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Penpulimab plus gemcitabine in combination with cisplatin or anlotinib as first-line treatment for metastatic nasopharyngeal carcinoma (M NPC): A phase II study.

Shuang Huang, Xiaozhong Chen, Song Qu, Shenhong Qu, Yaqian Han, Kunyu Yang, Shiting Huang, Min Li, Lin Zhang, Qian Ding; Cancer Hospital of the University of Chinese Academy of Sciences, Hangzhou, China; The Cancer Hospital of the University of Chinese Academy of Sciences, Zhejiang Cancer Hospital, Hangzhou, China; Guangxi Medical University Affiliated Tumor Hospital, Nanning, China; The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China; Hunan Cancer Hospital, Changsha, China; Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Background: Cisplatin (P)-based combination regimen is the backbone in the first-line treatment of M NPC while the toxicity limited its usage. This study investigated the efficacy and safety of penpulimab (an anti-programmed death-1 antibody) plus gemcitabine (G) in combination with cisplatin (P) or anlotinib (a multikinase inhibitor) as first-line treatment of these pts. **Methods:** This is a multicenter, three cohorts, randomized, phase II study (NCT04736810). Pts with histologically confirmed regional or distant M NPC who had measurable lesions per RECIST 1.1 and received no systemic treatment for metastatic lesions were enrolled. Other inclusion criteria included 18-75 years old and ECOG PS 0-1. Pts in cohort A, B and C were given G + P + penpulimab + anlotinib; G + P + penpulimab or G + penpulimab + anlotinib, respectively. G (1000mg/m^2, d1, d8) and P (80mg/m^2, d1) were given intravenously for 4 to 6 cycles, 3 weeks per cycle. Penpulimab (200mg, d1) and anlotinib (12mg, qd, d1-14) were given intravenously and orally respectively until confirmed disease progression, or unacceptable toxicities, or up to 2 years, whichever occurred firstly. Pts who developed disease progression but still had clinical benefit could receive penpulimab and anlotinib continuously based on the decision of physicians. The primary endpoint was objective response rate (ORR). Here we report the preliminary results of this study. **Results:** Between March 2021 and September 2021, 17 pts were randomly assigned to cohort A (n = 5), B (n = 5) or C (n = 7), and the median age was 52, 49 and 52 years old, respectively. Nearly half (7/17, 41.2%) had liver metastasis and the majority (5/7, 71.4%) was in the cohort C. At the data cutoff date on January 17, 2022, the median treatment cycles were 6, 8, 8 across three cohorts. All pts received tumor response and the confirmed ORR was 80.0%, 80.0% and 100%. The details of tumor response were summered in followed table. Notably, in cohort C, 1 pts achieved confirmed complete response (CR) and all others had confirmed partial response (PR). Replacement of cisplatin with anlotinib seemed to show better safety profile that ≥ grade 3 adverse events (AEs) occurred in 6 pts (85.7%) in cohort A, 5 (100%) in cohort B while only 4 (57.1%) in group C. Moreover, the overall incidence of serious AEs was 28.6%, 20%, 14.3% across three cohorts. The most common ≥ grade 3 AEs were white blood cell decreased and neutrophil count decreased. **Conclusions:** This preliminary analysis indicated that penpulimab plus gemcitabine and anlotinib had promising efficacy and favorable tolerance profile as first-line treatment for M NPC. Further investigate is ongoing. Clinical trial information: NCT04736810. Research Sponsor: None.

Cohort	A	B	C
Liver Metastasis at Baseline, n (%)	1 (20.0)	1 (20.0)	5 (71.4)
CR, n (%)	0 (0)	1 (20.0)	1 (14.3)
PR, n (%)	4 (80.0)	3 (60.0)	6 (85.7)
SD, n (%)	1 (20.0)	1 (20.0)	0 (0)
ORR, n (%)	4 (80.0)	4 (80.0)	7 (100)