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Clinical and biomarker data from a Phase 1/2 trial of ifinatamab deruxtecan (I-DXd) in advanced solid tumors

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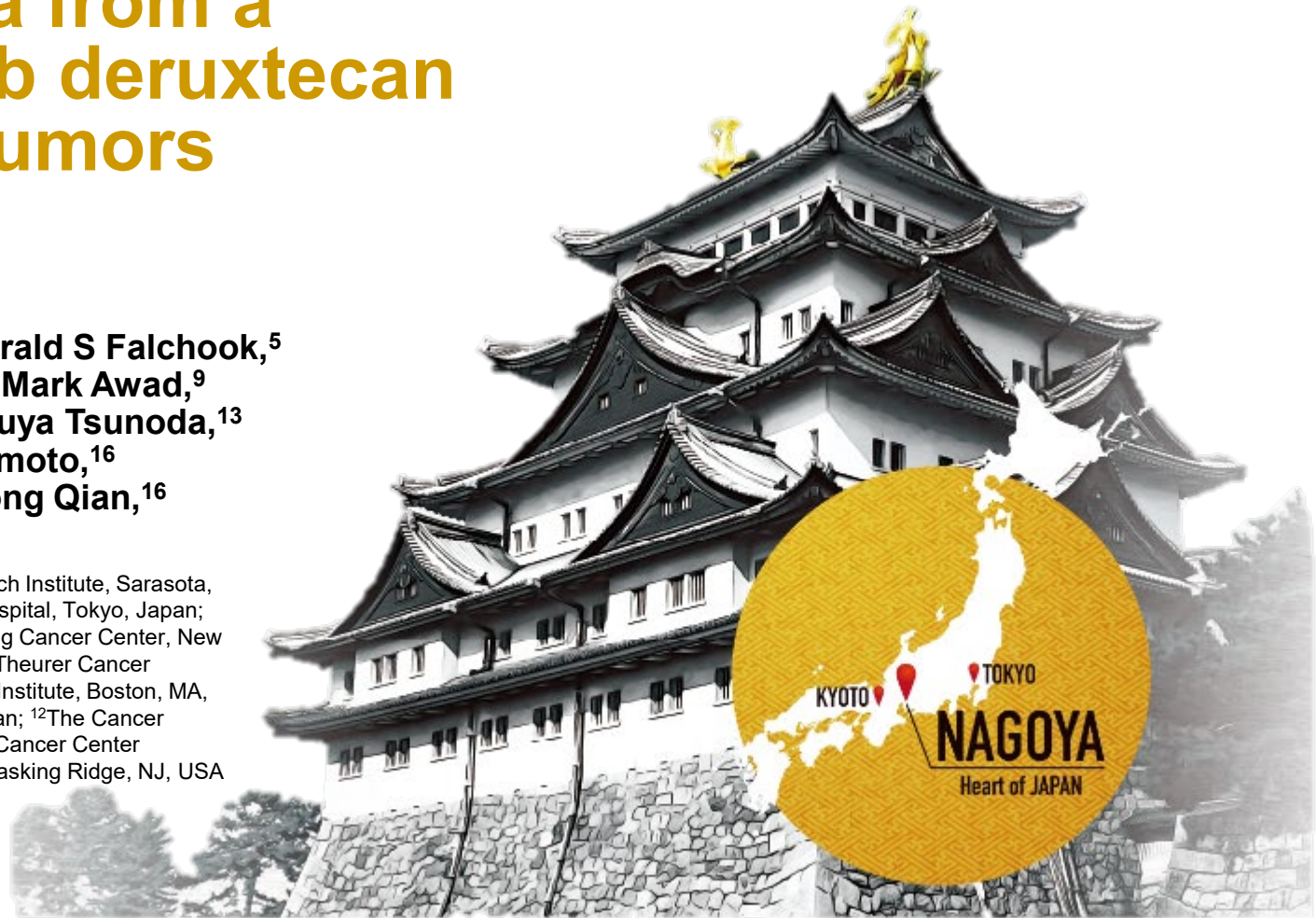

Presentation PS3-3

Declaration of interests

Research fund	□scientific research fund □contract □donation □other （ ） □N/A	Sponsor	Daiichi Sankyo, Inc. and Merck & Co., Inc.

Name of lead presenter	Toshihiko Doi	Institution or company/position	National Cancer Center Hospital East, Chiba, Japan

	No	If yes, please specify the name of company, organization, your status.
Employee or adviser of company and/or profit-making organization	✓	Rakuten Medical (Advisory fee)
Profit of stock	×	
Patent fee	×	
Lecturer fee	✓	Daiichi Sankyo
Manuscript fee	×	
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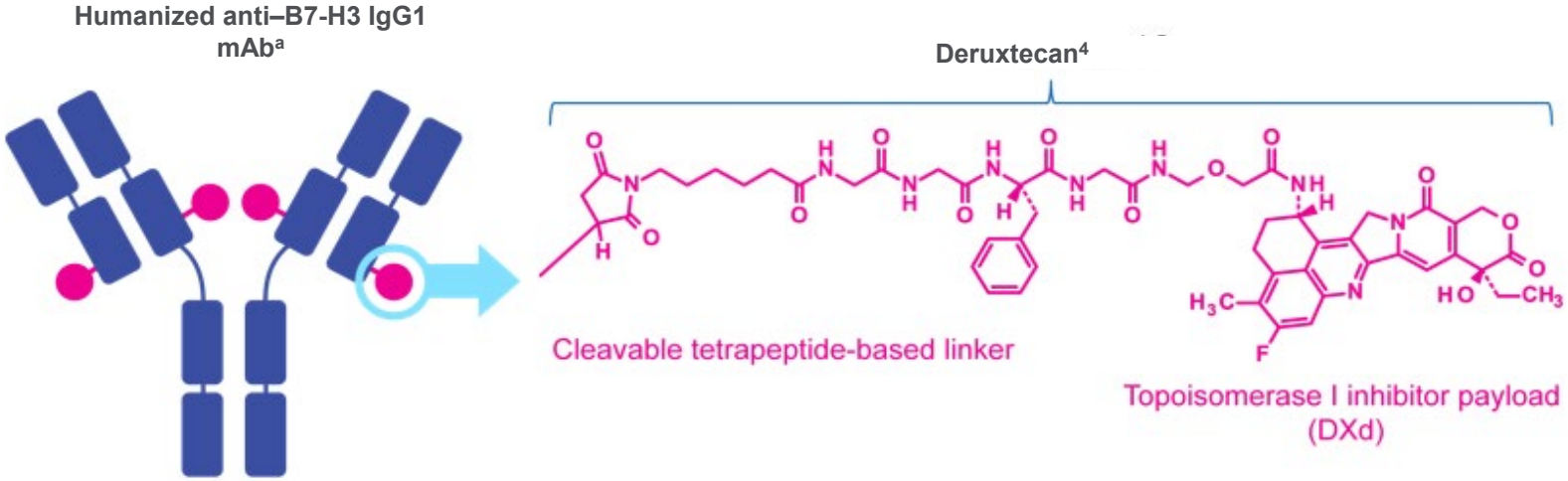
Contributions or endowed chair	×	
Fees of testimony, judgment, comment, etc.	×	
Presents or other payment	×	
Representative of organization for clinical study receiving research expenses from company	×	

