Iniciativa científica de:

GECP lung cancer research

Lung Cancer UPDATES

ESMO HIGHLIGHTS

23 - 27 OCTUBRE 2026

Madrid, Spain



#ESMOUPDATES

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Cáncer Pulmón Microcítico

Parte II

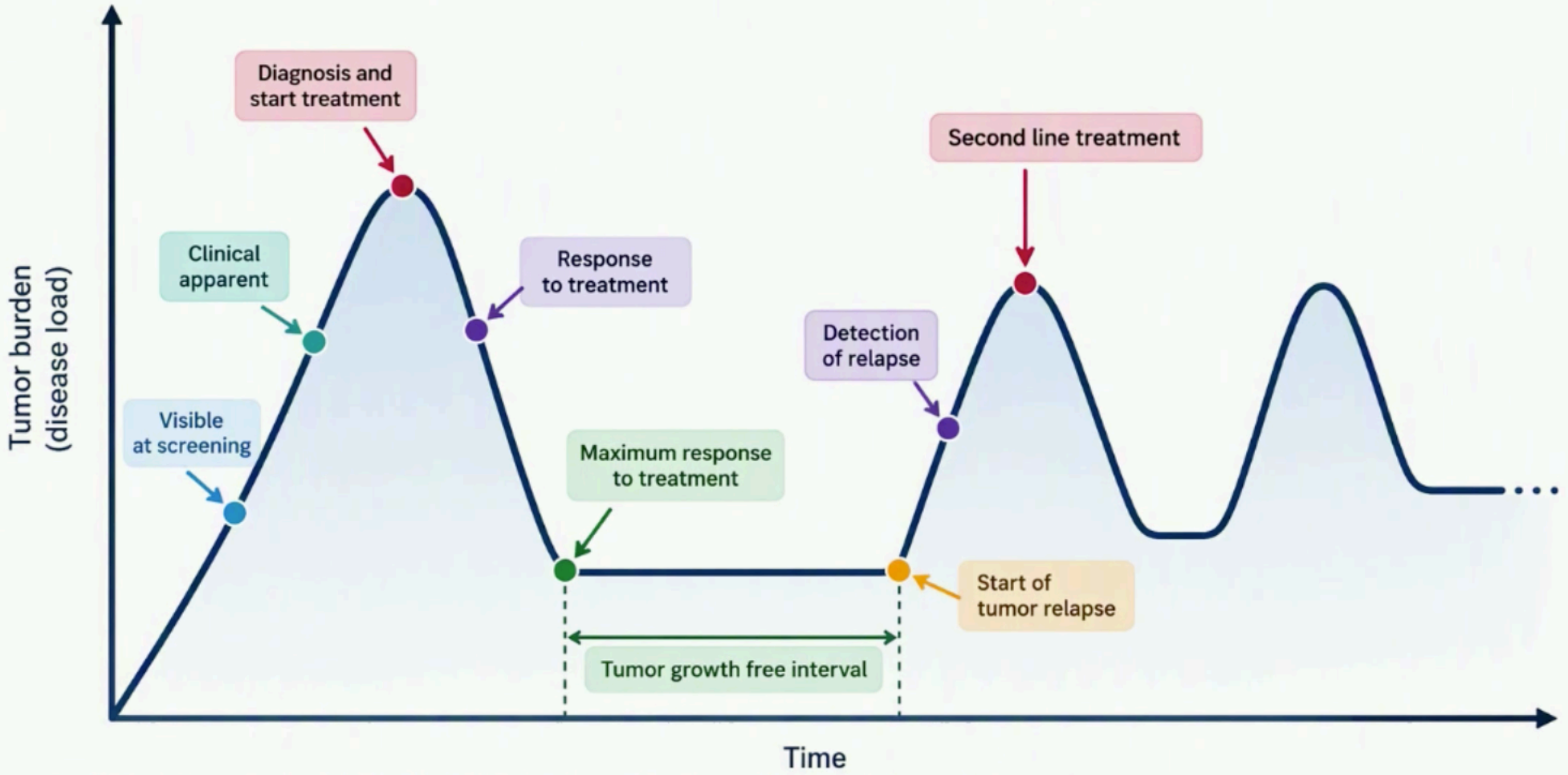
Manuel Dómine

Coordinador de Investigación Comprehensive Cancer Center Fundación Jiménez Díaz.

Director de Tumores Torácicos. Fundación Jiménez Díaz Campus hospitalario

Instituto de Investigación Sanitaria Fundación Jiménez Díaz (IIS-FJD)

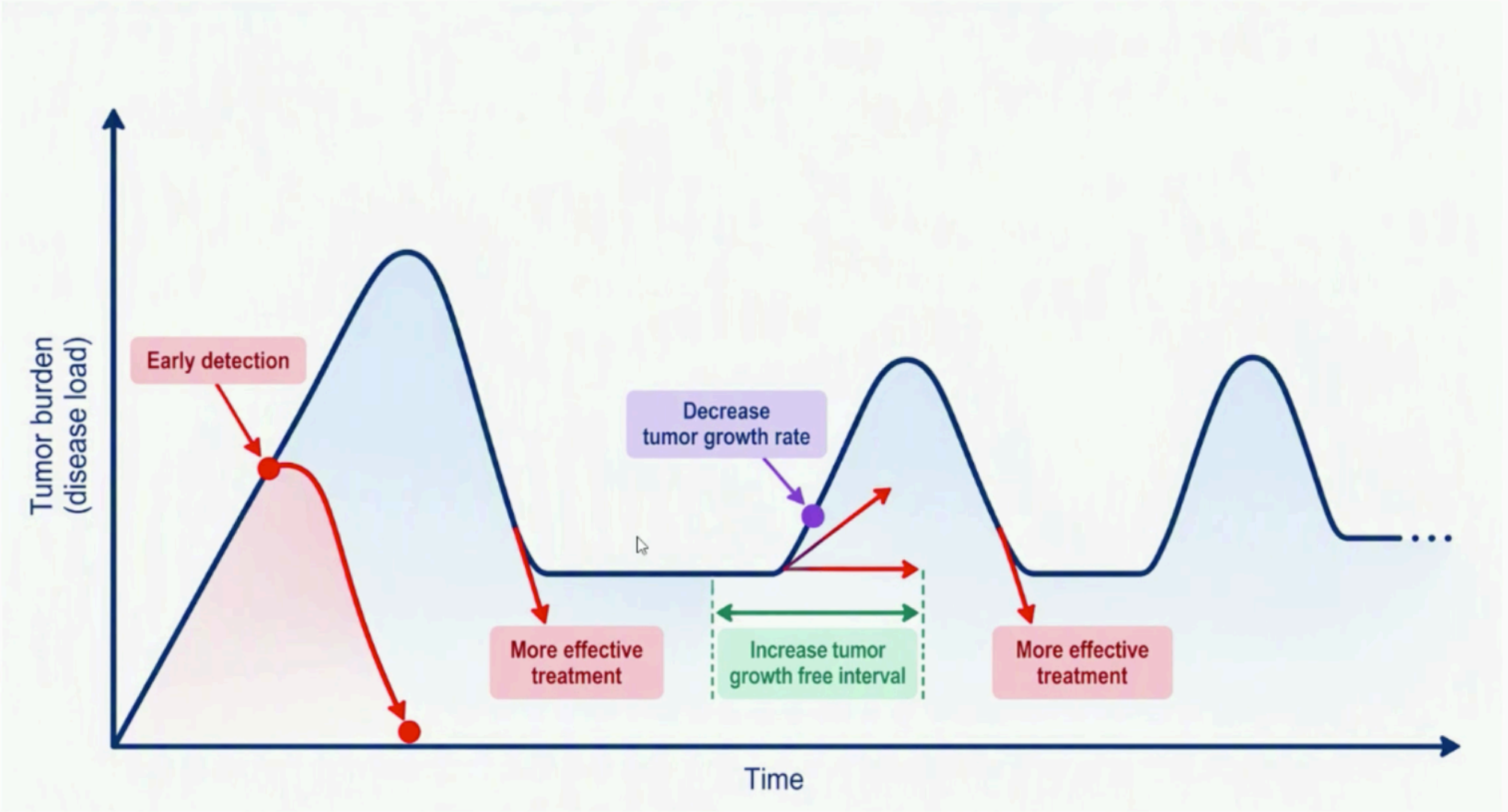
What is course of the disease with treatment



Joachim Aerts, Erasmus University Medical Centre Roterdam, image redrawn by co-pilot from original generated by presenter

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Where are we working on



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≥ 2L treatment options in ES-SCLC

Standard of care in rapidly evolving landscape

- **Rechallenge** platinum-based chemotherapy (>3-6 months after chemo)
- **Topotecan** mOS ~6 months
- **Lurbinectidin** (FDA approval 2020, EMA approval), mOS ~ 9 months
- **Tarlatamab** – FDA approval March 2024, EMA approval June 2026 – preferred option mOS 13.4 months

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Selected ≥ 2L treatments for ES-SCLC

TCE anti-DDL3

Tarlatamab

mOS 13.6 mo

phase 3
DeLLphi-304
ESMO 2026

ADC

SEZ6 (ABBV-706)

mOS 14.3 mo

phase 1 Part 2
ASCO 2026
ESMO 2026

B7-H3 (Tam-Peli)

mOS 13.3 mo

phase 3 TAISHAN-302
WCLC 2026

B7-H3 (Riz-Rez)

mOS 18.5 mo

phase 3 ARTEMIS-008
WCLC 2026

- All these novel agents, particularly ADCs have the potential to replace chemotherapy
- Optimal sequencing of these agents and upfront combination strategies

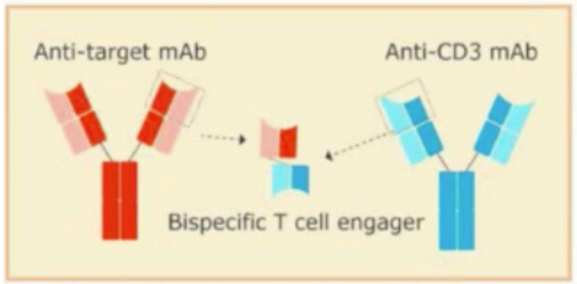
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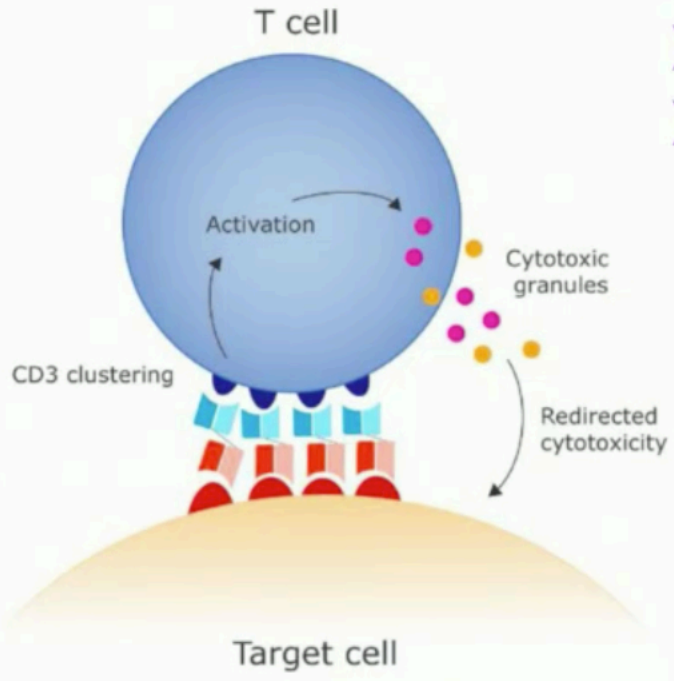
TARLATAMAB

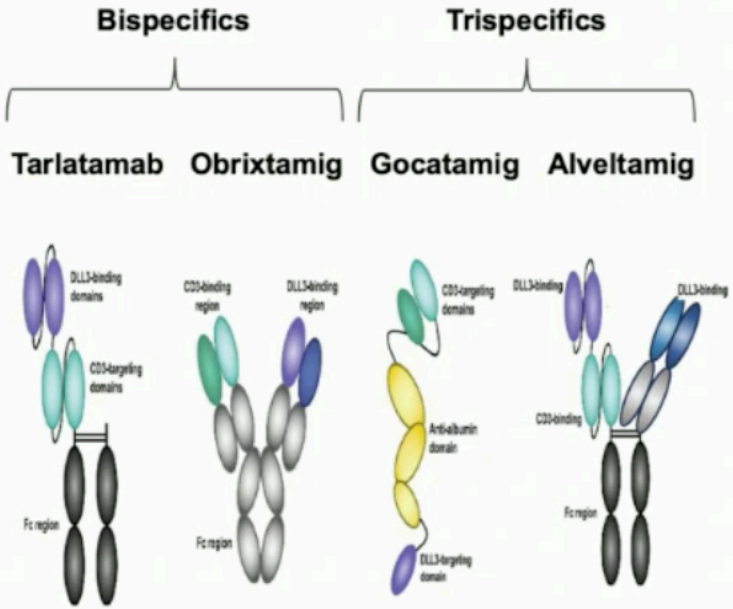
Delta Like Ligand 3 targeting T cell engager

Among solid tumours, clinical evidence supporting TCE is strongest for SCLC.

- DLL3 is highly expressed in SCLC (>70%)
- Inhibits Notch signaling
- SCLC immune desert







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K. Oselin, 26Oct2026

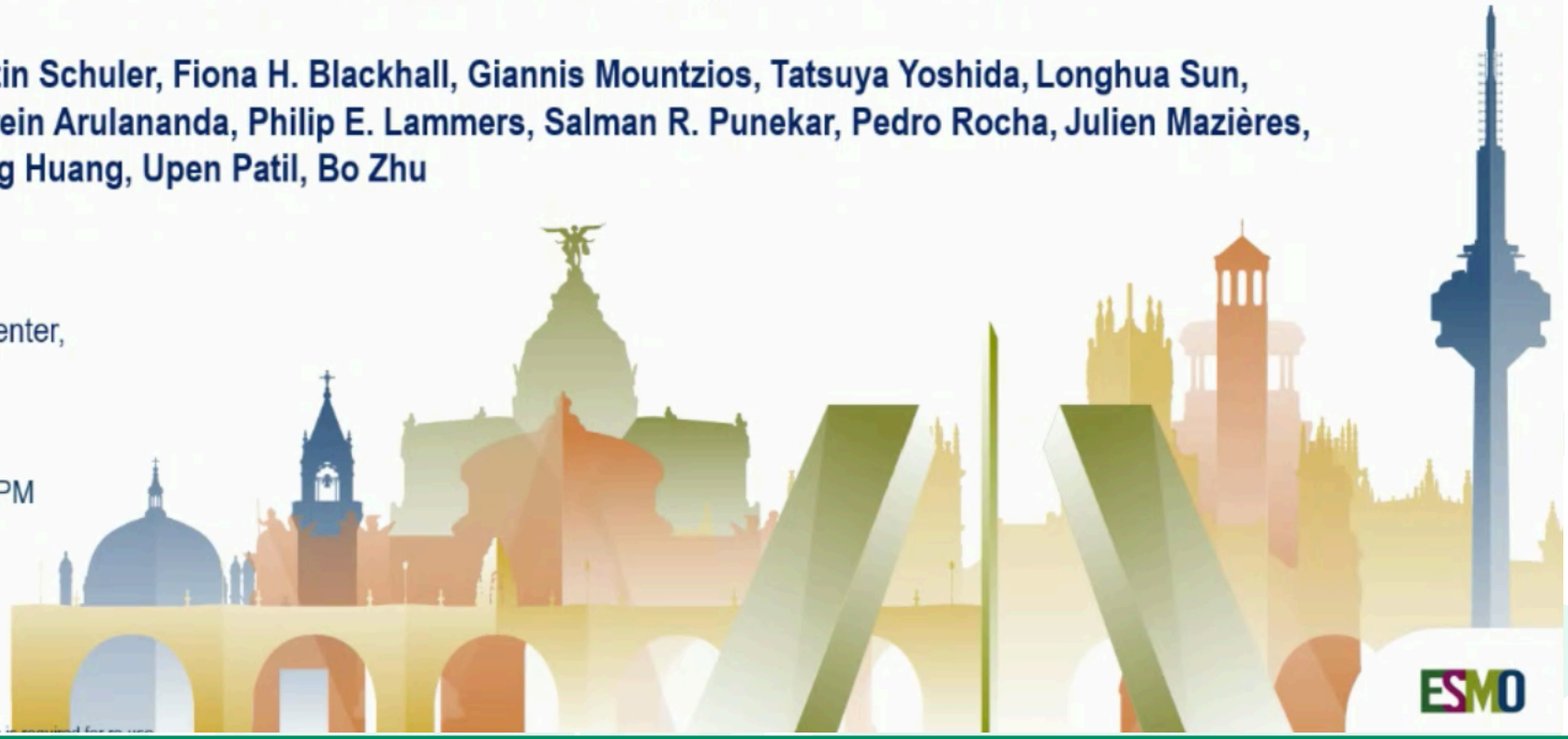
MADRID 2026 ESMO congress

Tarlatamab in Previously Treated SCLC: Extended Follow-up of Overall Survival From the Phase 3 DeLLphi-304 Trial

