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First-line HLX07 vs. Placebo Combined with Serplulimab and Chemotherapy for Recurrent or Metastatic Nasopharyngeal Cancer: a Randomised, Double-blind, Multicentre Phase 2 study

First-line HLX07 plus serplulimab and chemotherapy in R/M-NPC

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DECLARATION OF INTERESTS

Li Zhang

Consulting or Advisory Role:

AstraZeneca, Innovent Biologics

Speakers‘ Bureau:

AstraZeneca, BeiGene, HengRui Pharm., Innovent Biologics, Roche,

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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.

Study Design

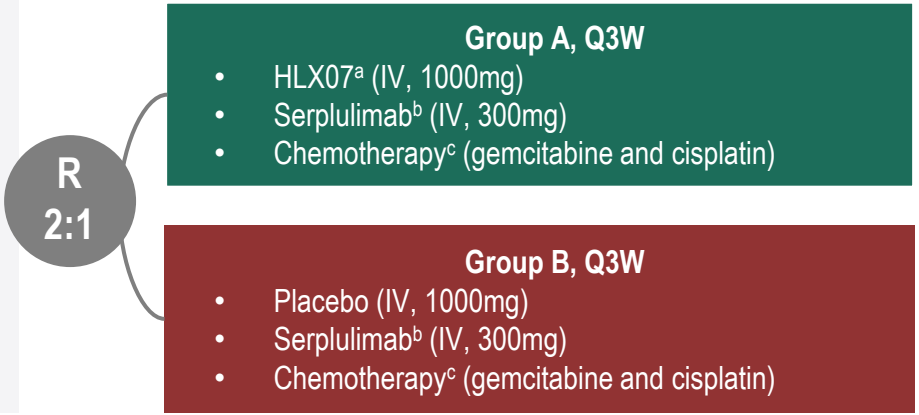
A randomised, double-blind, multicentre, phase 2 trial (NCT05513573)

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

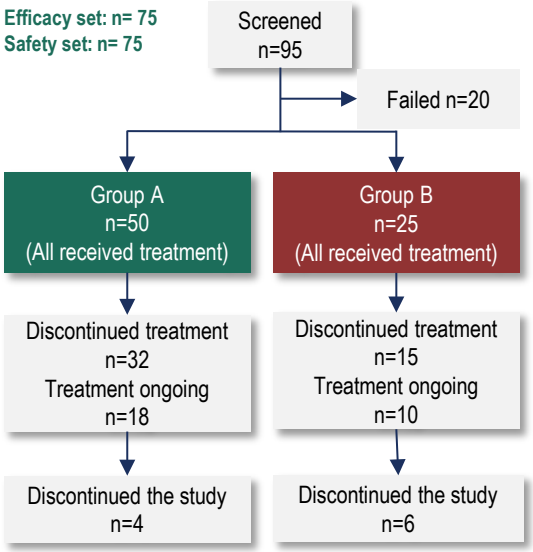
- liver metastasis (yes vs. no)



- **Primary endpoint: ORR (assessed by IRRC per RECIST v1.1)**
- **Secondary endpoints:** ORR (investigator-assessed per RECIST v1.1), DCR, DOR, TTR, PFS (IRRC and investigator-assessed per RECIST v1.1), 6 &12-month PFS rate, OS, 12 & 24-month OS rate, Safety, PK, Immunogenicity, Biomarker explorations

[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.
ECOG PS, Eastern Cooperative Oncology Group performance status; DCR, disease control rate; DOR, duration of response; IRRC, independent radiological review committee; IV, intraveneous; NPC, nasopharyngeal cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; Q3W, once every three weeks; RECIST, Response Evaluation Criteria in Solid Tumours; TTR, time to response

