Results from two phase II studies of SI-B001, an EGFR×HER3 bispecific antibody with/without chemotherapy in patients (pts) with recurrent and metastatic headand neck squamous cell carcinoma (HNSCC).

SYSTIMMUNE

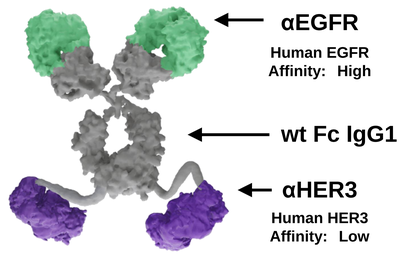
Abstract Number: 6037

Liqiong Xue[1], Kunyu Yang[2], Meiyu Fang[3], Xuelei Ma[4], Wen Zou[5], Muran Ding[5], Zhaoxiang Wang[5], Yujia Peng[5], Sa Xiao[5], Hongwei Wang[6], Hai Zhu[7], Martin Sebastian Olivo[7], Yi Zhu[5, 6, 7], Ye Guo[1]

[1] Shanghai East Hospital, School of Medicine, Tongji University, Shanghai, China; [2] Cancer Center ,Union Hospital, Tongji Medical College, Huazhong University ofScience and Technology, Wuhan, China; [3] Department of rare cancer & head and neckmedical oncology, Cancer Hospital of the University of Chinese Academy of Sciences, Zhejiang Cancer Hospital, Hangzhou, China; [4] West China Hospital, Sichuan University, Chengdu, China; [5] Baili-Bio (Chengdu) Pharmaceutical Co., Ltd., Chengdu, China; [6] Sichuan Baili-pharmaceutical Co., Ltd., Chengdu, China; [7] SystImmune,Inc., Redmond, WA.

Background and Methods

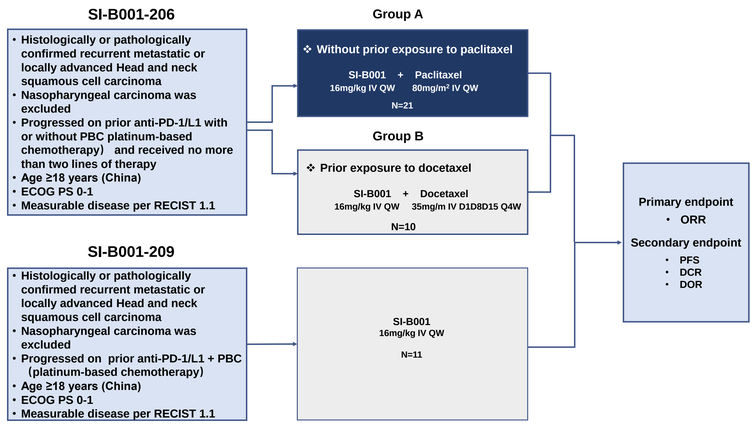
Background: SI-B001 (izalontamab) is a novel EGFR×HER3 bispecific antibody. We present the efficacy and safety results from two ongoing studies, SI-B001-206 and SI-B001-209, of patients with recurrent and metastatic HNSCC. Clinical trial information: NCT05044897 and NCT05054439.



SI-B001 (izalontamab)

Methods: SI-B001-209 enrolled pts with recurrent and metastatic HNSCC progressed on prior anti-PD-1/L1 plus platinum-based chemotherapy (PBC). Pts were treated with SI-B001 16mg/kg IV QW. SI-B001-206 enrolled pts with recurrent and metastatic HNSCC progressed on prior anti-PD-1/L1 with or without PBC and received no more than two lines of treatment. Pts enrolled in SI-B001-206 were divided into two groups: Group A, pts without prior exposure to paclitaxel were treated with SI-B001 (12mg/kg IV QW) plus paclitaxel (80mg/m IV QW); Group B, pts with prior exposure to paclitaxel were treated with SI-B001 (12mg/kg IV QW) plus docetaxel (35mg/m IV D1D8D15 Q4W). The study endpoints of the two studies were identical. The primary endpoint was objective response rate (ORR) by investigator per RECIST v1.1. The secondary endpoints were ORR by independent central review, progression-free survival (PFS), disease control rate (DCR), duration of response (DOR), overall Survival (OS), and safety.

Study design



Results

As of April 17, 2023, 11 pts in SI-B001-209 received SI-B001 single agent. Pts had a median of 4 prior lines of therapy. In 10 out of 11 pts who had at least one post-baseline tumor assessment in SI-B001-209, ORR (n/N) was 30% (3/10), mPFS [95%CI] was 2.7 [1.8-7.9] mo. 31 pts in SI-B001-206 received SI-B001 plus chemotherapy, including 21 pts in Group A and 10 pts in Group B. In 25 pts who had at least one post-baseline tumor assessment, ORR was 44% (11/25), mPFS was 3.7 [2.5-4] mo. One nasal sinus cancer pt enrolled had stable disease (SD). 17 out of the 20 pts who have at least one post-baseline tumor assessment in Group A, ORR was 58.2% (10/17), mPFS was 5.4[3.7-6.3] mo. 8 out of 10 pts who have at least one post-baseline tumor assessment in Group B, ORR was 12.5% (1/8), mPFS was 1.6 [1.2-3.7] mo.