Charles M. Rudin, Myung-Ju Ahn, Martin Schuler, Fiona H. Blackhall, Giannis Mountzios, Tatsuya Yoshida, Longhua Sun, Byoung Chul Cho, Antonio Lugini, Surein Arulananda, Philip E. Lammers, Salman R. Punekar, Pedro Rocha, Julien Mazières, Mahmut Gümüş, Umut Demirci, Shuang Huang, Upen Patil, Bo Zhu

Presenter: Charles M. Rudin, MD, PhD
Director, Memorial Sloan Kettering Cancer Center,
New York, NY, USA

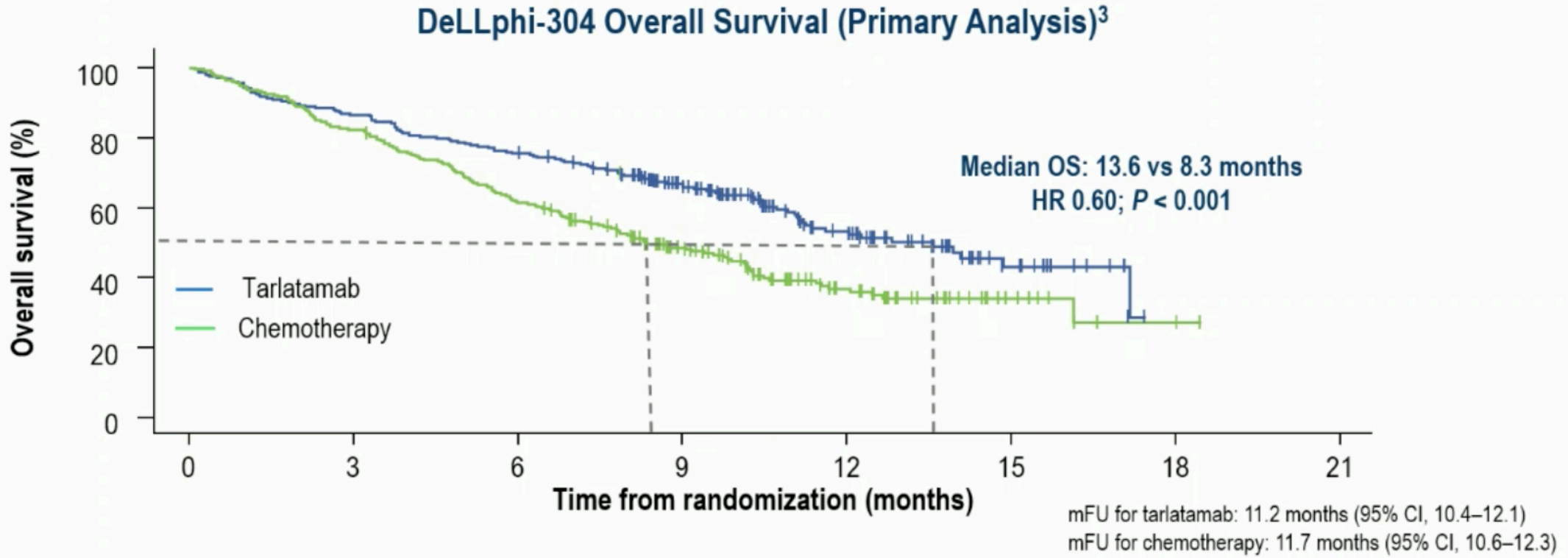
Presentation date & time: 26 October 2026; 2:45 PM



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Previously reported primary analysis: tarlatamab improved OS vs chemotherapy

- Prior to DeLLphi-304 results, median real-world overall survival in the 2L setting was poor (approximately 5-6 months)[1,2]

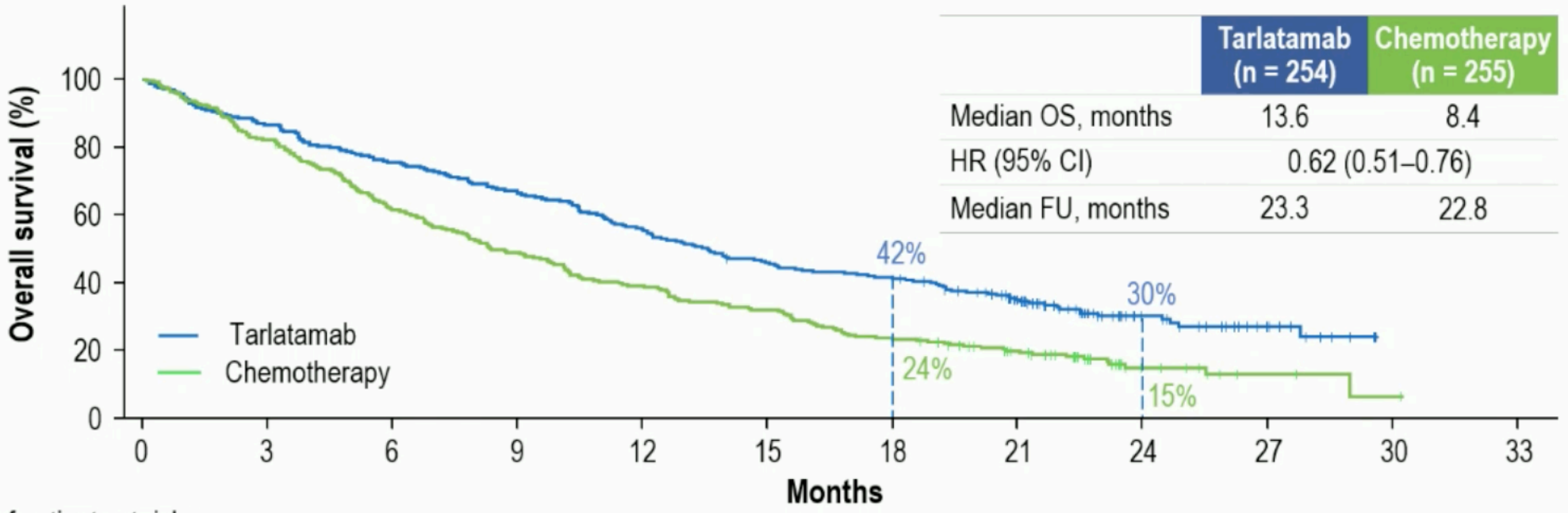


We now report results from the extended follow-up of DeLLphi-304 (median follow-up, 23 months) assessing the durability of clinical benefit and long-term safety of tarlatamab vs chemotherapy

2L, second-line; **CI**, confidence interval; **HR**, hazard ratio; **mFU**, median follow-up; **OS**, overall survival.

1. Shaw J, et al. *Oncologist*. 2024;29:1079-1089; 2. Aggarwal H, et al. *Front Oncol*. 2026;16:1846362; 3. Mountzios G, et al. *N Engl J Med*. 2025;393:349–361.

Extended follow-up confirms sustained OS benefit of tarlatamab



	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median OS, months	13.6	8.4
HR (95% CI)	0.62 (0.51–0.76)	
Median FU, months	23.3	22.8

Number of patients at risk:

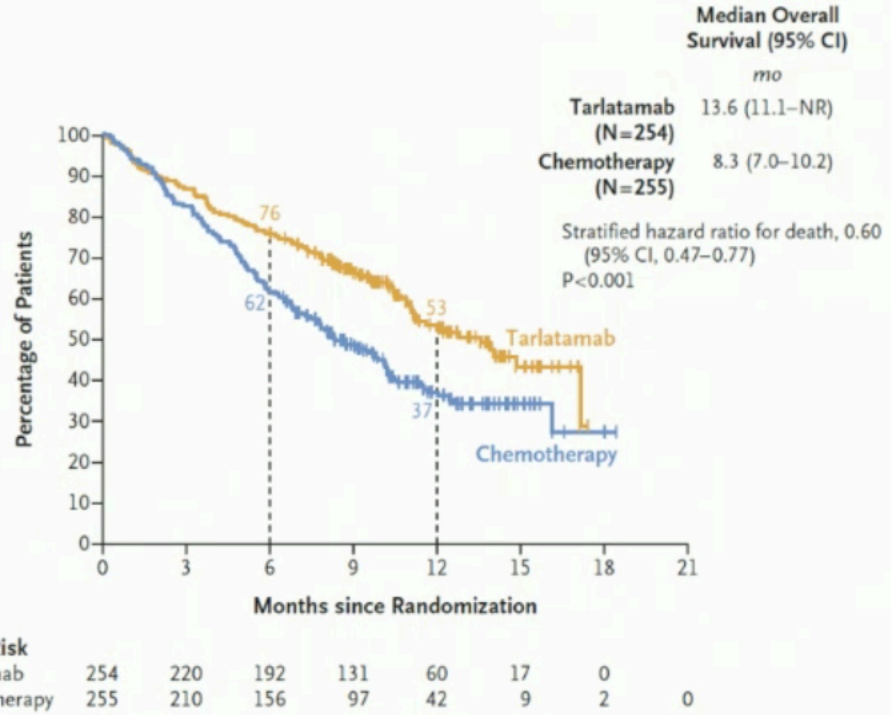
Tarlatamab	254	220	192	171	142	116	105	73	33	14	0	
Chemotherapy	255	210	156	124	99	81	60	40	13	4	1	0

Data cutoff date: 18 Feb 2026.

Tarlatamab showed sustained survival benefit vs chemotherapy, with reduced mortality risk, persistent separation of the Kaplan–Meier curves, and higher landmark OS rate

CI, confidence interval; **FU**, follow-up; **HR**, hazard ratio; **OS**, overall survival.

DeLLphi-304 phase III trial – Extended follow-up



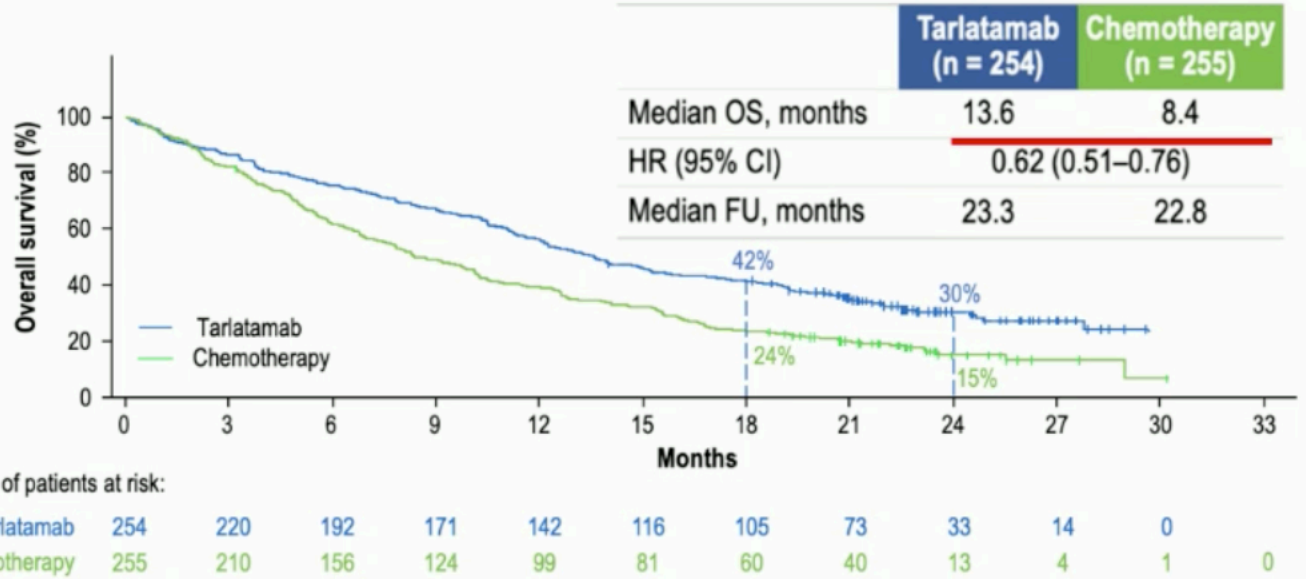


Figure 1. Overall Survival (Intention-to-Treat Population).
Shown are Kaplan–Meier estimates of overall survival in the intention-to-treat population, which included all the patients who had undergone randomization. Overall survival was defined as the time from randomization to death from any cause. A hazard ratio below 1.0 indicates better overall survival with tarlatamab than with chemotherapy. Tick marks indicate censored data. NR denotes not reached.

1-year OS 53% vs 37% - Interim analysis

2-year OS 30% vs 15% - Extended FU

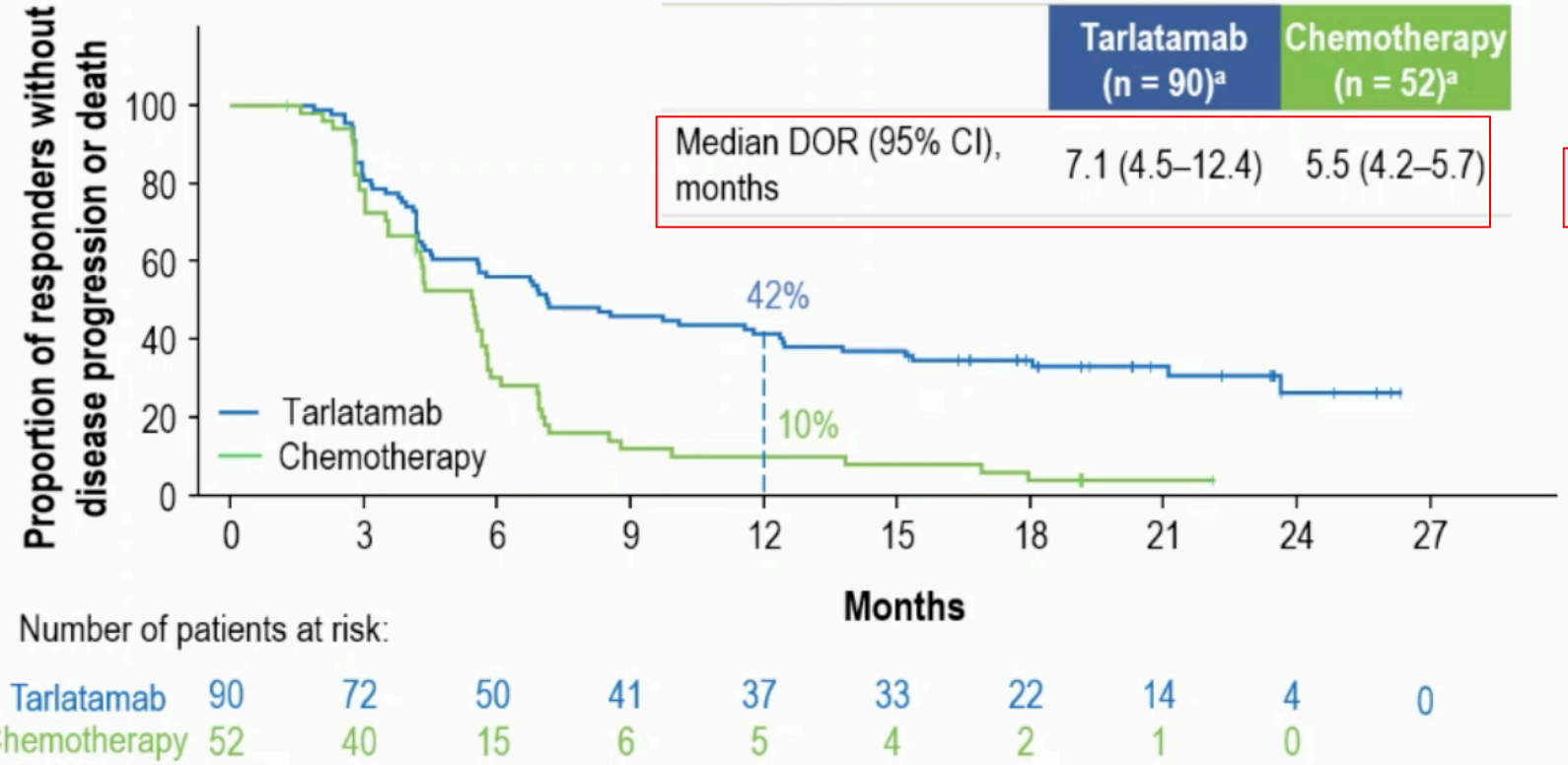
N Engl J Med 2025;393:349-61.

mFU 11 months

mFU 23 months

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Tarlatamab demonstrated durable responses compared with chemotherapy



	Tarlatamab (n = 90)[a]	Chemotherapy (n = 52)[a]
Median DOR (95% CI), months	7.1 (4.5–12.4)	5.5 (4.2–5.7)

Number of patients at risk:

Tarlatamab	90	72	50	41	37	33	22	14	4	0
Chemotherapy	52	40	15	6	5	4	2	1	0	

Data cutoff date: 18 Feb 2026.

