

A first-in-human, phase 1 study of BGB-15025 (hematopoietic progenitor kinase 1 [HPK1] inhibitor) as monotherapy and in combination (combo) with tislelizumab (TIS; anti-PD-1 antibody) in patients (pts) with advanced solid tumors (ST)

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Background: BGB-15025, a potent, selective, small-molecule HPK1 inhibitor, has shown preclinical antitumor effects in combo with TIS. Phase 1a results were presented (Deva, ASCO 2024). Now we report dose expansion results from a phase 1b, multicenter trial of BGB-15025 in combo with TIS ± chemotherapy (CT) (NCT04649385).

Methods: Eligible pts had treatment naïve advanced/metastatic non-small cell lung cancer (Cohort A [A]) or gastric/gastroesophageal junction adenocarcinoma (Cohort B [B]) or advanced/metastatic esophageal squamous cell carcinoma (Cohort C [C]) that progressed after ≤2 lines of prior therapy (checkpoint inhibitors allowed). Pts received BGB-15025 + TIS with CT (A, B) or without CT (C). Key endpoints were objective response rate (ORR; primary), progression-free survival (PFS), duration of response (DOR), disease control rate (DCR) and safety/tolerability.

Results: As of Mar 19, 2025, 45 pts (12, A; 20, B; 13, C) were treated. Median follow up was 9.6 (range 0.7-21.6) months (mo).

Overall, confirmed ORR was 33.3% (95% CI 20.0-49.0), with 1 complete response (CR) and 14 partial responses (PR); DCR was 75.6% (95% CI 60.5-87.1). By cohort, ORR was 25.0% (5.5-57.2) in A (3 PR), 60.0% (36.1-80.9) in B (1 CR, 11 PR), 0% (0-24.7) in C; median DOR was 7.0 mo (95% CI 6.0-not evaluable [NE]) in A, NE (3.0-NE) in B; and median PFS was 7.7 mo (4.1-8.3) in A, 8.4 mo (4.3-NE) in B, 1.3 mo (0.8-2.1) in C.

Treatment-emergent adverse events (TEAEs) occurred in 44 (97.8%) pts (60.0% grade ≥ 3 ; 42.2% serious AEs). AEs related to any treatment occurred in 40 (88.9%) pts; 48.9% were grade ≥ 3 . Most common treatment-related TEAEs (TR-TEAEs) were thrombocytopenia/platelet count decreased (48.9% overall; 66.7%, A; 65.0%, B; 7.7%, C), anemia (44.4% overall; 100.0%, A; 35.0%, B; 7.7%, C) and neutropenia/neutrophil count decreased (42.2% overall; 75.0%, A; 50.0%, B; 0%, C). TR-TEAEs leading to discontinuation occurred in 4 (8.9%) pts; there were no fatal TR-TEAEs. Immune-mediated AEs occurred in 13 (28.9%) pts.

Conclusions: These results show BGB-15025 in combo with TIS $\pm$ CT demonstrated antitumor activity and was generally tolerable in advanced ST.