Patients Disposition and Baseline Characteristics



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

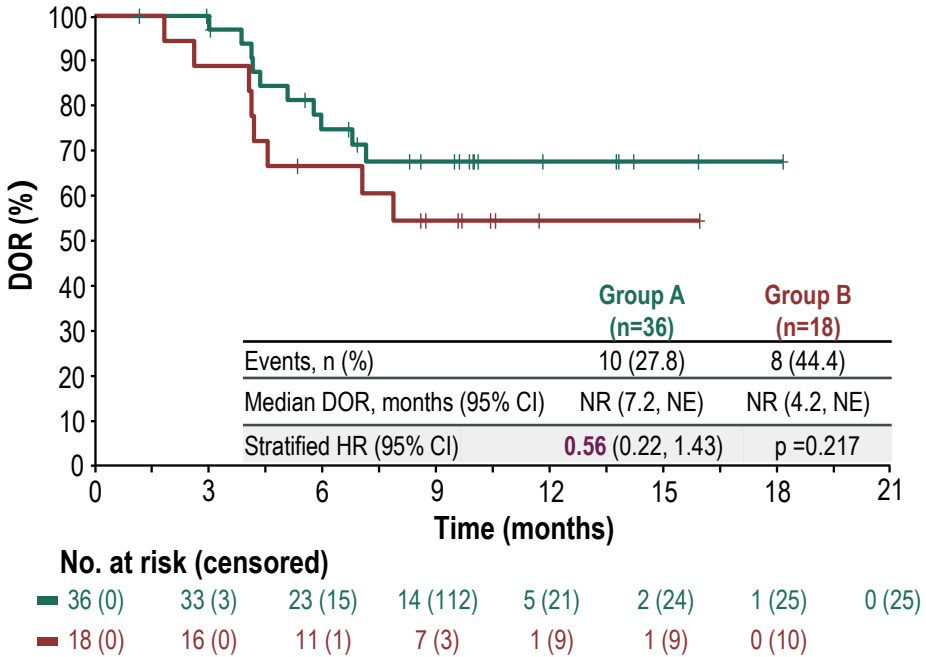
Characteristics	Group A (n = 50)	Group B (n = 25)
Age, median (range), years	50 (20-74)	51 (20-67)
Male, n (%)	43 (86.0)	21 (84.0)
Asian, n (%)	50 (100.0)	25 (100.0)
ECOG PS, n (%)		
0	32 (64.0)	13 (52.0)
1	18 (36.0)	12 (48.0)
Disease status, n(%)		
Local recurrent	7 (14.0)	4 (16.0)
Metastatic	43 (86.0)	21 (84.0)
Primary	30 (60.0)	11 (44.0)
Recurrent	13 (26.0)	10 (40.0)
Distant metastasis, n (%)		
Bone	19 (38.0)	15 (60.0)
Lung	19 (38.0)	9 (36.0)
Liver	18 (36.0)	9 (36.0)
Lymph node	18 (36.0)	7 (28.0)
Other	7 (14.0)	4 (16.0)

Characteristics	Group A (n = 50)	Group B (n = 25)
Histology, n (%)		
KSCC	0	1 (4.0)
Non-KSCC	49 (98.0)	22 (88.0)
Other	1 (2.0)	2 (8.0)
PD-L1 expression		
TPS ≤1	20 (40.0)	10 (40.0)
TPS >1	28 (56.0)	15 (60.0)
Not available	2 (4.0)	0
EGFR expression		
H-score ≤185	25 (50.0)	13 (52.0)
H-score >185	22 (44.0)	12 (48.0)
Not available	3 (6.0)	0
Baseline plasma EBV DNA copy no., n (%)		
≤ 2000	16 (32.0)	11 (44.0)
> 2000	34 (68.0)	14 (56.0)

