Bortezomib-melphalan-prednisone *versus* lenalidomide-dexamethasone in elderly patients with multiple myeloma: the Real MM phase IV trial

In patients with newly diagnosed multiple myeloma (NDMM) ineligible for autologous stem-cell transplantation (NTE), the standard first-line therapies until the introduction of daratumumab were bortezomib-melphalan-prednisone (VMP) and lenalidomide-dexamethasone (Rd),[1] which were approved on the basis of data from the VISTA and FIRST phase III trials.[2,3] To our knowledge, the Real MM trial reported here (clinicaltrials.gov NCT03829371), funded by the Italian Medicines Agency AIFA (Independent Research program), is the first prospective, multicenter, randomized trial comparing VMP *versus* Rd in a real-life elderly population of NDMM patients.

Transplant ineligibility was defined by age ≥65 years or comorbidities. Patients were stratified by frailty (International Myeloma Working Group [IMWG] Frailty Score: fit *vs*. intermediate-fit *vs*. frail patients)[4] and cytogenetic risk (high risk [presence of t(4;14), t(14;16), or del(17p)] by fluorescence *in situ* hybridization [FISH] *vs*. standard risk) and randomized 1:1 to receive VMP (9 cycles) or continuous Rd per approved schedule. The primary endpoint was progression-free survival (PFS); secondary endpoints included overall response rate (ORR), overall survival (OS), progression after the next line of therapy (PFS2), time to next treatment (TNT), quality of life (QoL), and safety. This trial was reviewed and approved by the institutional review boards or independent ethics committees at each of the participating centers. All patients provided written informed consent before participating in the trial, which was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Following the introduction of daratumumab in first-line treatment for NTE patients, the protocol was amended, and, as of July 2022, enrolled patients have been randomized to receive daratumumab-VMP or daratumumab-Rd.

Between 10th January 2019 and 26th January 2022, 231 patients were randomized to receive VMP (N=114) *versus* Rd (N=117). Baseline characteristics were well balanced (Table 1). At the data cut-off (29th May 2023), the median follow-up among surviving patients was 28.94 months (Interquartile Range [IQR]: 20.21-37.13), and 56% of VMP patients completed therapy, while 33.3% of Rd patients remained on treatment, with a median duration of treatment of 16 months (IQR: 5.7-32) (*Online Supplementary Figure S1*).

The median PFS was 28.8 *versus* 26.6 months in the VMP *versus* Rd arms (Hazard Ratio [HR]: 0.93, 95% Confidence Interval [CI]: 0.63-1.38, *P*=0.72) (Figure 1A). However, the HR changed over time (*P* from the Grambsch and Therneau test =0.076): 0.64 during the first year of treatment (95% CI: 0.37-1.12, *P*=0.12) and, thereafter, 1.32 (95% CI: 0.74-2.36, *P*=0.34). The prespecified subgroup analysis according to cytogenetic risk showed a significant effect modification in terms of PFS between VMP and Rd (interaction *P*=0.018), with a median PFS of 30.0 (95% CI: 16.5-not reached [NR]) *versus* 10.4 months (95% CI: 7.8-NR) in the high-risk group (HR: 0.33, 95% CI: 0.12-0.92) and of 22.7 (95% CI: 17.7-39.4) *versus* 33.3 months (95% CI: 26.1-NR) in the standard-risk group (HR: 1.30, 95% CI: 0.80-2.09). No significant differences in terms of PFS were observed in other subgroups (Figure 1B).

Overall response rate (71% *vs*. 73%, *P*=0.90) and the rates of very good partial response or better (≥VGPR) (49% *vs*. 44%, *P*=0.56) were similar in the two arms, with a trend toward a higher complete response or better (≥CR) in the VMP arm (13% *vs*. 5%, *P*=0.058).

