MADRID 2026 ESMO congress

1542RO

Phase II study of izalontamab brengitecan (iza-bren) plus pembrolizumab in patients with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC)

D. Ji[1], C. Hu[2], Z. Liu[3], C. Hao[4], C. Sun[5], S. Qu[6], J. Xia[7], M. Cai[8], R. Liu[9], X.F. Liu[10], S. Xiao[11], H. Zhu[12], Y. Zhu[13]

[1] Department of Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai, China, [2] Department of Head & Neck Surgery, Fudan University Shanghai Cancer Center, Shanghai, China, [3] Department of Oncology, The Tenth Affiliated Hospital, Southern Medical University (Dongguan People's Hospital), Dongguan, China, [4] Department of Head and Neck Radiotherapy, Harbin Medical University Cancer Hospital, Harbin, China, [5] Department of Head Neck and Thyroid Surgery, Yunnan Cancer Hospital, Kunming, China, [6] Department of Head and Neck Radiotherapy, Guangxi Medical University Cancer Hospital, Nanning, China, [7] Department of Palliative Care, Anyang Tumor Hospital, Anyang, China, [8] Department of Oncology Head And Neck & Pelvic Tumor, The First Affiliated Hospital Of University Of South China, Hengyang, China, [9] Department of Radiation Oncology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [10] Department of Oncology, The Central Hospital of Shaoyang, Shaoyang, China, [11] Medical and Pharmacological Research Department, Baili-Bio (Chengdu) Pharmaceutical Co., Ltd., Chengdu, China, [12] Department of Biometrics, SystImmune Inc., Redmond, United States of America[13] President and CSO, Sichuan Biokin Pharmaceutical Co., Ltd, Chengdu, China

Background

EGFR and HER3 are commonly expressed in HNSCC. Iza-bren is a potential first-in-class antibody-drug conjugate (ADC) comprised of an EGFRxHER3 bispecific antibody conjugated to a novel topoisomerase I inhibitor payload (Ed-04) via a stable tetrapeptide-based cleavable linker. Results from a phase II study evaluating iza-bren plus pembrolizumab in patients (pts) with R/M HNSCC are reported.

Methods

This study consisted of two stages: Stage I, the safety run-in phase, and Stage II, the expansion phase. First-line R/M HNSCC pts were enrolled in stage II and treated with iza-bren at 2.5 mg/kg or at 2.75 mg/kg D1D8 Q3W plus pembrolizumab (200mg D1 Q3W). The primary endpoints were ORR and RP2D for combination treatment.

Results

As of Mar 2, 2026, a total of 78 first-line R/M HNSCC pts from China were enrolled in stage II, including 38 pts receiving iza-bren at 2.5 mg/kg and 40 pts at 2.75 mg/kg plus pembrolizumab. The median follow-up was 11.9 mo. At 2.5 mg/kg D1D8 Q3W, ORR was 55.3%, cORR was 47.4%, mDOR was 13.6 months, and mPFS was 8.2 months. Detailed efficacy was summarized in the table below.Table: 1542RO

	Total(N = 78)	2.5 mg/kgD1D8 Q3W(N = 38)	2.75 mg/kg D1D8 Q3W(N = 40)
BOR, n			
CR	2	1	1
cCR	2	1	1
PR	44	20	24
cPR	36	17	19
SD	19	10	9
PD	8	6	2
NE	5	1	4
ORR, % (95% CI)	59.0 (47.3, 70.0)	55.3 (38.3, 71.4)	62.5 (45.8, 77.3)
cORR, % (95% CI)	48.7 (37.2, 60.3)	47.4 (31.0, 64.2)	50.0 (33.8, 66.2)
DCR, % (95% CI)	83.3 (73.2, 90.8)	81.6 (65.7, 92.3)	85.0 (70.2, 94.3)
mDOR, mo (95% CI)	13.6 (9.3, NR)	13.6 (6.5, 13.6)	NR (4.3, NR)
mPFS, mo (95% CI)	7.1 (4.5, 9.7)	8.2 (4.4, 15.0)	5.8 (3.8, 10.8)

cCR: confirmed CR. cPR: confirmed PR. The most frequent hematologic TRAEs (all grades) were anemia (94.9%), leukopenia (80.8%), neutropenia (70.5%), and thrombocytopenia (53.8%); the most frequent non-hematologic TRAEs (all grades) were decreased appetite (50.0%) and asthenia (41.0%). Grade 3 and above TRAEs were predominantly hematologic in nature and could be effectively managed with standard supportive measures including dose reductions, and 4 (5.1%) pts discontinued treatment due to iza-bren related AE. No interstitial lung disease was reported.

Conclusions

Iza-bren plus pembrolizumab has demonstrated promising anti-tumor activity with a manageable safety profile in treatment-naive R/M HNSCC pts. Iza-bren 2.5 mg/kg D1D8 Q3W was selected as the RP2D for combination therapy and phase III study is in planning.

Clinical trial identification

NCT06437522.

Legal entity responsible for the study

Baili-Bio (Chengdu) Pharmaceutical Co, Ltd.

Funding

Baili-Bio (Chengdu) Pharmaceutical Co, Ltd.

Disclosure

S. Xiao: Financial Interests, Personal, Full or part-time Employment: Baili-Bio (Chengdu) Pharmaceutical Co., Ltd. H. Zhu: Financial Interests, Personal, Full or part-time Employment: SystImmune Inc; Financial Interests, Personal, Stocks/Shares: SystImmune Inc. Y. Zhu: Financial Interests, Personal, Full or part-time Employment: SystImmune Inc; Financial Interests, Personal, Ownership Interest: SystImmune Inc, Baili Pharmaceutical. All other authors have declared no conflicts of interest.

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