ELSEVIER

Blood 142 (2023) 1693–1695

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

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

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

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Introduction: Programmed cell death protein 1 (PD-1) inhibitors such as pembrolizumab play an important role in the treatment of patients with relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL), but treatment failure remains a significant challenge. Lymphocyte-activation gene 3 (LAG-3) is an immune checkpoint receptor that downregulates T-cell activity and plays a role in regulating T-cell function. Dual blockade of PD-1 and LAG-3 demonstrated antitumor activity in patients with advanced melanoma in the RELATIVITY-047 trial, which led to FDA approval in this setting. Favezelimab is a humanized IgG4 monoclonal antibody directed against LAG-3 that is being investigated in combination with pembrolizumab in patients with R/R hematologic malignancies in a multicohort phase 1/2 study (NCT03598608). Prior analyses of this study demonstrated that pembrolizumab 200 mg plus favezelimab 800 mg every 3 weeks (Q3W) exhibited sustained antitumor activity and acceptable safety in the cohort of patients with anti-PD-1-naive R/R cHL (cohort 1). We present updated results from this cohort.
Methods: A safety lead-in phase to determine the recommended phase 2 dose (RP2D) was followed by a dose-expansion phase. Eligible patients were ≥18 years of age; had R/R cHL after autologous stem cell transplantation (ASCT), were ineligible for ASCT, or did not respond to salvage chemotherapy; had not received prior anti-PD-1 therapy; and had an ECOG performance status of 0 or 1. In the safety lead-in, patients received pembrolizumab 200 mg IV Q3W and favezelimab at a starting dose of 200 mg that was escalated to 800 mg IV Q3W using a modified toxicity probability interval method. In the dose-expansion phase, patients received pembrolizumab 200 mg Q3W plus favezelimab at the established RP2D of 800 mg Q3W for up to 35 cycles (~2 years). CT was performed every 12 weeks and PET at weeks 12 and 24. The primary end point was safety. Objective response rate (ORR) per IWG 2007 criteria by investigator review was a secondary end point. Duration of response (DOR) and progression-free survival (PFS) per IWG 2007 criteria by investigator review and overall survival (OS) were exploratory.
Results: Thirty patients with anti-PD-1-naive cHL were enrolled in cohort 1. The median age was 40.5 years (range, 19-82), 17 patients (57%) were male, 16 (53%) had an ECOG performance status of 0, and 24 (80%) had received 3 or fewer prior lines of therapy. At data cutoff (March 2, 2023), 13 patients (43%) had completed 35 cycles of study treatment, 16 (53%) had

discontinued treatment (10 [33%] progressive disease, 5 [17%] adverse event [AE], 1 [3%] noncompliance with study drug), and 1 (3%) was ongoing on treatment. The median time from first dose to data cutoff was 31.5 months (range, 24.0-43.2). Treatment-related AEs occurred in 27 patients (90%), of which the most common (≥20%) were hypothyroidism (27%), infusion-related reaction (23%), and fatigue (20%). Grade 3/4 treatment related AEs occurred in 9 patients (30%). Five patients (17%) discontinued treatment because of treatment-related AEs. No deaths due to treatment-related AEs were reported. AEs of clinical interest occurred in 20 patients (67%); 3 patients (10%) had grade 3 events (colitis, pneumonitis, severe skin reaction) and 1 patient (3%) had a grade 4 event (hepatitis). Of 5 patients who received allogeneic stem cell transplantation after discontinuation or completion of study treatment, 1 had a grade 3/4 AE (increased blood bilirubin) that was unrelated to study treatment and resolved. The ORR was 80% (n = 24; 95% CI, 61-92); 10 patients (33%) had a complete response and 14 (47%) had a partial response. Twenty-nine patients (97%) had any reduction in target lesions size from baseline, and 25 (83%) had a reduction of ≥50%. Median DOR was 17.0 months (range, 2.6-30.2), and an estimated 47% of responders remained in response ≥24 months. Median PFS was 19.4 months (95% CI, 9.0-28.5), and the 24-month PFS rate was 46%. Median OS was not reached (NR; 95% CI, NR-NR), and the 24-month OS rate was 93%.

Conclusion: With additional follow-up, the combination of favezelimab and pembrolizumab continued to demonstrate sustained antitumor activity and manageable safety in patients with anti-PD-1-naive R/R cHL. Analyses are underway to identify biomarkers predictive of response to the combination of favezelimab and pembrolizumab. Further studies to investigate this combination are warranted.

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*AstraZeneca/MedImmune:* Consultancy; *Allogene Therapeutics:* Consultancy; *Gilead Sciences:* Research Funding; *Seattle Genetics:* Consultancy, Research Funding; *BMS:* Consultancy, Other: Travel/Accommodations/Expenses, Research Funding; *Adicet Bio:* Consultancy; *AstraZeneca:* Research Funding. **Vucinic:** *Takeda:* Consultancy, Honoraria; *Sobi:* Honoraria, Other: Travel/Accommodations/Expenses; *Amgen:* Honoraria; *MSD:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *BMS/Celgene:* Consultancy, Honoraria, Other: Travel/Accommodations/Expenses; *Gilead/Kite:* Consultancy, Honoraria; *Janssen:* Honoraria; *AstraZeneca:* Honoraria; *Abbvie:* Honoraria. **Armand:** *Kite - a Gilead company:* Research Funding; *ADC Therapeutics:* Consultancy; *GenMab:* Consultancy; *Enterome:* Consultancy; *Genentech/Roche:* Consultancy, Research Funding; *ATB Therapeutics:* Consultancy; *IGM:* Research Funding; *Adaptive Biotechnologies:* Research Funding; *Xencor:* Consultancy; *Affimed Therapeutics:* Research Funding; *Foresight Diagnostics:* Consultancy; *Regeneron:* Consultancy; *AstraZeneca:* Consultancy, Research Funding; *MSD:* Consultancy, Research Funding; *Tessa Therapeutics:* Consultancy; *Bristol Myers Squibb:* Consultancy, Research Funding; *Merck:* Consultancy, Honoraria, Research Funding. **Avigdor:** *Gilead:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board of Directors or advisory committees; *Roche:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Membership on an entity's Board of Directors or advisory committees, Other: Travel/Accommodations/Expenses; *Takeda:* Membership on an entity's Board of Directors or advisory committees; *MSD:* Research Funding. **Gasiorowski:** *Abbvie:* Honoraria; *Janssen:* Honoraria; *Astellas:* Honoraria; *Novartis:* Honoraria; *Otsuka:* Honoraria; *MSD:* Honoraria; *Antengene:* Honoraria. **Herishanu:** *Medison:* Honoraria; 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Co., Inc.: Research Funding; *BMS:* Other: Travel/Accommodations/Expenses, Research Funding; *Oncovalent Therapeutics:* Consultancy; *Kite/Gilead:* Consultancy, Honoraria, Research Funding.

https://doi.org/10.1182/blood-2023-182128