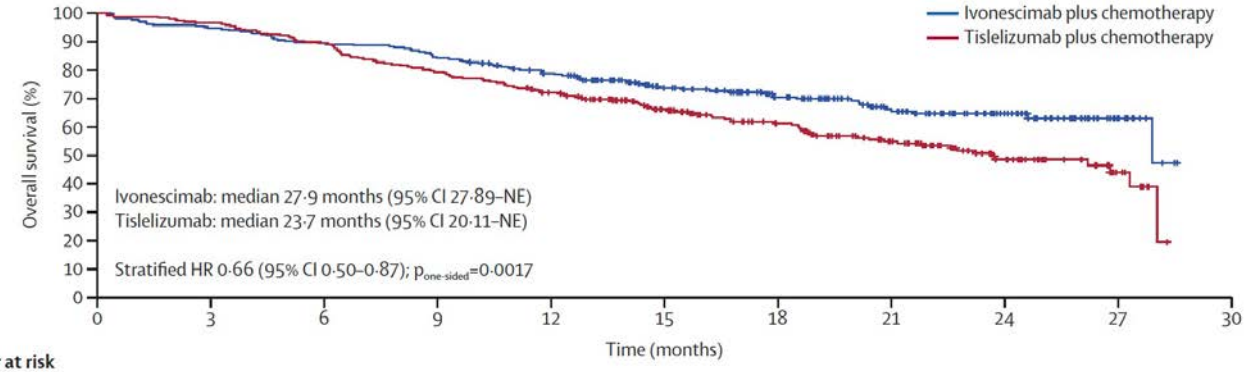


	Ivonescimab + chemo (N=266)	Tislelizumab + chemo (N=266)
mPFS, months (95% CI)	11.14 (9.86, NE)	6.90 (5.82, 8.57)
Stratified HR (95% CI)	0.60 (0.46, 0.78)	
p-value	<0.0001	

Median Follow-up: 10.28 months

OS

Consistent PFS benefit by investigator-assessment: HR = 0.64 (95% CI: 0.50, 0.84)



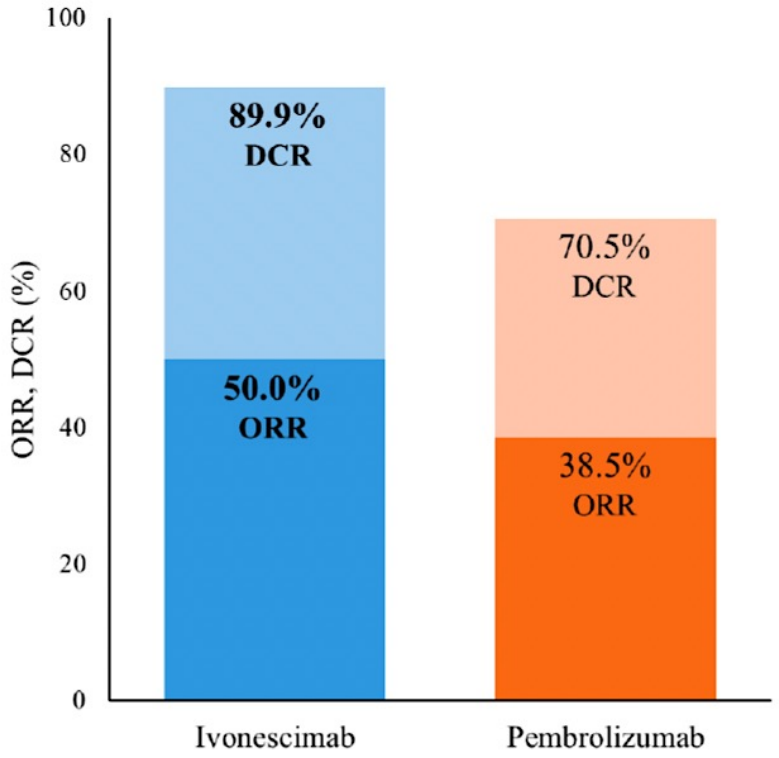
Number at risk (censored)											
Ivonescimab plus chemotherapy	266 (0)	252 (0)	238 (0)	224 (0)	202 (8)	152 (46)	119 (73)	85 (100)	49 (135)	15 (168)	0 (182)
Tislelizumab plus chemotherapy	266 (0)	257 (0)	238 (0)	211 (0)	186 (6)	142 (36)	113 (55)	80 (77)	43 (107)	12 (136)	0 (146)

Lu S et al. ESMO 2025;Abstract LBA4. Lu S et al. *Lancet* 2026;407(10548):2620-9.

