北京陈菊梅公益基金会
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Key updates on HLX43, an anti-PD-L1 ADC, in non-small cell lung cancer

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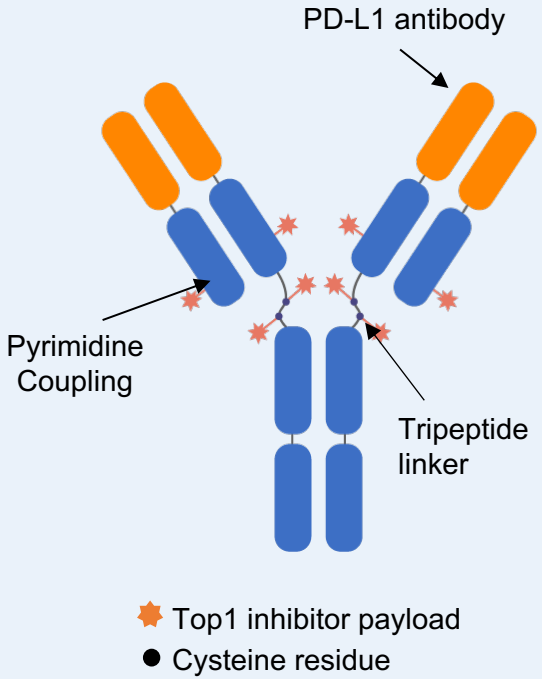
Background

- Despite the approval of multiple PD-1/PD-L1 inhibitors for advanced NSCLC, the majority of patients still face resistance, including both de novo and acquired resistance.[1, 2]
- By specifically delivering cytotoxic payloads to tumor cells, antibody-drug conjugates (ADCs) represent an effective strategy for patients who are refractory to PD-1/PD-L1 therapies.[3]
- HLX43 is the second PD-L1-targeting ADC in global development.

Molecular components of HLX43



Key Features

- High-affinity, internalizable PD-L1 antibody
- Highly stable linker in circulating blood
- Cleavable and **TME-activatable tripeptide linker**
- Potent cytotoxic payload Top1 inhibitor (DAR=8)

1. Sharma P, et al. Cell. 2023;186(8):1652-1669. 2. Doroshow DB, et al. Nat Rev Clin Oncol. 2021;18(6):345-362. 3. Fu Z, et al. Sig Transduct Target Ther. 2022;7(1):93.

DAR, drug-to-antibody ratio; NSCLC, non-small-cell lung cancer; PD-L1, programmed cell death 1-ligand 1; PD-1, programmed cell death 1; TME, tumor microenvironment; Top1, topoisomerase 1.

Data Analysis

cutoff date 2025/10/22

HLX43-FIH101

Key inclusion criteria

- For **phase 1a**, histologically or cytologically confirmed advanced malignant **solid tumors**
- For **phase 1b**, histologically or cytologically confirmed advanced **NSCLC** refractory or not amenable to standard therapy

Screening

Phase 1a CN only	Phase 1b CN only
4.0 mg/kg 3.0 mg/kg 2.5 mg/kg 2.0 mg/kg 1.0 mg/kg 0.5 mg/kg HLX43, Q3W N=20	**3.0 mg/kg Q3W N=20** **2.5 mg/kg Q3W N=~50** **2.0 mg/kg Q3W N=~50**

HLX43-NSCLC201

Key inclusion criteria

- Locally advanced or metastatic NSCLC confirmed by histology or cytology, and not suitable for radical treatment
- Has failed at least one prior line of standard therapy

R 1:1

Part A Global	Part B Global
2.5 mg/kg HLX43, Q3W N=50 **2.0 mg/kg HLX43, Q3W N=50**	**Selected dose HLX43, Q3W N=143**

Pooled analysis to evaluate the efficacy of RP2/3D dosing

- **2.5 mg/kg NSCLC HLX43, Q3W N=85**
- **2.0 mg/kg NSCLC HLX43, Q3W N=89**

CN, China; N, number; NSCLC, non-small cell lung cancer; RP2/3D, recommended phase 2/3 dose; Q3W, every 3 weeks.

