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Daiichi-Sankyo

WCLC 2025 Highlights

DAIICHI SANKYO CO., LTD.

September 17th (US)/ 18th (JP), 2025

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WCLC 2025 Highlights: Speakers

Ken Takeshita
Head of Global R&D

Abderrahmane Laadem
Head of Late-Stage Clinical Development

Agenda

1. **SCLC overview**

2. **I-DXd program overview**
   - I-DXd scientific profile
   - IDeate-Lung01 WCLC presentation
   - I-DXd clinical development plan

3. **Other program updates from WCLC 2025**

4. **Q&A**

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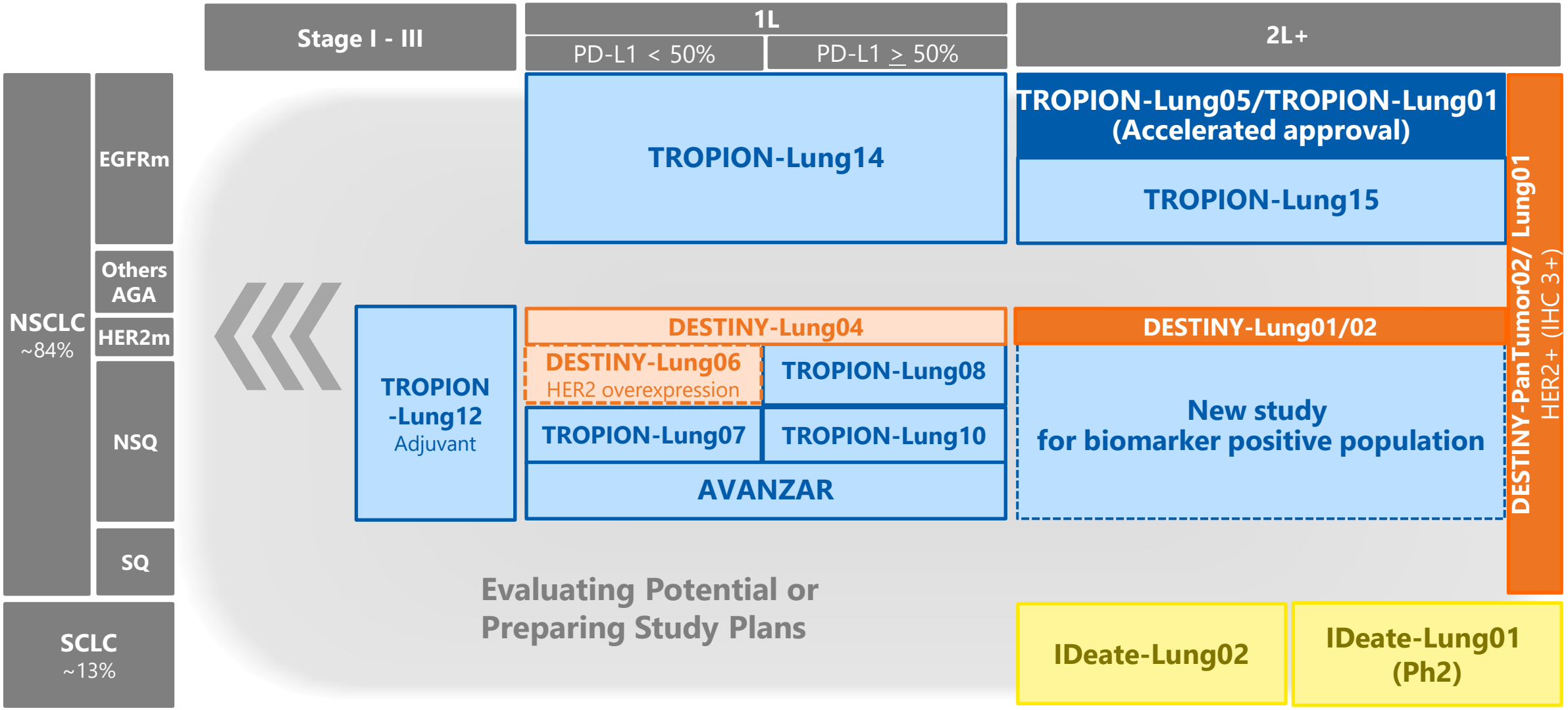
4. **Q&A**

Establish and Expand DXd ADCs to Address the Broad Spectrum of Lung Cancer



Launched | On-going | Planning | ENHERTU® | DATROWAY® | I-DXd

- Pivotal studies and major Ph2 only, not exhaustive
- Box size does not reflect the patient population
- Box indicates current potential target segment

AGA: actionable genomic alteration, IHC: immunohistochemistry, NSQ: non- squamous, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, SQ: squamous

Patients with SCLC face a poor prognosis; 5-year survival is 9% (all stages)

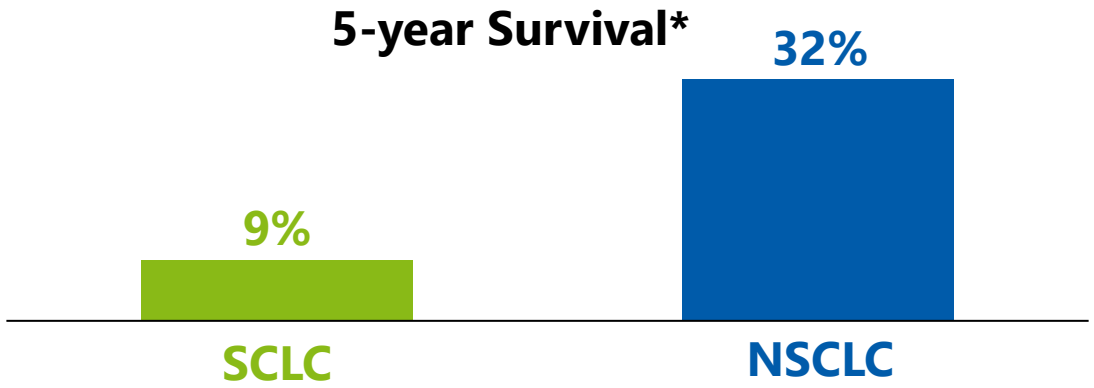
SCLC Patient[1-3]

Relatively uncommon (13.8% of all lung cancer), with an annual incidence of 250K globally

more common in men	Median age of diagnosis is 63-69 years	~90% of cases are attributed to smoking	~32% pts develop brain mets by 2L/3L

Prognosis[1,2, 4]

- Highly aggressive form of lung cancer
- ~70% of patients are diagnosed with extensive stage disease
- No actionable biomarkers
- Poor survival outcomes



NSCLC: non-small cell lung cancer, SCLC, small cell lung cancer

Mets: metastasis, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer

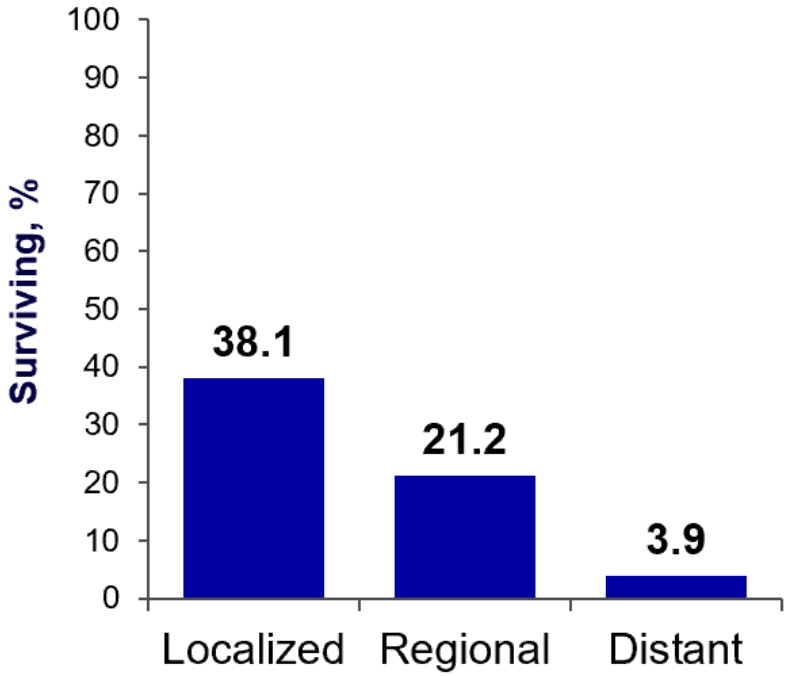
1) Cittolin-Santos GF, et al. Cancer. 2024;130(14):2453-2461. 2) Thomas Anish, et al. Nat Cancer. 2025 (6):938-953.
3) EClinicalMedicine 2024 Oct 3:77:102871. 4) American Cancer Society 5-Year Survival Rates

*These numbers are based on people diagnosed with SCLC between 2012 and 2018 and with NSCLC between 2015 and 2021.

Patients with ES-SCLC have rapid tumor progression and few effective 2L+ treatment options

As of Aug 2025

5-Year OS in patients with SCLC by stage at diagnosis in the US[2,a]



- >70% of patients diagnosed with SCLC have extensive-stage (metastatic) disease[1,2]
- Despite high initial response rates to combination platinum-based chemotherapy ± immunotherapy in 1L ES-SCLC, the median PFS is <6 months and the median OS is ≤13 months[3–5]
- Standard chemotherapy options for 2L+ treatment of ES-SCLC have limited efficacy, with median OS of 6.0–9.3 months[6–9]
- In 2024, the DLL3/CD3–directed T-cell engager tarlatamab was approved for the treatment of ES-SCLC in 2L in the US (accelerated approval) and Japan, and in 3L+ in the UK, based on efficacy observed in a population of patients treated in 2L+[10–13]

ES-SCLC: extensive-stage small cell lung cancer, OS: overall survival, PFS: progression-free survival, SCLC: small cell lung cancer.

[a]Rates in 2021. 1. Saltos A, et al. *Front Oncol*. 2020;10:1074. 2. SEER (Surveillance, Epidemiology, and End Results Program), National Cancer Institute. Available at: https://seer.cancer.gov/statistics-network/explorer/. Accessed March 24, 2025. 3. Horn L, et al. *N Engl J Med*. 2018;379:2220–2229. 4. Paz-Ares L, et al. *Lancet*. 2019;394:1929–1939. 5. Goldman JW, et al. *Lancet Oncol*. 2021;22:51–65. 6. Eckardt JR, et al. *J Clin Oncol*. 2007;25:2086–2092. 7. O'Brien ME, et al. *J Clin Oncol*. 2006;24:5441–5447. 8. Trigo J, et al. *Lancet Oncol*. 2020;21:645–654. 9. von Pawel J, et al. *J Clin Oncol*. 2014;32:4012–4019. 10. FDA. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-tarlatamab-dlle-extensive-stage-small-cell-lung-cancer. Accessed March 24, 2025. 11. IMDELLTRA™ (tarlatamab-dlle) [prescribing information]. Thousand Oaks, CA: Amgen. 2024. 12. Amgen. https://www-amgen-co-jp.translate.goog/media/press-releases/2024/12/20241227?_x_tr_sl=ja&_x_tr_tl=en&_x_tr_hl=ja&_x_tr_pto=wapp. Accessed March 24, 2025. 13. IMDYLLTRA™ (tarlatamab-dlle) [summary of product characteristics]. Cambridge, UK: Amgen. 2025.

ES-SCLC has a high incidence of brain metastasis leading to its poor prognosis

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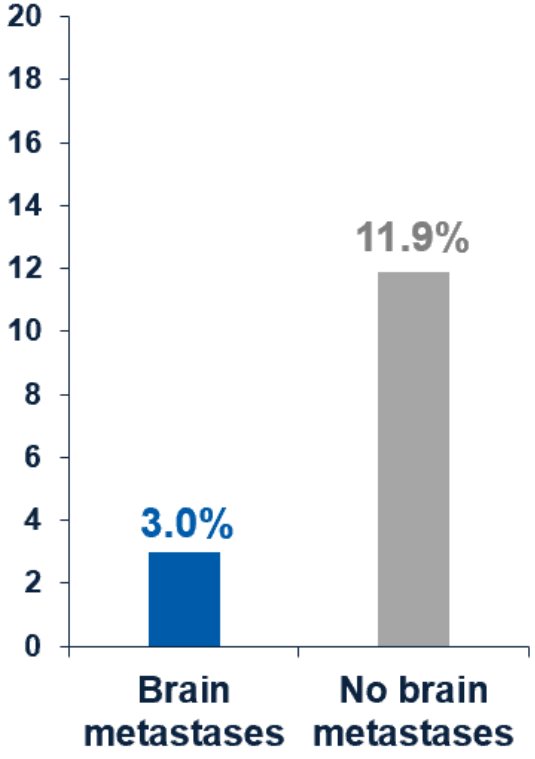
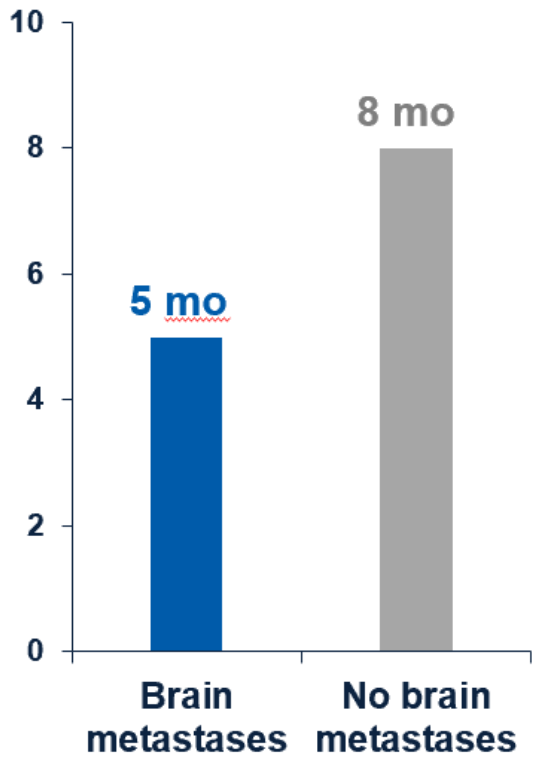
3-Year cancer-specific survival[2,a]



Median OS[2,a]