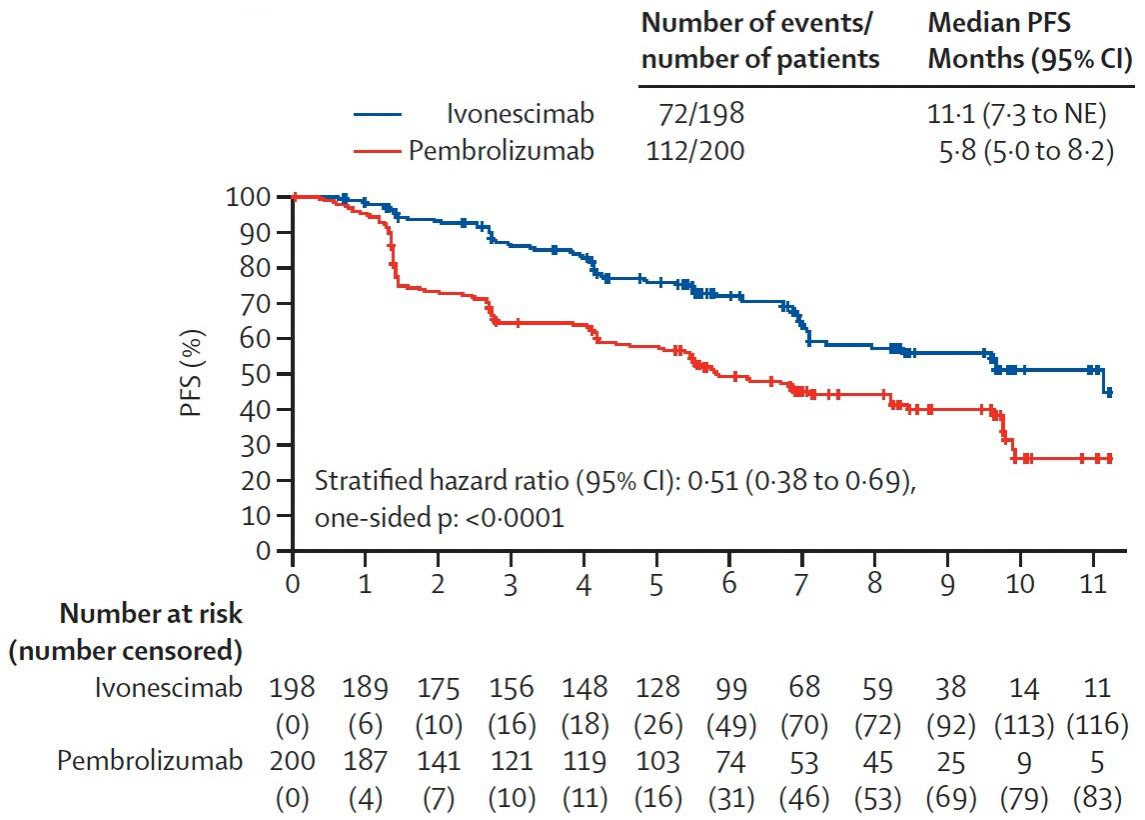
RTP RESEARCH TO PRACTICE

HARMONi-2 Study: First-Line Ivonescimab versus Pembrolizumab for PD-L1-Positive NSCLC

ORR and DCR



PFS

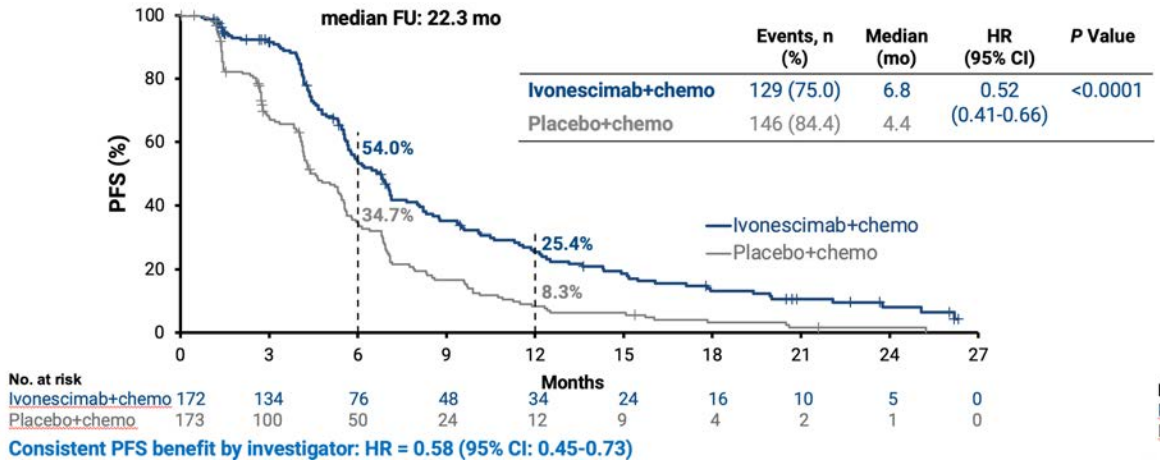


ORR = objective response rate

Zhou C et al. WCLC 2024;Abstract PL02.04. Xiong A et al. *Lancet 2025*;405(10481):839-49.

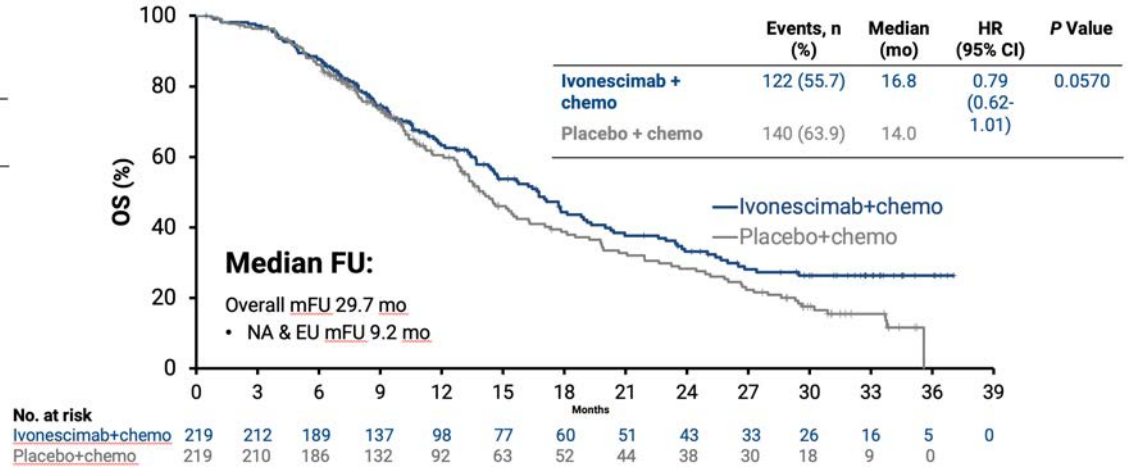
RTP RESEARCH TO PRACTICE

HARMONi Trial: Ivonescimab with Chemotherapy for EGFR-Mutated NSCLC After EGFR TKI



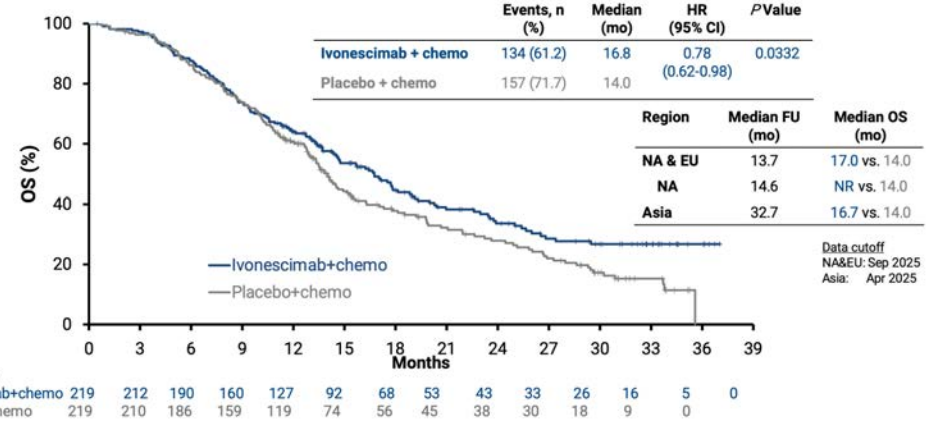
	Events, n (%)	Median (mo)	HR (95% CI)	*P* Value
Ivonescimab+chemo	129 (75.0)	6.8	0.52 (0.41-0.66)	<0.0001
Placebo+chemo	146 (84.4)	4.4		

Consistent PFS benefit by investigator: HR = 0.58 (95% CI: 0.45-0.73)



	Events, n (%)	Median (mo)	HR (95% CI)	*P* Value
Ivonescimab + chemo	122 (55.7)	16.8	0.79 (0.62-1.01)	0.0570
Placebo + chemo	140 (63.9)	14.0		