Baseline demographic and disease characteristics

Data cutoff: Oct 22, 2025
Median follow-up: ~4.0 months

	2.0 mg/kg (n = 89)	2.5 mg/kg (n = 85)
Median age (range), years	59 (36–75)	62 (43–74)
Male, n (%)	66 (74.2)	62 (72.9)
ECOG PS, n (%)		
0	20 (22.5)	24 (28.2)
1	69 (77.5)	61 (71.8)
Smoking status, n (%)		
Never	38 (42.7)	33 (38.8)
Current	6 (6.7)	8 (9.4)
Former	45 (50.6)	44 (51.8)
NSCLC subtype		
Squamous	42 (47.2)	40 (47.1)
Non-squamous	47 (52.8)	45 (52.9)
EGFR wild type	29 (32.6)	26 (30.6)
EGFR mutant	18 (20.2)	19 (22.4)
Metastases, n (%)		
Bone	23 (25.8)	22 (25.9)
Brain	12 (13.5)	6 (7.1)
Liver	12 (13.5)	10 (11.8)

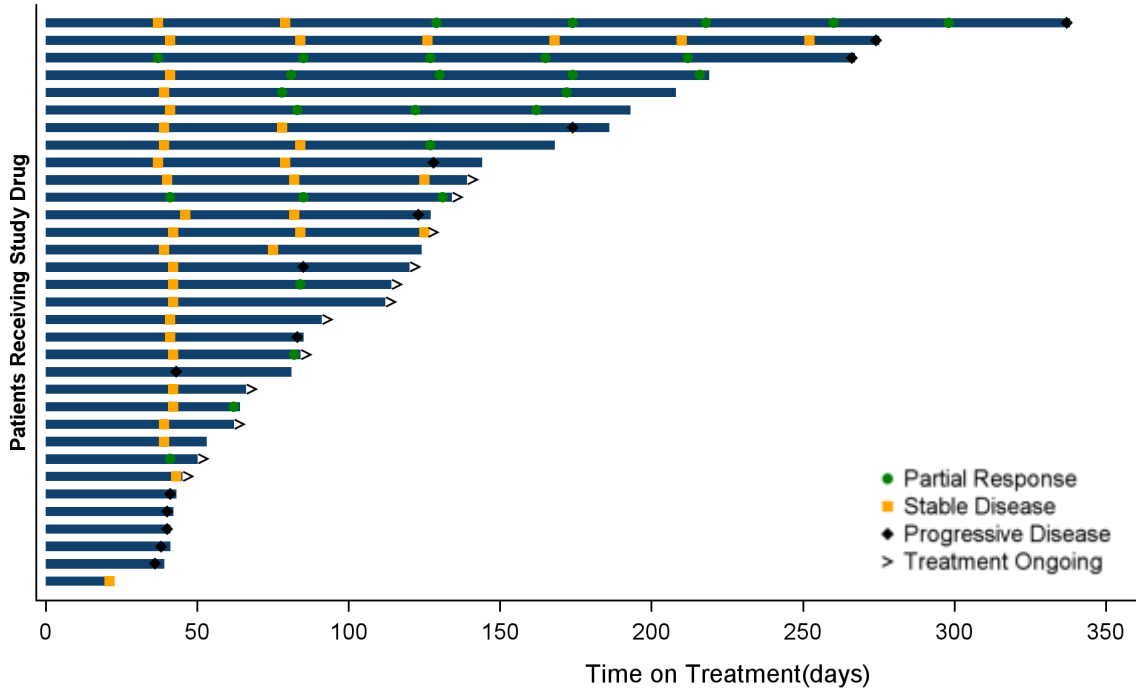
	2.0 mg/kg (n = 89)	2.5 mg/kg (n = 85)
PD-L1 expression by TPS[#], n (%)		
TPS < 1%	31 (34.8)	28 (32.9)
1% ≤ TPS < 50%	20 (22.5)	22 (25.9)
TPS ≥ 50%	10 (11.2)	6 (7.1)
Not available	28 (31.5)	29 (34.1)
Prior lines of therapy		
1	25 (28.1)	27 (31.8)
2	29 (32.6)	27 (31.8)
3	15 (16.9)	21 (24.7)
≥ 4	20 (22.5)	10 (11.8)
Median, range	2 (1–7)	2 (1–7)
Median, range for squamous	2 (1–7)	2 (1–6)
Median, range for non-squamous	2 (1–6)	2 (1–7)
EGFR wild type	2 (1–6)	2 (1–6)
EGFR mutant	3 (1–6)	2 (1–7)
Prior platinum-based chemo, n (%)	89 (100.0)	85 (100.0)
Prior immunotherapy, n (%)	71 (79.8)	64 (80.0)
Prior target therapy, n (%)	34 (38.2)	27 (31.8)
Prior docetaxel, n (%)	26 (29.2)	15 (17.6)

