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Ifinatamab deruxtecan (I-DXd) in extensive-stage small cell lung cancer: Asian subgroup analysis from the Phase 2 IDeate-Lung01 study

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Declaration of interests

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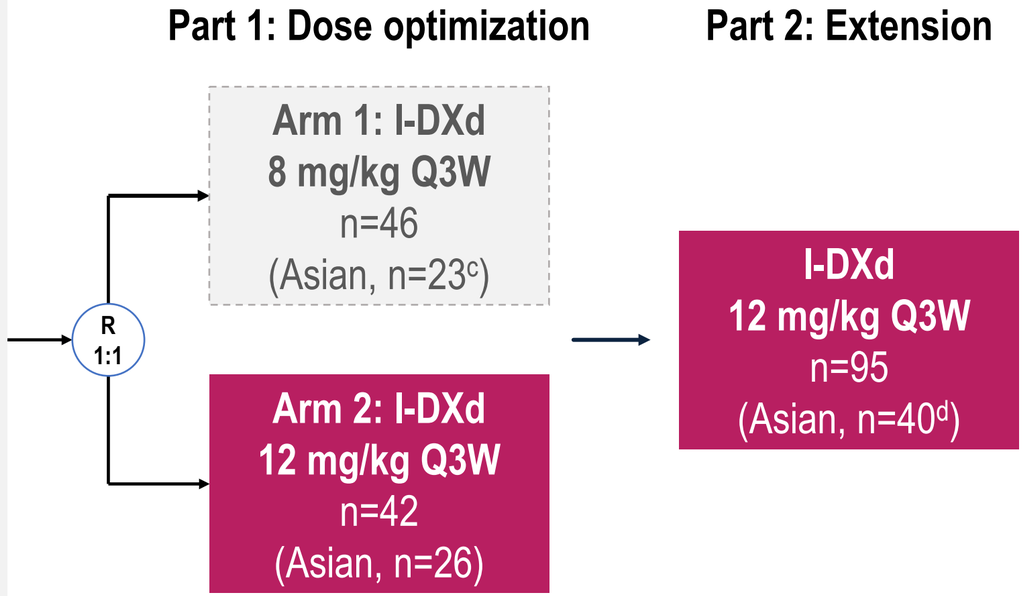
IDeate-Lung01 study design

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



Primary endpoint:

- ORR by BICR[e]

Secondary endpoints:

- DOR by BICR and inv[e]
- PFS by BICR and inv[e]
- OS
- DCR by BICR and inv[e]
- TTR by BICR and inv[e]
- ORR by inv[e]
- Safety
- PK
- Immunogenicity

[a]Or local legal age of consent. [b]Patients must also have had ≥1 lesion that had not been irradiated and was amenable to biopsy. [c]In total, 24 patients were treated with I-DXd 8 mg/kg in Part 1: 23 at sites in Asia and 1 at a site in the United States. [d]In total, 41 Asian patients were treated with I-DXd 12 mg/kg in Part 2; however, 1 of these patients was treated at a site in the United States and was not included in this analysis. [e]Per RECIST 1.1.
BICR, blinded independent central review; 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; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; TTR, time to response.

Hidetoshi Hayashi

I-DXd demonstrated a manageable safety profile and encouraging efficacy in the total 12-mg/kg population

	Total I-DXd 12-mg/kg population (N=137)[1]		
	Total (N=137)	2L (n=32)	3L+ (n=105)
cORR, % (95% CI)	**48.2 (39.6–56.9)**	56.3 (37.7–73.6)	45.7 (36.0–55.7)
mDOR (95% CI), months	**5.3 (4.0–6.5)**	7.2 (3.6–NE)	4.3 (3.7–5.8)
mTTR (range), months	**1.4 (1.0–8.1)**	1.4 (1.2–4.0)	1.4 (1.0–8.1)
mPFS (95% CI), months	**4.9 (4.2–5.5)**	5.6 (3.9–8.1)	4.5 (4.2–5.4)
mOS (95% CI), months	**10.3 (9.1–13.3)**	12.0 (7.3–19.1)	10.3 (9.1–13.0)

We present efficacy and safety data for Asian patients treated with I-DXd 12 mg/kg across the dose-optimization and extension parts of IDeate-Lung01

2L, second-line; 3L+; third-line and beyond; CI, confidence interval; cORR, confirmed objective response rate; mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; mTTR, median time to response; NE, not estimable.

