Phase 2, open-label study of pembrolizumab in children and young adults with newly diagnosed classical hodgkin lymphoma (cHL) with slow early response (SER) to frontline chemotherapy: KEYNOTE-667

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Introduction

Higher risk for relapse is seen in cHL patients (pts) with SER to initial chemotherapy (chemo), and the burden of late organ toxicities may be higher after dose intensification. The phase 2, open-label KEYNOTE-667 (NCT03407144) study evaluates the efficacy and safety of pembrolizumab (pembro) plus chemo in pts with cHL and SER to frontline chemo. The results of an interim safety analysis are presented.

Methods

Eligible pts aged 3-17 (children) or 18-25 years (young adults) with newly-diagnosed, confirmed stage IA, IB, or IIA cHL without bulky disease (Group 1 [low-risk]) or stage IIEB, IIIEA, IIIEB, IIIB, IVA, or IVB cHL (Group 2 [high-risk]) were enrolled to receive induction with doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD; Group 1) or vincristine, etoposide/etoposide phosphate, prednisone/prednisolone, doxorubicin (OEPA; Group 2) for 2 cycles. After induction, pts with rapid early response (RER) received non-study consolidation chemo, and pts with SER received consolidation with pembro plus 2 cycles AVD (Group 1) or 4 cycles cyclophosphamide, vincristine, prednisone/prednisolone, dacarbazine (COPDAC-28; Group 2). Pts received maintenance pembro Q3W, for 17 doses. Pts with SER (Group 1) with CR could stop pembro after 8 doses (including 2 doses after initial CR). Primary endpoint was ORR per Cheson 2007 IWG criteria in pts with SER. An interim safety analysis was performed after 10 pts with SER completed one dose pembro plus chemo (cycle 2, day 1). Adverse events (AEs) were defined by CTCAE criteria (v4.0). All pts

with 2 pembro doses (cycle 1) and all chemo doses (cycle 2, day 1 consolidation) are included. Data cut-off was Jan 18, 2021.

Results

At data cut-off, median (range) follow-up was 7.2 mo (3.7-11.1). 10 pts with SER are included (Group 1 [n=1]; Group 2 [n=9]. Median (range) age was 16y (13-19), 5 had bulky disease, 6 had stage IV disease. No pt had a treatment-related dose delay. All were ongoing on treatment, with median time on treatment of 4.5 mo. Nine pts had an AE, most commonly (in ≥2 pts) diarrhea, pyrexia, alanine aminotransferase increased, and 1 pt had grade ≥3 AEs of anemia, leukopenia, and neutropenia. Treatment-related AEs occurred in 2 pts, most commonly diarrhea. There were no grade ≥3 treatment-related AEs. No pts had an AE leading to dose-reduction, treatment interruption, or discontinuation.

Conclusion

Pembro in combination with AVD or COPDAC 28 has a manageable safety profile in pts with cHL with SER to induction chemotherapy.

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