OS stable with longer term Western data, nominal p=0.0332



	Events, n (%)	Median (mo)	HR (95% CI)	*P* Value
Ivonescimab + chemo	134 (61.2)	16.8	0.78 (0.62-0.98)	0.0332
Placebo + chemo	157 (71.7)	14.0		

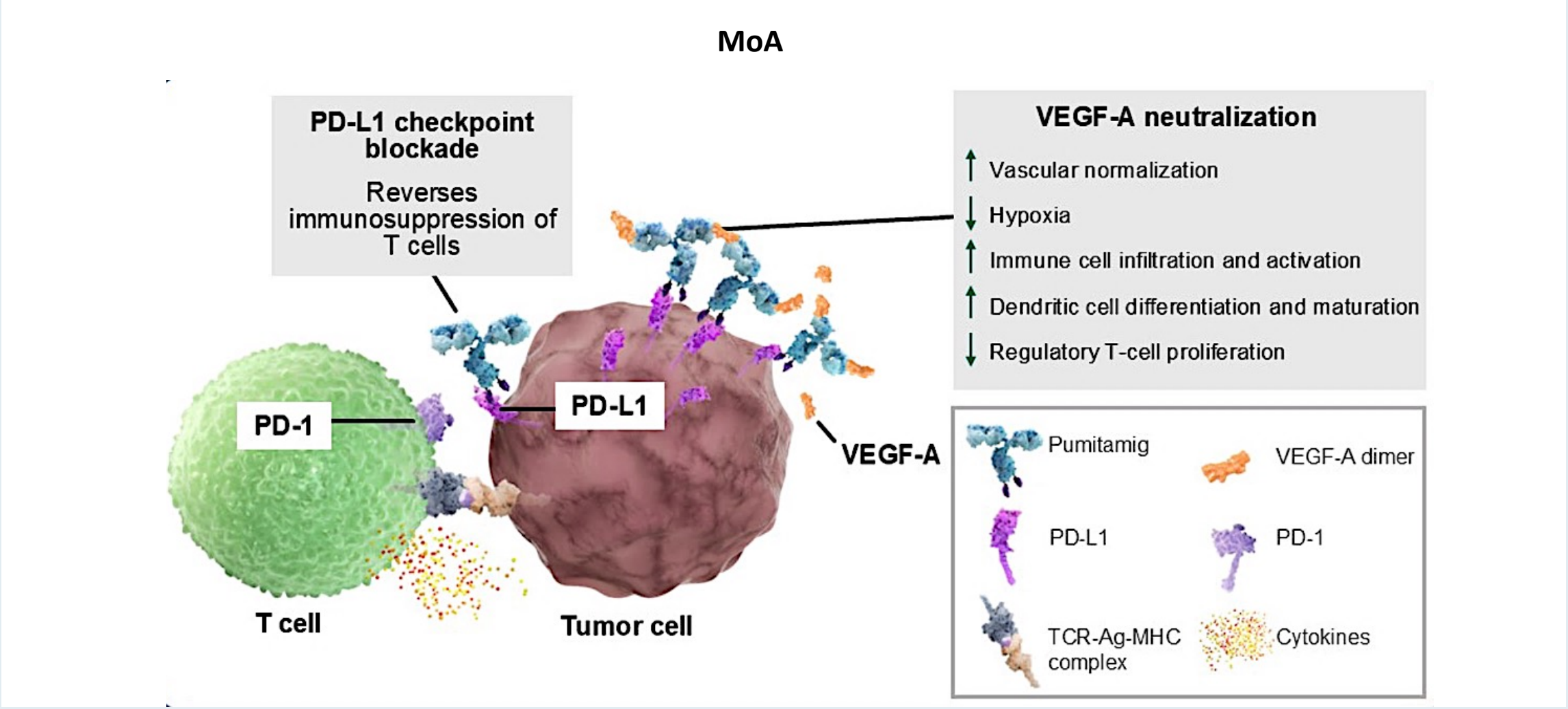
Region	Median FU (mo)	Median OS (mo)
NA & EU	13.7	17.0 vs. 14.0
NA	14.6	NR vs. 14.0
Asia	32.7	16.7 vs. 14.0

Data cutoff
NA&EU: Sep 2025
Asia: Apr 2025

Goldman J et al. WCLC 2025;Abstract PL02.12.

RTP RESEARCH TO PRACTICE

Pumitamig: A PD-L1 x VEGF-A Bispecific Antibody

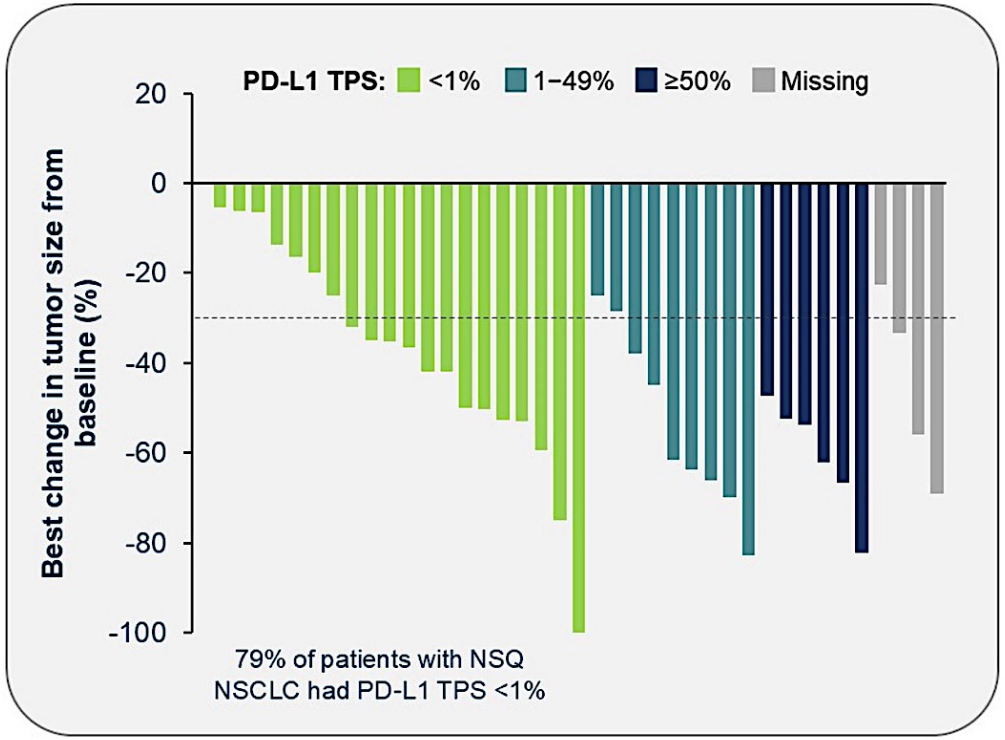


Peters S et al. ASCO 2026;Abstract 8513.