1. Rudin CM, et al. *J Clin Oncol.* 2025. Online ahead of print. doi:10.1200/JCO-25-02142

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Baseline characteristics

Characteristic	I-DXd 12-mg/kg Asian subgroup (n=66)	Total I-DXd 12-mg/kg population (N=137)
Age, median (range), years	63 (34–79)	63 (34–79)
Male, n (%)	54 (81.8)	90 (65.7)
Country of enrollment, n (%)		
China	19 (28.8)	19 (13.9)
Japan	22 (33.3)	22 (16.1)
Republic of Korea	19 (28.8)	19 (13.9)
Taiwan	6 (9.1)	6 (4.4)
ECOG PS 1, n (%)	55 (83.3)	106 (77.4)
ES-SCLC at diagnosis, n (%)	52 (78.8)	111 (81.0)
Brain / liver metastases at baseline,[a] n (%)	16 (24.2) / 25 (37.9)	52 (38.0) / 55 (40.1)
CTFI, n (%)		
≤30 days / >30 to <90 days / ≥90 days	10 (15.2) / 21 (31.8) / 35 (53.0)	18 (13.1) / 40 (29.2) / 72 (52.6)
Prior lines of systemic therapy, median (range)	2 (1–3)	2 (1–3)
1 / 2 / 3, n (%)	14 (21.2) / 40 (60.6) / 12 (18.2)	32 (23.4) / 75 (54.7) / 30 (21.9)
Select prior anticancer therapy, n (%)		
Topoisomerase I inhibitor	29 (43.9)	44 (32.1)
Amrubicin	12 (18.2)	12 (8.8)
Lurbinectedin	2 (3.0)	29 (21.2)
DLL3-targeting T-cell engager[b]	1 (1.5)	11 (8.0)
Prior anti–PD-(L)1 therapy, n (%)	49 (74.2)	111 (81.0)

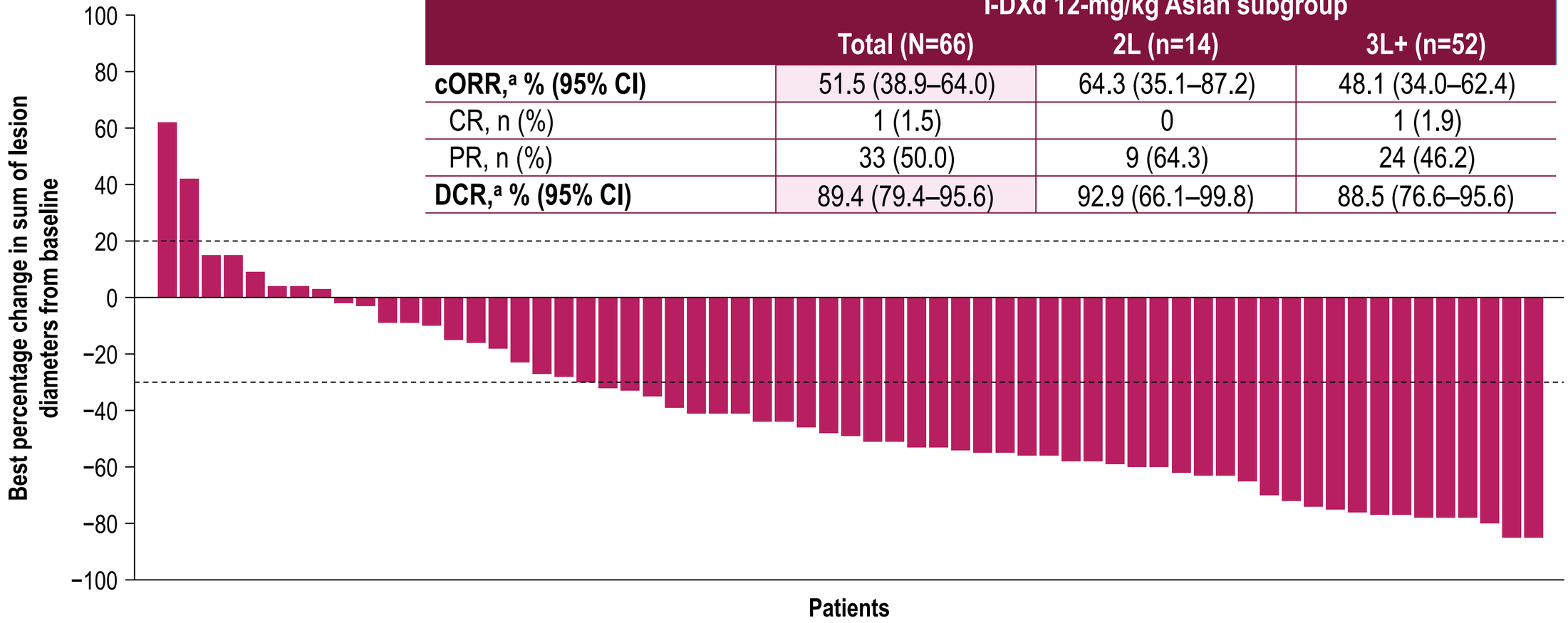
Data cutoff: March 3, 2025.