The estimated 36-month OS was 83% with VMP *versus* 67% with Rd (HR: 0.52, 95% CI: 0.29-0.93, *P*=0.028) (Figure 2A). This advantage was also confirmed after censoring for daratumumab use in second line (HR: 0.53, 95% CI: 0.28-0.99, *P*=0.045). A survival advantage of VMP over Rd was also observed in both high-risk and standard-risk subgroups, with a greater benefit in high-risk patients (HR: 0.23 *vs*. 0.66) (Figure 2B), while frail patients (HR 0.41, 95% CI: 0.19-0.91) and intermediate-fit patients (HR: 0.46, 95% CI: 0.12-1.79) obtained a slight benefit from VMP as compared with fit patients (HR: 1.11, 95% CI: 0.29-4.15, interaction *P*=0.45).

The estimated 36-month PFS2 was significantly better with VMP (82% *vs*. 63%, HR: 0.52, *P*=0.017) (*Online Supplementary Figure S2A*). Following disease progression (91 events), 67% of patients received second-line treatment. A second subsequent therapy line including daratumumab was more commonly used in the VMP *versus* Rd arm (60% *vs*. 23%). TNT was similar between the two arms (*Online Supplementary Figure S2B*).

Grade (G)3-4 treatment-emergent adverse events (AE) occurred in 42% of VMP *versus* 52% of Rd patients (*Online Supplementary Table S1*). The incidence of G3-4 neutropenia was similar in the two arms (19% *vs*. 25%); G3-4 thrombocytopenia occurred in 15% *versus* 0% (*P*<0.0001); G3-4 infections in 4% *versus* 9% of patients (*P*=0.17), of which 2% *versus* 4% were pneumonia; G3-4 peripheral neuropathy (PNP) in 6% *versus* 1% (*P*=0.06), while G1-2 PNP in 48% *versus* 10% (*P*<0.001); the incidence of G3-4 gastrointestinal disorders was similar in the two arms (5% *vs*. 4%); skin-related disorders occurred in 1% *versus* 11% (*P*=0.003).

Serious AE occurred in 37% *versus* 47% of patients in the VMP *versus* Rd arms: cardiac failure was the most common (8%) with VMP, while SARS-CoV-2 pneumonia was the most common (10%) with Rd. Treatment-emergent deaths were rare (≤1% in both arms).

Dose reductions were frequent in both arms. In the VMP arm, 66% of patients had ≥1 dose reduction, mainly in bortezomib (52%). Of note, 39% switched to once-weekly bortezomib administration before the fifth cycle. Rd patients also frequently required dose reductions of lenalidomide (49%) and dexamethasone (47%). In both arms, more treatment discontinuations occurred in frail (41% in the VMP *vs*. 67% in the Rd arm) than in intermediate-fit (36% *vs*. 59%) and fit (38% *vs*. 63%) patients.

Although this trial showed no significant difference in PFS between the VMP (median, 28.8 months) and Rd arm (median, 26.6), the results compared favorably with those of prior studies, likely reflecting better management over time through dose reductions, weekly bortezomib administration, and longer treatment durations. Interestingly, the HR for PFS changed over time, favoring VMP during the first 12 months (HR: 0.64), while favoring Rd thereafter (HR: 1.32), likely reflecting the benefit of continuous lenalidomide therapy, already confirmed in prior trials (e.g., FIRST and MM-015).[5,6]

The aim of this study was also to identify the subgroups who would benefit most from each combination. In high-risk patients, VMP significantly improved PFS compared with Rd (HR: 0.33, interaction *P*=0.0018). No difference in PFS was observed in standard-risk, frail, or renally impaired

Table 1. Baseline patient characteristics in the intention-to-treat population.

