A Phase 1 Study of the OX40 Agonist, BGB-A445, With or Without PD-1 Monoclonal Antibodies, in Patients with Advanced Solid Tumors

Conclusions

Background

• OX40 is an immune costimulatory receptor, expressed on activated CD8+ and CD4+ T-cells, that promotes T-cell proliferation and survival in the tumor microenvironment.

• BGB-A445 is a novel monoclonal antibody (mAb) agonist that does not compete with endogenous OX40 ligand binding.

• In preclinical studies, BGB-A445 has demonstrated antitumor activity as a single agent and in combination with an anti-PD-1 mAb.

• In preclinical models, BGB-A445 had dose-dependent antitumor effects, without the toxic effects that have been observed in high-antibody concentrations with ligand-complexed OX40 antibodies (Figure 1).

• This ongoing dose-escalation part of a multicenter, phase 1 study (NCT04215978) is investigating BGB-A445 alone or in combination with tislelizumab in patients with advanced solid tumors.

Methods

• Eligible patients were enrolled into 1 dose-escalation cohorts to receive BGB-A445 intravenous (IV) as monotherapy (Part A) or to receive 5 dose levels of BGB-A445 IV in combination with tislelizumab (Part B) on day 1 and every 28 days (Figure 2).

• Dose-escalation was guided by a Bayesian modified toxicity probability interval 2 approach.

• The primary objective of the dose-escalation phase of the study was to assess safety and tolerability of BGB-A445 by adverse events (AEs) and to determine the maximum tolerated or administered dose.

• Secondary objectives included characterizing the BGB-A445 pharmacokinetic (PK) profile and preliminary antitumor activity and the relationship of PK and antitumor activity in solid tumors (RECIST 1.1).

• This ongoing dose-escalation part of a multicenter, phase 1 study (NCT04215978) is investigating BGB-A445 alone or in combination with tislelizumab in patients with advanced solid tumors.

• Of 50 patients in the efficacy-evaluable population of Part A, 2 patients (4.0%) achieved unconfirmed partial response (PR), 13 patients (26.0%) had stable disease (SD), and 8 patients (16.0%) had disease progression.

• Of 33 patients in the efficacy-evaluable population of Part B, 7 patients (21.2%) achieved confirmed partial response (PR), 15 patients (45.5%) had stable disease (SD), and 11 patients (33.3%) had disease progression.

Results

Patients

• Of 50 patients in the efficacy-evaluable population of Part A, 2 patients (4.0%) achieved unconfirmed partial response (PR), 13 patients (26.0%) had stable disease (SD), and 8 patients (16.0%) had disease progression.

• Of 33 patients in the efficacy-evaluable population of Part B, 7 patients (21.2%) achieved confirmed partial response (PR), 15 patients (45.5%) had stable disease (SD), and 11 patients (33.3%) had disease progression.

Pharmacokinetics and Pharmacodynamics

• BGB-A445 exposure was similar as monotherapy and in combination with tislelizumab (Table 3).

• Treatment-related AEs leading to treatment discontinuation occurred in 1 patient (1.7%) in Part A and 2 patients (6.2%) in Part B.

• Baseline demographics were similar between Part A and Part B (Table 1).

• Of 54 patients enrolled, 50 patients were included in the efficacy-evaluable population (Part A: 28 patients; Part B: 22 patients).

• Of 44 patients with available PD-1 expression data, 42 (95.5%) had >1% of tumor cells stained positive for PD-1.

• Of 50 patients in the efficacy-evaluable population of Part A, 2 patients (4.0%) achieved unconfirmed partial response (PR), 13 patients (26.0%) had stable disease (SD), and 8 patients (16.0%) had disease progression.

• Of 33 patients in the efficacy-evaluable population of Part B, 7 patients (21.2%) achieved confirmed partial response (PR), 15 patients (45.5%) had stable disease (SD), and 11 patients (33.3%) had disease progression.

Table 1: Baseline Characteristics

Table 2: Summary of Adverse Events: Part B Combination BGB-A445 + Tislelizumab

Table 3: Summary of Adverse Events: Part B Combination BGB-A445 + Tislelizumab

Disclosures

No other reports, grants, personal fees, and nonfinancial support from BMS; no financial support from other sources.

References