[#] Detected with SP263.

chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; ITT, intention-to-treat; NSCLC, non-small cell lung cancer; PD-L1, programmed cell death 1 ligand 1; RES, response evaluable set; SS, safety set; TPS, tumor proportion score.

Efficacy in squamous NSCLC patients per RECIST v1.1

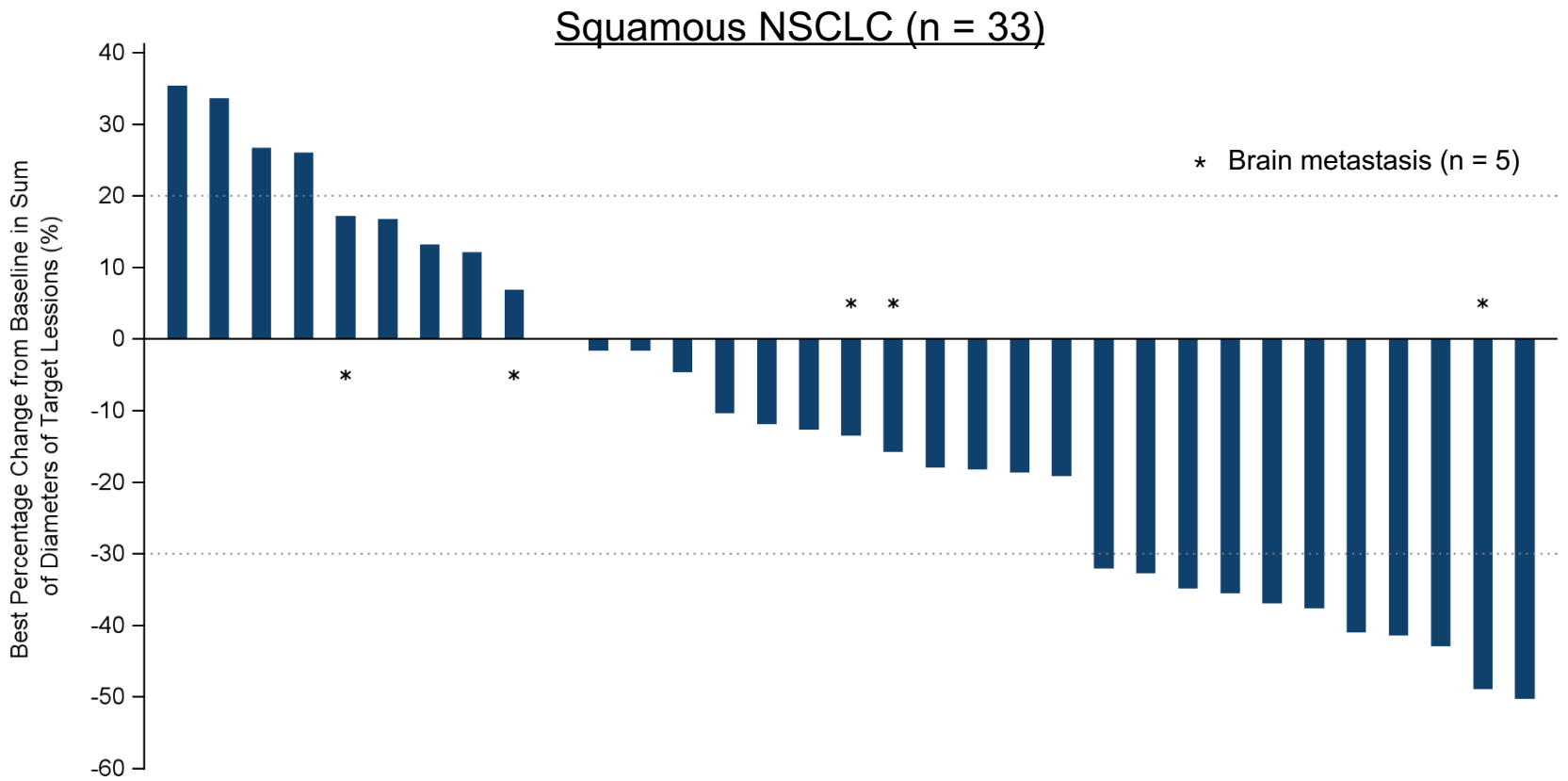
Efficacy*	2.0 mg/kg squamous NSCLC (n = 33)
CR, n (%)	0
PR, n (%)	11 (33.3)
SD, n (%)	14 (42.4)
PD, n (%)	6 (18.2)
NE, n (%)	2 (6.1)
ORR, % (95% CI)	33.3 (18.0–51.8)
DCR, % (95% CI)	75.8 (57.7–88.9)



