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Background

Nasopharyngeal cancer (NPC) is common cancer in South-East Asia with an estimated 120,416 new cases globally in 2022[1].

R/M-NPC is associated with a poor prognosis[2]. Traditional chemotherapy involves gemcitabine plus cisplatin (GP) [3]. First-line PD-1 inhibitors plus GP became SOC in R/M-NPC[4,5]. However, the improvement in survival benefits remains limited.

High EGFR expression is found in nearly 85 % of NPC cases and is associated with poor outcomes[6,7], suggesting that targeting this pathway can be a potential therapeutic strategy.

HLX07 is a novel, humanised anti-EGFR monoclonal antibody with a higher binding affinity and reduced immunogenicity. Safety and preliminary efficacy of HLX07 were demonstrated in a previous phase 1 study[8].

Here we report the efficacy and safety results from a phase 2 study of HLX07 vs. placebo, combined with serplulimab (PD-1 inhibitor) and GP in recurrent or metastatic nasopharyngeal cancer (R/M-NPC)

PD-1, Programmed cell death protein 1

1. Bray F, *et al. CA Cancer J Clin*. 2024;74(3):229–263. 2. Perri F, *et al. Onco Targets Ther*. 2019;12:1583-1591. 3. Zhang L, *et al. Lancet*. 2016;388(10054):1883-1892. 4. Yang Y, *et al. Lancet Oncol*. 2021;22(8):1162-1174. 5. Mai HQ, *et al. JAMA*. 2023;330(20):1961-1970. 6. Chua DT, *et al. Int J Radiat Oncol Biol Phys*. 2004;59(1):11-20. 7. Ma BB, *et al. Head Neck*. 2003;25(10):864-872. 8. Hou MM, *et al. Invest New Drugs*. 2021;39(5):1315-1323.

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Study Design

A randomised, double-blind, multicentre, phase 2 trial (NCT05513573)

Patients

- Age ≥18 years
- Pathohistologically confirmed unresectable, recurrent, or metastatic NPC that is not amenable to local or radical treatment
- ECOG PS 0/1
- Provision of fresh or archived tumour tissue
- No prior systemic therapy

Stratification factor

- liver metastasis (yes vs. no)

R 2:1

Group A, Q3W
HLX07[a] (IV, 1000mg)
Serplulimab[b] (IV, 300mg)
Chemotherapy[c] (gemcitabine and cisplatin)

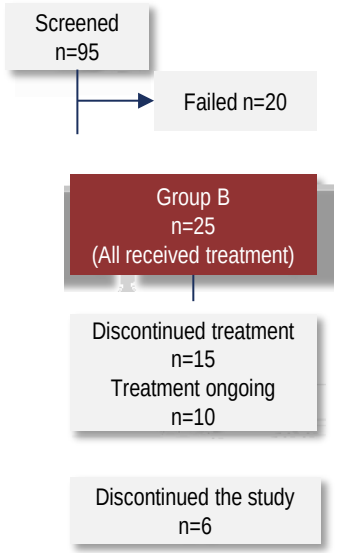
Group B, Q3W
Placebo (IV, 1000mg)
Serplulimab[b] (IV, 300mg)
Chemotherapy[c] (gemcitabine and cisplatin)

[a] until disease progression, intolerable toxicity, withdrawal of consent, initiation of new antitumour therapy, or death (whichever occurred first); [b] up to two years; [c] IV gemcitabine (1000 mg/m^2) + IV capecitabine (80 mg/m^2) up to 6 cycles.

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Patients Disposition and Baseline Characteristics

Efficacy set: n= 75
Safety set: n= 75



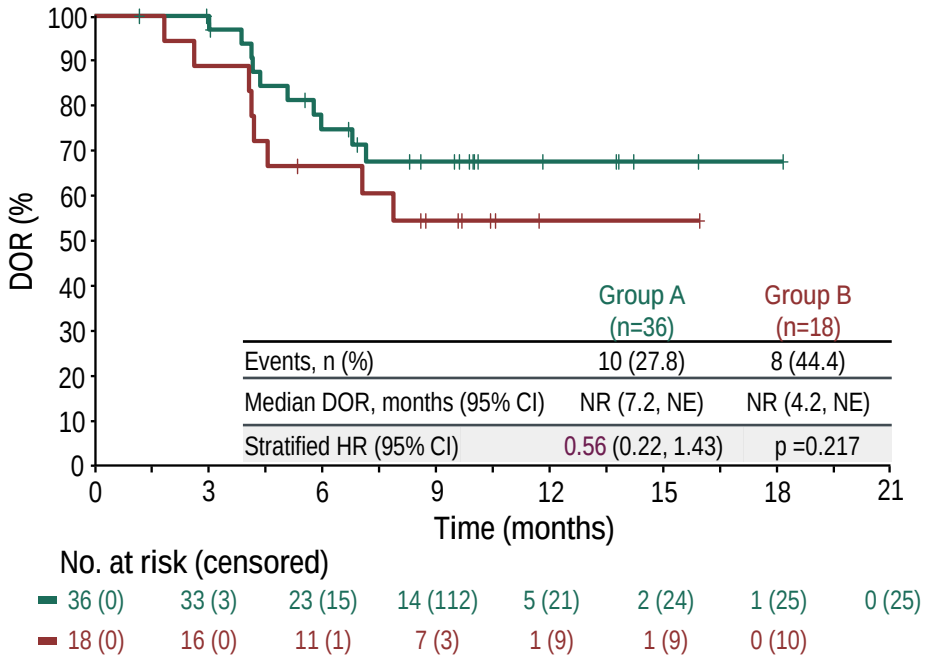
Median duration of follow-up: 10.84 months
Range: 0.03-19.38

