Abstract Submission

14. Myeloma and other monoclonal gammopathies - Clinical
EHA-2702

HORIZON (OP-106): UPDATED EFFICACY AND SAFETY OF MELFLUFEN IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) REFRACTORY TO DARATUMUMAB (DARA) AND/OR POMALIDOMIDE (POM)

Paul G. Richardson1, Albert Oriol2, Alessandra Larocca3, Paula Rodriguez Otero4, Maxim Norkin5, Joan Bladé6, Michele Cavo7, Hani Hassoun8, Xavier Leleu9, Adrián Alegre10, Christopher Maisel11, Agne Paner12, Amitabha Mazumder13, Jeffrey A. Zonder14, Noemi Puig15, John Harran1, Johan Haramberg16, Sara Thuresson16, Hanan Zubair16, Maria-Victoria Mateos16

1Dana-Farber Cancer Institute, Harvard Medical School, Boston, United States, 2Hospital Germans Trias i Pujol, Badalona, Spain, 3A.O.U. Città della Salute e della Scienza di Torino - S.C. Ematologia U. Torino, Italy, 4Clinica Universidad de Navarra, Pamplona, Spain, 5University of Florida Health Cancer Center, Gainesville, United States, 6Hospital Clinica de Barcelona - Servicio de Onco-Hematologia, Barcelona, Spain, 7Policlinico S. Orsola Malpighi, Bologna, Italy, 8Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, United States, 9CHU de Poitiers, Poitiers, France, 10Hospital Universitario La Princesa, Madrid, Spain, 11Baylor Scott & White Charles A. Sammons Cancer Center, Dallas, 12Rush University Medical Center, Chicago, 13The Oncology Institute of Hope and Innovation, Glendale, 14Karmanos Cancer Institute, Detroit, United States, 15Hospital Clinico Universitario de Salamanca, Salamanca, Spain, 16Oncopeptides AB, Stockholm, Sweden

Does the study abide by applicable national and international regulations and guidelines, including but not limited to ethical committees, data protection and privacy regulations, informed consent and off-label use of drugs?: Yes

Background: Despite recent advances in MM therapy, the disease remains incurable. Patients (pts) with late-stage RRMM refractory to pom and/or dara have limited effective treatment options. Melflufen is a novel peptide-conjugated alkylator potentiated by intracellular aminopeptidases, which are markedly overexpressed in MM. In a previous data cut for the phase 2 HORIZON study, melflufen + dexamethasone (dex) showed encouraging efficacy in pts with RRMM exposed to IMiDs and proteasome inhibitors (PIs) and refractory to dara and/or pom (overall response rate [ORR], 33%; clinical benefit rate [CBR], 39%) and was well tolerated (Richardson, et al. ASH 2018; Oral 600).

Aims: To present the updated efficacy and safety of melflufen + low-dose dex in pts refractory to pom and/or dara (HORIZON, NCT02963493).

Methods: Pts with RRMM must have received ≥2 prior lines and have been exposed to IMiDs and PIs and refractory to pom and/or dara. Pts receive 40 mg melflufen intravenously on d 1 of each 28-d cycle + 40 mg weekly dex (20 mg for pts aged ≥75 y). The primary endpoint is ORR (≥ partial response [PR]; investigator assessed per International Myeloma Working Group criteria). Secondary endpoints include safety, CBR (≥ minimal response), progression-free survival (PFS), overall survival (OS), and duration of response (DOR). Pts are treated until progressive disease (PD) or unacceptable toxicity.

Results: As of 6 Feb 2019, 95 pts were treated. Median age was 63 y (35-86); median time since diagnosis was 6.3 y (0.7-24.6); 39% of pts were International Staging System stage 3; 61% of the pts with available cytogenetic data (n=66) had high-risk cytogenetics at study entry. Median no. of prior lines was 5 (2-13). All pts were pom or dara refractory and received prior PIs and IMiDs. In total, 91% were refractory to pom, 73% to dara and 63% to both pom and dara; 87% were refractory to a PI, 97% to an IMiD, 86% to a PI and an IMiD (double refractory). In addition, 65% were double + anti-CD38 + last-line refractory (triple class + last-line); 82% had received prior alkylator therapy (57% alkylator refractory), and 69% had ≥1 prior autologous transplant. A median of 3 cycles (range, 1-17) of melflufen were administered. Treatment was ongoing in 22% of pts and discontinued in 57% of pts due to PD, 14% due to adverse events (AEs), and 7% for other reasons. Treatment-related grade 3/4 AEs were reported in 68 pts (72%), most commonly (>20%) neutropenia (55%), thrombocytopenia (52%), and anemia (26%). The most common treatment-related nonhematologic grade 3/4 AE was pneumonia (3%). AEs outside of infections and infestations and the blood and lymphatic system were infrequent, with grade 3/4 treatment-related AEs occurring in 9 pts (9%). Sixteen pts (17%) experienced treatment-related serious AEs. No treatment-related deaths were reported. In total, 90 pts had available response data. ORR was 30%; 1 pt achieved stringent complete response (sCR), 11% very good PR (VGPR), and 18% PR. CBR was 40%. Median PFS for all pts treated (N=95) was 4 mo (95% CI, 3.3-4.7), median OS was 10 mo (95% CI, 8.1-not reached [NR]), and median DOR (n=27) was 4.8 mo (95% CI, 3.6-NR).

Summary/Conclusion: Melflufen continues to have promising activity in pts with late-stage RRMM refractory to dara and/or pom and was generally well tolerated, with infrequent nonhematologic AEs and low rates of discontinuation due to AEs.
Keywords: Clinical trial, Imids, Multiple myeloma, Phase II