SI-B001 plus chemotherapy in patients with locally advanced or metastatic EGFR/ALK wild-type non-small cell lung cancer: A phase II, multicenter, open-label study

SYSTIMMUNE

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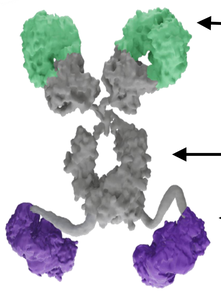
Background



- SI-B001 (izalontamab): a novel EGFR×HER3 bispecific antibody.
- Currently, 6 phase II clinical studies of SI-B001, either alone or in combination with chemotherapy, are being conducted in different epithelial carcinomas. The indication in this study (SI-B001-201) is EGFR/ALK wild-type NSCLC.
- Clinical trial information: NCT05020457

Objective

- To investigate the efficacy and safety of SI-B001 in combination with chemotherapy in patients with locally advanced or metastatic EGFR/ALK wild-type NSCLC.

Methods

- This phase II study enrolled patients with locally advanced or metastatic EGFR/ALK wild-type NSCLC who had failed first-line anti-PD-1/L1 therapy, with or without platinum-based chemotherapy (PBC).
- This study consisted of three cohorts: Cohort A pts received SI-B001 plus PBC as second-line treatment after failure to first-line anti-PD-1/L1 antibody monotherapy; Cohort B pts received SI-B001 plus docetaxel as second-line treatment after failure to first-line anti-PD-1/L1 therapy plus PBC; Cohort C pts received SI-B001 plus docetaxel as third-line or higher treatment after failure to first-line anti-PD-1/L1 therapy and PBC.
- This study evaluated SI-B001 in three distinct dosing schedules: Schedule 1 (16+9mg/kg once weekly), Schedule 2 (14mg/kg on Days 1 and 8 every 3 weeks), and Schedule 3 (21+12mg/kg once weekly).
- The primary endpoints of the study were to determine the objective response rate (ORR) in evaluable patients and to identify the optimal dose. The secondary endpoints included assessment of progression-free survival (PFS), disease control rate (DCR), duration of response (DOR), and safety.

Acknowledgments

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

References

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 combination with paclitaxel and carboplatin. Cancer Res (2023) 83 (7_Supplement): 6309.

Study Design

Eligibility criteria

- Locally advanced or metastatic EGFR/ALK wild-type NSCLC
- Previously treated with anti-PD-1/L1 therapy
- Docetaxel-Naïve
- Eastern Cooperative Oncology Group performance status of 0-1
- At least one measurable lesion per RECIST v1.1
- No autoimmune, inflammatory illnesses
- Adequate organ and marrow function
- Either no brain metastases or stable brain metastases at screening

Cohorts

- **Cohort A: SI-B001 + PBC（2L）** first-line anti-PD-1/L1 antibody monotherapy
- **Cohort B: SI-B001 + docetaxel（2L）** first-line anti-PD-1/L1 therapy plus PBC
- **Cohort C: SI-B001 + docetaxel（≥3L）** first-line anti-PD-1/L1 therapy and PBC

Schedules

- **Schedule 1: 16+9mg/kg QW**
- **Schedule 2: 14mg/kg D1D8 Q3W**
- **Schedule 3: 21+12mg/kg QW**

Primary endpoints: ORR, optimal dose for combination
Secondary endpoints: PFS, DCR, DOR, safety

Patients

- As of the first data cutoff (Nov 11, 2022), 55 patients were enrolled, including 1 pt in Cohort A, 45 pts in Cohort B, 8 pts in Cohort C, and 1 pt based on the investigator's discretion. The data and analysis presented in this poster are based on the updated follow-up data as of April 17, 2023.