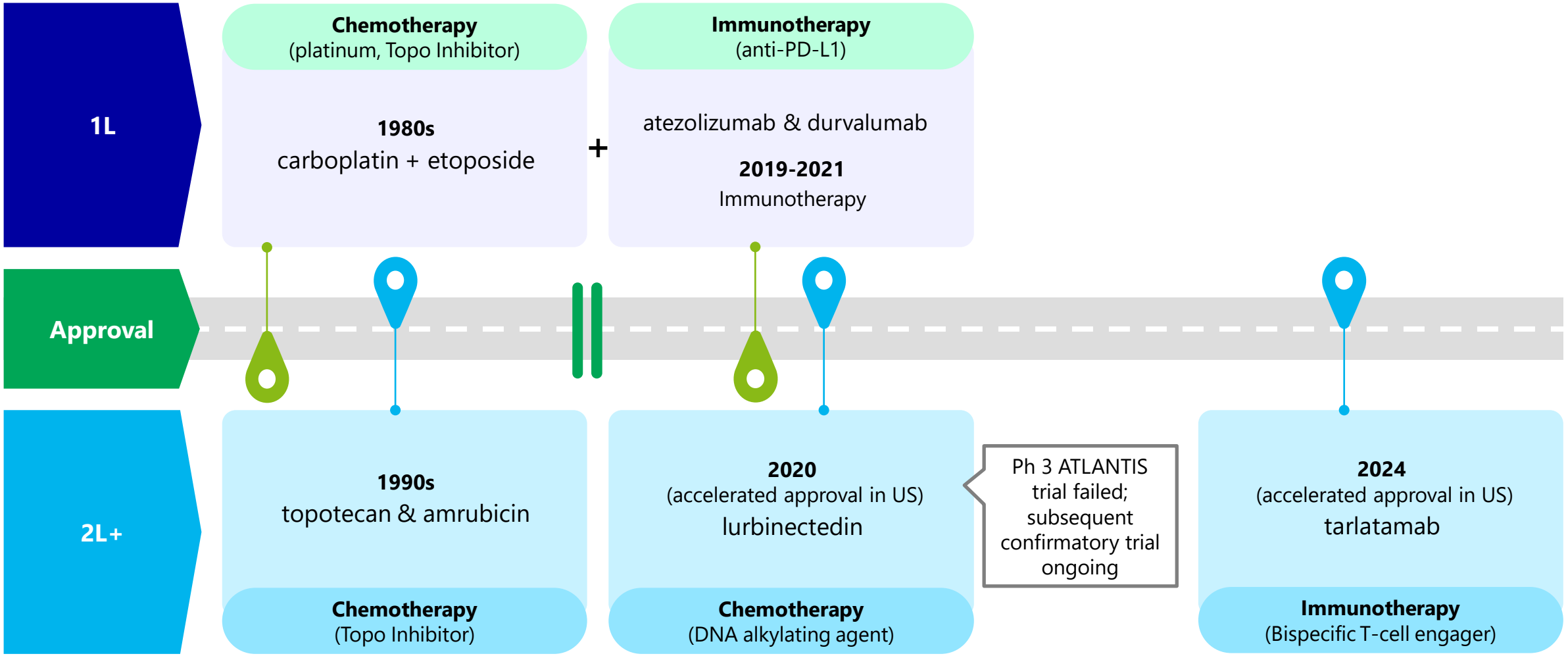


- Approximately 10–20% of patients with SCLC have brain metastases at diagnosis, with the incidence of brain metastases increasing to 80% after ~2 years[1–6]
- Patients with SCLC and brain metastases have poorer prognosis than those without brain metastases:[2]
  - 3-year survival rate is 3.0% vs 11.9%
  - Median OS is 5 vs 8 months
- Many systemic therapies have limited activity in the brain[7]
  - Although brain radiation therapy is effective in some patients, it can be associated with neurocognitive decline, and re-irradiation can be challenging due to the risk of neurotoxicity[8,9]

ES-SCLC: extensive-stage small cell lung cancer, OS: overall survival, SCLC, small cell lung cancer
[a]Among patients with SCLC and synchronous brain metastases at initial diagnosis (n=5711) or no brain metastases at initial diagnosis (n=27,458).
1. Rudin CM, et al. *Nat Rev Dis Primers*. 2021;7:3. 2. Zhou G, et al. *Cancer Med*. 2023;12:1195–1203. 3. Kromer C, et al. *J Neurooncol*. 2017;134:55–64. 4. Korfel A, et al. *Eur J Cancer*. 2002;38:1724-1729.
5. Lekic M, et al. *Radiol Oncol*. 2012;46:54–59. 6. Nugent JL, et al. *Cancer*. 1979;44:1885–1893. 7. Alvarez-Breckenridge C, et al. *Am Soc Clin Oncol Educ Book*. 2022;42:1–19.
8. Tang L, et al. *Front Oncol*. 2024;14:1382220. 9. Kepka L, et al. *J Thorac Dis*. 2021;13:3269–3278.

SCLC has had limited advancements in the past decades until recent approvals in 1L and 2L

As of Aug 2025



* Lurbinectedin and tarlatamab are approved for use in adult patients with disease progression on or after platinum-based chemotherapy; lurbinectedin approved in 17 territories worldwide & tarlatamab approved in US & conditional marketing authorization in JP as of July 2025

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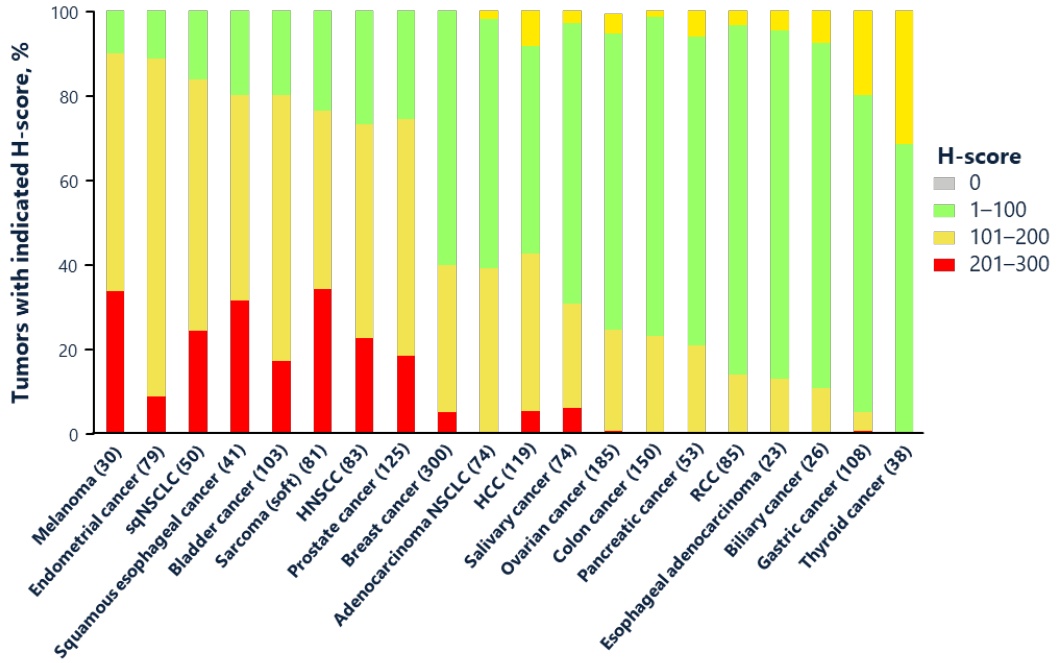
Why target B7-H3?

IHC analysis of B7-H3 expression on human tumor tissues[1,a]



B7-H3 is highly expressed in many solid tumors but is absent or expressed at low levels in normal tissues,[1–4] making it a potentially promising therapeutic target

HCC: hepatocellular carcinoma, HNSCC: head and neck squamous cell carcinoma, IHC, immunohistochemistry, NSCLC: non-small cell lung cancer, RCC: renal cell carcinoma, sqNSCLC, squamous non-small cell lung cancer.

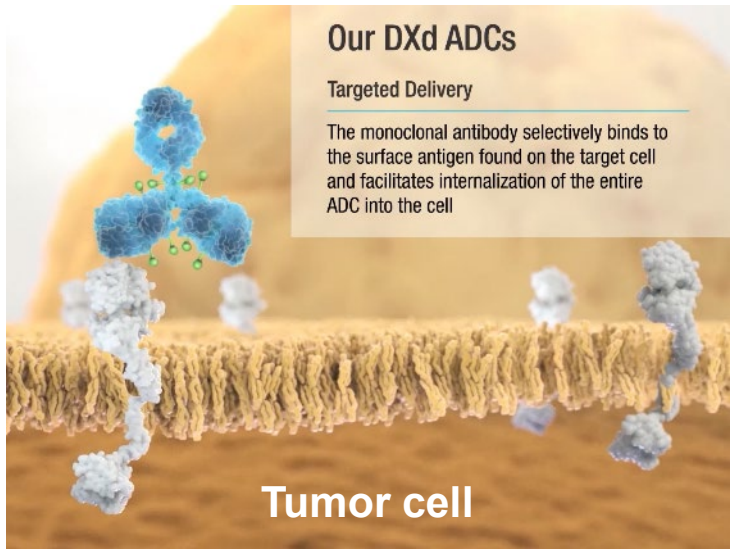
Yamato M, et al. *Mol Cancer Ther*. 2022;21:635–646. H-score was calculated using the HALO image analysis software (Indica Labs): H-score = (3× % tumor cells with strong membrane staining) + (2× % tumor cells with moderate membrane staining) + (1× % tumor cells with weak membrane staining). The H-score could range from 0 to 300.

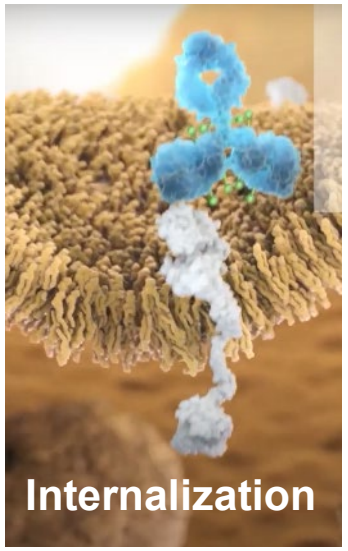
[a]Figures reproduced according to Creative Commons licence: http://creativecommons.org/licenses/by/4.0/.

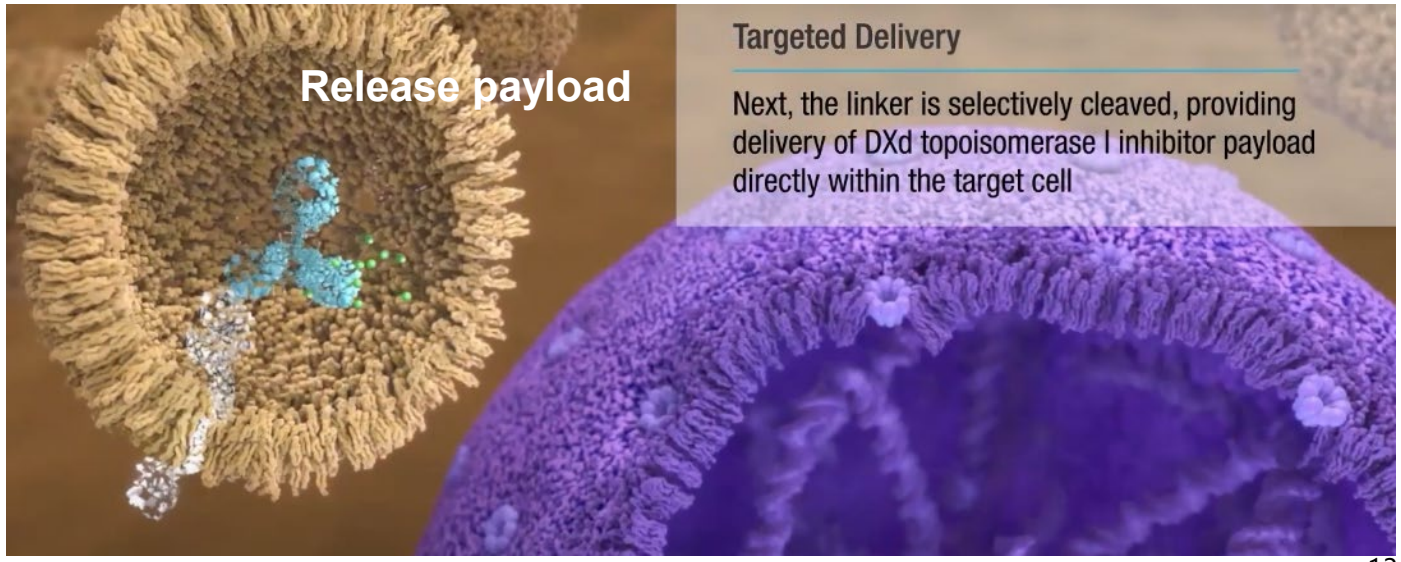
1. Yamato M, et al. *Mol Cancer Ther*. 2022;21:635–646. 2. Yang S, et al. *Int J Biol Sci*. 2020;16:1767–1773. 3. Dong P, et al. *Front Oncol*. 2018;8:264. 4. Wang L, et al. *Tumor Biol*. 2016;37:2961–2971.

I-DXd (B7-H3-directed ADC)

- I-DXd is an antibody-drug conjugate (ADC) utilizing Daiichi Sankyo's DXd technology.
  - ✓ Humanized B7-H3 antibody
  - ✓ Tetrapeptide cleavable linker
  - ✓ Potent Topoisomerase 1 inhibitor payload with bystander antitumor effect
- I-DXd can selectively bind to B7-H3, a protein overexpressed on the surface of tumor cells and not (or little) present on normal tissue.
- This high selectivity is achieved through the B7-H3-targeted antibody.







https://www.dxd-adc-technology.com/en

IDeate-PanTumor01 Study Design

Patients with advanced/ unresectable or metastatic solid tumors (unselected for B7-H3 expression) N≈205

Part 1: dose-escalation
- I-DXd IV q3w monotherapy for advanced solid tumors[a]

16.0 mg/kg
12.0 mg/kg
8.0 mg/kg
6.4 mg/kg
4.8 mg/kg
3.2 mg/kg
1.6 mg/kg
0.8 mg/kg

RDE

Part 2: dose-expansion (12.0 mg/kg)
- I-DXd IV q3w monotherapy for selected advanced solid tumors

Cohort 1: ESCC
(planned n≈40)

Cohort 2: mCRPC
(planned n=40)

Cohort 3: sqNSCLC
(planned n≈40)

Backfill Cohort: SCLC
(enrolled n=22)

Key primary endpoints

Dose escalation: Safety
Dose expansion: Efficacy: ORR, DOR, DCR, PFS, OS

Key secondary endpoints

PK
Immunogenicity

[a]Tumor types included advanced/unresectable or metastatic HNSCC, ESCC, mCRPC, sqNSCLC, SCLC, bladder cancer, sarcoma, endometrial cancer, melanoma, and breast cancer.

DCR: disease control rate, DOR: duration of response, ESCC: esophageal squamous cell carcinoma, IV: intravenous, mCRPC: metastatic castration-resistant prostate cancer, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, PK: pharmacokinetics, q3w: every 3 weeks, SCLC: small cell lung cancer, sqNSCLC: squamous non-small cell lung cancer

IDeate-PanTumor01 Efficacy Analysis Across Tumor

ESMO 2023

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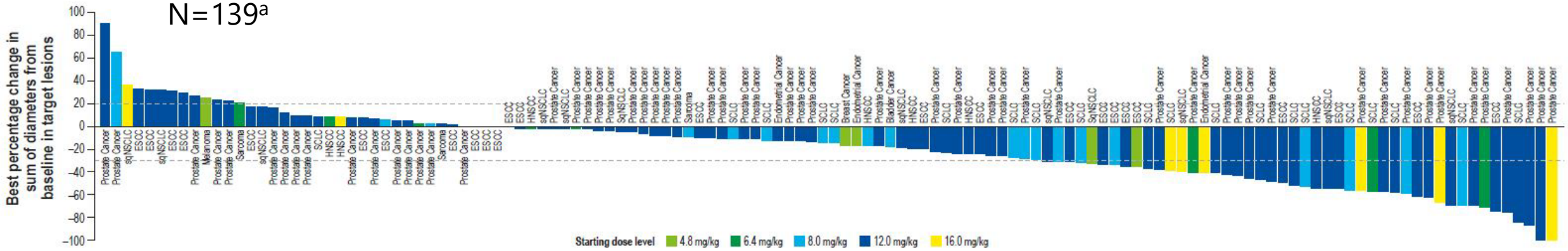
I-DXd showed anti-tumor efficacy across various tumor types, including SCLC, ESCC, HNSCC, mCRPC, and sqNSCLC



In the ≥4.8 mg/kg population, the confirmed ORR was 27.3% (38/139; 95% CI: 20.1%–35.5%)

[a]All 139 patients were evaluable at baseline but patients who did not have any post-baseline tumor assessments were not included in the waterfall plot.

