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POSTER ABSTRACTS

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

Open-Label, Randomized, Phase 3 Study of Coformulated Favezelimab and Pembrolizumab Versus Chemotherapy in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma Refractory to Anti-PD-1 Therapy: Keyform-008

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Background: The importance of PD-1 therapy in relapsed or refractory (R/R) classical Hodgkin Lymphoma (cHL) is well established, with PD-1 inhibitors such as pembrolizumab being a standard of care option for patients. However, most patients eventually develop progressive disease and optimal therapy after anti-PD-1 failure has not been determined. The inhibitory checkpoint receptor, lymphocyte-activation gene 3 (LAG-3) is expressed in cHL tumor microenvironments and upregulation of LAG-3 is considered to play an important role in anti-PD-1 resistance. Favezelimab (MK-4280) is a humanized immunoglobulin G4 antibody that binds to LAG-3 and blocks interaction with major histocompatibility complex Class II ligands. Results from the ongoing phase 1/2 MK-4280-003 study of the combination of favezelimab and pembrolizumab demonstrated manageable safety and promising antitumor activity in patients with anti-PD-1-refractory R/R cHL. The randomized, open-label, parallel group, active-controlled, phase 3 KEYFORM-008 study (NCT05508867) is designed to evaluate efficacy and safety of the coformulation of favezelimab and pembrolizumab versus physician's choice of chemotherapy in patients with anti-PD-1-refractory R/R cHL.

Study Design and Methods: Patients ≥18 years old, with histologically confirmed R/R cHL, an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0-2, and adequate organ function are eligible. Patients must have exhausted all available treatment options with known clinical benefit, including having progressed on anti-PD-1-based therapy and being ineligible for or having failed autologous stem cell transplant (ASCT). In addition, patients should also have been ineligible for brentuximab vedotin (BV), relapsed or failed to respond to BV or discontinued BV due to toxicity. Patients with a history of central nervous system (CNS) metastases or active CNS involvement are excluded. Approximately 360 patients will be enrolled and randomly assigned 1:1 to receive coformulated favezelimab 800 mg and pembrolizumab 200 mg intravenously (IV) every 3 weeks (Q3W) or physician's choice of chemotherapy (gemcitabine 800-1200 mg/m ^{2} IV on days 1 and 8 of a 21-day cycle or bendamustine 90-120 mg/m ^{2} IV on days 1 and 2 of either a 21- or 28-day cycle). Randomization will be stratified by prior ASCT (yes vs no) and ECOG PS (0 or 1 vs 2). Treatment will continue for ≤35 cycles for the favezelimab/pembrolizumab coformulation or ≤6 cycles for chemotherapy or until disease progression, unacceptable toxicity, or withdrawal. Patients receiving physician's choice of chemotherapy with progressive disease confirmed by blinded independent central review (BICR)

per Lugano criteria may be eligible to cross over to the favezelimab/pembrolizumab coformulation. Response assessments by positron emission tomography (PET) and computed tomography (CT) or magnetic resonance imaging (MRI) will be performed every 12 weeks (Q12W) until disease progression or trial discontinuation. Adverse events will be monitored throughout the study and graded per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0. The primary end point is progression-free survival (PFS) per Lugano criteria by BICR. Overall survival (OS) is a key secondary end point. Other secondary end points are objective response rate (ORR), duration of response (DOR) per Lugano criteria by BICR, and safety. Exploratory end points include PFS on subsequent anticancer therapy and health-related quality of life. PFS, OS, and DOR rates in each treatment group will be estimated using the Kaplan-Meier method. The Clopper-Pearson method will be used to estimate ORR with 95% CI. Patient-reported outcomes will be assessed using EORTC Quality Of Life Questionnaire C30 and the EuroQuol 5-dimension, 5-level questionnaire. Enrollment for this study is open in sites in Australia, Belgium, Brazil, Canada, China, Czech Republic, France, Germany, Israel, Poland, Spain, South Korea, Sweden, Switzerland, Turkey, UK, and USA.

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