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Abstract Number:

6037

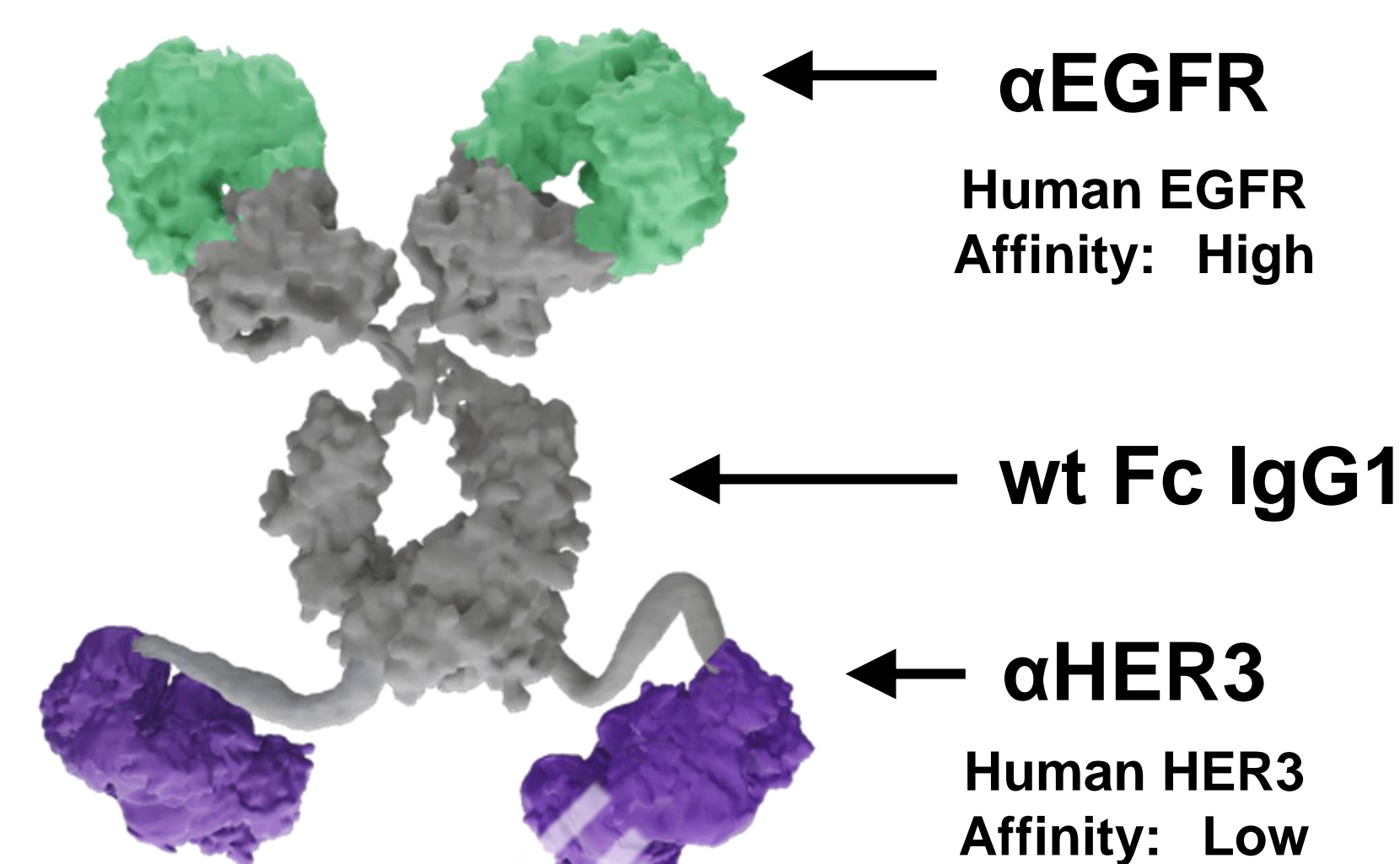
# Results from two phase II studies of SI-B001, an EGFR×HER3 bispecific antibody with/without chemotherapy in patients (pts) with recurrent and metastatic head and neck squamous cell carcinoma (HNSCC).