Ifinatamab deruxtecan (I-DXd) was designed with 7 key attributes

- B7-H3 (CD276) is expressed in many solid tumors but is absent or expressed at relatively low levels in normal tissue. High B7-H3 expression is associated with a poor prognosis[1–3]
- I-DXd is a B7-H3–directed ADC designed to enhance selective tumor-cell death with minimal systemic exposure. It comprises three parts: a humanized anti–B7-H3 IgG1 mAb, covalently linked to a potent topoisomerase I inhibitor payload (DXd) via a stable tetrapeptide-based cleavable linker[1–5]
- DS7300-A-J101 (NCT04145622) is an ongoing, multicenter, open-label, first-in-human Phase 1/2 study of I-DXd in heavily pretreated patients with advanced solid tumors. In previous analyses, I-DXd was generally well tolerated and showed preliminary efficacy[5,6]



Payload mechanism of action: topoisomerase I inhibitor[4,7,8,b]
High potency of payload[4,8,b]
Optimized drug-to-antibody ratio ≈4[4,7,9–11,b]
Payload with short systemic half-life[4,8,b,c]
Stable linker-payload[4,8,b]
Tumor-selective cleavable linker[4,8,b]
Bystander antitumor effect[4,7,8,11,b]

[a]Image is for illustrative purposes only; actual drug positions may vary. [b]The clinical relevance of these features is under investigation. [c]Based on animal data.
ADC, antibody–drug conjugate; B7-H3, B7 homolog 3; CD276, cluster of differentiation 276; DXd, deruxtecan; IgG1, immunoglobulin G1; mAb, monoclonal antibody.

1. Dong P, et al. *Front Oncol.* 2018;8:264. 2. Kontos F, et al. *Clin Cancer Res.* 2021;27:1227–1235. 3. Rasic P, et al. *World J Gastrointest Oncol.* 2021;13:799–821. 4. Yamato M, et al. *Mol Cancer Ther.* 2022;21:635–646. 5. Doi T, et al. *Ann Oncol.* 2022;33(Suppl. 7):S197–S224. 6. Johnson ML, et al. *Ann Oncol.* 2021;32(Suppl. 5):S583–S620. 7. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67:173–185. 8. Daiichi Sankyo, Inc. Data on file. 9. Okajima D, et al. *Mol Cancer Ther.* 2021;20:2329–2340. 10. Ogitani Y, et al. *Clin Cancer Res.* 2016;22:5097–5108. 11. Ogitani Y, et al. *Cancer Sci.* 2016;107:1039–1046.

Study design

Patients with advanced/unresectable or metastatic solid tumors (not selected 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)

Key primary endpoints
- Dose escalation: DLTs, SAEs, TEAEs, AESIs
- Dose expansion: ORR, DOR, DCR, PFS, OS

Key secondary endpoints
- PK
- Immunogenicity

- The overall study population comprised 174 patients with 10 different tumor types (including SCLC, ESCC, mCRPC, and sqNSCLC) from the dose-escalation and -expansion cohorts, who received I-DXd doses of between 0.8 and 16.0 mg/kg
- Fifty-six of these patients were in the Japanese subgroup
- We present extended follow-up data from the overall study population[1] and the Japanese subgroup
  - The safety analysis included patients with SCLC, ESCC, mCRPC, sqNSCLC, and other tumor types, who received I-DXd 0.8–16.0 mg/kg
  - The efficacy and B7-H3 correlation analyses included patients who received doses at or above the minimal effective dose (≥4.8 mg/kg)

[a]Tumor types included advanced/unresectable or metastatic HNSCC, ESCC, mCRPC, sqNSCLC, SCLC, bladder cancer, sarcoma, endometrial cancer, melanoma, and breast cancer.
AESI, adverse events of special interest; B7-H3, B7 homolog 3; DCR, disease control rate; DLT, dose-limiting toxicity; DOR, duration of response; ESCC, esophageal squamous cell carcinoma; HNSCC, head and neck 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; RDE, recommended dose for expansion; SAE, serious adverse event; SCLC, small cell lung cancer; sqNSCLC, squamous non-small cell lung cancer, TEAE, treatment-emergent adverse event.
1. Patel MR, et al. ESMO 2023. Poster #690P.

Patient baseline characteristics and disposition

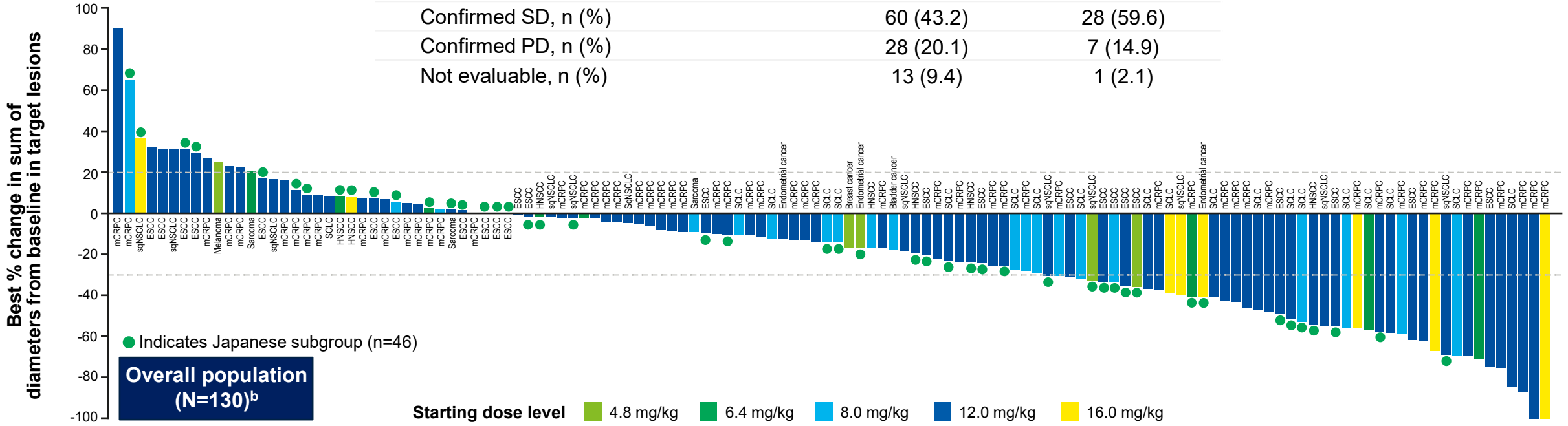
Baseline characteristics	Overall population (N=174)[1,a]	Japanese subgroup (n=56)[a]
Age, years, median (range)	66 (35–84)	65 (35–80)
Sex, n (%)		
Male	145 (83.3)	50 (89.3)
Female	29 (16.7)	6 (10.7)
ECOG PS, n (%)		
0	69 (39.7)	34 (60.7)
1	105 (60.3)	22 (39.3)
Country of enrollment, n (%)		
United States	118 (67.8)	0 (0)
Japan	56 (32.2)	56 (100)
Cancer type, n (%)		
ESCC	29 (16.7)	21 (37.5)
mCRPC	75 (43.1)	12 (21.4)
SCLC	22 (12.6)	5 (8.9)
sqNSCLC	18 (10.3)	5 (8.9)
Other	30 (17.2)	13 (23.2)

