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)

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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