[a]By blinded independent central review. [b]One patient in the Asian subgroup and 7 patients in the total 12-mg/kg population received prior tarlatamab.

CTFI, chemotherapy-free interval; DLL3, delta-like ligand; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; PD-(L)1, programmed death (ligand) 1.

I-DXd 12 mg/kg demonstrated strong antitumor activity

	I-DXd 12-mg/kg Asian subgroup		
	Total (N=66)	2L (n=14)	3L+ (n=52)
cORR,[a] % (95% CI)	51.5 (38.9–64.0)	64.3 (35.1–87.2)	48.1 (34.0–62.4)
CR, n (%)	1 (1.5)	0	1 (1.9)
PR, n (%)	33 (50.0)	9 (64.3)	24 (46.2)
DCR,[a] % (95% CI)	89.4 (79.4–95.6)	92.9 (66.1–99.8)	88.5 (76.6–95.6)



Total I-DXd 12-mg/kg population (N=137): cORR, 48.2% (95% CI, 39.6–56.9)

Data cutoff: March 3, 2025. Median follow-up: 13.1 months (95% CI, 12.2–NE).

[a]By blinded independent central review per Response Evaluation Criteria in Solid Tumours, version 1.1.

2L, second-line; 3L+, third-line and beyond; CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; DCR, disease control rate; NE, not estimable; PR, partial response.

