TISLELIZUMAB (BGB-A317) FOR RELAPSED/REFRACTORY CLASSICAL HODGKIN LYMPHOMA: UPDATED FOLLOW-UP EFFICACY AND SAFETY RESULTS FROM A PHASE 2 STUDY

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Background

Programmed cell death protein 1 (PD-1) inhibitors have broadened therapeutic options in relapsed/refractory classic Hodgkin Lymphoma (cHL). Tislelizumab is a humanized IgG4 monoclonal antibody with high affinity/specificity for PD-1. Tislelizumab was engineered to minimize binding to FcγR on macrophages, thereby decreasing antibody-dependent phagocytosis, a potential mechanism of T-cell clearance and resistance to anti–PD-1 therapy.

Aims

The primary endpoint was overall response rate (ORR) assessed by an independent review committee (IRC) using the Lugano criteria. Secondary endpoints included progression-free survival (PFS), duration of response (DOR), rate of complete response (CRR), time to response (TTR) assessed by IRC, and safety and tolerability.

Methods

This is an ongoing, single-arm, multicenter phase 2 study (ClinicalTrials.gov: NCT03209973) of tislelizumab given at 200 mg intravenously every 3 weeks until disease progression (PD) or unacceptable toxicity. Patients with relapsed/refractory cHL were eligible if they: failed to achieve a response or progressed after autologous stem cell transplant (ASCT), or: received ≥2 lines of prior systemic chemotherapy for cHL and were ineligible for ASCT.

Results

Seventy patients from 11 centers in China were enrolled and treated; patient characteristics are shown in the table below. As of data cutoff date (July 23, 2018), the median follow-up was 9.8 months (range, 3.4-14.7 mos). Fifty-three patients (75.7%) remained on treatment; 17 patients (24.2%) discontinued (11 for PD; 4 for adverse events [AEs]; 1 withdrew consent; 1 due to pregnancy). The ORR was 87.1% and the CRR was 62.9% by IRC. The median TTR by IRC was12.0 weeks (range, 8.9-42.1). The median PFS was not reached and estimated 9-month PFS rate was 74.5%. The median DOR was not reached. The most frequently reported AEs were pyrexia (54.3%), hypothyroidism (32.9%), increased weight (30.0%), upper respiratory tract infection (30.0%), cough (17.1%) and pruritus (17.1%). Grade ≥3 AEs reported in ≥2 patients were upper respiratory tract infection (2.9%) and pneumonitis (2.9%). Immune-related AEs were reported in 27 patients (38.6%); grade ≥3 in 6 patients (8.6%): pneumonitis (interstitial lung disease, organizing pneumonia, pneumonitis, n=3); skin adverse reactions (erythema nodosum), nephritis (focal segmental glomerulosclerosis), and musculoskeletal (increased creatine phosphokinase) (each n=1).

Table. Patient Demographics and Baseline Characteristics

Characteristic	N = 70
Median age, y	32.5
<65 y, n (%)	66 (94.3)
≥65 and <75 y, n (%)	4 (5.7)
Gender, n (%)	
Female	30 (42.9)
Male	40 (57.1)
Median time from initial cHL diagnosis to study entry, mo	25.3
Stage IV disease, n (%)	42 (60.0)
Bulky disease[a], n (%)	8 (11.4)
Bone marrow involvement, n (%)	22 (31.4)
B-symptom(s), n (%)	26 (37.1)
Patients with any prior radiation therapy, n (%)	21 (30.0)
Ineligible for prior ASCT[b], n (%)	57 (81.4)
Failure to achieve an objective response to salvage chemotherapy	53 (75.7)
Inadequate stem cell collection or unable to collect stem cells	2 (2.9)
Comorbidities	2 (2.9)
Type of prior systemic therapy, n (%)	
Chemotherapy	70 (100.0)
ASCT	13 (18.6)
Immunotherapy[c]	15 (21.4)
Median lines of prior therapy (range)	3 (2-11)

[a]Bulky disease defined as mediastinal mass ratio of 0.33 or size of any single node/nodal mass ≥10 cm in diameter.
[b]All received ≥2 prior regimens.
[c]Immunotherapy included brentuximab vedotin, rituximab, cytokine-induced killer cell transfusion, thalidomide, or lenalidomide.

Conclusion

Updated results of this study further demonstrated the substantial therapeutic activity of tislelizumab in patients with heavily pre-treated R/R cHL, as shown by a high rate of durable deep responses. The treatment of tislelizumab was well tolerated in patients with R/R cHL.