	VMP arm N=114	Rd arm N=117
Median age, years (range)	76.5 (66-91)	76 (67-86)
Age, years, N (%)		
≤75	48 (42)	57 (49)
75-80	41 (36)	40 (34)
>80	25 (22)	20 (17)
ISS stage, N (%)		
I	23 (20)	33 (28)
II	47 (41)	38 (32)
III	44 (39)	46 (39)
R-ISS stage, N (%)		
I	17 (16)	22 (21)
II	74 (70)	66 (62)
III	15 (14)	18 (17)
Missing	8	11
ECOG PS, N (%)		
0	56 (49)	44 (38)
1	41 (36)	44 (38)
2	15 (13)	17 (15)
3	2 (2)	11 (9)
4	-	1 (1)
Serum LDH ≥ULN, N (%)	18 (16)	17 (15)
Frailty Score, N (%)		
Fit	30 (26)	27 (25)
Intermediate-fit	27 (24)	31 (26)
Frail	57 (50)	59 (50)
Creatinine clearance: mL/min, N (%)		
0-30	10 (9)	11 (10)
30-50	30 (27)	25 (22)
>50	73 (65)	79 (69)
Missing	1	2
Cytogenetic profile, N (%)		
Standard	82 (83)	77 (81)
High*	17 (17)	18 (19)
Missing	15	22

*High cytogenetic risk was defined as the presence of t(4;14), t(14;16), or del(17p). del: deletion; ECOG PS: Eastern Cooperative Oncology Group Performance Status; ISS: International Staging System; LDH: lactate dehydrogenase; N: number; Rd: lenalidomide-dexamethasone; R-ISS: Revised International Staging System; t: translocation; ULN: upper limit of normal; VMP: bortezomib-melphalan-prednisone.

patients. These findings are consistent with previous data, like those from the VISTA trial,[7] suggesting that bortezomib may overcome poor outcomes associated with high-risk cytogenetics. At the same time, Real MM, with the support of centralized FISH testing and patient stratification by frailty and cytogenetics, confirmed the limited benefit of lenalid-

