Final Publication Number IFPN1: 257P

Phase 1 Clinical Trial of Ragistomig (ABL503/TJ-L14B: PD-L1 × 4-1BB Bispecific Antibody) Q6W Dosing Balances Favorable Safety and Sustained Efficacy Through Extended Immunologic Memory and Expansion of CD8⁺ T Cells

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Background

- Ragistomig (ABL503/TJ-L14B) is a bi-Fab-Fab bispecific anti-PD-L1 mAb (PD-L1) and human IgG1 fused with anti-4-1BB scFv, Figure 1
- Ragistomig, a bispecific antibody targeting PD-L1 and 4-1BB, has been engineered to restrict 4-1BB costimulation to PD-L1 expressing tumor microenvironment, thereby reducing systemic hepatotoxicity associated with 4-1BB monospecific antibodies, while enhancing enhancer activity and overcoming resistance to PD-L1/L2 checkpoint inhibitors.
  - PD-L1 mAb blocks immune tumor immunity by reprogramming suppressive and stimulatory signals leading to more effective cancer control.
  - 4-1BB (CD137), a costimulatory receptor of TNFR superfamily, enhances T-cell proliferation and memory functions, through costimulatory signals. 4-1BB promotes the effective expansion and differentiation of memory CD8⁺ T cells, supporting robust and durable antitumor immunity.
- Preliminary results from Registering monotherapy administered Q6W demonstrated encouraging clinical efficacy, achieving an ORR of 26.9% and a DCR of 69.2% with manageable toxicity, including in subjects who were diagnosed refractory to prior anti-PD-L1/L1 therapy.[1]
- To optimize the safety profile while preserving encouraging efficacy for combination strategy, an extended-interval Q9W regimen was subsequently investigated in the phase 1 trial.

Figure 1 Registering (ABL503/TJ-L14B) and Mechanism of Action, PD-L1 Dependent 4-1BB Activation

Method

- First-in-human, multicenter, open-label, phase 1 trial of Ragistomig in advanced or metastatic advanced/refractory solid tumor, to assess safety, preliminary anti-tumor efficacy and pharmacokinetic (PK)/pharmacodynamic (PD) relationship, (NCT04785941)
- The phase 1 trial consists of dose escalation (completed) and expansion part (ongoing). To further optimize the dosing strategy, especially for the combination regimen, 3 mg/kg Q6W cohort was introduced in the dose expansion part 2B, following the dose expansion part 2A with Q2W regimen, Figure 2
- Registering was administered intravenously at 3 mg/kg Q6W to subjects with prior immuno-oncology(IO)-treated relapsed or refractory solid tumors expressing PD-L1, IC25 or TPS ≥ 1%
- This study presents initial clinical data from the newly investigated Q6W regimen, with data from the 3 mg/kg Q2W cohort included for reference.

Figure 2 Phase 1 Study Design (Dose Escalation Part and Expansion Part)

Result

Baseline Demographics and Clinical Characteristics

- As of October 22, 2025, a total of 20 subjects had been enrolled in the 3 mg/kg Q6W cohort, with treatment ongoing in 3 subjects.
- The Q6W cohort enrolled subjects with solid tumors who had previously received IO treatment and had subsequently exhausted all available treatment options, representing a population with significant unmet medical needs.
- All subjects in Q6W cohort had an ECOG performance status of 0-1, with the majority (80%) classified as ECOG 1, indicating mild functional limitation in activity.
- Subjects were heavily pretreated, with 70.0% having received ≥ 3 prior lines of systemic anti-cancer treatment in 3 mg/kg Q6W cohorts.

Table 1 Baseline Demographics and Clinical Characteristics

	3 mg/kg Q6W (N=20)	3 mg/kg Q2W (N=16)
Age	62	61
Sex		
Female, n (%)	10(50.0%)	8(50.0%)
Male, n (%)	10(50.0%)	8(50.0%)
ECOG		
ECOG 0, n (%)	4 (20%)	3(18.8%)
ECOG 1, n (%)	16(80%)	13(81.2%)
Prior Systemic Cancer Therapy		
≥ 1	20(100%)	16(100%)
≥ 2	19(95.0%)	15(93.8%)
≥ 3	14(70.0%)	9(56.3%)
Number of prior lines, median	3.5	3
≥ 4	6(30.0%)	6(37.5%)
≥ 5	4(20.0%)	4(25.0%)
≥ 6	3(15.0%)	3(18.8%)
≥ 7	2(10.0%)	2(12.5%)
≥ 8	1(5.0%)	1(6.3%)
≥ 9	1(5.0%)	1(6.3%)
≥ 10	1(5.0%)	1(6.3%)