Patient disposition	Overall population (N=174)[1,a]	Japanese subgroup (n=56)[a]
Ongoing study treatment, n (%)	8 (4.6)	0 (0.0)
Patients by dose, n (%)		
0.8 mg/kg	5 (2.9)	2 (3.6)
1.6 mg/kg	5 (2.9)	2 (3.6)
3.2 mg/kg	7 (4.0)	2 (3.6)
4.8 mg/kg	5 (2.9)	3 (5.4)
6.4 mg/kg	8 (4.6)	3 (5.4)
8.0 mg/kg	20 (11.5)	6 (10.7)
12.0 mg/kg	108 (62.1)	34 (60.7)
16.0 mg/kg	16 (9.2)	4 (7.1)

Data cutoff: January 31, 2023.
[a]Includes patients with SCLC, ESCC, mCRPC, sqNSCLC, and other tumor types.
ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma; mCRPC, metastatic castration-resistant prostate cancer; SCLC, small cell lung cancer; sqNSCLC, squamous non-small cell lung cancer.
1. Patel MR, et al. ESMO 2023. Poster #690P.

Antitumor activity across tumor types

Responses by RECIST v1.1	Overall population (N=139)[1,a]	Japanese subgroup (n=47)[a]
Confirmed ORR, n (%)	38 (27.3)	11 (23.4)
95% CI	20.1–35.5	12.3–38.0
Confirmed CR, n (%)	1 (0.7)	0 (0.0)
Confirmed PR, n (%)	37 (26.6)	11 (23.4)
Confirmed SD, n (%)	60 (43.2)	28 (59.6)
Confirmed PD, n (%)	28 (20.1)	7 (14.9)
Not evaluable, n (%)	13 (9.4)	1 (2.1)



Data cutoff: January 31, 2023.

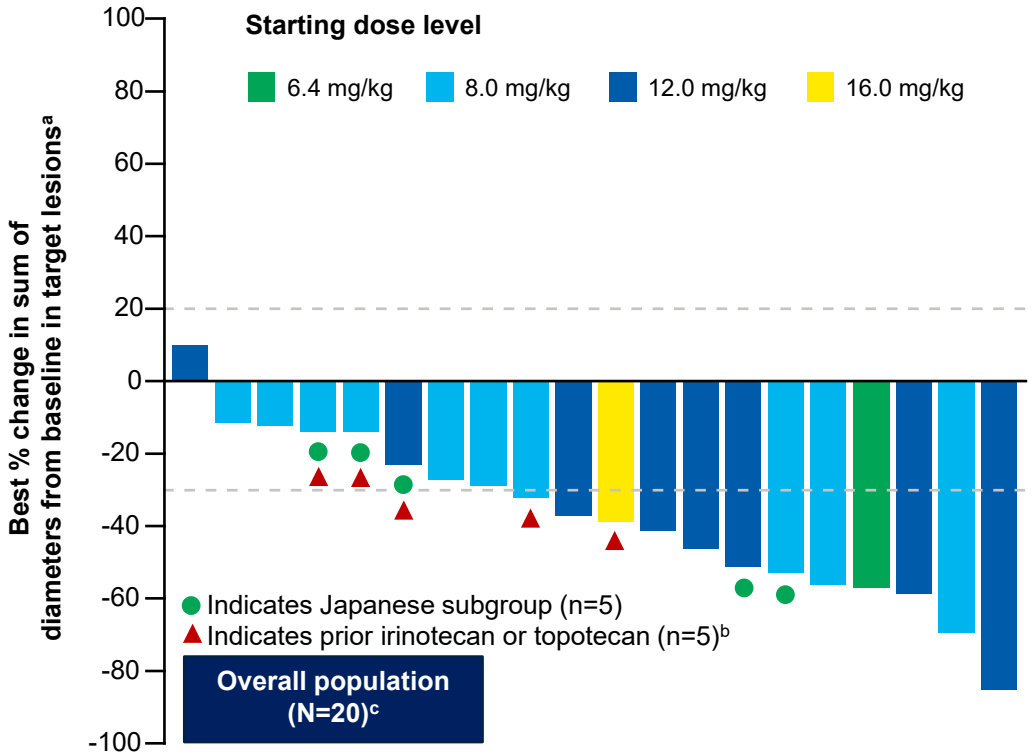
[a]ORR analysis was based on patients who received I-DXd at a dose of ≥4.8 mg/kg who had measurable disease at baseline. [b]All 139 patients were evaluable at baseline, but 9 patients who did not have any post-baseline tumor assessments were not included in the waterfall plot.

CI, confidence interval; CR, complete response; ESCC, esophageal squamous cell carcinoma; HNSCC, head and neck squamous cell carcinoma; mCRPC, metastatic castration-resistant prostate cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; SCLC, small cell lung cancer; SD, stable disease; sqNSCLC, squamous non-small cell lung cancer.

