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POSTER ABSTRACTS

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Favezelimab in Combination with Pembrolizumab in Patients with Heavily Pretreated Anti-PD-1-Refractory Classical Hodgkin Lymphoma: Updated Analysis of an Open-Label Phase 1/2 Study

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Background: Programmed cell death protein 1 (PD-1) inhibitors are a standard of care for relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL), but better treatment options are needed for patients with anti-PD-1-refractory disease. Lymphocyte-activation gene 3 (LAG-3) is an immune checkpoint receptor with a role in regulating T-cell function. Dual blockade of PD-1 and LAG-3 has demonstrated antitumor activity in patients with advanced melanoma. Combination therapy with favezelimab (anti-LAG-3) and pembrolizumab (anti-PD-1) is currently being investigated in a phase 1/2 study (NCT03598608) in patients with R/R hematologic malignancies. Prior analyses showed that the combination had antitumor activity and manageable safety in patients with heavily pretreated anti-PD-1-refractory cHL (cohort 2). Updated results for this cohort are presented.

Methods: The study consisted of a safety lead-in (part 1) followed by a dose-expansion phase (part 2). Eligible patients were ≥18 y; had R/R cHL after autologous stem cell transplantation (ASCT), were ineligible for ASCT, or did not respond to salvage chemotherapy; had an ECOG performance status of 0 or 1; and had experienced disease progression after ≥2 doses of anti-PD-1-based therapy and within 12 weeks of the last dose of anti-PD-1 therapy. In part 1, patients received pembrolizumab 200 mg IV Q3W + favezelimab starting at 200 mg and escalating to 800 mg IV Q3W per a modified toxicity probability interval design. In part 2, patients received pembrolizumab + favezelimab at the established RP2D of 800 mg Q3W for ≤35 cycles (~2 y). The primary end point was safety. ORR per IWG 2007 criteria by investigator review was a secondary end point. DOR and PFS per IWG 2007 criteria by investigator review and OS were exploratory end points.

Results: 34 patients with anti-PD-1-refractory cHL were enrolled in cohort 2. The median age was 37.5 y (range, 25-79), 16 patients (47%) were male, 21 (62%) had an ECOG performance status of 0, and 94% had received ≥4 prior lines of therapy. Seventeen patients (50%) had received an anti-PD-1-based regimen as their most recent therapy. At database cutoff (March 2, 2023), 8 patients (24%) had completed 35 cycles of treatment and 26 (76%) had discontinued treatment (14 [41%] progressive disease, 7 [21%] AEs, 5 [15%] other reasons). The median time from first dose to data cutoff was 35.3 mo (range, 15.0-49.4). Treatment-related AEs occurred in 28 patients (82%), of which the most common (≥15%) were hypothyroidism (18%), nau-

sea (18%), and fatigue (15%). Grade 3/4 treatment-related AEs occurred in 6 patients (18%). 6 patients (18%) discontinued treatment because of treatment-related AEs. No deaths due to treatment-related AEs were reported. AEs of clinical interest occurred in 17 patients (50%); 2 patients (6%) had grade 3 events (encephalitis, hepatitis) and 1 patient (3%) had a grade 4 event (type 1 diabetes mellitus). Of the 2 patients who underwent allogeneic hematopoietic stem cell transplantation after discontinuation or completion of study treatment, 1 had a grade 3 AE (acute graft versus host disease) unrelated to study treatment that resolved. The ORR in cohort 2 was 29% (10/34; 95% CI, 15-48), with 3 (9%) complete responses (CR) and 7 (21%) partial responses (PR). Of the 10 responders, 7 had received ≥5 prior lines of therapy (3 CR/4 PR). The ORR in patients with anti-PD-1 as their most recent therapy was 35% (6/17; 95% CI, 14-62; 1 CR/5 PR); the ORR in patients with non-anti-PD-1 as their most recent therapy was 24% (4/17; 95% CI, 7-50; 2 CR/2 PR). Of 28 patients with a baseline and postbaseline assessment available, 25 (89%) had any reduction in target lesion size from baseline, and 12 (43%) had ≥50% reduction. Median DOR was 21.9 mo (range, 0.0+ to 26.1+) and an estimated 17% of responders remained in response ≥24 mo. Median PFS was 9.7 mo (95% CI, 5.1-14.7); 24-mo PFS rate was 21%. Median OS was 34.3 mo (95% CI, 25.7-NR); 24-mo OS rate was 76%.
Conclusion: After additional follow-up, the combination of favezelimab + pembrolizumab continued to demonstrate manageable safety and antitumor activity in patients with heavily pretreated anti-PD-1-refractory cHL. Analyses are underway to identify biomarkers predictive of response to the combination of favezelimab and pembrolizumab. The phase 3 KEYFORM-008 study (NCT05508867) is being conducted to evaluate a coformulation of favezelimab and pembrolizumab in patients with anti-PD-1-refractory cHL.

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