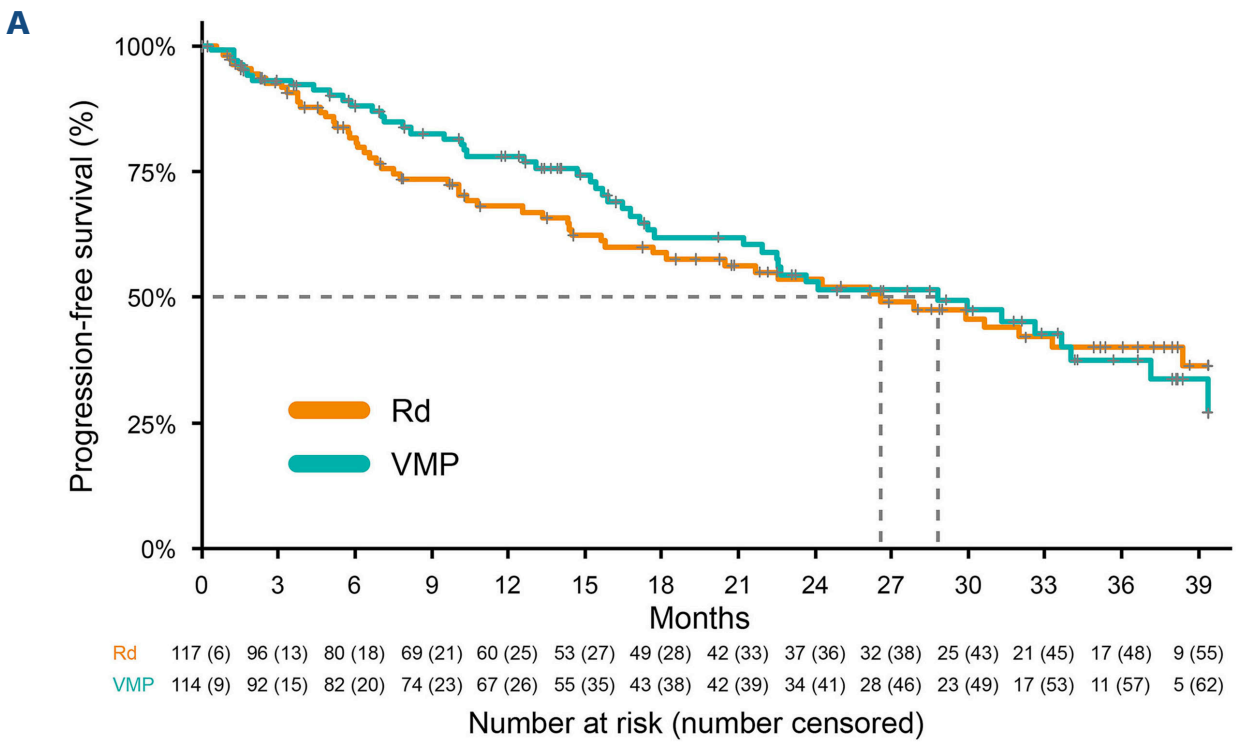

Figure 1. Progression-free survival in the intention-to-treat population. (A) Progression-free survival (PFS). (B) PFS subgroup analysis. CI: confidence interval; ECOG PS: Eastern Cooperative Oncology Group Performance Status; HR: Hazard Ratio; IMWG: International Myeloma Working Group; ISS: International Staging System; Rd: lenalidomide-dexamethasone; VMP: bortezomib-melphalan-prednisone.

omide in high-risk patients observed in the FIRST trial.[5] Although age has recently been associated with poorer PFS and OS in older patients,[8] no significant interaction between age and treatment arm was observed in our trial. This is consistent with findings from the BENEFIT trial, in which the rate of minimal residual disease negativity was

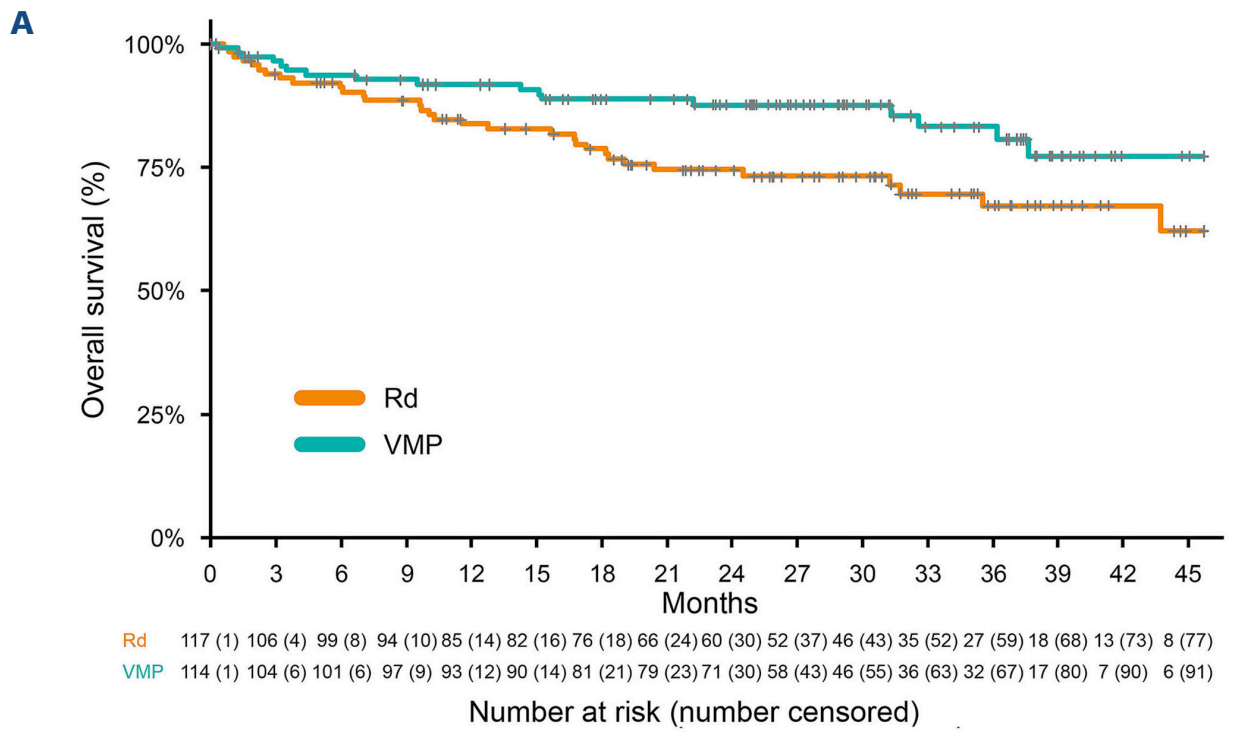

Figure 2. Overall survival in the intention-to-treat population. (A) Overall survival (OS). (B) OS: subgroup analysis. CI: confidence interval; ECOG PS: Eastern Cooperative Oncology Group Performance Status; HR: Hazard Ratio; IMWG: International Myeloma Working Group; ISS: International Staging System; Rd: lenalidomide-dexamethasone; VMP: bortezomib-melphalan-prednisone.

