Final Analysis of a Multicenter, Open-Label, Phase 2 Study Evaluating the Efficacy and Safety of Tislelizumab (TIS) in Combination With Fruquintinib (F) in Patients (Pts) With Selected Solid Tumors

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CONCLUSIONS

- Tislelizumab has demonstrated potential as an immuno-oncology backbone that can be successfully combined with different agents, such as fruquintinib, for the treatment of various solid tumors
- Tislelizumab plus fruquintinib demonstrated moderate antitumor activity in patients with gastric cancer/gastroesophageal junction adenocarcinoma (GC/GEJC), microsatellite-stable colorectal cancer (MSS CRC), and programmed death-ligand 1–positive (PD-L1+) non-small cell lung cancer (NSCLC)
- Tislelizumab plus fruquintinib was tolerable for patients with advanced solid tumors
- Further investigation of tislelizumab plus fruquintinib is warranted in the GC/GEJC, MSS CRC, and PD-L1+ NSCLC settings

INTRODUCTION

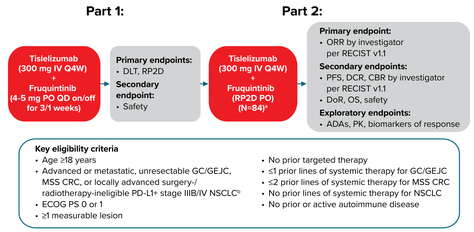
- Combining immune checkpoint inhibitors with antiangiogenic agents has demonstrated promising antitumor activity, often surpassing the efficacy of either approach alone[1,2]
- Tislelizumab, an anti-programmed cell death protein-1 (anti–PD-1) antibody, and fruquintinib, a selective vascular endothelial growth factor receptor-1/2/3 tyrosine kinase inhibitor, have shown clinical efficacy across various indications[3,4]
- The phase 2 BGB-A317-Fruquintinib-201 trial (NCT04716634) evaluated the efficacy and safety of tislelizumab plus fruquintinib in patients with advanced solid tumors
- Here, we present the final analysis of the BGB-A317-Fruquintinib-201 trial (data cutoff: February 22, 2024)

METHODS

- BGB-A317-Fruquintinib-201 was an open-label, multicenter, two-part study with a safety run-in followed by dose expansion
- The study design is shown in **Figure 1**
- Survival endpoints (progression-free survival [PFS], overall survival [OS], duration of response [DoR]) were estimated using Kaplan–Meier methodology, with 95% confidence intervals (CIs) calculated using the Brookmeyer and Crowley method
- Overall response rate (ORR), disease control rate (DCR), and clinical benefit rate (CBR) were calculated with 95% CIs using the Clopper–Pearson method
- DCR: proportion of patients with complete response (CR), partial response (PR), or stable disease (SD) as determined by the investigator per Response Evaluation Criteria in Solid Tumours (RECIST) v1.1
- CBR: proportion of patients with CR, PR, or durable SD (≥24 weeks) as determined by the investigator per RECIST v1.1

METHODS (CONT.)

Figure 1. BGB-A317-Fruquintinib-201 Study Design



[a]All patients enrolled in Part 1 (n=6) were treated with the RP2D and were counted towards Part 2; up to approximately 30 patients per cohort were enrolled to receive the RP2D. In Part 2, treatment was administered until disease progression, intolerable toxicity, death, withdrawal of consent, or until the study was terminated, whichever occurred first. [b]PD-L1 positive was defined as tumor cell expression ≥1% by VENTANA PD-L1 (SP263) immunohistochemistry assay conducted by a central laboratory. Excludes patients with NSCLC and known *EGFR* or *ALK* mutations.
Abbreviations: ADA, anti-drug antibody; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; PK, pharmacokinetics; PO, orally; Q4W, once every 4 weeks; QD, once daily; RP2D, recommended phase 2 dose.

RESULTS

Patient Disposition and Baseline Characteristics

- A total of 84 patients were enrolled (GC/GEJC, n=31; MSS CRC, n=31; PD-L1+ NSCLC, n=22), all of which received treatment and were included in the safety analysis set
- As of February 22, 2024, median study follow-up was 11.6 months (range: 0.4-32.8)
- By the end of the study period, 60.7% of patients had discontinued treatment due to progressive disease
- Patient demographics and baseline characteristics were representative of the target cancer patient population (**Table 1**)

Table 1. Patient Demographic and Baseline Characteristics (Safety Analysis Set)

