2026 ASCO® ANNUAL MEETING

Efficacy and Safety of HLX43 (Anti-PD-L1 ADC) in Patients with Advanced Non-small Cell Lung Cancer

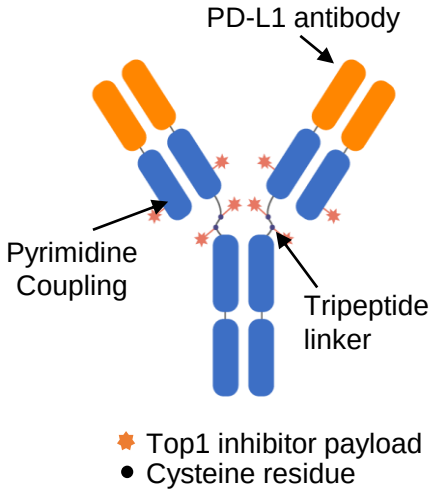
Investigators: Jie Wang, Jianjun Zhang, Ning Li, Rui Wan, Xin Wang, Shan Zeng, Lin Wu, Hua Zhong, Jingxun Wu, Runxiang Yang, Shaozhang Zhou, Guowu Wu, Bin Yang, Donglin Wang, Chuan Jin, Haifeng Liu, Xiaolong Yan, Fred.R. Hirsch, Jie He

Leading PI: Jie Wang, M.D
Presenter: Rui Wan, M.D
Affiliation: Department of Internal Medicine, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China.

Background

- The majority of NSCLC 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 demonstrated encouraging efficacy with a manageable safety in patients with advanced solid tumors, including CC, NPC, ESCC.

Molecular components of HLX43



- 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)

Here, we present the pooled findings from the phase 1 (HLX43-FIH101) and the global phase 2 study (HLX43-NSCLC201) investigating HLX43 in patients with NSCLC.

CC, cervical cancer; DAR, drug-to-antibody ratio; ESCC, esophageal squamous cell carcinoma; NPC, nasopharyngeal carcinoma; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; PD-1, programmed death-1; TME, tumor microenvironment; Top1, topoisomerase 1.

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.

Study design

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
China 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

Phase 1b
China only

- **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

- **2.5 mg/kg HLX43, Q3W n = 50**
- **2.0 mg/kg HLX43, Q3W n = 50**

Part B
Global

- **Selected dose HLX43, Q3W n = 143**

Pooled analysis to evaluate the efficacy in NSCLC patients

- **4.0 mg/kg HLX43, Q3W n = 5**
- **3.0 mg/kg HLX43, Q3W n = 23**
- **2.5 mg/kg HLX43, Q3W n = 85**
- **2.0 mg/kg HLX43, Q3W n = 89**
- **1.0 mg/kg HLX43, Q3W n = 3**

n, number; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks; R, randomization.

Baseline characteristics

Data cutoff: Feb 28, 2026
Median follow-up: 7.5 months

Of the total patients, 5 were from the United States, 2 from Australia, and the remainder from China.

	NSCLC (n = 205) 1, 2, 2.5, 3, 4 mg/kg
Median age (range), years	60 (36–75)
Male, n (%)	147 (71.7)
ECOG PS, n (%)	
0	54 (26.3)
1	151 (73.7)
Smoking status, n (%)	
Never	90 (43.9)
Current	15 (7.3)
Former	100 (48.8)
NSCLC subtype	
Squamous	95 (46.3)
Non-squamous	110 (53.7)
EGFR wild type	63 (30.7)
EGFR mutant	47 (22.9)
Metastases, n (%)	
Bone	57 (27.8)
Liver	28 (13.7)
Brain	28 (13.7)

	NSCLC (n = 205) 1, 2, 2.5, 3, 4 mg/kg
PD-L1 expression by TPS[#], n (%)	
TPS < 1%	85 (41.5)
1% ≤ TPS < 50%	66 (32.2)
TPS ≥ 50%	30 (14.6)
Not available	24 (11.7)
Prior lines of therapy, n (%)	
1	59 (28.8)
2	66 (32.2)
3	43 (21.0)
≥ 4	37 (18.0)
Median, (range)	2 (1–9)
Median, (range) for squamous	2 (1–7)
Median, (range) for non-squamous	2 (1–9)
EGFR wild type	2 (1–6)
EGFR mutant	3 (1–9)
Prior platinum-based chemo, n (%)	203 (99.0)
Prior immunotherapy, n (%)	168 (82.0)
Prior target therapy, n (%)	84 (41.0)
Prior docetaxel, n (%)	50 (24.4)

[#] Detected with SP263. chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; TPS, tumor proportion score.