ROSETTA Lung-02: A Phase II/III Trial of First-Line Pumitamig and Chemotherapy for NSCLC

Efficacy

	Overall NSCLC (NSQ + SQ)				
	TPS <1% (n = 21)	TPS 1–49% (n = 9)	TPS ≥50% (n = 6)	Missing* (n = 4)	Overall (N = 40)
uORR, % (95% CI)	61.9 (38.4–81.9)	77.8 (40.0–97.2)	100.0 (54.1–100.0)	75.0 (19.4–99.4)	72.5 (56.1–85.4)
cORR, % (95% CI)	**47.6** (25.7–70.2)	77.8 (40.0–97.2)	100.0 (54.1–100.0)	50.0 (6.8–93.2)	62.5 (45.8–77.3)
cBOR, n (%)					
CR	0	1 (11.1)	0	0	1 (2.5)
PR	10 (47.6)	6 (66.7)	6 (100.0)	2 (50.0)	24 (60.0)
SD	11 (52.4)	2 (22.2)	0	2 (50.0)	15 (37.5)

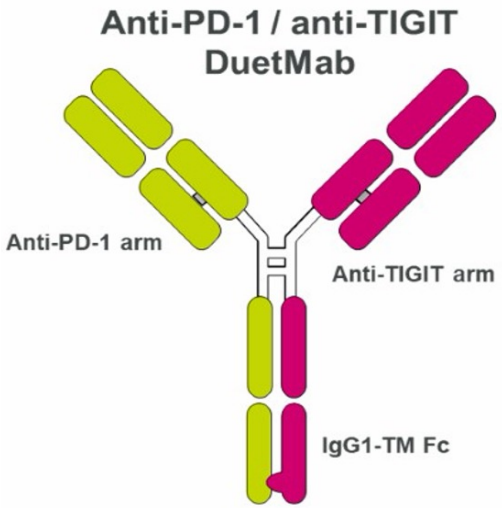


uORR = unconfirmed objective response rate; NSQ = nonsquamous

Peters S et al. ASCO 2026;Abstract 8513.

RTP RESEARCH TO PRACTICE

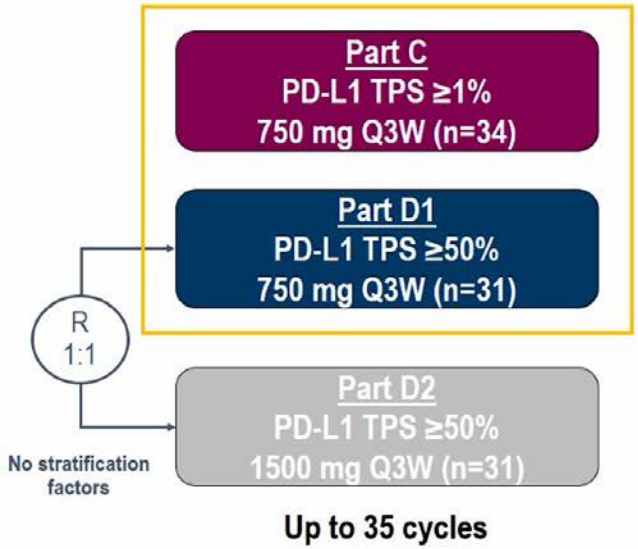
ARTEMIDE-01 Trial: Rilvegostomig for Checkpoint Inhibitor-Naïve NSCLC



CPI-naïve, PD-L1 TPS ≥1% Stage IV NSCLC

- Up to 1 prior chemotherapy regimen for metastatic disease
- PD-L1 TPS per local test
- *EGFR/ALK* wild-type

Part A (dose escalation) and Part B (dose expansion) in CPI-resistant NSCLC not pictured



Primary endpoints

- ORR per investigator per RECIST v1.1
- Safety

Key secondary endpoints

- DoR
- PFS

ORR and DoR

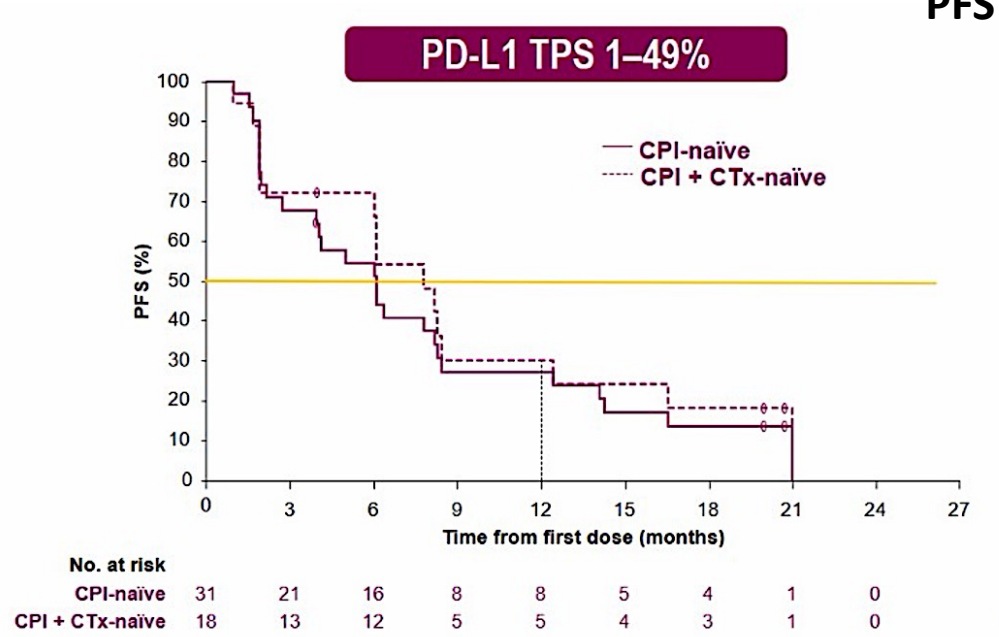
	PD-L1 TPS 1–49%		PD-L1 TPS ≥50%	
	CPI-naïve (n=31)	CPI + CTx-naïve (n=18)	CPI-naïve (n=34)	CPI + CTx-naïve (n=31)
ORR, % (95% CI)	29.0 (14.2–48.0)	44.4 (21.5–69.2)	61.8 (43.6–77.8)	67.7 (48.6–83.3)
Median DoR, months (range)	9.9 (4.1–NC)	8.5 (4.1–NC)	NR (10.3–NC)	NR (10.3–NC)