CI: confidence interval, ESCC: esophageal squamous cell carcinoma, HNSCC: head and neck squamous cell carcinoma, mCRPC: metastatic castration-resistant prostate cancer, ORR: objective response rate, SCLC: small cell lung cancer, sqNSCLC: squamous non-small cell lung cancer

IDeate-PanTumor01 Efficacy Analysis: ESCC, mCRPC, sqNSCLC

ESMO 2023

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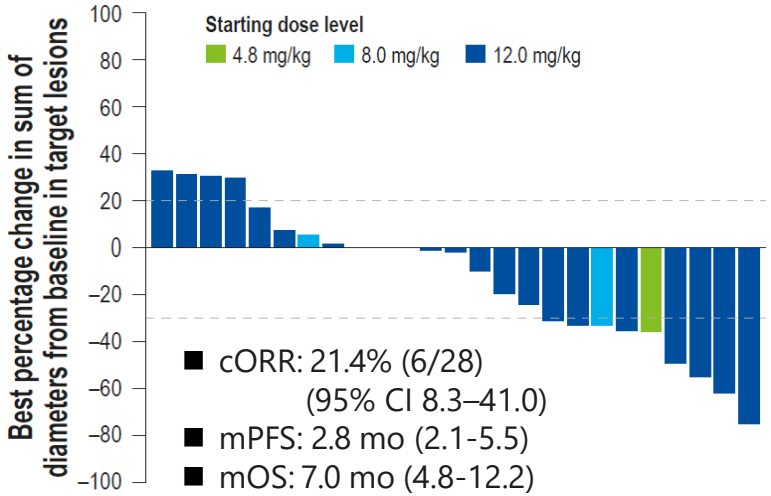
I-DXd continued to show durable efficacy in patients with heavily pretreated solid tumors, including ESCC, mCRPC, and sqNSCLC

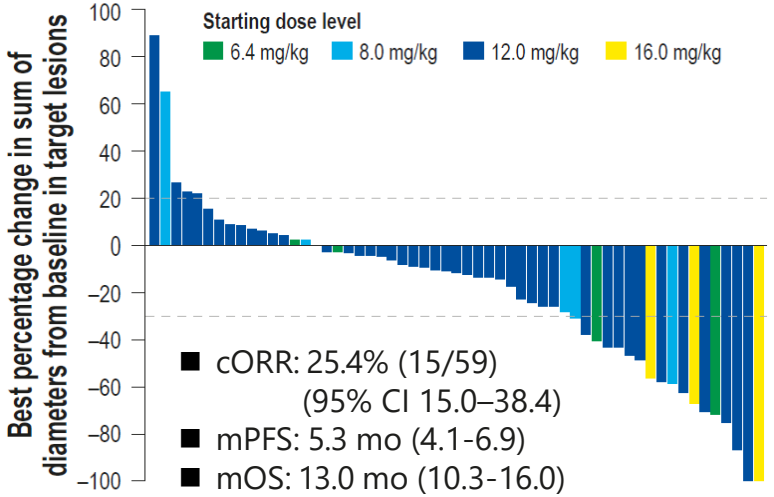
Efficacy in selected tumor types

ESCC



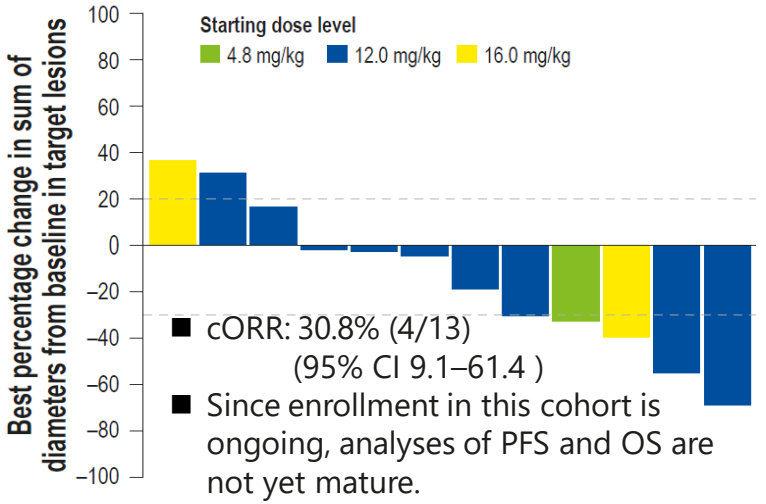
- cORR: 21.4% (6/28)
  (95% CI 8.3–41.0)
- mPFS: 2.8 mo (2.1-5.5)
- mOS: 7.0 mo (4.8-12.2)
- No. of prior treatments, median: 4 (1-7)

mCRPC*



- cORR: 25.4% (15/59)
  (95% CI 15.0–38.4)
- mPFS: 5.3 mo (4.1-6.9)
- mOS: 13.0 mo (10.3-16.0)
- No. of prior treatments, median: 6 (1-11)

sqNSCLC



- cORR: 30.8% (4/13)
  (95% CI 9.1–61.4)
- Since enrollment in this cohort is ongoing, analyses of PFS and OS are not yet mature.
- No. of prior treatments, median: 3 (1-12)

Data cutoff: Jan 2023

- Observed safety profile was manageable and tolerable
- No new safety signals were observed, and the safety profile was consistent with previous data. The most common (≥3%) Grade ≥3 TEAEs were anemia (19.0%), neutropenia (4.0%), and nausea and lymphocyte count decreased (3.4% each)
- Incidence of ILD was consistent with the previously observed data; 10 (5.7%) confirmed cases of adjudicated ILD were observed, of which two cases were Grade ≥3 (one grade 4 in 12 mg/kg cohort and one grade 5 in 16 mg/kg cohort)

* n=73, including patients with bone metastases who were not evaluable for ORR. The ORR is calculated based on 59 patients who received ≥1 dose ≥4.8 mg/kg, had measurable disease at baseline, ≥2 postbaseline scans, and/or discontinued treatment for any reason at data cutoff.

CI: confidence interval, cORR: confirmed objective response rate, ESCC: esophageal squamous cell carcinoma, ILD: interstitial lung disease, mCRPC: metastatic castration-resistant prostate cancer, mOS: median overall survival, mPFS: median progression-free survival, NE: not estimable, OS: overall survival, PFS: progression-free survival, SCLC: small cell lung cancer, sqNSCLC: squamous non-small cell lung cancer

IDeate-PanTumor01 Efficacy Analysis: SCLC

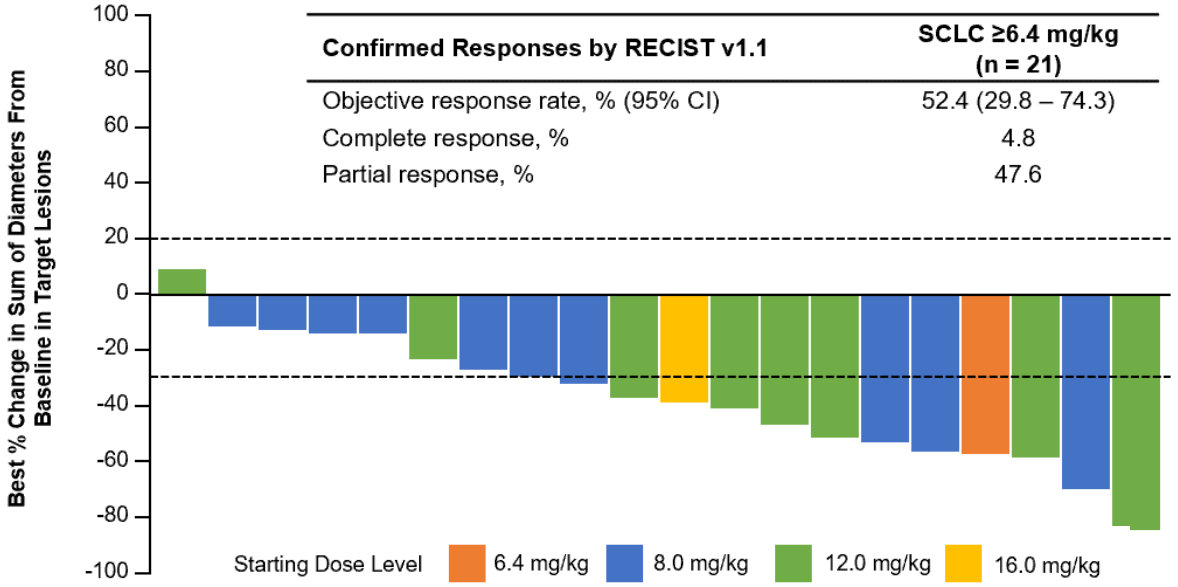
ESMO 2023

Daiichi-Sankyo

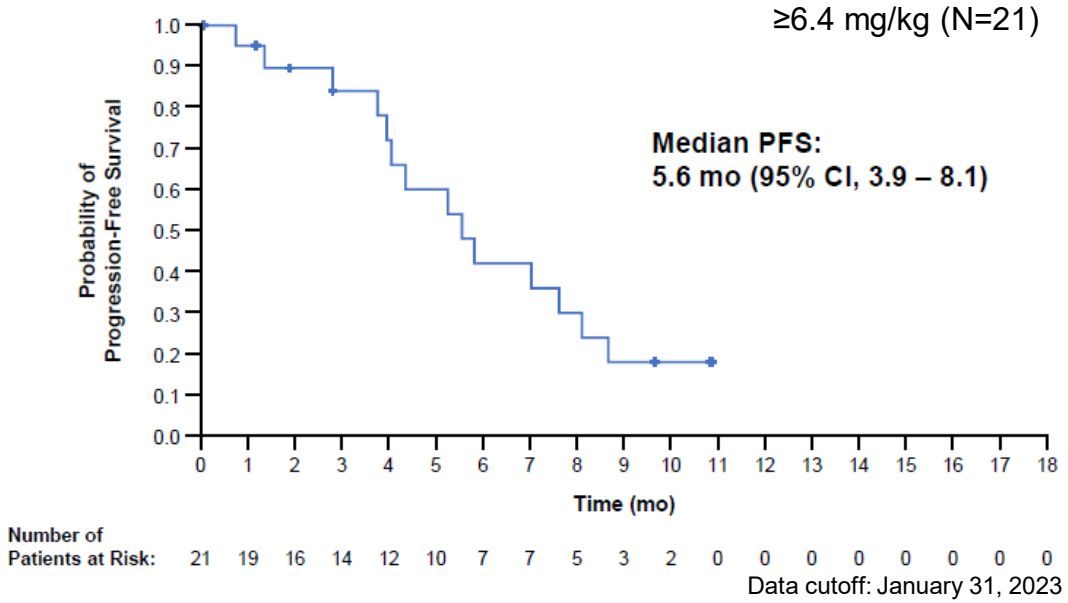
I-DXd, a novel B7-H3-directd DXd ADC, continues to demonstrate robust and durable efficacy in patients with heavily pretreated SCLC

ORR

Confirmed Responses by RECIST v1.1	SCLC ≥6.4 mg/kg (n = 21)
Objective response rate, % (95% CI)	52.4 (29.8 – 74.3)
Complete response, %	4.8
Partial response, %	47.6



PFS



Data cutoff: January 31, 2023

- Median number of prior systemic treatments: 2 (range: 1-7)
- ORR 52.4% (95% CI, 29.8-74.3), mDOR 5.9 mo (2.8-7.5), mPFS 5.6 mo (3.9-8.1), mOS 12.2 mo (6.4-NA)
- Generally well tolerated; no new safety signals and safety profile was consistent with previous reports
- Data support further development including a Ph2 of patients with extensive stage SCLC (IDeate-1)

ADC: antibody-drug conjugate, CI: confidence interval, RECIST: response evaluation criteria in solid tumors, mDOR: median duration od response, mo: months, mOS: median overall survival, mPFS: median progression free survival, ORR,: objective response rate, SCLC: small cell lung cancer

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Ifinatamab Deruxtecan (I-DXd) in Extensive-Stage Small Cell Lung Cancer: Primary Analysis of the Phase 2 IDeate-Lung01 Study

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

[1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [2]Sarah Cannon Research Institute, Nashville, TN, USA; [3]Hospital Universitario 12 de Octubre, Madrid, Spain; [4]The Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Tokyo, Japan; [5]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [6]Institut Curie, Paris, France; [7]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [8]Kindai University, Osaka, Japan; [9]National Cancer Center Hospital East, Kashiwa, Japan; [10]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea; [11]Merck & Co., Inc., Rahway, NJ, USA; [12]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [13]Daiichi Sankyo SAS, Paris, France; [14]Memorial Sloan Kettering Cancer Center, New York, NY, USA.

WCLC 2025 OA06.03. (Oral)

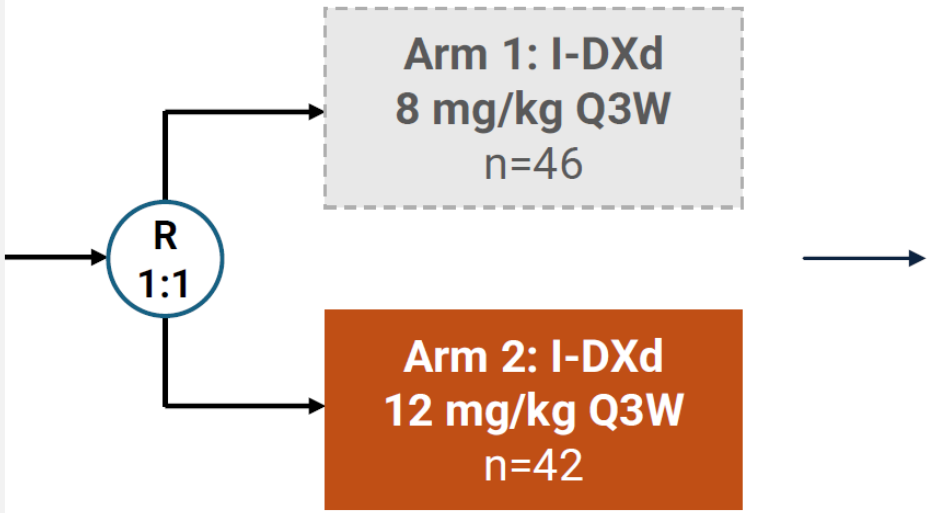
IDeate-Lung01 study design

Phase 2, multicenter, randomized, open-label study (NCT05280470)

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

Part 1: Dose optimization



Stratification factors:

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

Part 2: Extension

I-DXd 12 mg/kg Q3W
n=95

Primary endpoint

- ORR by BICR[c]

Secondary endpoints

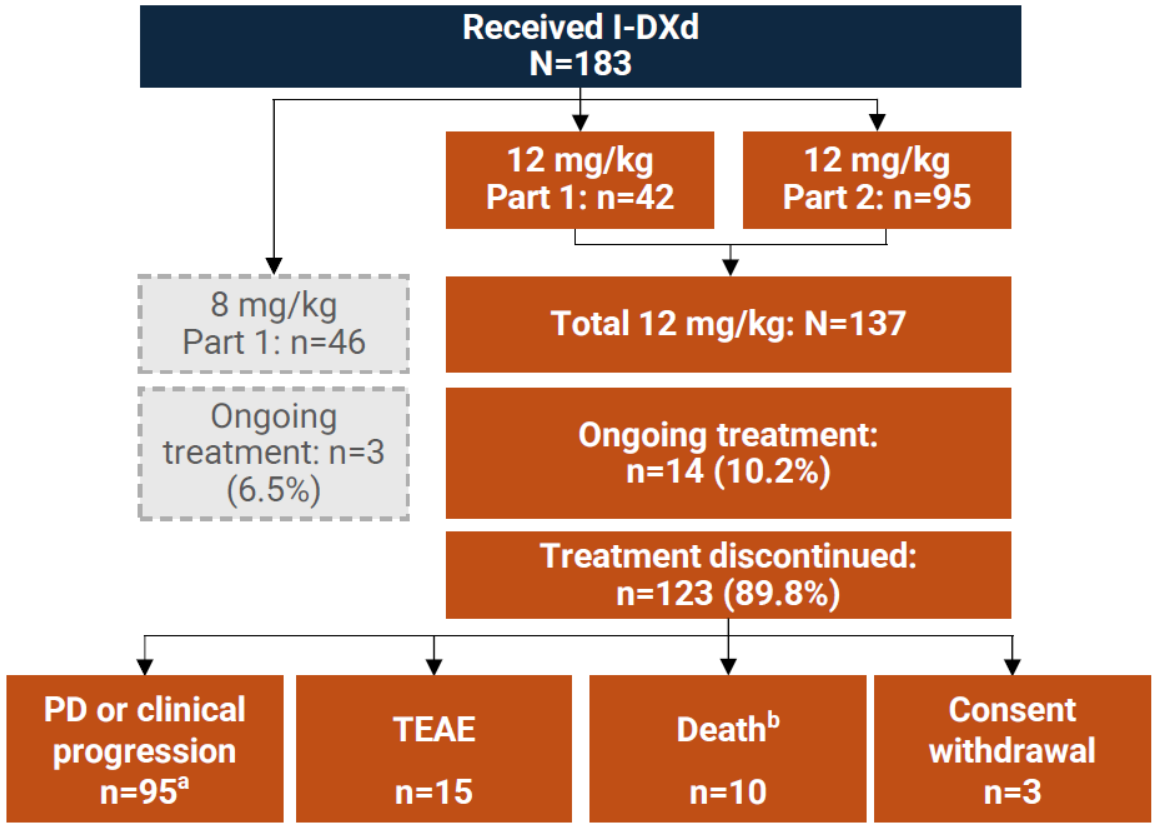
- DOR by BICR and inv[c]
- PFS by BICR and inv[c]
- OS
- DCR by BICR and inv[c]
- TTR by BICR and inv[c]
- ORR by inv[c]
- Safety
- Pharmacokinetics
- Immunogenicity

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..

