BGB-A317-212: A Multicenter, Open-label, Phase II Study to Evaluate the Efficacy and Safety of Tislelizumab in Combination With Lenvatinib in Patients With Selected Solid Tumors

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Conclusions

Results from the interim analysis of the phase II study show that the combination of tislelizumab and lenvatinib demonstrated preliminary antitumor activity in patients with selected tumor types. The treatment combination exhibited a manageable safety profile, without identifying new safety signals.

Longer follow-up is needed to further investigate the potential of this combination to benefit patients with advanced solid tumors.

Background

Tislelizumab (BGB-A317) is a humanized monoclonal antibody that targets the programmed cell death protein 1 (PD-1)[1,2] and has demonstrated promising efficacy in various advanced solid tumors.[3,4] However, some patients fail to respond or develop resistance to tislelizumab monotherapy.[5,6]

Combining PD-1 checkpoint inhibitors with antiangiogenic agents has shown improved anticancer efficacy and prolonged survival compared with each agent alone.[7] Lenvatinib, a receptor tyrosine kinase inhibitor that targets vascular endothelial growth factors 1-3, fibroblast growth factor receptors 1-4, platelet-derived growth factor receptor alpha, stem cell factor receptor, and rearranged during transfection, has shown potentially superior effects when combined with anti–PD-1 therapy.[8,9]

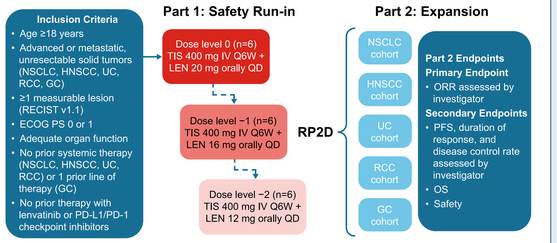
Here, we present the primary results of the open-label, multicenter, phase II BGB-A317-212 study evaluating the safety and preliminary anticancer activity of tislelizumab and lenvatinib in Chinese patients with various solid tumors (NCT05014828).

Methods

Study Design

- BGB-A317-212 is an open-label, multicenter, phase II study (**Figure 1**)
- Part 1 (safety run-in) determined the recommended phase II dose (RP2D) of lenvatinib 20 mg orally per day in combination with tislelizumab 400 mg intravenously every 6 weeks
- In part 2 (expansion), patients received lenvatinib at the RP2D plus tislelizumab per the part 1 regimen until disease progression, withdrawal, death, loss to follow-up, new anticancer therapy, study termination by sponsor, or unacceptable toxicity
- The primary endpoints were safety and RP2D determination (part 1) and overall response rate (ORR) assessed by investigator (part 2) in the Safety Analysis Set and Evaluable Analysis Set
- The secondary endpoints in part 2 were progression-free survival (PFS), duration of response, and disease control rate assessed by investigator, overall survival in the intent-to-treat population, and safety
- The non-small cell lung cancer (NSCLC), urothelial cancer (UC), and gastric cancer (GC) cohorts were closed early for reasons not related to safety

Figure 1. Study Design



Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; GC, gastric cancer; HNSCC, head and neck squamous cell carcinoma; IV, intravenously; LEN, lenvatinib; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q6W, once every 6 weeks; QD, once daily; RCC, renal cell carcinoma; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; RP2D, recommended phase II dose; TIS, tislelizumab; UC, urothelial cancer.