1. Patel MR, et al. ESMO 2023. Poster #690P.

Efficacy analysis in SCLC

SCLC

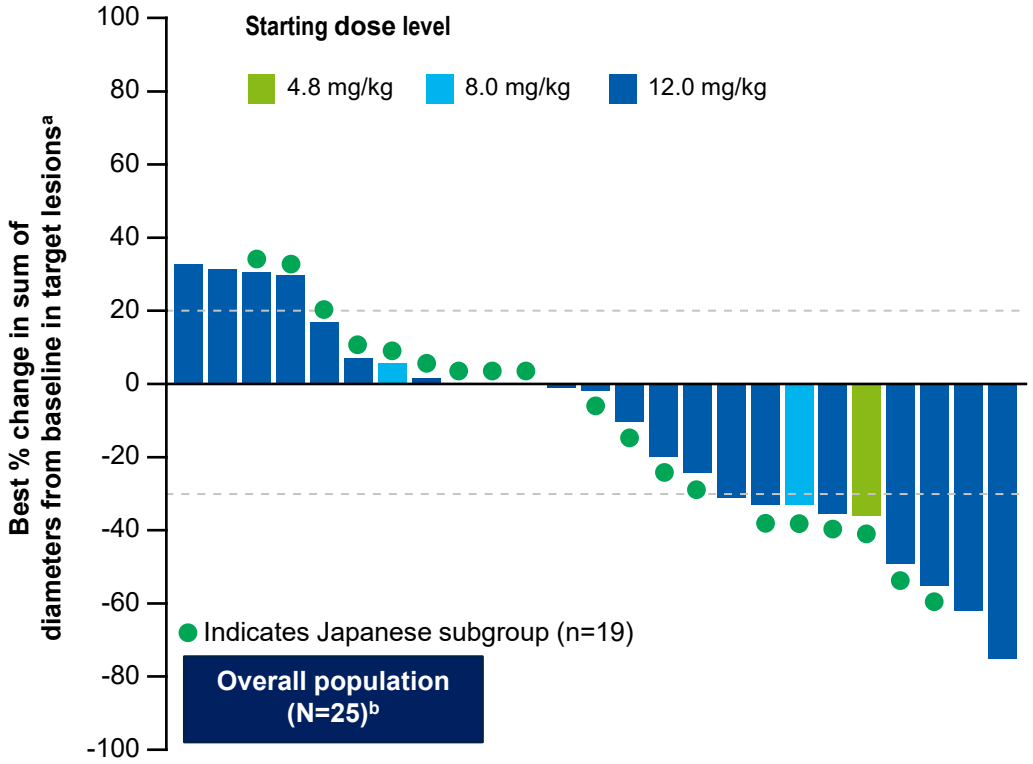


	Overall population[1,2]	Japanese subgroup
Efficacy population (≥4.8 mg/kg)	**n=21**	**n=5**
Confirmed ORR, n (%) 95% CI	11 (52.4) 29.8–74.3	2 (40.0) 5.3–85.3
Confirmed CR, n (%)	1 (4.8)	0 (0)
Confirmed PR, n (%)	10 (47.6)	2 (40.0)
Confirmed SD, n (%)	6 (28.6)	3 (60.0)
Confirmed PD, n (%)	2 (9.5)	0 (0)
Not evaluable, n (%)	2 (9.5)	0 (0)
TTR, months, median (95% CI)	1.2 (1.2–1.4)	1.2 (1.2–NE)
DOR, months, median (95% CI)	5.9 (2.8–7.5)	NE (4.4–NE)
Median PFS, months (95% CI)	5.6 (3.9–8.1)	4.7 (2.8–NE)
Median OS, months (95% CI)	12.2 (6.4–NE)	NE (NE–NE)
Follow-up, months, median (95% CI)	11.7 (4.6–12.9)	6.7 (2.3–NE)
Safety population (all doses)	**n=22**	**n=5**
Number of prior systemic regimens, median (range)	2 (1–7)	3 (2–6)
Platinum-based chemotherapy, n (%)	22 (100)	5 (100)
Immunotherapy, n (%)	18 (81.8)	3 (60.0)
Irinotecan or topotecan, n (%)	5 (22.7)[b]	4 (80.0)[b]
B7-H3 at baseline	**n=22**	**n=4**
B7-H3 combined mem/cyto H-score, median (range)[d]	115 (10–190)	23.5 (0–184)

Data cutoff: January 31, 2023.
[a]Change from baseline in target lesions was assessed per RECIST v1.1. [b]One patient received both. [c]All 21 patients were evaluable at baseline, but one did not have any post-baseline tumor assessments and so was not included in the waterfall plot. [d]The H-score quantifies biomarker expression by taking into account the proportion and the intensity of biomarker staining. Due to the unique immunostaining pattern of B7-H3 in SCLC, the B7-H3 expression level was quantified according to the combined mem/cyto H-score, in contrast to the membrane H-score used for other tumor types, which was based on membrane staining only.
B7-H3, B7 homolog 3; CI, confidence interval; CR, complete response; cyto, cytosol; DOR, duration of response; H-score, histochemical score; mem, membrane; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; SCLC, small cell lung cancer; SD, stable disease; TTR, time to response.
1. Johnson ML, et al. WCLC 2023. Oral 3258. 2. Patel MR, et al. ESMO 2023. Poster #690P.

