BACKGROUND

A combination of anti-PD-1 and anti-PD-L1 can therefore potentially elicit stronger signals in tumor microenvironments leading to T-cell exhaustion and T-cell receptor activation and attenuates T-cell proliferation and functional activities, resulting in T-cell anergy induction.

METHODS

Overall Design and Study Objectives

The primary objectives of phase 2A will be to assess the objective response rate (ORR), per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, of BGB-A333 alone and in combination with tislelizumab, is also a co-primary endpoint following the safety, tolerability, pharmacokinetics, and preliminary antitumor activity of anti-PD-L1 monoclonal antibody BGB-A333 alone and in combination with anti-PD-1 monoclonal antibody tislelizumab in patients with advanced solid tumors.

Patients

- Adult patients, aged ≥18 years, will be eligible for the study if they have:
  - For phase 1: only patients with histologically or cytologically confirmed advanced or metastatic solid tumors from any tissue type, who have been previously treated with at least one standard therapy or for which treatment is not available, not tolerated, or refused for further treatment.
  - For phase 2: patients with locally advanced or metastatic urothelial carcinoma who have progressed on or after first-line platinum-based chemotherapy or who were ineligible for platinum-based chemotherapy.

TREATMENT

- Phase 1A (BGB-A333 dose escalation): BGB-A333 monotherapy at approximately 3–5 dose levels (450 mg Q3W to 1350 mg Q3W or higher if needed) will be evaluated in patients with solid tumors who will be treated with BGB-A333 and tislelizumab (200 mg, Q3W).


dose level -1

- Any condition requiring systemic treatment with either corticosteroids (>10 mg daily of prednisone equivalent) or other immunosuppressive medication within 14 days before study treatment.

- Known history of HIV infection, hepatitis B virus or hepatitis C virus infection except for patients with hepatitis B who must also meet Clevudidine criteria. And

- Cardiac chest pain episode of syncope, uncontrolled hypertension (systolic pressure ≥160 mmHg or diastolic pressure ≥100 mmHg), or symptomatic pulmonary embolism within 28 days before study drug administration; or

- History of or active cerebrovascular accident, all within 6 months before administration of the study drug.

- Includes patients with hepatocellular carcinoma who must also meet Child-Pugh A classification.

- Patients will be excluded if they have:

- Coexisting conditions that will impair their ability to understand or follow study instructions.

- The primary objective of the phase 2A (BGB-A333 dose escalation) will enroll approximately 20 patients with urothelial carcinomas, with the potential to add dose cohorts of patients with other tumor types.

- The primary objective of the phase 2B (combination dose escalation) will enroll approximately 20 patients with urothelial carcinomas, with the potential to add more cohorts of patients with other tumor types.

- Phase 1B (dose expansion) will enroll a cohort of approximately 6 patients with solid tumors who will be treated with BGB-A333 alone and in combination with tislelizumab, in patients with advanced solid tumors.

- Secondary objectives will be to assess the preliminary antitumor activity, characterize the pharmacodynamics, and evaluate the immunogenicity of BGB-A333 alone and in combination with tislelizumab.

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