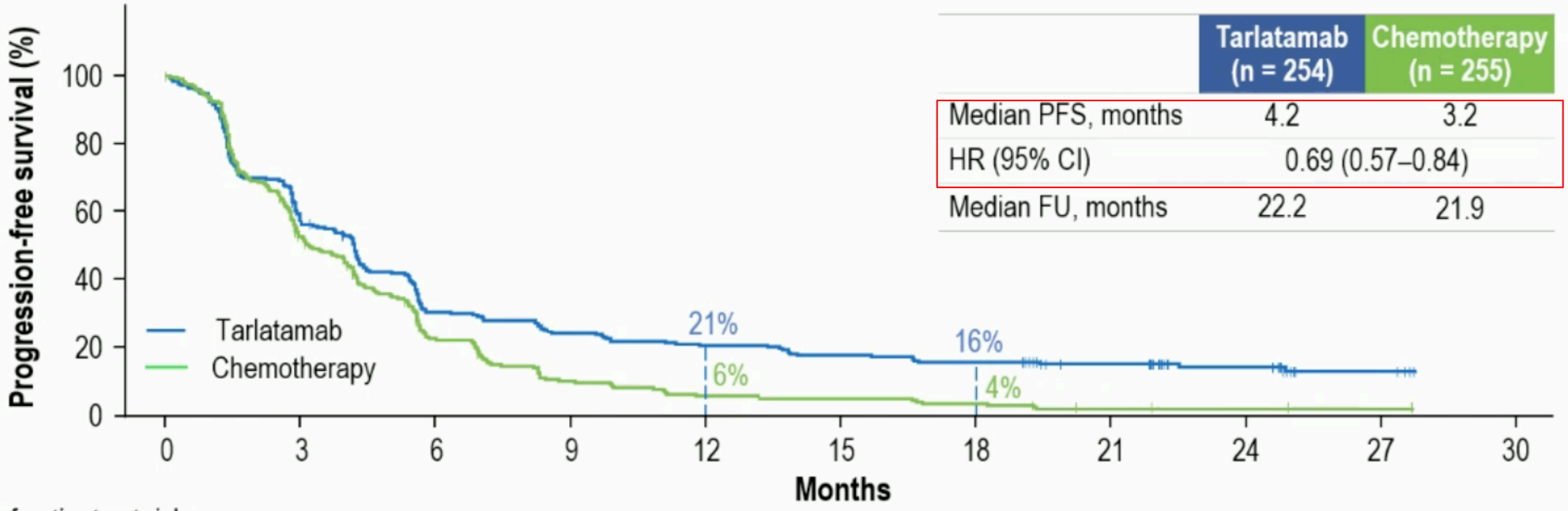
Outcomes (%)	Tarlatamab (n = 254)	Chemotherapy (n = 255)
ORR (95% CI)	35 (30–42)	20 (16–26)
KM estimate of DOR (95% CI) at 6 months	56 (45–66)	30 (18–43)
KM estimate of DOR (95% CI) at 12 months	42 (31–52)	10 (4–20)
Sustained DC (≥ 52 weeks)	24	4

mFU for tarlatamab: 20.7 months (95% CI, 18.2–23.5)
mFU for chemotherapy: 19.2 months (95% CI, 19.2–NE)

- **Tarlatamab demonstrated longer responses, with a greater proportion of ongoing responses at 12 months**
- **Approximately six-fold more patients achieved sustained DC (≥ 52 weeks) with tarlatamab vs chemotherapy**

[a]Number of confirmed responders as assessed by investigator (ITT analysis).
CI, confidence interval; **DC**, disease control; **DOR**, duration of response; **ITT**, intention-to-treat; **KM**, Kaplan-Meier; **mFU**, median follow-up; **NE**, not estimable; **ORR**, objective response rate.

Tarlatamab demonstrated sustained PFS benefit during extended follow-up



	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median PFS, months	4.2	3.2
HR (95% CI)	0.69 (0.57–0.84)	
Median FU, months	22.2	21.9

Number of patients at risk:

Tarlatamab	254	142	74	59	50	43	38	27	15	4	0
Chemotherapy	255	119	48	21	12	11	8	3	2	1	0

Data cutoff date: 18 Feb 2026.

The PFS benefit observed with tarlatamab in the primary analysis was sustained during extended follow-up, with higher landmark PFS rates than chemotherapy

CI, confidence interval; **FU**, follow-up; **HR**, hazard ratio; **PFS**, progression-free survival.

Tarlatamab had a more favorable safety profile compared with chemotherapy

Adverse event, n (%)	Tarlatamab (n = 252)	Chemotherapy (n = 244)
Median duration of treatment (range), weeks	18.2 (0.1–128.9)	10.9 (0.1–118.1)
Any grade TEAEs	249 (98.8)	243 (99.6)
Any grade TRAEs	235 (93.3)	223 (91.4)
Grade ≥ 3	70 (27.8)	153 (62.7)
Serious	72 (28.6)	76 (31.1)
Leading to dose interruption and/or dose reduction	49 (19.4)	135 (55.3)
Leading to treatment discontinuation	8 (3.2)	16 (6.6)
Fatal*	1 (0.4)	4 (1.6)

Data cutoff date: 18 Feb 2026.

- **Tarlatamab was associated with a lower incidence of grade ≥ 3 TRAEs vs chemotherapy**
- **Fewer TRAEs leading to dose modification or treatment discontinuation were observed with tarlatamab**

*The single grade 5 TRAE observed with tarlatamab was attributed to ICANS in the setting of progressive neurological decline concurrent with persistent fever, hypoxemia, and hypotension. Grade 5 TRAEs observed with chemotherapy were attributed to general physical health deterioration (n = 1), pneumonia (n = 1), respiratory tract infection (n = 1), and tumor lysis syndrome (n = 1).

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

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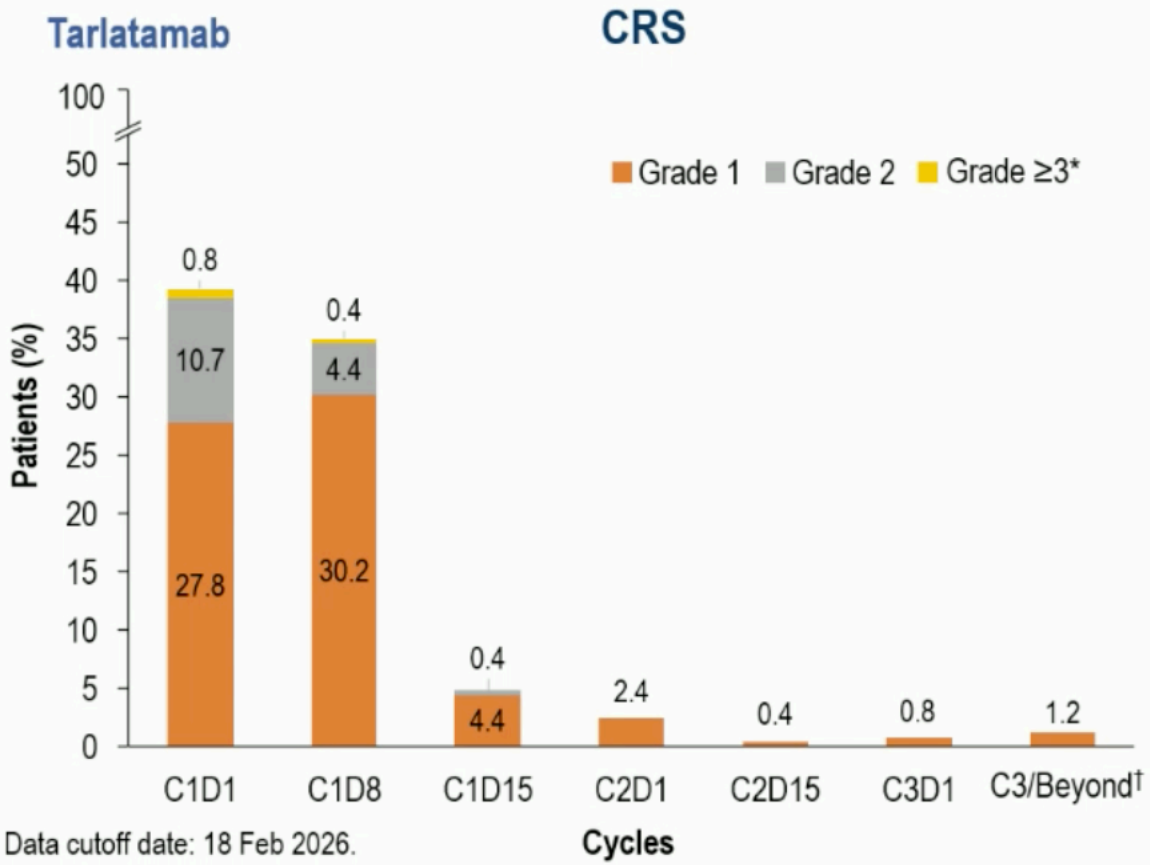
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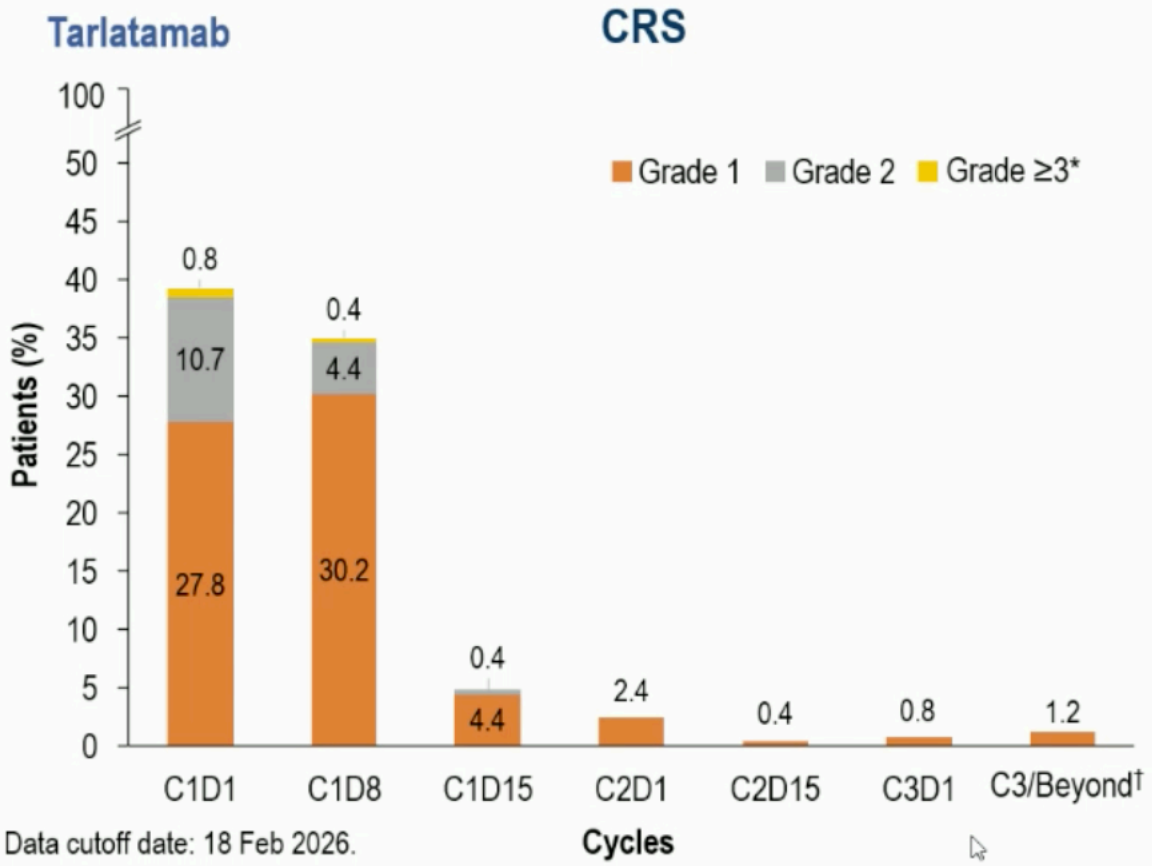
CRS and ICANS were predominantly early-onset events, with rare incidence in subsequent cycles



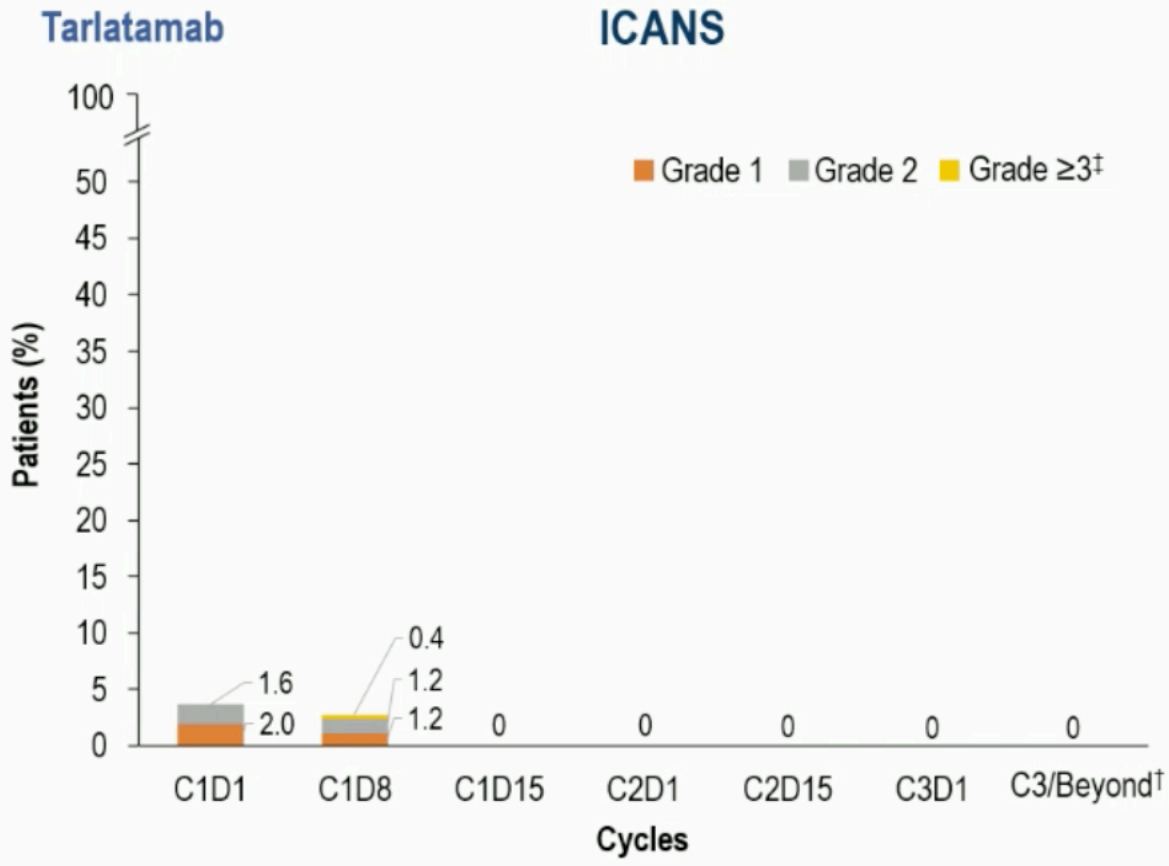
Data cutoff date: 18 Feb 2026.

*There were no grade 4 or 5 CRS events.
†For cycle 3 and beyond, the cumulative incidence of CRS and ICANS are presented respectively.
‡All ICANS events were grade 1–2 with one grade 5 event; the patient's death was attributed to ICANS in the context of progressive neurologic decline concurrent with persistent fever, hypoxemia, and hypotension.
C, cycle; **CRS**, cytokine release syndrome; **D**, day; **ICANS**, immune effector cell-associated neurotoxicity syndrome.

CRS and ICANS were predominantly early-onset events, with rare incidence in subsequent cycles



Data cutoff date: 18 Feb 2026.



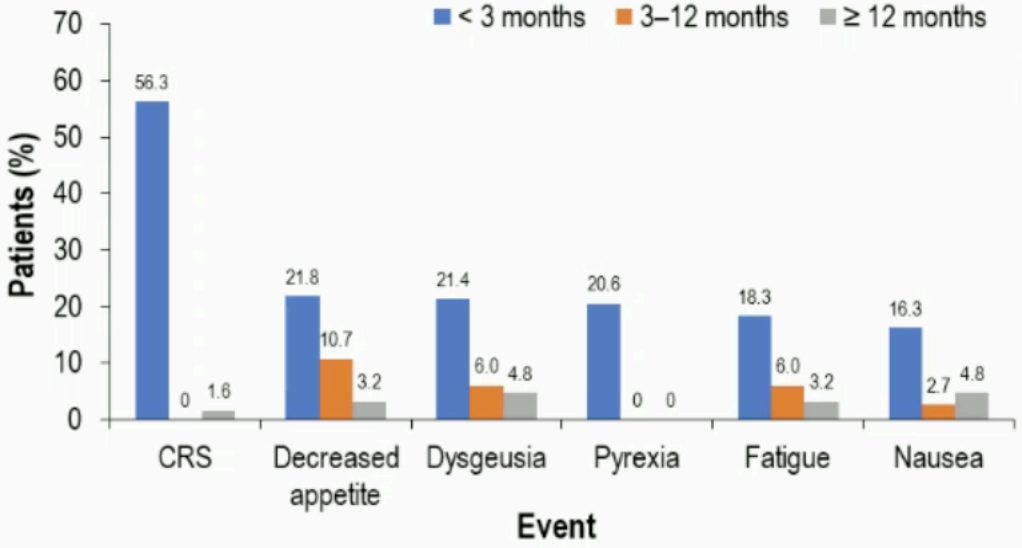
CRS and ICANS occurred predominantly during the first two doses and were primarily grade 1–2

*There were no grade 4 or 5 CRS events.
†For cycle 3 and beyond, the cumulative incidence of CRS and ICANS are presented respectively.
‡All ICANS events were grade 1–2 with one grade 5 event; the patient's death was attributed to ICANS in the context of progressive neurologic decline concurrent with persistent fever, hypoxemia, and hypotension.
C, cycle; **CRS**, cytokine release syndrome; **D**, day; **ICANS**, immune effector cell-associated neurotoxicity syndrome.