Efficacy analysis in ESCC

ESCC

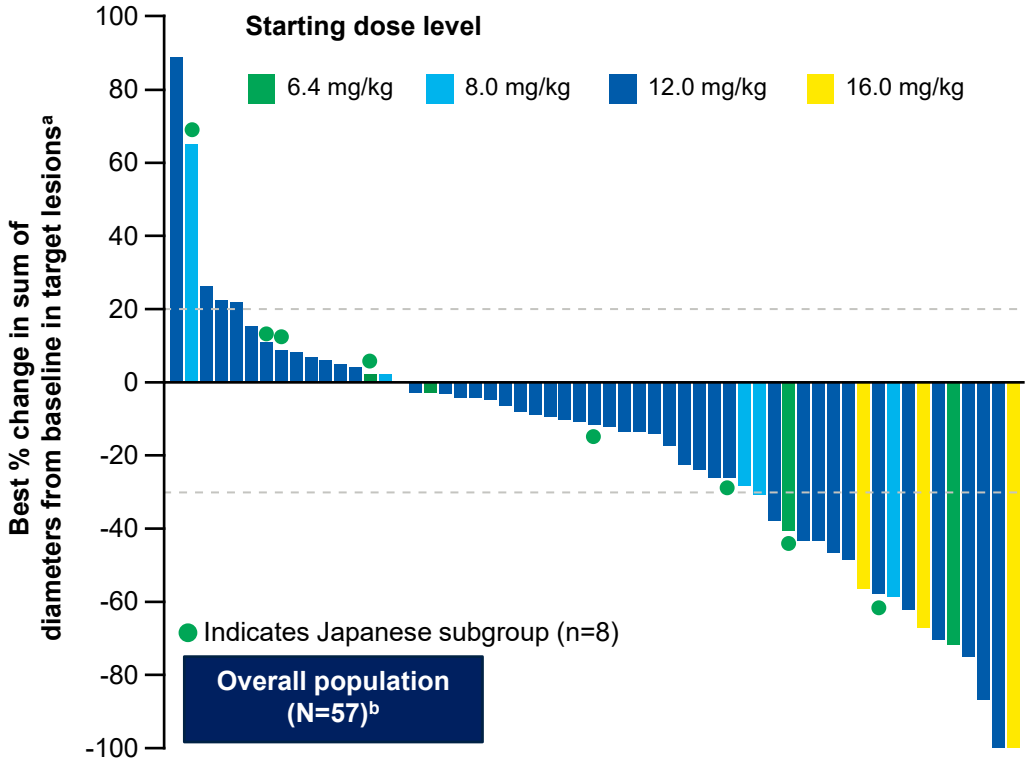


	Overall population[1]	Japanese subgroup
Efficacy population (≥4.8 mg/kg)	**n=28**	**n=20**
Confirmed ORR, n (%) 95% CI	6 (21.4) 8.3–41.0	4 (20.0) 5.7–43.7
Confirmed PR, n (%)	6 (21.4)	4 (20.0)
Confirmed SD, n (%)	13 (46.4)	12 (60.0)
Confirmed PD, n (%)	5 (17.9)	3 (15.0)
Not evaluable, n (%)	4 (14.3)	1 (5.0)
TTR, months, median (95% CI)	1.4 (1.2–NE)	1.6 (1.2–NE)
DOR, months, median (95% CI)	3.5 (2.4–NE)	2.8 (2.4–NE)
Median PFS, months (95% CI)	2.8 (2.1–5.5)	3.9 (2.5–5.5)
Median OS, months (95% CI)	7.0 (4.8–12.2)	9.7 (4.4–14.3)
Follow-up, months, median (95% CI)	14.9 (6.3–NE)	14.9 (8.1-NE)
Safety population (all doses)	**n=29**	**n=21**
Number of prior systemic regimens, median (range)	4 (1–7)	4 (2–7)
Platinum-based chemotherapy, n (%)	29 (100)	21 (100)
Taxane, n (%)	21 (72.4)	17 (81.0)
Immunotherapy, n (%)	27 (93.1)	20 (95.2)
B7-H3 baseline analysis for evaluable patients	**n=29**	**n=17**
B7-H3 membrane H-score at baseline, median (range)	190 (2–297)	207.0 (40–297)

Data cutoff: January 31, 2023.
[a]Change from baseline in target lesions was assessed per RECIST v1.1. [b]Of 28 patients with measurable disease at baseline, three did not have post-baseline tumor assessments, and so were not included in the waterfall plot.
B7-H3, B7 homolog 3; CI confidence interval; CR, complete response; DOR, duration of response; ESCC, esophageal squamous cell carcinoma; H-score, histochemical score; NE, not estimable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; SD, stable disease; TTR, time to response.
1. Patel MR, et al. ESMO 2023. Poster #690P.

Efficacy analysis in mCRPC

mCRPC

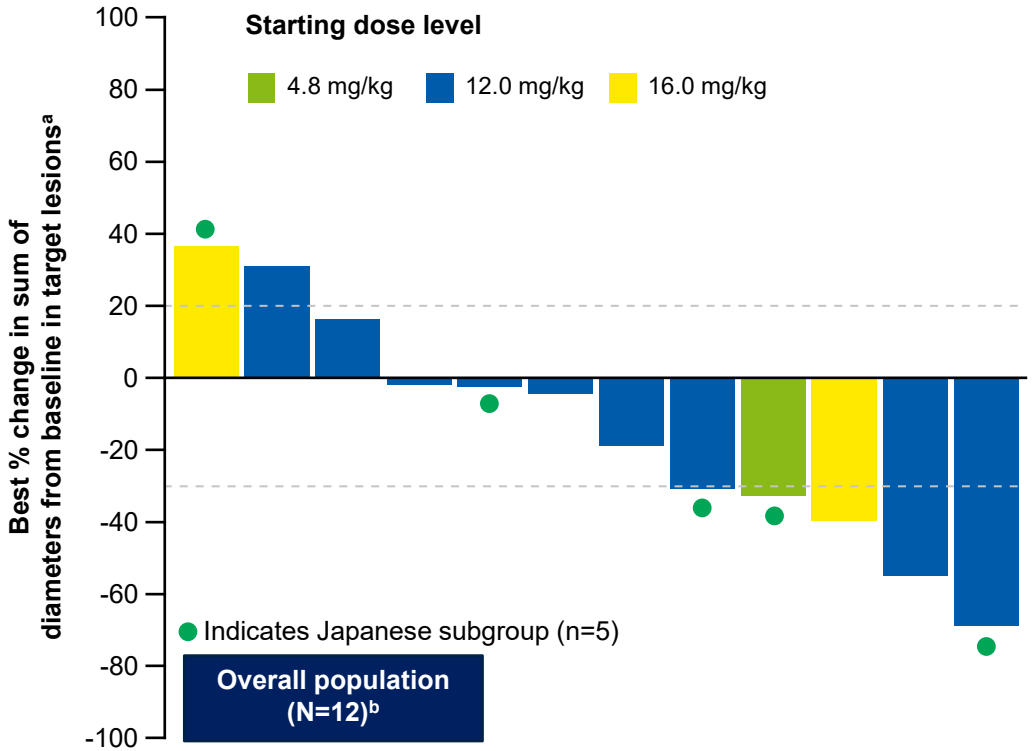


	Overall population[1]	Japanese subgroup
Efficacy population (≥4.8 mg/kg)	**n=59**	**n=8**
Confirmed ORR, n (%) 95% CI	15 (25.4) 15.0–38.4	1 (12.5) 0.3–52.7
Confirmed PR, n (%)	15 (25.4)	1 (12.5)
Confirmed SD, n (%)	28 (47.5)	5 (62.5)
Confirmed PD, n (%)	14 (23.7)	2 (25.0)
Not evaluable, n (%)	2 (3.4)	0 (0.0)
TTR, months, median (95% CI)	1.4 (1.2–2.6)	2.9 (NE–NE)
DOR, months, median (95% CI)	6.4 (3.0–10.0)	2.8 (NE–NE)
Median PFS, months (95% CI)	5.3 (4.1–6.9)[c]	4.4 (1.6–NE)[c]
Median OS, months (95% CI)	13.0 (10.3–16.0)[c]	11.4 (5.5–NE)[c]
Follow-up, months, median (95% CI)	16.6 (14.5–18.6)[c]	14.5 (5.0, NE)[c]
Safety population (all doses)	**n=75**	**n=12**
Number of prior systemic regimens, median (range)	6 (1–11)	5.5 (4–10)
Taxane, n (%)	61 (81.3)	12 (100)
NHA, n (%)	72 (96.0)	12 (100)
B7-H3 baseline analysis for evaluable patients	**n=75**	**n=7**
B7-H3 membrane H-score at baseline, median (range)	202 (5–300)	212.0 (140–300)

Data cutoff: January 31, 2023.
[a]Change from baseline in target lesions was assessed per RECIST v1.1. [b]Two patients did not have any post-baseline tumor assessments and were not included in the waterfall plot. [c]n=73 (overall population) and n=11 (Japanese subgroup), including patients with bone metastases who were not evaluable for response per RECIST v1.1.
B7-H3, B7 homolog 3; CI, confidence interval; DOR, duration of response; H-score, histochemical score; mCRPC, metastatic castration-resistant prostate cancer; NE, not estimable; NHA, novel hormonal agents; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; SD, stable disease; TTR, time to response.
1. Patel MR, et al. ESMO 2023. Poster #690P.