Table 1. Patient demographics

	ALL (N=55)	Cohort-A (N=1)	Cohort-B (N=45)	Cohort-C (N=8)	Other (N=1)
Age (Median, Range)					
	61.0 (33.0 - 76.0)	57.0 (57.0 - 57.0)	61.0 (33.0 - 76.0)	63.5 (42.0 - 69.0)	64.0 (64.0 - 64.0)
Weight (Mean, Range)					
	62.5 (44.0 - 82.0)	60.4 (60.4 - 60.4)	62.2 (44.0 - 82.0)	63.2 (52.5 - 79.0)	71.8 (71.8 - 71.8)
BMI (Mean, Range)					
	22.9 (17.5 - 30.3)	22.7 (22.7 - 22.7)	22.6 (17.5 - 30.1)	23.9 (20.5 - 30.3)	28.4 (28.4 - 28.4)
BSA (Mean, Range)					
	1.7 (1.4 - 2.0)	1.7 (1.7 - 1.7)	1.7 (1.4 - 2.0)	1.7 (1.5 - 2.0)	1.8 (1.8 - 1.8)
Smoking History					
Never	11/55 (20%)	0/1 (0%)	9/45 (20%)	2/8 (25%)	0/1 (0%)
Previous	38/55 (69%)	1/1 (100%)	32/45 (71%)	4/8 (50%)	1/1 (100%)
Current	6/55 (11%)	0/1 (0%)	4/45 (9%)	2/8 (25%)	0/1 (0%)
UNK	0/55 (0%)	0/1 (0%)	0/45 (0%)	0/8 (0%)	0/1 (0%)
ECOG					
0	6/55 (11%)	0/1 (0%)	4/45 (9%)	2/8 (25%)	0/1 (0%)
1	48/55 (87%)	1/1 (100%)	40/45 (89%)	6/8 (75%)	1/1 (100%)
UNK	1/55 (2%)	0/1 (0%)	1/45 (2%)	0/8 (0%)	0/1 (0%)

Safety

- The most common Grade ≥3 treatment-related adverse events (TRAEs) were neutropenia (15%), myelosuppression (13%), and leukopenia (9%).
- No drug-related death was observed.

Table 2. TRAE Summary (≥G3 occurred)

	SI-B001 plus chemotherapy (N=55)				
PT Term	G1	G2	G3	G4	All Grade
Rash	20 (36%)	10 (18%)	3 (5%)		33 (60%)
Mouth ulceration	6 (11%)	7 (13%)	1 (2%)		14 (25%)
Leukopenia	6 (11%)	2 (4%)	5 (9%)		13 (24%)
Anemia	6 (11%)	5 (9%)	2 (4%)		13 (24%)
Pyrexia	9 (16%)	3 (5%)	1 (2%)		13 (24%)
Neutropenia	4 (7%)		7 (13%)	1 (2%)	12 (22%)
Diarrhea	8 (15%)	3 (5%)	1 (2%)		12 (22%)
Myelosuppression	1 (2%)	2 (4%)	2 (4%)	5 (9%)	10 (18%)
Paronychia	5 (9%)	2 (4%)	1 (2%)		8 (15%)
Hypokalemia	3 (5%)	2 (4%)	2 (4%)		7 (13%)
Dermatitis acneiform	6 (11%)		1 (2%)		7 (13%)
Pneumonia		2 (4%)	4 (7%)		6 (11%)
Asthenia	3 (5%)	2 (4%)	1 (2%)		6 (11%)
Lymphopenia	3 (5%)		2 (4%)		5 (9%)
Chest discomfort	2 (4%)	2 (4%)	1 (2%)		5 (9%)
Hypersensitivity			4 (7%)		4 (7%)
Hypoaesthesia	1 (2%)		1 (2%)		2 (4%)
Respiratory failure	1 (2%)		1 (2%)		2 (4%)
Cardiomyopathy			1 (2%)		1 (2%)
Gastritis			1 (2%)		1 (2%)
Soft tissue infection			1 (2%)		1 (2%)
Heart rate increased			1 (2%)		1 (2%)
Interstitial lung disease			1 (2%)		1 (2%)
Tachypnoea			1 (2%)		1 (2%)
Cardiac failure				1 (2%)	1 (2%)
Septic shock				1 (2%)	1 (2%)

Efficacy

- Among the 55 enrolled pts, 52 were evaluable for efficacy; ORR (n/N, [95%CI]) was 28.9% (15/52, [17.1, 43.1]), DCR was 75.0% (39/52, [61.1, 86.0]) (Table 3).
- In Cohort B, 42 pts were evaluable for efficacy. Among them, 23 were treated on schedule 1 (16+9mg/kg, QW), the ORR was 43.5% (10/23, [23.2, 65.5]) and the DCR was 69.6% (16/23, [47.1, 86.8]) (Table 4).
- Among the 23 evaluable pts in Cohort B treated on schedule 1 (16+9mg/kg, QW), 19 had no actionable genomic alterations (AGA), the ORR was 47.4% (9/19, [24.5, 71.1]), the DCR was 73.7% (14/19, [48.8, 90.9]), and the mPFS was 7.2m (Table 5, Figure 1-3).

