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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 Low-Risk Classical Hodgkin Lymphoma (cHL) with Slow Early Response (SER) to Front-Line Chemotherapy (chemo): Early Results from the Phase 2 Keynote-667 Study

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Background: Pediatric patients (pts) with low-risk cHL achieve high cure rates with standard chemo. However, those with a SER to front-line chemo are at higher risk of relapse than pts with a rapid early response (RER). Current treatment options are also associated with long-term toxicities such as secondary malignancies, cardiovascular disease, and pulmonary and gonadal toxicity. Novel treatment approaches are needed to optimize outcomes while minimizing long-term toxicity. KEYNOTE-667 (NCT03407144) is an open-label, phase 2 study that included an analysis of safety and efficacy of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) induction in pediatric pts with low-risk cHL followed by consolidation with pembro plus AVD and involved-site radiotherapy (ISRT) and pembro maintenance in those with SER to front-line ABVD. We present an interim analysis of pts with low-risk cHL enrolled in this trial.

Methods: Eligible pts were 3-25 y old and had newly diagnosed stage IA, IB, or IIA cHL without bulky disease, measurable disease per investigator assessment, and a Lansky Play-Performance Scale ≥50 (aged <16 y) or a Karnofsky score of ≥50 (aged ≥16 y). Pts initially received 2 cycles of induction with ABVD. Response was then assessed by PET/MRI/CT (early response assessment). Pts with RER received nonstudy therapy per treating physician. Pts with SER (Deauville score [DS], 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) in combination with 2 cycles of AVD followed by a late response assessment (LRA) with PET/MRI/CT. All pts with a SER then received ISRT (21.6 Gy for pts with a complete PET response [DS, 1-3]; 30.6-36 Gy for pts with a partial PET response [DS, 4 or 5]) plus maintenance pembro Q3W for up to 17 cycles. Primary end point was ORR by blinded independent central review (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 rate of PET negativity after consolidation, EFS, OS, and safety.

Results: 73 pts with low-risk cHL were enrolled, 9 of whom had SER to ABVD induction. 64 pts had a RER and received nonstudy treatment. At data cutoff (March 1, 2023), 2 of 9 pts (22%) with SER had completed consolidation and maintenance therapy, 5 (56%) were ongoing, and 2 (22%) had discontinued, both because of complete response. Median time from enrollment to data cutoff was 8.7 mo (range, 2.2-32.9). Median age was 16 y (range, 7-20), 5 pts (56%) were male, 2 (22%) had Ann Arbor stage I disease, and 7 (78%) had Ann Arbor stage II disease. Pts with SER had received a median of 8 doses of pembro (range, 1-17); median time on pembro was 4.8 mo (range, <0.1-11.3). Of 9 pts who received consolidation therapy with pembro plus AVD, 6 (67%) had a LRA (3 are still in consolidation and have not reached the LRA timepoint), of whom 3 (50%) were PET negative by BICR (2 [33%] were PET negative by investigator review). Of 73 pts who received ABVD induction, 66 (90%) had an AE regardless of causality. 33 pts (45%) experienced grade 3/4 AEs, most commonly (≥10%) neutrophil count decreased (n = 19; 26%) and neutropenia (n = 9; 12.3%). One pt experienced grade 4 febrile neutropenia. Twelve pts (16%) had serious AEs. No pts discontinued treatment or died because of AEs. Treatment-related AEs due to ABVD induction occurred in 59 pts (81%), with grade 3/4 events in 31 (42%). Of the 9 pts with SER to ABVD induction who received consolidation and maintenance therapy, 7 (78%) experienced an AE regardless of causality. Two pts (22%) had grade 3/4 AEs. No serious AEs were reported during consolidation and maintenance therapy, and no pts discontinued treatment or died because of AEs. Treatment-related AEs occurred in 6 pts (67%) who received consolidation and maintenance therapy; with grade 3/4 events in 2 pts (22%). Six pts (67%) experienced AEs related to pembro; most commonly (≥3 pts) anemia, nausea, vomiting (n = 3 each [33%]). Two pts experienced grade 3/4 AEs related to pembro (vomiting, white blood cell count decreased). One pt (11%) experienced an immune-mediated AE (grade 2 hyperthyroidism).

Conclusion: Early results from the low-risk cHL cohort of KEYNOTE-667 suggest that induction therapy with ABVD and consolidation with pembro plus AVD had a manageable safety profile. Among the relatively small number of pts with a SER to ABVD, 50% with a LRA had a PET-negative response by BICR and received a reduced dose of RT.

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