Abstract: P1068

Title: UPDATED RESULTS FROM AN OPEN-LABEL PHASE 1/2 STUDY OF FAVEZELIMAB IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH RELAPSED OR REFRACTORY CLASSICAL HODGKIN LYMPHOMA AFTER ANTI–PD-1 TREATMENT

Abstract Type: Poster Presentation

Session Title: Hodgkin lymphoma - Clinical

Background:

Programmed death 1 (PD-1) inhibitors are standard of care for relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL), but optimized treatment strategies are needed for patients (pts) with progressive disease after anti–PD-1 therapy. Dual blockade of PD-1 and lymphocyte-activation gene 3 (LAG-3) has demonstrated antitumor activity, leading to FDA approval of the combination in unresectable or metastatic melanoma. Favezelimab, a humanized IgG-4 LAG-3 inhibitor, plus pembrolizumab (anti–PD-1) is being investigated in a phase 1/2 efficacy and safety study (NCT03598608) in pts with R/R hematologic malignancies. Initial results showed effective antitumor activity and tolerable safety of pembrolizumab 200 mg QW3 and favezelimab 800 mg QW3 in heavily pretreated pts with R/R cHL whose disease progressed after anti–PD-1 therapy (cohort 2; Timmerman J et al. *J Clin Oncol*. 2022;40(16 suppl):7545).

Aims:

Evaluate efficacy and safety of favezelimab + pembrolizumab in pts with R/R cHL whose disease progressed after anti–PD-1 therapy.

Methods:

Eligible pts in cohort 2 had R/R cHL after autologous stem cell transplantation (ASCT) or were ineligible for ASCT or did not respond to salvage chemotherapy, an ECOG PS ≤1, and disease progression after ≥2 doses of anti–PD-1-based therapy. In part 1 (safety lead-in), pts from all cohorts received favezelimab IV 200 mg or 800 mg Q3W plus pembrolizumab IV 200 mg Q3W. Dose finding based on occurrence of dose-limiting toxicities (DLTs) was determined using a modified toxicity probability interval design. In part 2 (dose expansion), pts received pembrolizumab plus favezelimab at the established RP2D (800 mg Q3W) for ≤35 cycles (~2 years). Primary end points were safety and RP2D. Secondary end points included ORR. Duration of response (DOR), progression-free survival (PFS), and overall survival (OS) were exploratory.

Results:

Cohort 2 enrolled 34 pts. Median age was 37.5 years, 62% had ECOG PS of 0, and 94% had ≥4 prior lines of therapy; 17 pts (50%) had an anti–PD-1–based regimen as their most recent line of therapy. At database cutoff (August 31, 2022), 8 pts (24%) had completed 2 years of study treatment and 25 (74%) had discontinued (including 13 because of progressive disease and 7 because of adverse events). After a 29.3-month (range, 9.0-43.4) median follow-up (first dose to data cutoff), 10 pts had an objective response (ORR, 29% [95% CI, 15-48]; complete response [CR], 3 [9%]; partial response [PR], 7 [21%]). 25 of 28 pts (89%) with a postdose scan had reduction in target lesion size from baseline, and 12 pts (43%) had ≥50% reduction from baseline. Median DOR was 21.9 months (range, 0.0+ to 24.0); an estimated 52% of responders remained in response ≥15 months. Median PFS was 10.7 months (95% CI, 5.1-14.7); 15-month PFS rate was 33%. Median OS was not reached (NR; 95% CI, 25.7-NR); 15-month OS rate was 87%. Of the 10 responders, 7 had ≥5 prior lines of therapy (CR, 3; PR, 4); 3 responders (all PR) had ≤4 prior lines of therapy. Among 28 pts (82%) who had a treatment related AE the most common (≥15%) were hypothyroidism and nausea (18% each), diarrhea and fatigue (15% each). Grade 3 or 4 treatment related AEs occurred in 6 pts (18%). No deaths were treatment related. 1 patient who received allogeneic hematopoietic stem cell transplantation after completion of study treatment had a grade 3 AE unrelated

to study treatment that resolved.

Summary/Conclusion:

The combination of favezelimab plus pembrolizumab continued to demonstrate antitumor activity and manageable safety in pts with R/R cHL whose disease progressed following anti–PD-1 therapy.

Keywords: Clinical trial, Immunotherapy, Hodgkin’s lymphoma