Iberdomide, daratumumab, and dexamethasone in transplant-ineligible/deferred newly diagnosed multiple myeloma: updated results from the CC-220-MM-001 trial

MM-578

Anna Sureda Balari,[1] Abdullah M. Khan,[2] Albert Oriol,[3] Mercedes Gironella Mesa,[4] Faiz Anwer,[5] Cristina Encinas Rodríguez,[6] Brea C. Lipe,[7] Paula Rodríguez-Otero,[8] Michael Amatangelo,[9] Danny Jeyaraju,[9] Kexin Jin,[9] Thomas Solomon,[9] Lilia Taningco,[9] Olumoroti Aina,[9] Paulo Maciag,[9] Sagar Lonial[10]

[1]Hematology Department, Institut Català d'Oncologia - Hospitalet, IDIBELL, University of Barcelona, Barcelona, Spain; [2]The James Cancer Hospital and Solove Research Institute, The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [3]Catalan Institute of Oncology and Josep Carreras Institute, Hospital Germans Trias i Pujol, Badalona, Spain; [4]Hematology Department, Vall d'Hebron Hospital, Barcelona, Spain; [5]Department of Hematology and Medical Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, USA; [6]Hospital General Universitario Gregorio Marañón (HGUGM), IiSGM, Madrid, Spain; [7]Department of Medicine, University of Rochester Medical Center, Rochester, NY, USA; [8]Clínica Universidad de Navarra, CIMA, IDISNA, CIBERONC, Pamplona, Spain; [9]Bristol Myers Squibb, Princeton, NJ, USA; [10]Winship Cancer Institute, Emory University, Atlanta, GA, USA

Introduction

- Lenalidomide (LEN) plus an anti-CD38 monoclonal antibody and dexamethasone (DEX) is a standard of care for patients with transplant-ineligible (TNE)/transplant-deferred newly diagnosed multiple myeloma (NDMM)[1]
  - In the MAIA and BENEFIT trials, minimal residual disease (MRD) negativity was achieved by less than one-third of patients, suggesting a high-unmet need for therapies that achieve deep and durable responses in patients with TNE NDMM[2,3]
- Iberdomide (IBER) is a CELMoD agent with superior potency than LEN and may provide additional therapeutic benefit when given in combination with daratumumab (DARA) and DEX (IberDd)[4] (**Figure 1**)
  - IBER binds cereblon (CRBN) with higher affinity and unique interactions compared with immunomodulatory drug (IMiD®) agents; preclinically, IBER has shown deep MM-cell killing in combination with DARA versus IMiD agents[4,5]
- The synergistic activity of IberDd has been observed in the ongoing phase 1/2 CC-220-MM-001 clinical trial (NCT02773030)
  - Preliminary results show high response rates (94.7%) and a manageable safety profile in TNE/transplant-deferred NDMM[6]

Figure 1. IBER mechanism of action

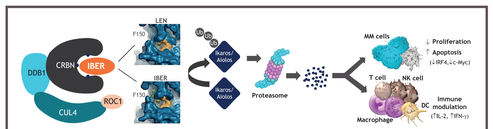


Figure adapted with permission from Lonial S, et al. *Future Oncol* 2025;21:1761-1769. © The Authors 2025. Permission granted by The Authors. *c-Myc*, cellular Myc; CUL4, cullin 4; DC, dendritic cell; DDB1, DNA damage-binding protein 1; IFN, interferon; IL, interleukin; IRF4, interferon regulatory factor 4; NK, natural killer; ROC1, regulator of cullins-1; Ub, ubiquitin.