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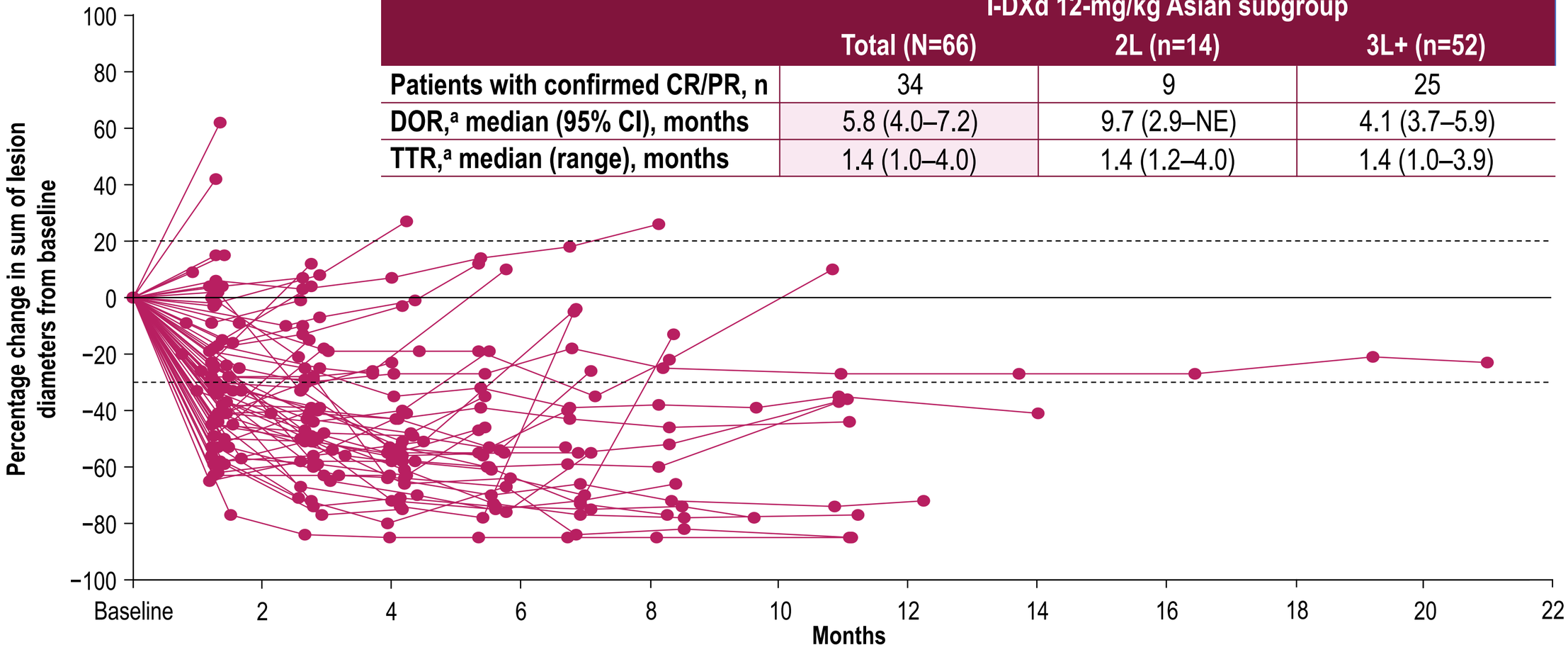
Responses to I-DXd 12 mg/kg were rapid and durable

	I-DXd 12-mg/kg Asian subgroup		
	Total (N=66)	2L (n=14)	3L+ (n=52)
Patients with confirmed CR/PR, n	34	9	25
DOR,[a] median (95% CI), months	5.8 (4.0–7.2)	9.7 (2.9–NE)	4.1 (3.7–5.9)
TTR,[a] median (range), months	1.4 (1.0–4.0)	1.4 (1.2–4.0)	1.4 (1.0–3.9)



Total I-DXd 12-mg/kg population (N=137): Median DOR, 5.3 months (95% CI, 4.0–6.5); median TTR, 1.4 months (range, 1.0–8.1)

Data cutoff: March 3, 2025. Median follow-up: 13.1 months (95% CI, 12.2–NE).

[a]By blinded independent central review per Response Evaluation Criteria in Solid Tumours, version 1.1.

2L, second-line; 3L+, third-line and beyond; CI, confidence interval; CR, complete response; DOR, duration of response; NE, not estimable; PR, partial response; TTR, time to response.