* Unconfirmed tumor response as assessed by investigator in the response-evaluable set.

CI, confidence interval; CR, complete response; DCR, disease control rate; NE, not evaluable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

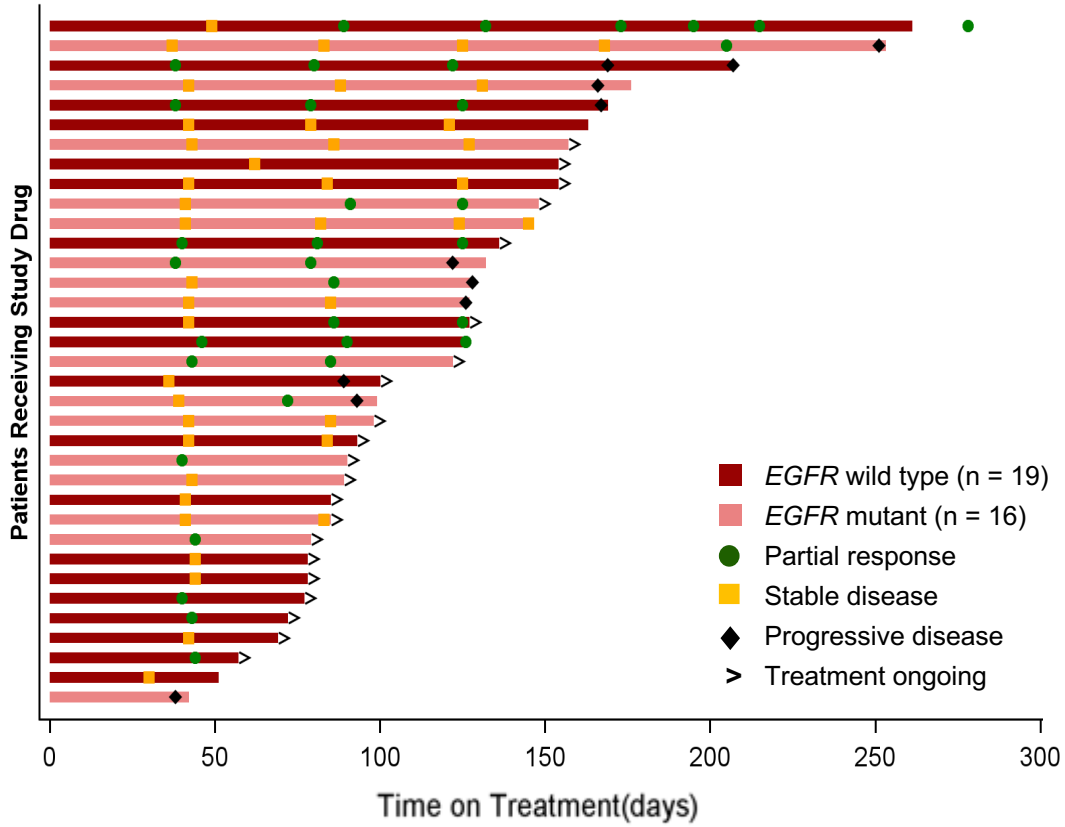
Efficacy in squamous NSCLC patients per RECIST v1.1



NSCLC, non-small cell lung cancer; RECIST, Response Evaluation Criteria in Solid Tumors.

