Pomalidomide, daratumumab, and dexamethasone after lenalidomide treatment in patients with relapsed or refractory multiple myeloma: final overall survival analysis of the phase 2 MM-014 study

MM-371

Nizar J. Bahlis,[1] Christy Samaras,[2] Donna Reece,[3] Michael Sebag,[4] Jeffrey Matous,[5] Jesús G. Berdeja,[6] Jesse Shustik,[7] Gary J. Schiller,[8] Siddhartha Ganguly,[9] Kevin Song,[10] Christopher S. Seet,[11] Mirelis Acosta-Rivera,[12] Donald Quick,[13] Bertrand Anz,[14] Gustavo Fonseca,[15] Hongjuan Liu,[16] Christian Gentili,[17] David S. Siegel[18]

[1]University of Calgary, Calgary, Canada; [2]Cleveland Clinic, Cleveland, OH, USA; [3]Princess Margaret Hospital, Toronto, Canada; [4]McGill University Health Centre, Montreal, Canada; [5]Colorado Blood Cancer Institute, Sarah Cannon Research Institute, Denver, CO, USA; [6]Sarah Cannon Research Institute, Nashville, TN, USA; [7]Fraser Valley Cancer Centre, Surrey, Canada; [8]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [9]Houston Methodist Hospital Neal Cancer Center, Houston, TX, USA; [10]Vancouver General Hospital, Vancouver, Canada; [11]UCLA Medical Center, Los Angeles, CA, USA; [12]Fundacion de Investigacion de Diego, San Juan, Puerto Rico; [13]Joe Arrington Cancer Research and Treatment Center, Lubbock, TX, USA; [14]Tennessee Oncology, Nashville, TN, USA; [15]Florida Cancer Specialists, Lecanto, FL, USA; [16]Bristol Myers Squibb, Princeton, NJ, USA; [17]Bristol Myers Squibb, Boudry, Switzerland; [18]John Theurer Cancer Center, Hackensack, NJ, USA

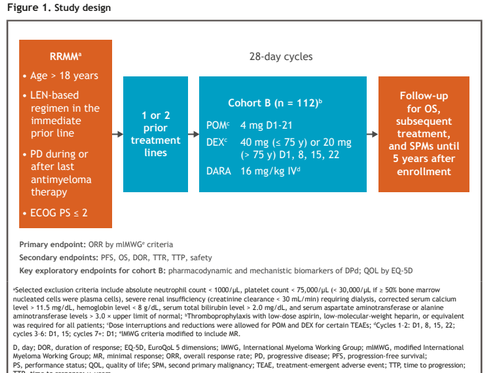
Introduction

- Treatment choice after the first line is important for patients with multiple myeloma (MM)
- Though the treatment landscape has evolved, there is no consensus on optimal sequence
- Lenalidomide (LEN) is a standard of care in MM and, as such, nearly all patients receive LEN in the first or second line of therapy[1]
- Improved treatment options are needed for patients who have exhausted the benefits of LEN in early lines
- In the phase 2 MM-014 trial (NCT01946477), which comprised 3 cohorts, the outcomes of pomalidomide (POM)-based therapy after failure of first- or second-line LEN-based therapy were investigated in patients with relapsed or refractory MM (RRMM)
- In cohort B of MM-014, at a median follow-up of 28.4 months, POM plus daratumumab (DARA) and low-dose dexamethasone (DEX) (DPd) showed promising efficacy, but overall survival (OS) data were immature[2]
- Here, we report final OS in MM-014 cohort B at a median (range) follow-up of 41.9 (0.4-73.1) months

Methods

- The study design of cohort B in MM-014 is shown in **Figure 1**

Figure 1. Study design



Primary endpoint: ORR by mIMWG[e] criteria

Secondary endpoints: PFS, OS, DOR, TTR, TTP, safety

Key exploratory endpoints for cohort B: pharmacodynamic and mechanistic biomarkers of DPd; QOL by EQ-5D

*Selected exclusion criteria include absolute neutrophil count < 1000/μL, platelet count < 75,000/μL (< 30,000/μL if ≥ 50% bone marrow nucleated cells were plasma cell(s), severe renal insufficiency (creatinine clearance < 30 mL/min) requiring dialysis, corrected serum calcium level > 11.5 mg/dL, hemoglobin level < 8 g/dL, serum total bilirubin level > 2.0 mg/dL, and serum aspartate aminotransferase or alanine aminotransferase levels > 3.0 × upper limit of normal; †Thromboprophylaxis with low-dose aspirin, low-molecular-weight heparin, or equivalent was required for all patients; ‡Dose interruptions and reductions were allowed for POM and DEX for certain TEAEs; §Cycles 1-2: D1, 8, 15, 22; cycles 3-6: D1, 15; cycles 7+: D1; ¶IMWG criteria modified to include MR.