higher in the bortezomib-based arm among patients both above and below 75 years of age.[9]

Overall survival was notably longer in the VMP arm, with 17 deaths after a median follow-up of 28.9 months *versus* 32 in the Rd arm (HR: 0.52, *P*=0.028). This may reflect the PFS benefit in high-risk patients treated with VMP, lenalidomide refractoriness in the Rd arm, and differences in salvage therapy. More patients in the VMP arm received daratumumab at relapse, potentially improving outcomes. However, this benefit persisted after censoring for daratumumab use, highlighting the importance of treatment sequencing.

Our analysis is the first prospective evaluation of patients stratified by the IMWG frailty score. Frailty impacted discontinuation rates and mortality in both arms. However, no PFS differences emerged between the two arms in different frailty classes, while a slight OS benefit was observed in frail patients receiving VMP.

Our data showed that real-world practice can differ from the trial schedules, with 39% of patients in the VMP arm receiving once-weekly instead of twice-weekly bortezomib during the first four cycles, a strategy that has already been successfully explored with other modified regimens, such as lenalidomide-bortezomib-dexamethasone (RVD)-lite.[10] The improved tolerability of bortezomib has also helped its integration into more intensive regimens incorporating anti-CD38 antibodies, showing promising results in the IMROZ, CEPHEUS, and BENEFIT trials, even in elderly patients.[9,11,12] Nonetheless, the optimal schedule for bortezomib remains unclear, as it was administered twice weekly in the IMROZ trial and once weekly – but for a longer duration – in the BENEFIT trial.

In our study, fixed-duration VMP led to a longer treatment-free interval, which translated into better health-related QoL compared with continuous Rd.[13]

Regarding safety, both regimens exhibited known toxicity profiles.[2,7,14] As expected, thrombocytopenia and peripheral neuropathy were more common with VMP, whereas infections and dermatologic reactions were more common with Rd. The higher incidence of infections observed with Rd could have been influenced by glucocorticoid use. Reduced doses of dexamethasone, switching to prednisone, or early discontinuation could be better options for elderly or frail patients.[14]

Based on our data, both VMP and Rd remain effective and well-tolerated regimens, but VMP proved to be a preferable option due to its advantages in terms of PFS (particularly in patients with high cytogenetic risk) and OS. This real-world, prospective evidence may help guide front-line choices, particularly in settings where access to daratumumab is limited or in patients who are ineligible for more intensive approaches.

Enrollment in the daratumumab-VMP and daratumumab-Rd arms is ongoing, and their future comparison will further clarify the role of daratumumab in these combinations.

Authors

Sara Bringhen,[1] Lorenzo Cani,[2] Nicola Giuliani,[3] Silvia Mangiacavalli,[4] Giulia Benevolo,[1] Elisabetta Antonioli,[5] Renato Zambello,[6] Roberto Ria,[7] Iolanda Donatella Vincelli,[8] Sonia Ronconi,[9] Sonia Morè,[10] Antonietta Pia Falcone,[11] Alessandro Allegra,[12] Mattia D'Agostino,[2] Andrea Evangelista,[13] Andrea Capra,[14] Elisa Sciorsci,[15] Paola Curci,[16] Patrizia Tosi,[17] Anna Marina Liberati,[18] Anna Maria Cafro,[19] Angelo Belotti,[20] Francesca Patriarca,[21] Donato Mannina,[22] Katia Mancuso,[23,24] Francesco Cattel,[15] Giovannino Ciccone,[13] Benedetto Bruno,[2] Mario Boccadoro[14,25] and Alessandra Larocca[2]

