haematologica
Journal of the Ferrata Storti Foundation

Pomalidomide, bortezomib and dexamethasone in multiple myeloma refractory to lenalidomide and anti-CD38 monoclonal antibodies: outcomes from a real-world experience

by Carmine Liberatore, Virginia Valeria Ferretti, Paola Tacchetti, Concetta Conticello, Gregorio Barilà, Elisabetta Antonioli, Angelo Belotti, Anna Maria Cafro, Laura Paris, Velia Bongarzoni, Massimo Gentile, Matteo Da Vià, Barbara Gamberi, Sara Pezzatti, Fabrizio Ciambelli, Mariagrazia Garzia, Ombretta Annibali, Francesca Fazio, Giusy Antolino, Sonia Morè, Nicola Sgherza, Francesca Farina, Annalisa Citro, Paola Stefanoni, Vittorio Del Fabro, Claudio Salvatore Cartia, Francesca Fioritoni, Katia Mancuso, Irene Attucci, Maria Luisa Pioltelli, Michele Puppi, Sofia Terlizzi, Chiara Lisi, Michele Palumbo, Massimo Offidani, Maria Teresa Petrucci and Silvia Mangiacavalli

Received: September 15, 2025.
Accepted: March 13, 2026.

Citation: Carmine Liberatore, Virginia Valeria Ferretti, Paola Tacchetti, Concetta Conticello, Gregorio Barilà, Elisabetta Antonioli, Angelo Belotti, Anna Maria Cafro, Laura Paris, Velia Bongarzoni, Massimo Gentile, Matteo Da Vià, Barbara Gamberi, Sara Pezzatti, Fabrizio Ciambelli, Mariagrazia Garzia, Ombretta Annibali, Francesca Fazio, Giusy Antolino, Sonia Morè, Nicola Sgherza, Francesca Farina, Annalisa Citro, Paola Stefanoni, Vittorio Del Fabro, Claudio Salvatore Cartia, Francesca Fioritoni, Katia Mancuso, Irene Attucci, Maria Luisa Pioltelli, Michele Puppi, Sofia Terlizzi, Chiara Lisi, Michele Palumbo, Massimo Offidani, Maria Teresa Petrucci and Silvia Mangiacavalli. Pomalidomide, bortezomib and dexamethasone in multiple myeloma refractory to lenalidomide and anti-CD38 monoclonal antibodies: outcomes from a real-world experience.
Haematologica. 2026 Mar 26. doi: 10.3324/haematol.2025.289143 [Epub ahead of print]

LETTER TO THE EDITOR

Pomalidomide, bortezomib and dexamethasone in multiple myeloma refractory to lenalidomide and anti-CD38 monoclonal antibodies: outcomes from a real-world experience

Short title

PVd in anti-CD38 lenalidomide refractory myeloma

Authors

Carmine Liberatore[1,2*], Virginia Valeria Ferretti[3], Paola Tacchetti[4], Concetta Conticello[5], Gregorio Barilà[6], Elisabetta Antonioli[7], Angelo Belotti[8], Anna Maria Cafro[9], Laura Paris[10], Velia Bongarzoni[11], Massimo Gentile[12,13], Matteo Da Vià[14], Barbara Gamberi[15], Sara Pezzatti[16], Fabrizio Ciambelli[17], Mariagrazia Garzia[18], Ombretta Annibali[19], Francesca Fazio[20], Giusy Antolino[21], Sonia Morè[22], Nicola Sgherza[23], Francesca Farina[24], Annalisa Citro[25], Paola Steffanoni[10], Vittorio Del Fabro[26], Claudio Salvatore Cartia[27], Francesca Fioritoni[2], Katia Mancuso[4,28], Irene Attucci[7], Maria Luisa Pioltelli[9], Michele Puppi[4], Sofia Terlizzi[8], Chiara Lisi[20], Michele Palumbo[27], Massimo Offidani[22], Maria Teresa Petrucci[20], Silvia Mangiacavalli[27].

