Preliminary Results of a Phase 1/2 Study of BGB-A317, an anti-PD-1 mAb in Chinese Patients (pts) with Advanced Tumors

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Background: BGB-A317 is a humanized IgG4 anti-PD-1 mAb that blocks PD-L1/L2 binding to PD-1, thereby restoring T cell-mediated tumor inhibition. In the first-in-human phase 1 trial, which was conducted in Australia, New Zealand, USA, Taiwan, and Korea, doses up to 10mg/kg Q2W were well tolerated and a flat dose of 200 mg Q3W was selected as RP2D. Here, we report the preliminary results from a multi-center, phase 1/2 clinical trial of BGB-A317 at 200 mg Q3W in Chinese pts with advanced solid tumors.

Methods: Phase 1 and 2 parts of the study were designed to confirm the RP2D of 200mg Q3W and assess its anti-tumor activity in select tumor types, respectively. Pts with histologically or cytologically confirmed advanced solid tumors were enrolled and intravenously treated with BGB-A317 at 200 mg Q3W. Adverse events (AE) were evaluated using NCI-CTCAE v4.03 and tumor response was assessed Q9W in the first year and Q12W thereafter per RECIST v1.1.

Results: As of May 26, 2017, 20 pts (including 5 MSI-H colorectal cancer (CRC), 3 hepatocellular cancer (HCC), 3 urothelial bladder cancer (UBC), 2 gastric cancer (GC), 2 melanoma, 2 esophageal cancer (EC) and 3 others) were dosed at least once in Phase 1. Among 15 pts that have been followed up for $\geqslant$ 21 days, no DLT was observed. The most common drug related AEs (drAEs) were blood bilirubin (bil) increase (n=7), blood bil unconjugated increase (n=6), anemia (n=4), and AST increase (n=4), while $\geqslant$ grade 3 drAEs were AST increase, bil conjugated increase, and blood bil unconjugated increase (n=1 each). One possibly drug-unrelated death was reported. PK analyses from 19 Chinese pts after single dose showed that the mean C_{max} and $AUC_{0\text{-}14d}$ were 68 μg/mL and 480 μg·day/mL. Of 9 evaluable pts, 2 pts, one each with GC and UBC, had an unconfirmed PR.

Conclusions: BGB-A317 has been generally well tolerated to date and the safety profile in Chinese pts is consistent with that observed in other populations. Preliminary PK is similar between distinct ethnic pts. Evidence of tumor regression has been showed and a more robust assessment of anti-tumor activity will occur in phase 2. Clinical trial information: CTR20160872.