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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Favezelimab (anti-LAG-3) Plus Pembrolizumab in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL): Cohort 3 of a Multicohort Open-Label Phase 1/2 Study

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Background: Lymphocyte-activation gene 3 (LAG-3) is involved in the regulation of T-cell function and is commonly co-expressed with PD-1 on anergic T cells. Favezelimab (MK-4280), a humanized IgG4 anti-LAG-3 monoclonal antibody, plus pembrolizumab (anti-PD-1) is being investigated in the multicohort phase 1/2 MK-4280-003 efficacy and safety study (NCT03598608) in patients with relapsed or refractory (R/R) hematologic malignancies. Prior analyses of the combination demonstrated antitumor activity and manageable safety in patients with anti-PD-1-naive R/R classical Hodgkin lymphoma (cHL; cohort 1; ORR, 73%; CR, 30%) (Johnson NA et al. Blood. 2022;140(suppl 1):6540-2) and anti-PD-1-refractory cHL (cohort 2; ORR, 29%; CR, 9%) (Timmerman J et al. Blood. 2022;140(suppl 1):768-70). We present results from analysis of patients with R/R DLBCL enrolled in cohort 3.
Methods: In this study, a safety lead-in phase (part 1) to determine the recommended phase 2 dose (RP2D) was followed by a dose-expansion phase (part 2). In cohort 3, eligible patients were ≥18 years old, had histologically confirmed R/R DLBCL that had progressed after ≥2 lines of previous therapy, including progression after autologous stem cell transplant (ASCT), had declined ASCT, or were ineligible for ASCT. Patients with Richter transformation were not permitted. In part 1, patients received favezelimab at a starting dose of 200 mg that was escalated to 800 mg plus pembrolizumab at 200 mg IV every 3 weeks (Q3W) per the modified toxicity probability interval method. In the dose-expansion phase, patients received favezelimab at the established RP2D of 800 mg plus pembrolizumab 200 mg Q3W for ≤35 cycles (~2 years). Response assessments were performed at weeks 12 and 24 (PET) and Q12W (CT). Adverse events (AEs) were graded per the NCI CTCAE v4.0. The primary end point was safety. ORR per IWG 2007 criteria by investigator review was a secondary end point. Exploratory end points included duration of response (DOR) and progression-free survival (PFS) per IWG 2007 criteria by investigator review and overall survival (OS).
Results: A total of 25 patients with R/R DLBCL were enrolled. Patients had a median age of 73 years (range, 25-87), 10 (40%) had ECOG PS 0, and 15 (60%) had ≥3 prior lines of therapy. Most common subtypes of DLBCL were unspecified DLBCL (n = 12; 48%) and germinal center B-cell DLBCL (n = 6; 24%). At database cutoff (March 2, 2023), 1 patient (4%) was ongoing

on treatment and 24 (96%) had discontinued because of progressive disease (n = 14), AEs (n = 2), clinical progression (n = 5), or patient noncompliance/nonstudy anticancer therapy (n = 3); 1 patient (4%) discontinued because of treatment-related AEs. No treatment-related deaths occurred. Sixteen patients (64%) had a treatment-related AE; the most common (≥5%) were cough (16%), increased blood alkaline phosphatase (12%), and hypothyroidism, constipation, infusion related reaction, increased AST, muscle spasms, headache and pruritis (8% each). Grade 3 or 4 treatment-related AEs occurred in 4 patients (16%; 1 grade 3 lymphocytic hypophysitis, 1 grade 3 infectious enterocolitis, 1 grade 3 increased AST, 1 grade 3 increased ALT, 1 grade 3 increased amylase, and 1 grade 4 decreased neutrophil count). AEs of clinical interest occurred in 5 patients (20%); only one grade ≥3 occurred (grade 3 hypophysitis). The median (range) time from first dose to data cutoff was 25.9 (19.7-52.1) months. The objective response rate was 12% (95% CI, 2.5-31.2; [2 CR, 1 PR]). Among 17 patients with a postdose scan, 7 (41%) had a reduction from baseline in target lesion size, and 6 (35%) had ≥50% reduction from baseline. Median DOR was not reached (range, 3.0+ to 16.9+ months); 1 responder had an observed response duration of ≥12 months. Median PFS was 2.1 months (95% CI, 1.1-2.7); 12-month PFS rate was 12%. As of the data cutoff, 20 patients (80%) had died. Median OS was 6.4 months (95% CI, 2.3-15.8); 12-month OS rate was 43%.

Conclusion: Favezelimab 800 mg plus pembrolizumab 200 mg had limited antitumor activity in patients with DLBCL in cohort 3. Analyses are underway to identify biomarkers predictive of response to the combination of favezelimab and pembrolizumab. The safety profile was manageable and consistent with that observed in other cohorts in the study.

Disclosures Santoro: *Roche:* Speakers Bureau; *Abbvie:* Speakers Bureau; *Amgen:* Speakers Bureau; *Celgene (BMS):* Speakers Bureau; *AstraZeneca:* Speakers Bureau; *Eli Lilly:* Speakers Bureau; *Sandoz:* Speakers Bureau; *Novartis:* Speakers Bureau; *Arqule:* Other; *Takeda:* Speakers Bureau; *Merck MSD:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Bayer:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Eisai:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Pfizer:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Gilead:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Servier:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *BMS:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Incyte:* Consultancy; *Sanofi:* Consultancy. **Johnson:** *Gilead:* Consultancy; 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