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P1086 FAVEZELIMAB (ANTI–LAG-3) AND PEMBROLIZUMAB CO-BLOCKADE IN ANTI–PD-1–NAIVE PATIENTS WITH RELAPSED OR REFRACTORY CLASSICAL HODGKIN LYMPHOMA: AN OPEN-LABEL PHASE 1/2 STUDY

Topic: 17. Hodgkin lymphoma - Clinical

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Background: Programmed cell death 1 (PD-1) inhibitors are a standard of care in patients with relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL), but clinical interest persists for new approaches to deepen and lengthen responses. Dual blockade of PD-1 and lymphocyte-activation gene 3 (LAG-3) has demonstrated antitumor activity in preclinical models.

Aims: The multicohort phase 1/2 MK-4280-003 study (NCT03598608) evaluated the safety and efficacy of favezelimab (MK-4280), a humanized Immunoglobulin G4 LAG-3 inhibitor, plus pembrolizumab (a PD-1 inhibitor) in patients with R/R hematologic malignancies. This analysis focused on anti–PD-1–naïve patients with R/R cHL (cohort 1).

Methods: This study included a safety lead-in phase (part 1) to determine the recommended phase 2 dose (RP2D) followed by a dose-expansion phase (part 2). Eligible patients in cohort 1 must have had R/R cHL after autologous stem cell transplantation (ASCT) or been ineligible for ASCT and have had no prior anti–PD-1 therapy. In part 1, patients from all cohorts received intravenous (IV) pembrolizumab 200 mg every 3 weeks (Q3W) and favezelimab IV 200 mg or 800 mg Q3W. Dose-finding based on occurrence of dose-limiting toxicities (DLTs) was determined using a modified toxicity probability interval design. In part 2, patients received pembrolizumab + favezelimab at the established RP2D for up to 2 years (35 cycles), or until documented disease progression, adverse events (AEs), or withdrawal from the study. Primary end point was safety, including DLTs and AEs. Secondary end point was objective response rate (ORR). Duration of response (DOR), progression-free survival (PFS), and overall survival (OS) were exploratory end points.

Results: Only 1 DLT (autoimmune hepatitis [grade 4]) was identified among the first 6 patients from all cohorts included in part 1 at the favezelimab 200 mg dose; thus, the dose was escalated to 800 mg. No DLTs were observed in the 15 additional patients treated at the 800 mg dose. The RP2D for the combination was defined as 800 mg Q3W + pembrolizumab 200 mg Q3W. In cohort 1, 30 patients were enrolled; median age was 40 years, 53% had ECOG PS 0, and 80% had no more than 3 prior lines of therapy. As of the database cutoff (Nov 1, 2021), 9 of 30 (30%) patients had discontinued treatment either due to adverse events (n=3) or disease progression (n=6). After a median follow-up of 13.5 months, ORR for cohort 1 was 73% (95% CI, 54-88; complete response, 7 patients [23%]; partial response, 15 patients [50%]). 28 of 30 patients (93%) had a reduction from baseline in target lesions. Median DOR was not reached ([NR]; 95% CI, 0+ to 23+ months) and 6 patients (51%) had response ≥12 months. The median PFS was 19 months (95% CI, 8-NR) and the 12-month PFS rate was 57%. The median OS was NR (95% CI, NR-NR) and the 12-month OS rate was 94%. Treatment-related AEs (TRAE) occurred in 26 patients (87%); most common

(≥10%) were hypothyroidism (27%), fatigue (20%), infusion-related reactions (20%), headache (17%), and arthralgia, hyperthyroidism, myalgia, and nausea (10% each). Grade 3 or 4 TRAEs occurred in 6 patients (20%) and 10% of patients discontinued due to TRAEs. No treatment-related deaths occurred.

Summary/Conclusion: Favezelimab 800 mg + pembrolizumab 200 mg Q3W demonstrated an acceptable safety profile and effective antitumor activity in anti–PD-1–naïve patients with R/R cHL. Further studies are merited to compare the activity of this combination to that of pembrolizumab alone.