Tarlatamab demonstrated no new or increase in toxicity with longer-term treatment

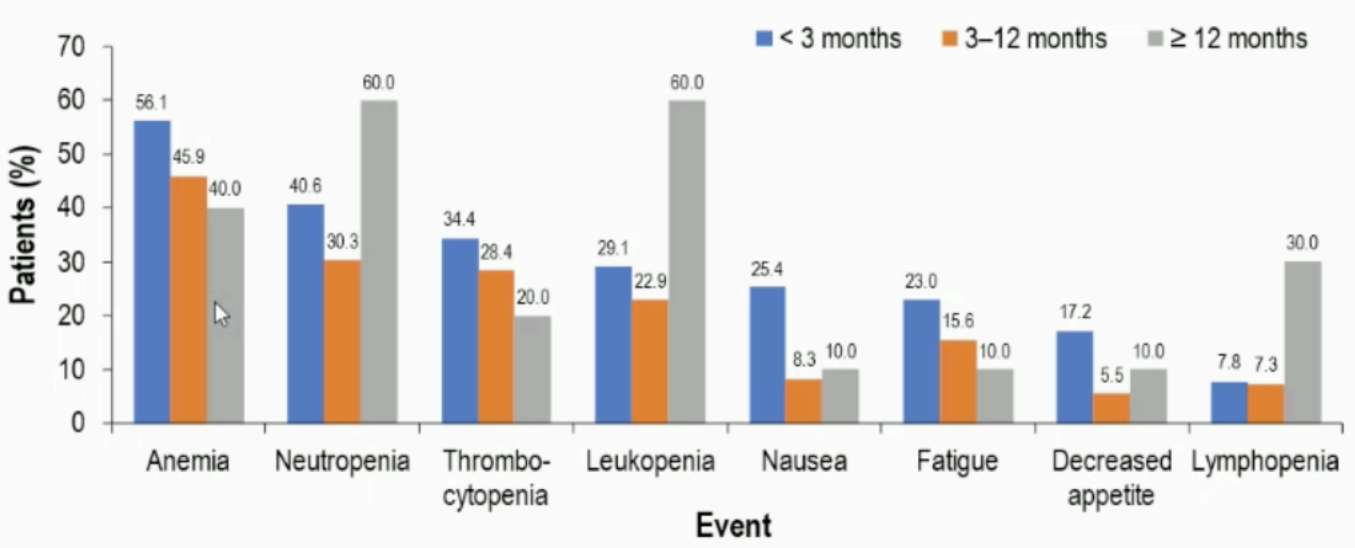
TRAEs reported by time period for patients on treatment

Tarlatamab



On treatment < 3 months: Tarlatamab (n = 252)
On treatment 3–12 months: Tarlatamab (n = 149)
On treatment ≥ 12 months: Tarlatamab (n = 62)

Chemotherapy



On treatment < 3 months: Chemotherapy (n = 244)
On treatment 3–12 months: Chemotherapy (n = 109)
On treatment ≥ 12 months: Chemotherapy (n = 10)

Data cutoff date: 18 Feb 2026.

- **The differing temporal patterns of TRAEs support the favorable long-term tolerability of tarlatamab relative to chemotherapy**
- **No new safety signals were identified with extended follow-up**

TRAEs with incidence of ≥ 15% by treatment period are presented.
CRS, cytokine release syndrome; **TRAE**, treatment-related adverse event.

Conclusions on DeLLphi-304

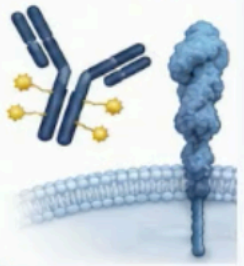
Standard of care in previously treated ES-SCLC

- ✓ Tarlatamab demonstrated statistically and clinically meaningful improvement in overall survival (**mOS 13.4 mo**) with extended follow up (median 23 mo).
- ✓ There were **no new safety concerns** with longer time on treatment, better safety profile than with chemo, grade 1/2 CRC is common, ICANs management.
- ✓ Tarlatamab also **improves CNS control** in patients with and without baseline CNS involvement.

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The Expanding Landscape of ADCs in SCLC

DLL3



ZL 1310 (Zoci)
R-DXd (DS-6000)
SHR-4849 (IDE849)
SHR-7787
IBI3009
FZ-AD005

SHARED PAYLOAD CLASS

TOP1 Inhibitors

(deruxtecan, exatecan, pelitecan, SN-38)



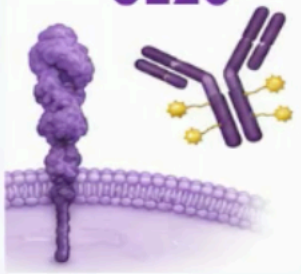
TROP2



SG
SHR-A1921 (Tize)

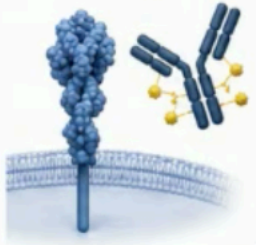
SEZ6

ABBV-706
HS-20108

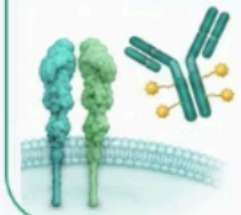


B7-H3

I-DXd (DS-7300)
HS-20093 (Ris-Rez)
YL201 (Tam-Peli)
BNT324 (Elfe-D)
MHB088C
SKB500



HER3 x EGFR



BL-B01D1
(Iza-bren)

I-DXd ▯ Ifinatamab Deruxtecan
R-DXd ▯ Raludotatug Deruxtecan
HS-20093 (GSK5764227) ▯ Risvutatug Rezetecan (Ris- Rez)
ZL 1310 ▯ Zocilurtatug Pelitecan (Zoci)
BL-B01D1 (BMS-986507) ▯ Izalontamab Brengitecan (Iza-Bren)
YL201 ▯ Tambotatug Pelitecan (Tam-Peli)
SHR-A1921 ▯ Tizetatug Rezetecan (Tize)
BNT324 ▯ Elfetabart Drozuntecan (Elfe-D)

1.- Reguart N. ASCO 2026

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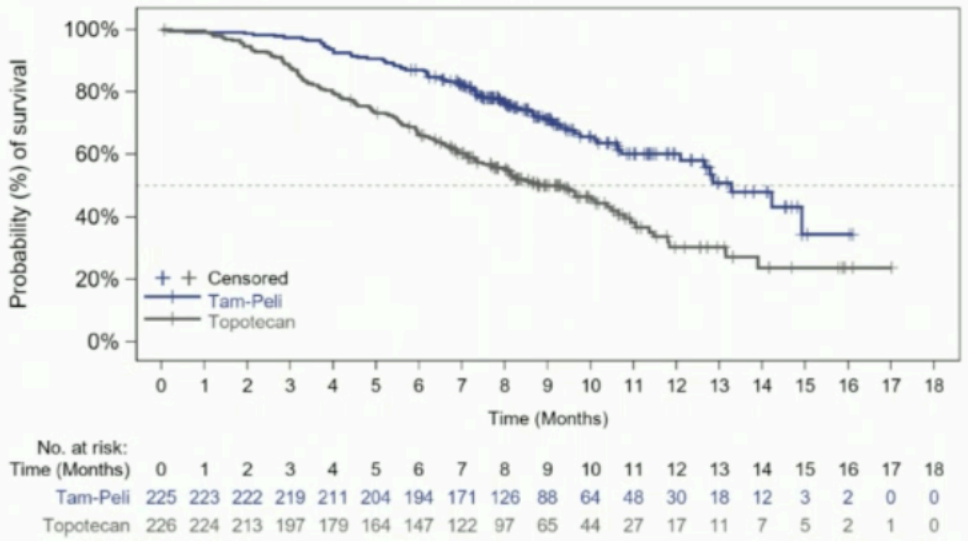
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TAISHAN-302

ARTEMIS-008

Antibody Drug Conjugates targeting B7-H3

Tambotatug pelitecan



No. at risk:

Time (Months)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Tam-Peli	225	223	222	219	211	204	194	171	126	88	64	48	30	18	12	3	2	0	0
Topotecan	226	224	213	197	179	164	147	122	97	65	44	27	17	11	7	5	2	1	0

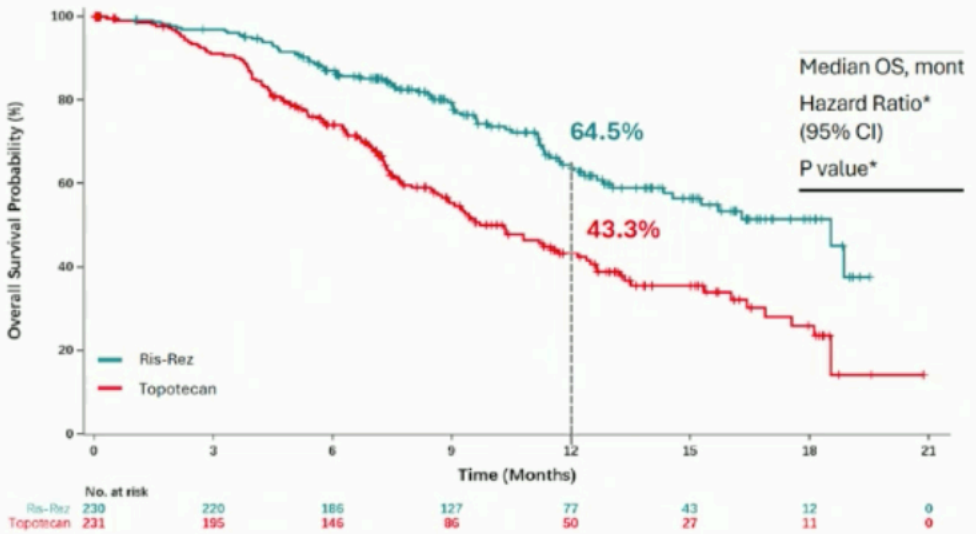
	Tam-Peli (N = 225)	Topotecan (N = 226)
OS events, n (%)	76 (33.8)	124 (54.9)
Median OS, months (95% CI)	**13.3** (12.1, NE)	**9.4** (7.7, 10.5)

HR 0.46 (95% CI: 0.35, 0.62)

P <0.0001*

J. Wang WCLC 2026

Risvutatug Rezetecan



No. at risk

Ris-Rez	230	220	186	127	77	43	12	0
Topotecan	231	195	146	86	50	27	11	0

	Ris-Rez N=230	Topotecan N=231
Median OS, months	**18.5**	**10.3**
Hazard Ratio* (95% CI)	**0.46** (0.35, 0.62)	
P value*	**<0.0001**	

L. Zhang WCLC 2026

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K. Oselin, 26Oct2026

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ABBV-706: A First-in-Class SEZ6-Targeted Topoisomerase 1 Inhibitor Antibody-Drug Conjugate With Robust Antitumor Activity in Relapsed/Refractory Small Cell Lung Cancer

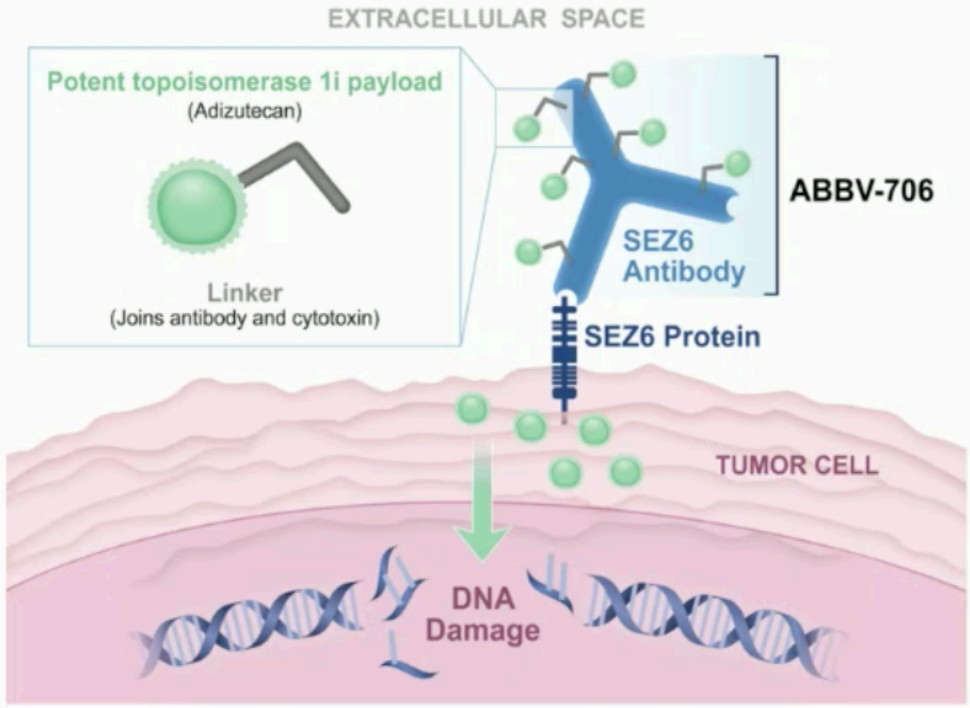
Anne C. Chiang,[1] Nadine Jahchan,[2] Emily Faivre,[2] Irene Lee,[2] Lujia Wang,[2] Klea Richardson,[2] Axel Hernandez,[2] Michael Barnes,[2] Sheila Bheddah,[2] Weilong Zhao,[2] Lloyd T. Lam,[2] Song Wang,[2] Tammy Palenski,[2] Daniel Martins,[2] Noura Choudhury,[3] Alissa J. Cooper,[4] Afshin Dowlati,[5] Lauren Byers,[6] Luis Paz-Ares[7]

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ABBV-706 is a first-in-class SEZ6-targeting ADC being evaluated in ES-SCLC

- Relapsed SCLC is a highly aggressive disease with poor outcomes and limited effective treatment options following first-line platinum-based chemoimmunotherapy[1,2]
- SEZ6, is a neuroendocrine lineage marker overexpressed in SCLC with limited expression in normal tissues,[3–5] and still expressed across molecular subtypes[6]
- ABBV-706 is a first-in-class ADC consisting of a SEZ6-targeting monoclonal antibody conjugated via a stable linker to a potent Top1i payload (adizutecan)[7]



Here, we characterize SEZ6 as a clinical biomarker for SCLC in the ongoing FIH phase 1 study in patients with R/R SCLC treated with ABBV-706 at the RP2D of 1.8 mg/kg Q3W

1. Canova S, et al. *Curr Oncol Rep*. 2023;25(11):1277-1294. **2.** Meriggi F. *Cancers (Basel)*. 2024;16(2):255. **3.** Wiedemeyer WR, et al. *Mol Cancer Ther*. 2022;21:986-998. **4.** Marks JA, et al. *Lung Cancer*. 2026;213:108913. **5.** Gezelius E, et al. *Clin Cancer Res*. 2025;31:4419-4428. **6.** Jahchan et al. WCLC 2026. Poster P3.340 **7.** Byers LA, et al. *Nat Med*. 2026;32(8):2898-2908. ADC, antibody-drug conjugate; ES-SCLC, extensive stage small cell lung cancer; FIH, first-in-human; Q3W, once every 3 weeks; RP2D, recommended phase 2 dose; R/R, relapsed/refractory; SCLC, small cell lung cancer; SEZ6, seizure-related homolog protein 6; Top1i, topoisomerase 1 inhibitor.

