678 **UPDATED SAFETY AND EFFICACY OF TORIPALIMAB COMBINED WITH CETUXIMAB IN PLATINUM-REFRACTORY RECURRENT OR METASTATIC HEAD AND NECK SQUAMOUS CELL CARCINOMA (R/M-HNSCC): A PHASE IB/II CLINICAL TRIAL**

[1]Ye Guo*, [2]Zhendong Li, [3]Desheng Hu, [4]Song Qu, [3]Youhua Zhu, [5]Meiyu Fang, [6]Wantao Chen, [7]Chuanzheng Sun, [8]Hao Jiang, [9]Jingfeng Zong, [10]Jinguan Lin, [11]Siyang Wang, [10]Wei Wang, [12]Chuan Jin, [13]Guochun Cao, [14]Minghua Ge, [15]Xiaoming Huang, [16]Xudong Wang, [17]Zhiming Li, [18]Mo Wang, [18]Xianming Luo, [18]Shuanghui Wei, [18]Yuteng Shen. *[1]Shanghai East Hospital, Shanghai, China; [2]Liaoning Cancer Hospital and Institute, Shenyang, China; [3]Hubei Cancer Hospital, Wuhan, China; [4]Guangxi Medical University Cancer Hospital, Nanning, China; [5]Zhejiang Cancer Hospital, Hangzhou, China; [6]Shanghai Ninth People's Hospital, Shanghai Jiao Tong Univetsity School of Medicine, Shanghai, China; [7]Yunnan Cancer Hospital, Kunming, China; [8]The First Affiliated Hospital of Bengbu Medical College, Bengbu, China; [9]Fujian Cancer Hospital, Fuzhou, China; [10]Hunan Cancer Hospital, Changsha, China; [11]The Fifth Affiliated Hospital Sun Yat-sen University, Zhuhai, China; [12]Affiliated Cancer Hospital and Institute of Guangzhou Medical University, Guangzhou, China; [13]Jiangsu Cancer Hospital, Nanjing, China; [14]Zhejiang Provincial People's Hospital, Hangzhou, China; [15]Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China; [16]Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [17]Sun Yat-sen University Cancer Center, Guangzhou, China; [18]Shanghai Junshi Biosciences, Shanghai, China*

Background PD-1 inhibitors and EGFR inhibitors are effective and may provide potential synergy in R/M HNSCC. An open-label, multicenter phase Ib/II study of toripalimab (a humanized IgG4K monoclonal antibody specific for PD-1) with cetuximab was conducted in platinum-refractory or PD-L1 positive previously untreated R/M-HNSCC (NCT04856631). Here we report the results of Cohort A (platinum-refractory).

Methods Eligible patients with R/M HNSCC progressed upon 1st-line platinum-containing treatment or developed R/M disease within 6 months of platinum-containing neo-adjuvant/adjuvant or chemo-radiation therapy who had no prior immunotherapy or EGFR inhibitors therapy were enrolled. Toripalimab was administered at 240mg intravenously (IV) Q3W and cetuximab was given as a loading dose of 400mg/m^2 IV followed by 250mg/m^2 QW. The primary endpoint was objective response rate (ORR) by an independent review committee (IRC) per RECIST v1.1. Secondary endpoints included ORR, disease control rates (DCR), duration of response (DOR), progression-free survival (PFS) by the investigators and IRC, overall survival (OS), and safety.

Results By the data cutoff date of Apr. 14, 2023, a total of 45 patients including 35 (77.8%) males were enrolled in Cohort A, with the median follow-up duration of 10.0 months. The median age of the patients was 59 (range 32–74) years. Eighteen (40.0%) patients had distant metastases and 31 (68.9%) were PD-L1 CPS $\geq$1. As assessed by the IRC, the confirmed ORR was 60% (95% CI 44.3%, 74.3%) with 1 CR and 26 PR, and the median DOR was 17.9 (95% CI 7.8, NA) months, the median PFS was 9.9 (95% CI 4.2, NA) months, 12 months PFS rate was 40.7%. Similar results were seen per investigators' assessment. The median OS was 15.4 (95% CI 8.5, 17.7) months, 12 months OS rate was 54.4%. Patients with positive PD-L1 expression (CPS$\geq$1) may benefit more than negative patients (ORR: 64.5% vs 40%, median PFS: 10.4 m vs 4.0 m, median OS: 15.4 m vs 11.7 m). Forty-two (93.3%) patients experienced treatment-related adverse events (TRAEs). Eleven (24.4%) patients experienced immune-related adverse events (irAEs). Ten (22.2%) patients occurred Grade$\geq$3 TRAEs and no Grade$\geq$3 irAEs occurred. No fatal AEs related to the study treatment was reported.

Conclusions Toripalimab combined with cetuximab were well tolerated and showed promising clinical efficacy in patients with R/M HNSCC.

Trial Registration NCT04856631

Ethics Approval The study obtained ethics approval from Shanghai East Hospital Drug clinical Trial Ethics Committee [[2020]临审第 (072) 号], and participants gave informed consent before taking part.

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