# TISLELIZUMAB (BGB-A317) FOR RELAPSED/REFRACTORY PERIPHERAL T-CELL LYMPHOMAS: SAFETY AND EFFICACY RESULTS FROM A PHASE 2 STUDY

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**Background**

Peripheral T-cell lymphomas (PTCL) are rare and generally aggressive. Relapsed/refractory (R/R) PTCL outcomes are poor. The T-cell lymphoma tumor microenvironment has increased programmed death-ligand 1 (PD-L1) expression, suggesting PD-1/PD-L1 pathway inhibition may be an effective T-cell lymphoma treatment. Tislelizumab, a humanized IgG4 monoclonal PD-1–blocking antibody, has high PD-1 affinity/specificity and minimized macrophage FCγR binding.

**Aims**

In cohort 2 of this phase 2 trial, the safety and antitumor activity of tislelizumab was evaluated in patients with R/R PTCL. The primary endpoint was investigator-assessed overall response rate (ORR) using 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), overall survival, and safety and tolerability.

**Methods**

This is an ongoing, single-arm, multicenter phase 2 study (NCT03493451) of tislelizumab given at 200 mg IV every 3 weeks until progressive disease (PD) or unacceptable toxicity. Three cohorts are enrolling patients with mature T- and NK-cell neoplasms by disease subtype. Reported here are results for cohort 2. Patient eligibility criteria were: R/R PTCL-not otherwise specified (NOS), angioimmunoblastic T-cell lymphoma (AITL), or anaplastic large cell lymphoma (ALCL); ECOG-PS ≤2; measurable disease by CT; ≥1 previous appropriate combination therapy (eg, CHOP, EPOCH, or similar); and PD during or after completing the most recent therapy.

**Results**

Patients (N = 44) at 19 sites in China, Italy, France, and Taiwan were enrolled and treated from April 27, 2018 to the Oct. 11, 2019 data cutoff. The cohort had 21 patients with PTCL-NOS, 11 with AITL, and 12 with ALCL. Median cohort follow-up at data cutoff was 7.4 months (range, 0.5-17.5). Six (13.6%) patients remained on treatment (median time on treatment 8.8 months) and 38 discontinued (28 for PD, 9 for adverse events [AEs], 1 withdrew consent). The ORR was 20.5% (95% CI: 9.8, 35.3). Three patients with PTCL-NOS (14.3%) achieved CR; one remained in CR for 11.2 months at the data cutoff. Median DOR was 8.2 months (95% CI: 2.69, NE). Median TTR was 2.9 months (range, 2.1-5.78). Median cohort PFS was 2.7 months (95% CI: 2.56, 4.76). The most frequently reported treatment-emergent AEs (TEAEs) were pyrexia (34.1%), asthenia and anemia (18.2%), arthralgia, cough, and thrombocytopenia (15.9%), pruritus (13.6%), and erythema, hypothyroidism, neutropenia, and upper respiratory tract infection (11.4%). Grade ≥3 TEAEs in ≥2 patients were neutropenia (9.1%), anemia (6.8%), thrombocytopenia (6.8%), general physical health deterioration (4.5%), pneumonia (4.5%), and pyrexia (4.5%). Immune-related

**Table 1:** Baseline Characteristics

| Characteristic | N = 44 |
|---|---|
| Median age, years, n (%) | 58 |
| <65 | 31 (70.5) |
| ≥65 | 13 (29.5) |
| Gender, n (%) | |
| Female | 15 (34.1) |
| Male | 29 (65.9) |
| ECOG performance status at baseline, n (%) | |
| 0 | 21 (47.7) |
| 1 | 21 (47.7) |
| 2 | 2 (4.5) |
| Median time from initial diagnosis to study entry, months (min, max) | 14.77 (3.7, 160.6) |
| Median number of prior regimens, n (min, max) | 2 (1, 8) |
| Stage at study entry, n (%) | |
| Stage II | 8 (18.2) |
| Stage III | 12 (27.3) |
| Stage IV | 24 (54.5) |
| Country enrollment, n (%) | |
| China | 22 (50.0) |
| Italy | 18 (40.9) |
| France | 3 (6.8) |
| Taiwan | 1 (2.3) |

**Table 2:** Disease Response by PTCL Subtype

| Response | PTCL-NOS (n = 21) | AITL (n = 11) | ALCL (n = 12) | Total (n = 44) |
|---|---|---|---|---|
| ORR, n (%) (95% CI) | 5 (23.8) 8.2, 47.2 | 2 (18.2) 2.3, 51.8 | 2 (16.7) 2.1, 48.4 | 9 (20.5) 9.8, 35.3 |
| CR rate, n (%) (95% CI) | 3 (14.3) 3.0, 36.3 | 0 (0.0) 0.0, 28.5 | 0 (0.0) 0.0, 26.5 | 3 (6.8) 1.4, 18.7 |
| DOR, months, median (95% CI) | NE (2.69, NE) | 3.2 (NE, NE) | 8.3 (8.18, 8.38) | 8.2 (2.69, NE) |
| TTR, months, median (range) | 4.6 (2.76-5.78) | 2.5 (2.10-2.86) | 2.7 (2.69-2.73) | 2.9 (2.10-5.78) |
| PFS, months, median (95% CI) | 2.7 (2.17, 5.42) | 3.4 (1.58, 5.29) | 2.7 (1.02, 10.87) | 2.7 (2.56, 4.76) |

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large cell lymphoma; CR, complete response; DOR, duration of response; NE, not estimable; ORR, overall response rate; PFS, progression-free survival; PTCL-NOS, peripheral T-cell lymphoma-not otherwise specified; TTR, time to response.

**Conclusion**

Tislelizumab showed modest activity in patients with mature T-cell neoplasms and toxicity was tolerable. Future development in this aggressive disease should consider a mechanism-based combination to drive more rapid, deep, and sustainable response.