



Check for updates

Blood 142 (2023) 2018-2021

## The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

## **653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS**

## Long-Term Outcomes from the Phase 3 OCEAN (OP-103) Study: Melflufen and Dexamethasone (Dex) Versus Pomalidomide (Pom) and Dex in Relapsed Refractory Multiple Myeloma (RRMM)

Fredrik Schiesvold, MDPhD<sup>1</sup>, Meletios A. Dimopoulos, MD PhD<sup>2</sup>, Sosana Delimpasi<sup>3</sup>, Pawel Robak<sup>4</sup>, Daniel Coriu, PhD<sup>5</sup>, Wojciech Maciej Legiec, MD<sup>6</sup>, Ludek Pour, MD<sup>7</sup>, Ivan Spicka<sup>8</sup>, Tamas Masszi<sup>9</sup>, Vadim Anatolievich Doronin, MD<sup>10</sup>, Jiri Minarik, MD PhD<sup>11</sup>, Galina Salogub <sup>12,13</sup>, Yulia Alexeeva <sup>14,15</sup>, Antonio Lazzaro <sup>16</sup>, Vladimir Maisnar <sup>17</sup>, Gabor Mikala, MDPhD<sup>18</sup>, Stefan Norin, MDPhD<sup>19</sup>, Marcus Thuresson<sup>20</sup>, Anna Bergan<sup>19</sup>, Jakob Obermüller<sup>19</sup>, Roman Hajek, MD<sup>21</sup>, Maria-Victoria Mateos<sup>22</sup>, Paul G. Richardson, MD<sup>23</sup>, Pieter Sonneveld, MD PhD<sup>24</sup>

- <sup>1</sup> KG Jebsen Center for B Cell Malignancies, University of Oslo, Oslo, Norway
- <sup>2</sup>Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece
- <sup>3</sup>General Hospital Evangelismos, Athens, Greece
- <sup>4</sup>Medical University of Lodz, Lodz, Poland
- <sup>5</sup>Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
- <sup>6</sup>St. John of Dukla Oncology Center of Lublin Land, Department of Hematology and Bone Marrow Transplantation, Lublin,
- <sup>7</sup> Department of Internal Medicine, University Hospital Brno, Brno, Czech Republic
- <sup>8</sup>Charles University Hospital Kralovske Vinohrady, Prague, Czech Republic
- <sup>9</sup> Department of Internal Medicine and Hematology, Semmelweis University, Budapest, Hungary
- <sup>10</sup>Department, State Budget Healthcare Institution of Moscow, City Clinical Hospital #40 of Moscow Healthcare Department, Moscow, Russian Federation
- <sup>11</sup> Department of Hemato-Oncology, Faculty of Medicine and Dentistry, Palacky University and University Hospital Olomouc, Olumouc, Czech Republic
- <sup>12</sup>V.A. Almazov National Medical Research Centre, St. Petersburg, Russian Federation
- <sup>13</sup>V.A. Almazov Chemotherapy of Oncohematology Diseases and Bone Marrow Transplantation Department #2, St. Petersburg, Russian Federation
- <sup>14</sup>V.A. Almazov National Medical Research Centre, Saint Petersburg, RUS
- <sup>15</sup>V.A. Almazov Chemotherapy of Oncohematology Diseases and Bone Marrow Transplantation Department #1, St. Petersburg, Russian Federation
- <sup>16</sup>Division of Hematology and Bone Marrow Transplant Center, Hospital Guglielmo da Saliceto, PIACENZA PC, ITA
- <sup>17</sup>4th Department of Medicine Haematology, Charles University Hospital, Hradec Králové, CZE
- <sup>18</sup>South-Pest Central Hospital, National Institute for Hematology and Infectious Diseases, Budapest, Hungary
- <sup>19</sup>Oncopeptides AB, Stockholm, SWE
- <sup>20</sup>Oncopeptides AB, Stockholm, Sweden
- <sup>21</sup>Department of Hematooncology, University Hospital Ostrava, Ostrava, Czech Republic
- <sup>22</sup> Institute of Cancer Molecular and Cellular Biology, University Hospital of Salamanca, Salamanca, Spain
- <sup>23</sup>Dana-Farber Cancer Institute, Boston, MA
- <sup>24</sup>Department of Hematology, Erasmus MC Cancer Institute, Rotterdam, Netherlands