Table 3. Efficacy by Cohort

	Cohort A (N=1)	Cohort B (N=42)	Cohort C (N=8)	Other (N=1)	Total (N=52)
BOR					
CR	0	0	0	0	0
PR	1	13	1	0	15
SD	0	17	7	0	24
PD	0	9	0	1	10
NE	0	3	0	0	3
ORR % (95%CI)	100%	31.0% (17.6~47.1)	12.5% (0.3~52.7)	0	28.9% (17.1~43.1)
DCR % (95%CI)	100%	71.4% (55.4~84.3)	100%	0	75.0% (61.1~86.0)
DoR (m) (median, range)	5.5	4.2 (0.2~13.1+)	4.1	/	4.2 (0.2~13.1+)

Figure 1. PFS

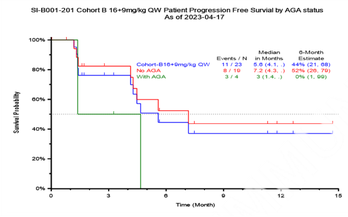


Table 4. Efficacy for Cohort B by dose

	21+12mg/kg QW (N=1)	14mg/kg D1D8 Q3W (N=18)	16+9mg/kg QW (N=23)	Total (N=42)
BOR				
CR	0	0	0	0
PR	0	3	10	13
SD	1	10	6	17
PD	0	5	4	9
NE	0	0	3	3
ORR % (95%CI)	0	16.7% (3.6~41.4)	43.5% (23.2~65.5)	31.0% (17.6~47.1)
DCR % (95%CI)	100%	72.2% (46.5~90.3)	69.6% (47.1~86.8)	71.4% (55.4~84.3)
DoR (m) (median, range)	/	2.9 (0.9~4.2)	NR (0.2~13.1+)	4.2 (0.2~13.1+)

Figure 2. Change in Tumor Size

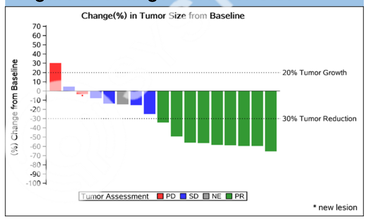
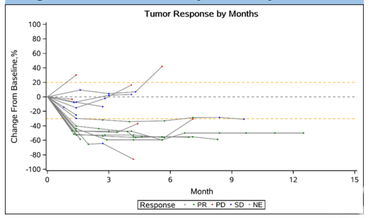


Table 5. Efficacy for Cohort B 16+9mg/kg by AGA

	No AGA (N=19)	With AGA (N=4)	Total (N=23)
BOR			
CR	0	0	0
PR	9	1	10
SD	5	1	6
PD	2	2	4
NE	3	0	3
ORR % (95%CI)	47.4% (24.5~71.1)	25.0% (0.6~80.6)	43.5% (23.2~65.5)
DCR % (95%CI)	73.7% (48.8~90.9)	50.0% (6.8~93.2)	69.6% (47.1~86.8)
DoR (m) (median, range)	NR (0.2~13.1+)	3.8	NR (0.2~13.1+)
PFS (m) (median, 95% CI)	7.2 (4.3, NR)	3.0 (1.4, NR)	5.6 (4.1, NR)

Figure 3. Tumor Response by Months



Conclusions

- SI-B001 (16+9 mg/kg QW) + docetaxel in NSCLC patients without AGA in 2nd line setting achieved ORR of 47.4% and mPFS of 7.2 months.
- The toxicity of SI-B001 + docetaxel was deemed to be manageable.
- A phase III study of SI-B001 + docetaxel in NSCLC patients without AGA is on-going.