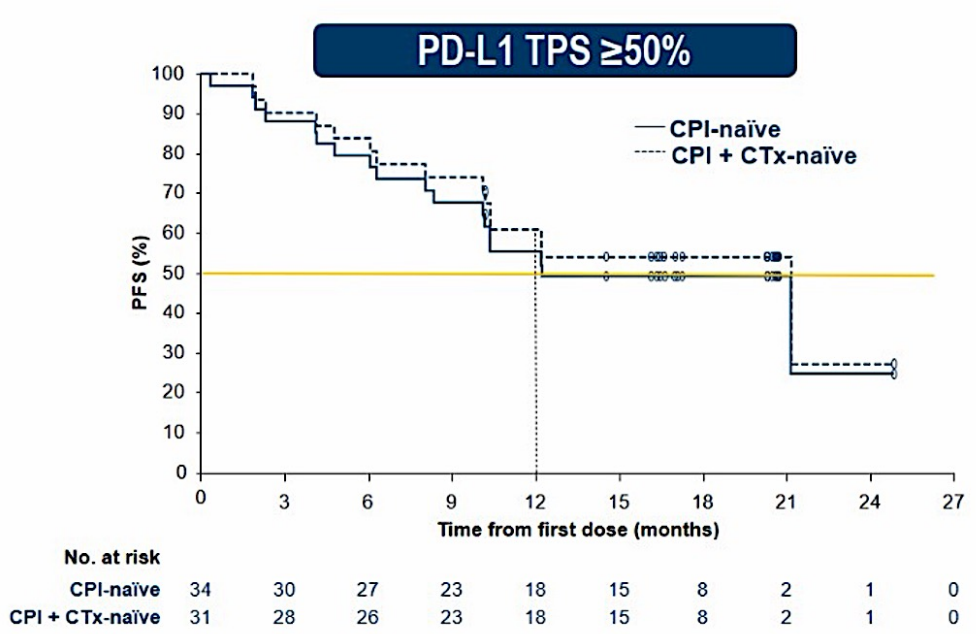
ORR = objective response rate

Cho BC et al. ESMO 2025;Abstract 1853MO.

ARTEMIDE-01: PFS

PFS





	PD-L1 TPS 1–49%		PD-L1 TPS ≥50%	
	CPI-naïve (n=31)	CPI + CTx-naïve (n=18)	CPI-naïve (n=34)	CPI + CTx-naïve (n=31)
Median PFS, months (95% CI)	6.1 (2.7–8.3)	7.8 (1.9–12.5)	12.3 (8.4–NC)	21.2 (10.2–NC)
12-month PFS, % (95% CI)	27.2 (12.9–43.6)	30.1 (11.1–52.0)	55.5 (37.3–70.3)	60.8 (41.4–75.6)

Cho BC et al. ESMO 2025;Abstract 1853MO.

Select Ongoing Phase III Trials of Bispecific Therapy for NSCLC

Trial identifier	N	Setting	Treatment arms	Key endpoints	Estimated completion date
HARMONi-3 (NCT05899608)	1,600	1L metastatic NSCLC	Ivonescimab + chemotherapy versus pembrolizumab + chemotherapy	PFS, OS	2029-12-31
HARMONi-7 (NCT06767514)	780	1L metastatic NSCLC with high PD-L1 expression (≥50%)	Ivonescimab versus pembrolizumab	PFS, OS	2029-06
ARTEMIDE-Lung02 (NCT06692738)	1,160	1L metastatic squamous NSCLC with PD-L1 expression (≥1%)	Rilvegostomig + chemotherapy versus pembrolizumab + chemotherapy	PFS, OS	2030-07-01
ARTEMIDE-Lung03 (NCT06627647)	1,160	1L metastatic nonsquamous NSCLC with PD-L1 expression (≥1%)	Rilvegostomig + chemotherapy versus pembrolizumab + chemotherapy	PFS, OS	2030-11-18
ARTEMIDE-Lung04 (NCT06868277)	830	1L metastatic NSCLC with high PD-L1 expression (≥50%)	Rilvegostomig versus pembrolizumab	PFS, OS	2030-12-02

RTP RESEARCH TO PRACTICE

Agenda

Module 5 — Lung Cancer: *Dr Liu*

- **EGFR Mutations**
- **HER2 Alterations**
- **ALK Fusions**
- **Available and Investigational Immunotherapies**
- **Small Cell Lung Cancer**

RTP RESEARCH TO PRACTICE

Cases and Discussion Questions

70-year-old woman, a former smoker with a PMH of breast cancer, develops extensive-stage SCLC and receives cisplatin/etoposide/durvalumab.

Zanetta S Lamar, MD

How do you think through the use of maintenance lurbinectedin? Would you be comfortable administering it with durvalumab for a patient such as this one who already started on that agent?

When and for whom are you thinking about tarlatamab? Does tarlatamab have similar tolerability concerns to those with the bispecific antibodies that we use in other diseases, such as lymphoma and multiple myeloma?

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Cases and Discussion Questions (Continued)

Based on available data, would you like to have access to ifinatamab deruxtecan (I-DXd) for your patients with ES-SCLC? If so, where would you envision using it opposite other available options?

What are the primary side effects associated with I-DXd? How do rates and severity of ILD compare to other DXd-based antibody-drug conjugates that we use in lung cancer?

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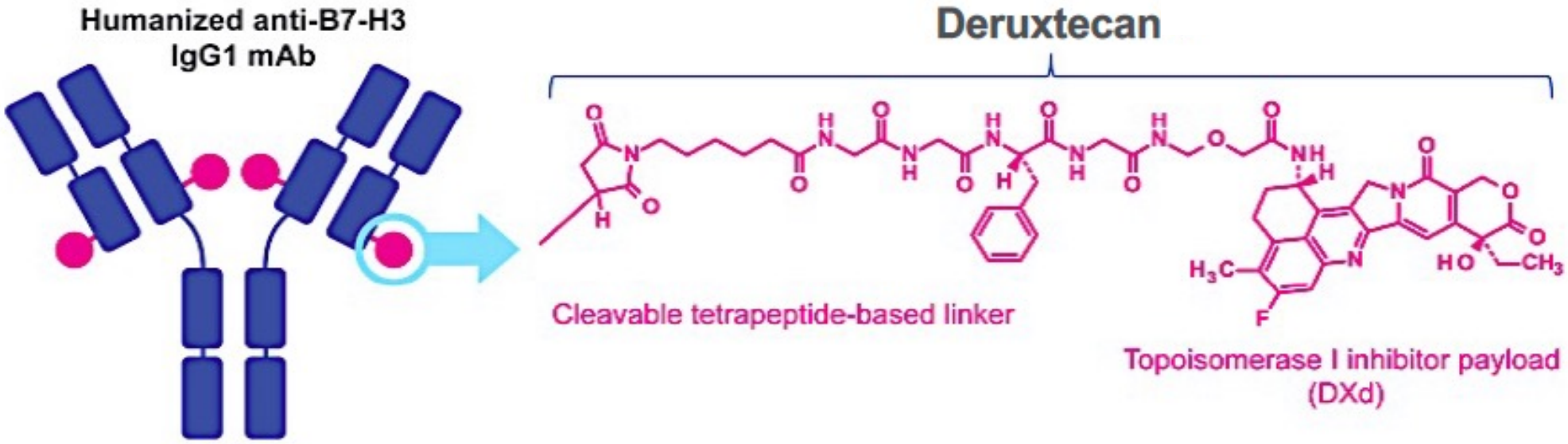
Targeting B7-H3 in SCLC

