Abstract Submission

14. Myeloma and other monoclonal gammopathies - Clinical

EHA-2692

ANCHOR (OP-104): A PHASE 1 STUDY UPDATE OF MELFLUFEN AND DEXAMETHASONE PLUS BORTEZOMIB OR DARATUMUMAB IN RELAPSED/REFRACTORY MULTIPLE MYELOMA PATIENTS REFRACTORY TO AN IMID OR A PROTEASOME INHIBITOR

Ludek Pour1, Yvonne A. Efebera2, Miquel Granell3, Roman Hajek4, Albert Oriol5, Jacques Delaunay6, Katell Le Du7, Jean-Richard Eveillard8, Lionel Karlin9, Vladmir Maisnar10, Joaquin Martinez-Lopez11, Maria-Victoria Mateos12, Maxim Norkin13, Vincent Ribrag14, Paul G. Richardson15, Jan Straub16, Catriona Byrne17, Christian Jacques17, Malin Sydvardner17, Enrique Ocio18

1Fakultní nemocnice Brno, Brno, Czech Republic, 2Division of Hematology, The Ohio State University, Columbus, United States, 3Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, 4Department of Hemato- oncology, University Hospital Ostrava, Ostrava, Czech Republic, 5Hospital Germans Trias i Pujol, Badalona, Spain, 6Hôpital privé du Confluent, Nantes, 7Department of Hematology, Centre Jean Bernard - Clinique Victor Hugo, Le Mans, 8Hôpital Morvan, Brest, 9Department of Hematology, Centre Hospitalier Lyon-Sud, University Claude Bernard Lyon 1, Pierre-Benite, France, 10Fourth Department of Medicine - Hematology, FN and LF UK Hradec Králové, Hradec Králové, Czech Republic, 11Hospital Universitario 12 de Octubre, Madrid, 12Hospital Clinico Universitario de Salamanca, Salamanca, Spain, 13University of Florida Health Cancer Center, Gainesville, United States, 14DITEP, Gustave Roussy, Université Paris-Saclay, Villejuif, France, 15Dana-Farber Cancer Institute, Harvard Medical School, Boston, United States, 16Všeobecná fakultní nemocnice, Prague, Czech Republic, 17Oncopeptides AB, Stockholm, Sweden, 18Hospital Universitario Marques de Valdecilla, Santander, Spain

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 therapy, multiple myeloma (MM) remains incurable, showing the need for novel therapies. Melflufen is a novel peptide-conjugated alkylator potentiated by intracellular aminopeptidases, which are markedly overexpressed in MM. In the phase 1/2 study O-12-M1, melflufen + dexamethasone (dex) had promising activity in relapsed/refractory MM (RRMM; overall response rate [ORR], 31%; median overall survival, 20.7 mo), with acceptable safety (Richardson et al. Blood. 2017). Melflufen is now being explored in triplet regimens.

Aims: To assess the safety and efficacy of melflufen + dex in a triplet regimen with bortezomib (BTZ) or daratumumab (dara) in patients (pts) with RRMM (ANCHOR, NCT03481556).

Methods: Pts must have RRMM and be refractory (or intolerant) to an IMiD and/or proteasome inhibitor (PI) with 1-4 prior lines of therapy. Pts who receive BTZ or dara cannot be refractory to a PI or have had prior anti-CD38 therapy, respectively. Melflufen (30, 40 or 20 mg intravenously [IV]) is administered on d 1 of each 28-d cycle in 1 of 2 regimens selected based on prior therapy and investigator choice. Regimen A: BTZ 1.3 mg/m² subcutaneous + dex 20 mg on d 1, 4, 8 and 11 and dex 40 mg on d 15 and 22. Regimen B: dara 16 mg/kg IV qw (8 doses), every 2 w (8 doses), then every 4 w + dex 40 mg qw. Pts are treated until disease progression (PD)/unacceptable toxicity. The phase 1 primary objective is to determine the optimal melflufen dose in the combination.

Results: As of 6 Feb 2019, 15 pts were treated: 5 in the BTZ combination with melflufen 30 mg (n=3) or 40 mg (n=2) and 10 in the dara combination with melflufen 30 mg (n= 4) or 40 mg (n= 6). Regimen A (BTZ combination): Median age was 70 yr (63-82). Median no. of prior lines was 2 (2-4); 2 pts were refractory to last therapy. Median time since diagnosis was 5.8 yr (1.2-7.4). No dose-limiting toxicities (DLTs) were observed in the melflufen 30 mg cohort. The 40 mg cohort is recruiting. After 27 cycles, 3 pts (60%) experienced grade 3/4 treatment-related adverse events (TRAEs), most commonly thrombocytopenia (60%) and neutropenia (40%). One pt experienced treatment-related serious AEs (TRSAEs; grade 3 neutropenia and grade 3 pneumonia). All pts were ongoing on treatment. ORR was 100% for the melflufen 30 mg cohort (median 9 cycles [6-9]) and 0% for the 40 mg cohort (median, 1.5 cycles [1-2]).

Regimen B (dara combination): Median age was 63 yr (35-78). Median no. of prior lines was 2.5 (1-3); 6 pts were refractory to last therapy. Median time since diagnosis was 5.0 yr (1.9-8.2). No DLTs were observed in the melflufen 30 mg and 40 mg cohorts. After 59 cycles, 6 pts experienced grade 3/4 TRAEs, most commonly neutropenia (40%) and thrombocytopenia (30%). No pts experienced TRSAEs. Nine pts were ongoing on treatment; 1 pt discontinued after 2 cycles due to PD (best response, stable disease). ORR was
100% for the melflufen 30 mg cohort (median, 8 cycles [6-10]) and 50% for the 40 mg cohort (median, 3 cycles [2-8]). The non-responders (n=3) completed a median of 2 cycles. Phase 2 was initiated with melflufen 40 mg.

**Summary/Conclusion:** Melflufen + dex is feasible as a triplet regimen with BTZ or dara, with promising tolerability and efficacy in pts with RRMM. All pts were ongoing except 1 (dara combination). The longest treatment duration was 10 and 9 cycles for the combination with dara and BTZ, respectively; ORR in pts with ≥ 2 cycles was 78% and 100%, respectively. The study is actively recruiting. Phase 2 has been initiated for the dara combination with melflufen 40 mg.

**Keywords:** Bortezomib, Clinical trial, Multiple myeloma, Phase I