BICR assessed confirmed tumor response

	2.0 mg/kg			2.5 mg/kg			3.0 mg/kg		
Tumor response[a]	Sq-NSCLC (n = 33)	Nsq-NSCLC *EGFR* wild type (n = 23)	Nsq-NSCLC *EGFR* mutant (n = 13)	Sq-NSCLC (n = 29)	Nsq-NSCLC *EGFR* wild type (n = 19)	Nsq-NSCLC *EGFR* mutant (n = 16)	Sq-NSCLC (n = 8)	Nsq-NSCLC *EGFR* wild type (n = 6)	Nsq-NSCLC *EGFR* mutant (n = 7)
Complete response	0	0	0	0	0	0	0	0	0
Partial response	11 (33.3)	1 (4.3)	2 (15.4)	4 (13.8)	7 (36.8)	6 (37.5)	1 (12.5)	2 (33.3)	0
Stable disease	16 (48.5)	15 (65.2)	7 (53.8)	20 (69.0)	11 (57.9)	8 (50.0)	5 (62.5)	3 (50.0)	3 (42.9)
Progressive disease	5 (15.2)	5 (21.7)	3 (23.1)	5 (17.2)	0	1 (6.3)	1 (12.5)	0	1 (14.3)
Not evaluable	1 (3.0)	2 (8.7)	1 (7.7)	0	1 (5.3)	1 (6.3)	1 (12.5)	1 (16.7)	3 (42.9)
Objective response rate, % (95% CI)	**33.3** (18.0, 51.8)	4.3 (0.1, 21.9)	15.4 (1.9, 45.4)	13.8 (3.9, 31.7)	**36.8** (16.3, 61.6)	**37.5** (15.2, 64.6)	12.5 (0.3, 52.7)	33.3 (4.3, 77.7)	0
Disease control rate, % (95% CI)	81.8 (64.5, 93.0)	69.6 (47.1, 86.8)	69.2 (38.6, 90.9)	82.8 (64.2, 94.2)	94.7 (74.0, 99.9)	87.5 (61.7, 98.4)	75.0 (34.9, 96.8)	83.3 (35.9, 99.6)	42.9 (9.9, 81.6)

Data are in n (%), unless specified.
[a] as assessed by BICR according to RECIST v1.1 in response-evaluable patients;
BICR, blinded independent central review; CI, confidence interval; NSCLC, non-small cell lung cancer; Nsq, nonsquamous; sq, squamous.

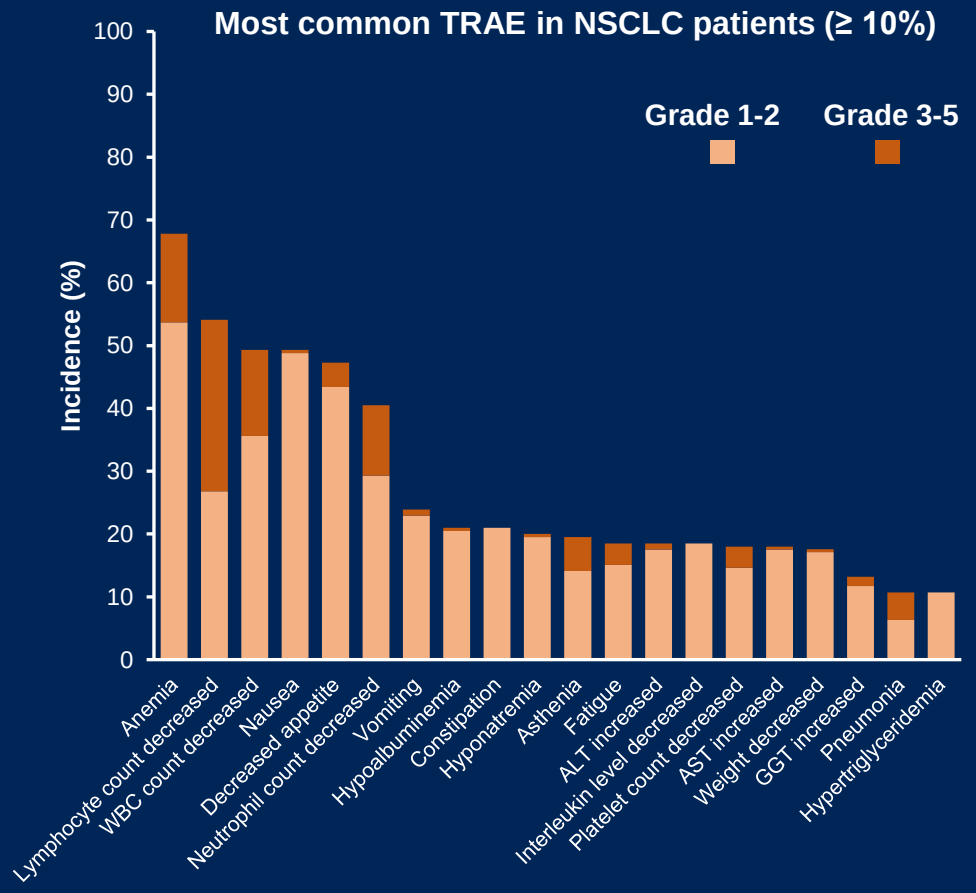
BICR assessed efficacy at the potential RP3D and in subgroups