Efficacy in non-squamous NSCLC patients per RECIST v1.1

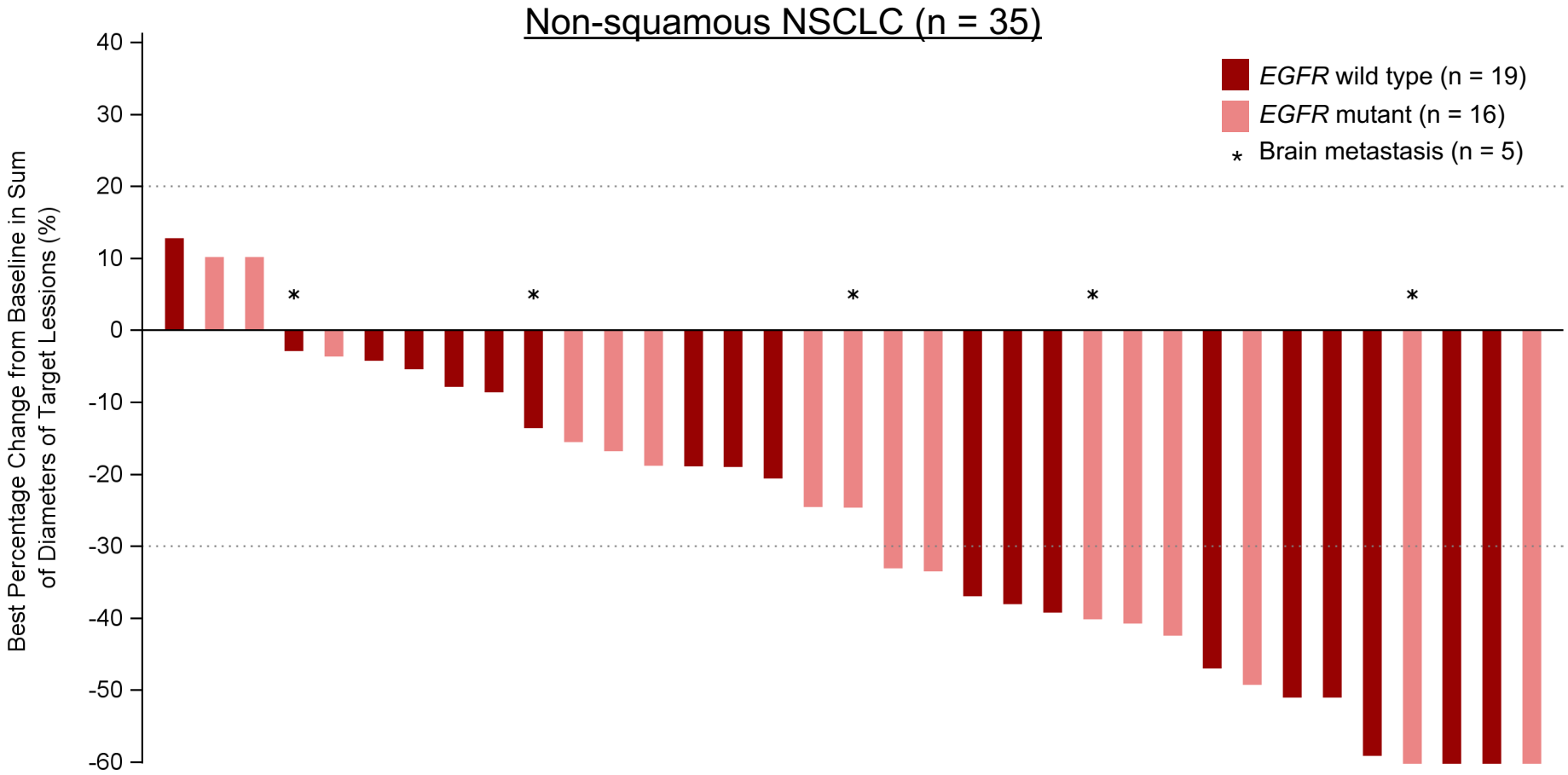
Efficacy*	2.5 mg/kg Non-squamous NSCLC (n = 35)
CR, n (%)	0
PR, n (%)	17 (48.6)
SD, n (%)	16 (45.7)
PD, n (%)	1 (2.9)
NE, n (%)	1 (2.9)
ORR, % (95% CI)	48.6 (31.4–66.0)
DCR, % (95% CI)	94.3 (80.8–99.3)



* Unconfirmed tumor response as assessed by investigator in the response-evaluable set.