[1]SSD Clinical Trial in Oncoematologia e Mieloma Multiplo, Department of Oncology, AOU Città della Salute e della Scienza di Torino, University of Torino, Torino; [2]Division of Hematology, AOU Città della Salute e della Scienza di Torino, University of Torino and Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino; [3]University of Parma & AOU Parma, Parma; [4]Division of Hematology, IRCCS Fondazione Policlinico San Matteo, Pavia; [5]Hematology Unit, AOU Careggi, Florence; [6]Department of Medicine (DIMED), Hematology, Padua University, Padua; [7]University of Bari Aldo Moro Medical School, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), Bari; [8]Divisione di Ematologia, Grande Ospedale Metropolitano "Bianchi-Melacrino-Morelli", Reggio Calabria; [9]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola; [10]AOU delle Marche, Università Politecnica delle Marche, Ancona; [11]Hematology, IRCCS "Casa Sollievo della Sofferenza" Hospital, San Giovanni Rotondo; [12]Division of Hematology, Department of Human Pathology in Adulthood and Childhood "Gaetano Barresi", University of Messina, Messina; [13]Unit of Clinical Epidemiology, AOU Città della Salute e della Scienza di Torino and CPO Piemonte, Torino; [14]European Myeloma Network (EMN); [15]SC Farmacia Ospedaliera, AOU Città della Salute e della Scienza di Torino, Torino; [16]Hematology and Stem Cell Transplantation Unit, AOU Consorziale Policlinico, Bari; [17]UO Ematologia, Ospedale di Rimini, Rimini; [18]A.O. Santa Maria di Terni – Università degli Studi di Perugia, Terni–Perugia; [19]SC Ematologia, GOM Niguarda, Milano; [20]Department of Hematology, ASST Spedali Civili di Brescia, Brescia; [21]Hematologic Clinic and Transplant Center, University Hospital of Central Friuli, DMED, University of Udine, Udine; [22]Oncology-Hematology Department, Papardo Hospital, Messina; [23]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna; [24]Dipartimento di Scienze Mediche e Chirurgiche, Università di Bologna, Bologna and [25]Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy

Correspondence:
S. BRINGHEN - sarabringhen@yahoo.com

https://doi.org/10.3324/haematol.2025.287510

Received: February 11, 2025.
Accepted: July 22, 2025.
Early view: July 31, 2025.