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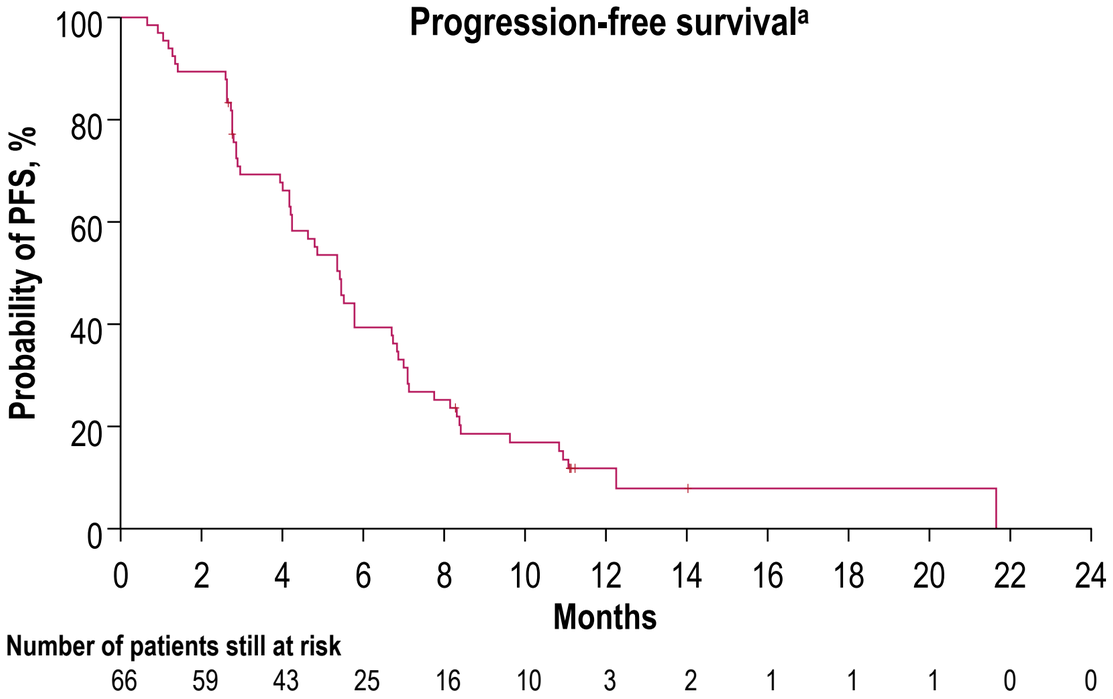
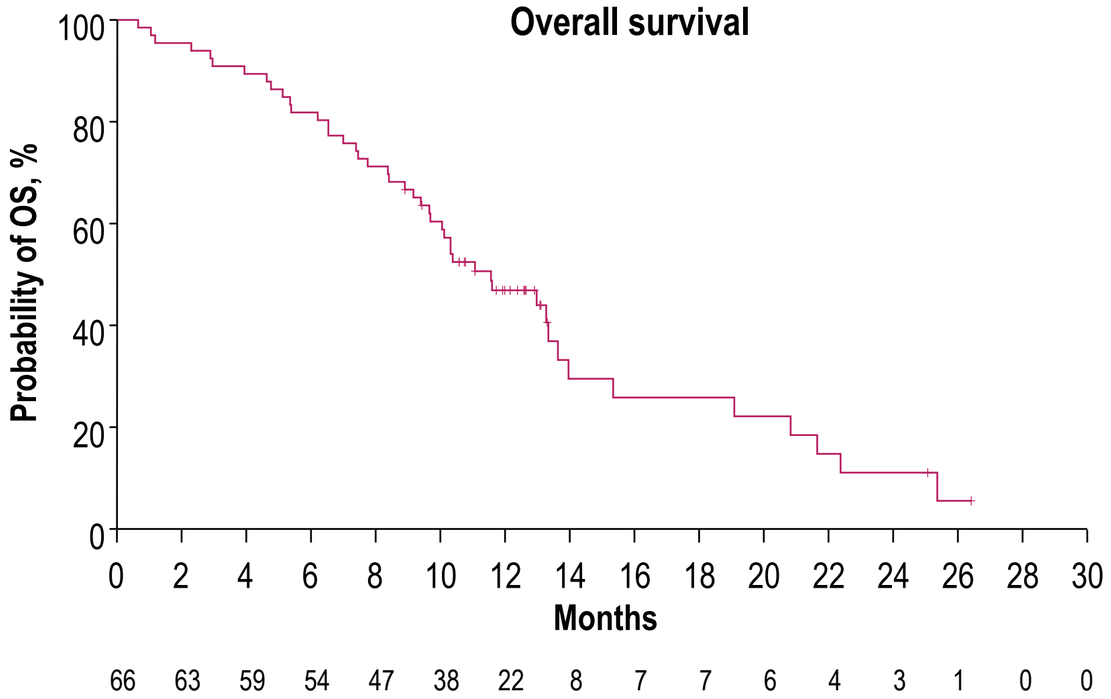
mPFS was 5.4 months and mOS was 11.6 months





	I-DXd 12-mg/kg Asian subgroup		
	Total (N=66)	2L (n=14)	3L+ (n=52)
PFS,[a] median (95% CI), months	5.4 (4.2–6.7)	8.0 (3.9–NE)	4.9 (4.0–5.8)
OS, median (95% CI), months	11.6 (9.7–13.6)	15.3 (3.9–NE)	10.4 (9.4–13.3)

Total I-DXd 12-mg/kg population (N=137): Median PFS, 4.9 months (95% CI, 4.2–5.5); median OS, 10.3 months (95% CI, 9.1–13.3)

Data cutoff: March 3, 2025. Median follow-up: 13.1 months (95% CI, 12.2–NE).