D, day; DOR, duration of response; EQ-5D, EuroQol 5 dimensions; IMWG, International Myeloma Working Group; mIMWG, modified International Myeloma Working Group; MR, minimal response; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PS, performance status; QOL, quality of life; SPM, second primary malignancy; TEAE, treatment-emergent adverse event; TTP, time to progression; TTR, time to response; y, years.

- Patients were followed for OS, subsequent treatment, and SPM for up to 5 years after the last patient was enrolled
- OS was calculated as the time from start of treatment until time of death from any cause
  - Patients were censored at the date last known to be alive
- Dose interruptions and reductions were allowed for certain TEAEs

Results

Baseline demographics and disease characteristics

- Among 112 patients enrolled in cohort B, 85 (75.9%) had disease refractory to LEN and 27 (24.1%) had relapsed disease following LEN (**Table 1**)
- In total, 69 (61.6%) and 43 (38.4%) patients had received 1 and 2 prior lines of treatment, respectively

Table 1. Baseline demographics and disease characteristics

	MM-014 cohort B (n = 112)
Median (range) age, years	66.5 (39-83)
≤ 65 years	50 (44.6)
> 65 to ≤ 75 years	50 (44.6)
> 75 years	12 (10.7)
Male/Female	76 (67.9)/36 (32.1)
Race	
White	91 (81.3)
Black or African American	10 (8.9)
Asian	6 (5.4)
Other	5 (4.5)
ECOG PS[a]	
0	44 (39.3)
1	67 (59.8)
R-ISS stage	
I	31 (27.7)
II	52 (46.4)
III	8 (7.1)
NE	21 (18.8)
Median (range) time from first diagnosis, years	3.4 (0.5-11.5)
Status of most recent prior LEN-containing treatment	
LEN-relapsed	27 (24.1)
LEN-refractory	85 (75.9)
Prior lines of therapy	
1	69 (61.6)
2	43 (38.4)
Prior stem cell transplant	78 (69.6)

Presented as n (%) unless otherwise indicated.

[a]One patient had an ECOG PS of 2.

NE, not evaluable; R-ISS, revised International Staging System.

Patient disposition and drug exposure

- At a median (range) follow-up of 41.9 (0.4-73.1) months, with a data cutoff of December 16, 2022, 97 (86.6%) patients had discontinued treatment, most commonly due to disease progression (**Table 2**)

Table 2. Patient disposition

Disposition, n (%)	MM-014 cohort B (n = 112)
Patients continuing treatment	15 (13.4)
Reasons for treatment discontinuation	
Disease progression	54 (48.2)
Withdrawal by patient	23 (20.5)
AE	10 (8.9)
Death	3 (2.7)
Transition to commercially available treatment	2 (1.8)
Other	3 (2.7)
Unknown	2 (1.8)
Patients continuing in follow-up	22 (19.6)
Reasons for discontinuation from study	
Death	50 (44.6)
Withdrawal by patient	19 (17.0)
Lost to follow-up	2 (1.8)
Other	4 (3.6)

AE, adverse event.

- At follow-up, 75 (67.0%) patients had discontinued from the study, most commonly due to death
  - Of the 50 patients who died, 47 died off treatment, during the long-term follow-up
- Patients received POM, DEX, and DARA for median (range) durations of 15.7 (0.3-73.1), 13.7 (< 0.1-72.5), and 15.2 (< 0.1-72.7) months, respectively (**Table 3**)

Efficacy

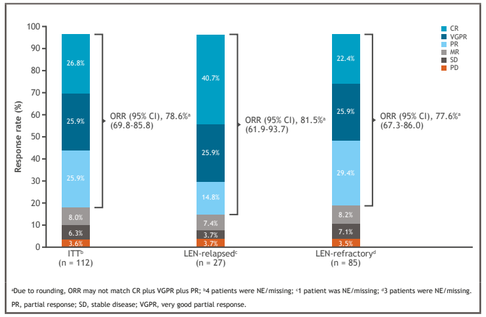
Overall response rate

- The ORR was 78.6% in the ITT population, 81.5% in the LEN-relapsed population, and 77.6% in the LEN-refractory population (**Figure 2**)
- The complete response (CR) rate was 26.8% in the ITT population, 40.7% in the LEN-relapsed population, and 22.4% in the LEN-refractory population

