OCEAN (OP-103): Patients With Relapsed/Refractory Multiple Myeloma Treated With Melflufen Plus Dexamethasone or Pomalidomide Plus Dexamethasone - a Resource Utilization Analysis of Adverse Events Leading to Hospitalizations

Poster EE73

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CONCLUSIONS

- There was limited usage of inpatient services for treatment-emergent adverse events (TEAEs) in the OCEAN study
- The most common reason for hospitalization was infections in both the melflufen + dexamethasone and pomalidomide + dexamethasone treatment arms
- Overall, TEAEs leading to hospitalization were less frequent with melflufen + dexamethasone compared with pomalidomide + dexamethasone, with few of the hematologic TEAEs requiring hospitalization
- Fewer cardiac TEAEs required hospitalization with melflufen + dexamethasone compared with pomalidomide + dexamethasone, confirming the absence of this potential safety signal, and supporting the tolerability of melflufen + dexamethasone previously seen in older patients[1-4]

BACKGROUND

- The economic burden in relapsed/refractory multiple myeloma (RRMM) is driven by:
  - Drug costs, with substantial burden following exposure to multiple drug classes and combinations[5]
  - The use of inpatient services[6]
- Melphalan flufenamide (melflufen) is a first-in-class peptide-drug conjugate that utilizes increased peptidase expression to selectively release potent alkylating agents inside tumor cells
- Melflufen plus dexamethasone is approved in Europe for the treatment of patients with triple-class refractory RRMM who have received ≥3 prior lines of therapy and progressed >36 months after a previous autologous stem cell transplant, if one was received
  - Approval was based on results from the phase 2 HORIZON study and further supported by the phase 3 OCEAN study[1,2]

OBJECTIVE

- This analysis evaluates resource utilization in the OCEAN study (OP-103; NCT03151811), of patients with RRMM treated with melflufen + dexamethasone or pomalidomide + dexamethasone, by determining the frequency of TEAEs leading to hospitalization

METHODS

- The OCEAN study was a randomized, phase 3, head-to-head study of melflufen plus dexamethasone compared with pomalidomide plus dexamethasone in patients with RRMM who had disease refractory to lenalidomide and last line of therapy (**Figure 1**)
  - Patients must have received 2-4 prior lines of therapy including lenalidomide and a proteasome inhibitor
- All patients who received study treatment (safety population) were analyzed for:
  - The proportion of patients in each treatment arm with TEAEs leading to hospitalization for >24 hours
  - The number of TEAEs leading to hospitalization for >24 hours per treatment year

Figure 1. OCEAN Study Design: A Head-to-Head Comparison Study

A phase 3, randomized, open-label, global study[1]

Patients with RRMM[a]
- Aged ≥18 years
- 2-4 prior lines of therapy including lenalidomide and a PI
- Refractory to lenalidomide and last line of therapy
- ECOG PS ≤2

(N=495)

1 cycle = 28 days

R 1:1

Melflufen (40 mg IV, day 1 of each 28-day cycle)
Dexamethasone (40 mg PO weekly)[b,c]

Pomalidomide (4 mg PO, Days 1-21 of each 28-day cycle)
Dexamethasone (40 mg PO weekly)[b,c]

Patients treated until disease progression or unacceptable toxicity

Patients stratified by:
- Age (<75 vs ≥75 years)
- Prior lines of therapy (2 vs 3-4)
- ISS score (I vs II/III)

Primary endpoint:
- PFS assessed by IRC per IMWG Uniform Response Criteria[7,8]

Key secondary endpoints:
- ORR
- OS
- Safety[d]

ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IRC, Independent Review Committee; ISS, International Staging System; IV, intravenously; melflufen, melphalan flufenamide; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PO, orally; R, randomization; RRMM, relapsed/refractory multiple myeloma.
[a]Select inclusion criteria. Other criteria apply. [b]Days 1, 8, 15, and 22 of each 28-day cycle. [c]The starting dexamethasone dose will be reduced to 20 mg in patients aged ≥75 years. [d]An independent data safety monitoring committee will monitor the risk-benefit ratio at regular intervals.[1]