*corresponding author

Affiliations

[1]Department of Medicine and Aging Sciences, "G d'Annunzio" University, Chieti, Italy;

[2]Hematology Unit, Santo Spirito Hospital, Pescara, Italy;

[3]Unit of Biostatistics and Clinical Trial Center, Fondazione IRCCS Policlinico S. Matteo, Pavia, Italy

[4]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna, Italy;

[5]AOU Policlinico G. Rodolico-San Marco, University School of Medicine, Catania, Italy;

[6]Hematology Unit, San Bortolo Hospital; Vicenza, Italy;

[7]Department of Hematology, Careggi Hospital and University of Florence, Italy;

[8]Department of Hematology, ASST Spedali Civili di Brescia; Brescia, Italy;

[9]Department of Hematology, GOM Niguarda Hospital, Milano, Italy;

[10]Department of Hematology, ASST Papa Giovanni XXIII, Bergamo, Italy;

[11]Department of Hematology, San Giovanni-Addolorata Hospital, Roma, Italy;

[12]Department of Onco-hematology, Hematology Unit, Azienda Ospedaliera Annunziata, Cosenza, Italy;

[13]Department of Pharmacy, Health and Nutritional Science, University of Calabria, Rende, Italy;

[14]Hematology & BMT Unit, Fondazione IRCCS Ospedale Maggiore Policlinico di Milano, University of Milan, Milano, Italy;

[15]Azienda USL - IRCCS di Reggio Emilia, Reggio Emilia, Italy;

[16]Department of Hematology and Transplantation, ASST di Monza, S Gerardo Hospital, Monza, Italy;

[17]S.C. Ematologia ASST Valle Olona Ospedale di Circolo Busto Arsizio, Italy;

[18]Azienda Ospedaliera San Camillo Forlanini, UOC Hematology and Stem Cell Transplant, Roma, Italy;

[19]Division of Hematology, Stem Cell Transplantation, Fondazione Policlinico Universitario Campus Bio Medico, Roma, Italy;

[20]Division of Hematology, Department of Translational and Precision Medicine, Azienda Ospedaliera Universitaria Policlinico Umberto I di Roma, Sapienza University of Rome, Roma, Italy;

[21]Azienda Ospedaliero Universitaria S. Andrea, Roma, Italy;

[22]Clinica di Ematologia Azienda Ospedaliero Universitaria delle Marche, Ancona, Italy;

[23]Hematology and Stem Cell Transplantation Unit, AOUC Policlinico di Bari, Bari, Italy;

[24]Hematology and BMT Unit, IRCCS Ospedale San Raffaele, Milano, Italy;

[25]UOC Ematologia, Ospedale Civile di Legnano, Legnano, Italy;

[26]Faculty of Medicine and Surgery, "Kore" University of Enna, Enna, Italy;

[27]Division of Hematology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy;

[28]Dipartimento di Scienze Mediche e Chirurgiche, Università di Bologna, Bologna, Italy;

Keywords

Pomalidomide, Bortezomib, Dexamethasone, Relapsed refractory multiple myeloma, lenalidomide refractoriness, anti-CD38 refractoriness.

Clinical trial

protocol DARE-MM vers. 1; NCT06541860

Authorship Contributions

All co-authors (C.L., V.V.F., P.T., C.C., B.G., E.A., A.B., A.M.C., L.P., V.B., M.G., M.D.V., B.G., S.P., F.C., M.G., O.A., F.F., G.A., S.M., N.S., F.F., A.C., P.S., V.D.F., C.S.C., F.F., K.M., I.A., M.L.P., M.P., S.T., C.L., M.P., M.O., M.T.P., S.M.) contributed to patients' clinical care. C.L., V.V.F., C.S.C and S.M. wrote the manuscript. C.L., V.V.F., C.S.C. and S.M. revised the manuscript. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest Disclosures

The authors declare no conflict of interest.