Efficacy analysis in sqNSCLC

sqNSCLC



	Overall population[1]	Japanese subgroup
Efficacy population (≥4.8 mg/kg)	**n=13**	**n=5**
Confirmed ORR, n (%) 95% CI	4 (30.8) 9.1–61.4	2 (40.0) 5.3–85.3
Confirmed PR, n (%)	4 (30.8)	2 (40.0)
Confirmed SD, n (%)	4 (30.8)	2 (40.0)
Confirmed PD, n (%)	2 (15.4)	1 (20.0)
Not evaluable, n (%)	3 (23.1)	0 (0.0)
TTR, months, median (95% CI)	1.3 (0.7–NE)	0.9 (0.7–NE)
DOR, months, median (95% CI)	4.1 (2.8–NE)	4.0 (3.0–NE)
Follow-up, months, median (95% CI)	5.2 (1.7–NE)	4.4 (1.7, NE)
Safety population (all doses)	**n=18**	**n=5**
Number of prior systemic regimens, median (range)	3 (1–12)	4 (3–6)
Platinum-based chemotherapy, n (%)	18 (100)	5 (100)
Immunotherapy, n (%)	18 (100)	5 (100)
Taxane, n (%)	16 (88.9)	4 (80.0)
B7-H3 baseline analysis for evaluable patients	**n=18**	**n=2**
B7-H3 membrane H-score at baseline, median (range)	42 (0–210)	200.0 (190–210)

Data cutoff: January 31, 2023.

[a]Change from baseline in target lesions was assessed per RECIST v1.1. [b]One patient did not have any post-baseline tumor assessments and was not included in the waterfall plot. Since enrollment in the sqNSCLC cohort is ongoing, analyses of PFS and OS in this cohort are not yet mature.

B7-H3, B7 homolog 3; CI, confidence interval; DOR, duration of response; H-score, histochemical score; NE, not estimable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; SD, stable disease; sqNSCLC, squamous non-small cell lung cancer; TTR, time to response.

1. Patel MR, et al. ESMO 2023. Poster #690P.

Overall safety summary

	Overall population (N=174)[1,a]	Japanese subgroup (n=56)[a]
Treatment duration, weeks, median (range)	12.3 (0.1–74.3)	12.3 (0.1–45)
Any TEAEs[b], n (%)	172 (98.9)	56 (100)
TEAE of CTCAE grade ≥3, n (%)	76 (43.7)	22 (39.3)
TEAE associated with drug discontinuation, n (%)	14 (8.0)[c]	5 (8.9)[d]
TEAE associated with dose interruption, n (%)	38 (21.8)	15 (26.8)
TEAE associated with dose reduction, n (%)	18 (10.3)	7 (12.5)
Treatment-related TEAE associated with death, n (%)	1 (0.6)	1 (1.8)

- The 16.0 mg/kg cohort was closed due to the observed clinical risk:benefit ratio in the overall population: higher rates of serious and grade ≥3 TEAEs occurred within a shorter median treatment duration than in the 8.0 and 12.0 mg/kg cohorts

Data cutoff: January 31, 2023.
[a]Includes patients with SCLC, ESCC, mCRPC, sqNSCLC and other tumor types. [b]Adverse events were coded using MedDRA, version 25.1. [c]The most common TEAEs associated with discontinuation in the overall population were pneumonitis (n=3) and ILD (n=2). [d]The most common TEAE associated with discontinuation in the Japanese subgroup was ILD (n=2).
CTCAE, Common Terminology Criteria for Adverse Events; ESCC, esophageal squamous cell carcinoma; mCRPC, metastatic castration-resistant prostate cancer; SCLC, small cell lung cancer; sqNSCLC, squamous non-small cell lung cancer; TEAE, treatment-emergent adverse event.
1. Patel MR, et al. ESMO 2023. Poster #690P.

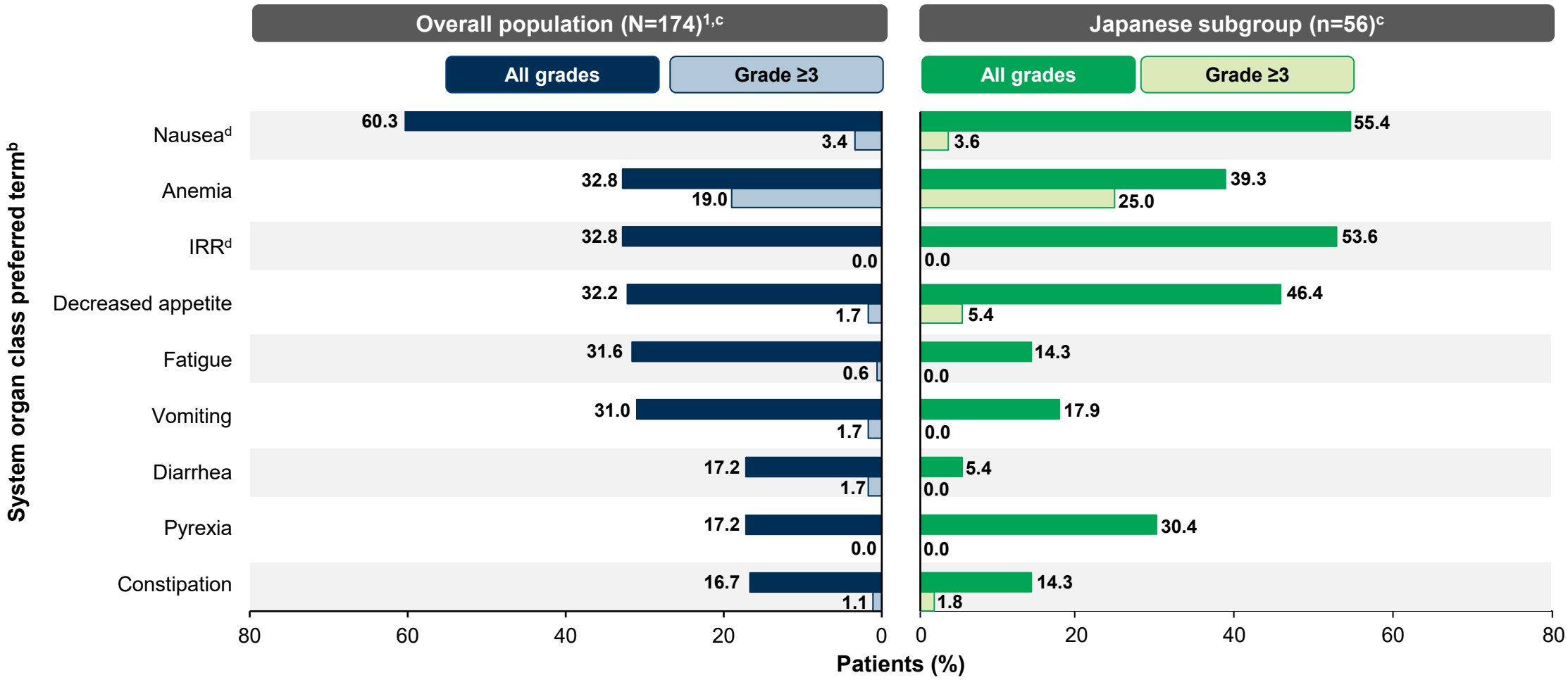
Incidence of ILD

Adjudicated ILD, n (%) (All were adjudicated as treatment-related)	Overall population (N=144)[1,a]			Japanese subgroup (n=44)[a]		
	8.0 mg/kg	12.0 mg/kg	16.0 mg/kg	8.0 mg/kg	12.0 mg/kg	16.0 mg/kg
Total confirmed ILD cases	10 (6.9)			6 (13.6)		
Grade 1	1 (0.7)	5 (3.5)	1 (0.7)	1 (2.3)	3 (6.8)	0
Grade 2	0	1 (0.7)	0	0	0	0
Grade 3	0	0	0	0	0	0
Grade 4	0	1 (0.7)	0	0	1 (2.3)	0
Grade 5	0	0	1 (0.7)	0	0	1 (2.3)