ABBV-706 FIH phase 1 study design and published results

Phase 1 R/R ES-SCLC[a]

- Prior platinum-etoposide chemotherapy and/or immuno-oncology regimens
- Prior treated or untreated stable brain metastases were eligible
- History of ILD/pneumonitis requiring treatment or active disease were excluded

Total monotherapy patient population: ABBV-706 1.3–3.5 mg/kg (N=124)

1.8 mg/kg RP2D for monotherapy

ABBV-706 1.8 mg/kg as 2L+ (n=41)

IV Q3W in 21-day cycles until disease progression or unacceptable toxicity

Key Endpoints
Safety, ORR, PFS, OS, SEZ6 by IHC

Key Methods[1]

- Archival or fresh tissue biopsy at screening
- SEZ6 IHC (AbbVie proprietary assay)
- Plasma ctDNA and serum proGRP were collected at baseline, start of each cycle 1–4, odd cycles thereafter, and end of treatment
- The Guardant INFINITY™ ctDNA assay (Guardant Health) was used to monitor methylation-based tumor fraction responses
- proGRP was used to monitor tumor response using the Roche Cobas® electrochemiluminescence immunoassay (LabCorp)

Patient Characteristics 1.8 mg/kg (n=41)[1]

Median age, years (range)	64 (48–85)
Median prior LoT, n (range)	2 (1–6)
Brain mets at baseline	39% (n=16)
Chemo-free interval	61% (<90 days) 27% (<30 days)

Results 1.8 mg/kg (n=41)[1]

Safety Grade ≥3

All TRAEs	88% (n=36)
Anemia	42% (n=17)
Neutropenia	20% (n=8)

Efficacy[b]

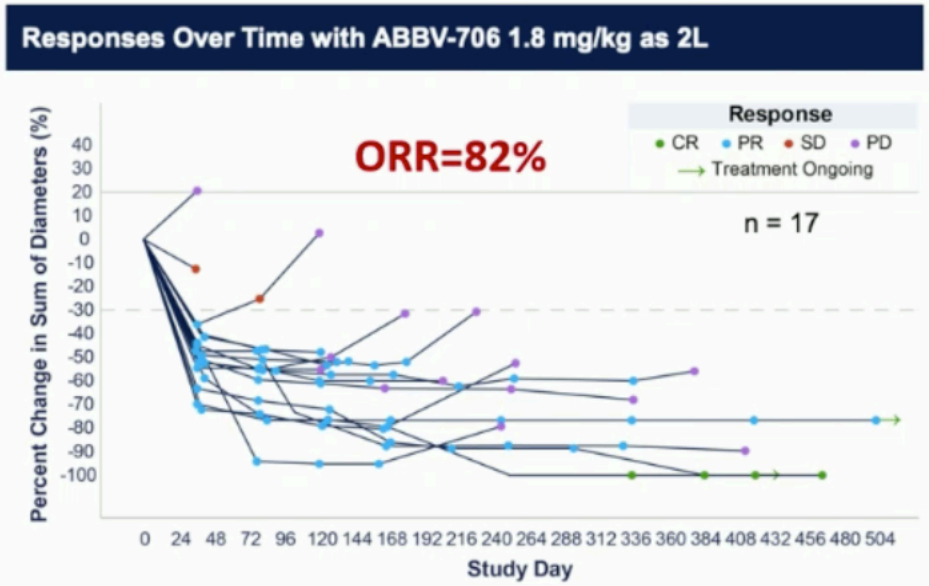
ORR	56% (n=23)
mPFS	6.4 months (4.0–8.1)
mOS	12.4 months (8.2–17.3)

1. Byers LA, et al. *Nat Med*. 2026;32(8):2898-2908. [a]ClinicalTrials.gov. NCT05599984. [b]Similar efficacy was observed in the ITT and biomarker eligible populations. 2L+, second-line and later; chemo, chemotherapy; ctDNA, circulating tumor DNA; ES-SCLC; extensive stage small cell lung cancer; FIH, first-in-human; IHC, immunohistochemistry; ILD, interstitial lung disease; ITT, intention to treat; IV, intravenous; LoT, lines of treatment; mets, metastases; mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; proGRP, pro-gastrin releasing peptide; Q3W, every 3 weeks; RP2D, recommended phase 2 dose; R/R, relapsed/refractory; SEZ6, seizure-related homolog protein 6; TRAE, treatment-related adverse event.

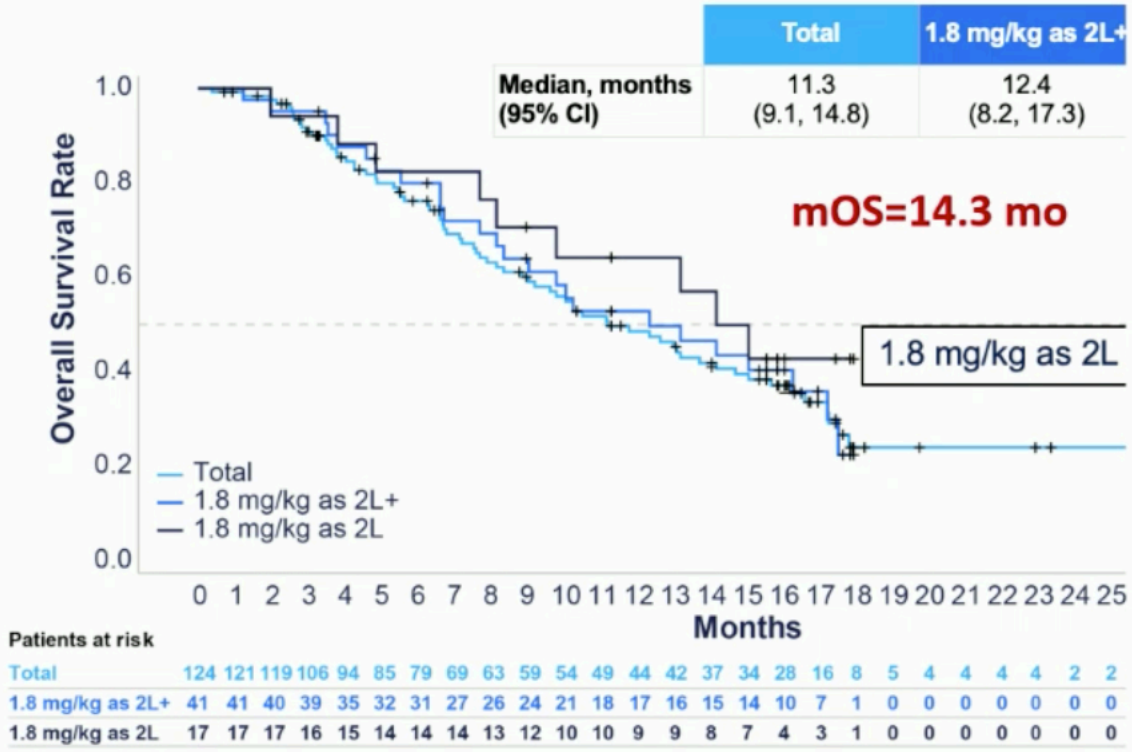
ABBV-706 first-in-class ADC targets SEZ6

First-in-human study as monotherapy and combination with budigalimab

Second line



LA. Byers ASCO 2026



Chiang et al. ESMO 2026 – 3837RO

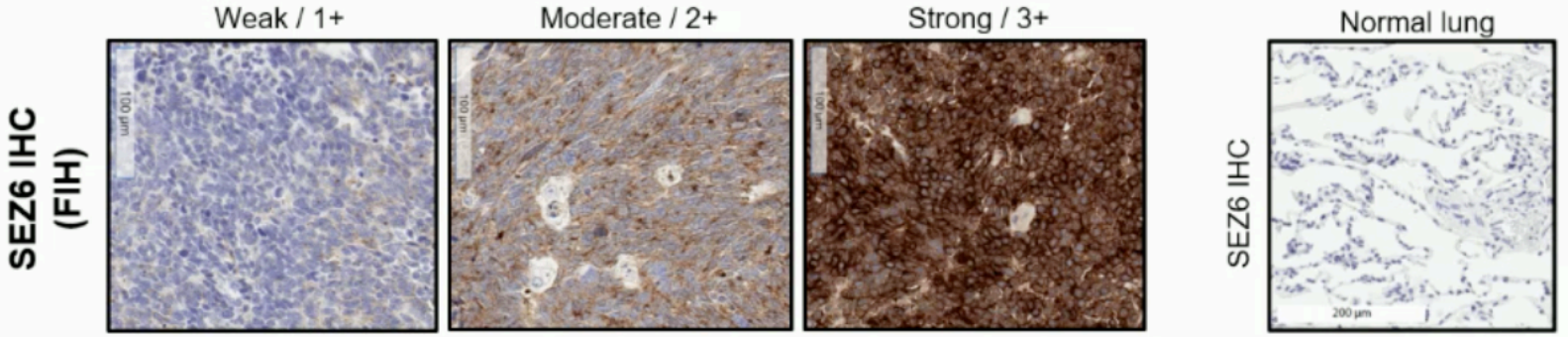
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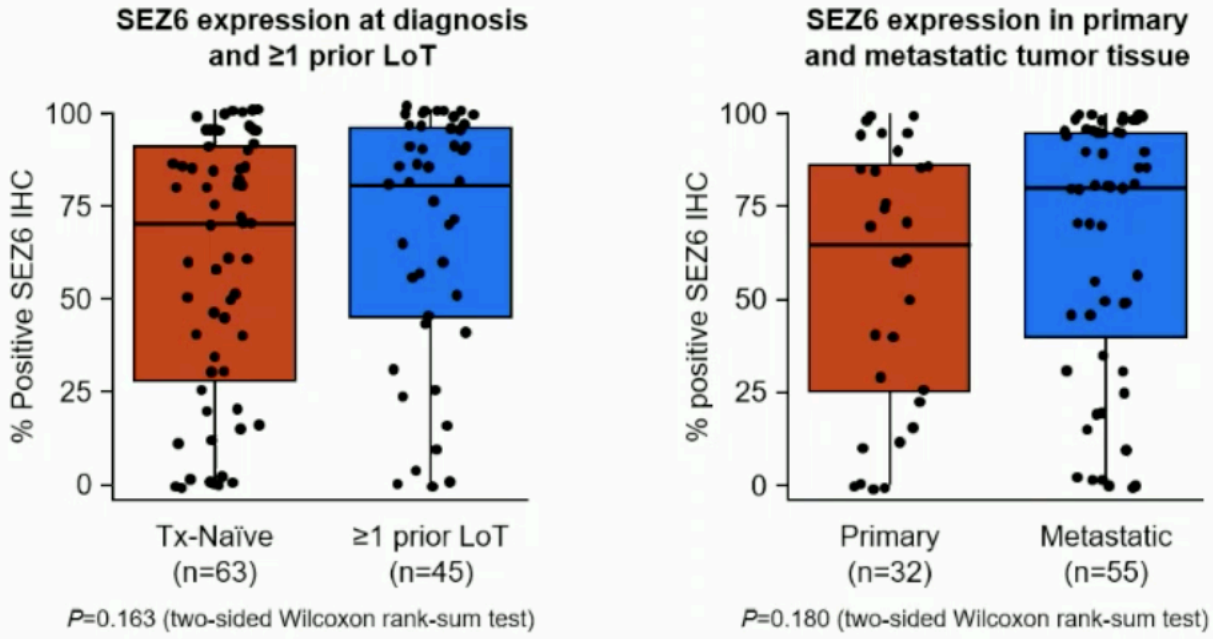
SEZ6: A compelling ADC target with high and stable expression in SCLC

In the FIH study, tumors expressing SEZ6 are prevalent in patients with SCLC[a]

SEZ6 expression in SCLC is not affected by prior treatment or biopsy from primary cancer or metastases



(93% above a 1% [1+ cutoff] and median H-score of 145)[1]

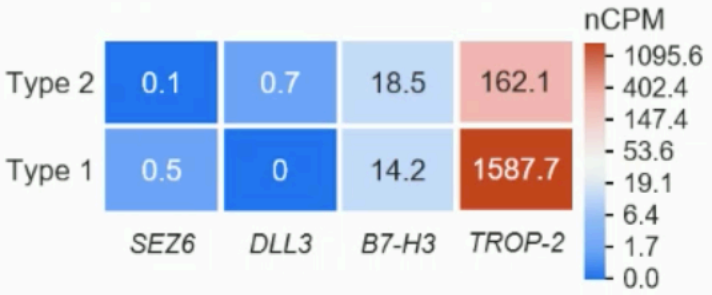


1. Byers LA, et al. *Nat Med*. 2026;32(8):2898-2908. [a]SEZ6 IHC was performed on all SCLC tumors collected at screening n=108.8 ADC, antibody-drug conjugate; FIH, first-in-human; IHC, immunohistochemistry; LoT, line of treatment; SCLC, small cell lung cancer; SEZ6, seizure-related homolog protein 6; Tx, treatment.

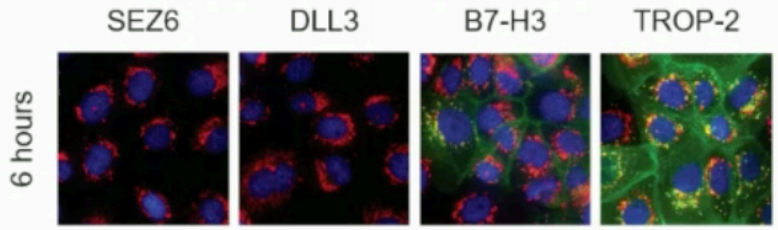
Minimal SEZ6 expression in normal lung alveolar epithelial cells translates into limited antibody binding and internalization

- ADCs have been associated with a higher risk of pneumonitis/ILD
- DLL3, B7-H3, and TROP-2 are well known targets in SCLC
- Both SEZ6 and DLL3 have low expression in normal lung alveolar cells compared with B7-H3 and TROP-2
- Low expression translates to low binding, internalization, and trafficking to normal alveolar lung lysosomes

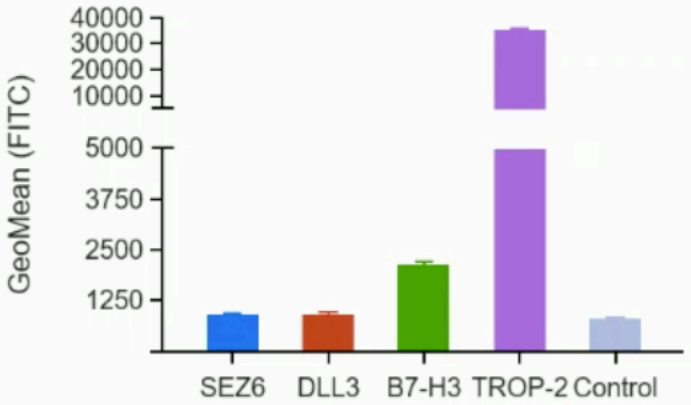
Lung Alveolar Cell Gene Expression[a]



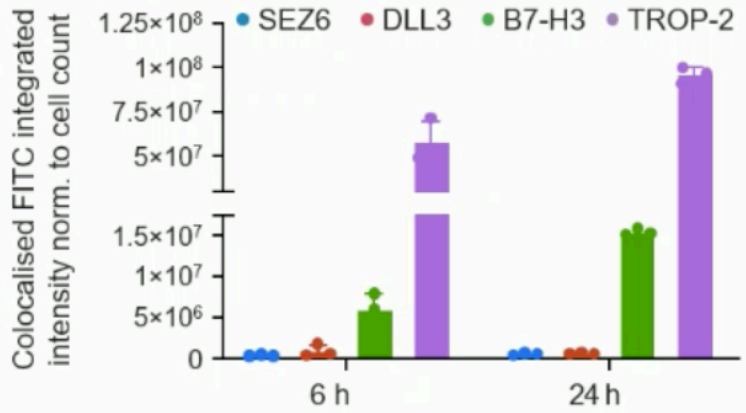
Internalization and Trafficking to Normal Alveolar Lung Lysosomes[b]



Lung Alveolar Cell Target Binding



Colocalization to Lysosomal Compartment



Limited expression in normal lung tissue may support low incidence of lung toxicity such as ILD

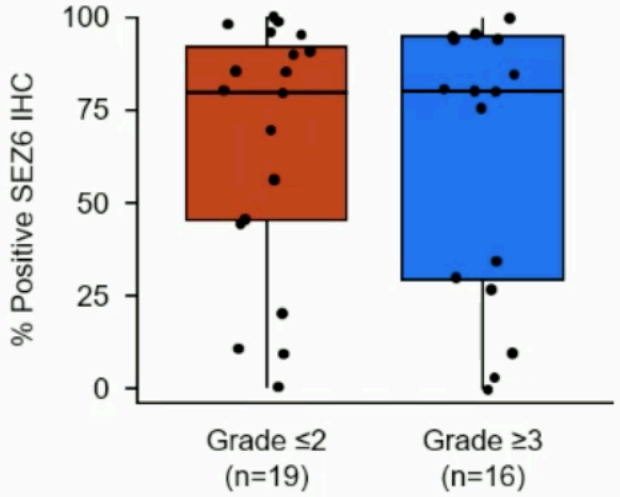
[a]From single-cell expression data across available lung cell types in Human Protein Atlas (SciLifeLab, Solna, Sweden). [b]DAPI nuclear staining (Blue), AF488-labeled antibody (Green), Lysotracker (Red), colocalization to lysosome (Yellow). Trafficking, AF488-labeled antibodies internalization and colocalization with the lysosomal compartment were assessed by live cell imaging. ADC, antibody-drug conjugate; B7-H3, B7 homolog 3; DAPI, 4′,6-diamidino-2-phenylindole; DLL3, delta-like canonical notch ligand 3; FITC, fluorescein isothiocyanate; GeoMean, geometric mean; h, hour; ILD, interstitial lung disease; nCPD, normalized counts per million; norm., normalized; TROP-2, trophoblast cell surface antigen 2; SCLC, small cell lung cancer; SEZ6, seizure-related homolog protein 6.

