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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Background: Immunotherapy in combination with antiangiogenic agents has shown promising antitumor activity compared with either agent alone. We report efficacy and safety data from the final analysis of the phase 2 BGB-A317-Fruquitinib-201 trial evaluating the programmed cell death-1 antibody TIS combined with the selective vascular endothelial growth factor receptor (VEGFR)-1, -2, and -3 inhibitor F in pts with advanced solid tumors.

Methods: This was an open-label, multicenter, two-part study with a safety run-in followed by dose-expansion. Eligible pts were adults with advanced or metastatic unresectable gastric cancer (GC), microsatellite stable colorectal cancer (MSS CRC), or locally advanced surgery-/radiotherapy-ineligible and programmed death ligand-1–positive (PD-L1+; defined as PD-L1 $\geqslant$1%) stage IIIB/IV non-small cell lung cancer (NSCLC). F 5 mg daily (3 weeks on, 1 week off) plus TIS (300 mg IV Q4W) was administered as second-line therapy for pts with GC, third-line therapy for pts with MSS CRC, and first-line therapy for pts with PD-L1+ NSCLC. The primary outcome measure was overall response rate (ORR) per RECIST v1.1. Secondary endpoints included other efficacy measures and safety.

Results: The median study follow-up was 11.6 months (mo; range, 0.4-32.8). A total of 84 pts were enrolled (GC, n=31; MSS CRC, n=31; PD-L1+ NSCLC, n=22). One study treatment component-related death was reported in the GC cohort and 1 in the PD-L1+ NSCLC cohort. The recommended phase 2 dose was established at F 5 mg daily (3 weeks on, 1 week off) in combination with TIS with no observed dose-limiting toxicities. Efficacy and safety are reported in the **Table**. Any-grade treatment-emergent adverse events (TEAEs) occurred in 83 (98.8%) pts; proteinuria (32.1%), hypoalbuminemia (27.4%), and hypothyroidism (25.0%) were most common. 9/32 (10.7%) pts had grade ≥3 immune-mediated AEs.

Conclusions: Despite the limited sample size, TIS+F demonstrated moderate antitumor activity in pts with advanced solid tumors, with manageable safety observed in pts with GC and MSS CRC. Further investigation of TIS+F is warranted in the GC and MSS CRC settings.

	GC (N=31)	**MSS CRC (N=31)**	**PD-L1+ NSCLC (N=22)**
ORR, n (%)	4 (12.9)	3 (9.7)	9 (40.1)
Disease control rate, n (%)	23 (74.2)	23 (74.2)	15 (68.2)
Clinical benefit rate, n (%)	10 (32.3)	12 (38.7)	13 (59.1)
Median progression-free survival, mo (95% CI)	4.6 (3.4, 7.4)	4.6 (3.6, 7.2)	15.6 (1.8, NE)
Median overall survival, mo (95% CI)	10.5 (5.2, 14.6)	10.0 (4.7, 15.2)	NR (6.0, NE)
Median duration of response, mo (95% CI)	NR (5.6, NE)	11.9 (3.7, NE)	NR (7.7, NE)
Grade ≥3 TRAE, n (%)	10 (32.3)	12 (38.7)	14 (63.6)
Serious TRAE, n (%)	3 (9.7)	3 (9.7)	9 (40.9)
TEAE leading to discontinuation of any study treatment, n (%)	5 (16.1)	3 (9.7)	7 (31.8)

CI, confidence interval; NE, not evaluable; NR, not reached.