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Adverse event patterns and management with pomalidomide, dexamethasone, and daratumumab in patients with relapsed or refractory multiple myeloma: a safety analysis of the phase 2 MM-014 study

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Introduction

- Lenalidomide is a standard of care in multiple myeloma (MM), but patients with relapsed or refractory MM (RRMM) previously treated with lenalidomide have been poorly represented in recent trials investigating triplet regimens after ≤ 3 treatment lines
- Improved treatment options are needed for patients who have exhausted the benefits of lenalidomide in early lines of therapy
- Over the course of the disease, health-related quality of life deteriorates due in part to treatment toxicities[1,2]
- In the phase 2 MM-014 trial (NCT01946773), which comprised 3 cohorts, the outcomes of pomalidomide-based therapy after failure of first- or second-line lenalidomide-based therapy were investigated in patients with RRMM.
- In cohort B of MM-014, at a median follow-up of 28.4 months, pomalidomide plus daratumumab and low-dose dexamethasone (DPd) showed promising efficacy, with an overall response rate (ORR) of 77.7% and median progression-free survival (PFS) of 30.8 months[3]
  - Neutropenia was the most frequent treatment-emergent adverse event (TEAE), occurring in 67.0% of patients, with grade 3/4 neutropenia events occurring in 64.3% of patients
- The objective of this analysis was to assess the TEAEs that occurred in cohort B and whether they could be resolved by dose modification without affecting efficacy

Methods

Figure 1. Study design

Results

Drug-relatedness and onset of most common TEAEs

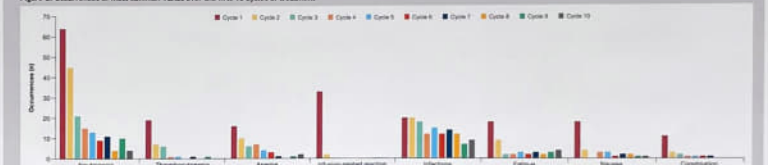
- In cohort B (n = 112), TEAEs of interest were those that were most common (occurring in ≥ 10% of patients) during the first treatment cycle: neutropenia, thrombocytopenia, anemia, infusion-related reaction, infections, fatigue, nausea, and constipation (**Figure 2**)
  - The rate of onset for all TEAEs tended to decrease each cycle for the first 10 cycles, except for infections
- Most patients experienced TEAEs related to pomalidomide (**Table 1**)
- Median time to onset was < 1 month for all most common TEAEs except infections, fatigue, and nausea (**Table 2**)

Duration, resolution, and management of most common TEAEs

- All most common TEAEs persisted for a median of < 1 month except for fatigue, nausea, and constipation; cases that resolved did so in a median of ≤ 1.2 months for each TEAE except fatigue (**Table 3**)
- TEAEs related to pomalidomide were mostly managed by dose interruption, reduction, or both; few patients discontinued pomalidomide due to most common TEAEs (**Table 4**)

The most common TEAEs (≥ 10% of patients in first treatment cycle) were neutropenia, thrombocytopenia, anemia, infusion-related reaction, infections, fatigue, nausea, and constipation. Occurrences tended to decrease over the first 10 cycles of treatment

Figure 2. Occurrences of most common TEAEs over the first 10 cycles of treatment



Include TEAEs of an grades and all causality. Infections included pneumonia, influenza, and upper respiratory infections

Table 1. Drug-relatedness of most common TEAEs

Related TEAE, n (%)	Pomalidomide	Daratumumab	Dexamethasone
Patients reporting ≥ 1 related TEAE	105 (93.8)	90 (80.4)	96 (76.8)
Patients reporting ≥ 1 related TEAE of interest			
Neutropenia	71 (63.4)	40 (35.7)	4 (6.4)
Thrombocytopenia	22 (19.6)	14 (12.5)	2 (1.6)
Anemia	21 (18.8)	15 (13.4)	0
Infusion-related reaction	2 (1.8)	23 (20.5)	1 (0.8)
Infections	29 (25.9)	28 (25.0)	28 (22.4)
Fatigue	36 (32.1)	19 (17.0)	19 (17.0)
Nausea	9 (8.0)	9 (8.0)	7 (6.3)
Constipation	8 (7.1)	3 (2.7)	3 (2.7)

Table 2. Onset of most common TEAEs

TEAE	n	Months from first dose to onset, median (range)
Neutropenia	75	0.99 (0.03–23.53)
Thrombocytopenia	28	0.49 (0.03–43.76)
Anemia	30	0.99 (0.03–32.95)
Infusion-related reaction	34	0.03 (0.01–1.44)
Infections	84	0.40 (0.16–47.75)
Fatigue	52	1.22 (0.03–55.56)
Nausea	40	1.00 (0.03–32.22)
Constipation	20	0.77 (0.10–31.80)