Patient disposition and baseline characteristics



- Median treatment duration: total 12 mg/kg, 4.8 months (range, 0.7–22.7)
- Median follow-up: total 12 mg/kg, 12.8 months (95% CI, 12.2–13.1)[c]

Characteristic	Total I-DXd 12 mg/kg (N=137)
Age, median (range), years	63 (34–79)
Male, n (%)	90 (65.7)
Race, n (%)	
Asian / White / Other or multiple	67 (48.9) / 63 (46.0) / 7 (5.1)
Region, n (%)	
Asia / Europe / North America	66 (48.2) / 40 (29.2) / 31 (22.6)
ECOG PS 1, n (%)	106 (77.4)
ES-SCLC at diagnosis, n (%)	111 (81.0)
Brain / liver metastases at baseline,[d] n (%)	52 (38.0) / 55 (40.1)
CTFI, n (%)[e]	
≤30 days / >30 to <90 days / ≥90 days	18 (13.1) / 40 (29.2) / 72 (52.6)
Number of prior lines of systemic therapy, n (%)	
1 / 2 / 3	32 (23.4) / 75 (54.7) / 30 (21.9)
Select prior anticancer therapy, n (%)	
TOPO I inhibitor	44 (32.1)
Lurbinectedin	29 (21.2)
Amrubicin	12 (8.8)
DLL3-targeting TCE[f]	11 (8.0)
Prior anti–PD-(L)1 therapy, n (%)	111 (81.0)

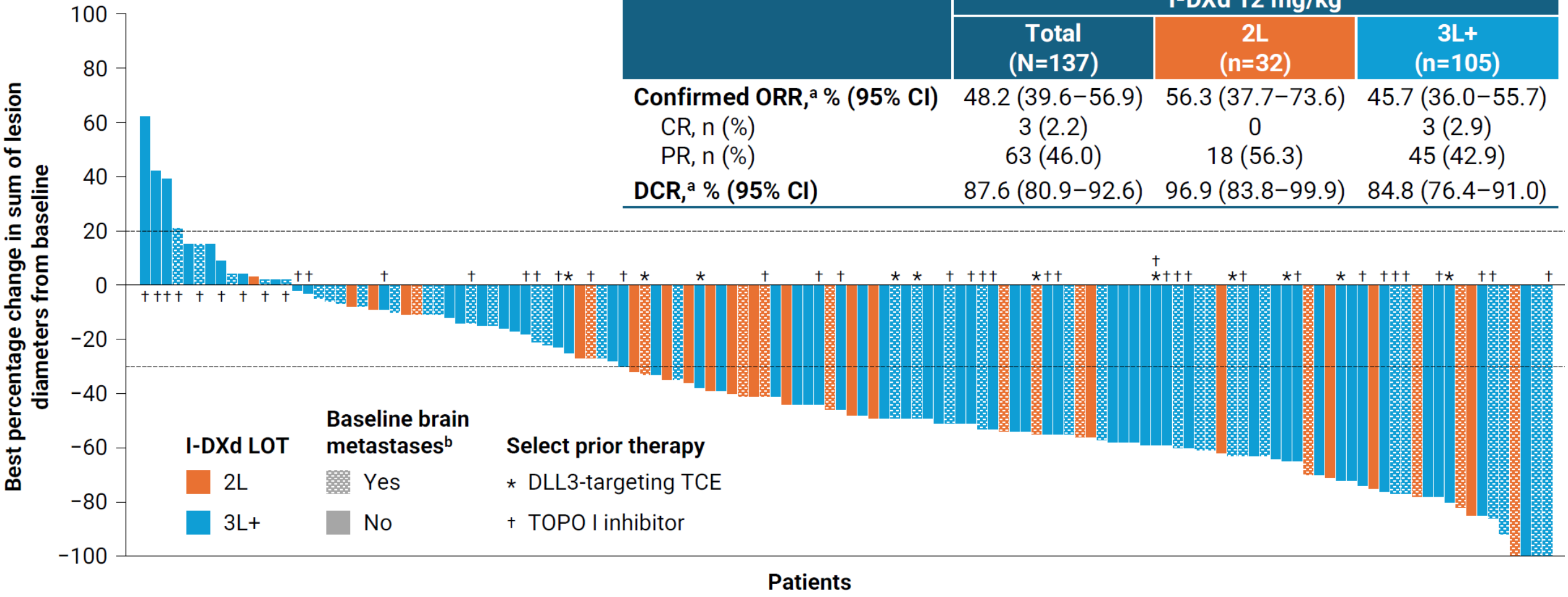
Data cutoff: March 3, 2025.

[a]Included 8 patients with clinical progression. [b]Death due to any reason, not limited to TEAEs associated with death. [c]Median (95% CI) follow-up in Part 1: 26.4 months (22.3–NE); median follow-up in Part 2: 12.2 months (11.3–12.5). [d]By BICR. [e]Seven (5.1%) patients had missing CTFI data (based on a 90-day cutoff). [f]Seven patients received prior tarlatamab.

BICR, blinded independent central review; CI, confidence interval; CTFI, chemotherapy-free interval; DLL3, delta-like ligand 3; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; NE, not estimable; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; TCE, T-cell engager; TEAE, treatment-emergent adverse event; TOPO I, topoisomerase I.

I-DXd 12 mg/kg demonstrated promising antitumor activity

	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)

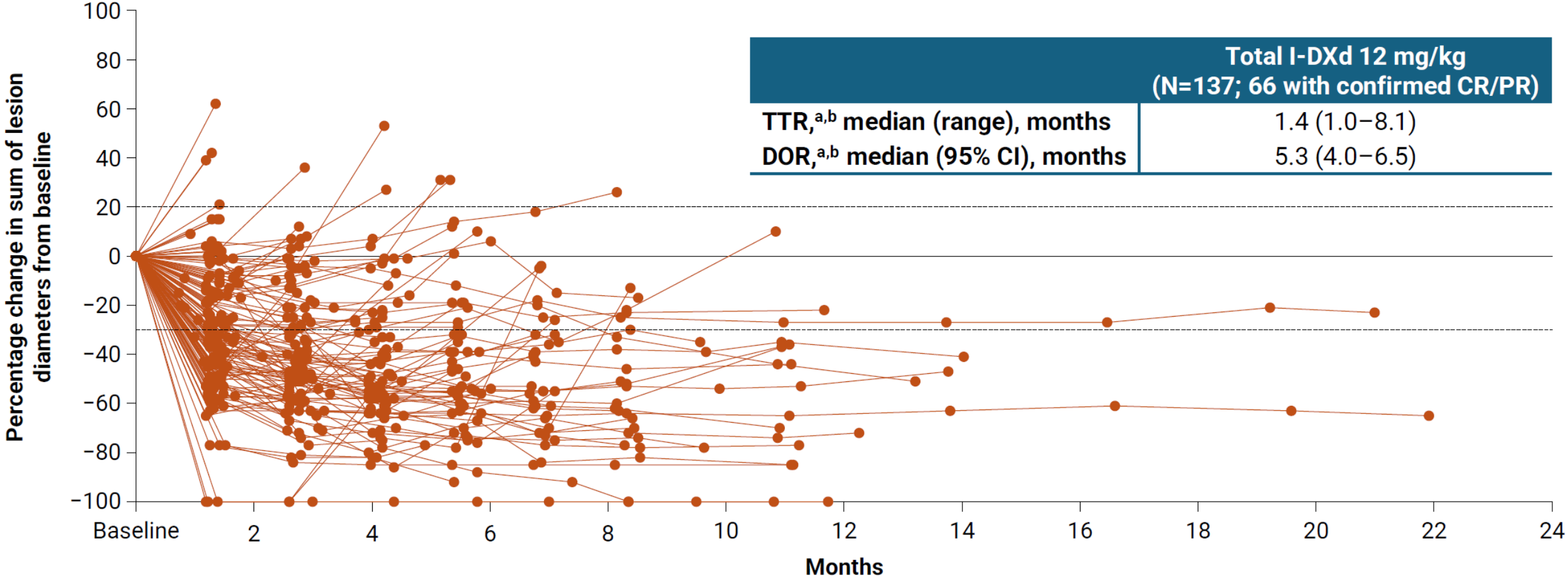


Data cutoff: March 3, 2025.

[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.

Responses with I-DXd 12 mg/kg were rapid and durable

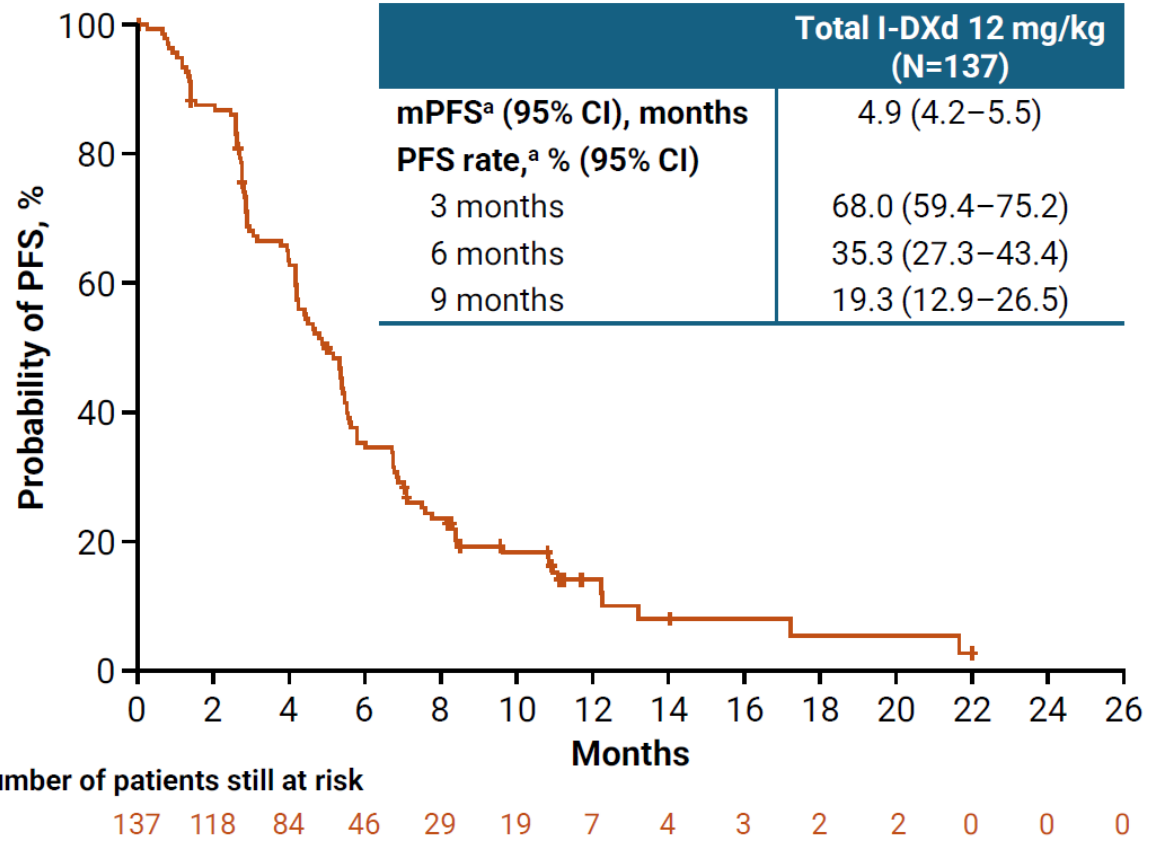


	Total I-DXd 12 mg/kg (N=137; 66 with confirmed CR/PR)
TTR,[a,b] median (range), months	1.4 (1.0–8.1)
DOR,[a,b] median (95% CI), months	5.3 (4.0–6.5)

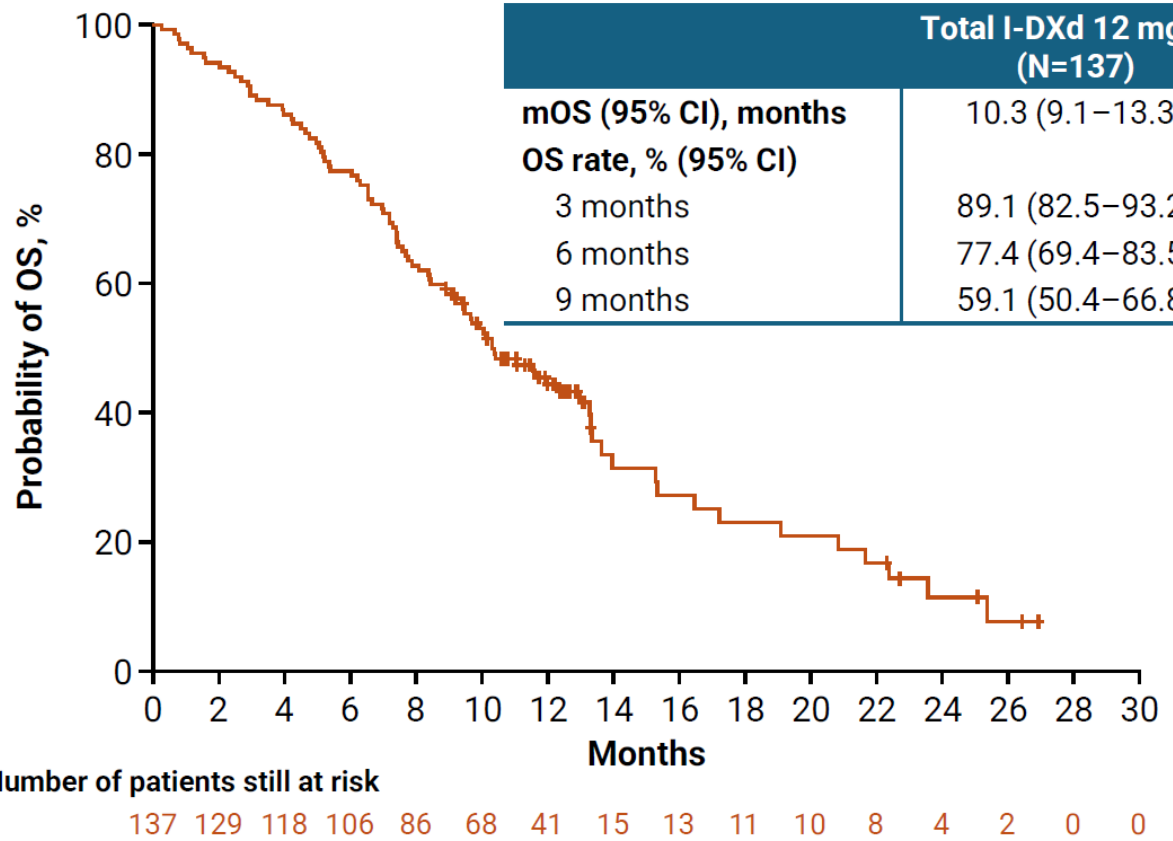
Among patients who received I-DXd 12 mg/kg as 2L therapy (n=32), median TTR was 1.4 months (range, 1.2–4.0) and median DOR was 7.2 months (95% CI, 3.6–NE)