B7 homologue 3 (B7-H3) is overexpressed in a wide range of cancer types and is associated with disease progression and lower overall survival.[1-5]



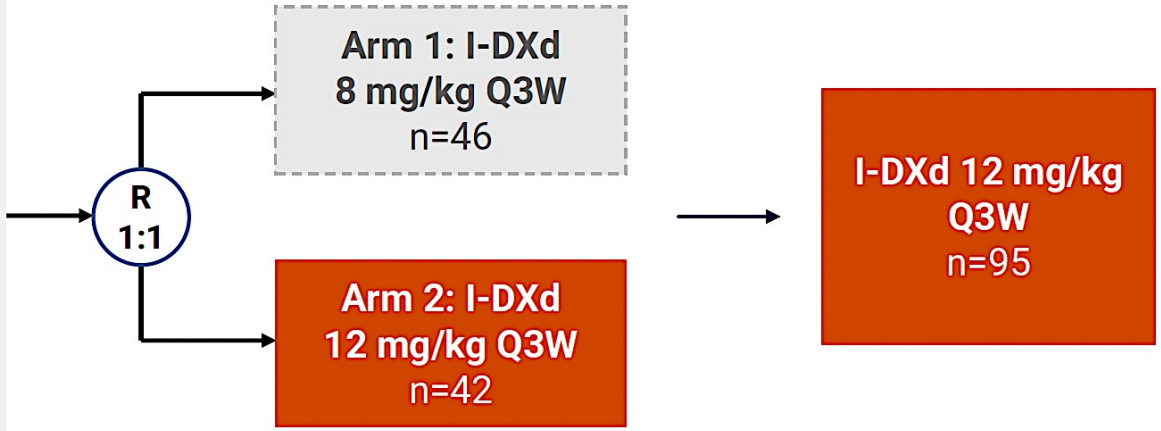
1. Yamato M et al. AACR-NCI-EORTC 2020;Abstract 28. 2. Dong P et al. *Front Oncol* 2018;8:264. 3. Picarda E et al. *Clin Cancer Res* 2016;22(14):3425-31. 4. Bendell JC et al. *J Clin Oncol* 2020;39(15 suppl 1). Abstract TPS3646. 5. Kontos F et al. *Clin Cancer Res* 2021;27(5):1227-35. 6. Doi T et al. ESMO 2022;Abstract 4530.

RTP RESEARCH TO PRACTICE

IDeate-Lung01 Trial: Ifinatamab Deruxtecan (I-DXd) for ES-SCLC

Patient eligibility

- Histologically or cytologically documented ES-SCLC
- Age ≥18 years[a]
- ≥1 prior line of PBC and ≤3 prior lines of systemic therapy
- Radiologically documented PD on or after most recent prior systemic therapy
- ECOG PS 0–1
- ≥1 measurable lesion per RECIST 1.1[b]
- Patients with asymptomatic brain metastases (untreated or previously treated) were eligible



Stratification factors:

- 2L CTFI <90 days; 2L CTFI ≥90 days; 3L or 4L
- Prior anti–PD-(L)1 treatment (yes or no)

Primary endpoint

- ORR by BICR[c]

Secondary endpoints

- DOR by BICR and inv[c]
- PFS by BICR and inv[c]
- OS
- DCR by BICR and inv[c]
- TTR by BICR and inv[c]
- ORR by inv[c]
- Safety
- Pharmacokinetics
- Immunogenicity

Exploratory analysis

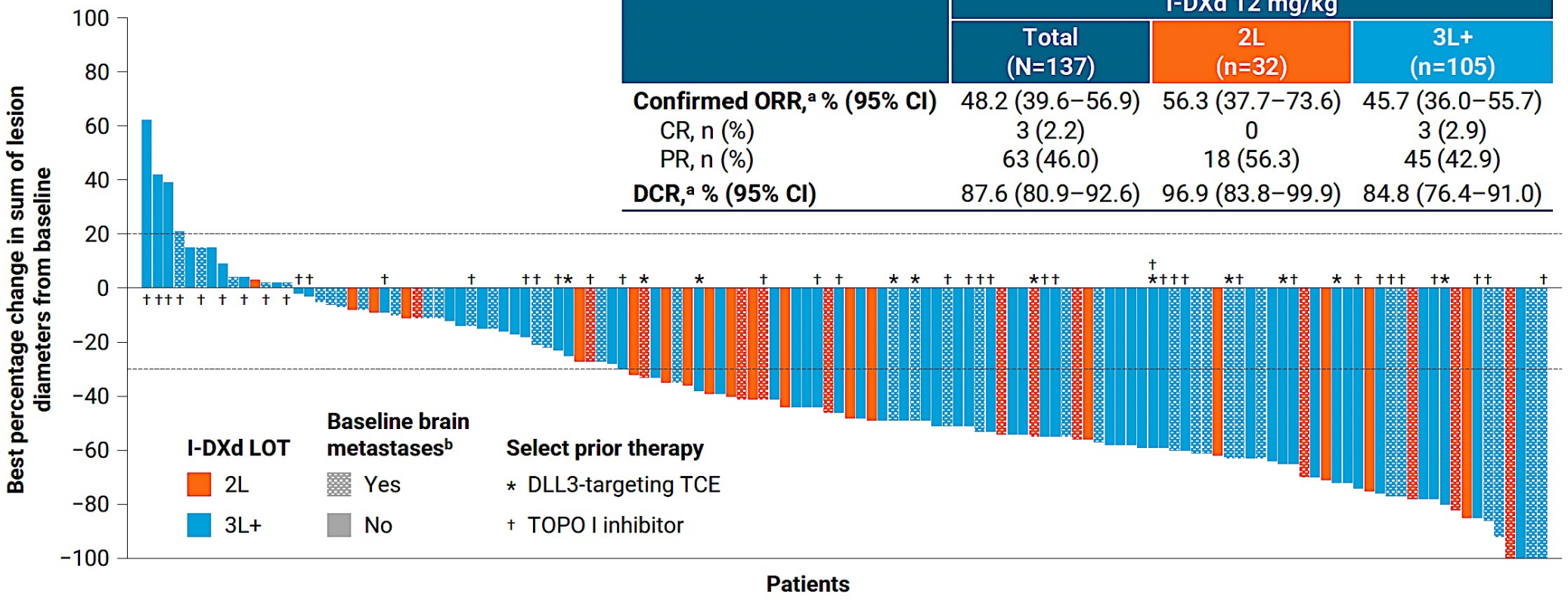
- Intracranial ORR by BICR[d]

[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]Per 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; CNS, central nervous system; 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; TTR, time to response.