Results

Patient Disposition and Baseline Characteristics

- Patient disposition and baseline characteristics are presented in **Table 1**

Table 1. Baseline Characteristics

	RCC (n=23)	HNSCC (n=27)	GC (n=3)	NSCLC (n=5)
Number of patients treated, n (%)	23 (100.0)	27 (100.0)	3 (100.0)	5 (100.0)
Patients remaining on treatment, n (%)	14 (60.9)	6 (22.2)	1 (33.3)	0
Median study follow-up (range), mo	12.1 (10.8-15.7)	10.8 (5.7-14.4)	14.8 (13.7-16.2)	22.0 (13.3-22.9)
Median age (range), years	62.0 (51.0-73.0)	59.0 (35.0-80.0)	64.0 (51.0-69.0)	67.0 (57.0-75.0)
Age group, n (%)				
<65 years	12 (52.2)	15 (55.6)	2 (66.7)	2 (40.0)
≥65 years	11 (47.8)	12 (44.4)	1 (33.3)	3 (60.0)
Male sex, n (%)	17 (73.9)	19 (70.4)	3 (100.0)	4 (80.0)
Median weight (range), kg	68.0 (55.0-96.0)	54.0 (38.1-85.0)	60.0 (57.5-62.0)	55.0 (50.0-80.0)
ECOG PS, n (%)				
0	14 (60.9)	7 (25.9)	0	0
1	9 (39.1)	20 (74.1)	3 (100.0)	5 (100.0)

Data cutoff: October 20, 2023. **Abbreviations:** ECOG PS, Eastern Cooperative Oncology Group performance status; GC, gastric cancer; HNSCC, head and neck squamous cell carcinoma; mo, months; NSCLC, non-small cell lung cancer; RCC, renal cell carcinoma.

Efficacy

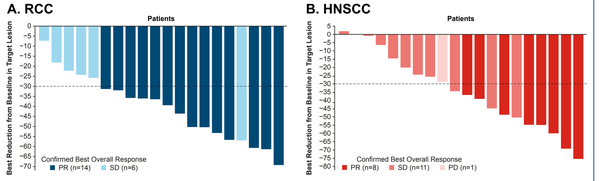
- The ORR was 66.7% in patients with RCC, 33.3% in patients with HNSCC or GC, and 20.0% in patients with NSCLC (**Table 2** and **Figure 2**)
- Median PFS was 15.4 months for patients with RCC, 6.1 months for patients with HNSCC, not estimable for patients with GC, and 6.0 months for patients with NSCLC (**Table 3** and **Figure 3**)

Table 2. Response Endpoints (Evaluable Analysis Set)

	RCC (n=21)	HNSCC (n=24)	GC (n=3)	NSCLC (n=5)
ORR,[a] % (95% CI)[b]	66.7 (43.0, 85.4)	33.3 (15.6, 55.3)	33.3 (0.8, 90.6)	20.0 (0.5, 71.6)
PR, n (%)	14 (66.7)	8 (33.3)	1 (33.3)	1 (20.0)
SD, n (%)	6 (28.6)	11 (45.8)	1 (33.3)	4 (80.0)
PD, n (%)	0	2 (8.3)	1 (33.3)	0
mDoR, mo (95% CI)[c]	NE (10.8, NE)	9.6 (2.8, NE)	NE (NE, NE)	18.5 (NE, NE)
DCR, % (95% CI)	95.2 (76.2, 99.9)	79.2 (57.8, 92.9)	66.7 (9.4, 99.2)	100.0 (47.8, 100.0)

The Evaluable Analysis Set includes all patients who received ≥1 dose of study drugs, have evaluable disease at baseline, and have ≥1 evaluable postbaseline tumor response assessment unless any clinical PD or death occurred before the first postbaseline tumor assessment. [a] Confirmed by investigator. [b] The 95% CI was estimated using the Clopper-Pearson method. [c] mDOR was estimated using the Kaplan-Meier method, with 95% CIs estimated using the Brookmeyer and Crowley method with log-log transformation. Data cutoff: October 20, 2023. **Abbreviations:** CI, confidence interval; DCR, disease control rate; GC, gastric cancer; HNSCC, head and neck squamous cell carcinoma; mDoR, median duration of response; mo, months; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, overall response rate; PD, progressive disease; PR, partial response; RCC, renal cell carcinoma; SD, stable disease.

Figure 2. Best Percentage Change from Baseline in Target Lesion by Best Overall Response[a] for (A) RCC and (B) HNSCC (Safety Analysis Set)



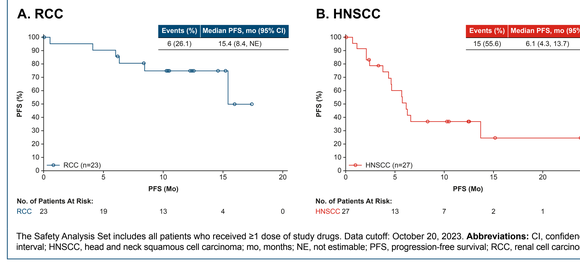
[a] Confirmed by investigator. Data cutoff: October 20, 2023. The dotted lines represent the cutoff for ≤30% tumor reduction from baseline. **Abbreviations:** HNSCC, head and neck squamous cell carcinoma; PD, progressive disease; PR, partial response; RCC, renal cell carcinoma; SD, stable disease.