Disclosures

SB has participated in the speakers' bureaus for Amgen, Bristol Myers Squibb, GlaxoSmithKline, Janssen, Sanofi, and AbbVie; has served on the advisory boards for Bristol Myers Squibb, Janssen, Takeda, Pfizer, Stemline Therapeutics, and Oncopeptides; has received consultancy fees from Sanofi. NG has received fees for participation in consultancy advisory boards from Takeda, Amgen, Oncopeptides, and Bristol Myers Squibb; has received research support from Pfizer; has participated in the speakers' bureaus for Amgen, Sanofi, and Takeda. SM has received honoraria from Bristol Myers Squibb, Sanofi, Amgen, GlaxoSmithKline, Takeda, Pfizer, and Janssen; has served on the advisory boards for Sanofi, Takeda, Bristol Myers Squibb, Pfizer, and Janssen. GB has served on the advisory boards and participated in the speakers' bureaus for Bristol Myers Squibb, Novartis, GlaxoSmithKline, Menarini, and Janssen. EA has served on the advisory boards for GlaxoSmithKline, Sanofi, Pfizer, and Menarini Stemline. RZ has served on the advisory boards for Janssen, Amgen, GlaxoSmithKline, Sanofi, Menarini Stemline, Oncopeptides, and Pfizer. RR has participated in the speakers' bureaus for Amgen, Bristol Myers Squibb, CSL Behring, Janssen Cilag, Octapharma, and Takeda; has provided consultancy for Amgen, Bristol Myers Squibb, CSL Behring, Janssen Cilag, Pfizer, Sanofi, and Takeda. SM has received honoraria from GlaxoSmithKline, Janssen, Menarini, and Pfizer. MD has received honoraria from GlaxoSmithKline, Sanofi, and Janssen; has served on the advisory boards for GlaxoSmithKline, Sanofi, Bristol Myers Squibb, and Adaptive Biotechnologies; has received research support from Janssen. AML has received sponsored research funding for her institution from Takeda, Roche, Celgene, AbbVie, Millennium, Janssen, Sanofi, Verastem, Novartis, Morphosys, GlaxoSmithKline, Oncopeptides, Karyopharm, Onconova, Archigen, Fibrogen, Dr. Reddy's Lab., LoxoOncology, Beigene, Bristol Myers Squibb, and PSI; has received honoraria from IQVIA, Incyte, Celgene, AbbVie, Bristol Myers Squibb, and Janssen; has received support for travel from Takeda, Roche, Janssen, Celgene, Bristol Myers Squibb, AbbVie, Novartis, Sanofi, IQVIA, and Verastem. AMC has received honoraria for her participation in advisory boards from Amgen, Takeda, Bristol Myers Squibb, Janssen, and Sanofi. AB has served on the advisory boards for Amgen, Pfizer, Janssen, GlaxoSmithKline, and Menarini Stemline. FP has received honoraria for lectures from Menarini and Sanofi; has served on the advisory boards for Sanofi and Bristol Myers Squibb. KM has received honoraria from Sanofi, Amgen, Janssen, GlaxoSmithKline, Celgene, and Oncopeptides. MB has received honoraria from Sanofi, Celgene, Amgen, Janssen, Novartis, Bristol Myers Squibb, and AbbVie; has served on the advisory boards for Janssen and GlaxoSmithKline; has received research funding from Sanofi, Celgene, Amgen, Janssen, Novartis, Bristol Myers Squibb, and Mundipharma. AL has received honoraria from and served on the advisory boards for Johnson & Johnson, GlaxoSmithKline, Menarini, and Sanofi. All the other authors have no conflicts of interest to disclose.

Contributions

All authors contributed equally to the acquisition, analysis, or interpretation of data for this work. All authors critically reviewed the work for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors had access to all the data reported in the study and had final responsibility for the decision to submit this manuscript for publication.

Acknowledgments

We thank the University of Torino (Italy), which sponsored the Real MM trial, and the Italian Medicines Agency AIFA - Independent Research, which provided the funding to conduct the trial. We are also grateful to the European Myeloma Network (EMN). We are grateful to all patients, caregivers, physicians, nurses, and data managers involved in the Real MM trial at the following participating centers: Torino, Italy (Alessandra Larocca); Parma (Nicola Giuliani); Pavia (Silvia Mangiacavalli); Firenze (Elisabetta Antonioli); Padova (Renato Zambello); Bologna (Michele Cavo, Elena Zamagni); Bari (Roberto Ria); Reggio Calabria (Iolanda Donatella Vincelli); Messina (Donato Mannina); Meldola (Sonia Ronconi); Udine (Francesca Patriarca); Ancona (Massimo Offidani); Brescia (Giuseppe Rossi, Angelo Belotti); Milano (Anna Maria Cafro); San Giovanni Rotondo (Nicola Cascavilla, Antonietta Pia Falcone); Rimini (Patrizia Tosi); Messina (Caterina Musolino, Alessandro Allegra); Terni (Anna Marina Liberati, Gaetano Vaudo, Arcangelo Liso); Camposampiero (PD) (Ercole De Biasi, Maide Maria Cavalli); Modena (Giovanna Leonardi); Novara (Lorenzo De Paoli, Gloria Margiotta Casaluci); Bari (Paola Curci); Roma (Maurizio Martelli); Aviano (Mariagrazia Michieli); Cuneo (Mariella Grasso, Francesco Vassallo); Ascoli Piceno (Piero Galieni); Milano (Fabio Ciceri); Rionero in Vulture (Giuseppe Pietrantuono); Cagliari (Antonio Ledda, Rita Floris); Napoli (Fabrizio Pane); Reggio Emilia (Barbara Gamberi); Roma (Maria Cantonetti, Luca Franceschini); Biella (Annarita Conconi); Civitanova Marche (Riccardo Centurioni, Milena Mirabile); Monza (Sara Pezzatti); Pescara (Antonio Spadano, Francesca Fioritoni).