CI, confidence interval; CR, complete response; DCR, disease control rate; EGFR, epidermal growth factor receptor; NE, not evaluable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Efficacy in non-squamous NSCLC patients per RECIST v1.1



EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; RECIST, Response Evaluation Criteria in Solid Tumors.

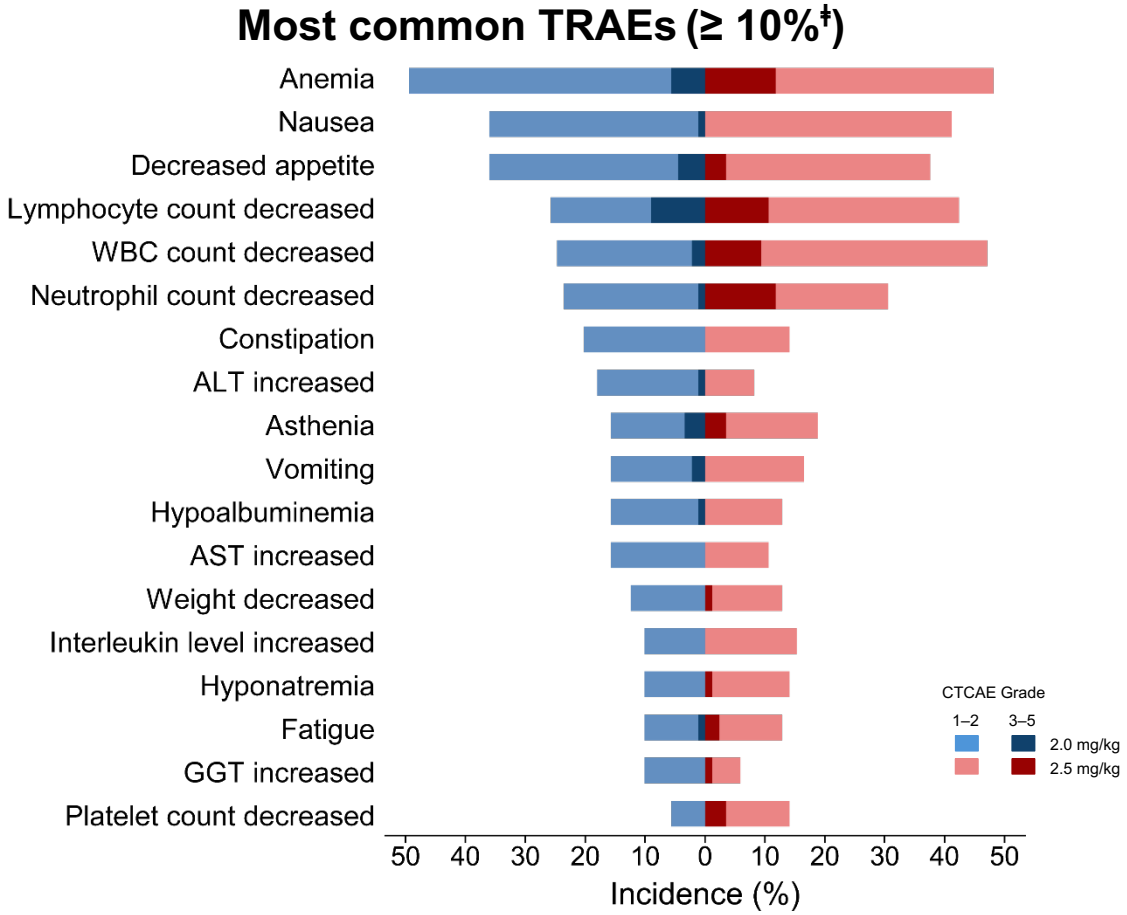
Subgroup analysis of tumor response per RECIST v1.1