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

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

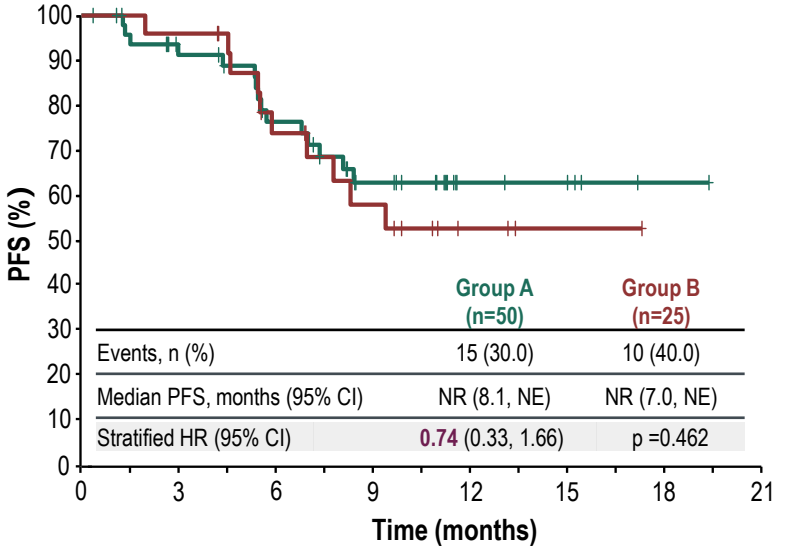
	Group A (n = 50)	Group B (n = 25)
Best overall response, n (%)		
CR	0	0
PR	36 (72.0)	18 (72.0)
SD	8 (16.0)	7 (28.0)
PD	3 (6.0)	0
NE	3 (6.0)	0
ORR, % (95% CI), n	72.0 (57.5, 83.8), 36	72.0 (50.6, 87.9), 18
DCR, % (95% CI), n	88.0 (75.7, 95.5), 44	100 (86.3, 100), 25
Median DOR, months (95% CI)	NR (7.2, 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

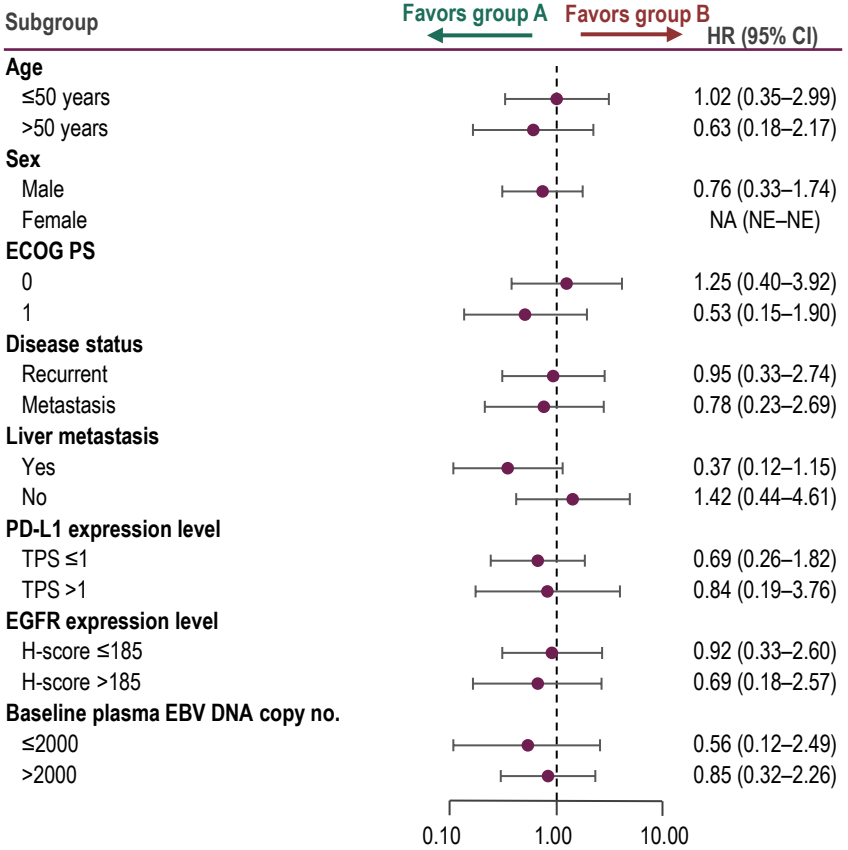
Efficacy- PFS (by IRRC per RECIST v1.1)



	Group A (n=50)	Group B (n=25)
Events, n (%)	15 (30.0)	10 (40.0)
Median PFS, months (95% CI)	NR (8.1, NE)	NR (7.0, NE)
Stratified HR (95% CI)	**0.74** (0.33, 1.66)	p =0.462