Data cutoff: March 3, 2025.
Tumor assessments were performed every 6 weeks (±7 days) in the first 36 weeks and every 12 weeks (±7 days) thereafter, until disease progression, death, loss to follow-up, or withdrawal of consent, whichever occurred first.
[a]Assessed by BICR per RECIST 1.1. [b]Patients with confirmed objective response.
2L, second-line; BICR, blinded independent central review; CI, confidence interval; CR, complete response; DOR, duration of response; NE, not estimable; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; TTR, time to response.

mPFS was 4.9 months and mOS was 10.3 months with I-DXd 12 mg/kg



	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)



	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)

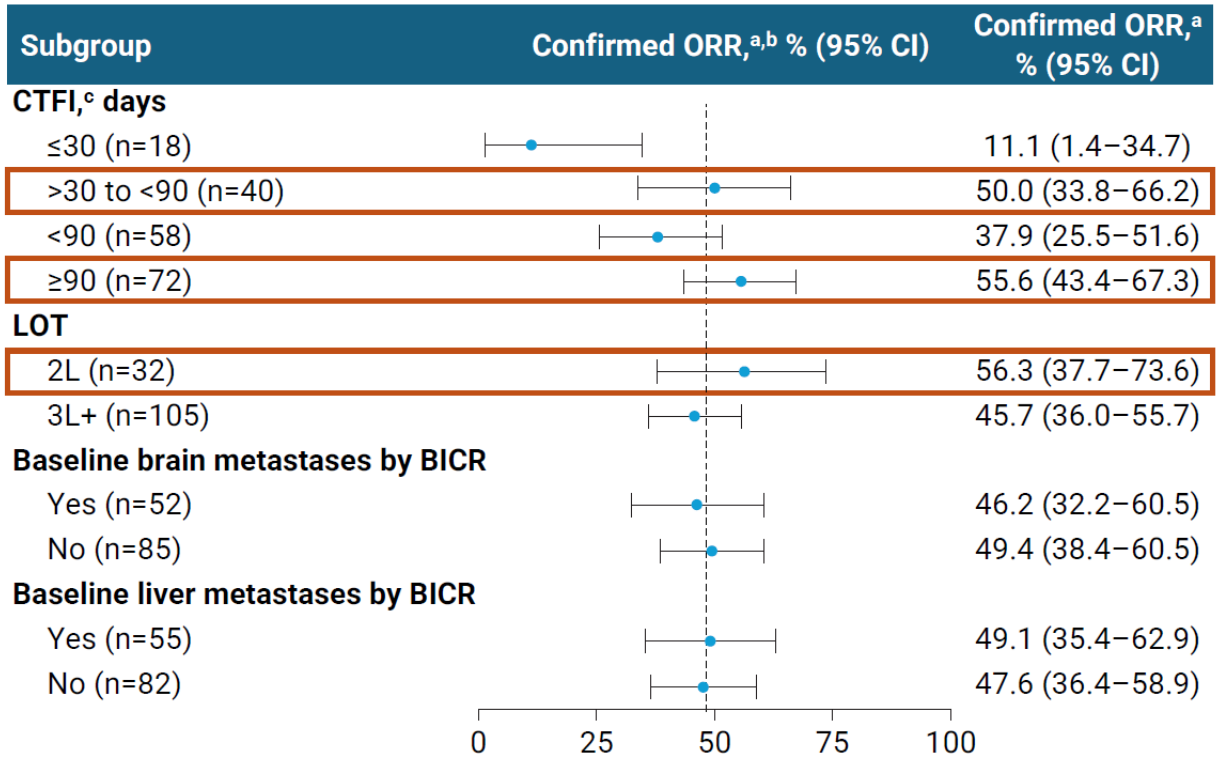
Among patients who received I-DXd 12 mg/kg as 2L therapy (n=32), mPFS was 5.6 months (95% CI, 3.9–8.1) and mOS was 12.0 months (95% CI, 7.3–19.1)

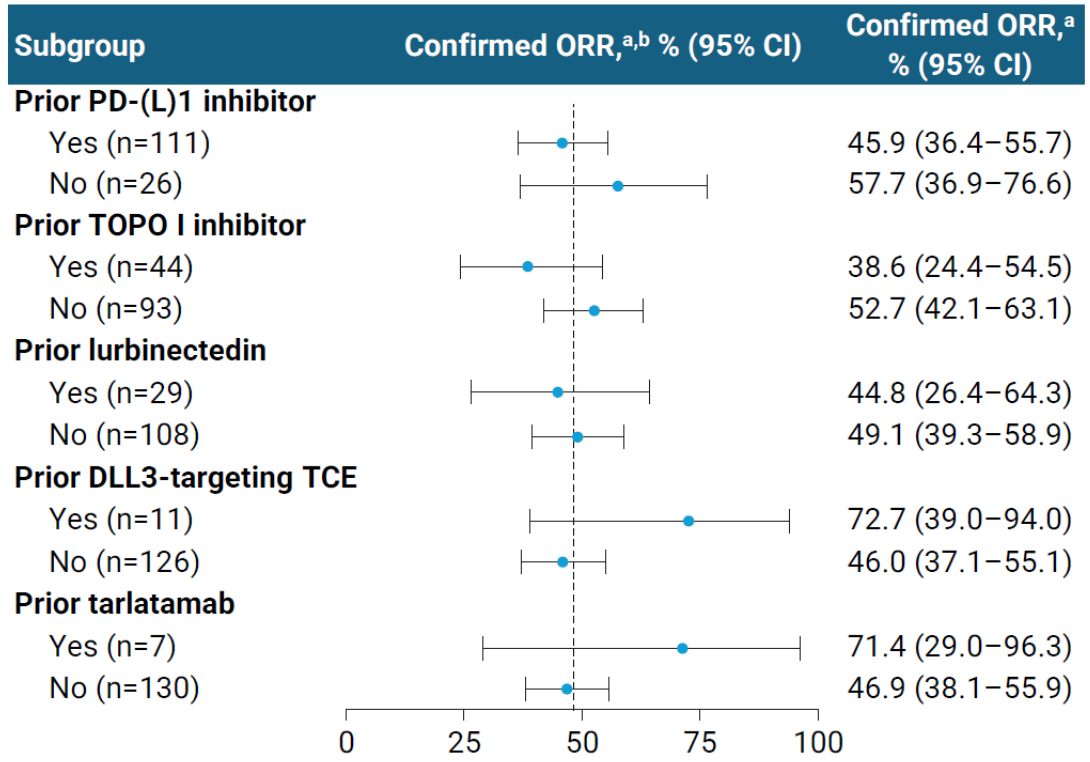
Data cutoff: March 3, 2025.

[a]Assessed by BICR per RECIST 1.1.

2L, second-line; BICR, blinded independent central review; CI, confidence interval; (m)OS, (median) overall survival; (m)PFS, (median) progression-free survival; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1

I-DXd demonstrated clinically meaningful benefit across subgroups of the total 12 mg/kg group





- The total 12-mg/kg population included 18 (13.1%) patients with CTFI ≤30 days; as expected, confirmed ORR was low in this population
- In 65 patients with baseline brain metastases identified using CNS BICR, CNS confirmed ORR was 46.2% (95% CI, 33.7–59.0)[d]

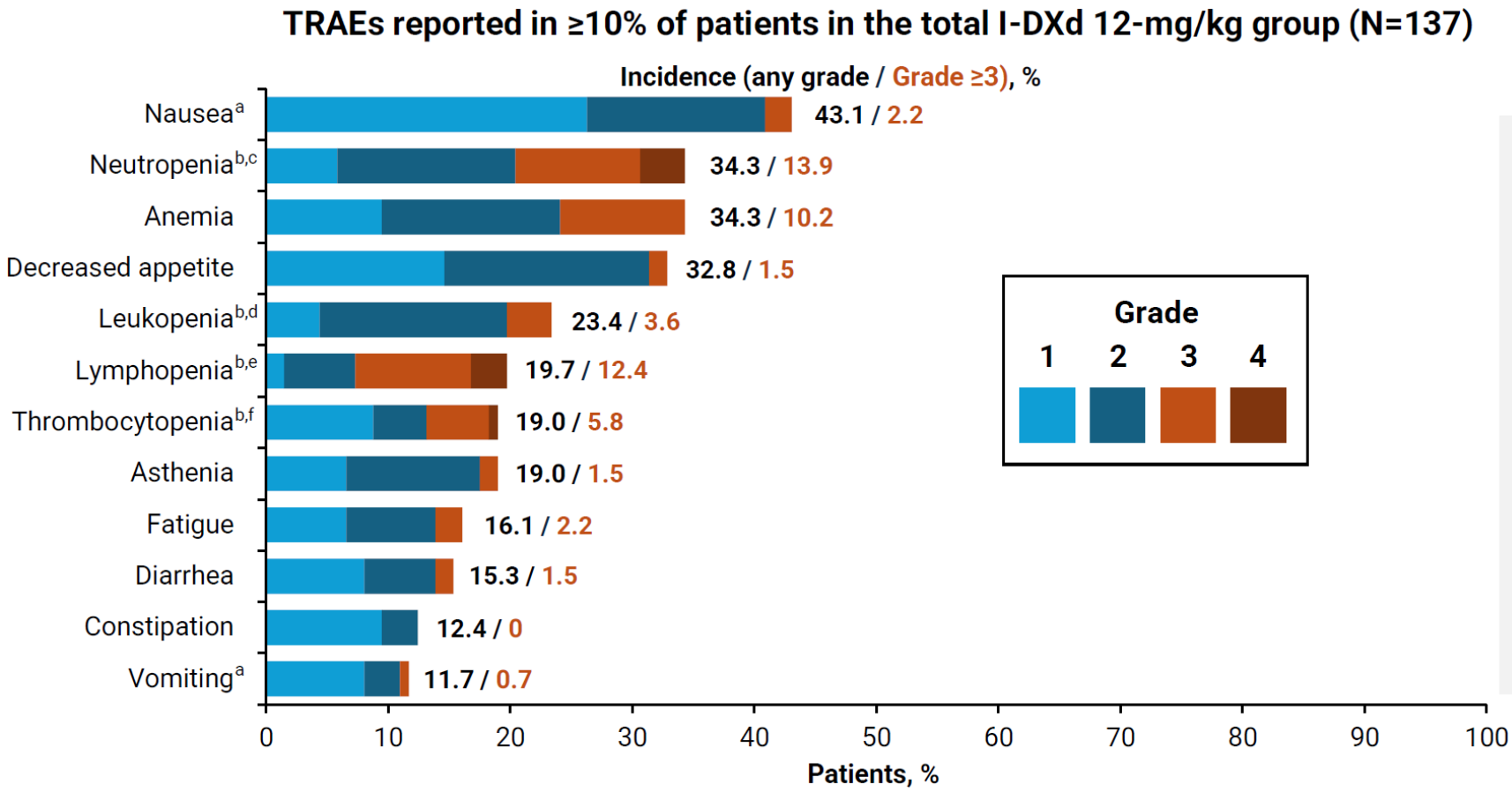
Data cutoff: March 3, 2025.
Median (95% CI) DOR,[a] months: CTFI ≤30 days, NE (NE–NE); **CTFI >30 to <90 days,** 3.7 (3.1–4.2); **CTFI <90 days,** 3.8 (3.1–4.4); **CTFI ≥90 days,** 6.5 (4.1–9.7); **2L,** 7.2 (3.6–NE); **3L+,** 4.3 (3.7–5.8); **baseline brain metastases by BICR "yes,"** 4.8 (3.0–8.3); **baseline brain metastases by BICR "no,"** 5.3 (4.1–7.0); **baseline liver metastases by BICR "yes,"** 5.3 (3.9–7.2); **baseline liver metastases by BICR "no,"** 4.9 (3.5–6.4); **prior PD-(L)1 inhibitor "yes,"** 4.5 (3.6–5.8); **prior PD-(L)1 inhibitor "no,"** 8.3 (3.9–NE); **prior TOPO I inhibitor "yes,"** 4.1 (3.0–9.8); **prior TOPO I inhibitor "no,"** 5.5 (3.9–6.5); **prior lurbinectedin "yes,"** 4.0 (2.6–5.5); **prior lurbinectedin "no,"** 5.8 (4.1–7.2); **prior DLL3-targeting TCE "yes,"** 5.1 (2.8–NE); **prior DLL3-targeting TCE "no,"** 5.3 (4.0–6.5); **prior tarlatamab "yes,"** 5.6 (2.8–NE); **prior tarlatamab "no,"** 5.1 (3.9–6.5).
[a]Assessed by BICR per RECIST 1.1. [b]Confirmed ORR for total I-DXd 12 mg/kg (N=137) was 48.2% (95% CI, 39.6–56.9) and is represented by the vertical dashed line. [c]Seven patients had missing CTFI data (based on a 90-day cutoff).
[d]Assessed using a version of RECIST 1.1 modified for assessment of CNS tumors.
2L, second-line; 3L+, third-line and beyond; BICR, blinded independent central review; CI, confidence interval; CNS, central nervous system; CTFI, chemotherapy-free interval; DLL3, delta-like ligand 3; DOR, duration of response; LOT, line of therapy; NE, not estimable; ORR, objective response rate; PD-(L)1, programmed death (ligand) 1; RECIST (1.1), Response Evaluation Criteria in Solid Tumours (version 1.1); TCE, T-cell engager; TOPO I, topoisomerase I.I.

The safety profile of I-DXd 12 mg/kg was manageable

	Total I-DXd 12 mg/kg (N=137)
Median treatment duration,[a] months (range)	4.8 (0.7–22.7)
Median cycles, n (range)	7.0 (1.0–32.0)
Any-grade TRAEs, n (%)	123 (89.8)
Grade ≥3	50 (36.5)
Associated with dose delay	35 (25.5)
Associated with dose reduction	21 (15.3)
Associated with treatment discontinuation[b]	13 (9.5)
Associated with death[c]	6 (4.4)

Data cutoff: March 3, 2025.
[a]Treatment duration (months) is calculated as (date of the last dose − date of the first dose + 21 days) × 12 ÷ 365.25. For patients who were still on treatment at data cutoff, the last available date of dose prior to data cutoff was used. [b]Grade 1: pneumonitis (n=1); Grade 2: ILD (n=3), pneumonitis (n=2), radiation pneumonitis (n=1), and fatigue (n=1); Grade 3: ILD (n=2), *Pneumocystis jirovecii* pneumonia (n=2), and nausea (n=1). [c]ILD/pneumonitis (n=3); *Pneumocystis jirovecii* pneumonia (n=2); pulmonary sepsis (n=1). Of the 3 treatment-related ILD/pneumonitis events associated with death per investigator, only 1 was subsequently adjudicated as treatment related by the ILD adjudication committee.
ILD, interstitial lung disease; TRAE, treatment-related adverse event.

The most common TRAEs were hematologic or gastrointestinal in nature, and fatigue



- 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.

Conclusions

- I-DXd 12 mg/kg demonstrated remarkable efficacy in patients with previously treated ES-SCLC, particularly given the inclusion of populations often excluded from clinical trials
  - 18/137 with CTFI ≤30 days; 52/137 with asymptomatic untreated or previously treated brain metastases[a]
- Confirmed ORR was 48.2%, median DOR was 5.3 months, median PFS was 4.9 months, and median OS was 10.3 months
- Clinically meaningful benefit was observed regardless of platinum sensitivity or LOT, with confirmed ORRs of:
  - 55.6% (CTFI ≥90 days) and 50.0% (CTFI >30 to <90 days)
  - 56.3% (2L) and 45.7% (3L+)
- Meaningful intracranial efficacy was observed; a full subgroup analysis of patients with baseline brain metastases will be presented at ESMO 2025 (Abstract 2760MO) The safety profile of I-DXd 12 mg/kg was manageable and consistent with previous reports[1–3]
- The ongoing global Phase 3 IDeate-Lung02 trial (NCT06203210) is comparing I-DXd 12 mg/kg vs treatment of physician's choice (topotecan, amrubicin, or lurbinectedin) in patients with relapsed SCLC with only 1 prior line of systemic treatment, which must have included PBC

Data cutoff: March 3, 2025.