SEZ6 expression is not associated with hematological TRAEs or response

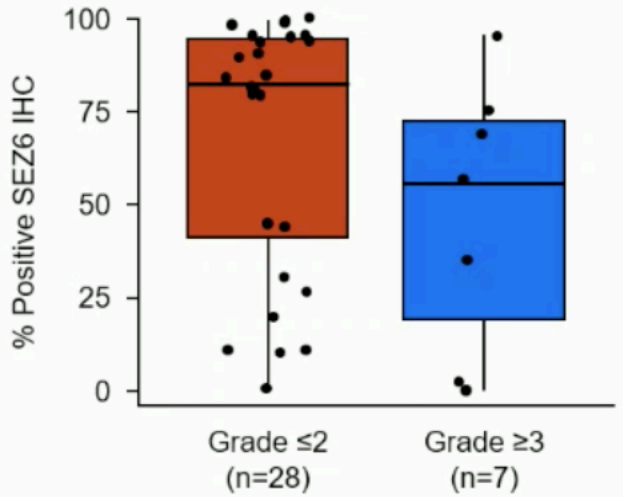
- Preliminary data from the phase 1 study of ABBV-706 monotherapy showed a manageable safety profile[1]
- Most common Grade ≥3 TRAEs in patients with SCLC treated with ABBV-706 1.8 mg/kg Q3W were hematological, including anemia and neutropenia
- SEZ6 expression did not correlate with development of any grade anemia or neutropenia[a]
- SEZ6 expression was comparable between responders[b] and nonresponders to ABBV-706 treatment, supporting a biomarker-unselected approach[a]

Hematological Toxicity

SEZ6 Expression in Patients With Anemia

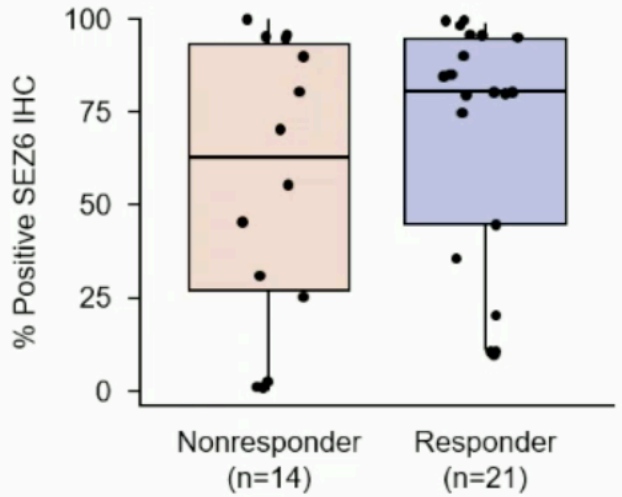


SEZ6 Expression in Patients With Neutropenia



Response

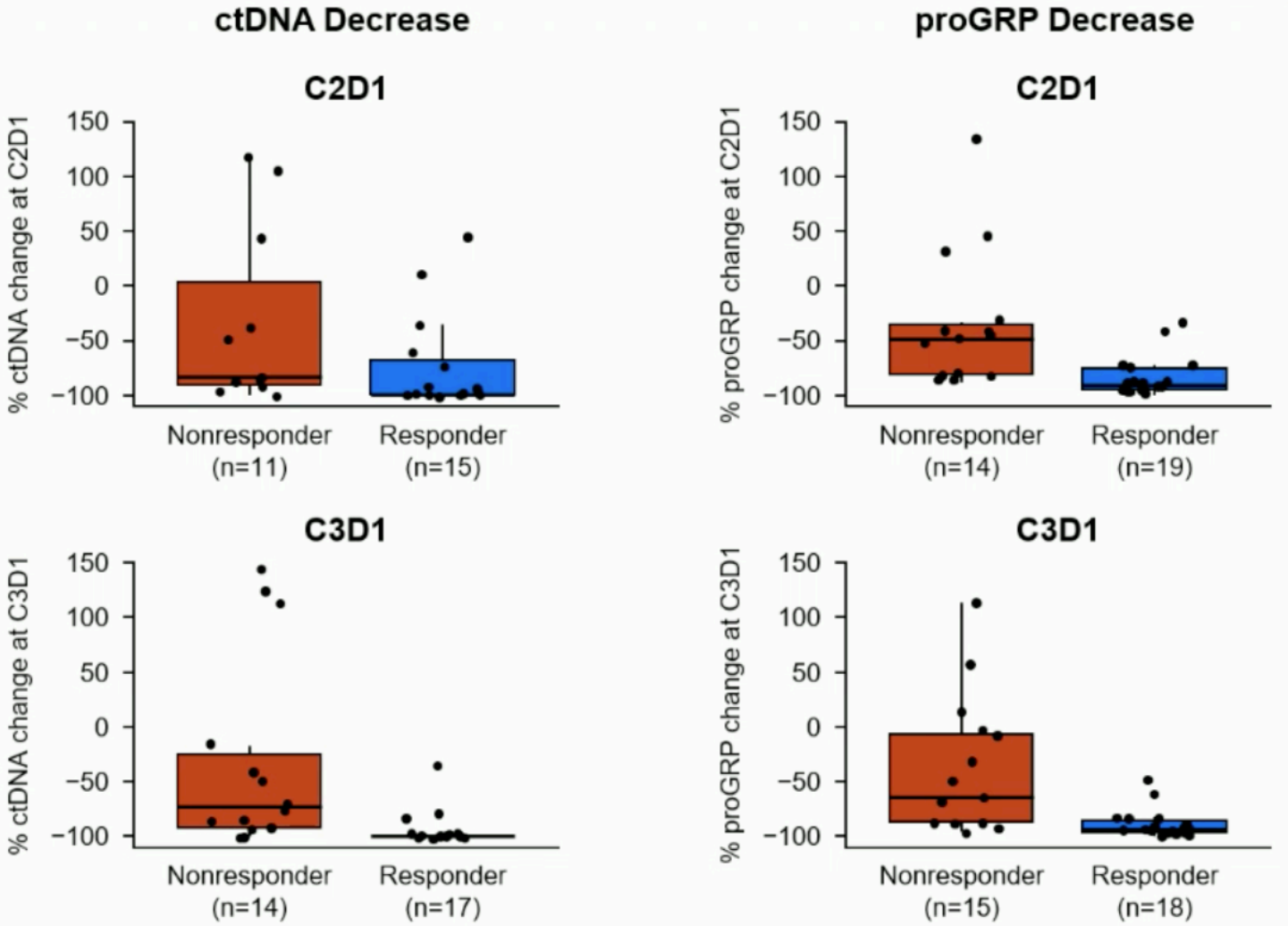
SEZ6 Expression in Nonresponders vs Responders



1. Byers LA, et al. *Nat Med*. 2026;32(8):2898-2908. [a]SEZ6 IHC correlation with ORR and safety in 35 evaluable tumor samples. [b]Responders defined as confirmed CR + PR. CR, complete response; IHC, immunohistochemistry; ORR, overall response rate; PR, partial response; Q3W, every 3 weeks; SCLC, small cell lung cancer; SEZ6, seizure-related homolog protein 6; TRAE, treatment-related adverse event.

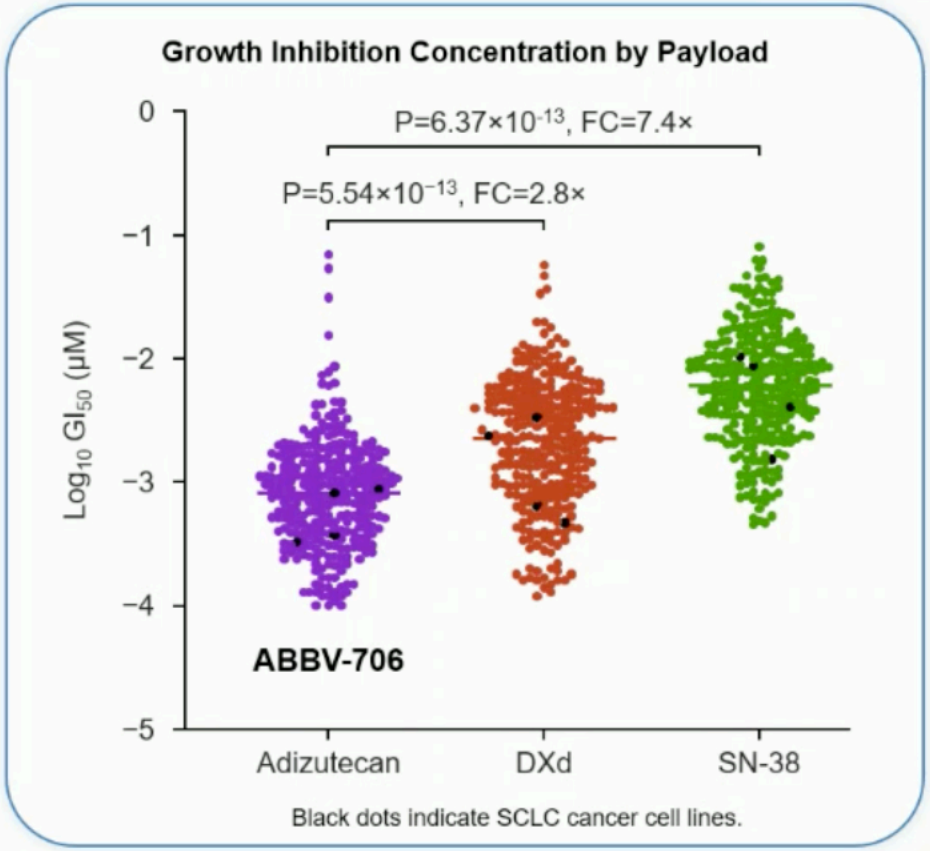
ABBV-706 monotherapy results in rapid ctDNA and proGRP decreases, which are more pronounced in responders compared to nonresponders

- ctDNA and proGRP are emerging clinical biomarkers in SCLC used to monitor the effectiveness of treatment and disease progression
- ABBV-706 monotherapy triggered rapid declines in ctDNA and proGRP as early as C2D1 among patients who received the 1.8 mg/kg dose
- ctDNA and proGRP decreases at C2D1 and C3D1 were more pronounced in responders compared with nonresponders[a]

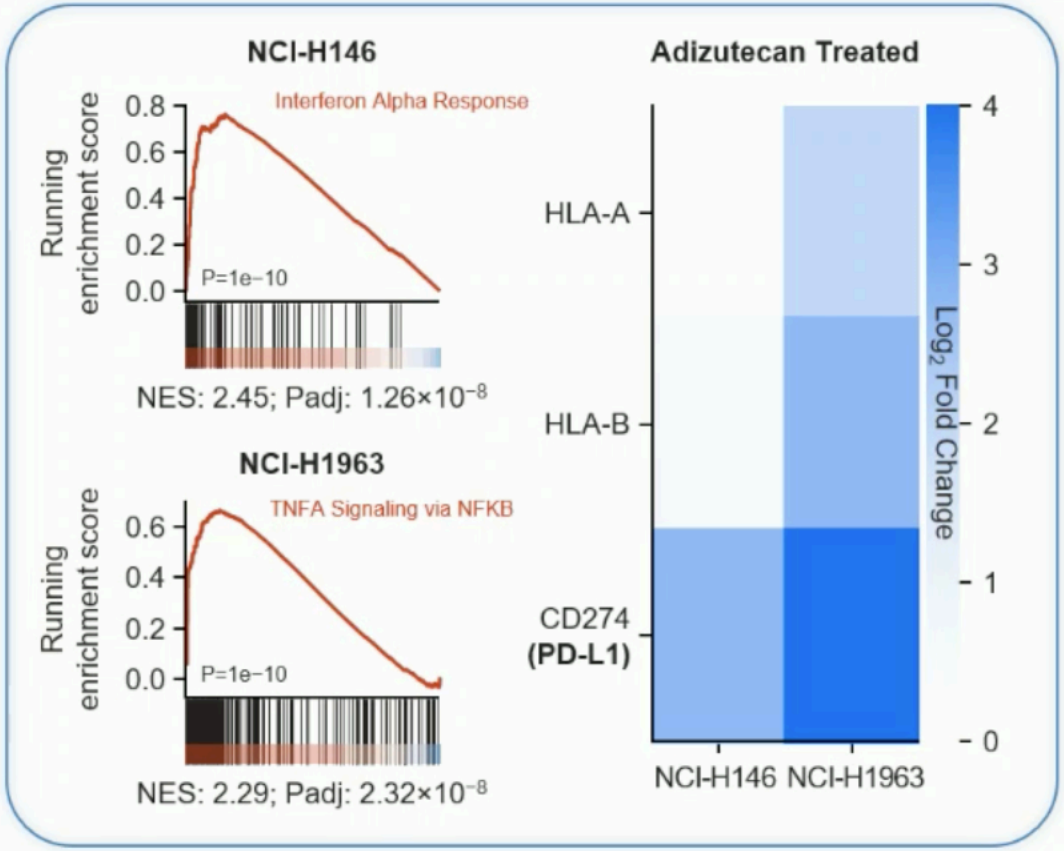


[a]Responders defined as confirmed CR + PR. C, cycle; CR, complete response; ctDNA, circulating tumor DNA; D, day; PR, partial response; proGRP, pro-gastrin releasing peptide; SCLC, small cell lung cancer.

The adizutecan Top1i payload has potent growth inhibitory activity and induces immunomodulatory effects in SCLC



Adizutecan payload more potently inhibits growth of cancer cell lines, including SCLC cell lines, compared with other Top1i payloads

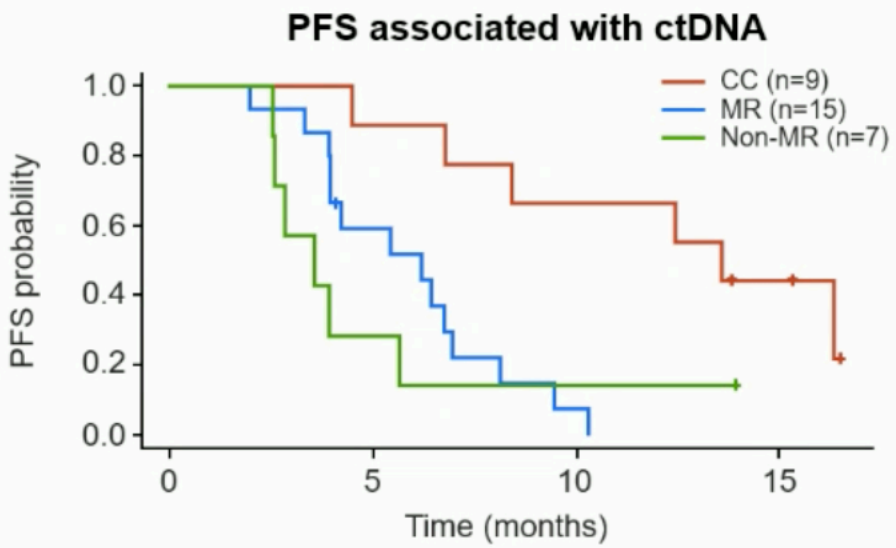


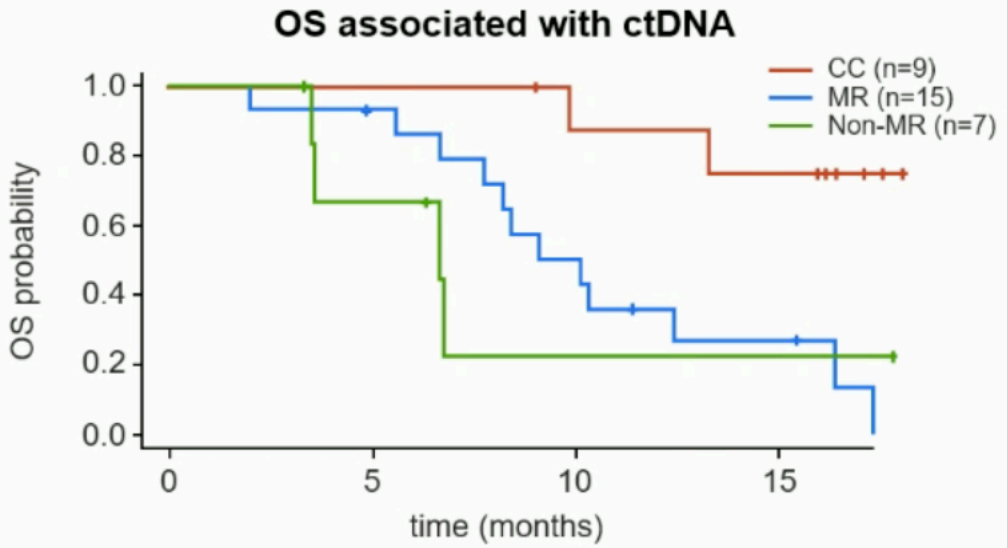
Adizutecan treatment in SCLC cell lines leads to enrichment in hallmark inflammatory signals and a significant increase in PD-L1 and MHC-I

DXd, deruxtecan; FC, fold change; GI_{50}, concentration causing 50% inhibition of cell growth; HLA, human leukocyte antigen; MHC-I, major histocompatibility complex class I; NCI, National Cancer Institute; NES, normalized enrichment score; NFKB, nuclear factor kappa-light-chain-enhancer of activated B cells; Padj, adjusted P-value; PD-L1, programmed death-ligand 1; SCLC, small cell lung cancer; SN-38, 7-ethyl-10-hydroxycamptothecin; TNFA, tumor necrosis factor alpha; Top1i, topoisomerase 1 inhibitor.

ctDNA clearance is associated with robust improvements in PFS and OS

- ABBV-706 induces rapid ctDNA reduction: ≥50% in 77% (n/N=24/31) and ≥95% in 52% (n/N=16/31) of patients by C3D1
- Complete ctDNA clearance observed in 29% of patients shows a significant trend toward improvements in PFS and OS





	PFS			OS		
Total patients N=31	**Non-MR (n=7)**	**MR (n=15)**	**CC (n=9)**	**Non-MR (n=7)**	**MR (n=15)**	**CC (n=9)**
Median outcome, months (95% CI)[a]	3.6 (2.6–NR)	6.2 (4.0–9.5)	13.6 (8.4–NR)	6.7 (3.6–NR)	10.1 (8.2–NR)	NR (NR–NR)

Rapid ctDNA reduction was sustained and was associated with improved outcomes

[a]Similar data were observed with 95% cutoff for ctDNA reductions, as a predictor of OS and PFS. Non-MR: ctDNA reduction <50%; MR: ctDNA reduction ≥50% and <100%; CC: 100% ctDNA reduction. Responder defined as PR+CR. C, Cycle; CC, complete clearance; CI, confidence interval; CR, complete response; ctDNA, circulating tumor DNA; D, day; mPFS, median progression-free survival; MR, molecular responder; NR, not reached; OS, overall survival; PFS, progression-free survival; PR, partial response.