	GC/GEJC (n=31)	MSS CRC (n=31)	PD-L1+ NSCLC (n=22)	Total (N=84)
Median age, years (range)	59 (33-75)	58 (37-72)	67 (33-76)	60 (33-76)
≥65 years, n (%)	7 (22.6)	8 (25.8)	14 (63.6)	29 (34.5)
Male, n (%)	21 (67.7)	20 (64.5)	17 (77.3)	58 (69.0)
Race, n (%)[a]				
American Indian or Alaska Native	1 (3.2)	0	0	1 (1.2)
Asian	31 (100.0)	31 (100.0)	22 (100.0)	84 (100.0)
ECOG performance status, n (%)				
0	9 (29.0)	14 (45.2)	3 (13.6)	26 (31.0)
1	22 (71.0)	17 (54.8)	19 (86.4)	58 (69.0)
Disease stage at initial diagnosis, n (%)				
I/II	1 (3.2)	1 (3.2)	2 (9.1)	4 (4.8)
III	0	3 (9.7)	4 (18.2)	7 (8.3)
IV	30 (96.8)	27 (87.1)	14 (63.6)	71 (84.5)
Unknown	0	0	2 (9.1)	2 (2.4)
Patients with metastatic disease at study entry, n (%)	31 (100.0)	31 (100.0)	17 (77.3)	79 (94.0)
Histology/cytology, n (%)				
Adenocarcinoma	31 (100.0)	31 (100.0)	9 (40.9)	71 (84.5)
Squamous cell carcinoma	0	0	13 (59.1)	13 (15.5)
Number of prior lines of therapy, n (%)				
0	1 (3.2)	0	22 (100.0)	23 (27.4)
1	30 (96.8)	1 (3.2)	0	31 (36.9)

[a]One patient in the GC/GEJC cohort was of mixed race and was counted in both the American Indian or Alaska Native and Asian categories.

RESULTS (CONT.)

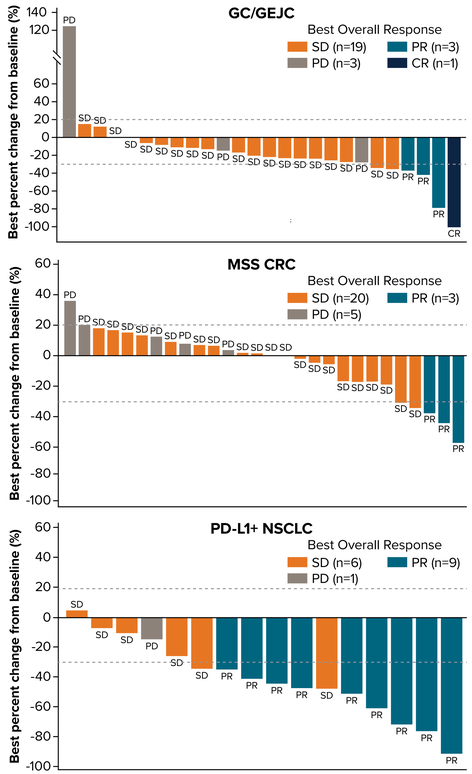
Recommended Phase 2 Dose

- No dose-limiting toxicities were observed with fruquintinib 5 mg daily (3 weeks on, 1 week off) plus tislelizumab 300 mg Q4W, establishing the RP2D

Efficacy

- Clinical response to treatment was observed across all cohorts (**Figure 2** and **Table 2**)
- Median PFS was 4.6 months in both the GC/GEJC and MSS CRC cohorts and 15.6 months in the PD-L1+ NSCLC cohort (**Figure 3**)
- Median OS was not reached in the PD-L1+ NSCLC cohort, and was 10.5 months and 10.0 months for the GC/GEJC and MSS CRC cohorts, respectively (**Figure 4**)

Figure 2. Best Percent Change From Baseline in Target Lesion Sum of Diameters by Best Overall Response per Investigator in (A) GC/GEJC, (B) MSS CRC, and (C) PD-L1+ NSCLC (Safety Analysis Set[a])



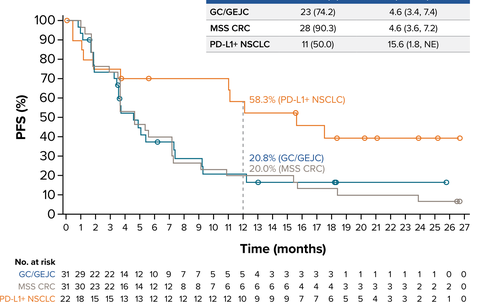
[a]Response not evaluable: GC/GEJC (n=4), MSS CRC (n=2), PD-L1+ NSCLC (n=6).