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## Background and Methods

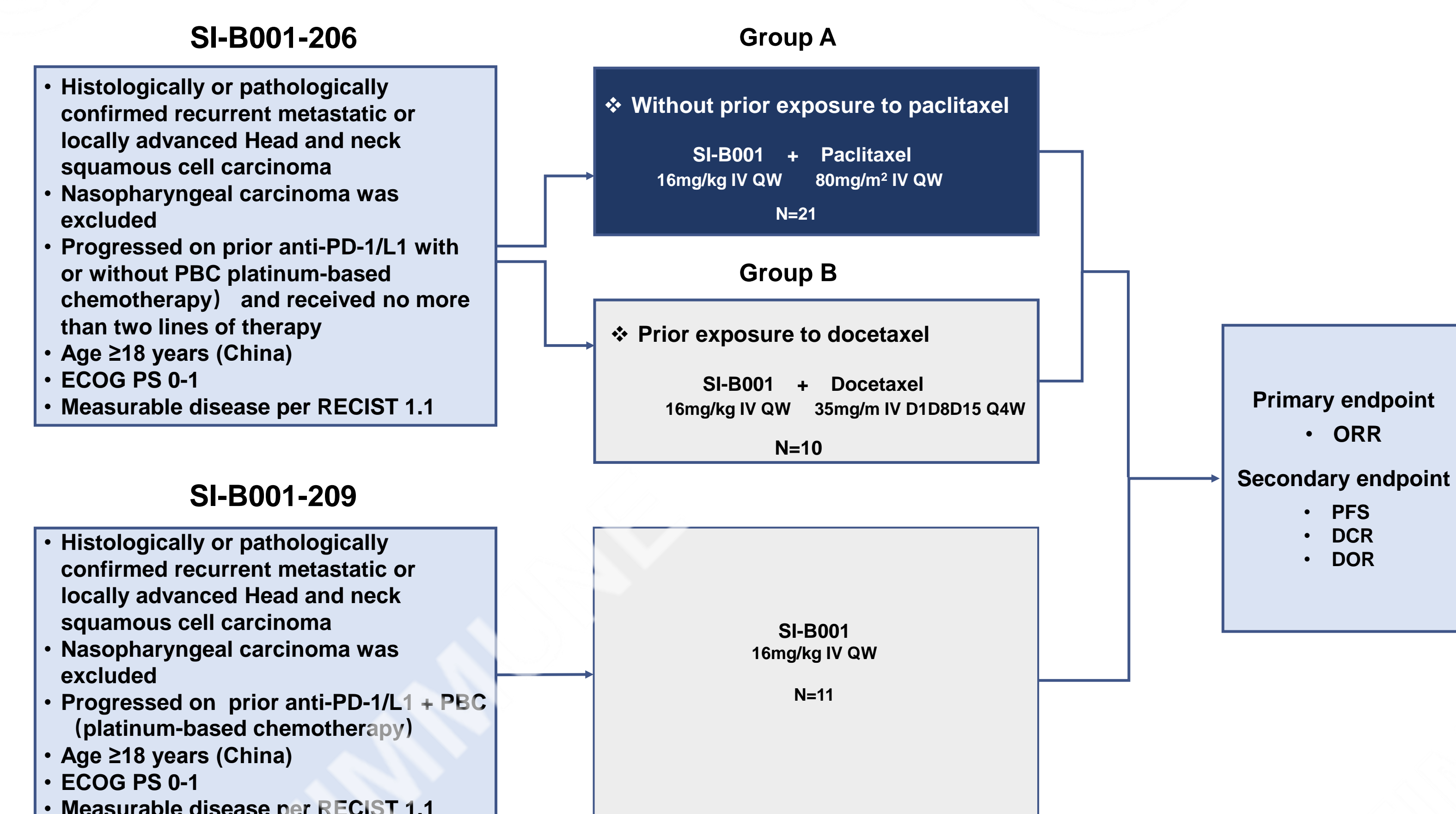
**Background:** SI-B001 (izalontamab) is a novel EGFR×HER3 bispecific antibody. We present the efficacy and safety results from two ongoing studies, SI-B001-206 and SI-B001-209, of patients with recurrent and metastatic HNSCC. Clinical trial information: NCT05044897 and NCT05054439.