Table 3. Duration and resolution of most common TEAEs

TEAE	n	Months of duration, median (range)	Recovered, n (%)	Months to recovery, median
Neutropenia	75	0.36 (0.03–5.29)	67 (89.3)	0.40
Thrombocytopenia	28	0.39 (0.03–40.79)	24 (85.7)	1.15
Anemia	30	0.31 (0.03–36.83)	19 (63.3)	0.26
Infusion-related reaction	34	0.03 (0.03–0.13)	34 (100.0)	0.04
Infections	84	0.53 (0.03–42.00)	76 (85.4)	1.20
Fatigue	52	7.57 (0.03–59.17)	22 (42.3)	1.85
Nausea	40	1.12 (0.03–61.01)	27 (64.3)	0.87
Constipation	20	35.14 (0.07–61.91)	9 (40.0)	0.99

Table 4. Management of most common TEAEs by drug-relatedness

TEAE	n	Dose unchanged, n (%)	Dose reduced, n (%)	Drug interrupted, n (%)	Drug withdrawn, n (%)	Drug interrupted and dose reduced, n (%)	Not applicable, n (%)
Related to pomalidomide							
Neutropenia	71	19 (26.1)	17 (23.9)	38 (53.5)	0	11 (15.5)	2 (2.8)
Thrombocytopenia	22	10 (46.9)	1 (4.5)	6 (18.2)	1 (4.5)	2 (9.1)	1 (4.5)
Anemia	21	10 (50.5)	2 (9.5)	2 (9.5)	0	1 (4.8)	1 (4.8)
Infusion-related reaction	2	2 (100.0)	0	0	0	0	0
Infections	29	20 (69.0)	1 (3.4)	13 (44.8)	2 (6.9)	1 (3.4)	2 (6.9)
Fatigue	36	22 (60.9)	2 (8.3)	3 (8.3)	0	1 (2.8)	0
Nausea	9	8 (88.9)	0	1 (11.1)	0	0	0
Constipation	8	8 (100.0)	0	0	0	0	0
Related to daratumumab							
Neutropenia	40	30 (75.0)	–	10 (25.0)	0	–	0
Thrombocytopenia	14	12 (85.7)	–	2 (21.4)	1 (7.1)	–	0
Anemia	15	15 (100.0)	–	1 (6.7)	0	–	0
Infusion-related reaction	23	7 (31.1)	–	14 (78.8)	1 (3.0)	–	0
Infections	28	21 (75.0)	–	6 (28.4)	2 (7.1)	–	1 (10.7)
Fatigue	19	16 (84.7)	–	3 (15.8)	0	–	0
Nausea	9	9 (100.0)	–	0	0	–	0
Constipation	3	3 (100.0)	–	0	0	–	0
Related to dexamethasone							
Neutropenia	4	3 (66.9)	0	1 (33.3)	0	0	0
Thrombocytopenia	2	2 (100.0)	0	0	0	0	0
Anemia	4	2 (75.0)	0	0	0	0	1 (25.0)
Infusion-related reaction	1	1 (100.0)	0	0	0	0	0
Infections	28	21 (75.0)	0	5 (18.1)	2 (10.7)	1 (3.6)	3 (10.7)
Fatigue	19	16 (84.2)	2 (15.8)	1 (5.3)	0	0	1 (5.3)
Nausea	7	6 (85.7)	1 (14.3)	0	0	0	0
Constipation	3	3 (100.0)	0	0	0	0	0

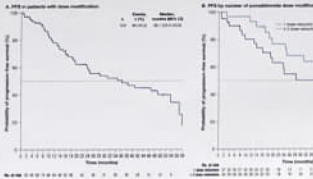
Categories are not mutually exclusive. There could have been > 1 action taken to manage the TEAE

- Pomalidomide-related neutropenia was more frequently managed by dose reduction than the other most common TEAEs related to pomalidomide (**Table 4**)
- Daratumumab and dexamethasone were withdrawn from very few patients, mostly due to infections (system organ class), and among the most common TEAEs, those related to daratumumab and dexamethasone were managed most frequently by dose interruption (**Table 4**)
- Among patients who received pomalidomide dose reductions, 34 (30.4%) received 1 reduction, 11 (9.8%) received 2 reductions, and 6 (5.4%) received 3 reductions

PFS

- Median PFS was 36.1 months in patients with ≥ 1 dose modification (**Figure 3A**)
- Median PFS was 38.2 and 53.6 months in patients with 1 and ≥ 2 pomalidomide dose modifications, respectively (**Figure 3B**)

Figure 3. PFS



HR, risk reduction

Conclusions

- TEAEs that occurred in ≥ 10% of patients in the first treatment cycle tended to decrease in frequency over the first 10 cycles, except for infections
- Patients previously treated with lenalidomide remained responsive to DPd when AEs were managed by dose modification
- There was no evidence of cumulative toxicity between lenalidomide and pomalidomide
- Patients with dose modification had a higher median PFS than that previously reported for the overall cohort[3]
- Managing AEs through dose modification may prolong the time to onset of AEs and may improve outcomes for patients with RRMM treated with DPd
- Patients with pomalidomide and dexamethasone dose adjustments can remain on treatment with favorable outcomes

References

1. Bell J et al Health Qual Life Out 2013;11:1-12.
2. Hansson L et al Int J Qual Ill 2011;6:65-72.
3. Siegel D S et al Br J Haematol 2015;169:787-797.
4. Bahlis N J et al. Lunch presentation EHA 2015; 100-101.

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