A phase 1 study of the OX40 agonist, BGB-A445, with or without tislelizumab, an anti-PD-1 monoclonal antibody, in patients with advanced solid tumors.

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Background: OX40 is an immune costimulatory receptor, expressed on activated $CD4^+$ and $CD8^+$ T cells, which promotes T cell proliferation and survival in the tumor microenvironment. BGB-A445 is a novel monoclonal antibody (mAb) OX40 agonist that does not compete with endogenous OX40 ligand binding. BGB-A445 has demonstrated antitumor activity as a single agent and in combination with an anti-PD-1 mAb in preclinical studies. Here, we report data from the ongoing dose-escalation part of a multicenter, phase 1 dose escalation/expansion study (NCT04215978) of BGB-A445 alone or in combination with tislelizumab (TIS) in patients (pts) with advanced solid tumors.

Methods: Eligible pts were enrolled into seven sequential dose escalation cohorts of BGB-A445 IV as monotherapy (Part A) or five increasing dose levels of BGB-A445 IV in combination with TIS 200 mg IV (Part B) on day 1 of 21-day cycles. Dose escalation was guided by a Bayesian (mTPI-2) approach. This study assessed safety, tolerability, pharmacokinetics (PK) profile, and preliminary antitumor activity (RECIST v1.1).

Results: As of August 31, 2022, 59 pts were enrolled in Part A and 32 pts in Part B. Median (range) age was 59 years (28-80) and 61 years (37-75) in Parts A and B, respectively; 26 (44%) and 13 (41%) pts were male, respectively. ≥Grade 3 treatment-emergent AEs (TEAEs) were reported in 24 (41%) and 17 (53%) pts in Parts A and B, respectively; the most commonly reported (≥3 reported) ≥grade 3 TEAEs were gastrointestinal disorders (diarrhea, nausea, and abdominal pain). Serious TEAEs were reported in 23 (39%) pts in Part A and 16 (50%) in Part B. Treatment-related AEs leading to treatment discontinuation were reported in 1 (2%) pt in Part A and 0 (0%) pts in Part B. In Part A, all grade immune-mediated AEs (imAEs) were reported in 11 (19%) pts; no pts reported ≥grade 3 imAEs. In Part B, all grade imAEs were reported in 14 (44%) pts; ≥grade 3 imAEs were reported in 1 (3%) pt (one event each of rash maculopapular and diarrhea). There were no dose-limiting toxicities or concerning patterns of safety/tolerability observed. BGB-A445 PK (maximum concentration [C_{max}] and area under the curve from day 0 to 21 [$AUC_{0\text{-}21}$]) were linear and dose proportional in all tested dose ranges. In the efficacy-evaluable population of Parts A (n=50) and B (n=30), respectively, partial response was observed in 2 (4%) pts (unconfirmed) and 7 (23%) pts (confirmed); stable disease in 18 (36%) and 13 (43%) pts (confirmed), and progressive disease in 26 (52%) and 8 (27%) pts.

Conclusions: In the dose escalation part of this study, BGB-A445 alone or in combination with TIS was generally well tolerated across all doses in pts with advanced solid tumors, and demonstrated preliminary antitumor activity as both a single and combination agent. The dose expansion part of the study is ongoing in pts with non-small cell lung cancer and head and neck squamous cell carcinoma.