HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

S215 KEYNOTE-667: OPEN-LABEL, PHASE 2 STUDY OF PEMBROLIZUMAB IN CHILDREN AND YOUNG ADULTS WITH NEWLY DIAGNOSED CLASSICAL HODGKIN LYMPHOMA (CHL) WITH SLOW EARLY RESPONSE TO FRONT-LINE CHEMOTHERAPY

Topic: Hodgkin Lymphoma - Clinical

Luciana Vinti*[1], Stephen Daw[2], Constantino Sabado Alvarez[3], Franca Fagioli[4], Auke Beishuizen[5], Gerard Michel[6], Maria Luisa Moleti[7], Michaela Cepelova[8], Anne Thorwarth[9], Charlotte Rigaud[10], Diego Plaza Lopez De Sabando[11], Judith Landman-Parker[12], Juan Shen[13], Pallavi Pillai[13], Patricia Marinello[13], Christine Mauz-Koerholz[14]

[1]Irccs Ospedale Pediatrico Bambino Gesu, Rome, Italy; [2]University College London Hospitals Nhs Foundation Trust, London, United Kingdom; [3]Hospital Universitari Vall D Hebron, Barcelona, Spain; [4]Regina Margherita Childrens Hospital And University Of Turin, Turin, Italy; [5]Princess Máxima Centrum, Utrecht, Netherlands; [6]Chu De Marseille Hopital De La Timone Enfants, Marseille, France; [7]Universita Degli Studi Di Roma La Sapienza, Rome, Italy; [8]University Hospital Motol, Prague, Czech Republic; [9]Charite-Universitaetsmedizin Berlin Campus Virchow-Klinikum, Berlin, Germany; [10]Gustave Roussy Cancer Campus, Villejuif, France; [11]Hospital Universitario La Paz, Madrid, Spain; [12]Hopital D'Enfants Armand Trousseau, Sorbonne University, Paris, France; [13]Merck & Co., Inc., Rahway, United States; [14]Justus-Liebig University Of Giessen, Giessen, Germany, And Medical Faculty Of The Martin-Luther-University Of Halle-Wittenberg, Halle, Germany

Background:

cHL is one of the most curable forms of childhood cancer, with 5-year survival rates exceeding 95%. However, patients (pts) who have a slow early response (SER) to initial chemotherapy (chemo) are at higher risk of relapse, and the approaches currently used to treat these pts, including chemo dose intensification and radiotherapy (RT), can result in significant long-term toxicity. An unmet need remains for novel therapeutic approaches that optimize outcomes in pts with SER while minimizing long-term toxicity. KEYNOTE-667 (NCT03407144) is an open-label, phase 2 study that is being conducted to evaluate the efficacy and safety of pembrolizumab (pembro) plus chemo in pts with cHL and SER to front-line chemo.

Aims:

To present results of an interim analysis of KEYNOTE-667 in pts with high-risk cHL (group 2) and SER.

Methods:

Eligible pts 3-17 old (children) or 18-25 y old (young adults) with newly diagnosed stage IIEB, IIIEA, IIIEB, IIIB, IVA, or IVB cHL received induction with vincristine, etoposide, prednisone/prednisolone, and doxorubicin (OEPA) for 2 cycles. After induction, (early) response was assessed by PET/MRI/CT. 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 a maximum of 200 mg IV Q3W (3-17 y old) or 200 mg IV Q3W (18-25 y old) plus 4 cycles of cyclophosphamide, vincristine, prednisone/prednisolone, dacarbazine (COPDAC-28). Pts with PET positivity (Deauville score, 4 or 5) after consolidation (late response assessment [LRA]) received involved-site RT (28.8 Gy) to late PET-positive residua while continuing pembro; pts with PET negativity continued pembro without RT. All pts with SER received maintenance pembro Q3W for up to 17 cycles. The primary end point was ORR by blinded independent central review (BICR) per Cheson 2007 International Working Group criteria in pts with SER. The rate of PET negativity after consolidation and safety were secondary end points.

Results:

49 pts with high-risk cHL with SER were included. Median follow-up at the data cutoff (Sept 2, 2022) was 15.3 mo

Abstract Book Citations: Authors, Title, HemaSphere, 2023;7(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.

(range, 3.2-30.5). Median age was 15 y (range, 6-22), 23 pts (47%) were male, 24 (49%) had bulky disease, and 31 (63%) had Ann Arbor stage IV disease. Of 49 pts, 22 (45%) had completed treatment, 24 (49%) were ongoing on consolidation or maintenance, and 3 (6.1%) had discontinued. Pts had received a median of 16 administrations (range, 2-17) of pembro; median time on pembro was 10.4 mo (range, 0.5-11.8). 42 pts (86%) had a LRA, of whom 27 (64%) were PET negative by BICR (30 [71%] PET negative by investigator review). 42 pts (86%) experienced adverse events (AEs), most commonly (≥15%) nausea (n = 10 [20%]), COVID-19 (n = 8 [16%]), and headache (n = 8 [16%]). Grade 3/4 AEs occurred in 13 pts (27%). 7 pts (14%) had a serious AE. 1 pt (2.0%) discontinued treatment because of an AE that was not considered treatment related (COVID-19). No pts died because of an AE. Treatment-related AEs occurred in 30 pts (61%), with 6 (12%) experiencing grade 3/4 treatment-related AEs. 4 pts (8%) experienced immune-mediated AEs (grade 1 hypothyroidism, n = 2; grade 2 hypothyroidism, n = 2).

Summary/Conclusion:

Pembro plus COPDAC-28 consolidation therapy had manageable safety and promising antitumor activity in pediatric pts with high-risk cHL with SER to front-line OEPA. 64% of pts with a LRA had a PET-negative response and were spared RT. These findings suggest adding pembro to COPDAC-28 consolidation may augment responses in this high-risk cHL population.

Copyright Information: (Online) ISSN: 2572-9241

Abstract Book Citations: Authors, Title, HemaSphere, 2023;7(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.