P38 PATIENT-REPORTED OUTCOMES (PRO) IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) TREATED WITH MELFLUFEN AND DEXAMETHASONE (DEX) OR POMALIDOMIDE (POM) AND DEX: ANALYSES FROM THE PHASE 3 OCEAN STUDY

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Background: The phase 3 OCEAN study (OP-103; NCT03151811) met its primary endpoint; melphalan flufenamide (melflufen) + dex showed superior progression-free survival vs pom+dex in patients with RRMM refractory to lenalidomide, but overall survival (secondary endpoint) numerically favored pom+dex (Schjesvold FH, et al. *Lancet Haematol*. 2022;9[2]:e98-e110). Hematologic adverse events (AEs) were more frequent with melflufen+dex, but grade 3/4 infections were more common with pom+dex. Melflufen+dex was approved in Europe for the treatment of patients with ≥3 prior lines of therapy and triple—class refractory RRMM; if patients had prior autologous stem cell transplant (ASCT), time to progression (TTP) must have been >36 months.

RRMM is associated with severe symptoms, of which pain, fatigue, physical functioning, and emotional functioning have been strongly linked to impairments in health-related quality of life (HRQoL) for patients. Because HRQoL is known to deteriorate with each subsequent line of therapy, treatment goals should include preserving or even improving HRQoL (Engelhardt M, et al. *Clin Lymphoma Myeloma Leuk*. 2020;21[2]:e160-e175).

Objective: To evaluate functional status and well-being based on PRO assessments in patients receiving treatment with either melflufen+dex or pom+dex in the OCEAN study. Secondly, to assess PROs in the subgroup of patients with TTP >36 months after an ASCT or had no prior ASCT to understand whether results are generalizable to patients in the global target population.

Methods: EORTC QLQ-C30, EORTC QLQ-MY20 and EQ-5D-3L were included in the OCEAN trial beginning with protocol version 4.1 and assessed before treatment in each cycle. Mean scores per cycle and change from baseline to cycle 6 were analyzed for Global Health Status/QoL, Physical Functioning, Emotional Functioning, Pain, Fatigue, Disease Symptoms, and Side Effects of Treatment. Within the melflufen+dex arm, the target population was compared vs the non–target population (ie, patients with TTP <36 months after an ASCT).

Results: Baseline characteristics were generally well matched between patients reporting PROs (n=158) and the overall study population (N=495). Overall, mean baseline scores before treatment were similar between melflufen+dex and pom+dex treatment groups: 63.8 vs 64.3 in Global Health Status/QoL, 72.4 vs 74.2 in Physical Functioning, 81.0 vs 79.8 in Emotional Functioning, 35.1 vs 32.6 in Fatigue, 30.2 vs 28.7 in Pain, 24.7 vs 22.6 in Disease Symptoms, 16.1 vs 16.1 in Side Effects of Treatment, and 64.0 vs 66.9 for the EQ-5D-3L VAS, respectively. Mean scores remained generally constant between baseline and follow-up timepoints (Figure). Mean baseline scores before treatment with melflufen+dex were similar between the target population and the non–target population groups: 65.3 vs 61.9 in Global Health Status/QoL, 73.2 vs 71.5 in Physical Functioning, 83.3 vs 78.0 in Emotional Functioning, 30.7 vs 40.7 in Fatigue, 26.2 vs 35.4 in Pain, 23.0 vs 27.1 in Disease Symptoms, 15.9 vs 16.3 in Side Effects of Treatment, and 64.8 vs 62.8 for the EQ-5D-3L VAS, respectively. Despite small patient numbers (n=44), the target population group showed a similar trend to that of the overall population.

Conclusion: Given the negative impact of treatment-related AEs on HRQoL in RRMM, results from OCEAN are encouraging. HRQoL was maintained throughout treatment with melflufen+dex, including in the target population, and was similar to that with pom+dex.
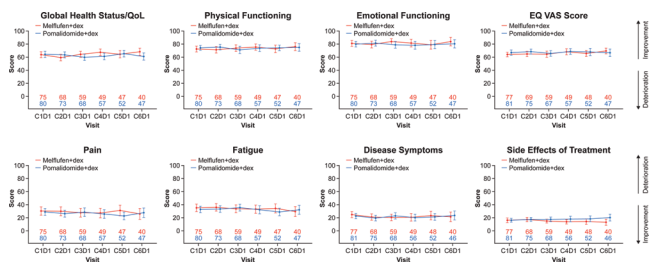
P39 DEDALO: PHASE II STUDY OF DARATUMUMAB PLUS POMALIDOMIDE AND DEXAMETHASONE (DPD) IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA AND 17P DELETION

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Introduction: Deletion of the short arm of chromosome 17 (del(17p)) is a well-established high-risk feature in multiple myeloma (MM) and is included in current disease staging criteria. Treatment of del(17p) MM is a major challenge due to rapid development of chemoresistance and short survival. The size of del(17p) clone correlates with prognosis, and the 55-60% threshold has the worst prognosis. Approximately 1/3 of pts have a concomitant TP53 mutation, with a complete abolition of the protein function. TP53 biallelic inactivation is defined as double-hit myeloma.