Table 3. Drug exposure

	MM-014 cohort B (n = 112)
Median treatment duration, months (range)	
POM	15.7 (0.3-73.1)
DEX	13.7 (< 0.1-72.5)
DARA	15.2 (< 0.1-72.7)
Median number of treatment cycles (range)	
POM	17.0 (1-77)
DEX	15.0 (1-77)
DARA	17.0 (1-78)
Patients with ≥ 1 dose reduction	
POM	52 (46.4)
DEX	52 (46.4)
DARA	3 (2.7)

Figure 2. Best overall response



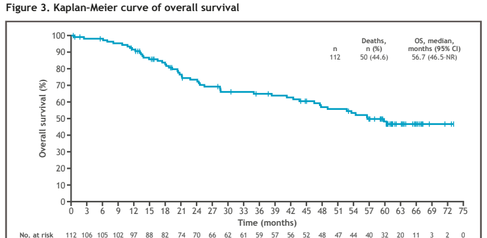
[a]Due to rounding, ORR may not match CR plus VGPR plus PR; [b]4 patients were NE/missing; [c]1 patient was NE/missing; [d]3 patients were NE/missing.

PR, partial response; SD, stable disease; VGPR, very good partial response.

Overall survival

- Fifty (44.6%) patients died, mostly due to PD (n = 28 [25.0%]; **Figure 3**)
- The median OS was 56.7 months (95% CI, 46.5-not reached [NR])
  - Median OS was NR (95% CI, 47.6-NR) for the LEN-relapsed group and 53.6 months (28.6-NR) for the LEN-refractory group

Figure 3. Kaplan-Meier curve of overall survival



	MM-014 cohort B (n = 112)
Deaths, n (%)	50 (44.6)
Causes of death, n (%)	
PD	28 (25.0)
AE	5 (4.5)
Other primary malignancy[a]	2 (1.8)
Other/unknown	15 (13.4)

[a]Includes complication due to other primary malignancy.

Presented at EHA 2023. Abstract P882.[3]

- Median OS was similar regardless of number of prior lines of therapy (**Figure 4**)
- Median OS was similar in pre-specified patient subgroups (**Figure 5**)

Figure 4. Kaplan-Meier estimate of overall survival by prior lines of therapy

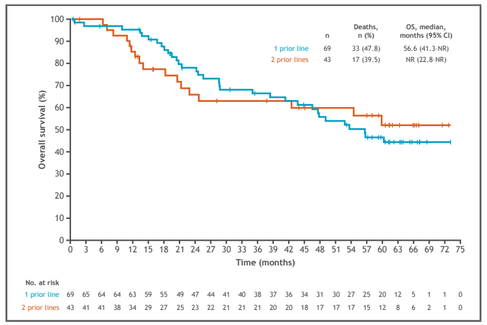
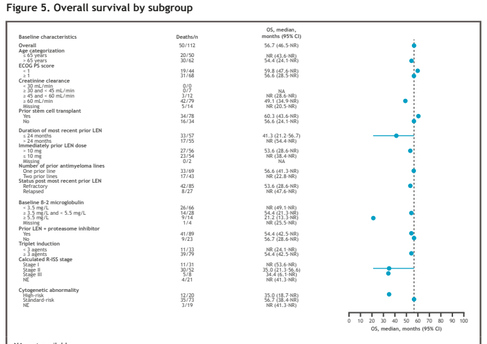


Figure 5. Overall survival by subgroup



NA, not available.

Progression-free survival

- At the data cutoff, the median PFS in the ITT population was 23.7 months (95% CI, 15.8-36.1)

Subsequent therapies

- A total of 64 (57.1%) patients received subsequent therapy, most commonly bortezomib/cyclophosphamide/DEX (n = 7 [6.3%])
- In the regimen following DPd treatment, only 1 patient each received chimeric antigen receptor T-cell therapy and T-cell engager therapy (elranatamab; data not shown)