Conclusions

SEZ6 is highly expressed in SCLC, stable across LoT, and not correlated with response rates or hematological adverse events following ABBV-706 monotherapy

The immunomodulatory effects induced by the adizutecan payload support the mechanistic rationale for combining ABBV-706 with PD-L1 in the ongoing phase 2 1L SCLC SEZanne study[a]

ctDNA clearance is associated with improvements in PFS and OS following ABBV-706 monotherapy

ABBV-706 monotherapy has demonstrated promising clinical benefit, with biomarker and preclinical data supporting SEZ6 as a therapeutic target in SCLC; the phase 3 SEZanne-02 study[b] in patients with R/R SCLC previously treated with tarlatamab is ongoing

AbbVie Inc. and the authors thank the participants, study sites, and investigators who participated in this clinical trial.

AbbVie funded this trial and participated in the trial design, research, analysis, data collection, interpretation of data, and the review and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship.

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[a]ClinicalTrials.gov. NCT07155174. clinicaltrials.gov/ct2/show/NCT07155174. Accessed October 2026. [b]ClinicalTrials.gov. NCT07365241. clinicaltrials.gov/ct2/study/NCT07365241. Accessed October 2026. 1L, first-line; ctDNA, circulating tumor DNA; LoT, lines of treatment; R/R, relapsed/refractory; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; SCLC, small cell lung cancer; SEZ6, seizure-related homolog protein 6.

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SKB500 (a novel B7-H3-targeted antibody-drug conjugate) in patients with extensive-stage small cell lung cancer (ES-SCLC): Results from a phase I study

Haifeng Liu[1], Xueying Zhang[1], Wei Zheng[2], Shengxiang Ren[3], Lang He[4], Qiming Wang[5], Wen Gao[6], Dingzhi Huang[7], Anwen Liu[8], Jian Li[8], Sanxing Guo[9], Zhangzhou Huang[10], Hongxu Liu[11], Zhiwei Li[12], Jinsheng Hong[13], Zhiye Zhang[14], Xiguang Cao[15], Yan Qing[15], Xiaoping Jin[15], Junyou Ge[15,16]

[1] Jilin Cancer Hospital, Changchun, China; [2] Shengjing Hospital, China Medical University, Shenyang, China; [3] Shanghai Pulmonary Hospital, Shanghai, China; [4] Chengdu Fifth People's Hospital, Chengdu, China; [5] The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Henan Academy of Innovations in Medical Science, Zhengzhou, China; [6] Jiangsu Province Hospital, Nanjing, China; [7] Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [8] The Second Affiliated Hospital of Nanchang University, Nanchang, China; [9] The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [10] Fujian Cancer Hospital, Fuzhou, China; [11] Liaoning Cancer Hospital, Shenyang, China; [12] Harbin Medical University Cancer Hospital, Harbin, China; [13] The First Affiliated Hospital of Fujian Medical University, Fuzhou, China; [14] The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, China; [15] Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China; [16] National Engineering Research Center of Targeted Biologics, Chengdu, China

Professor Haifeng Liu

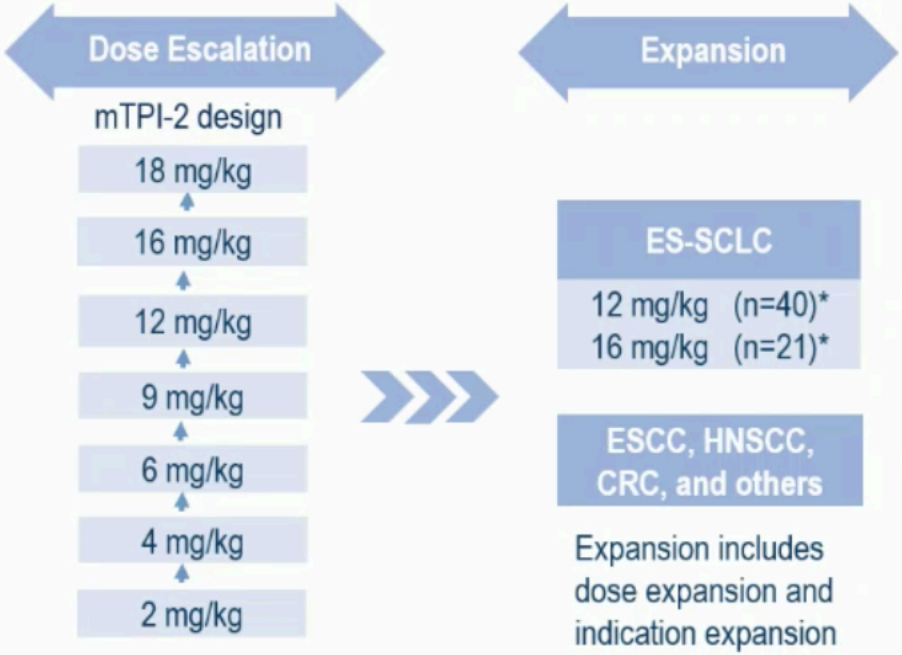
26 October 2026



ESMO

Background and Study Design

- B7-H3 is overexpressed in lung cancer and several other malignancies but has limited expression in normal tissues, where it promotes tumor progression and immune evasion[1].
- SKB500 is a B7-H3-targeted ADC comprising an antibody linked to a topoisomerase I inhibitor payload via a cleavable pyrimidine-tripeptide linker. As previously reported, SKB500 demonstrated favorable safety and antitumor activity across multiple tumor types[2].



Key Eligibility Criteria:

- Age 18-75 years
- ES-SCLC
- Progressed on ≥ 1 prior line of systemic therapy
- ECOG PS 0-1

Endpoints:

- **Primary Endpoints:**
  Safety (DLT, AE)
- **Secondary Endpoints:**
  Investigator-assessed ORR, DCR, DoR, and PFS; OS

Here we present updated safety and antitumor activity of SKB500 in ES-SCLC from the multicenter, open-label phase I study.

SKB500 was administered intravenously every 3 weeks (Q3W). *Sample sizes include patients enrolled in the dose escalation phase. Clinical trial identification: NCT06736327.
ADC, antibody-drug conjugate; B7-H3, B7 homolog 3; CRC, colorectal cancer; DCR, disease control rate; DLT, dose-limiting toxicity; DoR, duration of response; ECOG PS, eastern cooperative oncology group performance status; ESCC, esophageal squamous cell carcinoma; ES-SCLC, extensive-stage small cell lung cancer; HNSCC, head and neck squamous cell carcinoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

Professor Haifeng Liu

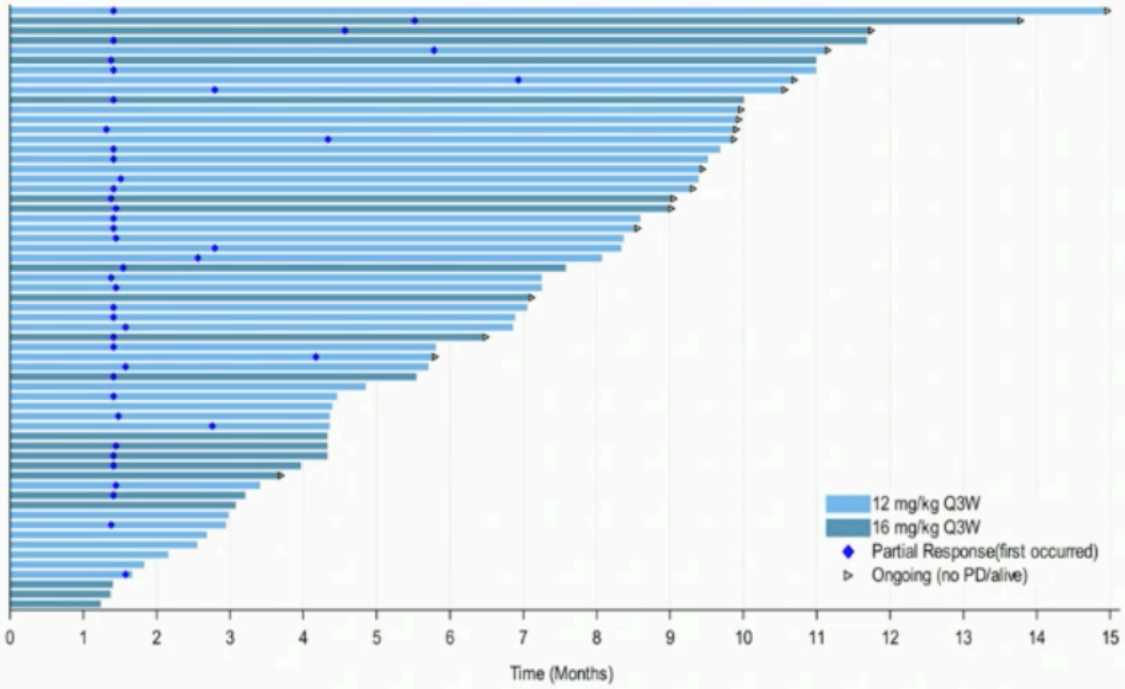
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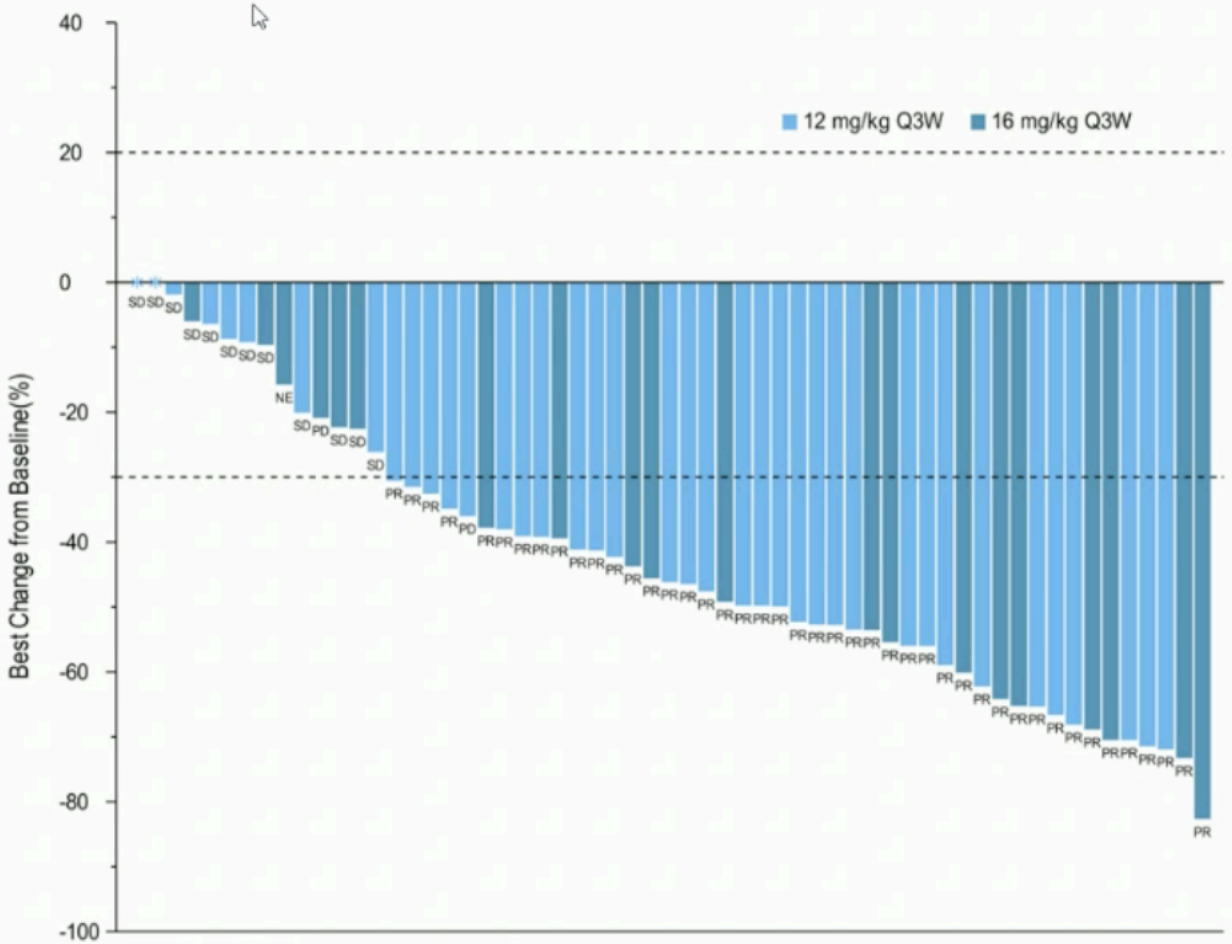
1. Yamato M et al. *Mol Cancer Ther*. 2022; 21(4):635-646.
2. Liu H et al. 2026 ASCO. Abstract 3011.

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Objective Response and Duration of Response

	12 mg/kg (n = 40)	16 mg/kg (n = 21)
ORR, % (95% CI)	75.0 (58.8, 87.3)	66.7 (43.0, 85.4)
cORR , % (95% CI)	62.5 (45.8, 77.3)	66.7 (43.0, 85.4)
DCR, % (95% CI)	95.0 (83.1, 99.4)	85.7 (63.7, 97.0)
DoR, median (95% CI), mo	5.7 (4.3, 7.1)	5.8 (2.7, NE)





* Percentage change from baseline for target lesions was 0%.

Data cutoff: September 16, 2026.

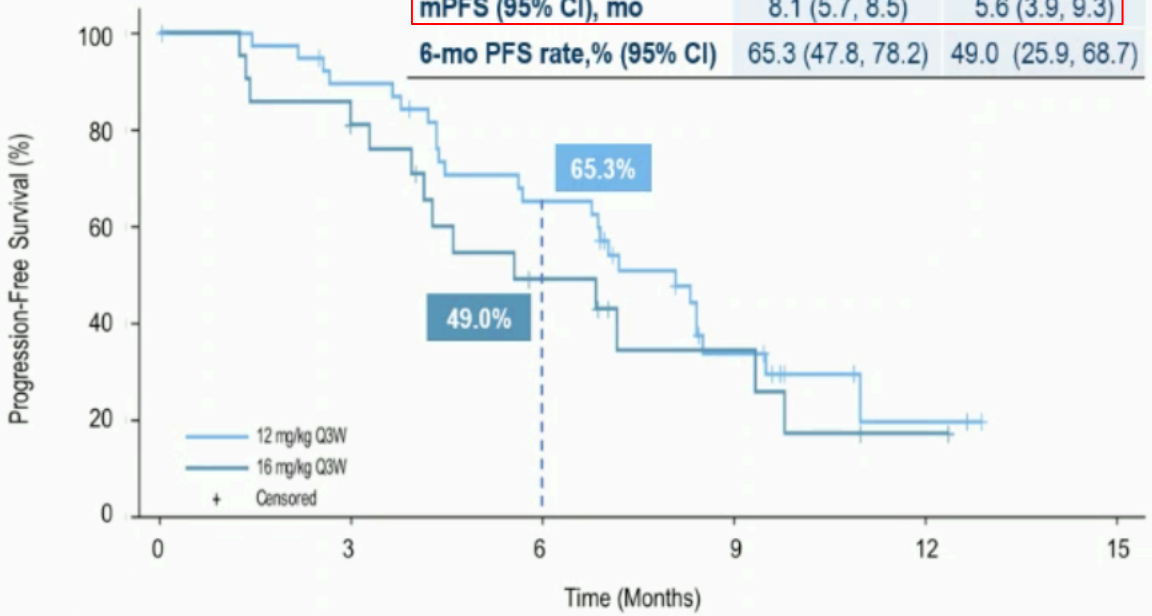
cORR, confirmed ORR; NE, not estimable; PD, progressive disease; PR, partial response; SD, stable disease.