Pomalidomide-dexamethasone showed promising results in this setting (Leleu et al, Blood 2014). Daratumumab is an attractive strategy for treatment of MM pts with del(17p).

In the phase II DEDALO trial (NCT04124497), we assessed daratumumab-pomalidomide-dexamethasone (DPd) in RRMM pts with del(17p).

Methods: Key eligibility criteria included: RRMM; up to 3 prior lines of therapy, del(17p) observed by FISH in at least 10% of plasma cells at any time of MM history, previous exposure to lenalidomide, no refractoriness or intolerance to pomalidomide, nor previous exposure to an anti-CD38 monoclonal antibody.

Continuous DPd treatment consisted of daratumumab (1800 mg subcutaneously or 16 mg/kg intravenously) weekly during cycles 1 and 2, every 2 weeks during cycles 3–6, and every 4 weeks thereafter; oral pomalidomide (4 mg, once daily on days 1–21); and oral or intravenous dexamethasone (40 mg once daily on days 1, 8, 15, and 22; 20 mg for pts ≥75 years) at each 28-day cycle. The primary endpoint was MRD 10-5 negativity within the first 12 months of treatment. NGF and NGS MRD analyses were performed. The key secondary endpoints were PFS, ORR and OS.

Results: Forty-five pts were enrolled. The median age was 63 (range 43-83) years (yrs), and 60%/29%/11% of pts had ISS stage I/II/III. All pts had >10% del(17p) and 14 pts had ≥55% del(17p); t(4;14) was observed in 6, t(14;16) in 6, del(1p) in 10, and 1q+ in 16 pts. Median number of prior lines of therapy was 1 (range 1-3); 100% had been previously exposed to lenalidomide and 86% to a proteasome inhibitor.

Three pts achieved MRD negativity by NGF, while NGS analysis is ongoing. ORR was 60%, including 13 pts with PR, 12 with VGPR, and 2 with ≥CR. Median time-to-response was 2.5 months. With a median follow-up of 8.5 months (range 6.3-13.9), median PFS was 7.1 months (range 5.9 – not reached [NR]; Figure).

By subgroup analysis, PFS was: 8.4 months in pts with del(17p) clone size <60% and 6.5 months in pts with del(17p) clone size ≥60% (HR, 0.75; 95% CI 0.33-1.7; P=0.48); 12.4 months in pts with ISS I vs 4.2 months in pts with ISS II-III (HR, 2.48; 95% CI 1.12-5.51; P=0.02); 6.6 months in pts at first relapse vs 7.1 months beyond first relapse (HR 0.95; 95% CI 0.42-2.12; P=0.89); 7.1 months in pts <65 yrs and 7.6 months in those ≥65 yrs of age (HR 0.84; 95% CI 0.37-1.92; P=0.68). Median OS was NR. No new safety concerns were observed. TP53 mutational analysis is underway.

Conclusion: In this difficult-to-treat population, DPd is a therapeutic option for pts of all ages and can be considered as a bridge to other immunotherapies, such as T-cell engagers and CAR-T cells.

Figure. Progression-free survival
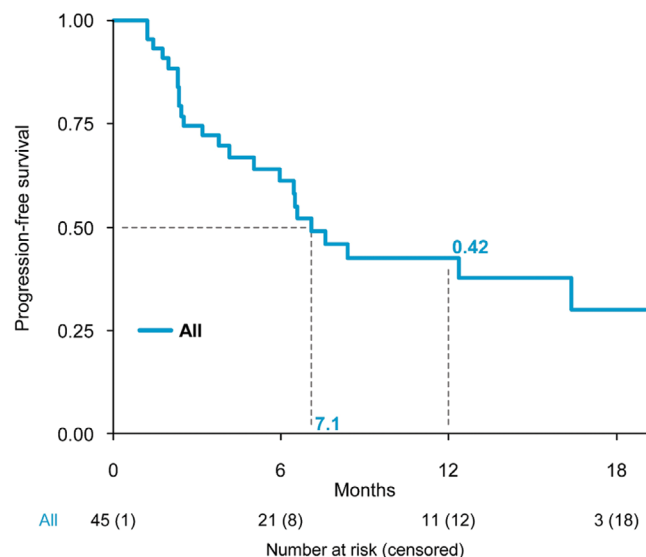
P40 REAL-WORLD TREATMENT PATTERNS OF PATIENTS INITIATING THIRD-LINE THERAPY IN RELAPSED/REFRACTORY MULTIPLE MYELOMA IN EUROPE