Data sharing statement

Original data are available in anonymous form upon request by contacting corresponding author.

Corresponding author

Carmine Liberatore

Hematology Unit

Ospedale Santo Spirito,

via Fonte Romana 8, 65124, Pescara

Phone +39 0854252853

Fax +39 0854252904

e-mail: carmine.liberatore@asl.pe.it

The introduction of triplets and quadruplets regimens combining anti-CD38 monoclonal antibodies (antiCD38), immunomodulatory agents, proteasome inhibitors (PI) either bortezomib (V) or carfilzomib (K) and dexamethasone in the frontline treatment of newly diagnosed (ND) multiple myeloma (MM) has markedly improved patients' outcomes.[1] However, the broader use of continuous treatments is leading to an earlier emergence of multidrug resistance.[2] Rates of patients refractory to both antiCD38 and lenalidomide (antiCD38-len-refractory) at first relapse are estimated to reach up to 30% by 2027.[2] This incidence may rise even more rapidly, given the outcomes of daratumumab-lenalidomide-dexamethasone (DRd) in the real-world setting.[3] Patients with early antiCD38-len-refractory MM represent a growing clinical challenge with dismal outcomes. In the MAMMOTH study, among 41 antiCD38-len-refractory patients the ORR was 36.6%, with median PFS and OS of 4.5 and 12.6 months, respectively.[4] Comparable findings were reported in the LocoMMotion trial.[5] The current therapeutic landscape for antiCD38-len-refractory patients remains limited. In relapsed/refractory (RR) MM patients, the latest NCCN and EHA–EMN guidelines recommend switching the mechanism of drug action, according to prior treatment exposure.[6] Anti-BCMA agents such as CAR-T and belantamab-mafodotin (bela) have shown to be highly effective in this setting, but their real-world applicability remains currently limited due to regulatory approval, fitness of patients, and manufacturing constraints.[7–9] In absence of anti-BCMA agents, other approved second-line regimens include Kd56, pomalidomide (P)Vd, and selinexor (S)Vd, while elotuzumab (E)Pd is indicated from the third line.[6] However, information are lacking on these combinations in antiCD38-len-refractory patients as they were rarely included in registrational trials. This limitation is clearly acknowledged by the EHA-EMN guidelines, stating that their recommendation is based on panel consensus rather than robust trial data.[6] Notably, PVd was one of the first approved regimens to offer a complete switch in the mechanism of action

for antiCD38-len-refractory patients.[10] However, its effectiveness in this setting remains poorly characterized.

To address this gap, we conducted a nationwide, multicenter, retrospective and prospective Italian study to assess the real-world effectiveness and safety of PVd in patients with antiCD38-len-refractory MM following one or two prior lines of therapy (LOTs). Here, we report findings from the retrospective phase.

Patients were consecutively enrolled from June 1st, 2023, to December 31st, 2024, at 20 hematological centers in Italy. Eligible patients had antiCD38-len-refractory MM after their immediate prior LOTs and were treated with on-label PVd salvage regimen. Exclusion criteria were diagnosis of plasma-cell leukemia, Waldenström's macroglobulinemia, POEMS syndrome, primary amyloid light chain amyloidosis, and disease status other than antiCD38-len-refractory. All patients received PVd in 21-days cycles according to OPTIMISMM trial, until disease progression or unacceptable toxicity.[10] Dose reductions followed the manufacturer's product guidelines. Primary endpoint was PFS, defined as time from PVd initiation to disease progression or death, whatever occurred first. Secondary endpoints were rates of disease response according to IMWG criteria; OS, defined as time from PVd initiation to death for any cause and finally safety. Categorical variables were described as counts and percentage, continuous variables as median and interquartile range (IQR). OS and PFS were estimated by Kaplan-Meier method. Patients were considered responsive if achieving ≥partial remission. After defining the median time to best response, the impact of response on PFS was assessed using a 3-month landmark analysis. The effect of predictors on PFS was evaluated by Cox regression model. All statistical analyses were performed using Stata 18. The study received approval of local ethics committee or institutional review board at each participating site (protocol DARE-MM vers. 1; NCT06541860). All patients provided written informed consent. The trial was conducted in accordance with the principles of

the Declaration of Helsinki and the International Conference on Harmonisation Good Clinical Practice guidelines.