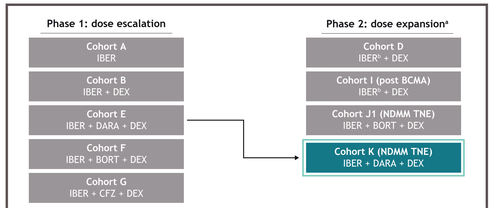
Objective

- To report updated results with extended follow-up from the IberDd dose-expansion cohort of the CC-220-MM-001 trial in patients with NDMM who are TNE or not receiving autologous stem cell transplant (ASCT) as their first therapy

Methods

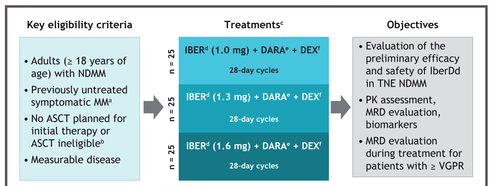
- CC-220-MM-001 is a phase 1/2 trial evaluating IBER with different treatment combinations in MM (**Figure 2**)
- Key patient eligibility criteria, treatments, and objectives are shown in **Figure 3**
- The data cutoff date for the analysis was March 3, 2025

Figure 2. CC-220-MM-001 study design



[a]Cohorts C (IBER monotherapy expansion) and J2 (IBER + BORT + DEX in patients with NDMM who are transplant eligible) were planned but not opened; [b]1.6 mg on D1-21 of 28-day cycles. BCMA, B-cell maturation antigen; BORT, bortezomib; CFZ, carfilzomib; D, day(s).

Figure 3. Patients, treatments, and endpoints



IBER: D1-21 of each cycle
DARA: 1800 mg SC, QW C1-2, Q2W C3-6, Q4W C ≥ 7
DEX: 40 mg (20 mg if > 75 years of age) QW

[a]Radiotherapy, bisphosphonates, or a single short course of steroids were permitted; [b]Due to age (≥ 65 years) or severe comorbidities; [c]Venous thromboembolism prophylaxis was administered from C1D1 until end of treatment; [d]IBER was given orally on D1-21; [e]DARA was given SC at 1800 mg on D1, 8, 15, and 22 during C1-2, D1 and 15 during C3-6, and D1 on C ≥ 7; [f]DEX was given orally at a dose of 40 mg on D1, 8, 15, and 22, or a dose of 20 mg in patients > 75 years of age. C, cycle; PK, pharmacokinetics; QW, once a week; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; VGPR, very good partial response.

Results

- Baseline characteristics are shown in **Table 1**

Table 1. Baseline characteristics

Characteristic[a]	IberDd TNE NDMM (N = 75)
Age, median (range), years	75 (44-90)
≥ 75 years of age, n (%)	44 (58.7)
Sex, n (%)	
Male	42 (56.0)
Race, n (%)	
White	53 (70.7)
Asian	11 (14.7)
Black or African American	4 (5.3)
Other or not reported	7 (9.3)
Time since diagnosis, median (range), years	0.1 (0-11.3)
ECOG PS, n (%)	
0	23 (30.7)
1	43 (57.3)
2	9 (12.0)
ISS stage at study entry,[b] n (%)	
I	30 (40.0)
II	30 (40.0)
III	14 (18.7)
Presence of plasmacytomas,[c] n (%)	6 (8.0)
High-risk cytogenetics,[d,e] n (%)	31 (41.3)

[a]Data cutoff: March 3, 2025; [b]1/75 patients was missing; [c]Including paraosseous and extramedullary lesions; [d]Defined as the presence of any abnormality for del(17p), and/or translocation t(4,14), and/or translocation t(14,16), and/or amplification 1q21; [e]9/75 patients were missing or not evaluable. del(17p), deletion of the short arm (p) of chromosome 17; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System.

- At almost 2 years median follow-up, 66.7% of patients remained on therapy (**Table 2**)
  - No deaths were attributed to study treatment

Table 2. Treatment disposition

Treatment disposition[a]	IberDd TNE NDMM (N = 75)
Follow-up, median (range), months	22.3 (0.4-28.5)
Ongoing, n (%)	50 (66.7)
Discontinued, n (%)	25 (33.3)
AE[b]	9 (12.0)
Progressive disease	7 (9.3)
Patient withdrawal	4 (5.3)
Death[c]	3 (4.0)
Physician decision	2 (2.7)

[a]Data cutoff: March 3, 2025; [b]9 patients discontinued treatment due to AEs: 3 general physical health deterioration, 1 cytomegalovirus chorioretinitis, 1 acute kidney injury, 1 hypoxia, 1 anemia/neutropenia, 1 peripheral neuropathy, and 1 peripheral sensory neuropathy; [c]3 patients died during the treatment period due to grade 5 AEs: 1 intestinal ischemia, 1 aspiration pneumonia with sepsis, and 1 death from an unknown cause. AE, adverse event.