Ahn MJ et al. WCLC 2025;Abstract OA06.03. Rudin CM et al. *J Clin Oncol 2026;*44(4):261-73.

IDeate-Lung01: ORR

	I-DXd 12 mg/kg		
	Total (N=137)	2L (n=32)	3L+ (n=105)
Confirmed ORR,[a] % (95% CI)	48.2 (39.6–56.9)	56.3 (37.7–73.6)	45.7 (36.0–55.7)
CR, n (%)	3 (2.2)	0	3 (2.9)
PR, n (%)	63 (46.0)	18 (56.3)	45 (42.9)
DCR,[a] % (95% CI)	87.6 (80.9–92.6)	96.9 (83.8–99.9)	84.8 (76.4–91.0)



Data cutoff: March 3, 2025.

[a]Assessed by BICR per RECIST 1.1. [b]By BICR.

2L, second-line; 3L+, third-line and beyond; BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; DLL3, delta-like ligand 3; LOT, line of therapy; ORR, objective response rate; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; TCE, T-cell engager; TOPO I, topoisomerase I.

Ahn MJ et al. WCLC 2025;Abstract OA06.03. Rudin CM et al. *J Clin Oncol 2026;*44(4):261-73.

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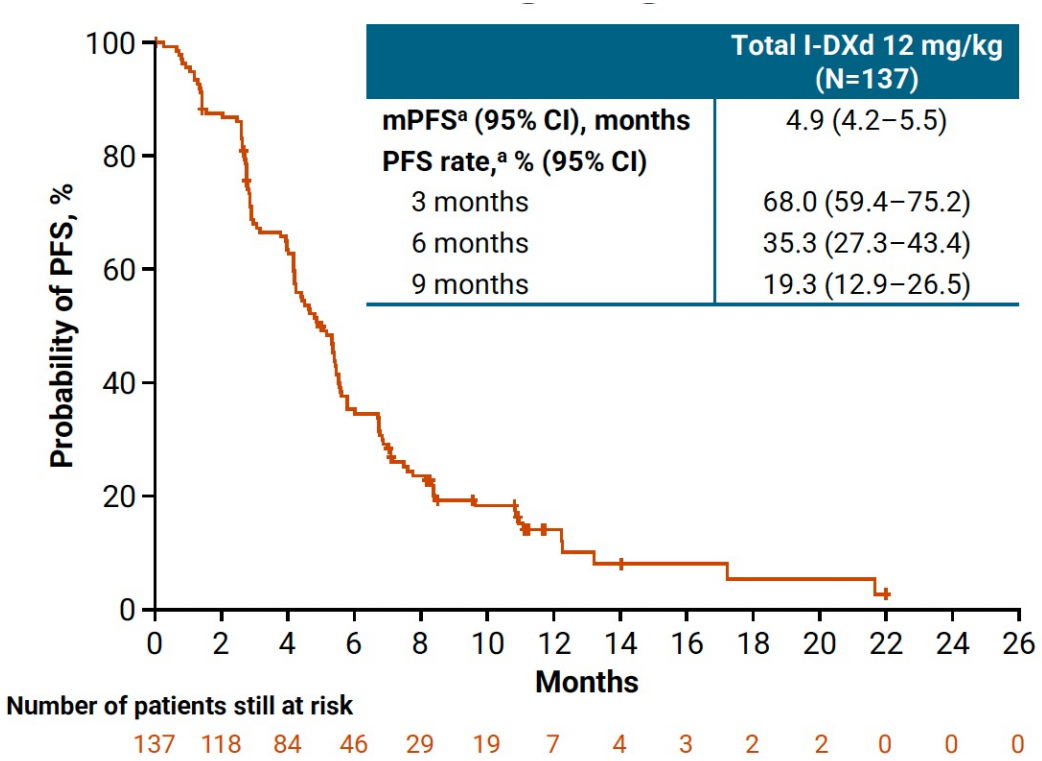
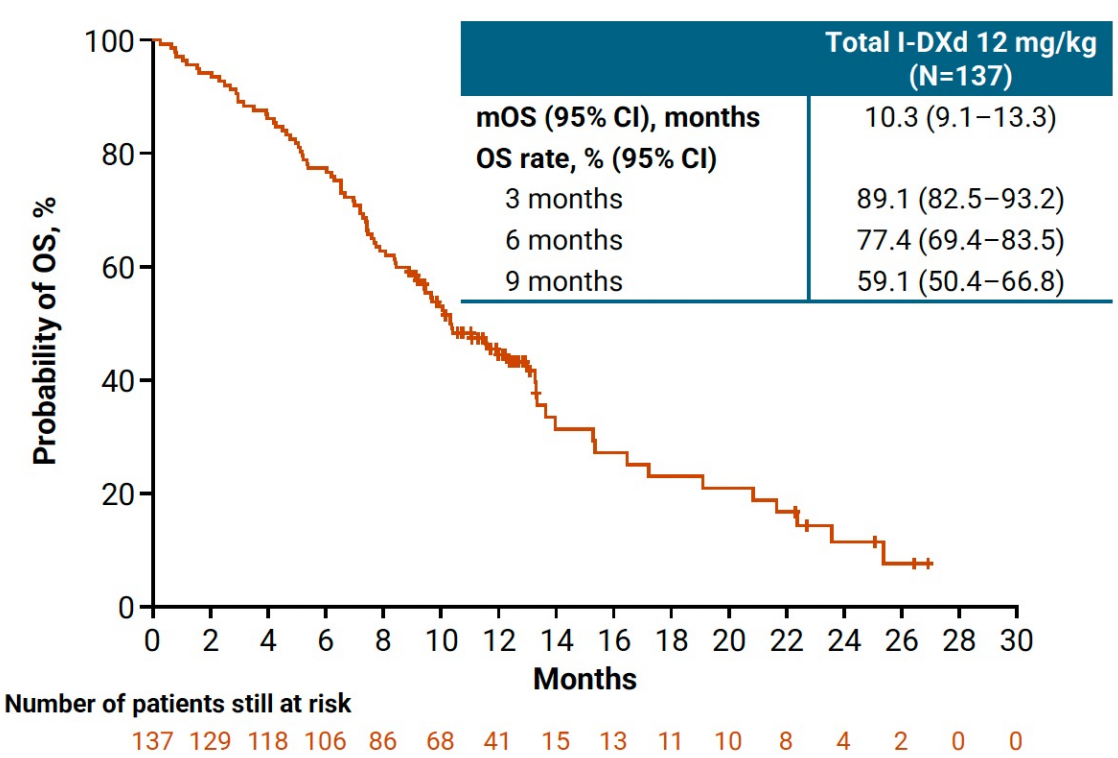
IDeate-Lung01: PFS and OS