The most common Grade ≥ 3 treatment-related adverse events (TRAEs) in SI-B001-209 was hypomagnesaemia (9%). The most common Grade ≥ 3 TRAEs in SI-B001-206 were rash (13%), anemia (6%) and leukopenia (9%). No SI-B001 drug-related deaths occurred in either study.

Table 1. Characteristics of Patients

The baseline of enrolled subjects of SI-B001-206 and SI-B001-209 are shown below in Table 1A and Table 1B respectively.

Table 1A. Baseline Characteristics of S206

	ALL (N=31)	SI-B001+ Paclitaxel (N=21)	SI-B001+Docetaxel (N=10)
Age (Median, Range)	58.0 (36.0 - 75.0)	59.0 (41.0 - 75.0)	52.5 (36.0 - 75.0)
Height (Mean, Range)	164.5 (145.0 - 184.0)	164.0 (145.0 - 184.0)	165.7 (162.0 - 170.0)
Weight (Mean, Range)	53.5 (29.8 - 66.4)	52.4 (29.8 - 65.8)	55.8 (38.0 - 66.4)
BMI (Mean, Range)	19.7 (14.0 - 24.8)	19.4 (14.2 - 24.2)	20.3 (14.0 - 24.8)
BSA (Mean, Range)	1.6 (1.1 - 1.8)	1.5 (1.1 - 1.8)	1.6 (1.3 - 1.8)
Ethic (Han)	26/31 (84%)	17/21 (81%)	9/10 (90%)
Sex (Male)	26/31 (84%)	17/21 (81%)	9/10 (90%)
Smoking History			
Never	15/31 (48%)	12/21 (57%)	3/10 (30%)
Previous	15/31 (48%)	8/21 (38%)	7/10 (70%)
Current	0/31 (0%)	0/21 (0%)	0/10 (0%)
UNK	1/31 (3%)	1/21 (5%)	0/10 (0%)
Alcohol History			
Never	25/31 (81%)	18/21 (86%)	7/10 (70%)
Previous	6/31 (19%)	3/21 (14%)	3/10 (30%)
Current	0/31 (0%)	0/21 (0%)	0/10 (0%)
UNK	0/31 (0%)	0/21 (0%)	0/10 (0%)
ECOG			
0	3/31 (10%)	1/21 (5%)	2/10 (20%)
1	28/31 (90%)	20/21 (95%)	8/10 (80%)

Table 1B. Baseline Characteristics of S209

	ALL(N=11)
Age (Median, Range)	57.0 (46.0 - 71.0)
Height (Mean, Range)	164.0 (146.0 - 172.0)
Weight (Mean, Range)	54.4 (40.0 - 73.5)
BMI (Mean, Range)	20.2 (16.0 - 25.4)
BSA (Mean, Range)	1.6 (1.3 - 1.9)
Ethic (Han)	11/11 (100%)
Sex (Male)	10/11 (91%)
Smoking History	
Never	3/11 (27%)
Previous	7/11 (64%)
Current	1/11 (9%)
UNK	0/11 (0%)
Alcohol History	
Never	6/11 (55%)
Previous	5/11 (45%)
Current	0/11 (0%)
UNK	0/11 (0%)
ECOG	
0	0/11 (0%)
1	11/11 (100%)

Table 2. Safety summary

TRAEs observed in SI-B001-206 and SI-B001-209 were summarized in below Table 2A and Table 2B respectively.

Table 2A. FREQ>=10% or G>=3 TRAE by PT

	SI-B001-206 (N=31)				
PT Name	*G1*	*G2*	*G3*	*G4*	*All Grade*
Rash	13 (42%)	2 (6%)	4 (13%)		19 (61%)
Anemia	7 (23%)	1 (3%)	2 (6%)		10 (32%)
Leukopenia	5 (16%)	2 (6%)	2 (6%)	1 (3%)	10 (32%)
Proteinuria	7 (23%)				7 (23%)
Stomatitis	2 (6%)	3 (10%)	1 (3%)		6 (19%)
Asthenia	3 (10%)	3 (10%)			6 (19%)
Weight decreased	6 (19%)				6 (19%)
Mouth ulceration		4 (13%)	1 (3%)		5 (16%)
Paronychia	2 (6%)	1 (3%)	1 (3%)		4 (13%)
Skin fissures	1 (3%)	2 (6%)	1 (3%)		4 (13%)
Nausea	1 (3%)	3 (10%)			4 (13%)
Dermatitis acneiform	2 (6%)		1 (3%)		3 (10%)
Hypoaesthesia	1 (3%)	1 (3%)	1 (3%)		3 (10%)
Neutropenia	1 (3%)		1 (3%)	1 (3%)	3 (10%)
ALT increased	3 (10%)				3 (10%)
Pyrexia	2 (6%)	1 (3%)			3 (10%)
Jaw fistula			1 (3%)		1 (3%)
Skin infection			1 (3%)		1 (3%)
Skin ulcer			1 (3%)		1 (3%)