Table 2. Disease Response per Investigator (Safety Analysis Set)

	GC/GEJC (n=31)	MSS CRC (n=31)	PD-L1+ NSCLC (n=22)
ORR, n (%)	4 (12.9)	3 (9.7)	9 (40.9)
95% CI (%)	3.6, 29.8	2.0, 25.8	20.7, 63.6
DCR, n (%)	23 (74.2)	23 (74.2)	15 (68.2)
95% CI (%)	55.4, 88.1	55.4, 88.1	45.1, 86.1
CBR, n (%)	10 (32.3)	12 (38.7)	13 (59.1)
95% CI (%)	16.7, 51.4	21.8, 57.8	36.4, 79.3
DoR, months, median (95% CI)	NR (5.6, NE)	11.9 (3.7, NE)	NR (7.7, NE)

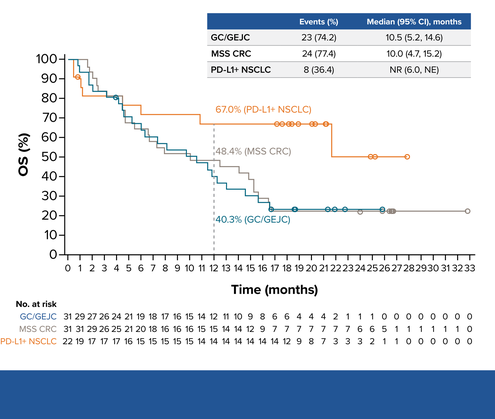
Abbreviations: NE, not estimable; NR, not reached.

Figure 3. Kaplan–Meier Plot for PFS per Investigator (Safety Analysis Set)



	Events (%)	Median (95% CI), months
GC/GEJC	23 (74.2)	4.6 (3.4, 7.4)
MSS CRC	28 (90.3)	4.6 (3.6, 7.2)
PD-L1+ NSCLC	11 (50.0)	15.6 (1.8, NE)

Figure 4. Kaplan–Meier Plot for OS (Safety Analysis Set)



	Events (%)	Median (95% CI), months
GC/GEJC	23 (74.2)	10.5 (5.2, 14.6)
MSS CRC	24 (77.4)	10.0 (4.7, 15.2)
PD-L1+ NSCLC	8 (36.4)	NR (6.0, NE)

Safety/Tolerability Profile

- The most frequently observed adverse events were consistent with the known profile of tislelizumab and fruquintinib treatment or underlying conditions in patients
- Treatment-emergent adverse events (TEAEs) were similar across cohorts, with higher rates of grade ≥3 and serious treatment-related TEAEs in the PD-L1+ NSCLC cohort due to longer treatment duration (**Table 3**)
- A total of 98.8% of patients experienced any-grade TEAEs; the most common were proteinuria (32.1%), hypoalbuminemia (27.4%), and hypothyroidism (25.0%)
- Overall, 10.7% (n=9) of patients had grade ≥3 immune-mediated adverse events (imAEs)
- No infusion-related reactions were reported
- Four (4.8%) patients experienced fatal TEAEs, with one treatment-related death in each of the GC/GEJC and PD-L1+ NSCLC cohorts

Table 3. Safety Overview (Safety Analysis Set)

n (%)	GC/GEJC (n=31)	MSS CRC (n=31)	PD-L1+ NSCLC (n=22)	Total (N=84)
Any-grade TEAEs	30 (96.8)	31 (100.0)	22 (100.0)	83 (98.8)
Any study treatment component-related TEAEs	25 (80.6)	27 (87.1)	19 (86.4)	71 (84.5)
Grade ≥3 TEAEs	18 (58.1)	21 (67.7)	18 (81.8)	57 (67.9)
Any study treatment component-related TEAEs	10 (32.3)	12 (38.7)	14 (63.6)	36 (42.9)
Serious TEAEs	13 (41.9)	14 (45.2)	13 (59.1)	40 (47.6)
Any study treatment component-related TEAEs	3 (9.7)	3 (9.7)	9 (40.9)	15 (17.9)
TEAEs leading to death[a]	3 (9.7)	0	1 (4.5)	4 (4.8)
Any study treatment component-related TEAEs	1 (3.2)	0	1 (4.5)	2 (2.4)
TEAEs leading to any treatment discontinuation	5 (16.1)	3 (9.7)	7 (31.8)	15 (17.9)
TEAEs leading to any dose modification	21 (67.7)	26 (83.9)	18 (81.8)	65 (77.4)
Any-grade imAEs	10 (32.3)	11 (35.5)	11 (50.0)	32 (38.1)
Grade ≥3 imAEs	1 (3.2)	2 (6.5)	6 (27.3)	9 (10.7)

[a]TEAEs leading to death in this table excluded death due to disease under study. Adverse events were graded using Common Terminology Criteria for Adverse Events v5.0.

REFERENCES

1. Xu Q and Shao D. *Front Immunol*. 2024;15:1487610.
2. Zhou Y, et al. *Immunotargets Ther*. 2024;13:813-829.
3. Abushanab AK, et al. *Expert Rev Clin Pharmacol*. 2023;16:1153-1161.
4. Stucchi E, et al. *Expert Opin Pharmacother*. 2024;25:371-382.

DISCLOSURES

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