Tumor response	Efficacy under RP2/3 dosing		WCLC reported results (0.5–4 mg/kg)	
	ORR % (95% CI)	DCR % (95% CI)	ORR % (95% CI)	DCR % (95% CI)
NSCLC subtype				
Squamous 2.0 mg/kg (n = 33)	33.3 (18.0–51.8)	75.8 (57.7–88.9)	28.6 (13.2–48.7)	82.1 (63.1–93.9)
Docetaxel failed (≥ 3L) (n = 13)	38.5 (13.9–68.4)	84.6 (54.6–98.1)	30.0 (6.7–65.3)	80.0 (44.4–97.5)
Non-squamous 2.5 mg/kg (n = 35)	48.6 (31.4–66.0)	94.3 (80.8–99.3)	46.2 (26.6–66.6)	96.2 (80.4–99.9)
EGFR wild type (n = 19)	47.4 (24.4–71.1)	94.7 (74.0–99.9)	46.7 (21.3–73.4)	93.3 (68.1–99.8)
EGFR mutant (n = 16)	50.0 (24.7–75.3)	93.8 (69.8–99.8)	45.5 (16.7–76.6)	90.9 (58.7–99.8)
Brain metastasis				
Yes (n = 10)	30.0 (6.7–65.2)	90.0 (55.5–99.7)	36.4 (10.9–69.2)	100 (71.5–100)
No (n = 58)	43.1 (30.2–56.9)	84.5 (72.6–92.0)	37.2 (23.0–53.3)	83.7 (69.3–93.2)
PD-L1 expression by TPS				
TPS ≥ 1% (n = 25)	44.0 (24.0–66.7)	84.0 (63.9–95.5)	34.4 (18.6–53.2)	87.5 (71.0–96.5)
TPS < 1% (n = 43)	39.5 (25.5–55.3)	86.0 (72.1–94.1)	38.1 (18.1–61.6)	85.7 (63.7–97.0)

CI, confidence interval; DCR, disease control rate; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD-L1, programmed cell death 1 ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors; TPS, tumor proportion score.

Safety and tolerability

Safety*, n (%)	2.0 mg/kg (n = 89)	2.5 mg/kg (n = 85)
Any TRAE	73 (82.0)	76 (89.4)
Grade ≥3	22 (24.7)	24 (28.2)
Most common Grade ≥3 (≥ 10% in either group)		
Lymphocyte count decreased	8 (9.0)	9 (10.6)
Anemia	5 (5.6)	10 (11.8)
Neutrophil count decreased	1 (1.1)	10 (11.8)
TRAE leading to Tx interruption	15 (16.9)	23 (27.1)
TRAE leading to Tx discontinuation	2 (2.2)	3 (3.5)
TRAE leading to Tx reduction	2 (2.2)	6 (7.1)
TRAE leading to death	0	1 (1.2)#