## 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<sup>2</sup> IV QW); Group B, pts with prior exposure to paclitaxel were treated with SI-B001 (12mg/kg IV QW) plus docetaxel (35mg/m<sup>2</sup> 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				Table 1B. Baseline Characteristics of S209	
	ALL (N=31)	SI-B001+ Paclitaxel (N=21)	SI-B001+Docetaxel (N=10)	ALL(N=11)	
Age (Median, Range)	58.0 (36.0 - 75.0)	59.0 (41.0 - 75.0)	52.5 (36.0 - 75.0)	57.0 (46.0 - 71.0)	
Height (Mean, Range)	164.5 (145.0 - 184.0)	164.0 (145.0 - 184.0)	165.7 (162.0 - 170.0)	164.0 (146.0 - 172.0)	
Weight (Mean, Range)	53.5 (29.8 - 66.4)	52.4 (29.8 - 65.8)	55.8 (38.0 - 66.4)	54.4 (30.0 - 73.5)	
BMI (Mean, Range)	19.7 (14.0 - 24.8)	19.4 (14.2 - 24.2)	20.3 (14.0 - 24.8)	20.2 (16.0 - 25.4)	
BSA (Mean, Range)	1.6 (1.1 - 1.8)	1.5 (1.1 - 1.8)	1.6 (1.3 - 1.8)	1.6 (1.3 - 1.9)	
Ethnic (Han)	26/31 (84%)	17/21 (81%)	9/10 (90%)	11/11 (100%)	
Sex (Male)	26/31 (84%)	17/21 (81%)	9/10 (90%)	10/11 (91%)	
Smoking History					
Never	15/31 (48%)	12/21 (57%)	3/10 (30%)	3/11 (27%)	
Previous	15/31 (48%)	8/21 (38%)	7/10 (70%)	7/11 (64%)	
Current	0/31 (0%)	0/21 (0%)	0/10 (0%)	1/11 (9%)	
UNK	1/31 (3%)	1/21 (5%)	0/10 (0%)	0/11 (0%)	
Alcohol History					
Never	25/31 (81%)	18/21 (86%)	7/10 (70%)	6/11 (55%)	
Previous	6/31 (19%)	3/21 (14%)	3/10 (30%)	5/11 (45%)	
Current	0/31 (0%)	0/21 (0%)	0/10 (0%)	0/11 (0%)	
UNK	0/31 (0%)	0/21 (0%)	0/10 (0%)	0/11 (0%)	
ECOG					
0	3/31 (10%)	1/21 (5%)	2/10 (20%)	0/11 (0%)	
1	28/31 (90%)	20/21 (95%)	8/10 (80%)	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.

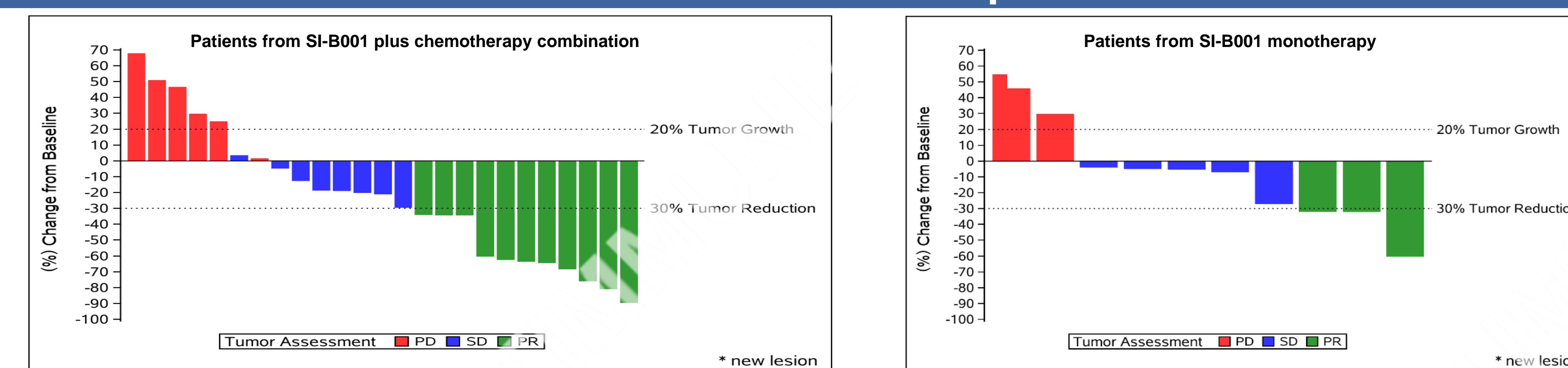
Table 2A. FREQ≥10% or G≥3 TRAE by PT						Table 2B. FREQ≥10% or G≥3 TRAE by PT				
PT Name	SI-B001-206 (N=31)					SI-B001-209 (N=11)				
	G1	G2	G3	G4	All Grade	G1	G2	G3	All Grade	
Rash	13 (42%)	2 (6%)	4 (13%)		19 (61%)	1 (9%)	2 (18%)		3 (27%)	
Anemia	7 (23%)	1 (3%)	2 (6%)		10 (32%)	2 (18%)	1 (9%)		3 (27%)	
Leukopenia	5 (16%)	2 (6%)	2 (6%)	1 (3%)	10 (32%)					
Proteinuria	7 (23%)				7 (23%)	3 (27%)			3 (27%)	
Stomatitis	2 (6%)	3 (10%)	1 (3%)		6 (19%)					
Asthenia	3 (10%)	3 (10%)			6 (19%)	1 (9%)	1 (9%)		2 (18%)	
Weight decreased	6 (19%)				6 (19%)	2 (18%)			2 (18%)	
Mouth ulceration		4 (13%)	1 (3%)		5 (16%)	2 (18%)			2 (18%)	
Paronychia	2 (6%)	1 (3%)	1 (3%)		4 (13%)					
Skin fissures	1 (3%)	2 (6%)	1 (3%)		4 (13%)	2 (18%)			2 (18%)	
Nausea	1 (3%)	3 (10%)			4 (13%)	1 (9%)	1 (9%)		2 (18%)	
Dermatitis acneiform	2 (6%)		1 (3%)		3 (10%)	2 (18%)			2 (18%)	
Hypoaesthesia	1 (3%)	1 (3%)	1 (3%)		3 (10%)	2 (18%)			2 (18%)	
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