ALT: Alanine aminotransferase

Table 2B. FREQ>=10% or G>=3 TRAE by PT

	SI-B001-209 (N=11)			
PT Name	*G1*	*G2*	*G3*	*All Grade*
Conjunctivitis	1 (9%)	2 (18%)		3 (27%)
Proteinuria	2 (18%)	1 (9%)		3 (27%)
Stomatitis	3 (27%)			3 (27%)
Paronychia		1 (9%)	1 (9%)	2 (18%)
AST increased	2 (18%)			2 (18%)
Blood ALP increased	2 (18%)			2 (18%)
Dermatitis acneiform	2 (18%)			2 (18%)
Mouth ulceration	1 (9%)	1 (9%)		2 (18%)
Rash maculo-papular	2 (18%)			2 (18%)
Skin fissures	2 (18%)			2 (18%)
Hypomagnesaemia			1 (9%)	1 (9%)

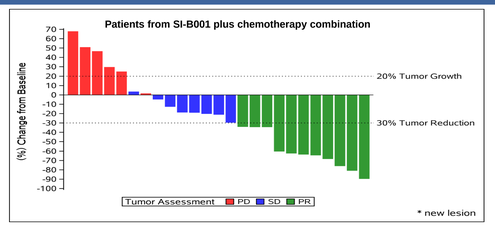
AST: Aspartate aminotransferase

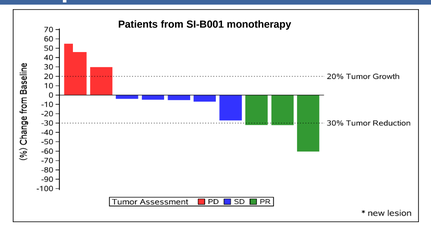
ALP: alkaline phosphatase

Efficacy of SI-B001 in HNSCC

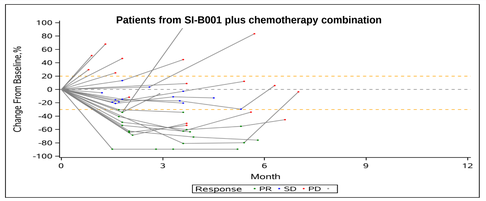
	Group A (in combination with paclitaxel)	Group B (in combination with docetaxel)	TOTAL (in combination with paclitaxel or docetaxel)	Single agent
	(N=17)	(N=8)	(N=25)	(N=10)
Best of response (BOR)				
CR	0	0	0	0
PR	10	1	11	3
SD	4	4	8	5
PD	3	3	6	2
ORR % (95%CI)	58.2% (32.9~81.6)	12.5% (0.3~52.7)	44.0% (24.4~65.1)	30.0% (6.7~65.3)
DCR % (95%CI)	82.4% (56.6~96.2)	62.5% (24.5~91.5)	76.0% (54.9~90.6)	80.0% (44.4~97.5)
DoR (m) (median, range)	3.9 (1.7~12.5+)	1.6	3.9 (1.6~12.5+)	3.3 (0.4~7.4)
PFS (m) (median, 95% CI)	5.4 (3.7, 6.3)	1.6 (1.2, 3.7)	3.7 (2.0, 5.4)	2.7 (1.8~7.9)

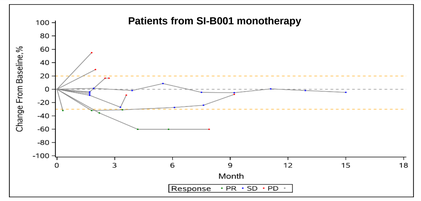
Antitumor Tumor Responses



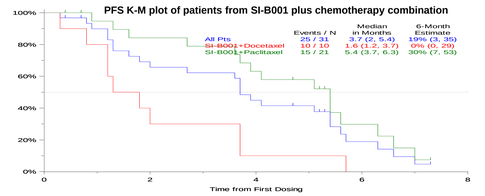


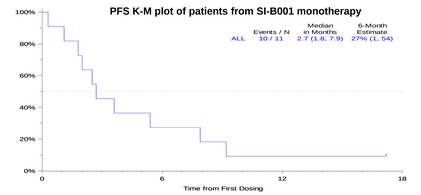
Tumor Responses Were Durable





Progression-Free Survival





Conclusions

- ❑ SI-B001 plus paclitaxel demonstrated encouraging anti-tumor activity in recurrent and metastatic HNSCC with ORR of 58.2%, DCR of 82.4%, DoR of 3.9 months and PFS of 5.4 months. The toxicity of SI-B001 plus taxane-based chemotherapy in HNSCC is deemed to be manageable and tolerable.
- ❑ A phase III study of SI-B001 in HNSCC is currently being prepared.

Acknowledgments

We thank all the patients and their families for their participation.
We thank also all the investigators, study nurses, and other study staffs for their contributions.

References

1.Blair Renshaw, Jahan Salar Khalili, Sa Xiao, Yi Zhu. Anti-tumor efficacy of SI-B001, a novel EGFR × HER3 bispecific antibody, against EGFR-driven epithelial tumors alone or in comba-nation with paclitaxel and carboplatin. Cancer Res (2023) 83 (7_Supplement): 6309.