[a]By BICR.

2L, second-line; 3L+, third-line and beyond; BICR, blinded independent central review; CTFI, chemotherapy-free interval; DOR, duration of response; (ES)-SCLC, (extensive-stage) small cell lung cancer; LOT, line of therapy; ORR, objective response rate; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression-free survival.

1. Johnson M, et al. Oral presentation at the 2023 IASLC World Conference on Lung Cancer. September 9–12, 2023; Singapore. Presentation OA05.05. 2. Patel MR, et al. Poster presentation at the European Society for Medical Oncology Congress 2023.

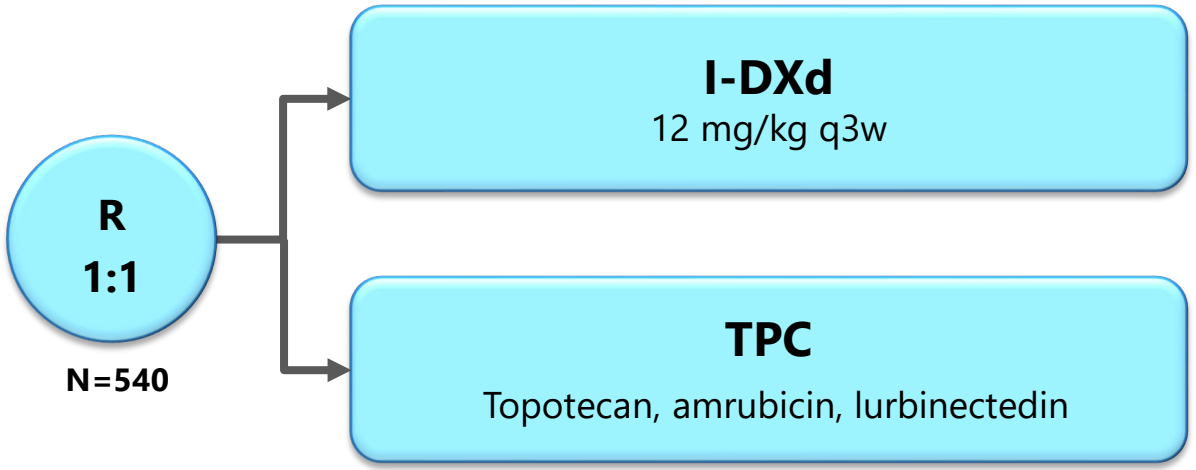
IDeate-Lung02 study

Ph3 study to evaluate I-DXd monotherapy for SCLC 2L

IDeate-Lung02 Study Design

Eligible Patients

- Relapsed SCLC
- ECOG PS 0 to 1
- Prior treatment with one-platinum based line

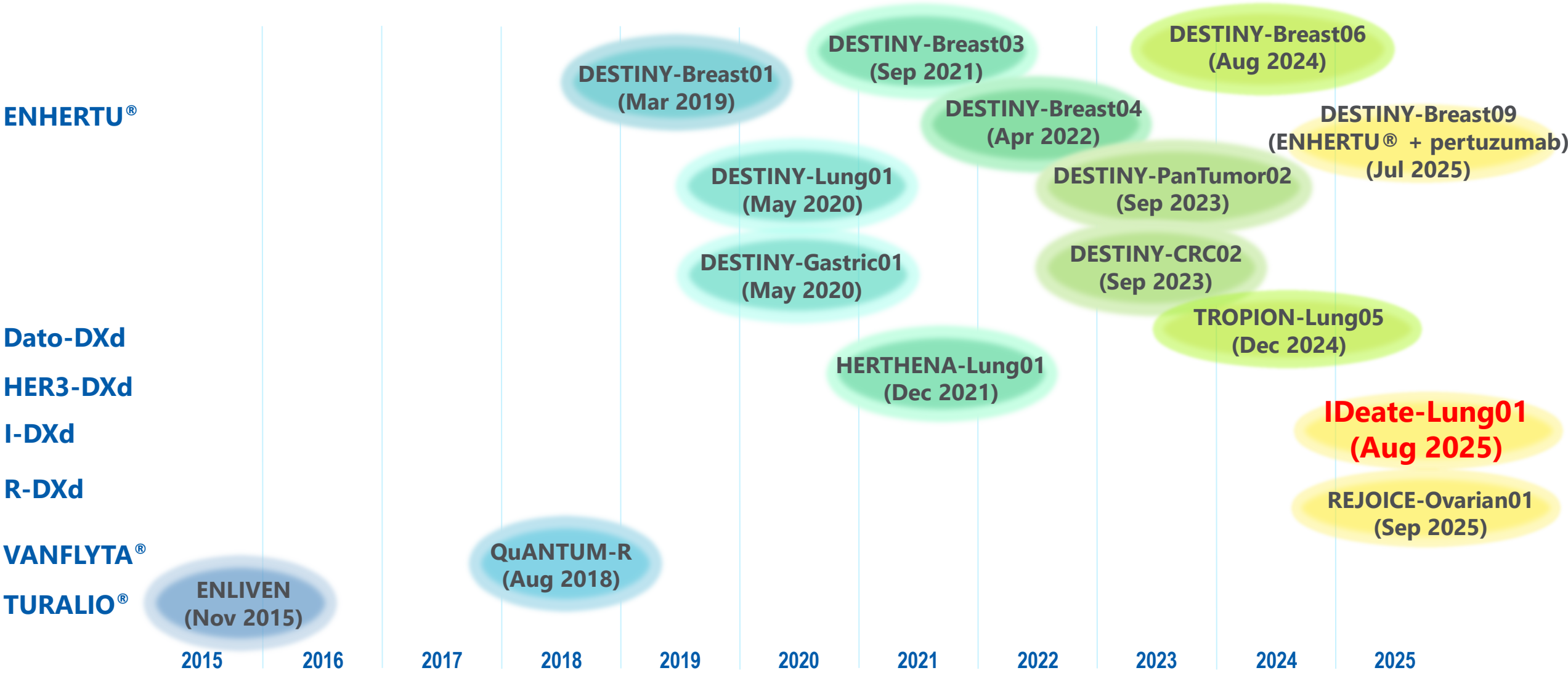


Primary Endpoint: ORR by BICR, OS
Secondary Endpoint: ORR by investigator, PFS, DOR, DCR, TTR, safety, etc.

- FPD is achieved in Aug 2024
- Estimated enrolment is updated to 540 from 468 in Nov 2024

BICR: blinded independent central review, DCR: disease control rate, DOR: duration of response, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, q3w: every 3 weeks, SCLC: small cell lung cancer, TPC: treatment of physician's choice, TTR: time to response

15 Breakthrough Therapy Designations



Agenda

1. SCLC overview

2. **I-DXd program overview**
   - I-DXd scientific profile
   - IDeate-Lung01 WCLC presentation
   - **I-DXd clinical development plan**

3. Other program updates from WCLC 2025

4. Q&A

I-DXd will support transformative outcomes for patients across a broad range of tumors, beginning in SCLC

VISION
Redefine the treatment paradigm for a broad range of patients with solid tumors through our innovative B7-H3 directed ADC

Rapidly enter SCLC as the anchor indication

2L+ SCLC Focus
Near-Term

Expand to ESCC, mCRPC, & 1L SCLC

ESCC & mCRPC & 1L SCLC
Mid-Term

Ph3 in ESCC and mCRPC have been initiated

Extend to earlier lines and other solid tumors

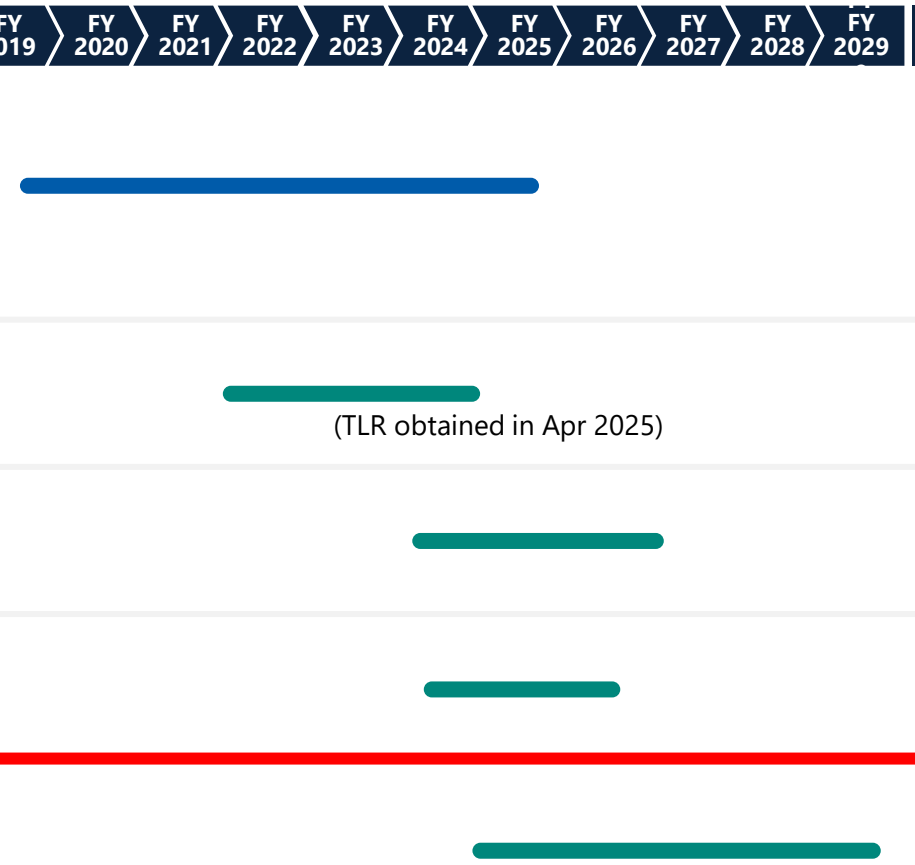
Across Solid Tumors
Long-Term

ADC: antibody-drug conjugate, ESCC: esophageal squamous cell carcinoma, mCRPC: metastatic castration-resistant prostate cancer, SCLC: small cell lung cancer

Ongoing I-DXd clinical trials: FIH and SCLC

As of Aug 2025

	Study	Phase	Patients / Design	Primary endpoint
FIH	**IDeate-PanTumor01** NCT04145622	**Ph1/2**	Single-agent I-DXd , **recurrent or metastatic solid tumors** (HNSCC, ESCC, NSCLC, SCLC, bladder cancer, sarcoma, EC, melanoma, prostate cancer, breast cancer, or mCRPC)	**Safety and tolerability, antitumor effect**
SCLC	**IDeate-Lung01** NCT05280470	**Ph2**	Single-agent I-DXd , **3L+ ES-SCLC** in extension part	**ORR by BICR**
	IDeate-Lung02 NCT06203210	**Ph3**	I-DXd vs TPC[a], **2L relapsed SCLC**	**ORR by BICR, OS**
	IDeate-Lung03 NCT06362252	**Ph1b/2**	I-DXd in combination with atezolizumab ± carboplatin, **1L ES-SCLC**	**Safety**
	MK-6070-002 NCT06780137	**Ph1/2**	Gocatamig (MK-6070; DS3280) and I-DXd in combination and as monotherapy, **2L+ SCLC**	**Safety and tolerability, ORR**



a Topotecan, amrubicin, or lurbinectedin

I-DXd trials current as of Aug 2025 posted on ClinicalTrials.gov. The displayed timeline shows the period from "study start date" to "primary completion date" as published

BICR: blinded independent central review, EC: endometrial cancer, ESCC: esophageal squamous cell carcinoma; ES-SCLC: extensive-stage small cell lung cancer, FIH: first in human, HNSCC: head and neck squamous cell carcinoma,, mCRPC: metastatic castration-resistant prostate cancer, NSCLC: non-small cell lung cancer, ORR: objective response rate, OS: overall survival, SCLC: small cell lung cancer, TPC: treatment of physician's choice

Ongoing I-DXd clinical trials: NSCLC and mCRPC

As of Aug 2025

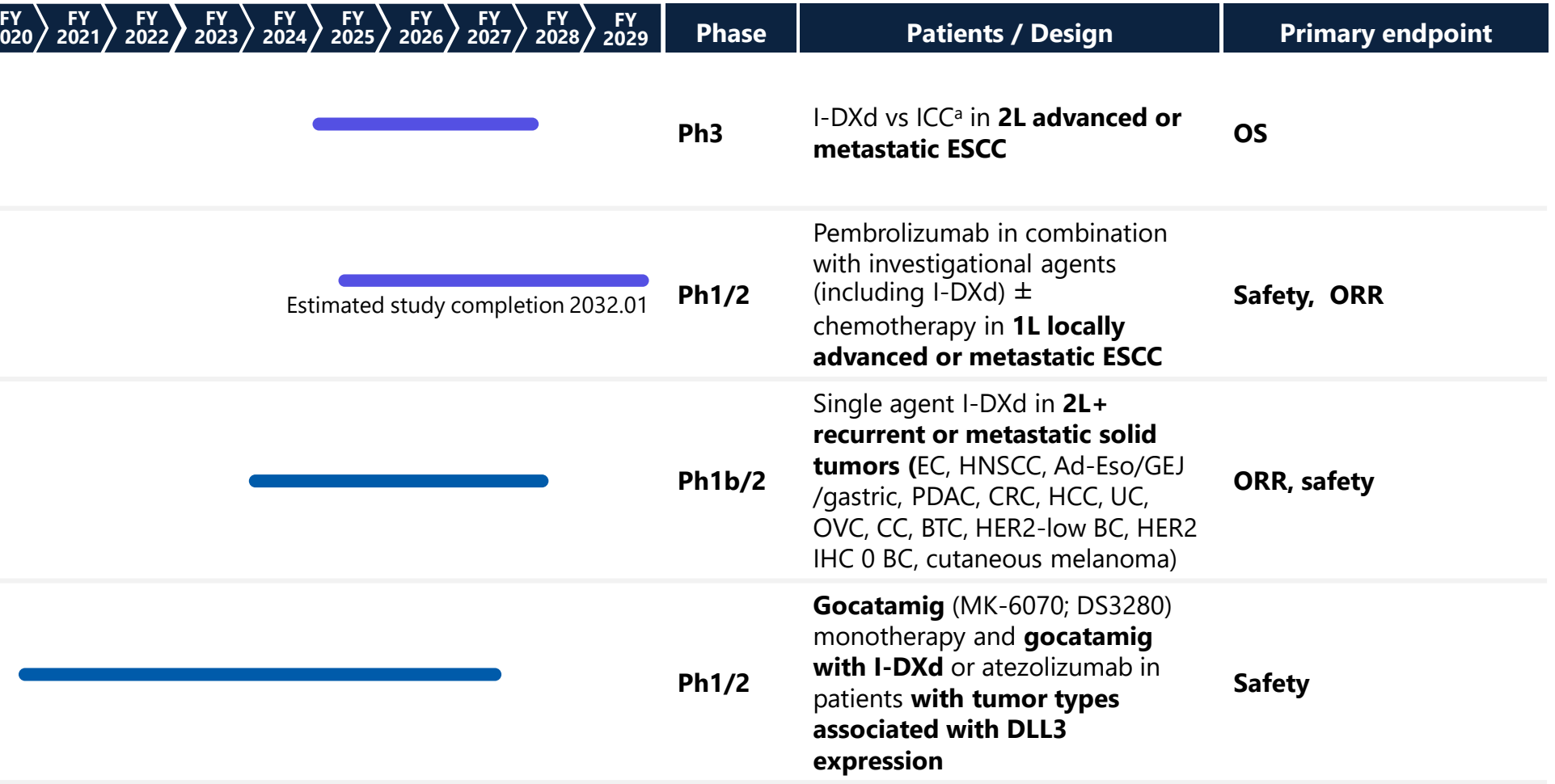
	Study	FY 2019 – FY 2029	Phase	Patients / Design	Primary endpoint
NSCLC	**KEYMAKER-U01A** NCT04165070	Estimated primary completion 2032.02	**Ph1/2**	Pembrolizumab ± chemotherapy with I-DXd or other agents[a], **treatment-naive NSCLC**	**Safety and tolerability** (for I-DXd combination arm)
NSCLC	**KEYMAKER-U01H** NCT06780085	Estimated primary completion 2032.03	**Ph2**	Single-agent I-DXd or R-DXd vs docetaxel, **2L non-squamous NSCLC**	**ORR, safety**
NSCLC	**KEYMAKER-U01I** NCT06780098	Estimated primary completion 2032.03	**Ph2**	Single-agent I-DXd (8 mg/kg or 12 mg/kg) or R-DXd vs docetaxel, **2L squamous NSCLC**	**ORR, safety**
mCRPC	**IDeate-Prostate01** NCT06925737		**Ph3**	Single-agent I-DXd vs docetaxel, **mCRPC**	**OS, rPFS**
mCRPC	**IDeate-Prostate02** NCT06863272	Estimated primary completion 2030.02	**Ph1/2**	Single-agent I-DXd, or I-DXd + opevesostat (MK-5684) or ARPI (abiraterone or enzalutamide) vs docetaxel, **mCRPC**	**Safety and tolerability** (safety lead-in phase) **PSA response rate** (efficacy phase)

a For full details of other agents included in the trial, please refer to ClinicalTrials.gov.
I-DXd trials current as of Aug 2025 posted on ClinicalTrials.gov. The displayed timeline shows the period from "study start date" to "primary completion date" as published
ARPI: androgen receptor pathway inhibitor(s), mCRPC: metastatic castration-resistant prostate cancer, NSCLC: non-small cell lung cancer, ORR: objective response rate, OS: overall survival, fPFS: radiographic progression-free survival, PSA: prostate psecific antigen