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Objectives: Real-world (RW) evidence can provide valuable insights into clinical practice and help identify and address unmet medical needs. We report RW treatment utilisation in patients from European data sets who initiated third-line (3L) treatment for relapsed/refractory multiple myeloma (RRMM).
Methods: This retrospective, noninterventional analysis used claims data from the German AOK PLUS health insurance fund and Italian Local Health Units (2012–2020). Patients initiating 3L treatment from 2016–2020 (index) were identified using an algorithm based on prescription and procedure codes. New lines of treatment were defined as introduction of a new agent not part of the prior line. Agents given ≤30 days of start of the line defined the regimen. Retreatments after >6 months of discontinuation were considered a new line. Baseline characteristics and treatment patterns were reported.
Results: Patients were identified from Germany (N=276) and Italy (N=289) (Table). Baseline characteristics were similar between countries. Prior to 3L treatment, immunomodulatory imide drug (IMiD) use was higher (74% vs 56%) and proteasome inhibitor (PI) use was lower (52% vs 96%) among patients in Italy versus Germany. At 3L, the proportion of double-class exposed patients in Italy was lower versus Germany (33% vs 52%).
In Germany, common first-line (1L) regimens were bortezomib (BORT) + dexamethasone (DEX; Vd, 46%), BORT + melphalan (MEL) + prednisone (PRED; VMP, 14%), and Vd + cyclophosphamide (CyBORD, 8%). The most common second-line (2L) treatment regimens were lenalidomide (LEN) + DEX (Rd, 30%), Vd (11%), and carfilzomib (CFZ) + Rd (KRd, 8%). By 3L, 95% and 54% of patients had received prior BORT- and LEN-based regimens, respectively. In 3L, combinations were often LEN- and/or CFZ-based with daratumumab (DARA) monotherapy and pomalidomide + DEX (Pd) also contributing ~4% each (Table).

Baseline (12 months) and treatment characteristics in patients with relapsed/refractory multiple myeloma who initiated 3L treatment

Characteristic	Germany (N=276)	Italy (N=289)
Male, n (%)	139 (50)	141 (49)
Median age at index (interquartile range), years	75 (65–80)	73 (66–79)
Median time since diagnosis (range), years	2.7 (0.4–7.4)	2.1 (0.3–6.7)
Year of 3L treatment initiation, n (%)		
2016	58 (21)	35 (12)
2017	57 (21)	48 (17)
2018	57 (21)	52 (18)
2019	54 (20)	80 (28)
2020	50 (18)	74 (26)
Prior treatment (excluding maintenance), n (%)		
PI	264 (96)	151 (52)
Immunomodulatory drug	154 (56)	213 (74)
anti-CD38	30 (11)	13 (4.5)
LEN + PI-exposed and POM-naive	135 (49)	61 (21)
Double-class exposed	144 (52)	96 (33)
Triple-class exposed	15 (5)	8 (3)
Stem cell transplant	75 (27)	43 (15)
3L treatment regimens ≥4% in either country, n (%)		
Rd	53 (19)	79 (27)
KRd	27 (10)	11 (4)
Kd	22 (8)	9 (3)
DRd	22 (8)	15 (5)
DVd	18 (7)	≤3[a]
Pd	11 (4)	35 (12)
DARA	11 (4)	0 (0)
Melphalan + prednisone	0 (0)	21 (7)

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Not issuable due to anonymisation regulations.
Rd, LEN + DEX; KRd, CFZ + LEN + DEX; Kd, CFZ + DEX; DRd, DARA + LEN + DEX; DVd, DARA + BORT + DEX; Pd, POM + DEX.
3L, third-line; BORT, bortezomib; CFZ, carfilzomib; DARA, daratumumab; DEX, dexamethasone; LEN, lenalidomide; PI, proteasome inhibitor; POM, pomalidomide.

In Italy, common 1L regimens included MEL ± DEX ± PRED (22%), Vd (6%), and thalidomide (THAL) + DEX (5%). Rd (40%) and Vd (8%) were the most common 2L regimens; by 3L, 56% and 49% of patients had received prior LEN- and BORT-containing regimens, respectively.
Overall, use of Pd in 3L in Italy was higher than in Germany (12% vs 4%), whereas use of CFZ- (10% vs 21%) and DARA-based (9% vs 29%) regimens was lower. In 3L, use of conventional therapies, such as MEL (15% vs 3%), was higher in Italy versus Germany.
Retreatment patterns in Germany and Italy showed that 60% and 82% of patients initiating 3L treatment, respectively, had prior exposure to the same agent class (IMiD, PI, monoclonal antibodies). Of 50 patients in Germany receiving BORT in 3L, 47 (94%) had prior BORT; of 135 patients receiving LEN in 3L, 47 (35%) had prior LEN. Of 40 patients in Italy receiving BORT in 3L, 31 (78%) had prior BORT; of 131 patients receiving LEN in 3L, 82 (63%) had prior LEN. Additionally, of 13 patients in Italy who received prior THAL, all were retreated with THAL in 3L.
Conclusions: This study provides a perspective of RW clinical practice from 2012-2020 for comparison with the evolving treatment landscape for RRMM.

P41 NO EVIDENCE OF B-CELL MATURATION ANTIGEN (BCMA) EXPRESSION LOSS OR SYSTEMIC IMMUNE IMPAIRMENT AFTER TREATMENT WITH THE BCMA-TARGETED ANTIBODY-DRUG CONJUGATE BELANTAMAB MAFODOTIN IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Objectives: Belantamab mafodotin (belamaf)—an antibody-drug conjugate targeting B-cell maturation antigen (BCMA)—demonstrated deep and durable responses in the DREAMM-2 trial of patients with relapsed/refractory