Table 3. Survival Endpoints (Safety Analysis Set)

	RCC (n=23)	HNSCC (n=27)	GC (n=3)	NSCLC (n=5)
Median PFS (95% CI),[a] mo	15.4 (8.4, NE)	6.1 (4.3, 13.7)	NE (1.4, NE)	6.0 (2.5, NE)
12-mo PFS rate, % (95% CI)[b]	74.9 (49.6, 88.8)	37.2 (17.9, 56.5)	66.7 (5.4, 94.5)	40.0 (5.2, 75.3)
12-mo OS[c] rate, % (95% CI)[b]	91.3 (69.5, 97.8)	62.5 (41.4, 77.8)	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)

The Safety Analysis Set includes all patients who received ≥1 dose of study drugs. [a] Median PFS was estimated using the Kaplan-Meier method, with 95% CIs estimated using the Brookmeyer and Crowley method with log-log transformation. [b] The 12-month PFS and OS rates were estimated using the Kaplan-Meier method, with 95% CIs estimated using the Greenwood formula. [c] Median OS was NE for all cohorts. Data cutoff: October 20, 2023. **Abbreviations:** CI, confidence interval; GC, gastric cancer; HNSCC, head and neck squamous cell carcinoma; mo, months; NE, not estimable; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; RCC, renal cell carcinoma.

Figure 3. Kaplan-Meier Curves for PFS by Investigator for (A) RCC and (B) HNSCC (Safety Analysis Set)



The Safety Analysis Set includes all patients who received ≥1 dose of study drugs. Data cutoff: October 20, 2023. **Abbreviations:** CI, confidence interval; HNSCC, head and neck squamous cell carcinoma; mo, months; NE, not estimable; PFS, progression-free survival; RCC, renal cell carcinoma.

Safety

- Median (range) exposure to tislelizumab and lenvatinib were 10.8 (0.5-18.7) and 10.8 (0.1-18.7) months for RCC, 4.6 (0.7-24.7) and 2.8 (0.1-16.2) months for HNSCC, 1.4 (1.4-16.2) and 1.9 (1.4-16.2) months for GC, and 7.0 (2.6-20.6) and 5.8 (2.0-20.6) months for NSCLC, respectively
- A summary of treatment-related adverse events (TRAEs) is presented in **Table 4**
- The most common grade ≥3 TRAE was hypertension (34.8% for RCC; 29.6% for HNSCC)
- No new safety signals were identified

Table 4. Summary of TRAEs (Safety Analysis Set)

	RCC (n=23)	HNSCC (n=27)	GC (n=3)	NSCLC (n=5)
Patients with ≥1 TRAE,[a] n (%)	22 (95.7)	25 (92.6)	3 (100.0)	5 (100.0)
Grade ≥3	18 (78.3)	16 (59.3)	1 (33.3)	3 (60.0)
Serious	10 (43.5)	10 (37.0)	2 (66.7)	2 (40.0)
Leading to death	1 (4.3)[b]	3 (11.1)[c]	0	0
Leading to treatment discontinuation	3 (13.0)	6 (22.2)	1 (33.3)	1 (20.0)

The Safety Analysis Set includes all patients who received ≥1 dose of study drugs. [a] Reported by the investigator. [b] Due to multiple organ dysfunction syndrome. [c] Due to pneumonia, arterial hemorrhage, and unknown cause. Data cutoff: October 20, 2023. **Abbreviations:** GC, gastric cancer; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer; RCC, renal cell carcinoma; TRAE, treatment-related adverse event.

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Disclosures

Wutong Ju is employed by BeiGene (Shanghai) Co., Ltd.

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