- Incidence of ILD was consistent with previous reports
  - One patient with endometrial cancer who received I-DXd at 16.0 mg/kg and was in the Japanese subgroup experienced Grade 5 ILD[1]

Data cutoff: January 31, 2023.
[a]Includes patients with SCLC, ESCC, mCRPC, sqNSCLC, and other tumor types, treated with I-DXd doses of 8.0–16.0 mg/kg. No cases of ILD were reported in patients treated with I-DXd doses ≤6.4 mg/kg.
ESCC, esophageal squamous cell carcinoma; ILD, interstitial lung disease; mCRPC, metastatic castration-resistant prostate cancer; SCLC, small cell lung cancer; sqNSCLC, squamous non-small cell lung cancer.
1. Patel MR, et al. ESMO 2023. Poster #690P.

Most common TEAEs (≥15%)[a] during I-DXd treatment



Data cutoff: January 31, 2023.

[a]Cutoff based on overall population. [b]Adverse events were coded using MedDRA, version 25.1. [c]Includes patients with SCLC, ESCC, mCRPC, sqNSCLC and other tumor types. [d]Prophylactic premedication for nausea, vomiting, and IRR was not permitted for primary prophylaxis during Cycle 1 of dose escalation.

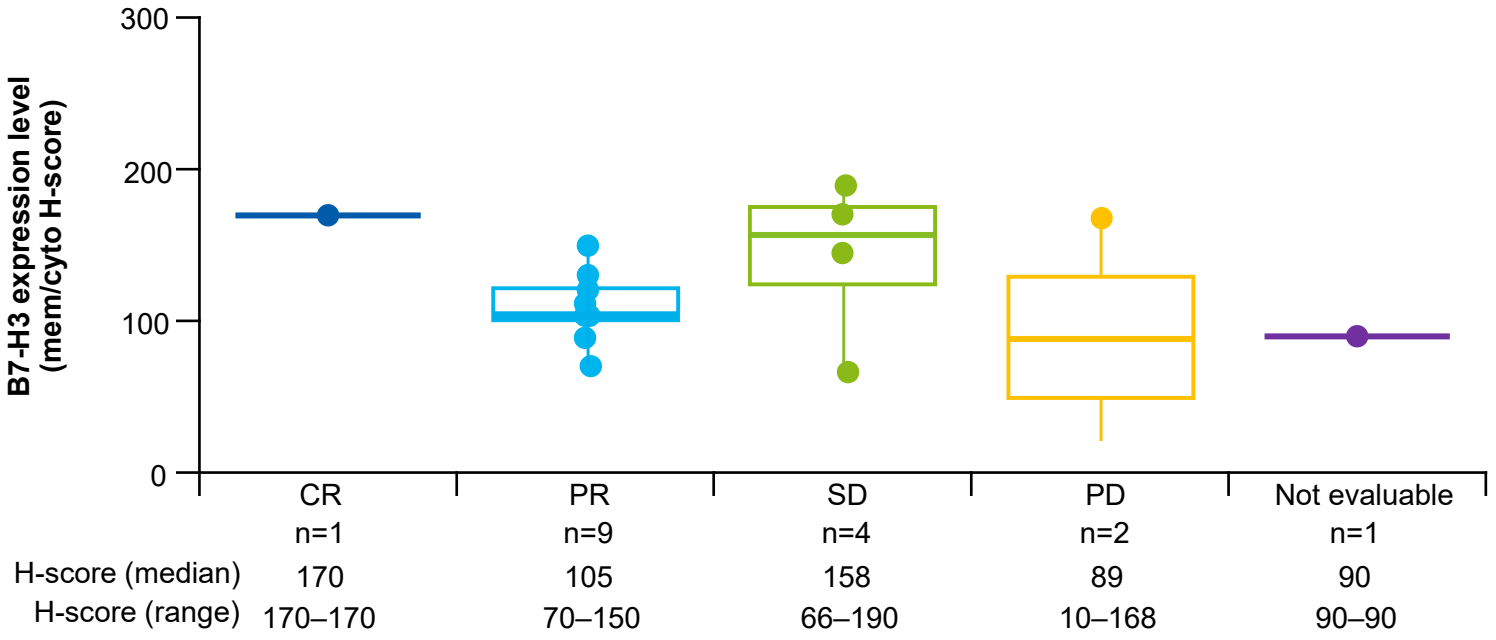
ESCC, esophageal squamous cell carcinoma; IRR, infusion-related reaction; MedDRA, Medical Dictionary for Regulatory Activities; mCRPC, metastatic castration-resistant prostate cancer; SCLC, small cell lung cancer; sqNSCLC, squamous non-small cell lung cancer; TEAE, treatment-emergent adverse event.

1. Patel MR, et al. ESMO 2023. Poster #690P.

B7-H3 correlative analysis in SCLC[a] for the overall population[1]

SCLC

SCLC : B7-H3 level by BOR status for evaluable patients (n=17)[1,b]



