(PS2021) PHARMACOKINETICS, EFFICACY, AND SAFETY OF SUBCUTANEOUS PEMBROLIZUMAB IN RELAPSED OR REFRACTORY CLASSIC HODGKIN LYMPHOMA (CHL) OR PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA (PMBCL): A PHASE 2 STUDY

Topic: 17. Hodgkin lymphoma - Clinical

Alejandro Berkovits*[1], Muhit Ozcan[2], Gabriel Barragan Ibanez[3], Ewa Paszkiewicz-Kozik[4], Wojciech Jurczak[5], Mauricio Chandía[6], Sergio Portino[7], Elifcan Aladag[8], Sebastian Giebel[9], Anna Sureda[10], Tae Min Kim[11], Brenda Garcia[12], Norma Gutierrez Gutierrez[13], Sebastian Hidalgo[14], Kirit Ardeshna[15], Antonia Rodriguez Izquierdo[16], Bastian von Tresckow[17, 18], Gina Song[19], Jessica Flynn[19], Katherine Ryland[19], Rushdia Yusuf[19], Elizabeth H. Phillips[20]

[1]Immunocel Chile, Providencia, Chile; [2]Ankara University, School of Medicine, Ankara, Türkiye; [3]Centro de Investigación Clínica de Oaxaca (CICLO), Oaxaca, Mexico; [4]Maria-Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [5]Maria-Skłodowska-Curie National Research Institute of Oncology, Krakow, Poland; [6]Biocenter, Concepción, Chile; [7]Bradford Hill Clinical Research Center and Finis Terrae University, Faculty of Medicine, Santiago, Chile; [8]Hacettepe University Faculty of Medicine, Ankara, Türkiye; [9]Maria Skłodowska-Curie National Research Institute of Oncology, Gliwice, Poland; [10]Institut Català d'Oncologia - L'Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain; [11]Seoul National University Hospital, Seoul, South Korea; [12]Health Pharma Professional Research, Mexico City, Mexico; [13]Hospital Universitario de Salamanca, IBSAL, Centro de Investigación del Cáncer, Salamanca, Spain; [14]Fundación Arturo López Pérez (FALP), Santiago, Chile; [15]University College London Hospitals NHS Foundation Trust, London, United Kingdom; [16]Hospital Universitario 12 de Octubre, Madrid, Spain; [17]German Hodgkin Study Group, University of Cologne, Cologne, Germany; [18]West German Cancer Center and German Cancer Consortium (DKTK partner site Essen), University Hospital Essen, University of Duisburg-Essen, Essen, Germany; [19]Merck & Co., Inc., Rahway, United States of America; [20]Division of Cancer Sciences, University of Manchester and The Christie NHS Foundation Trust, Manchester, United Kingdom;

Background

Pembrolizumab is a well-established intravenous PD-1 inhibitor for relapsed or refractory (R/R) cHL and PMBCL, administered Q3W or Q6W. MK-3475A is pembrolizumab with berahyaluronidase alfa (MK-5180) for subcutaneous administration (subcutaneous pembrolizumab). Berahyaluronidase alfa, a human hyaluronidase variant developed and manufactured by Alteogen Inc., is a permeation enhancer that enables subcutaneous administration of pembrolizumab. Subcutaneous pembrolizumab is approved globally (outside of the US) for the treatment of cHL and PMBCL.

Aims

To present pharmacokinetics (PK), efficacy, and safety from a single-arm, open-label, phase 2 study (NCT06504394) evaluating subcutaneous pembrolizumab in participants with R/R cHL or R/R PMBCL.

Methods

Eligible participants were ≥18 years with histologically confirmed, FDG-avid cHL or PMBCL per WHO criteria, radiographically measurable disease, and an ECOG PS of 0 or 1. Participants with cHL or PMBCL were anti–PD-1 naive and had disease that was refractory to, did not achieve CR with, or had relapsed after prior therapy. Participants with cHL had received ≥1 multiagent regimen, and participants with PMBCL had received ≥2 prior therapies (including ≥1 rituximab-based regimen). All participants were ineligible for or had relapsed after autologous stem cell transplant. Participants received subcutaneous pembrolizumab 790 mg Q6W for ≤18 cycles (~2 years) or until disease progression or other discontinuation criteria were met. Primary end points were PK exposure measures during cycle 1 (C1) and ORR per Lugano criteria by investigator. Intensive PK samples were collected during C1, and noncompartmental analysis methods were used to determine PK end points based on observed data. Secondary end points included safety. Data cutoff date was June 10, 2025.