Professor Haifeng Liu

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Progression-Free Survival and Overall Survival

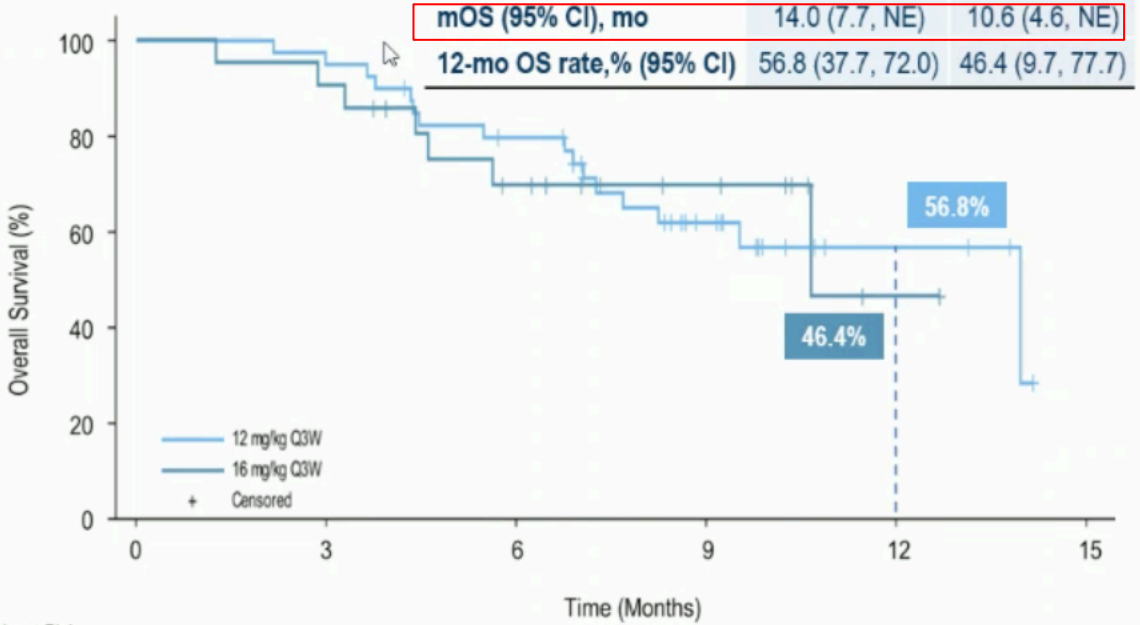
	12 mg/kg (n = 40)	16 mg/kg (n = 21)
mPFS (95% CI), mo	8.1 (5.7, 8.5)	5.6 (3.9, 9.3)
6-mo PFS rate,% (95% CI)	65.3 (47.8, 78.2)	49.0 (25.9, 68.7)



No. at Risk

12 mg/kg Q3W	40	34	24	9	2	0
16 mg/kg Q3W	21	16	8	4	1	0

	12 mg/kg (n = 40)	16 mg/kg (n = 21)
mOS (95% CI), mo	14.0 (7.7, NE)	10.6 (4.6, NE)
12-mo OS rate,% (95% CI)	56.8 (37.7, 72.0)	46.4 (9.7, 77.7)



No. at Risk

12 mg/kg Q3W	40	38	30	15	4	0
16 mg/kg Q3W	21	19	12	7	1	0

Median follow-up: 9.3 months (12 mg/kg) and 8.3 months (16 mg/kg).

Data cutoff: September 16, 2026.

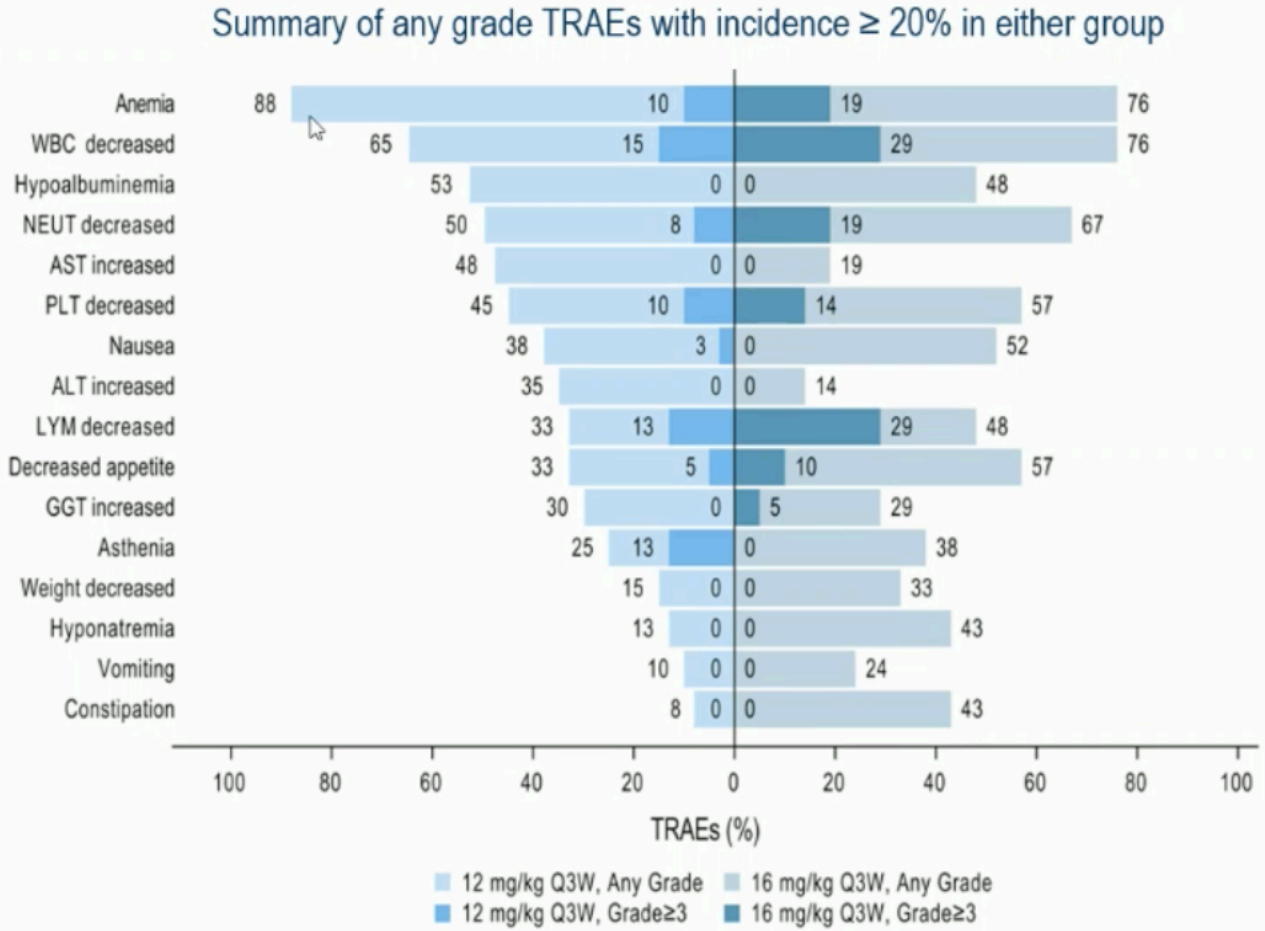
Professor Haifeng Liu

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Safety Summary

	12 mg/kg (n = 40)	16 mg/kg (n = 21)
Median duration of exposure, mo (range)	5.5 (1.4, 14.8)	4.3 (0.7, 13.0)
TRAEs, n (%)	40 (100)	20 (95.2)
Grade ≥ 3 TRAEs	21 (52.5)	14 (66.7)
Serious TRAEs	15 (37.5)	9 (42.9)
TRAEs leading to dose reduction	5 (12.5)	8 (38.1)
TRAEs leading to discontinuation	1 (2.5)	1 (4.8)
TRAEs leading to death	0	0



Data cutoff: September 16, 2026.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; LYM, lymphocyte count; NEUT, neutrophil count; PLT, platelet count; WBC, white blood cell count.

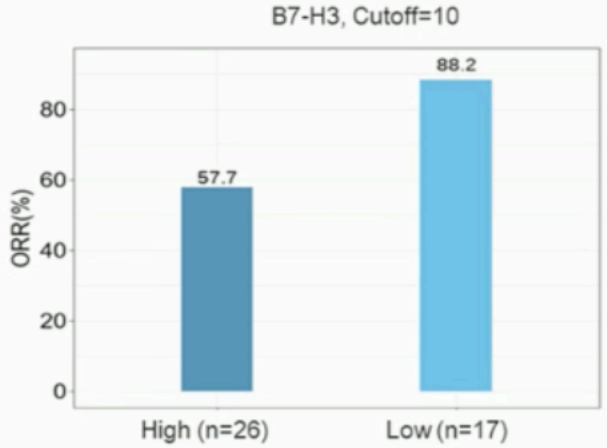
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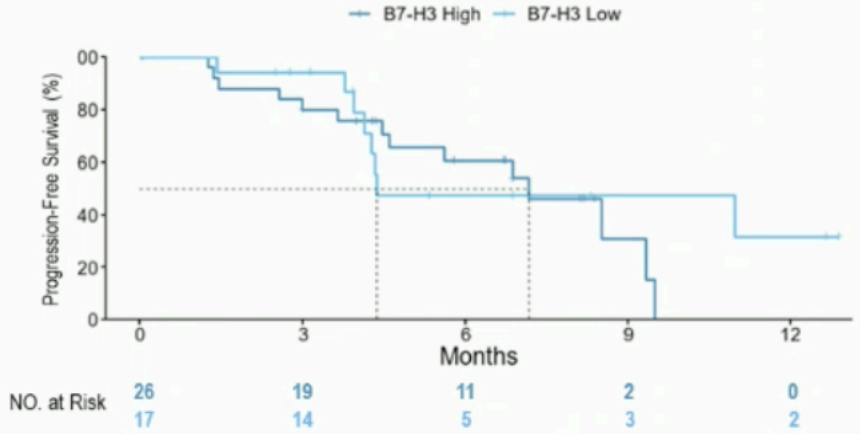
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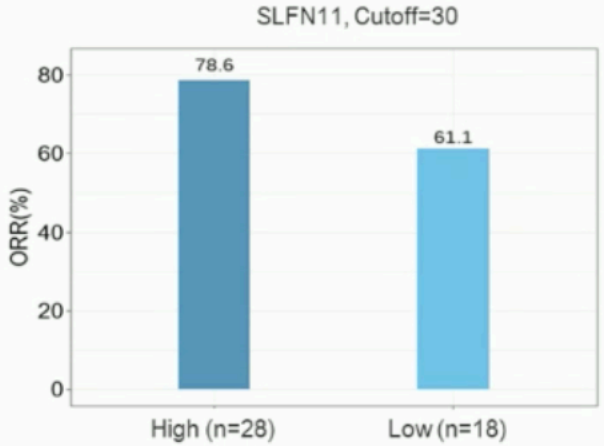
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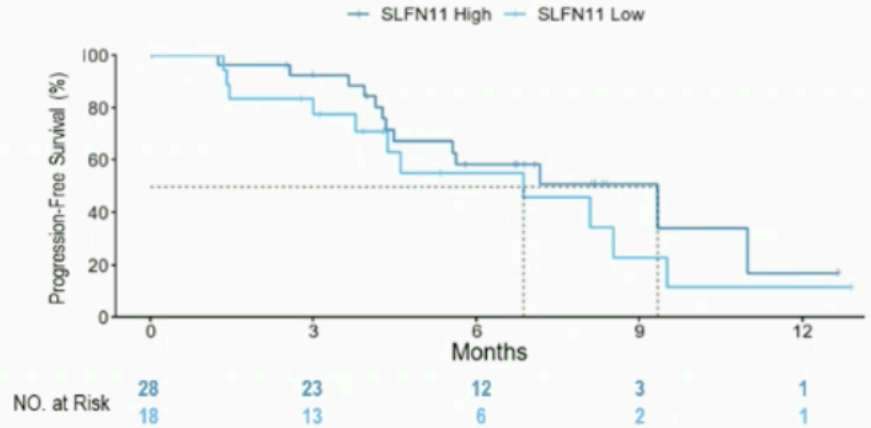
Biomarker

No correlation was observed between B7-H3 expression and tumor response, whereas SLFN11 exhibited a trend toward association with clinical activity.









Data cutoff: July 28, 2026.

Professor Haifeng Liu

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Conclusions

- **SKB500 demonstrated promising activity in ES-SCLC at both 12 and 16 mg/kg.**
  - 12 mg/kg: confirmed ORR 62.5%; median PFS 8.1 months; median OS 14.0 months.
  - 16 mg/kg: confirmed ORR 66.7%; median PFS 5.6 months; median OS 10.6 months.
- **SKB500 had a manageable safety profile, with no unexpected safety signals.**
  - The most common TRAEs were hematologic and gastrointestinal toxicities, which were manageable and typically resolved with dose modification and supportive care.
  - TRAEs leading to treatment discontinuation were low (2.5% vs 4.8% at 12 and 16 mg/kg, respectively).
  - No treatment-related deaths occurred.
- **B7-H3 expression showed no correlation with tumor response, whereas SLFN11 exhibited a trend toward association with clinical activity.**

These safety and efficacy results support further clinical development of SKB500 in ES-SCLC.

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response rates are promising

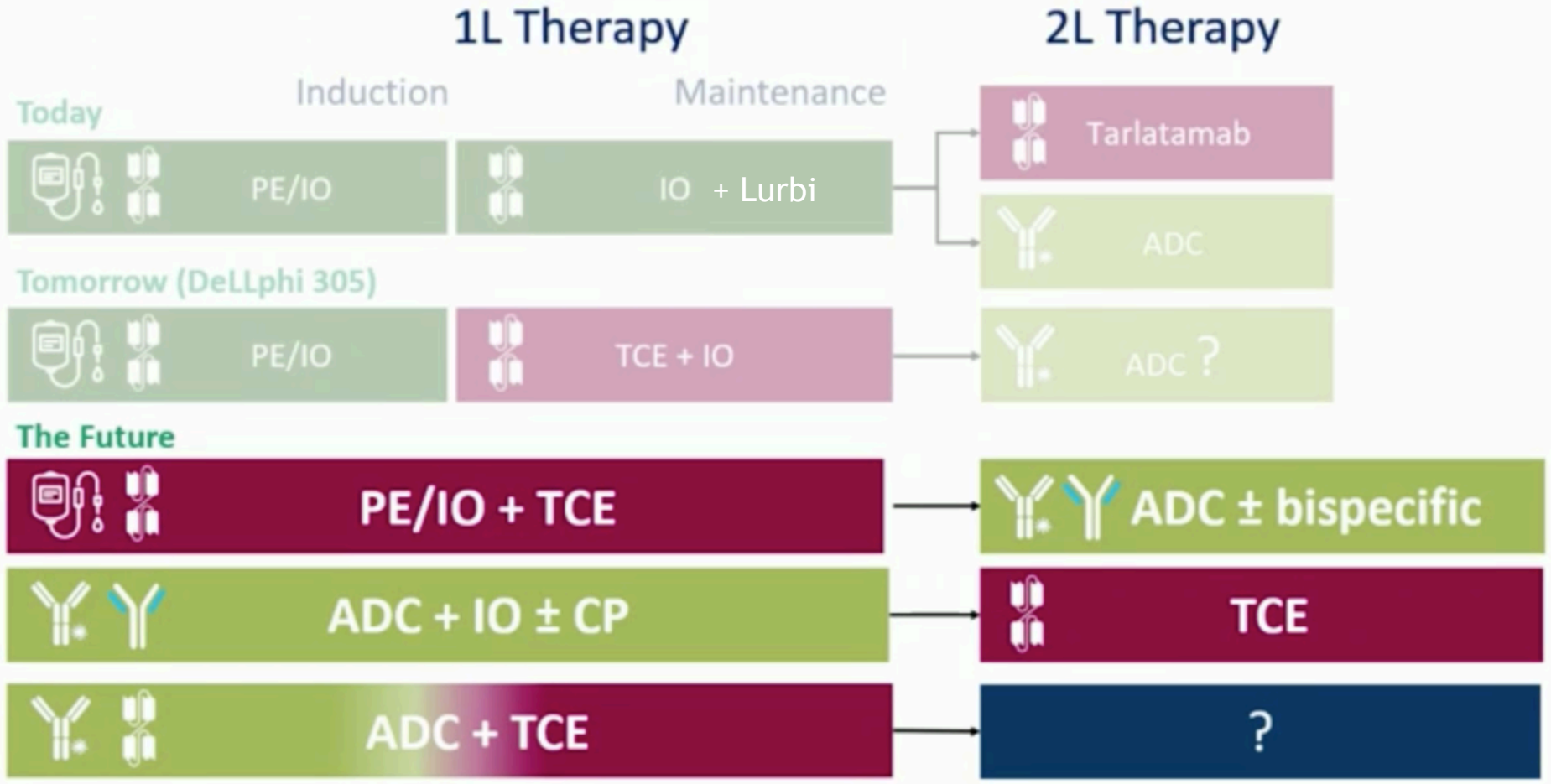
ABBV 706	SKB 500	topotecan
RR = 56%	ORR= 75%	RR = 21.6%
PFS = 6.4 months	DoR, 5.7 mo	PFS= 3.3 mo

Joachim Aerts, Erasmus University Medical Centre Roterdam

Resumen

- Dellphi 304 muestra en seguimiento extendido un beneficio y eficacia larga y una toxicidad favorable a largo plazo
- Estudios fase I con nuevos ADC de última generación como ABBV-706 (SEZ6) y SBK500 (B7-H3) muestran datos muy prometedores de eficacia con un buen perfil de toxicidad.
    - **Pendientes de estudios fase III y de su integración en primera línea**

WHAT'S NEXT? ADC COMBINATIONS



Gracias