Ongoing I-DXd clinical trials: ESCC and advanced solid tumors

As of Aug 2025

	Study	Phase	Patients / Design	Primary endpoint
ESCC	**IDeate-Esophageal01** NCT06644781	**Ph3**	I-DXd vs ICC[a] in **2L advanced or metastatic ESCC**	**OS**
ESCC	**KEYMAKER-U06** NCT06780111	**Ph1/2**	Pembrolizumab in combination with investigational agents (including I-DXd) ± chemotherapy in **1L locally advanced or metastatic ESCC**	**Safety, ORR**
Advanced solid tumors	**IDeate-PanTumor02** NCT06330064	**Ph1b/2**	Single agent I-DXd in **2L+ recurrent or metastatic solid tumors (**EC, HNSCC, Ad-Eso/GEJ /gastric, PDAC, CRC, HCC, UC, OVC, CC, BTC, HER2-low BC, HER2 IHC 0 BC, cutaneous melanoma)	**ORR, safety**
Advanced solid tumors	**MK-6070-001** NCT04471727	**Ph1/2**	**Gocatamig** (MK-6070; DS3280) monotherapy and **gocatamig with I-DXd** or atezolizumab in patients **with tumor types associated with DLL3 expression**	**Safety**



[a]Paclitaxel, docetaxel, irinotecan.

I-DXd trials current as of Aug 2025 posted on ClinicalTrials.gov. The displayed timeline shows the period from "study start date" to "primary completion date" as published

Ad-Eso: adenocarcinoma of the esophagus, BTC: biliary tract cancer, CC: cervical cancer, CRC: colorectal cancer, EC: endometrial cancer, ESCC: esophageal squamous cell carcinoma, ES-SCLC: extensive-stage small cell lung cancer, GEJ: gastroesophageal junction, HCC: hepatocellular carcinoma, HNSCC: head and neck squamous cell carcinoma, ICC: investigators' choice of chemotherapy, IHC: immunohistochemistry, mCRP: metastatic castration-resistant prostate cancer, NSCLC: non-small cell lung cancer, OVC: ovarian cancer, ORR: objective response rate, OS: overall survival, PDAC: pancreatic ductal adenocarcinoma, sqNSCLC: squamous non-small cell lung cancer, UC: urothelial carcinoma.

Agenda

1. SCLC overview

2. I-DXd program overview
   - I-DXd scientific profile
   - IDeate-Lung01 WCLC presentation
   - I-DXd clinical development plan

3. **Other program updates from WCLC 2025**

4. Q&A

Trastuzumab Deruxtecan + Pembrolizumab as First-Line Treatment in HER2-Overexpressing, PD-L1 TPS <50% NSCLC (DESTINY-Lung06)

Pasi A. Jänne,[1] Cai-Cun Zhou,[2] Egbert F. Smit,[3] Enriqueta Felip,[4] Koichi Goto,[5] William N. William Jr,[6] Chihiro Abe,[7] Qing Zhou,[7] Takahiro Kamio,[7] Kaline Pereira[7]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]East Hospital Affiliated to Tongji University, Shanghai, China; [3]Leiden University Medical Center, Leiden, Netherlands; [4]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [5]National Cancer Center Hospital East, Kashiwa, Japan; [6]Grupo Oncoclínicas, São Paulo, Brazil; [7]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA

WCLC 2025 P3.18.58. (Poster/TIP)

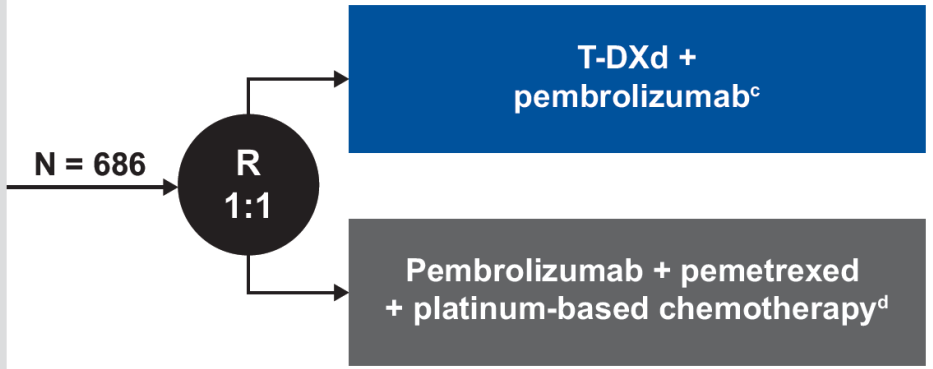
DESTINY-Lung06 Study

Global, open-label, randomized, phase 3 trial designed to evaluate the safety and efficacy of T-DXd + pembrolizumab versus platinum-based chemotherapy + pembrolizumab as a 1L therapy in patients with HER2-overexpressing, PD-L1 TPS <50%, unresectable/metastatic, non-squamous NSCLC

Study design

Patient population

- Locally advanced unresectable/metastatic non-squamous NSCLC
- No prior systemic treatment for advanced/metastatic NSCLC
- Centrally confirmed HER2 overexpression and PD-L1 TPS <50%
- No known actionable genomic alterations (AGAs)[a] with locally available therapies in 1L
- No known *HER2* mutation based on existing test results[b]



[a]For example, *ALK, ROS1, EGFR, NTRK, BRAF, RET, or MET* (by local testing).
[b]If approved or validated local test is available.
[c]T-DXd 5.4 mg/kg + pembrolizumab 200 mg IV Q3W.
[d]Pembrolizumab 200 mg + pemetrexed 500 mg/m^2 + platinum-based chemotherapy [cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL*min] IV Q3W.

Study start: September, 2025 | Recruiting

DESTINY-Lung06 is planned to be conducted at approximately 250 trial sites located in Asia, Europe, North America, and South America

Endpoints

Primary
- PFS by blinded independent central review (BICR)[a]

Key secondary
- OS

Other secondary
- PFS by investigator assessment[a]
- Overall response rate by BICR and investigator assessment[a]
- DOR by BICR and investigator assessment[a]
- Safety and tolerability
- Patient-reported outcomes

[a]By Response Evaluation Criteria in Solid Tumours, version 1.1

1L, first-line; AGA, actionable genomic alteration; AUC, area under the concentrationtime curve; BICR, blinded independent central review; DOR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ILD, interstitial lung disease; NSCLC, non–small cell lung cancer; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPS, tumor proportion score.

KEYMAKER-U01 Substudy 01G: Pembrolizumab + Patritumab Deruxtecan (HER3-DXd) ± Chemotherapy in Previously Untreated Stage IV NSCLC

M. Johnson[1]*; T. Csoszi[2]; Z. Szalai[3]; J. Bar[4,5]; N. Peled[6]; B. Chul Cho[7]; Y.J. Kim[8]; D. Kowalski[9]; E. Nadal[10]; J. Niu[11]; J.F. Gainor[12]; C. Aggarwal[13]; D.P. Carbone[14]; K.H. Dragnev[15]; K. Chen[16]; D. Sternberg[17]; B. Zhao[18]; H. Zhou[18]; A. Namakydoust[18]; V. Velcheti[19]

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KEYMAKER-U01 Substudy 01G

Ph2, rolling-arm, multicenter, open-label, signal-finding study that is evaluating pembrolizumab in combination with HER3-DXd, with or without platinum-based chemotherapy, in previously untreated participants with stage IV NSCLC with no actionable genomic alterations

Study design

Key Eligibility Criteria

- Treatment-naive stage IV squamous or nonsquamous NSCLC
- ECOG PS 0 or 1
- PD-L1 all comers
- Not eligible for *EGFR*-, *ALK*-, or *ROS1-directed* therapy
- No pneumonitis or ILD

Stratification Factors

- Tumor histology (squamous vs nonsquamous)
- PD-L1 tumor proportion score (<50% vs ≥50%)

R 1:2
N = 90

Arm 1
n = 30

Pembrolizumab 200 mg IV Q3W for up to 35 cycles + Platinum-based chemotherapy[a]

Arm 2
n = 60

HER3-DXd 5.6 mg/kg until discontinuation criterion is met + Pembrolizumab 200 mg IV Q3W for up to 35 cycles

Endpoints

Primary

- ORR*
- Safety and tolerability assessed by AEs and treatment discontinuations due to AEs

Secondary

- DOR*
- PFS*
- OS

* assessed per RECIST version 1.1 by BICR

AEs: adverse events, *ALK*, anaplastic lymphoma kinase; AUC, area under the curve; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; ILD, interstitial lung disease; IV, intravenous; Q3W, once every 3 weeks; R, randomized; *ROS1*, c-ros oncogene 1.

[a]The platinum-based chemotherapy regimen includes carboplatin (AUC 5 mg/mL•min [nonsquamous] or 6 mg/mL•min [squamous] IV on day 1 Q3W for up to 4 cycles) with either paclitaxel (200 mg/m^2 IV on day 1 Q3W for up to 4 cycles) or nab-paclitaxel (100 mg/m^2 IV on days 1, 8, and 15 Q3W for up to 4 cycles) for tumors with squamous histology or pemetrexed (500 mg/m^2 IV Q3W until discontinuation criteria met) for tumors with nonsquamous histology.

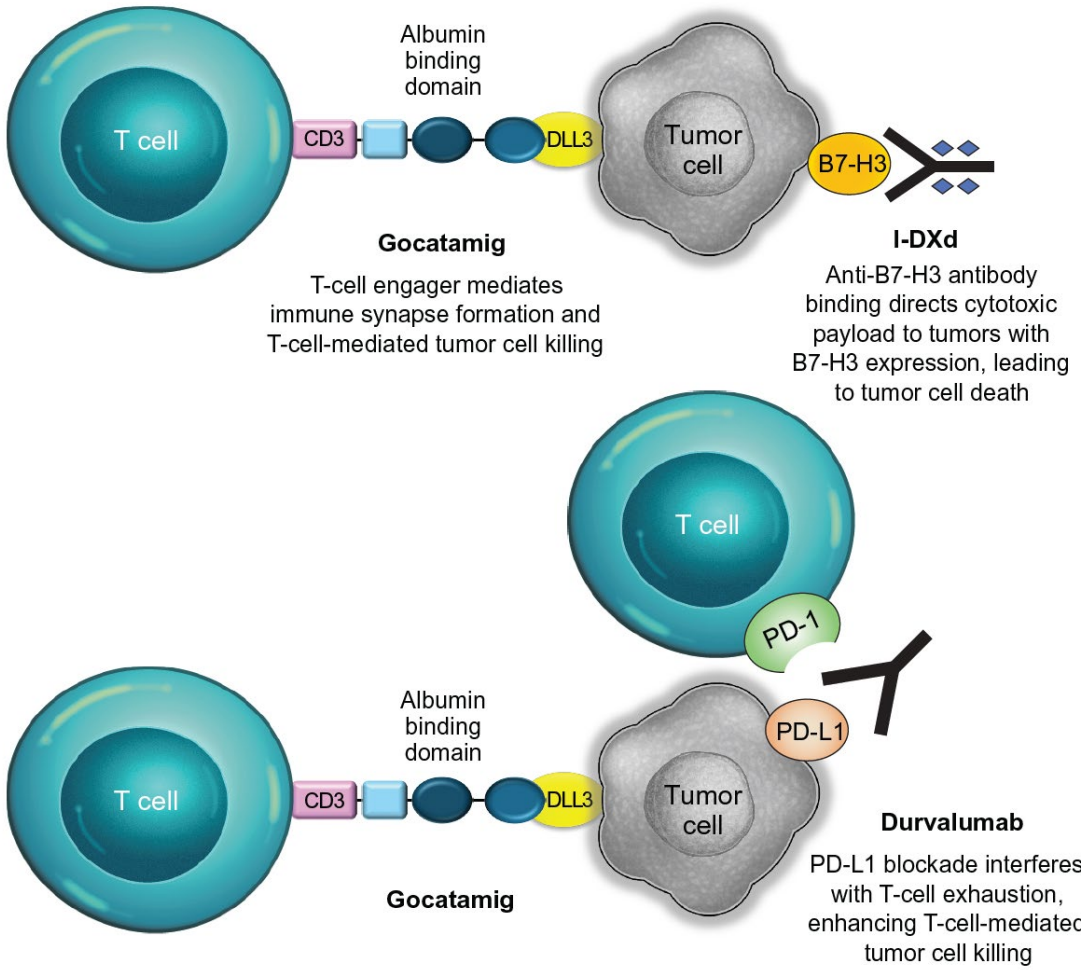
A phase 1b/2 study of gocatamig and ifinatamab deruxtecan for relapsed or refractory extensive-stage small cell lung cancer

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

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

WCLC 2025 P3.18.73. (Poster/TIP)

Mechanisms of action of gocatamig, I-DXd, and durvalumab



- DLL3 and B7-H3 are two proteins highly expressed on the surface of SCLC cells[1,2]
- Gocatamig (MK-6070, HPN328) is a DLL3-directed T-cell engager developed using the TriTAC® platform[3]
- I-DXd is an ADC comprising a B7-H3 monoclonal antibody covalently linked to a topoisomerase linhibitor[4]
- Both gocatamig and I-DXd have shown encouraging antitumor activity and manageable safety profiles when administered as monotherapy in participants with ES-SCLC relapsed or refractory to one or more prior lines of systemic chemotherapy[5,6]
- Durvalumab is a PD-L1 inhibitor approved for use in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of ES-SCLC[7]
- Because of their distinct mechanisms of action and minimally overlapping toxicities, combining gocatamig with an ADC or a checkpoint inhibitor may enhance efficacy without compromising tolerability

1. Owen DH, et al. J Hematol Oncol. 2019;12:61., 2. Dong P, et al. Front Oncol. 2018;8:264., 3. Austin RJ, et al. Mol Cancer Ther. 2021;20:109-120., 4. Yamato M, et al. Mol Cancer Ther. 2022;21(4):635-646., 5. Beltran H, et al. J Clin Oncol. 2024;42(16_suppl):8090., 6. Rudin CM, et al. J Thorac Oncol. 2024;19(10_suppl):OA04.03., 7. Imfinzi. Package insert. AstraZeneca. 2025.
ADC: antibody-drug conjugate, ES-SCLC: extensive-stage small cell lung cancer

Study design

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

Objectives

Primary

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

Secondary

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

DOR: duration of response, ORR: objective response rate, PFS: progression-free survival