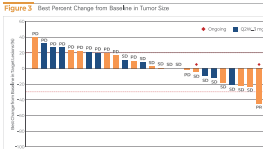
Efficacy

- Extending the dosing interval from Q2W to Q6W is expected to demonstrate encouraging antitumor activity.
- In 3 mg/kg Q6W cohort, two cPR (12%) were achieved out of 17 evaluable subjects, including those with anti-PD-L1 relapsed HNSCC and anti-PD-L1 refractory anal malignancy, Figure 3
- In addition, subjects with stable disease exhibited meaningful tumor reductions (-47% in anti-PD-L1 relapsed NSCLC and -22% in anti-PD-L1 relapsed neuroendocrine tumor, even in heavily pretreated subjects (3 prior lines), Figure 3
- Despite reduced dosing frequency, the Q6W regimen presented disease control rate of 58.8%, comparable to that observed in the Q2W regimen (62.5%), Table 2

Table 2 Efficacy Profiles

ABL503 monotherapy efficacy profile	3 mg/kg Q6W (N=17)	3 mg/kg Q2W (N=16)
Objective Response Rate, n (%)	2 (11.8%)	4 (25.0%)
Disease Control Rate, n (%)	10 (58.8%)	9 (56.3%)
Complete response	0 (0.0%)	1 (6.1%)
Partial response	2 (11.8%)	3 (21.4%)
Stable disease	8 (47.1%)	5 (35.7%)
Progressive disease	7 (41.2%)	5 (35.7%)

Figure 3 Best Percent Change from Baseline in Tumor Size

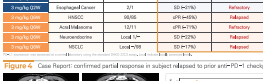


- Ragistomig demonstrated clinical activity across multiple solid tumor types.
- 72.7% of responders, including those with significant tumor reduction, had relapsed or were refractory to prior anti-PD-L1/L1 therapies, Table 3
- These findings suggest that Ragistomig reinvigorates exhausted T-cell subsets via 4-1BB-mediated costimulation, restoring effector activity in PD-L1 refractory tumors.[1]
- Durable disease control was observed, with stable disease for over 6 months in a patient with PD-L1-refractory bladder cancer.

Table 3 Responders in the 3 mg/kg Q2W and Q6W cohorts

Dose level	Tumor type	PD-L1 expression (CPS/TPS)	ABL503 BoR	Response to Prior anti-PD-L1	Prior anti-PD-L1/L1
3 mg/kg Q6W	Ovarian Cancer	100/1	cCR	Relapsed	Pembro+MEK inhibitor
3 mg/kg Q2W	Ovarian Cancer	10/5	uPR (-94%)	Naive	–
3 mg/kg Q2W	Head and Neck	20/10	uPR (-94%)	Relapsed	Nivolumab+DNA vaccine
3 mg/kg Q2W	Gastric	–	uPR (-91%)	Naive	–
3 mg/kg Q2W	Esophageal Cancer	2/1	SD (+21%)	Refractory	Nivolumab
1 mg/kg Q2W	HNSCC	90/50	uPR (-44%)	Relapsed	Nivolumab
3 mg/kg Q2W	Anal Malignancy	12/11	uPR (-77%)	Refractory	Pembrolizumab, Nivolumab
3 mg/kg Q2W	Neuroendocrine	Local 1.*	SD (+22%)	Relapsed	Atezolizumab
3 mg/kg Q2W	NSCLC	Local >50	SD (+17%)	Relapsed	Pembrolizumab

Figure 4 Case Report: confirmed partial response in subject relapsed to prior anti-PD-L1 checkpoint inhibitor.



- Demography
  - HNSCC, 65y, Male, CPS/TPS 90/85
- Tumor and Prior Treatment History
  - Surgery in 2021
  - Chemo+Cetuxi (Jun~Nov2021, 2bytt PD)
  - Radiologic recurrence confirmed in Aug 2021,
  - 1st line treatment, Nivolumab (Aug2021~Nov2023, 25yrtt SD)
  - Disease progression in Feb2025,
- ABL503 Treatment
  - The first infusion on 12Mar2025, (3 mg/kg Q6W)
  - At the initial tumor assessment at Week 6, tumor shrinkage of -60.0%, achieving PR,
  - At the second tumor assessment at Week 12, confirmed PR,
  - The tumor response is maintained beyond 6 month, and treatment is ongoing.