PFS



	Total I-DXd 12 mg/kg (N=137)
mPFS[a] (95% CI), months	4.9 (4.2–5.5)
PFS rate,[a] % (95% CI)	
3 months	68.0 (59.4–75.2)
6 months	35.3 (27.3–43.4)
9 months	19.3 (12.9–26.5)

OS



	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)

Ahn MJ et al. WCLC 2025;Abstract OA06.03. Rudin CM et al. *J Clin Oncol 2026;*44(4):261-73

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IDeate-Lung01: CNS Activity

	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)

- **Concordance** between systemic and CNS **objective response: 75.4%**
- **Concordance** between systemic and CNS **disease control: 86.2%**

- OS and PFS were similar for patients with and without baseline BM

In 29 patients with baseline brain target lesions, intracranial cORR was 65.5% (9 CR, 10 PR), and almost all patients experienced intracranial disease control (96.6%)

Rocha P et al. ESMO 2025;Abstract 2760MO.

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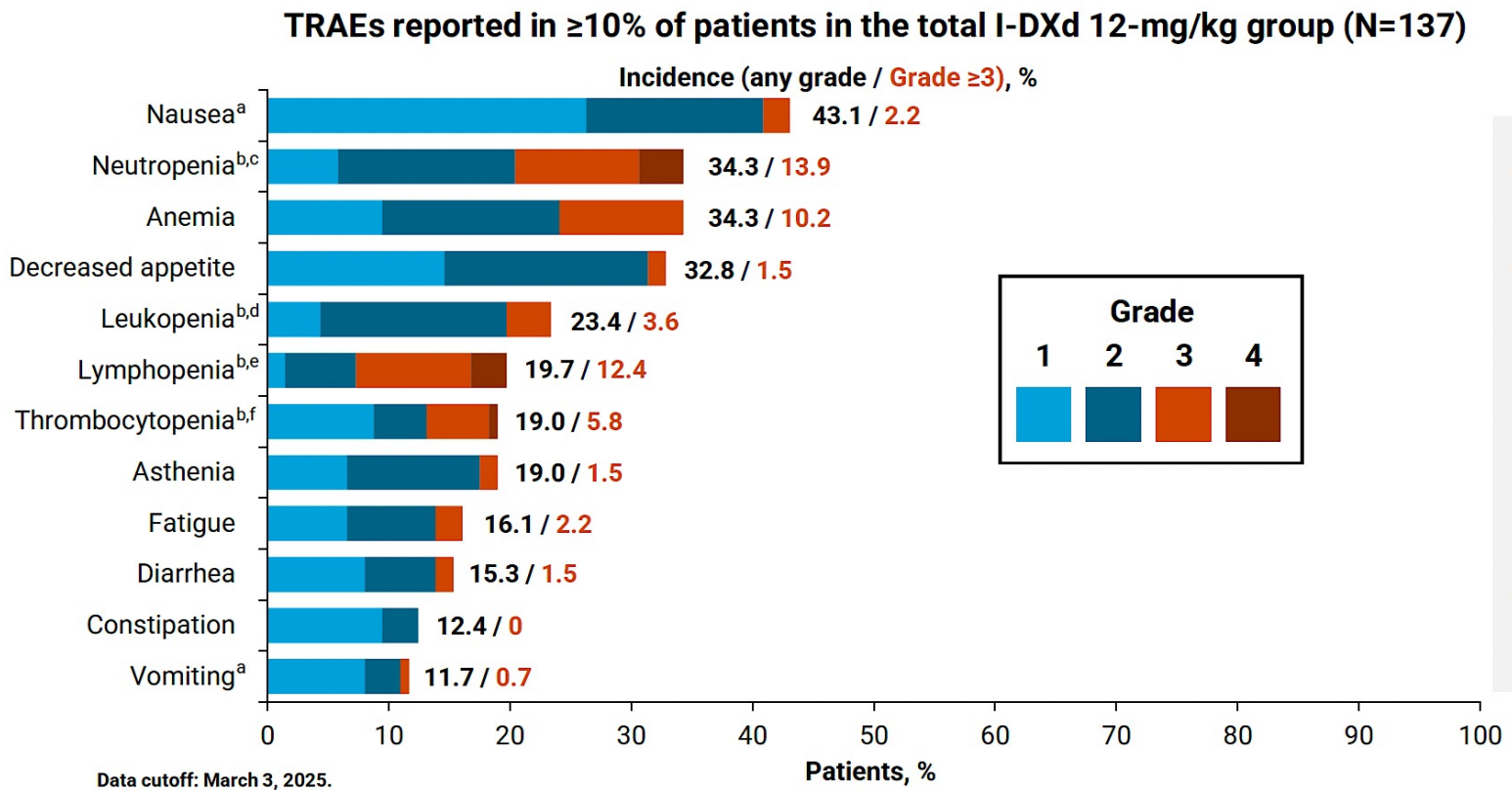
IDeate-Lung01: Safety



- Among the most common TRAEs, the majority were Grade 1 or 2
- Adjudicated treatment-related ILD/pneumonitis was reported in 17 (12.4%) patients:
  - Grade 1 or 2, n=11 (8.0%)
  - Grade 3, n=4 (2.9%)
  - Grade 5, n=2 (1.5%)[g]
- No ILD events were pending adjudication at data cutoff

Data cutoff: March 3, 2025.

[a]Prior to each I-DXd dose, antiemetic premedication with a 2- or 3-drug combination was mandatory across both study parts. [b]For prophylaxis or treatment of hematologic toxicity, trilaciclib, hematopoietic growth factors, or transfusion of blood, red blood cells, and platelets could be administered. [c]Includes the preferred terms "neutrophil count decreased" and "neutropenia." [d]Includes the preferred terms "white blood cell count decreased" and "leukopenia." [e]Includes the preferred terms "lymphocyte count decreased" and "lymphopenia." [f]Includes the preferred terms "platelet count decreased" and "thrombocytopenia". [g]Both patients were deemed to have adjudicated Grade 5 treatment-related ILD by the ILD adjudication committee; however, only 1 of these patients also had treatment-related ILD associated with death per investigator.

ILD, interstitial lung disease; TRAE, treatment-related adverse event.

Ahn MJ et al. WCLC 2025;Abstract OA06.03; Rudin CM et al. *J Clin Oncol 2026;*44(4):261-73.

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