[a]By blinded independent central review per Response Evaluation Criteria in Solid Tumours, version 1.1.

2L, second-line; 3L+, third-line and beyond; CI, confidence interval; NE, not estimable; (m)OS, (median) overall survival; (m)PFS, (median) progression-free survival.

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

	I-DXd 12-mg/kg Asian subgroup (n=66)	Total I-DXd 12-mg/kg population (N=137)
Any-grade TRAEs, n (%)	62 (93.9)	123 (89.8)
Grade ≥3	27 (40.9)	50 (36.5)
Associated with dose delay	20 (30.3)	35 (25.5)
Associated with dose reduction	12 (18.2)	21 (15.3)
Associated with treatment discontinuation	9 (13.6)	13 (9.5)
Associated with death	4 (6.1)	6 (4.4)[a]
Adjudicated treatment-related ILD/pneumonitis,[b] n (%)		
Any grade	12 (18.2)	17 (12.4)[c]
Grade 1	2 (3.0)	3 (2.2)
Grade 2	5 (7.6)	8 (5.8)
Grade 3	3 (4.5)	4 (2.9)
Grade 4	0	0
Grade 5	2 (3.0)	2 (1.5)
Time to onset of first event, median (range), days	104 (18–332)	78 (18–332)
Duration of first resolved event, median (range), days	23 (10–180)	26 (6–180)

Data cutoff: March 3, 2025. Median treatment duration: Asian subgroup, 5.1 months (range, 0.7–20.7); total 12-mg/kg population, 4.8 months (range, 0.7–22.7). Median number of cycles: Asian subgroup, 6.5 (range, 1–30); total 12-mg/kg population, 7.0 (range, 1–32).

[a]ILD/pneumonitis (n=3 [Asian, n=2]); *Pneumocystis jirovecii* pneumonia (n=2 [Asian, n=2]); pulmonary sepsis (n=1 [Asian, n=0]). Of the 3 ILD/pneumonitis events associated with death, only 1 (in a non-Asian patient) was subsequently adjudicated as Grade 5 treatment-related ILD/pneumonitis by the ILD adjudication committee. [b]At data cutoff, all suspected ILD/pneumonitis events had been adjudicated. [c]At data cutoff, 10 events had resolved (Asian, n=6), 4 events were ongoing (Asian, n=4), and there had been 3 deaths (Asian, n=2).