ABL503 induced a rapid, deep and durable antitumor response for HNSCC subject who had relapsed from prior anti-PD-L1 Nivolumab.

Safety

- A substantially improved safety profile was observed with the 3 mg/kg Q6W regimen.
- Only 1 of 20 subjects (5%) experienced ≥ Grade 3 treatment-emergent LFT elevation in the Q6W cohort.
- All ≥ Grade 3 treatment-related adverse events were recovered within 3-14 days with or without treatment interventions, and reduced LFT elevations, decreased platelet count, anemia, and decreased neutrophil count.
- No subjects discontinued treatment due to treatment-emergent adverse events (TEAEs) in the Q6W cohort. Importantly, no cases of cytokine release syndrome (CRS) were reported.
- Overall, the Q6W regimen was identified as potential optimal regimen for combination strategies with Ragistomig.

Table 4 Overall Safety Profiles

Category	3 mg/kg Q6W (N=20)	3 mg/kg Q2W (N=15)
Any adverse event	19 (95.0%)	15 (100.0%)
Any adverse event related to Ⓟ	10 (50.0%)	12 (80.0%)
Grade ≥ 3 AE	10 (50.0%)	10 (66.7%)
Grade ≥ 3 AE related to Ⓟ	3 (15.0%)	7 (46.7%)
Grade ≥ 3 Liver function test(LFT) elevation	1 (5.0%)	6 (40.0%)
Grade ≥ 3 Liver function test(LFT) elevation related to Ⓟ	1 (5.0%)	5 (33.3%)
AE leading to discontinuation of Ⓟ	0 (0.0%)	4 (26.7%)
AE related to Ⓟ leading to discontinuation	0 (0.0%)	2 (13.3%)
Any Cytokine release syndrome	0 (0.0%)	0 (0.0%)

Pharmacokinetics, Pharmacodynamic Biomarker (Peripheral Blood)

- Although overall exposure (C_{max}) was lower in the Q6W regimen compared with Q2W, antitumor efficacy remained preserved, Table 5
- Both effector and central memory CD8⁺ T-cell subsets were increased following treatment, with comparable fold-changes observed under the Q2W and Q6W, despite the extended dosing interval, Figure 5
- The Q6W regimen induced proliferation of effector CD8⁺ T cells. Notably, CTLA4⁺ Treg frequencies remained near baseline with Q6W, in contrast to the increase observed with Q2W, suggesting a more favorable effector-to-regulatory balance, Figure 5
- The preserved activation and expansion of key CD8⁺ T-cell subsets under Q6W suggest that immune-mediated pharmacodynamic activity may contribute to efficacy, supporting comparable antitumor effects to Q2W even under reduced drug exposure.

Table 5 Pharmacokinetics Parameters, mean (SD) After the First Dose

Parameters	3 mg/kg Q2W (N=15)	3 mg/kg Q6W (N=20)
C_{max} (ng/mL)	7,8 (5,6)	2,2 (1,1)
AUC$_{last}$ (hr*ng/mL)	8,710 (2,140)	8,690 (2,820)
C_{trough} (ng/mL)	82,5 (42,2)	8,4 (2,4)

Figure 5 Change in Immune Cell Subsets

Conclusion

- Ragistomig (ABL503/TJ-L14B) monotherapy Q6W demonstrated encouraging antitumor activity with a favorable safety profile in patients with heavily pretreated solid tumors.
- Despite the extended dosing interval, 3 mg/kg Q6W regimen presented antitumor efficacy, with confirmed responses and meaningful tumor stabilization in IO-relapsed or refractory subjects with unmet medical needs.
- Q6W exhibited a favorable safety profile, with only 1 of 20 subjects experiencing Grade ≥ 3 LFT elevations, no treatment discontinuations due to TEAEs, and no reported CRS.
- Immune cell pharmacodynamics demonstrated expansion of effector memory and CDR T cells under the Q6W regimen, while showing attenuated Treg expansion, indicating durable immune engagement despite the extended dosing interval.
- The 3 mg/kg Q6W regimen demonstrates an optimized safety-efficacy balance, supporting continued development of Ragistomig in future combination development, Evaluation of the 3 mg/kg Q6W cohort is ongoing.

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