Trastuzumab Deruxtecan in Patients From China With Pretreated HER2-Mutant NSCLC: Final Results From the DESTINY-Lung05 Study

Ying Cheng,[1] Dairong Li,[2] Lin Wu,[3] Xingya Li,[4] Yun Fan,[5] Mingjun Zhang,[6] Jun Guo,[7] Yu Yao,[8] Zizheng Song,[9] Rui Ma,[10] Yongqian Shu,[11] Buhai Wang,[12] Xiaorong Dong,[13] Qibin Song,[14] Yanjun Mi,[15] Jianhua Shi,[16] Yunru Chen,[17] Rui Mao,[17] Victor Zhang,[18] Yong Fang[19]

[1]Department of Oncology, Jilin Cancer Hospital, Changchun, China; [2]Department of Medical Oncology, Chongqing University Cancer Hospital & Chongqing Cancer Institute & Chongqing Cancer Hospital, Chongqing, China; [3]2nd Department of Thoracic Medicine, Hunan Cancer Hospital, Changsha, China; [4]Department of Oncology Second Ward, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [5]Department of Medical Thoracic Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [6]Oncology Department, The Second Hospital of Anhui Medical University, Hefei, China; [7]Department of Oncology, Shandong Cancer Hospital, Jinan, China; [8]Medical Oncology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China; [9]Department of Medical Oncology, Affiliated Hospital of Hebei University, Hebei, China; [10]Medical Oncology Department of Thoracic Cancer, Liaoning Cancer Hospital & Institute, Liaoning, China; [11]Department of Oncology, Jiangsu Province Hospital, Nanjing, China; [12]Cancer Institute, Northern Jiangsu People's Hospital, Yangzhou, China; [13]Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [14]Department of Oncology, Renmin Hospital of Wuhan University, Wuhan, China; [15]Department of Medical Oncology, The First Affiliated Hospital of Xiamen University, Xiamen, China; [16]Department of Medical Oncology, Linyi Cancer Hospital, Shandong, China; [17]Oncology R&D, AstraZeneca, Shanghai, China; [18]Biometrics Department, AstraZeneca, Shanghai, China; [19]Medical Oncology, Sir Run Run Shaw Hospital School of Medicine, Zhejiang University, Hangzhou, China

DESTINY-Lung05 study design

Patient population*

- Aged ≥18 years
- Metastatic nonsquamous NSCLC
- Locally or centrally confirmed activating *HER2* exon 19 or 20 mutation†
- Disease progression on or after ≥1 prior anticancer therapy‡
- RECIST 1.1-evaluable lesion
- WHO or ECOG performance status 0–1
- Patients with previously treated CNS metastases were allowed if asymptomatic / neurologically stable§

T-DXd 5.4 mg/kg every 3 weeks

Treatment continued until disease progression per RECIST 1.1, unacceptable toxicities, or trial discontinuation

Key endpoints

Primary: Confirmed ORR by ICR¶

Secondary:

- Confirmed ORR by INV¶
- DOR, DCR, PFS by ICR/INV¶
- OS
- CNS-PFS by ICR¶
- Safety

Exploratory:

- Best percentage change from baseline in the sum of diameters of target lesions

*Approximately 80 patients were planned for enrollment, with 72 patients enrolled at data cutoff; †based on a pre-existing tissue test result from a local laboratory or prospective central confirmation of the HER2 tissue mutation test result (retrospective central confirmation was performed for those enrolled based on existing local HER2 mutation results); ‡treatment with prior HER2-directed therapy, except for pan-HER class tyrosine kinase inhibitors, and prior treatment with an antibody-drug conjugate that consists of an exatecan derivative that is a topoisomerase I inhibitor were not allowed; §patients with asymptomatic CNS disease at baseline were eligible if they did not need ongoing corticosteroid or anticonvulsant treatments, had recovered from acute radiotherapy toxicity, and ≥2 weeks had passed since whole-brain radiotherapy; ¶per RECIST 1.1

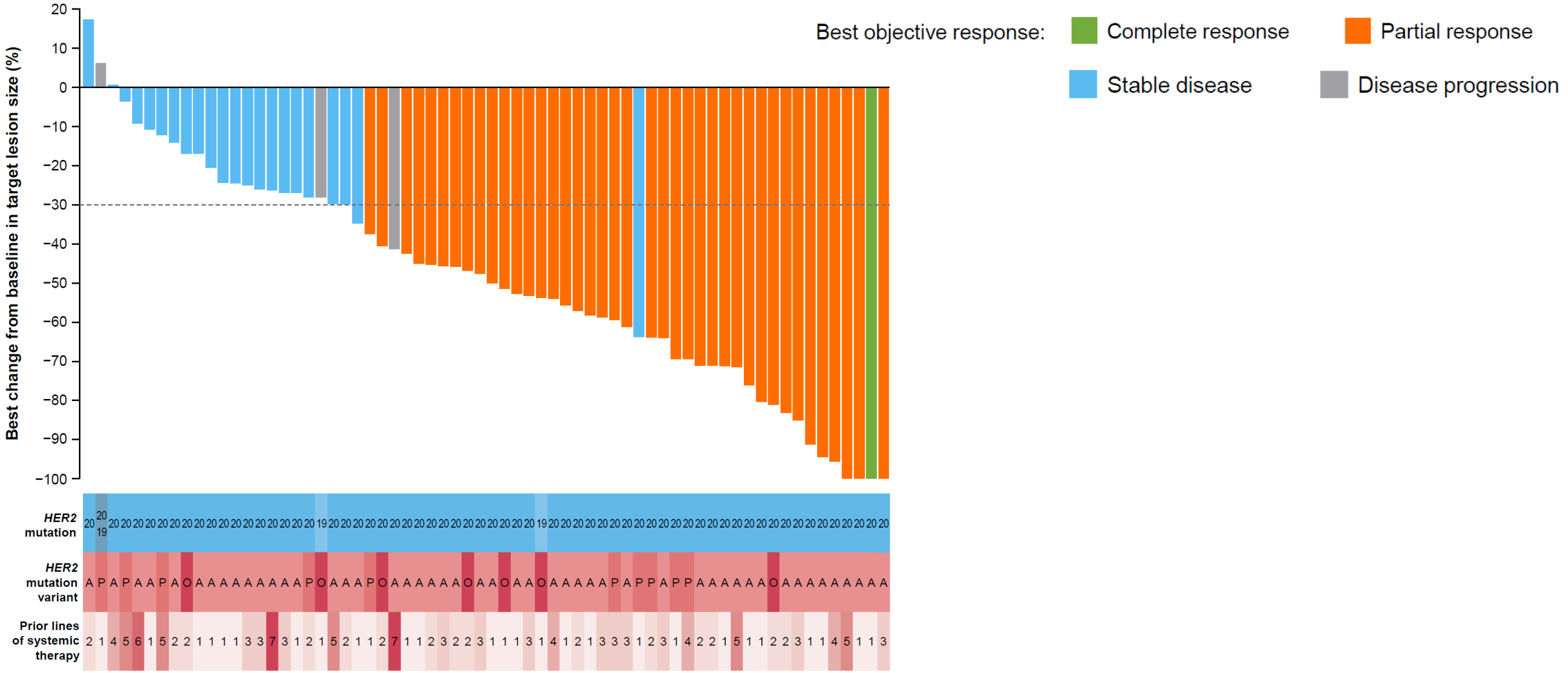
CNS, central nervous system; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; ICR, independent central review; INV, investigator assessed; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization

Response outcomes

	ICR N=72	INV N=72
Confirmed ORR, % (n)	**56.9 (41)**	**59.7 (43)**
95% CI	**44.7, 68.6**	**47.5, 71.1**
Best objective response, n (%)		
Complete response	1 (1.4)	0
Partial response	40 (55.6)	43 (59.7)
Stable disease*	25 (34.7)	24 (33.3)
Disease progression†	5 (6.9)	4 (5.6)
Not evaluable	1 (1.4)	1 (1.4)
DCR, % (95% CI)	91.7 (82.7, 96.9)	93.1 (84.5, 97.7)
Median DOR, months (95% CI)	11.6 (5.8, NE)	9.4 (7.2, 13.5)

Confirmed ORR required confirmation after at least 4 weeks *Included two patients who had PR/CR, but either no confirmation assessment was performed, or a confirmation assessment was performed but response was not confirmed; †included RECIST 1.1-defined disease progression, and death ≤13 weeks without RECIST 1.1-defined disease progression
CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; ICR, independent central review; INV, investigator assessment; NE, not evaluable; ORR, objective response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours

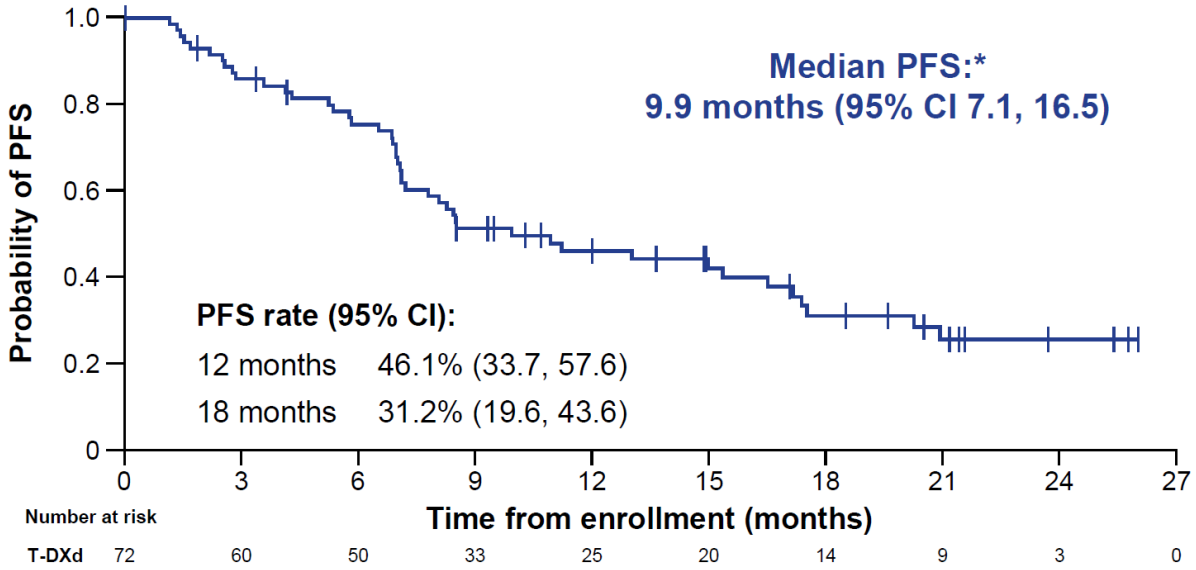
Best percentage change from baseline in target lesion size

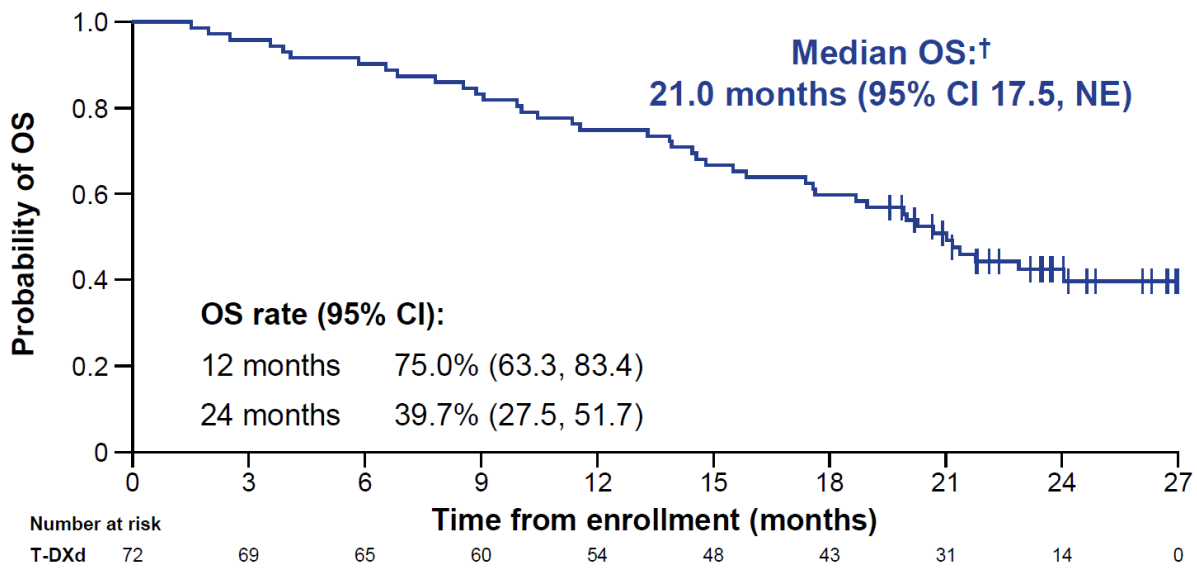


Best percentage change in target lesion size was assessed by ICR per RECIST 1.1 and was defined as the maximum reduction from baseline or the minimum increase from baseline in the absence of a reduction. The dashed reference line at −30% indicates the threshold for a partial response. Analyses were performed in patients with HER2m NSCLC by central testing with at least one post-baseline target lesion assessment (n=66). Only visits prior to subsequent anticancer therapy are included. The color of each bar indicates the confirmed best objective response per RECIST 1.1 determined by ICR. Numbers in the *HER2* mutation row indicate the exon in which the mutation occurred. Letters in the *HER2* mutation variant row correspond to the specific mutation: A, A775_G776insYVMA; P, P780_Y781insGSP; O, other (G776delinsVC, L755P, I767M)

HER2, human epidermal growth factor receptor 2; HER2m, *HER2* mutant; ICR, independent central review; NSCLC, non-small cell lung cancer; RECIST, Response Evaluation Criteria in Solid Tumours

Kaplan-Meier estimates of PFS by ICR and OS





Symbols indicate a censored observation. PFS was assessed by ICR per RECIST 1.1 *Progression events that did not occur within two missed visits of the last evaluable assessment or enrollment date were censored; †patients not known to have died at the time of analysis were censored at the last recorded date on which they were known to be aliveCI, confidence interval; ICR, independent central review; NE, not evaluable; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan

Summary of drug-related AEs

Safety analysis set, n (%)*	N=72
AEs	71 (98.6)
Grade ≥3 AEs	40 (55.6)
Serious AEs	23 (31.9)
AEs leading to discontinuations	4 (5.6)
AEs leading to dose reductions	16 (22.2)
AEs leading to dose interruptions	32 (44.4)
Adjudicated ILD/pneumonitis†	
Any grade	9 (12.5)
Grade 1	1 (1.4)
Grade 2	7 (9.7)
Grade 3	1 (1.4)
Left ventricular dysfunction	
Any grade	4 (5.6)‡
Grade 2	4 (5.6)‡

*Analyses include all patients who received ≥1 dose of T-DXd; †assessed by the ILD adjudication committee; ‡ejection fraction decreased
AE, adverse event; ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan

Conclusions

- With a median follow-up time of more than 20 months, results of the DESTINY-Lung05 final analysis build on primary data from the study1 and affirm that T-DXd (5.4 mg/kg) induces durable responses and
  clinically meaningful survival benefit in patients from China with pretreated metastatic HER2m NSCLC
- Antitumor activity was observed across *HER2* mutation subgroups
- No new safety signals were identified, and the safety profile was consistent with the known profile of T-DXd[1,2]
- These data further support the use of T-DXd (5.4 mg/kg) as a treatment option in China for patients with previously treated metastatic HER2m NSCLC[1]

1. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67:173–185; 2. Ogitani Y, et al. *Clin Cancer Res*. 2016;22:5097–5108;

Agenda

1. **SCLC overview**

2. **I-DXd program overview**
   - I-DXd scientific profile
   - IDeate-Lung01 WCLC presentation
   - I-DXd clinical development plan

3. **Other program updates from WCLC 2025**

4. **Q&A**

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