RESULTS

ADVERSE EVENTS OVERALL

- There were 226 of 228 (99.1) and 241 of 246 (98.0%) patients in the melflufen + dexamethasone and pomalidomide + dexamethasone arms experiencing 3919 and 2306 TEAEs, respectively (**Table 1**)
  - The most common types of TEAEs per MedDRA System Order Class in the melflufen + dexamethasone and pomalidomide + dexamethasone arms were blood and lymphatic system disorders (93.9% and 69.1%, respectively), infections and infestations (50.0% and 55.7%), and general disorders and administration site conditions (41.2% and 43.5%)
  - Among other notable TEAEs, cardiac TEAEs occurred in 7.5% and 9.8% of patients, respectively

Table 1. Occurrence of Adverse Events Overall

TEAE by System Organ Class n (%) / Number of Events	Melflufen + Dexamethasone (n=228)	Pomalidomide + Dexamethasone (n=246)
Blood and lymphatic system disorders[a]	214 (93.9%) / 2584	170 (69.1%) / 876
Infections and infestations	114 (50.0%) / 231	137 (55.7%) / 281
General disorders and administration site conditions	94 (41.2%) / 186	107 (43.5%) / 202
Investigations[b]	62 (27.2%) / 184	51 (20.7%) / 82
Musculoskeletal and connective tissue disorders	74 (32.5%) / 120	73 (29.7%) / 129
Gastrointestinal disorders	75 (32.9%) / 157	70 (28.5%) / 135
Respiratory, thoracic and mediastinal disorders	54 (23.7%) / 99	53 (21.5%) / 97
Nervous system disorders	41 (18.0%) / 64	58 (23.6%) / 90
Metabolism and nutrition disorders	48 (21.1%) / 81	50 (20.3%) / 92
Psychiatric disorders	37 (16.2%) / 44	39 (15.9%) / 58
Vascular disorders	29 (12.7%) / 33	32 (13.0%) / 55
Cardiac disorders	17 (7.5%) / 20	24 (9.8%) / 46
Renal and urinary disorders	17 (7.5%) / 23	23 (9.3%) / 34
Skin and subcutaneous tissue disorders	16 (7.0%) / 16	40 (16.3%) / 52
Ear and labyrinth disorders	10 (4.4%) / 13	11 (4.5%) / 12
Eye disorders	8 (3.5%) / 11	10 (4.1%) / 15
Surgical and medical procedures	4 (1.8%) / 5	1 (0.4%) / 1
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	3 (1.3%) / 4	9 (3.7%) / 12
Hepatobiliary disorders	2 (0.9%) / 2	1 (0.4%) / 1
Reproductive system and breast disorders	1 (0.4%) / 1	2 (0.8%) / 2
Endocrine disorders	1 (0.4%) / 1	2 (0.8%) / 2
Immune system disorders	1 (0.4%) / 1	2 (0.8%) / 2

TEAE, treatment-emergent adverse event.
[a]MedDRA SOC 'Blood and Lymphatic System Disorders,' including 'Platelet count decreased' and 'Neutrophil count decreased.' [b]MedDRA SOC 'Investigations,' excluding 'Platelet count decreased' and 'Neutrophil count decreased.'

ADVERSE EVENTS LEADING TO HOSPITALIZATIONS

- A total of 131 TEAEs in 30.7% of patients in the melflufen + dexamethasone arm and 166 TEAEs in 35.0% of patients in the pomalidomide + dexamethasone arm led to hospitalizations (**Table 2**)
  - The most common type of TEAEs leading to hospitalizations was infections, occurring in 12.7% and 19.5% of patients, respectively, including infective pneumonia, which occurred in 5.7% and 9.8% of patients, respectively
  - Hematologic TEAEs led to hospitalization in 7.5% and 3.7% of patients, respectively
  - Cardiac TEAEs led to hospitalization in 2.2% and 4.5% of patients, respectively (atrial fibrillation, 0 vs 3.3%)
  - Other TEAEs that led to hospitalization included "injury, poisoning, and procedural complications" in 3.9% and 3.7% of patients, respectively
- The median duration of hospitalization due to TEAEs was the same (7 days) between both arms; however, median duration of hospitalization due to hematologic TEAEs and infections was shorter in the melflufen + dexamethasone arm (5.0 days; range, [1-33]) than in the pomalidomide + dexamethasone arm (8.0 days; range, [1-82])