Background/Introduction: Melphalan flufenamide (melflufen) is a first-in-class peptide-drug conjugate that targets aminopeptidases resulting in rapid release of alkylating agents inside tumor cells. Based on the phase 2 HORIZON study and supported by the phase 3, randomized, controlled OCEAN study, melflufen was approved in Europe for use in patients (pts) with triple-class refractory RRMM with >3 prior lines of therapy (LoTs) and without prior autologous stem cell transplantation (ASCT) or with a time to progression (TTP) > 36 mo after prior ASCT. In the OCEAN study (NCT03151811), melflufen + dex showed superior progression-free survival (PFS) compared with pom + dex (6.8 vs 4.9 mo; hazard ratio [HR]: 0.79; P=0.032); PFS benefit in the melflufen + dex group was mainly driven by pts who had not received prior ASCT. Overall survival (OS) trended in favor of melflufen + dex in pts without prior ASCT and favored pom + dex in pts with prior ASCT (Schjesvold et al.

**POSTER ABSTRACTS** Session 653

Lancet Haematol. 2022;9:e98). Post-hoc analyses of OCEAN and HORIZON demonstrated that a TTP < 36 mo after prior ASCT was a negative prognostic factor for OS with melflufen + dex (Sonneveld et al. Clin Lymphoma Myeloma Leuk. 2023;S2152). Here, we present long-term OS and safety data from the final analysis of the OCEAN study.

Methods: Pts with RRMM (2-4 prior LoTs including lenalidomide [len] and a proteasome inhibitor) refractory to len and last LoT were randomized 1:1 (stratified by age, no. of prior LoTs, and International Staging System score) to receive 28-day (d) cycles of melflufen 40 mg intravenously on d1 or pom 4 mg orally (PO) daily on d1 to 21. All pts received dex 40 mg (20 mg for pts ≥75 y) PO on d1, 8, 15, and 22. Pts received therapy until disease progression or unacceptable toxicity. The primary endpoint was PFS, as assessed by independent review committee per IMWG Uniform Response Criteria, and key secondary endpoints were overall response rate, OS, and safety.

Results: As of 3 Feb 2023, 495 pts were randomized (246 to melflufen; 249 to pom); median age was 68 y (range, 39-91) and median prior LoTs was 3. In the intent-to-treat (ITT) melflufen and pom populations, median OS was 20.2 mo vs 24.0 mo (HR, 1.09 [95% CI, 0.88-1.35]), at a median follow-up of 40.3 mo and 38.1 mo, respectively. In the target subgroup of the melflufen and pom groups (pts without a prior ASCT or TTP > 36 mo after an ASCT), median OS was 23.6 mo vs 19.1 mo (HR, 0.88 [95% CI, 0.67-1.16]); in the non-target population (pts with TTP <36 mo after ASCT), median OS was 15.7 mo vs 27.5 mo (HR, 1.60 [95% CI, 1.15-2.21]), respectively.

While any grade hematologic toxicities were more common with melflufen, the occurrence of non-hematologic toxicities was similar in the 2 groups. Grade 3/4 (G3/4) treatment-emergent adverse events (TEAEs) in the safety population (melflufen [n=228] and pom [n=246]) occurred in 90% vs 76% of pts, respectively; most commonly thrombocytopenia (78% vs 13%; occurring with G3/4 hemorrhage in 1% vs 0%), neutropenia (64% vs 50%; occurring with G3/4 infections in 4% vs 7%), anemia (43% vs 19%), and infection and infestations (14% vs 24%). Serious AEs occurred in 43% vs 50% of pts (including pneumonia [6% vs 9%], COVID-19 pneumonia [5% vs 6%], and anemia [4% vs 2%]), and fatal AEs in 14% vs 15% (including COVID-19 pneumonia [4% vs 2%] and pneumonia [2% vs 2%]) in the melflufen and pom groups, respectively. With melflufen and pom, TEAEs led to dose reductions in 52% vs 28% of pts (most frequently thrombocytopenia [32% vs 2%] and neutropenia [12% vs 8%]), and discontinuations in 30% vs 24% of pts, respectively. Deaths occurred in 74% vs 68% of pts in the melflufen and pom groups, with AEs being the primary cause of death <30 d after last dose in 8% and 11%, respectively.

Conclusion: Long-term results were consistent with those of previous analyses (Schjesvold, et al. Lancet Haematol. 2022;9:e98e110). While OS trended in favor of pom in the ITT population, OS outcomes continued to be more favorable with melflufen in pts with no prior ASCT or with TTP > 36 mo after ASCT. No new safety signals were reported, and AEs were manageable with dose modifications, consistent with previous reports. This long-term follow-up of OCEAN confirms the favorable safety and OS outcomes of melflufen + dex in the target population and supports its continued use as an alternative treatment choice for pts with RRMM who have received ≥2 prior LoT and who have not received ASCT.