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

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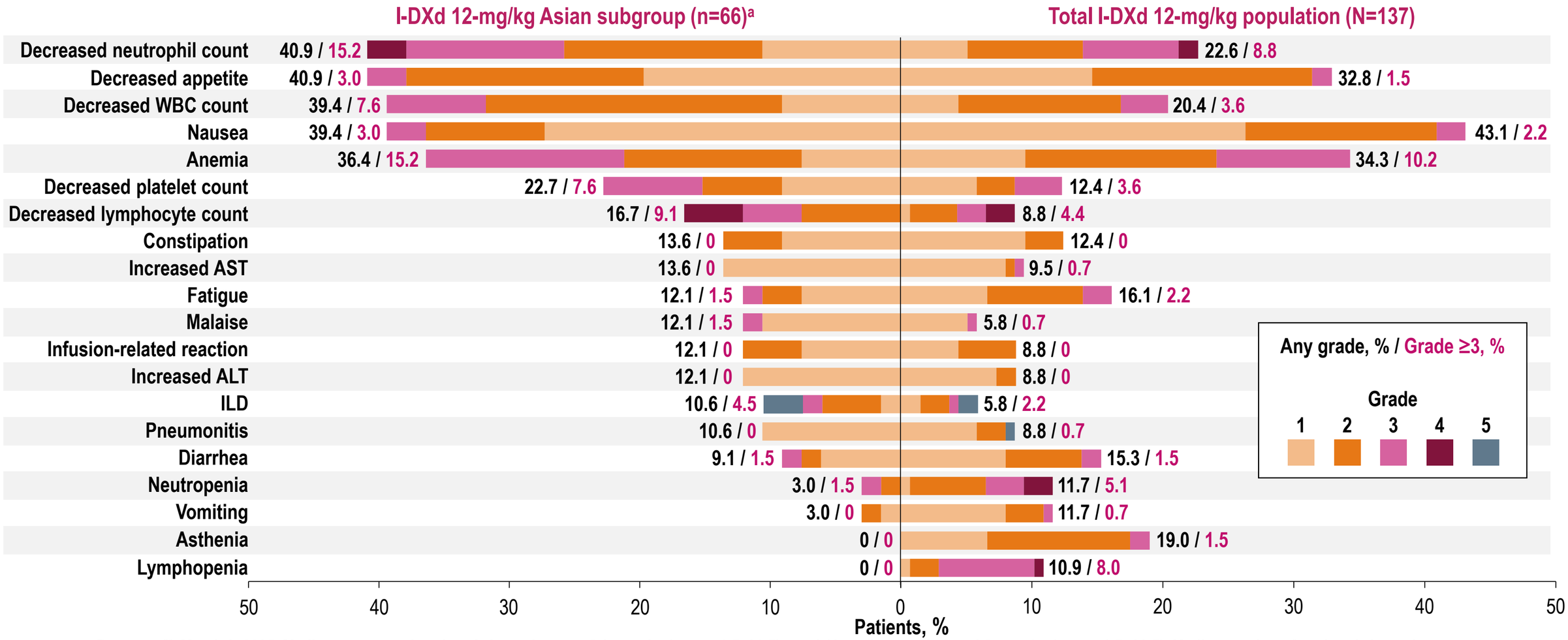
The safety profile of I-DXd 12 mg/kg was manageable

TRAEs reported at any grade in ≥10% of patients in the total 12-mg/kg population or Asian subgroup



Data cutoff: March 3, 2025. Median treatment duration: Asian subgroup, 5.1 months (range, 0.7–20.7); total 12-mg/kg population, 4.8 months (range, 0.7–22.7). Median number of cycles: Asian subgroup, 6.5 (range, 1–30); total 12-mg/kg population, 7.0 (range, 1–32).

[a]All TRAEs reported at Grade ≥3 in ≥5% of patients in the Asian subgroup were also reported in ≥10% of patients at any grade.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ILD, interstitial lung disease; TRAE, treatment-related adverse event; WBC, white blood cell.

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Conclusions

- In this subgroup analysis of IDeate-Lung01, I-DXd 12 mg/kg demonstrated similar efficacy in Asian patients to that seen in the total 12-mg/kg population:
  - cORR, 51.5% (vs 48.2%); mDOR, 5.8 months (vs 5.3 months); mTTR, 1.4 months (vs 1.4 months); mPFS, 5.4 months (vs 4.9 months); mOS, 11.6 (vs 10.3 months)
- Efficacy was particularly promising in patients who received I-DXd as 2L therapy, with a cORR of 64.3% (vs 56.3% in the total 12-mg/kg population)
- The safety profile was manageable and generally consistent with the total 12-mg/kg population (although comparisons are limited by a relatively small sample size in the Asian subgroup)
  - However, the incidence of any-grade and Grade ≥3 hematologic TRAEs was generally higher in the Asian subgroup than in the total 12-mg/kg population
  - Any-grade and Grade ≥3 adjudicated treatment-related ILD/pneumonitis was also more common in the Asian subgroup than in the total 12-mg/kg population
- The efficacy and safety of I-DXd 12 mg/kg in Asian patients will be investigated further in subgroup analyses of the ongoing global Phase 3 IDeate-Lung02 trial (NCT06203210)[a]

Data cutoff: March 3, 2025.

[a]IDeate-Lung02 is comparing I-DXd 12 mg/kg vs physician's choice of topotecan, amrubicin, or lurbinectedin in patients with relapsed small cell lung cancer with only 1 prior line of systemic treatment, which must have included platinum-based chemotherapy.

2L, second-line; cORR, confirmed objective response rate; ILD, interstitial lung disease; mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; mTTR, median time to response; TRAE, treatment-related adverse event.

Hidetoshi Hayashi

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