	Confirmed ORR % (95% CI)	Confirmed DCR % (95% CI)	Median PFS (95% CI), month
NSCLC subtype			
Squamous 2.0 mg/kg (n = 33)	33.3 (18.0, 51.8)	81.8 (64.5, 93.0)	**6.34 (4.07, 7.13)**
Docetaxel failed (≥ 3L) (n = 15)	46.7 (21.3, 73.4)	80.0 (51.9, 95.7)	**6.90 (1.35, 8.28)**
Non-squamous 2.5 mg/kg (n = 35)			
EGFR wild type (n = 19)	36.8 (16.3, 61.6)	94.7 (74.0, 99.9)	**6.67 (4.14, 8.25)**
EGFR mutant (n = 16)	37.5 (15.2, 64.6)	87.5 (61.7, 98.4)	5.55 (4.04, NE)
Brain metastasis			
Yes (n = 10)	20.0 (2.5, 55.6)	90.0 (55.5, 99.7)	5.36 (1.18, NE)
No (n = 58)	37.9 (25.5, 51.6)	86.2 (74.6, 93.9)	6.34 (4.30, 7.16)
PD-L1 expression by TPS			
TPS ≥ 1% (n = 29)	37.9 (20.7, 57.7)	89.7 (72.6, 97.8)	6.80 (4.04, 7.13)
TPS < 1% or NE (n = 39)	33.3 (19.1, 50.2)	84.6 (69.5, 94.1)	5.49 (4.76, 8.25)

BICR, Blinded Independent Central Review; CI, confidence interval; DCR, disease control rate; EGFR, epidermal growth factor receptor; L, line; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; PD-L1, programmed death-ligand 1; TPS, tumor proportion score.

Safety and tolerability

Event, n (%)	1.0 mg/kg (n = 3)	2.0 mg/kg (n = 89)	2.5 mg/kg (n = 85)	3.0 mg/kg (n = 23)	4.0 mg/kg (n = 5)	NSCLC (n = 205)
Any TRAE	3 (100.0)	85 (95.5)	83 (97.6)	23 (100.0)	5 (100.0)	199 (97.1)
Grade ≥3	0	37 (41.6)	46 (54.1)	14 (60.9)	3 (60.0)	100 (48.8)
Most common Grade ≥3 (≥ 10%)[#]						
Lymphocyte count decreased	0	18 (20.2)	29 (34.1)	8 (34.8)	1 (20.0)	56 (27.3)
Anemia	0	7 (7.9)	17 (20.0)	2 (8.7)	3 (60.0)	29 (14.1)
WBC count decreased	0	3 (3.4)	17 (20.0)	5 (21.7)	3 (60.0)	28 (13.7)
Neutrophil count decreased	0	2 (2.2)	13 (15.3)	6 (26.1)	2 (40.0)	23 (11.2)
TRAE leading to Tx interruption	0	27 (30.3)	37 (43.5)	9 (39.1)	5 (100.0)	78 (38.0)
TRAE leading to Tx discontinuation	0	5 (5.6)	7 (8.2)	4 (17.4)	0	16 (7.8)
TRAE leading to Tx reduction	0	3 (3.4)	13 (15.3)	4 (17.4)	5 (100.0)	25 (12.2)
TRAE leading to death	0	0	1 (1.2)	1 (4.3)	0	2 (1.0) *



[#] Occurring in at least 10% of all the 205 patients. [*] Due to respiratory failure (n = 1 in the 2.5 mg/kg group), and pneumonia (n = 1 in the 3.0 mg/kg group).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; NSCLC, non-small cell lung cancer; TRAE, treatment-related adverse event; Tx, treatment; WBC, white blood cell.

Conclusions

- **Efficacy at RP3D dose**
  - ✓ **IO- and chemo-treated Squamous NSCLC**
    - ✓ cORR: 33.3%; mPFS: 6.34 months
    - ✓ Docetaxel failed (≥ 3L) cORR: 46.7%; mPFS: 6.90 months
  - ✓ **IO- and chemo-treated, *EGFR* WT Non-squamous NSCLC**
    - ✓ cORR: 36.8%; mPFS: 6.67 months
- **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; cORR, confirmed objective response rate; DCR, disease control rate; EGFR, epidermal growth factor receptor; IO, immunotherapy; L, line; NSCLC, non-small-cell lung cancer; mPFS, median progression-free survival; PD-L1, programmed death-ligand 1; RP3D, recommended phase 3 dose; WT, wild type.

Lay Summary

What did this research tell us?

- HLX43 (an antibody-drug conjugate) provided promising clinical and survival benefits in patients with heavily pretreated advanced NSCLC, regardless of subtypes, brain metastasis, and PD-L1 expression
- HLX43 was well tolerated

Who does this research impact?

- People with advanced NSCLC, their caregivers and clinicians treating NSCLC

What does this mean for patients right now?

- HLX43 may potentially be a broad-spectrum treatment option for patients with previously treated advanced NSCLC regardless of subtypes, presence of brain metastasis and PD-L1 expression level.

Where can I access more information?

- Information on the medicine used in this study and the people who could participate can be found here: https://clinicaltrials.gov/study/NCT06115642; https://clinicaltrials.gov/study/NCT06907615

Acknowledgements

The authors would like to express their gratitude to all the patients who participated in this trial, their families, the study personnel at each study hospital, as well as the clinical study team from Shanghai Henlius Biotech, Inc., for their support with trial conduct.