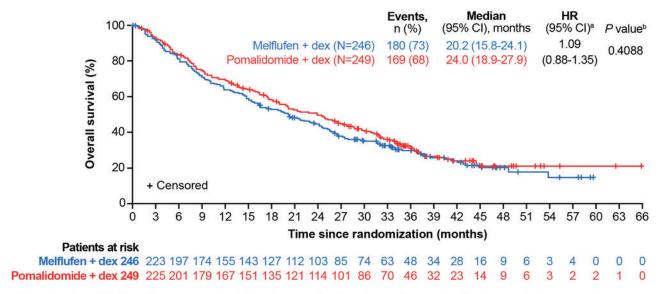
Disclosures Schjesvold: Targovax: Research Funding; Celgene: Consultancy, Other: Honoraria for lectures and educational material, Research Funding; Oncopeptides: Consultancy, Other: Honoraria for lectures and educational material, Research Funding; Pfizer: Other: Honoraria for lectures and educational material; Skylite DX: Other: Honoraria for lectures and educational material; Janssen-Cilag: Consultancy, Other: Honoraria for lectures and educational material, Research Funding; Novartis: Other: Honoraria for lectures and educational material; Amgen: Other: Honoraria for lectures and educational material; Abbvie: Consultancy, Other: Honoraria for lectures and educational material; GlaxoSmithKline: Consultancy, Honoraria, Research Funding; Takeda: Consultancy, Other: Honoraria for lectures and educational material; Sanofi: Consultancy, Other: Honoraria for lectures and educational material, Research Funding; Bristol Myers Squibb: Consultancy, Other: Honoraria for lectures and educational material; Daiichi Sankyo: Other: Honoraria for lectures and educational material; Schain: Other: Honoraria oraria for lectures and educational material. **Dimopoulos:** Sanofi: Honoraria, Membership on an entity's Board of Directors or advisory committees; Takeda: Honoraria, Membership on an entity's Board of Directors or advisory committees; Regeneron: Honoraria, Membership on an entity's Board of Directors or advisory committees; Menarini: Honoraria, Membership on an entity's Board of Directors or advisory committees; Janssen: Honoraria, Membership on an entity's Board of Directors or advisory committees; GlaxoSmithKline: Honoraria, Membership on an entity's Board of Directors or advisory committees; BeiGene Inc: Honoraria, Membership on an entity's Board of Directors or advisory committees; Bristol Myers Squibb: Honoraria, Membership on an entity's Board of Directors or advisory committees; Amgen: Honoraria, Membership on an entity's Board of Directors or advisory committees; AbbVie: Honoraria, Membership on an entity's Board of Directors or advisory committees. Delimpasi: Takeda: Honoraria; Amgen: Honoraria; Janssen: Honoraria; GSK: Honoraria. Coriu: Genesis BioPharma: Other: TRAVEL, ACCOMMODATIONS, EXPENSES; Accord Healthcare: Other: TRAVEL, ACCOMMODATIONS, EXPENSES. Spicka: GSK: Consultancy, Membership on an entity's Board of Directors or advisory committees; Janssen-Cilag: Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events; Sanofi: Consultancy, Other: Received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Participation on a Data Safety Monitoring Board or Advisory Board; Takeda: Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events; Amgen: Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events; Novartis: Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events;