Funding

The Real MM trial was funded by the Italian Medicines Agency AIFA - Independent Research.

Data-sharing statement

After the publication of this article, data collected for this analysis and related documents (including the trial protocol) will be made available to others upon reasonably justified request, which needs to be written and addressed to the attention of the corresponding author. The sponsor of the Real MM trial, the University of Torino, Italy, via the corresponding author, is responsible to evaluate and eventually accept or refuse every request to disclose data and their related documents, in conformance with the agreements in place with the involved subjects, the participating institutions, and all the other parties directly or indirectly involved in the conduct of this trial.

References

1. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol. 2014;15(12):e538-e548.
2. Facon T, Dimopoulos MA, Dispenzieri A, et al. Final analysis of survival outcomes in the phase 3 FIRST trial of up-front treatment for multiple myeloma. Blood. 2018;131(3):301-310.
3. San-Miguel JF, Schlag R, Khuageva NK, et al. Persistent overall survival benefit and no increased risk of second malignancies with bortezomib-melphalan-prednisone versus melphalan-prednisone in patients with previously untreated multiple myeloma. J Clin Oncol. 2013;31(4):448-455.
4. Palumbo A, Bringhen S, Mateos M-V, et al. Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report. Blood. 2015;125(13):2068-2074.
5. Benboubker L, Dimopoulos MA, Dispenzieri A, et al. Lenalidomide and dexamethasone in transplant-ineligible patients with myeloma. N Engl J Med. 2014;371(10):906-917.
6. Palumbo A, Hajek R, Delforge M, et al. Continuous lenalidomide treatment for newly diagnosed multiple myeloma. N Engl J Med. 2012;366(19):1759-1769.
7. San-Miguel JF, Schlag R, Khuageva NK, et al. Bortezomib plus melphalan and prednisone for initial treatment of multiple myeloma. N Engl J Med. 2008;359(9):906-917.
8. Pawlyn C, Schjesvold FH, Cairns DA, et al. Progression-free survival as a surrogate endpoint in myeloma clinical trials: an evolving paradigm. Blood Cancer J. 2024;14(1):134.
9. Leleu X, Hulin C, Lambert J, et al. Isatuximab, lenalidomide, dexamethasone and bortezomib in transplant-ineligible multiple myeloma: the randomized phase 3 BENEFIT trial. Nat Med. 2024;30(8):2235-2241.
10. O'Donnell EK, Laubach JP, Yee AJ, et al. A phase 2 study of modified lenalidomide, bortezomib and dexamethasone in transplant-ineligible multiple myeloma. Br J Haematol. 2018;182(2):222-230.
11. Facon T, Dimopoulos M-A, Leleu XP, et al. Isatuximab, bortezomib, lenalidomide, and dexamethasone for multiple myeloma. N Engl J Med. 2024;391(17):1597-1609.
12. Usmani SZ, Facon T, Hungria V, et al. Daratumumab plus bortezomib, lenalidomide and dexamethasone for transplant-ineligible or transplant-deferred newly diagnosed multiple myeloma: the randomized phase 3 CEPHEUS trial. Nat Med. 2025;31(4):1195-1202.
13. D'Agostino M, Bringhen S, Giuliani N, et al. Health-related quality of life in transplant-ineligible real-life multiple myeloma patients treated with fixed-duration bortezomib-melphalan-prednisone vs. continuous lenalidomide-dexamethasone. Hemasphere. 2023;7(S3):3264-3265, abstract P1680.
14. Larocca A, Bonello F, Gaidano G, et al. Dose/schedule-adjusted Rd-R vs continuous Rd for elderly, intermediate-fit patients with newly diagnosed multiple myeloma. Blood. 2021;137(22):3027-3036.