TISLELIZUMAB (BGB-A317) FOR RELAPSED/REFRACTORY EXTRANODAL NK/T-CELL LYMPHOMA: PRELIMINARY EFFICACY AND SAFETY RESULTS FROM A PHASE 2 STUDY

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Background

Extranodal NK/T-cell lymphoma (ENKTL) is a subtype of mature T-cell and NK-cell lymphoma more common in Asia and South America. Patients with relapsed/refractory (R/R) ENKTL have a poor prognosis after failure of an L-asparaginase (LASP)-based regimen. ENKTL cells are invariably infected by Epstein-Barr virus, which upregulates programmed death ligand 1 (PD-L1) expression on lymphoma cells. The PD-L1/PD-1 axis is therefore a potential target for NK/T-cell lymphomas. Tislelizumab, a humanized IgG4 monoclonal PD-1–blocking antibody, has high PD-1 affinity/specificity and minimized macrophage FCγR binding.

Aims

In cohort 1 of this phase 2 trial, the antitumor activity and safety of tislelizumab was evaluated in patients with R/R ENKTL. The primary endpoint was investigator-assessed overall response rate (ORR) using the Lugano criteria with the Lymphoma Response to Immunomodulatory Therapy Criteria modification. Secondary endpoints included progression-free survival (PFS), duration of response (DOR), complete response (CR) rate, time to response (TTR) assessed by investigator, overall survival, safety, and tolerability.

Methods

This is an ongoing, global, single-arm, multicenter, phase 2 study (ClinicalTrials.gov: NCT03493451) of tislelizumab given at 200 mg intravenously every 3 weeks until disease progression (PD) or unacceptable toxicity. Three cohorts enrolled patients with mature T- and NK-cell neoplasms by disease subtype. Reported here are results for cohort 1: R/R ENKTL. Patients with R/R ENKTL were eligible if they had ECOG-PS ≤2, ≥1 prior appropriate systemic therapies, eg, non-anthracycline-based regimens such as a LASP-based regimen, had PD during or after completing most recent therapy or refractory disease, and had measurable disease by CT scan.

Results

Patients (N = 22) from 12 centers in China, Italy, and France were enrolled and treated from April 13, 2018 to the Oct. 11, 2019 data cutoff date. Median follow-up was 8.4 months (range, 1.4-18.0). The median age was 47.5 years (range, 24-76); 63.6% were male. At study entry, 54.5% of patients had stage IV disease, and 86.4% had ECOG PS ≥1. The median number of prior regimens was 2 (range, 1-5). Eight (36.4%) patients had received a prior LASP-based regimen. One patient had a prior autologous stem cell transplant, and 72.7% had received prior radiotherapy. Cohort enrollment closed early due to slow accrual. At data cutoff, 6 patients (27.3%) remained on treatment and 16 patients (72.7%) discontinued treatment (12 for PD; 3 for adverse events [AEs]; 1 withdrew consent). The ORR was 31.8% (95% CI: 13.9, 54.9), and the CR rate was 18.2% (95% CI: 5.2, 40.3). Median TTR was 5.75 months (range, 2.14-14.29). Median DOR was not reached. Median PFS was 2.7 months (95% CI: 1.45, 5.32). The estimated 12-month PFS rate was 22.7% (95% CI: 8.27, 41.45). The most frequently reported (≥15%) AEs were anemia and pyrexia (27.3%, each) and hypoalbuminemia, hyperglycemia, and hypokalemia (18.2%, each). Grade ≥3 AEs reported in ≥2 patients were anemia (13.6%) and neutrophil count decrease (9.1%). Immune-related AEs (irAEs) were reported in 7 patients (31.8%); 1 was grade 3. One (4.5%) patient had an AE of respiratory failure (due to PD) that led to death. Four (18.2%) patients had AEs that led to dose delay.

Conclusion

Tislelizumab had modest antitumor activity in patients with R/R ENKTL and tolerable toxicity. Although several patients achieved CR, the PFS is short. Future studies in such aggressive diseases should include consideration for combination regimens and biomarker strategy.