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

- PD-1 inhibitors are highly effective in patients with relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL), but treatment options are limited for those with disease progression after PD-1 blockade
- There is an unmet need for effective therapies for anti–PD-1–resistant cHL
- Upregulation of lymphocyte-activation gene 3 (LAG-3) expression in cHL is proposed to contribute to anti–PD-1 resistance[1]
- The anti–LAG-3 antibody favezelimab plus the anti–PD-1 therapy pembrolizumab has shown promising antitumor activity and manageable safety in patients with R/R cHL after anti–PD-1 therapy[2]
- In the randomized, open-label, parallel-group, active-controlled, phase 3 trial, KEYFORM-008 (NCT05508867), we will evaluate the efficacy and safety of coformulated favezelimab and pembrolizumab versus chemotherapy in patients with R/R cHL that is refractory to anti–PD-1/L1 therapy

Objectives

Primary

- To evaluate progression-free survival (PFS) per Lugano criteria by blinded independent central review (BICR) of coformulated favezelimab and pembrolizumab versus chemotherapy

Secondary

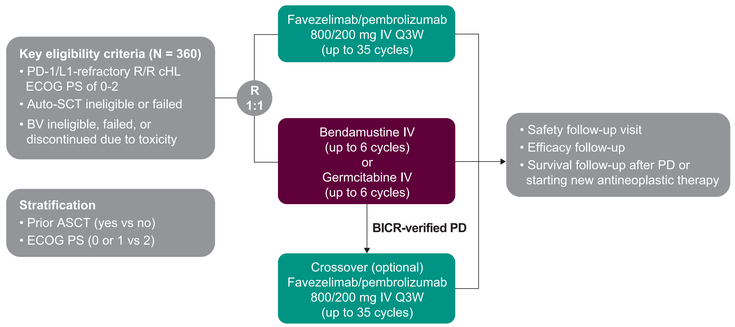
- To evaluate overall survival (OS), and objective response rate (ORR) and duration of response (DOR) per Lugano criteria by BICR of coformulated favezelimab and pembrolizumab versus chemotherapy
- To evaluate safety and tolerability of coformulated favezelimab and pembrolizumab

Exploratory

- To evaluate PFS on subsequent line of therapy (PFS2) coformulated favezelimab and pembrolizumab and chemotherapy
- To evaluate patient-reported quality of life coformulated favezelimab and pembrolizumab and chemotherapy
- To evaluate pharmacokinetic profile of coformulated favezelimab and pembrolizumab
- To identify molecular biomarkers indicative of clinical response/resistance, safety, pharmacodynamic activity, and/or mechanism of action of coformulated favezelimab and pembrolizumab

Methods

Study design



Auto-SCT, autologous stem-cell transplantation; BV, brentuximab vedotin; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; PD, progressive disease; Q3W, every 3 weeks.

Patient eligibility criteria

Key inclusion criteria	Key exclusion criteria
• Age ≥18 years • Histologically confirmed diagnosis of R/R cHL • Has progressed on treatment with anti–PD-1/L1 mAb, either monotherapy or combination[a] • Provision of a new or archival tumor tissue sample • ECOG performance status 0-2 • Adequate organ function • Measurable disease per Lugano criteria by investigator review • Must have had progressive disease after (or ineligible for): – Auto-SCT – Brentuximab vedotin	• Known active CNS metastases or active CNS involvement • Active infection requiring systemic therapy • Active autoimmune disease • Prior therapy with an anti–LAG-3 antibody • Clinically significant cardiovascular disease

CNS, central nervous system; mAb, monoclonal antibody; Q6W, every 6 weeks.

[a]PD-1 treatment progression is defined by meeting all of the following criteria: received at least 3 months of contiguous therapy (at least 2 doses if given on a Q6W schedule or at least 4 doses if given on a Q3W schedule), documented disease progression per Lugano criteria, and had progressive disease documented within 12 weeks from last dose of anti–PD-1/L1 mAb as determined by investigator.

Assessments and follow-up

Assessments	Detail
AEs	• AEs will be monitored and assessed by investigators throughout the trial and for 30 days (90 days for serious adverse events) after the last dose of trial treatment • Severity will be graded per NCI Common Terminology Criteria for Adverse Events, version 5.0
Tumor response	• Assessed by CT and PET or MRI every 12 weeks until disease progression or trial discontinuation

AE, adverse event; CT, computed tomography; MRI, magnetic resonance imaging; NCI, National Cancer Institute; PET, positron emission tomography.

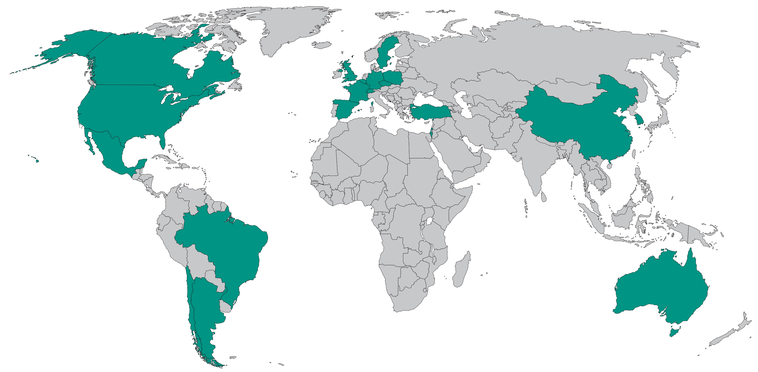
Analyses

Analysis	Detail
Safety	• Safety analyses will be conducted in the APaT population, consisting of all randomly assigned patients who received ≥1 dose of trial treatment
Efficacy	• Efficacy analyses will be conducted in the ITT population of all randomly assigned patients • OS, PFS, PFS2, and DOR will be summarized using the Kaplan-Meier method • ORR will be estimated and its 95% CI will be calculated using the Clopper-Pearson method • PFS and OS will be evaluated using a stratified log-rank test and HRs will be estimated using a stratified Cox regression model

APaT, all patients as treated; HR, hazard ratio; ITT, intention-to-treat.

Status

Sites of patient enrollment for KEYFORM-008 (green)



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1. Veldman J. et al. *Cancer Treat Rev.* 2020;82:101931.
2. Timmerman J. et al. *Blood.* 2022;140:768-770.

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624. Hodgkin Lymphomas and T/NK cell Lymphomas: Clinical and Epidemiological: Poster II
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