EBV, Epstein–Barr virus; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; KSCC, keratinizing squamous cell carcinoma; PD-L1, programmed death ligand 1; TPS, tumour proportion score

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Efficacy- Summary of Tumour Response[a] (by IRRC per RECIST v1.1)

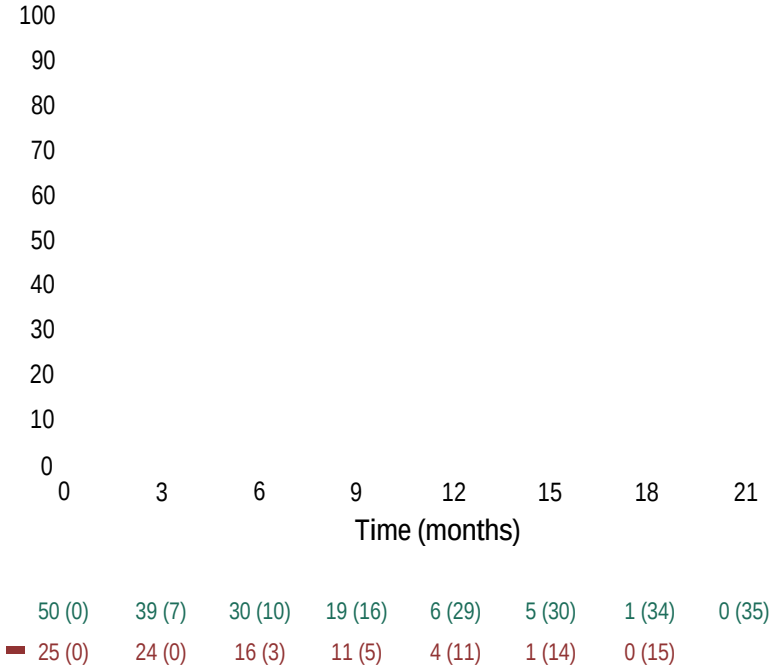
	Group A (n = 50)	Group B (n = 25)
Best overall response, n (%)		
CR	0	0
PR	36 (72.0)	18 (72.0)
SD	8 (16.0)	7 (28.0)
PD	3 (6.0)	0
NE	3 (6.0)	0
ORR, % (95% CI), n	72.0 (57.5, 83.8), 36	72.0 (50.6, 87.9), 18
DCR, % (95% CI), n	88.0 (75.7, 95.5), 44	100 (86.3, 100), 25
Median DOR, months (95% CI)	NR (7.2, NE)	NR (4.2, NE)
HR, 95% CI	0.56 (0.22, 1.43)	
12-month DOR rate, % (95% CI)	67.7 (48.1, 81.2)	54.6 (29.2, 74.2)



[a] Confirmed tumour response

CI, confidence interval; CR, complete response; DCR, disease control rate; PD, progressive disease; DOR, duration of response; HR, hazard ratio; IRRC, independent radiological review committee; NE, not evaluable; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease

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Subgroup	HR (95% CI)
Age	
≤50 years	1.02 (0.35–2.99)
>50 years	0.63 (0.18–2.17)
Sex	
Male	0.76 (0.33–1.74)
Female	NA (NE–NE)
ECOG PS	
0	1.25 (0.40–3.92)
1	0.53 (0.15–1.90)
Disease status	
Recurrent	0.95 (0.33–2.74)
Metastasis	0.78 (0.23–2.69)
Liver metastasis	
Yes	0.37 (0.12–1.15)
No	1.42 (0.44–4.61)
PD-L1 expression level	
TPS ≤1	0.69 (0.26–1.82)
TPS >1	0.84 (0.19–3.76)
EGFR expression level	
H-score ≤185	0.92 (0.33–2.60)
H-score >185	0.69 (0.18–2.57)
Baseline plasma EBV DNA copy no.	
≤2000	0.56 (0.12–2.49)
>2000	0.85 (0.32–2.26)

CI, confidence interval; EBV, Epstein–Barr virus; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; IRRC, independent radiological review committee; NA, not available; NE, not evaluable; NR, not reached; PD-L1, programmed death ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; TPS, tumour proportion score

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Conclusions

HLX07 combined with serplulimab+GP showed preliminary efficacy and tolerable safety profile in R/M-NPC patients

- Trend of PFS benefit (HR 0.74, 95% CI 0.33-1.66); 12-month PFS rate was 63.0% vs. 52.8%
- Trend of improved DOR (HR 0.56, 0.22-1.43), 12-month DOR rate was 67.7% vs. 54.6%
- The most common side-effect was skin rash (94% vs 56%) and manageable.

The sample size of the study is limited. The preliminary survival and clinical benefits warrant a further investigation of HLX07 plus Chemo-IO as a potential first-line treatment for R/M-NPC patients

AESI, adverse event of special interest; DOR, duration of response; GP, gemcitabine plus cisplatin; HR, hazard ratio; ORR, objective response rate; PFS, progression-free survival; R/M-NPC; recurrent or metastatic nasopharyngeal cancer; TEAE, treatment-emergent adverse event

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