- Neutropenia was the most common grade 3/4 hematologic treatment-emergent adverse event (TEAE) (78.7%); few grade 3/4 non-hematologic TEAEs, excluding infections, occurred (**Table 3**)
  - Grade 3/4 diarrhea not reported to date

Table 3. Common (≥ 25% all grade) TEAEs and TEAEs of interest

Most common (≥ 25% all grade) TEAEs and TEAEs of interest,[a] n (%)	IberDd TNE NDMM (N = 75)		
	All grade	Grade 3	Grade 4
Any TEAE	75 (100)	34 (45.3)	39 (52.0)
Hematologic TEAEs			
Neutropenia	62 (82.7)	26 (34.7)	33 (44.0)
Febrile neutropenia	9 (12.0)	9 (12.0)	0
Anemia	29 (38.7)	10 (13.3)	1 (1.3)
Lymphopenia	25 (33.3)	11 (14.7)	5 (6.7)
Leukopenia	17 (22.7)	8 (10.7)	3 (4.0)
Thrombocytopenia	16 (21.3)	2 (2.7)	1 (1.3)
Infections	68 (90.7)	35 (46.7)	4 (5.3)
Pneumonia[b]	29 (38.7)	24 (32.0)	3 (4.0)
COVID-19[c]	28 (37.3)	4 (5.3)	0
Non-hematologic TEAEs			
Peripheral edema	27 (36.0)	0	0
Constipation	27 (36.0)	0	0
Rash[d]	24 (32.0)	3 (4.0)	0
Fatigue	22 (29.3)	1 (1.3)	0
Pyrexia	22 (29.3)	3 (4.0)	0
Nausea	21 (28.0)	2 (2.7)	0
Diarrhea	20 (26.7)	0	0
Back pain	20 (26.7)	1 (1.3)	0
Insomnia	20 (26.7)	1 (1.3)	0
Asthenia	19 (25.3)	3 (4.0)	0
Hypocalcemia	19 (25.3)	2 (2.7)	1 (1.3)
Hypogammaglobulinemia	19 (25.3)	0	0
Peripheral sensory neuropathy	16 (21.3)	1 (1.3)	0
Second primary malignancies[e]	5 (6.7)	0	0
Deep vein thrombosis	2 (2.7)	1 (1.3)	0

[a]Data cutoff: March 3, 2025; [b]Including influenzal pneumonia, bacterial pneumonia, cryptococcal pneumonia, *Pneumocystis jirovecii* pneumonia, parainfluenzae viral pneumonia, Legionella pneumonia, pneumococcal pneumonia, and respiratory syncytial viral pneumonia; [c]Including COVID-19 pneumonia; [d]Including maculo-papular rash, macular rash, follicular rash, and pruritic rash; [e]Including only bladder neoplasm, basal cell carcinoma, and squamous cell carcinoma. COVID-19, coronavirus disease 2019.

- No significant safety trends were observed across IBER dose levels (**Table 4**)

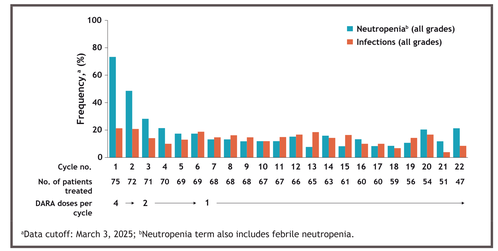
Table 4. TEAEs of interest by IBER dose level