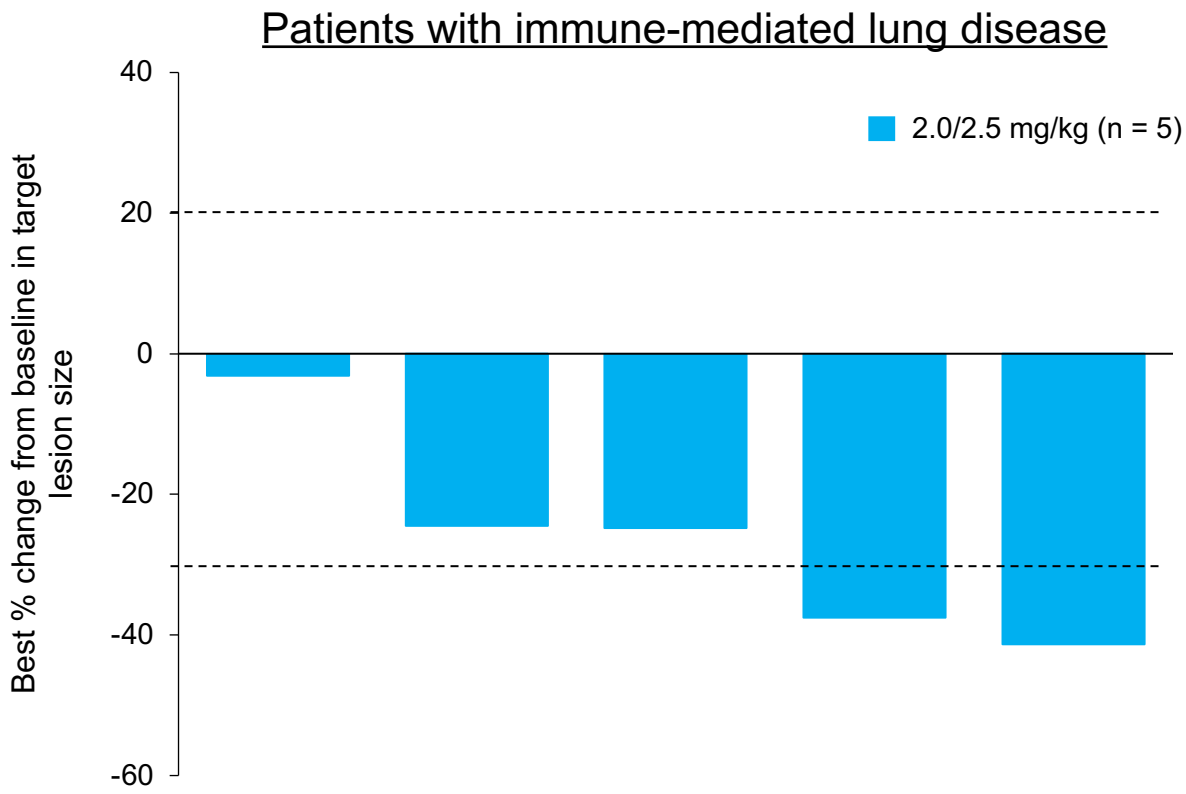
* Interstitial lung disease was reported as grade 3 in 2 patients in each group, and as grade 2 in 1 patient in each group; all are in recovery. # due to respiratory failure. ǂ ≥10% in either group.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; GGT, gamma-glutamyl transferase; TRAE, treatment-related adverse event; Tx, treatment; WBC, white blood cell.

Immune-related adverse events

	2.0 mg/kg (n = 89)	2.5 mg/kg (n = 85)
Any irAE, n (%)	10 (11.2)	7 (8.2)
Most common irAEs		
Immune-mediated lung disease	3 (3.4)	2 (2.4)
Grade 2	1 (1.1)	0
Grade 3	1 (1.1)	2 (2.4)
Grade 4	1 (1.1)	0
Grade 5	0	0

Confirmed ORR of **40% (2/5)** and **100% tumor shrinkage** in patients with immune-mediated lung disease indicated that **HLX43 is capable of eliciting immunotherapeutic effects** in addition to payload-mediated cytotoxic tumor cell killing.



irAE, immune-related adverse event; ORR, objective response rate.

Conclusions

- **Outstanding efficacy in NSCLC with HLX43 RP2/3D dosing**
  - ✓ **IO- and chemo-treated Squamous NSCLC**
    - ✓ ORR: 33.3%
    - ✓ Docetaxel failed (≥ 3L) ORR: 38.5%
  - ✓ **IO- and chemo-treated, *EGFR* WT Non-squamous NSCLC**
    - ✓ ORR: 47.4%
  - ✓ **NSCLC with brain metastasis:** ORR 30.0%; DCR 90.0%
- **Biomarker independent:** efficacy observed irrespective of *EGFR* mutation status or PD-L1 expression level
- **Favorable safety profile with low hematologic toxicities**

HLX43 demonstrated promising efficacy along with manageable safety in advanced NSCLC. Further investigation of HLX43 for this disease indication is warranted.

chemo, chemotherapy; DCR, disease control rate; EGFR, epidermal growth factor receptor; IO, immunotherapy; L, line; NSCLC, non-small-cell lung cancer; ORR, objective response rate; PD-L1, programmed cell death 1 ligand 1; WT, wild type.

Thank you!