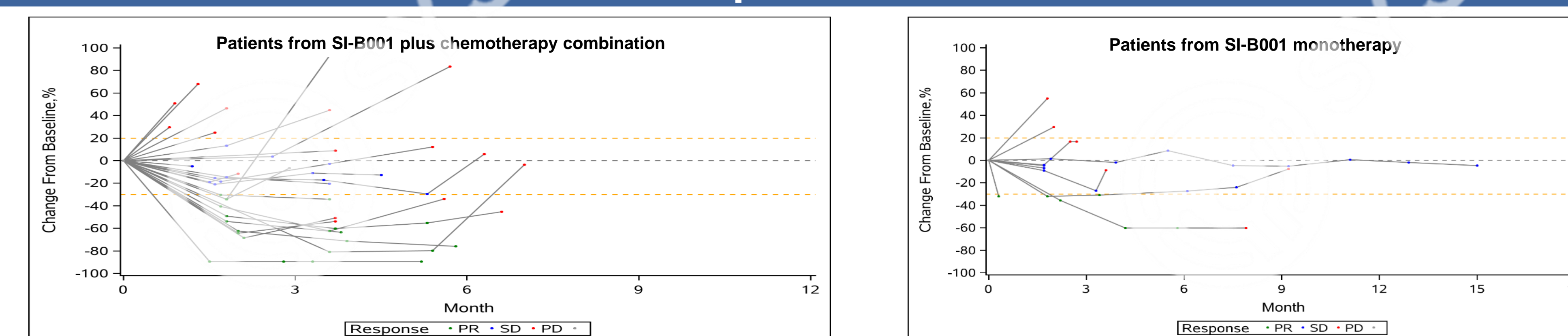
## Efficacy of SI-B001 in HNSCC

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

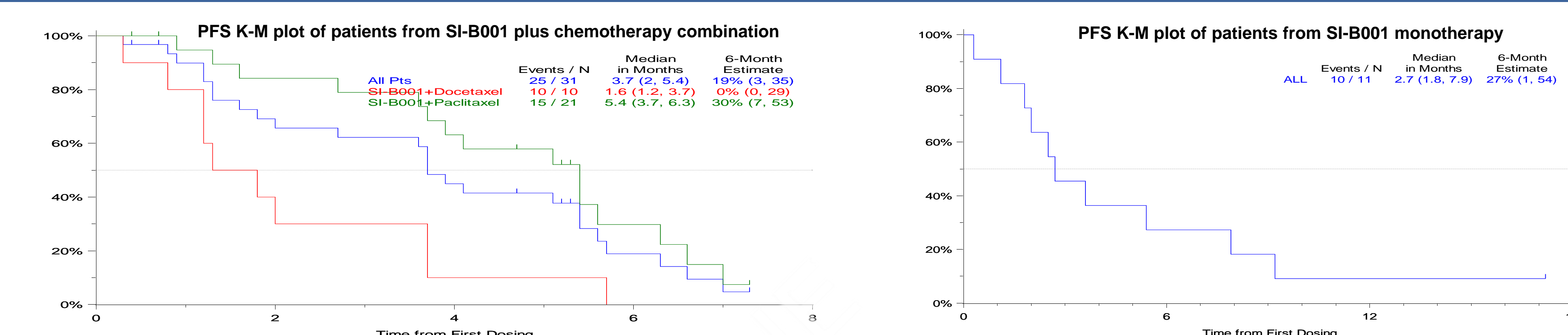
## Antitumor Tumor Responses



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