TEAEs of interest,[a] n (%)	IberDd 1.0 mg (n = 25)			IberDd 1.3 mg (n = 25)			IberDd 1.6 mg (n = 25)		
	All grade	Grade 3	Grade 4	All grade	Grade 3	Grade 4	All grade	Grade 3	Grade 4
Hematologic TEAEs									
Neutropenia	19 (76.0)	8 (32.0)	11 (44.0)	22 (88.0)	8 (32.0)	13 (52.0)	21 (84.0)	10 (40.0)	9 (36.0)
Febrile neutropenia	2 (8.0)	2 (8.0)	0	2 (8.0)	2 (8.0)	0	5 (20.0)	5 (20.0)	0
Anemia	8 (32.0)	1 (4.0)	0	13 (52.0)	4 (16.0)	0	8 (32.0)	5 (20.0)	1 (4.0)
Thrombocytopenia	5 (20.0)	0	1 (4.0)	5 (20.0)	1 (4.0)	0	6 (24.0)	1 (4.0)	0
Non-hematologic TEAEs									
Fatigue	8 (32.0)	1 (4.0)	0	8 (32.0)	0	0	6 (24.0)	0	0
Rash[b]	11 (44.0)	2 (8.0)	0	6 (24.0)	1 (4.0)	0	7 (28.0)	0	0
Diarrhea	5 (20.0)	0	0	6 (24.0)	0	0	9 (36.0)	0	0
Infections	23 (92.0)	12 (48.0)	0	22 (88.0)	12 (48.0)	2 (8.0)	23 (92.0)	11 (44.0)	2 (8.0)
Pneumonia[c]	9 (36.0)	8 (32.0)	0	12 (48.0)	10 (40.0)	2 (8.0)	8 (32.0)	6 (24.0)	1 (4.0)
COVID-19[d]	9 (36.0)	1 (4.0)	0	8 (32.0)	1 (4.0)	0	11 (44.0)	2 (8.0)	0

[a]Data cutoff: March 3, 2025; [b]Including maculo-papular rash, macular rash, follicular rash, and pruritic rash; [c]Including influenzal pneumonia, bacterial pneumonia, cryptococcal pneumonia, *P jirovecii* pneumonia, parainfluenzae viral pneumonia, Legionella pneumonia, pneumococcal pneumonia, and respiratory syncytial viral pneumonia; [d]Including COVID-19 pneumonia.

- The incidence of neutropenia was more frequent in the first 2 cycles, consistent with the more frequent DARA dosing, and decreased over time (**Figure 4**)

Figure 4. Neutropenia and infections by cycle



[a]Data cutoff: March 3, 2025; [b]Neutropenia term also includes febrile neutropenia.

- IBER treatment was generally well tolerated, and toxicities were managed by dose modifications (**Table 5**)

Table 5. Dose modifications and treatment exposure by IBER dose level

Dose modifications[a,b]	IberDd 1.0 mg (n = 25)	IberDd 1.3 mg (n = 25)	IberDd 1.6 mg (n = 25)	IberDd TNE NDMM (N = 75)
Patients with ≥ 1 IBER dose modification,[c] n (%)	24 (96.0)	25 (100)	24 (96.0)	73 (97.3)
IBER dose interruptions due to TEAEs, n (%)	22 (88.0)	22 (88.0)	20 (80.0)	64 (85.3)
IBER dose reductions due to TEAEs, n (%)	8 (32.0)	14 (56.0)	13 (52.0)	35 (46.7)
Treatment exposure[a,b]				
Treatment duration, median (range), months	22.6 (0.5-28.5)	22.4 (4.3-29.0)	21.9 (0.3-28.6)	22.4 (0.3-29.0)
Cycles received, median (range), n	23.0 (1.0-31.0)	22.0 (4.0-31.0)	23.0 (1.0-29.0)	23.0 (1.0-31.0)
RDI[d] of IBER, % (range)	91.6 (33.5-100)	79.6 (52.8-94.3)	80.1 (16.7-99.9)	82.2 (16.7-100)

[a]Data cutoff: March 3, 2025; [b]Data from the safety population; [c]Dose modification is defined as treatment adjustment for any reason; [d]Defined as (actual dose intensity/expected dose intensity) × 100. RDI, relative dose intensity.

