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POSTER ABSTRACTS

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

Pembrolizumab (pembro) in Children and Young Adults with High-Risk Classical Hodgkin Lymphoma (cHL) with Slow Early Response (SER) to Front-Line Chemotherapy (chemo): Updated Results from the Phase 2 Keynote-667 Study

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Background: cHL is one of the most curable forms of childhood cancer, but patients (pts) who have a SER to initial chemo are at high risk of relapse. The approaches currently used to treat pts with SER, such as dose intensification and radiotherapy (RT), can cause long-term toxicity.An unmet need remains to optimize treatment in pts with cHL and SER while minimizing long-term toxicity. The open-label, phase 2 KEYNOTE-667 study (NCT03407144) is being conducted to evaluate the efficacy and safety of pembro plus chemo in pediatric pts with cHL and SER to front-line chemo. Early analysis of pts in KEYNOTE-667 with high-risk cHL showed that pembro plus cyclophosphamide, vincristine, prednisone/prednisolone, and dacarbazine (COPDAC-28) consolidation had manageable safety and promising antitumor activity, with 66% of pts being spared RT. We present updated results for pts with high-risk cHL and SER.

Methods: Pts eligible for the high-risk group were 3-25 y old and had newly diagnosed stage IIEB, IIIEA, IIIEB, IIIB, IVA, or IVB cHL, measurable disease per investigator assessment, and a Lansky Play-Performance Scale ≥50 (<16 y old) or a Karnofsky score ≥50 (≥16 y old). All pts received 2 cycles of induction therapy with vincristine, etoposide, prednisone/prednisolone, and doxorubicin (OEPA). After induction, response was assessed by PET/MRI/CT (early response assessment). Pts with rapid early response received nonstudy therapy. Pts with SER (Deauville score, 4 or 5) received consolidation with pembro 2 mg/kg up to 200 mg IV Q3W (3-17 y) or 200 mg IV Q3W (18-25 y) plus 4 cycles of COPDAC-28. Response was then assessed by PET/CT/MRI (late response assessment [LRA]). Pts with PET positivity at LRA (Deauville score, 4 or 5) received involved-site RT (28.8 Gy) to late PET-positive residua plus maintenance pembro Q3W for up to 17 cycles; pts with PET negativity received maintenance pembro Q3W for up to 17 cycles without RT. The primary end point was ORR by BICR per Cheson 2007 IWG criteria in pts

with SER, determined at any time after starting pembro and before start of new anticancer therapy. Secondary end points included PET negativity after consolidation, EFS, OS, and safety.

Results: This analysis included 62 pts with high-risk cHL and SER to frontline OEPA. The median time from enrollment to data cutoff (March 1, 2023) was 16.8 mo (range, 2.3-36.4). At the data cutoff, 34 pts (55%) had completed consolidation and maintenance therapy, 23 (37%) were ongoing on treatment, and 5 (8%) had discontinued because of adverse events (AEs; n = 1), progressive disease (n = 2), or withdrawal by pt (n = 2). Median age was 14 y (range, 5-22), 30 pts (48%) were male, 29 (47%) had bulky disease, and 41 (66%) had Ann Arbor stage IV disease. Pts had received a median of 17 administrations of pembro (range, 1-17); the median time on pembro was 11.0 mo (range, <0.1-11.8). Of 62 pts who received consolidation with pembro plus COPDAC-28, 53 (85%) had a LRA (9 are still in consolidation and have not reached the LRA time point), of whom 35 (66%) were PET negative by BICR (37 [70%] PET negative by investigator review). AEs regardless of causality that occurred during consolidation and maintenance were reported in 54 pts (87%), most commonly (≥15%) headache (n = 11; 18%), nausea (n = 11; 18%), cough (n = 10; 16%), COVID-19 (n = 10; 16%), and pyrexia (n = 10; 16%). Grade 3/4 AEs occurred in 21 pts (34%). 13 pts (21%) had a serious AE. No pts died because of AEs. Treatment-related AEs occurred in 38 pts (61%). Grade 3/4 treatment-related AEs occurred in 10 pts (16%). One pt (2%) discontinued treatment because of a treatment-related AE (grade 3 AST increased). Pembro-related AEs occurred in 23 (37%) pts; most commonly (≥5%) hypothyroidism (n = 4; 6%), nausea (n = 3; 5%), and ALT increased (n = 3; 5%). Three pts (5%) experienced grade 3/4 pembro-related AEs. One serious AE was related to pembro (abdominal pain). Six pts (10%) experienced immune-mediated AEs (hypothyroidism, n = 4 [2 grade 1, 2 grade 2]; colitis, n = 1 [grade 2]; pneumonitis, n = 1 [grade 2]).

Conclusion: In this updated analysis, consolidation with pembro plus COPDAC-28 continued to have manageable safety and promising antitumor activity in pediatric pts with high-risk cHL and SER to front-line OEPA. Of pts with a LRA, 66% had a PET-negative response and were spared RT. These findings support the results of prior analyses and suggest that adding pembro to COPDAC-28 consolidation may augment responses in the high-risk cHL population.

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