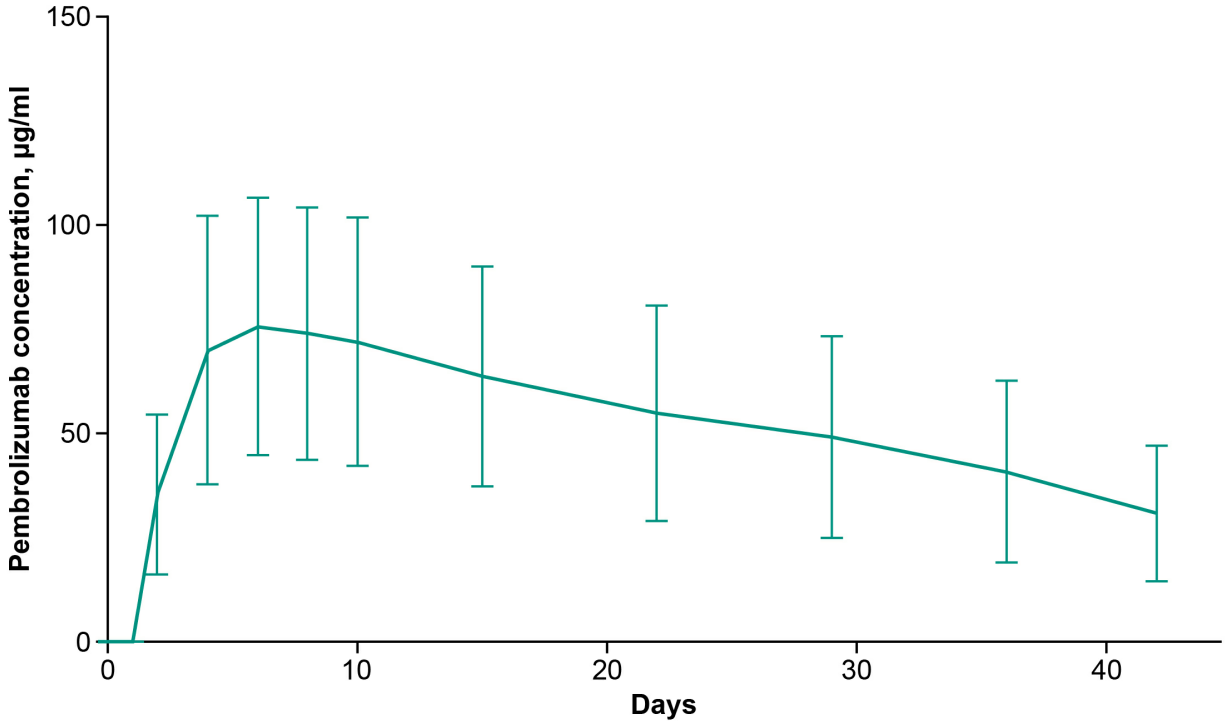
Results

At the time of this analysis, 53 participants had been enrolled and received ≥1 cycle of subcutaneous pembrolizumab (n=51, cHL; n=2, PMBCL); enrollment was ongoing. Median follow-up was 2.6 months (range, 0.0-7.4). Geometric mean (GM) of C1 overall pembrolizumab exposure of the area under the concentration-time curve from time 0 to 6 weeks ($AUC_{0\text{-}6}$; n=21) was 1716 mcg*day/mL, and variability was 47%. GM of C1 maximum concentration (C_{max}; n=47) was 75.06 mcg/mL with variability of 48%, and GM of C1 trough concentration (C_{trough}; n=25) at the end of dosing interval was 25.17 mcg/mL with variability of 62%. All participants who were efficacy evaluable (baseline and postbaseline assessment available) had cHL (n=21); the ORR was 71.4% (95% CI, 47.8-88.7), with 7 participants (33%) achieving a CR and 8 (38%) a PR. In all participants, treatment-related AEs (TRAEs) of any grade occurred in 27 participants (51%), most commonly (incidence ≥5%) pruritus (9%), rash (8%), arthralgia (6%), hypothyroidism (6%), and myalgia (6%). Grade 3 or 4 TRAEs occurred in 5 participants (9%). No participants discontinued or died due to TRAEs. Immune-mediated AEs and infusion reactions occurred in 5 participants (9%), with grade 3 or 4 events reported for 2 participants (4%).

Summary/Conclusion

The PK profile of subcutaneous pembrolizumab in participants with hematologic tumors was similar to that in solid tumors and was consistent with the typical PK profile for subcutaneous monoclonal antibodies (Figure). Subcutaneous pembrolizumab at a dose of 790 mg Q6W showed a manageable safety profile and efficacy consistent with intravenous pembrolizumab.

Mean Pharmacokinetic Profile for Subcutaneous Pembrolizumab 790 mg Q6W in Cycle 1.



Error bars represent the standard deviation of concentration.