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 specifically engineered to minimize binding to FcγR on macrophages, thereby abrogating 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) according to the Lugano criteria. Secondary endpoints included progression-free survival (PFS), duration of response (DOR), rate of complete response (CR), time to response (TTR) assessed by IRC, safety, and tolerability.

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

Results: Seventy patients from 11 Chinese centers were enrolled and treated; patient characteristics are in the table below. As of data cutoff date (Nov 26, 2018), the median follow-up was 13.93 months (range, 3.4-18.8 months). The ORR assessed by IRC was 87.1% based on PET/CT. A total of 44 patients (62.9%) achieved CR, and the median TTR assessed by IRC was12.0 weeks (range, 8.9-42.1). Fifty-two patients (74.3%) remained on treatment and 18 had discontinued (12 for PD; 4 for adverse events [AEs]; 1 withdrew consent; 1 due to pregnancy). The median PFS was not reached and estimated 9-month PFS rate was 75.9%. The median DOR was not reached as well. The most frequently reported (⩾15%) AEs due to any cause were pyrexia (57.1%), weight increased (34.3%), hypothyroidism and upper respiratory tract infection (32.9%, each), pruritus, WBC decreased and cough (18.6%, each), alanine aminotransferase increased (17.1%). Grade ⩾3 AEs reported in ⩾2 patients were weight increased, neutrophil count decreased, upper respiratory tract infection, pneumonitis, and hypertension (2.9%, each). Immune-related AEs were reported in 27 patients (38.6%); grade ⩾3 in 8 patients (11.4%): pneumonitis (interstitial lung disease, organizing pneumonia, pneumonitis, n=4); skin adverse reactions (erythema nodosum), nephritis (focal segmental glomerulosclerosis), musculoskeletal (increased creatine phosphokinase) and other immune-related reaction (lipase increased), n=1 each . No fatal AEs were reported. AEs leading to treatment discontinuation in 4 patients (5.7%) included pneumonitis (n=2), organizing pneumonia and focal segmental glomerulosclerosis (n=1 each). One patient died on study due to PD.

Conclusions: Updated results of this study further substantiated the high activity of tislelizumab resulting in a high rate of durable response in R/R cHL who had failed or were ineligible for ASCT. The favorable safety profile of tislelizumab was generally consistent with other PD-1-blocking antibodies.

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.