Table 2. Occurrence of Adverse Events Leading to Hospitalizations[a]

System Organ Class / Preferred Term n (%)	TEAEs Leading to Hospitalizations	
	Melflufen + Dexamethasone (n=228)	Pomalidomide + Dexamethasone (n=246)
Any AE	70 (30.7%)	86 (35.0%)
Infections and infestations	29 (12.7%)	48 (19.5%)
Pneumonia	10 (4.4%)	18 (7.3%)
Urinary tract infection	0 (0%)	6 (2.4%)
Influenza	0 (0%)	5 (2.0%)
Infective pneumonia[b]	13 (5.7%)	24 (9.8%)
Blood and lymphatic system disorders[c]	17 (7.5%)	9 (3.7%)
Anemia	7 (3.1%)	5 (2.0%)
Thrombocytopenia	7 (3.1%)	1 (0.4%)
Cardiac disorders	5 (2.2%)	11 (4.5%)
Atrial fibrillation	0 (0%)	8 (3.3%)

AE, adverse event; TEAE, treatment-emergent adverse event.
[a]2% cutoff. [b]MedDRA SMQ 'Infective Pneumonia (narrow scope).' [c]MedDRA SOC 'Blood and Lymphatic System Disorders,' including 'Platelet count decreased' and 'Neutrophil count decreased.'

ADVERSE EVENTS LEADING TO HOSPITALIZATIONS PER TREATMENT YEAR

- TEAEs leading to hospitalization occurred at frequencies of 0.86 and 1.12 per treatment year in the melflufen + dexamethasone and pomalidomide + dexamethasone arms, respectively (**Table 3**)
  - Infections leading to hospitalization occurred at frequencies of 0.27 and 0.41 per treatment year, respectively
  - Hematologic TEAEs leading to hospitalization occurred at frequencies of 0.18 and 0.11 per treatment year, respectively
  - Cardiac TEAEs leading to hospitalization occurred at frequencies of 0.04 and 0.1 per treatment year, respectively
- The cumulative treatment duration in years used for the respective arms was 151.7 for the melflufen + dexamethasone arm and 148.1 for the pomalidomide + dexamethasone arm

Table 3. Frequency of Adverse Events Leading to Hospitalizations Per Treatment Year

System Organ Class / Preferred Term	TEAEs Leading to Hospitalization Per Treatment Year (Events/Year)	
	Melflufen + Dexamethasone (n=228)	Pomalidomide + Dexamethasone (n=246)
Any AE	131 (0.86)	166 (1.12)
Infections and infestations	41 (0.27)	61 (0.41)
Pneumonia	12 (0.08)	19 (0.13)
Urinary tract infection	0 (0)	8 (0.05)
Influenza	0 (0)	5 (0.03)
Infective pneumonia[a]	16 (0.11)	25 (0.17)
Blood and lymphatic system disorders[b]	27 (0.18)	16 (0.11)
Anemia	9 (0.06)	12 (0.08)
Thrombocytopenia	9 (0.06)	1 (0.01)
Cardiac disorders	6 (0.04)	15 (0.1)
Atrial fibrillation	0 (0)	10 (0.07)

AE, adverse event; TEAE, treatment-emergent adverse event.
[a]MedDRA SMQ 'Infective Pneumonia (narrow scope).' [b]MedDRA SOC 'Blood and Lymphatic System Disorders,' including 'Platelet count decreased' and 'Neutrophil count decreased.'

REFERENCES

1. Schjesvold FH, et al. *Lancet Haematol*. 2022;9(2):e98-e110.
2. Richardson PG, et al. *J Clin Oncol*. 2021;39(7):757-767.
3. Mateos MV, et al. *Blood*. 2021;138(suppl 1):2741.
4. Larroca A, et al. *Blood*. 2020;136:44-46.
5. Yang J, et al. *J Manag Care Spec Pharm*. 2023;29(8):917-926.
6. Yeaw J, et al. *Value Health*. 2020;23(1):S37.
7. Rajkumar SV, et al. *Blood*. 2011;117(18):4691-4695.
8. Moreau P, et al. *Lancet Oncol*. 2021;22(3):e105-e118.

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