- MRD negativity was 64.0%, and MRD negativity with ≥ complete response (CR) was 56.0% (**Table 6**)

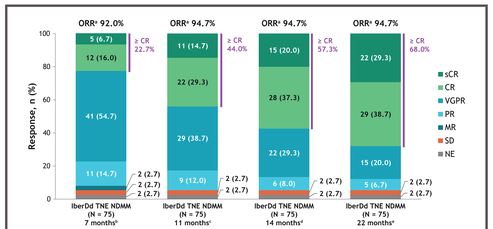
Table 6. MRD negativity rates and response

MRD negativity rates and response	IberDd TNE NDMM (N = 75)
MRD negativity (10^{-5}) rate,[a] n (%)	48 (64.0)
MRD negativity (10^{-5}) rate[a] with ≥ CR, n (%)	42 (56.0)
TTFR,[b] median (range), months	1.0 (0.9-11.3)
DOR,[b,c] median (range), months	NR (NR-NR)

Data cutoff: March 3, 2025; [a]MRD was assessed using the EuroFlow assay at a threshold of 10^{-5}; [b]As assessed in the 71 patients who achieved response; [c]Univariate analysis for all responders without adjusting for censoring. DOR, duration of response; NR, not reached; TTFR, time to first response.

- By 22 months, overall response rate (ORR) was 94.7% and responses deepened over time (**Figure 5**)
  - The rate of ≥ CR was 68.0%

Figure 5. Response over time



[a]PR or better; [b]Data cutoff: October 25, 2023; [c]Data cutoff: February 28, 2024; [d]Data cutoff: May 29, 2024; [e]Data cutoff: March 3, 2025. MR, minimal response; NE, not evaluable; PR, partial response; sCR, stringent complete response; SD, stable disease.

Conclusions

- At 22 months, IberDd continues to show deepening responses in TNE NDMM
  - Many responses were rapid, and ≥ CR rates improved from 44.0% to 68.0% within 12 months
  - MRD negativity rate with ≥ CR was 56.0% and no plateau has been observed, which is notable in the context of DARA, LEN, and DEX in NDMM[2]
- The safety profile of IberDd was manageable, with no new safety signals
  - Most common grade 3/4 TEAE was neutropenia
  - Few patients discontinued IBER due to AEs; 66.7% are still on treatment
- These results support the evaluation of IberDd in TNE NDMM and the role of novel therapies in achieving deep and durable responses in NDMM and RRMM
  - IberDd is also being investigated in the ongoing phase 3 EXCALIBER-RRMM trial (NCT04975997)

References

1. Facon T, et al. *Adv Ther* 2022;39:1976-1992.
2. Facon T, et al. *Leukemia* 2025;39:942-950.
3. Leleu X, et al. *Nat Med* 2024;30:2235-2241.
4. Bjorklund CC, et al. *Leukemia* 2020;34:1197-1201.
5. Ma P, et al. *Blood* 2023;142(suppl 1). Abstract 3289.
6. Sureda Balari A, et al. *Clin Lymphoma Myeloma Leuk* 2024;24(suppl 2):S35.

Acknowledgments

- The patients and families who are making the study possible
- The clinical study teams who participated
- All the investigators of the CC-220-MM-001 trial
- This study was supported by Celgene, a Bristol-Myers Squibb Company
- All authors contributed to and approved the presentation; professional medical writing and editorial assistance were provided by Ana Almeida, MSc, of the Publications Division of Omnicom Health Medical Communications, funded by Bristol Myers Squibb

Presented at the Society of Hematologic Oncology (SOHO) Annual Meeting; September 9-12, 2026, Chicago, IL, USA.
Previously presented at the International Myeloma Society (IMS) Meeting and Exposition; September 17-20, 2025; Toronto, ON, Canada.