Tislelizumab, an anti–PD-1 antibody, in patients with relapsed/refractory classical Hodgkin lymphoma in TIRHOL BGB-A317-210: a prospective, multicenter, phase 2 LYSA study conducted in Western countries

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ABSTRACT

Introduction: Tislelizumab, the anti-programmed-cell-death-protein-1 (anti-PD-1) antibody, was evaluated in an initial phase 2 study in Chinese patients with relapsed/refractory classical Hodgkin lymphoma (cHL); overall response rate (ORR) was 87%, complete response rate (CRR) was 63%, and 3-year progression-free survival (PFS) was 40%, warranting further evaluation in Western populations.

Patients and methods: TIRHOL (NCT04318080) is a phase 2 study in patients with cHL in France, Belgium, the US, and Australia (cohort 1 [C1]: prior autologous stem cell transplant [ASCT]; cohort 2 [C2]: ineligible for ASCT). Prior brentuximab vedotin (BV) therapy was an initial inclusion criterion, removed in 10/2021. Tislelizumab 200-mg was given intravenously every 3 weeks until progressive disease (PD), unacceptable toxicity, or study withdrawal. Disease assessments were performed every 12 weeks. The primary endpoint was investigator-assessed ORR (best overall response of complete response [CR] or partial response [PR]); secondary endpoints were CRR, time to response (TTR), duration of response (DOR), and safety/tolerability. Main exploratory endpoints were PFS and overall survival (OS).

Results: Between 08/2020-09/2022, 45 patients (C1: n=14; C2: n=31) who received ≥1 tislelizumab dose were included in the analysis. Median age was 64 years, 67% were male, and all had ECOG performance status 0-1. Most had advanced-stage disease (III, 38%; IV, 42%), 11% had bulky disease, 18% had B symptoms, and 29% had cHL refractory to last therapy. Median number of prior therapy lines was 2; 12 patients received ≥3 prior therapy lines, and 33 received prior BV. At last follow-up, the median treatment duration was 24 weeks. ORR was 64.4%; 14 patients achieved CR; 15 achieved PR. The remaining patients had stable disease (n=2) or PD (n=13) or were not evaluated (n=1). Both cohorts had similar ORRs (median TTR: 2.69 months; median DOR: 12.3 months). Three responsive patients underwent subsequent ASCT (n=1) or allogeneic SCT (n=2). With an 11.4-month median follow-up, median PFS was 5.6 (combined cohorts), 8 (C1), and 5 (C2) months. Thirteen patients with standardized update value increase had PD; their clinical benefit continued for a median 3.6 months afterwards. At last follow-up, 19 patients remained on tislelizumab. Median OS was not reached (1-year OS, 93.5%; 4 deaths), and no treatment-related deaths were reported. Fifteen patients experienced grade ≥3 treatment-emergent adverse events (AEs). Fifteen patients experienced immune-related AEs (irAEs); 3 had grade ≥3 irAEs.

Conclusion: The TIRHOL study met its primary endpoint, with an acceptable safety profile, confirming that tislelizumab is a promising treatment option in cHL.