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.

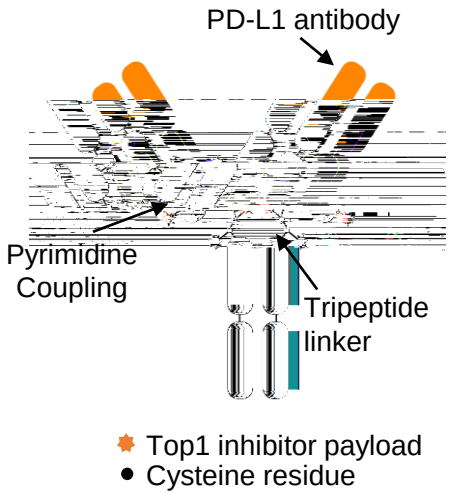
Background

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



High-affinity, internalizable PD-L1 antibody

Highly stable linker in circulating blood

Cleavable and **TME-activatable**

Potent cytotoxic payload Top1

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



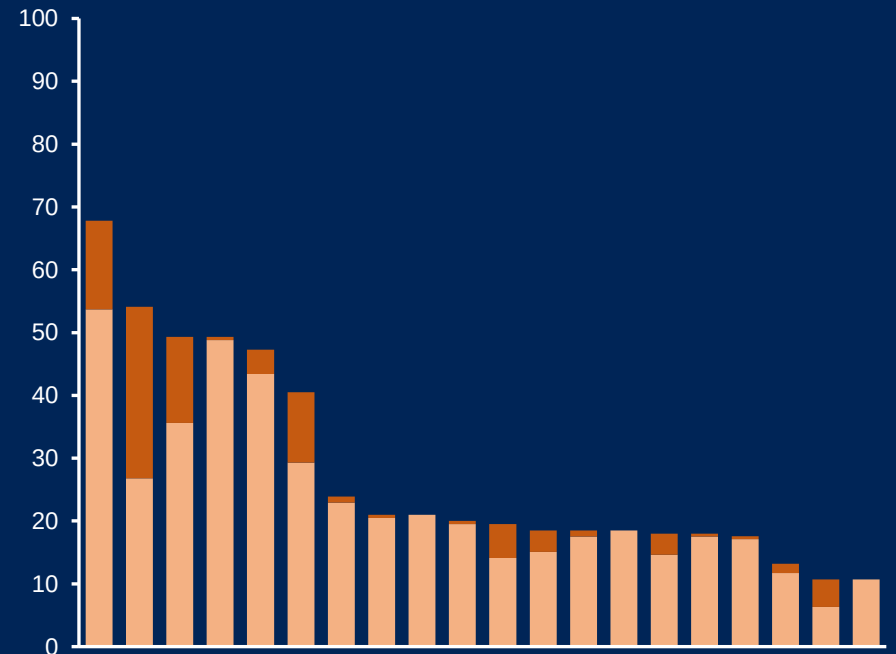
Baseline characteristics

	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)

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)
540 36W3gressiev116(e)16(di)-5(sease)]TJETQ EMC /Span <</MCID762/Lang(en-US)>>BDC q0.00000014305 0 960 540 reW* nBT/F2 10.56 Tf1 0 0 1 10(12.23 244.85									
	2 (7)	(7)	0		(8)	(12.5)	(65.7)	3 (42.9)	

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.


100
90
80
70
60
50
40
30
20
10
0

Conclusions

Efficacy at RP3D dose

- ✓ **IO- and chemo-treated Squamous NSCLC**
  - ✓ cORR: 33.3%; mPFS: 6.34 months
  - ✓ 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

Lay Summary

Acknowledgements

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