Tislelizumab, an anti-PD-1 antibody, in patients with relapsed/refractory classical Hodgkin lymphoma: final analysis from the LYSA phase 2 TIRHOL study BGB-A317-210

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ABSTRACT

Introduction: The phase 2 TIRHOL study (NCT04318080) was designed to evaluate the efficacy of PD-1 inhibitor tislelizumab in Western patients (pts) with relapsed/refractory (R/R) cHL and met its primary endpoint, with ORR of 64.4% at primary analysis. Here, we present the results of the TIRHOL final analysis.

Methods: Tislelizumab 200 mg was given intravenously every 3 weeks until progressive disease (PD), unacceptable toxicity, or study withdrawal; response was assessed by investigators, according to PET-CT International Lugano 2014 criteria, every 12 weeks. Cohort 1 included pts post-autologous stem cell transplant (ASCT); cohort 2 included pts ineligible for ASCT. The primary endpoint was ORR; secondary and exploratory endpoints included complete response (CR) rate, time to response (TTR), duration of response (DoR), safety and tolerability, PFS, overall survival (OS), pharmacokinetics (PK), and immunogenicity.

Results: Between Aug 2020 and Sept 2022, 45 pts (14 in cohort 1, 31 in cohort 2) were enrolled and dosed. The median age was 64 years (range 18-87), and all had ECOG performance status 0-1; 80% had stage III-IV disease, 11% had bulky disease, 18% had B symptoms, and 29% had refractory disease. The median prior lines of therapy received was 2 (1-4); 27% of pts received ≥3 prior lines of therapy and 73% received prior brentuximab vedotin. At study completion, the median treatment duration was 8 cycles (range 1-56), 27 weeks (range 3-168). The ORR was 66.7% (95% CI, 51%-80%) overall, 71.4% in cohort 1 and 64.5% in cohort 2; CR rate was 31% and 16 (36%) pts had PR. Remaining pts had stable disease (n=1), PD (n=13, 29%) or were not evaluated (n=1). The median TTR was 2.69 mos (range 0.3-19.5). The median DoR was 12.3 mos (95% CI, 3-NR) and was 25.6 mos (95% CI, 8.44-NR) for pts achieving CR. Four pts with objective responses underwent subsequent SCT. With a median follow-up of 30 mos (95% CI, 24.7-35.3), the median PFS was 5.6 (95% CI, 5.1-8.3), 6.8, and 5.6 mos for overall, cohort 1, and 2, respectively. Sixteen pts with PD continued to benefit clinically from tislelizumab treatment for a median of 9.1 mos (range 1.4-35.3) after PD. The 3-year OS rate was 70.1% (12 deaths; 95% CI, 51.9-82.4) with

no treatment-related deaths. Treatment-emergent adverse events (TEAEs) led to tislelizumab interruption or discontinuation in 13 pts, and in 9 pts these were considered treatment-related by investigators. Grade ≥3 TEAEs occurred in 16 (36%) pts and 3 pts had grade ≥3 immune-related TEAEs (maculo-papular rash, hepatitis, hemolytic anemia).

Conclusions: With a median follow-up of 30 mos, this study confirmed that tislelizumab is an effective therapeutic option for pts with R/R cHL, including those unfit for ASCT. Approximately 1/3 of the study population continued tislelizumab due to ongoing clinical benefit beyond SUV increase meeting PD criteria. The safety profile of tislelizumab remains acceptable, consistent with that of the PD-1 inhibitor class.