Abstract # 391

A Multicenter, Phase 1 Study of AB011, a Recombinant Humanized Anti-CLDN18.2 Monoclonal Antibody (AB011), as Monotherapy and Combined with Capecitabine and Oxaliplatin (CAPOX) in Patients with Advanced Solid Tumors

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Background

- Claudin18.2 (CLDN18.2) is a tight junction protein normally expressed in gastric mucosa and several cancer types.[1] CLDN18.2 is considered a potential therapeutic target.[2]
- AB011, a humanized, anti-CLDN18.2 monoclonal antibody (IgG1), showed synergy with cytotoxic agents in preclinical research.
- Here we report preliminary data for AB011 both as monotherapy and combined with capecitabine + oxaliplatin (CAPOX) in patients with advanced solid tumors (AB011-ST-01; NCT04400383).

Methods

- This multicenter, open-label, phase 1 study was to evaluate the safety and preliminary efficacy of AB011 first as monotherapy and then AB011 combined with chemotherapy in advanced solid tumors. Patients were enrolled from 22-July-2020 to 15-June-2022.
- **Monotherapy**: In the dose-escalation stage, AB011 dose levels of 1 mg/kg to 30 mg/kg were investigated using i3 + 3 design, and 20 mg/kg and 30 mg/kg doses were further evaluated in the dose-expansion stage. AB011 was infused on Day 1 and Day 15 of each 28-day cycle.
- **Combination treatment (Tx)**: AB011, at dose level of 20 mg/kg and 30 mg/kg, 21 days per cycle, combination with CAPOX were evaluated as first-line treatment in advanced gastric cancer/ gastroesophageal junction adenocarcinoma (GC/GEJA).
- **Data cutoff: 06-Sep-2022.**

Conclusion

- AB011 monotherapy and AB011 combined with chemotherapy showed a manageable and tolerable safety profile in advanced solid tumors.
- AB011 combined with chemotherapy (CAPOX) as first-line treatment demonstrated preliminary clinical benefit in patients with GC/GEJA.
- No differences were found in safety and preliminary efficacy between 20 mg/kg and 30 mg/kg doses in combined therapy.

Results

Table 1. Baseline Characteristics

Monotherapy	Total (N = 35)
Age, median (range), years	61.0 (26-77)
Male, n (%)	25 (71.4)
ECOG PS=1, n (%)	34 (97.1)
No. prior lines, n (%)	
< 3	22 (62.9%)
≥ 3	9 (25.7%)
	GC/GEJA (N=26)
Lauren classification, n (%)	
Intestinal type	3 (11.5)
Diffuse type	3 (11.5)
Mixed type	4 (15.4)
Unknown	16 (61.5)
Signet ring cell carcinoma, n (%)	4 (15.4)
No. metastatic organs, n (%)	
< 3	13 (50.0)
≥ 3	13 (50.0)
Peritoneal metastasis, n (%)	14 (53.8)
Liver metastasis, n (%)	9 (34.6)
	PC (N=9)
Metastatic PC, n (%)	8 (88.9)
Peritoneal metastasis, n (%)	1 (11.1)
Liver metastasis, n (%)	5 (55.6)

Combination Tx	GC/GEJA (N = 24)
Age, median (range), years	63.5 (35-78)
Male, n (%)	18 (75.0)
ECOG PS=1, n (%)	23 (95.8)
Primary lesion	
GC, n (%)	22 (91.7)
GEJA, n (%)	2 (8.3)
History of gastrectomy, n (%)	
Yes	6 (25.0)
No	18 (75.0)
Lauren classification, n (%)	
Intestinal type	4 (16.7)
Diffuse type	3 (12.5)
Mixed type	2 (8.3)
Unknown	15 (62.5)
Signet ring cell carcinoma, n (%)	2 (8.3)
No. metastatic organs, n (%)	
< 3	13 (54.2)
≥ 3	11 (45.8)
Peritoneal metastasis, n (%)	8 (33.3)
Liver metastasis, n (%)	9 (37.5)

ECOG PS: Eastern Cooperative Oncology Group performance status; PC: pancreatic cancer

Table 2. Drug Exposure & AE Summary (Monotherapy)

Monotherapy	AB011 dose levels					
	1 mg/kg (N=1)	3 mg/kg (N=1)	10 mg/kg (N=3)	20 mg/kg (N=13)	30 mg/kg (N=17)	Total (N=35)
No. infusions, median (range)	3	16	12.0 (3-12)	2.0 (1-12)	3.0 (1-40)	2.0 (1-40)
AB011-related TEAEs, n (%)	1 (100.0)	1 (100.0)	3 (100.0)	13 (100.0)	16 (94.1)	34 (97.1)
AB011-related serious TEAEs, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	3 (23.1)	4 (23.5)	7 (20.0)
DLTs, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	1 (7.1)
Gr ≥3 TEAEs, n (%)	0 (0.0)	1 (100.0)	0 (0.0)	6 (46.2)	7 (41.2)	14 (40.0)
AB011-related Gr ≥3 TEAEs, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	3 (23.1)	5 (29.4)	8 (22.9)

Table 3. Drug Exposure & AE Summary (Combination Tx)

Combination Tx	AB011 + CAPOX		
	20 mg/kg (N=13)	30 mg/kg (N=11)	Total (N=24)
No. infusions, median (range)	7.0 (1-17)	4.0 (1-9)	5.5 (1-17)
AB011-related TEAEs	13 (100.0)	11 (100.0)	24 (100.0)
AB011-related serious TEAEs	3 (23.1)	2 (18.2)	5 (20.8)
AB011- or CAPOX-related serious TEAEs, n (%)	4 (30.8)	2 (18.2)	6 (25.0)
DLTs, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Gr ≥3 TEAEs, n (%)	9 (69.2)	6 (54.5)	15 (62.5)
AB011 related Gr ≥3 TEAEs, n (%)	6 (46.2)	4 (36.4)	10 (41.7)
AB011- or CAPOX-related Gr ≥3 TEAEs, n (%)	9 (69.2)	5 (45.5)	14 (58.3)

Patients and Treatment

Monotherapy: 35 eligible patients enrolled (26 GC/GEJA, 9 PC) and treated with AB011 monotherapy.