No. at risk (censored)

50 (0)	39 (7)	30 (10)	19 (16)	6 (29)	5 (30)	1 (34)	0 (35)
25 (0)	24 (0)	16 (3)	11 (5)	4 (11)	1 (14)	0 (15)	



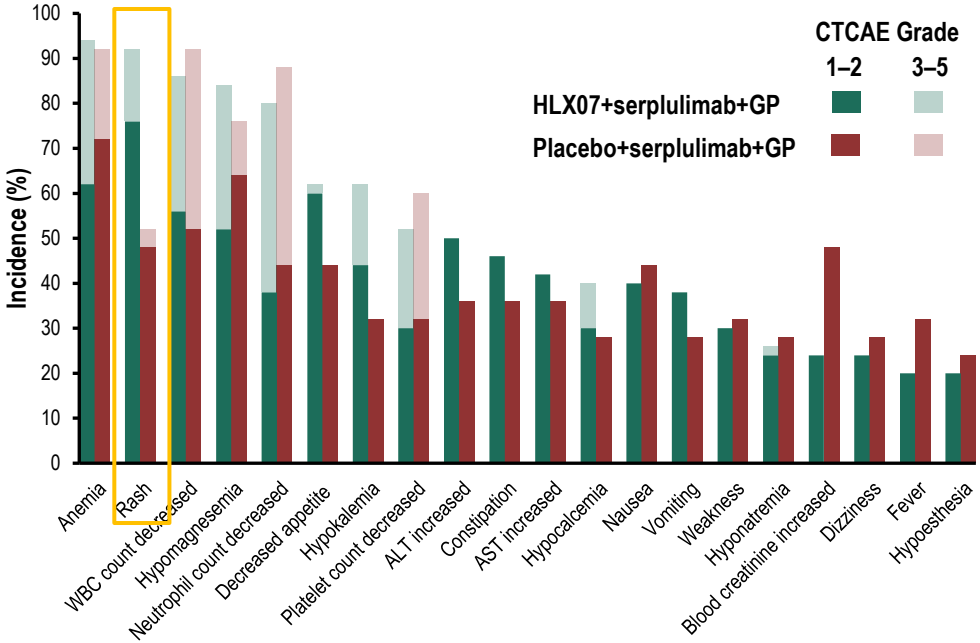
CI, confidence interval; EBV, Epstein–Barr virus; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; IRRC, independent radiological review committee; NA, not available; NE, not evaluable; NR, not reached; PD-L1, programmed death ligand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

Safety and Tolerability

Overview of Safety

	Group A (n = 50)	Group B (n = 25)
Any TEAEs, n (%)	49 (98.0)	25 (100)
CTCAE Grade 1	1 (2.0)	0
CTCAE Grade 2	7 (14.0)	6 (24.0)
CTCAE Grade ≥3	41 (82.0)	19 (76.0)
Leading to Tx discontinuation	8 (16.0)	5 (20.0)
Leading to death	1 (2.0)[a]	4 (16.0)[b]
Any TRAEs, n (%)	49 (98.0)	25 (100)
Related to HLX07/placebo	49 (98.0)	24 (96.0)
CTCAE Grade 5	1 (2.0)	0
Serious	14 (28.0)	8 (32.0)
Any AESIs, n (%)	48 (96.0)	22 (88.0)
Rash	47 (94.0)	14 (56.0)
Hypomagnesemia	42 (84.0)	19 (76.0)
irAE	6 (12.0)	4 (16.0)
Serious	5 (10.0)	2 (8.0)

Incidence of TEAEs by PT occurring in ≥20% patients[c]



[a] treatment-related bacterial pneumonia; [b] three patients had progressive disease leading to death; one had respiratory failure that was not treatment-related; [c] in both groups.

AESI, adverse event of special interest; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; GP, gemcitabine plus cisplatin; irAE, immune-related adverse event; PT, preferred terms; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; TX, treatment; WBC, white blood cell

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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