POSTER ABSTRACTS Session 653

Karyopharm: Membership on an entity's Board of Directors or advisory committees; Celgene: Consultancy, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events; Bristol Myers Squibb: Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; Support for attending meetings and/or travel events. Masszi: Takeda: Membership on an entity's Board of Directors or advisory committees; Janssen: Membership on an entity's Board of Directors or advisory committees; BMS: Membership on an entity's Board of Directors or advisory committees; Novartis: Membership on an entity's Board of Directors or advisory committees; Pfizer: Membership on an entity's Board of Directors or advisory committees; Abbvie: Membership on an entity's Board of Directors or advisory committees. Mikala: Janssen: Consultancy, Honoraria, Other: TRAVEL, ACCOMMO-DATIONS, EXPENSES, Research Funding; Bristol Myers Squibb: Consultancy, Honoraria; Celgene: Consultancy, Honoraria, Other: TRAVEL, ACCOMMODATIONS, EXPENSES; Amgen: Consultancy, Honoraria; Takeda: Consultancy, Honoraria, Other: TRAVEL, ACCOMMODATIONS, EXPENSES; AbbVie: Consultancy, Honoraria, Research Funding. Norin: Oncopeptides AB: Current Employment, Current equity holder in publicly-traded company, Current holder of stock options in a privately-held company. Thuresson: Oncopeptides: Consultancy, Current holder of stock options in a privately-held company. Bergan: Oncopeptides: Current Employment. Obermüller: Oncopeptides: Current Employment. Hajek: Sanofi: Consultancy, Membership on an entity's Board of Directors or advisory committees; Bristol Myers Squibb: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; Janssen: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings and/or travel, Research Funding; Takeda: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings and/or travel, Research Funding; Amgen: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings and/or travel, Research Funding; Celgene: Consultancy, Honoraria, Other: Support for attending meetings and/or travel, Research Funding; Oncopeptides: Consultancy, Membership on an entity's Board of Directors or advisory committees; Novartis: Consultancy, Research Funding; GlaxoSmithKline: Membership on an entity's Board of Directors or advisory committees; AbbVie: Consultancy; PharmaMar: Consultancy, Honoraria. Mateos: Janssen: Honoraria, Membership on an entity's Board of Directors or advisory committees; BMS/Celgene: Honoraria, Membership on an entity's Board of Directors or advisory committees; GSK: Honoraria, Membership on an entity's Board of Directors or advisory committees; Sanofi: Honoraria, Membership on an entity's Board of Directors or advisory committees; Pfizer: Honoraria, Membership on an entity's Board of Directors or advisory committees; Abbvie: Honoraria, Membership on an entity's Board of Directors or advisory committees; Stemline: Honoraria, Membership on an entity's Board of Directors or advisory committees; Oncopeptides: Honoraria, Membership on an entity's Board of Directors or advisory committees; Amgen: Honoraria; Takeda: Honoraria; Regeneron: Honoraria. Richardson: Bristol Myers Squibb: Consultancy, Other: Contracted research, Research Funding; Oncopeptides: Consultancy, Research Funding; GSK: Consultancy; Takeda: Research Funding; AstraZeneca Pharmaceuticals LP, Bristol-Myers, Squibb Company, Celgene Corporation, GlaxoSmithKline, Janssen Biotech Inc, Karyopharm Therapeutics, Oncopeptides, Sanofi, Secura Bio, Takeda Pharmaceuticals USA Inc;: Consultancy; Karyopharm: Consultancy, Research Funding; Sanofi: Consultancy. Sonneveld: Pfizer: Other: Advisory Board; Erasmus Medical Center: Current Employment; Celgene: Other: Advisory Board, Research Funding; Janssen: Other: Advisory Board, Research Funding; Amgen: Other: Advisory Board, Research Funding; Karyopharm: Other: Advisory Board, Research Funding; Bristol Myers Squibb: Other: Advisory Board, Research Funding.

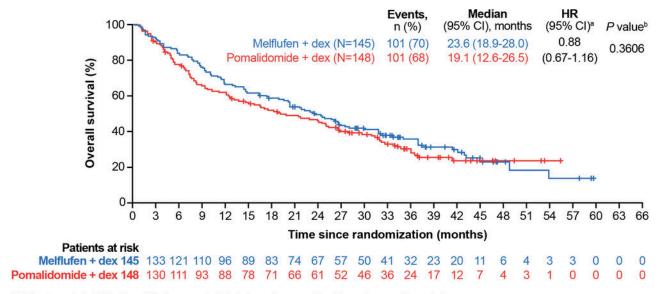
POSTER ABSTRACTS Session 653

Figure 1. Overall Survival in the ITT Population



<sup>a</sup>HR (and associated 95% CI) and P value are calculated using a Cox proportional hazards regression model stratified by randomization strata: age (<75, ≥75), number of lines of prior therapy (2, 3-4), and ISS Score (1, ≥2).

Figure 2. Overall Survival in Patients Without ASCT or Time to Progression >36 Months after ASCT



<sup>&</sup>lt;sup>9</sup>HR (and associated 95% CI) and P value are calculated using a Cox proportional hazards regression model.
<sup>b</sup>Unstratified log-rank test.

Figure 1

https://doi.org/10.1182/blood-2023-177945

<sup>&</sup>lt;sup>b</sup>Log-rank test stratified by randomization strata: age (<75, ≥75), number of lines of prior therapy (2, 3-4), and ISS Score (1, ≥2). Abbreviations: dex, dexamethasone; HR, hazard ratio; ISS, International Staging System; ITT, intention-to-treat.

Abbreviations: ASCT, autologous stem cell transplant; dex, dexamethasone; HR, hazard ratio.