- Baseline characteristics are shown in **Table 1**.
- Median follow-up: 13.14 months (IQR 6.05-19.81).

Combination Tx: 24 eligible patients with GC/GEJA were treated with AB011 plus CAPOX, with 13 patients received the 20mg/kg dose, and 11 patients received the 30mg/kg dose.

- 11 (45.8%) patients had ≥ 3 metastatic organs (**Table 1**).
- Median follow-up: 5.16 months (IQR 2.83-6.64).

Safety

- Adverse events (AEs), including treatment-emergent AEs (TEAEs) and dose-limiting toxicities (DLTs) are summarized in **Table 2**, **Table 3**, and **Table 4**.
- **Monotherapy**: 1 patient (30 mg/kg, GC) experienced grade 3 dyspnea and was considered as a DLT.
- **Combination Tx**: 9 (37.5%) patients reported serious TEAEs. No DLTs or treatment-related AEs leading to death occurred.

Efficacy

- **Monotherapy**: 1 (2.9%) patient achieved complete response (CR), 8 (22.9%) patients had stable disease (SD), and 3 (8.6%) patients had non-CR/non-progressive disease (NCNP).
- **Combination Tx**: Confirmed ORR was 52.2% among 23 pts with at least one post-treatment tumor assessment, with 53.8% ORR (20 mg/kg group) and 50.0% ORR (30 mg/kg group). Disease control rate was 100% (**Figure 1**, **Figure 2**).

Table 4. Most Common (≥20%) AB011-related TEAEs

Monotherapy Preferred term (PT), n (%)	Total (N=35)	
	Grade ≥3	Any grade
Vomiting	3 (8.6)	29 (82.9)
Nausea	0 (0.0)	22 (62.9)
Hypoalbuminemia	1 (2.9)	12 (34.3)
Hypophagia	0 (0.0)	10 (28.6)
Asthenia	0 (0.0)	10 (28.6)
Anemia	1 (2.9)	7 (20.0)

Combination Tx PT, n (%)	20 mg/kg (N=13)		30 mg/kg (N=11)		Total (N=24)	
	Gr ≥3	Any	Gr ≥3	Any	Gr ≥3	Any
Nausea	1 (7.7)	12 (92.3)	2 (18.2)	8 (72.7)	3 (12.5)	20 (83.3)
Vomiting	1 (7.7)	12 (92.3)	0 (0.0)	4 (36.4)	1 (4.2)	16 (66.7)
Hypoalbuminemia	0 (0.0)	6 (46.2)	2 (18.2)	7 (63.6)	2 (8.3)	13 (54.2)
Weight decreased	0 (0.0)	5 (38.5)	0 (0.0)	7 (63.6)	0 (0.0)	12 (50.0)
Anemia	1 (7.7)	5 (38.5)	1 (9.1)	3 (27.3)	2 (8.3)	8 (33.3)
Asthenia	0 (0.0)	2 (15.4)	0 (0.0)	4 (36.4)	0 (0.0)	6 (25.0)
Hyponatraenia	0 (0.0)	2 (15.4)	0 (0.0)	3 (27.3)	0 (0.0)	5 (20.8)

Figure 1. Tumor Shrinkage in Target Lesion (Combination Tx)

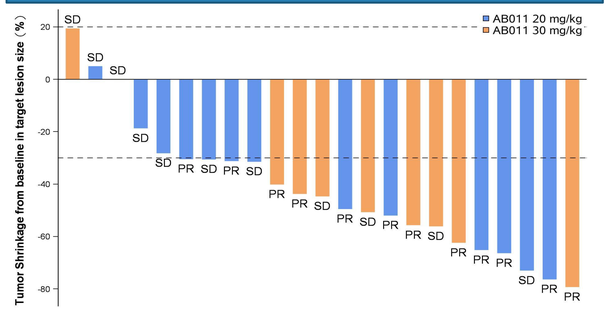
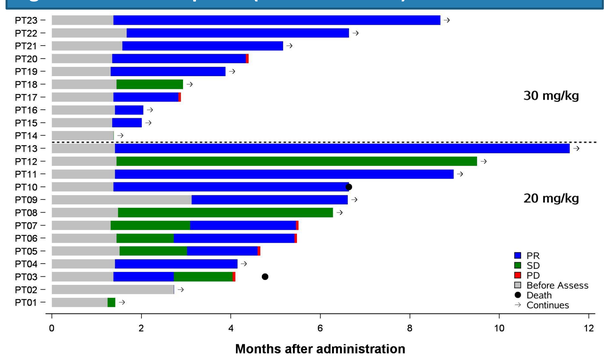


Figure 2. Tumor Response (Combination Tx)



Note: One patient did not have post-treatment tumor assessment

References: 1. Sahin U, et al. *Clin Cancer Res.* 2008;14(23):7624–7634.; 2. Cao W, et al. *Biomark Res*. 2022;10(1):38. Contact email: lijin@csco.org.cn