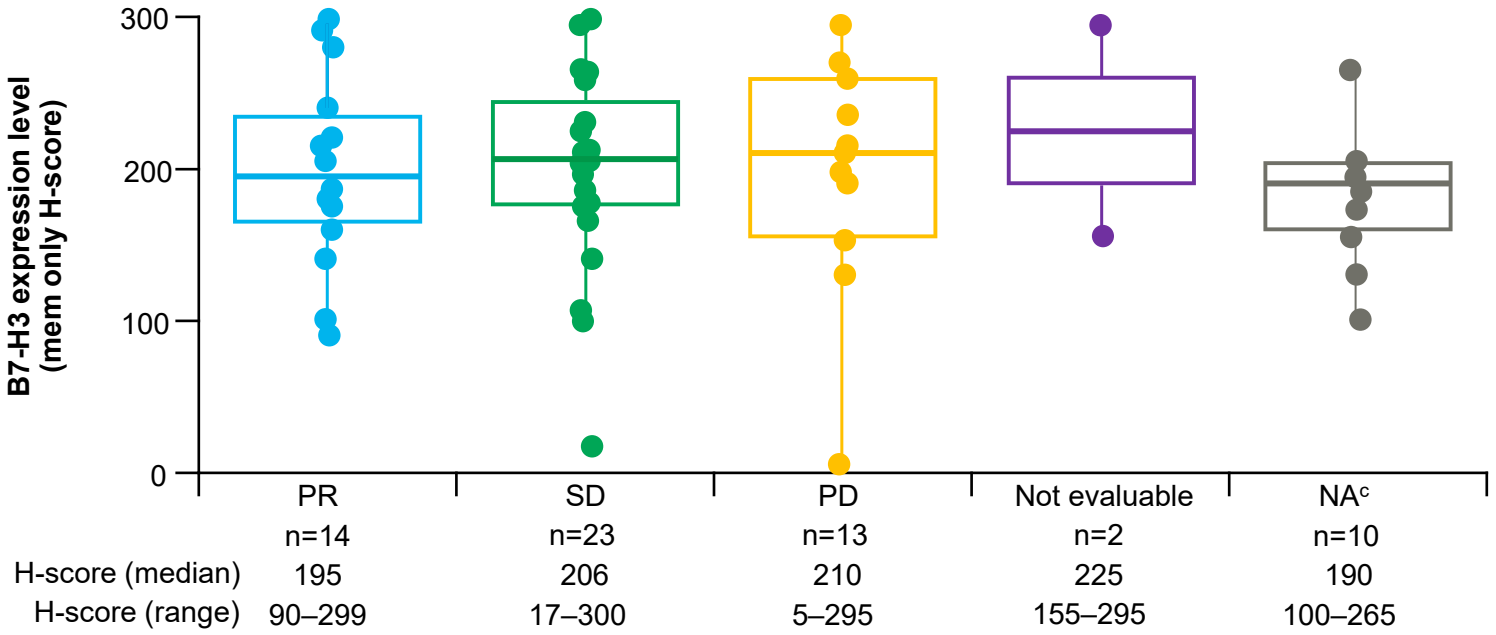
	Low B7-H3[b] (n=8)	High B7-H3[b] (n=9)
B7-H3 mem/cyto H-score at baseline, median (range)	115 (10–190)	
H-score at baseline, range	10–105	115–190
Unconfirmed ORR, n (%)	5 (62.5)	5 (55.6)
Median PFS, months (95% CI)	5.8 (0.7–NE)	5.3 (1.4–NE)
Median OS, months (95% CI)	12.2 (5.8–NE)	6.9 (2.8–NE)

Data cutoff: January 31, 2023.
[a]Enrollment and correlation analyses in the ESCC and sqNSCLC cohorts are ongoing. [b]At baseline. Low B7-H3 was defined as an H-score lower than the median H-score in the SCLC B7-H3-evaluable population. High B7-H3 was defined as an H-score higher than the median H-score in the SCLC B7-H3-evaluable population.
B7-H3, B7 homolog 3; BOR, best overall response; CI, confidence interval; CR, complete response; cyto, cytosol; ESCC, esophageal squamous cell carcinoma; H-score, histochemical score; mem, membrane; NE, not estimable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SCLC, small cell lung cancer; SD, stable disease; sqNSCLC, squamous non-small cell lung cancer.
1. Patel MR, et al. ESMO 2023. Poster #690P.

B7-H3 correlative analysis in mCRPC[a] for the overall population[1]

mCRPC

mCRPC : B7-H3 level by BOR status for evaluable patients (n=62)[1,b]



	Low B7-H3[b] (n=31)	High B7-H3[b] (n=31)
B7-H3 mem/cyto H-score at baseline, median (range)	202 (5–300)	
H-score at baseline, range	5–200	204–300
Unconfirmed ORR, n (%)	7/25 (28.0)	7/27 (25.9)
Median PFS, months (95% CI)	5.5 (3.3–9.6)	4.4 (2.9–5.7)
Median OS, months (95% CI)	13.5 (9.6–20.2)	13.0 (8.3–16.6)

Data cutoff: January 31, 2023.

[a]Enrollment and correlation analyses in the ESCC and sqNSCLC cohorts are ongoing. [b]At baseline. Low B7-H3 was defined as an H-score lower than the median H-score in the mCRPC B7-H3-evaluable population. High B7-H3 was defined as an H-score higher than the median H-score in the mCRPC B7-H3-evaluable population. [c]NA, not applicable, i.e. patients who do not have measurable disease at baseline and were not included in the ORR analysis.

B7-H3, B7 homolog 3; BOR, best overall response; CI, confidence interval; cyto, cytosol; ESCC, esophageal squamous cell carcinoma; H-score, histochemical score; mem, membrane; mCRPC, metastatic castration-resistant prostate cancer; NA, not applicable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; sqNSCLC, squamous non-small cell lung cancer.

1. Patel MR, et al. ESMO 2023. Poster #690P.

Conclusions

Efficacy[a]

- In the overall population[1] and Japanese subgroup, I-DXd showed durable efficacy in heavily pretreated patients with advanced solid tumors, including SCLC, ESCC, mCRPC, and sqNSCLC
- Efficacy data were consistent between the overall population[1] and the Japanese subgroup

Safety[a]

- In the overall population[1] and Japanese subgroup, no new safety signals were observed; the safety profile was manageable and tolerable with routine clinical practice and established dose-modification guidelines
- Safety data were consistent between the overall population[1] and the Japanese subgroup
- Incidence of ILD was consistent with previous data

B7-H3 correlative analysis

- In the overall population, there was no trend of correlation between B7-H3 expression and efficacy in the SCLC and mCRPC subsets[1]

Conclusion

- These data support further clinical investigation of I-DXd, including in the ongoing Phase 2 study of patients with advanced SCLC with 1–3 prior lines of therapy (NCT05280470)

[a]Patient numbers were small in the Japanese subgroup, so results in relation to the overall population should be interpreted with caution.
B7-H3, B7 homolog 3; ESCC, esophageal squamous cell carcinoma; ILD, interstitial lung disease; mCRPC, metastatic castration-resistant prostate cancer; SCLC, small cell lung cancer; sqNSCLC, squamous non-small cell lung cancer.
1. Patel MR, et al. ESMO 2023. Poster #690P.

Study sites

We would like to thank all the patients and their families, clinicians, and staff who participated in this study.

United States

- Dana Farber Cancer Institute, Boston, MA
- Florida Cancer Specialists, Sarasota, FL
- Henry Ford Hospital, Detroit, MI
- John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ
- MD Anderson Cancer Center, Houston, TX
- Memorial Sloan-Kettering Cancer Center, New York, NY
- Sarah Cannon Research Institute at HealthONE, Denver, CO
- Tennessee Oncology, Nashville, TN
- Washington University, Saint Louis, MO

Japan

- Aichi Cancer Center Hospital, Aichi
- Cancer Institute Hospital of JFCR, Tokyo
- National Cancer Center Hospital, Tokyo
- National Cancer Center Hospital East, Chiba
- Osaka University Hospital, Osaka
- Saitama Cancer Center, Saitama
- Shizuoka Cancer Center Hospital and Research Institute, Shizuoka
- Showa University Hospital, Tokyo

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