Safety

- The most common grade 3/4 TEAEs were neutropenia (n = 72 [64.3%]), anemia (n = 22 [19.6%]), pneumonia (n = 20 [17.9%]), and thrombocytopenia (n = 16 [14.3%]) (**Table 4**)
- TEAEs leading to discontinuation of POM, DEX, or DARA occurred in 7 (6.3%), 9 (8.0%), and 6 (5.4%) patients, respectively (**Table 5**)
- A total of 31 (27.7%) and 38 (33.9%) patients experienced treatment-related TEAEs leading to POM and DEX reduction, respectively, while 55 (49.1%), 17 (15.2%), and 65 (58.0%) experienced treatment-related TEAEs leading to POM, DEX, and DARA interruption, respectively
- Neutropenia was the most common treatment-related TEAE leading to dose modification of POM (reduction, n = 17 [15.2%]; interruption, n = 38 [33.9%]) and DARA (interruption, n = 30 [26.8%])
- Insomnia was the most common treatment-related TEAE leading to dose modification of DEX (reduction, n = 10 [8.9%]; interruption, n = 1 [0.9%])

Table 4. Grade 3/4 treatment-emergent adverse events

TEAEs occurring in ≥ 5% of patients, n (%)	MM-014 cohort B (n = 112)
Hematologic TEAEs	
Neutropenia	72 (64.3)
Anemia	22 (19.6)
Thrombocytopenia	16 (14.3)
Febrile neutropenia	11 (9.8)
Leukopenia	11 (9.8)
Non-hematologic TEAEs	
Pneumonia	20 (17.9)
Neutrophil count decreased	10 (8.9)
Hypertension	10 (8.9)
Dyspnea	8 (7.1)
Back pain	7 (6.3)
Fatigue	7 (6.3)
White blood cell count decreased	6 (5.4)
Sepsis	6 (5.4)
Chronic obstructive pulmonary disease	6 (5.4)
Hyperglycemia	6 (5.4)
Hypokalemia	6 (5.4)
Atrial fibrillation	6 (5.4)
Insomnia	6 (5.4)

Table 5. Treatment-emergent adverse events leading to dose modification or discontinuation

Patients reporting TEAEs, n (%)	MM-014 cohort B, ITT (n = 112)		
	POM	DEX	DARA
Leading to discontinuation of and related to study drug	7 (6.3)[a]	9 (8.0)[a]	6 (5.4)[b]
Leading to dose reduction of and related to study drug	31 (27.7)	38 (33.9)	0
Occurred in ≥ 5% of patients for any drug			
Neutropenia	17 (15.2)	0	0
Insomnia	0	10 (8.9)	0
Peripheral edema	0	6 (5.4)	0
Leading to dose interruption of and related to study drug	55 (49.1)	17 (15.2)	65 (58.0)
Occurred in ≥ 5% of patients for any drug			
Neutropenia	38 (33.9)	3 (2.7)	30 (26.8)
Pneumonia	7 (6.3)	5 (4.5)	5 (4.5)
Leukopenia	4 (3.6)	0	6 (5.4)
Infusion-related reaction	0	0	26 (23.2)

[a]Included 1 case each of leukopenia and thrombocytopenia; [b]Included 1 case each of leukopenia, thrombocytopenia, and febrile neutropenia.

Conclusions

- At a median follow-up of 41.9 months, patients in MM-014 cohort B demonstrated a favorable median OS of 56.7 months (95% CI, 46.5-NR)
  - In patients who had relapsed disease following LEN, median OS was NR (95% CI, 47.6-NR) and in patients whose disease was LEN-refractory, median OS was 53.6 months (95% CI, 28.6-NR)
- The safety profile of DPd was similar to that which has been reported previously with no new safety signals identified
- Given the high response rates and encouraging safety profile of DPd, a class switch may not be necessary in patients who experience PD on or after LEN
- These results suggest DPd may be beneficial for patients with RRMM who have exhausted the benefits of LEN in early lines of therapy

References

1. Holstein SA, et al. *Ther Adv Hematol* 2018;9:175-190.
2. Bahlis NJ, et al. *Leuk Lymphoma* 2022;63:1407-1417.
3. Bahlis NJ, et al. *HemaSphere* 2023;7(S3):1660-1661.

Acknowledgments

- The patients, families, and caregivers who made the study possible
- All the MM-014 co-investigators
- This study was supported by Bristol Myers Squibb
- All authors contributed to and approved this poster
- Writing and editorial assistance were provided by Richard Sora, PhD, of Caudex, funded by Bristol Myers Squibb

These data were previously presented at the European Hematology Association (EHA) Congress 2023 in Frankfurt, Germany (June 8-11, 2023)

Scientific Content on Demand
To request this poster
Scan QR code via a barcode reader application
QR codes are used for ad-hoc requests. For congress presentations only.

Copies of this poster obtained through Quick Response (QR) code are for personal use only and may not be reproduced without permission from the author of this poster