First-in-human, phase 1 study of BGB-26808 (hematopoietic progenitor kinase 1 [HPK1] inhibitor) ± tislelizumab (TIS; anti-PD-1) in advanced solid tumors (STs)

Authors: Aung Naing,[1] Xinjun Liang,[2] Sarwan Bishnoi,[3] Jie Li,[4] Sanjeev Deva,[5] Funan Liu,[6] John Park,[7] Dan Feng,[8] Victoria Chang,[9] Cunjing Yu,[10] Jiwon Seo,[9] Heather Zhang,[9] Yue Tian,[10] Kirsha Naicker,[11] Caicun Zhou[12]

Affiliations: [1]The University of Texas - MD Anderson Cancer Center, Houston, TX, USA; [2]Hubei Cancer Hospital, Wuhan Hubei, China; [3]Ashford Cancer Centre Research, Glandore, SA, Australia; [4]Jining First People's Hospital, Jining, Shandong, China; [5]Auckland City Hospital, Auckland, New Zealand; [6]The First Hospital of China Medical University Hunnan Campus, Shenyang, Liaoning, China; [7]Macquarie Medical School, Macquarie University, North Ryde, NSW, Australia; [8]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [9]BeOne Medicines, Inc., San Carlos, CA, USA; [10]BeOne Medicines (Beijing) Co, Ltd, Beijing, China; [11]BeOne Medicines UK Ltd, London, UK; [12]Shanghai East Hospital, Shanghai, China

Background: BGB-26808 is a potent and selective second-generation HPK1 inhibitor with preclinical antitumor activity. We report dose-escalation results from the phase 1a trial of BGB-26808 alone (Part A [A]) or + TIS (Part B [B]) (NCT05981703).

Methods: Eligible patients (pts) were ≥18 with advanced, metastatic and unresectable STs who previously received standard systemic therapy or for whom treatment is not available, not tolerated or not appropriate, and not received prior HPK1-targeting therapies (prior checkpoint inhibitors allowed). Oral BGB-26808 was escalated through 5 dose levels in A and B. Key primary objective: safety/tolerability; secondary objectives: preliminary antitumor activity and pharmacokinetics.

Results: As of February 28, 2025, 97 pts were enrolled (55 in A; 42 in B). Median (range) lines of prior systemic therapy was 3.0 (1-8) in A and B. The most common treatment-related (TR)-treatment-emergent adverse events (TEAEs) were diarrhea (30.9%; 17/55) and platelet count decreased (21.8%; 12/55) in A, and diarrhea and fatigue (16.7%; 7/42 each) in B. The most common grade ≥3 TR-TEAE was diarrhea (5.5%; 3/55) in A and anemia (4.8%; 2/42) in B. The most common immune-mediated adverse events were rash and hypothyroidism (3.6%; 2/55 each) in A and dermatitis, rash, hepatitis, diabetes mellitus and myositis (2.4%; 1/42 each) in B. There were no responders in A; in B, unconfirmed objective response rate (ORR) was 11.9% (1 complete response [CR] and 4 partial responses [PR]), of which 1 CR and 3 PRs were confirmed with subsequent tumor assessments. Median $T_{½}$ was 11 h and median T_{max} was 2-4 h. Exposure increased with doses evaluated. pSLP76 showed a trend of dose dependent inhibition in A and B.

Conclusion: Preliminary data show BGB-26808 ± TIS was generally tolerable and potential antitumor activity of BGB-26808 was shown combined with TIS. Further study of BGB-26808 + TIS ± chemotherapy is ongoing in the expansion.

Safety

	Part A BGB-26808 monotherapy (N=55)	Part B BGB-26808 + TIS (N=42)
Any TEAE	53 (96.4)	38 (90.5)
Grade ≥3	21 (38.2)	16 (38.1)
Serious	20 (36.4)	14 (33.3)
Leading to death	1 (1.8)	2 (4.8)
Leading to treatment discontinuation	1 (1.8)	5 (11.9)
Any treatment-related TEAE	39 (70.9)	27 (64.3)
Grade ≥3	11 (20.0)	8 (19.0)
Serious	8 (14.5)	5 (11.9)
Any imAE	6 (10.9)	4 (9.5)

Pts with multiple AEs are counted once. All AEs are listed as n (%).

Median (range) study follow-up was 4.2 (0.3-12.9) for A and 3.4 (0.4-10.7) months for B.

AE, adverse event; imAE, immune-mediated AE; pt, patient; TEAE, treatment-emergent AE; TIS, tislelizumab.