Seventy-seven patients were included in this analysis, with a median follow-up for the entire cohort of 2.7 years (IQR: 2.1–3.8). Table 1 summarizes baseline patients' characteristics at PVd initiation, compared to characteristics of patients enrolled in the OPTIMISMM trial.[10] In our cohort, the median number of prior LOTs was 1 (IQR: 1–2). Among 45 evaluable patients (58%), high-risk cytogenetic abnormalities were present in 31 (68.9%; 20.3% overall). Notably, 56 patients (70%) became antiCD38-len-refractory after 1 LOT (54 patients after DRd and 2 patients after DVRd), whereas 21 patients received a V-based upfront therapy (18 underwent autologous stem-cell transplantation) and developed antiCD38-len-refractoriness following second-line DRd. Patients received a median of 7 treatment cycles (IQR: 4.0–10.0), with a median duration of PVd of 5.7 months (95%CI: 2.9–9.0). The ORR and ≥very good partial remission (VGPR) were 75.7% and 47.1%, respectively (Table 1). Median time to best response was 3.0 months (95%CI: 1.9–4.5). Dose reductions occurred in 32 patients (41.5%): most frequently bortezomib (n=21, 65.6%), then pomalidomide (n=16, 50%) and dexamethasone (n=14, 43.7%). Overall, 64 adverse events were reported during treatment, with cytopenias, peripheral neuropathy, and infections being the most common (Table 2). Adverse events were manageable with dose modifications, while discontinuations due to toxicity remained uncommon (n=3, 3.8%). Median PFS and OS were 9.4 months (95%CI: 7–13.6 months) and 22.6 months (95%CI: 14.4–not reached), respectively (Figure 1). In the 3-months landmark analysis from PVd initiation, the depth of response (≥VGPR) did not significantly impact PFS (HR=1.1; 95% CI: 0.6–2.1; p=0.753) (Figure S1). Similarly, the emergence of antiCD38-len-refractoriness at 12-, 18-, and 24-months had no significant impact on PFS and OS (Figure S2). In univariate analysis, ISS stage III at diagnosis was significantly associated with shorter PFS (HR=1.92; 95% CI: 1.02–3.61; p=0.043) (Table S1). At disease progression, 45 patients (59%)

received a subsequent LOT, among them only 5 patients (6%) received anti-BCMA therapy (ide-cel, n=1; elranatamab, n=3; belantamab-mafodotin, n=1). The ORR to subsequent LOT was 22% and PFS2 was 3.2 months in the overall cohort.

In this study, we report for the first time the real-world outcomes of PVd in antiCD38-len-refractory MM patients who received one or two prior LOT, a population that is rapidly expanding and with a consequent need for effective salvage regimens. Compared with OPTIMISMM, our cohort appeared clinically enriched for high‐risk features, both cytogenetic, due to the inclusion of 1q21 abnormalities, and functional, since most patients experienced early relapses following antiCD38 and lenalidomide-based frontline therapy. Overall, the effectiveness of PVd in our study appeared roughly consistent although inferior to OPTIMISMM trial.[10] Response rates were comparable, but duration of response as well as survival in real-world cohort were shorter than previously reported. Notably, no survival advantage was observed even among patients who achieved deeper responses or those treated earlier. The safety profile was superimposable with registrational trial, with cytopenias, polyneuropathy and infections as the most common adverse events.[10] In this early antiCD38-len-refractory population, therapeutic challenges persisted at subsequent relapse, as reflected by the limited PFS2 and OS observed in the overall cohort. Approximately half of the patients were able to receive additional LOTs. In a minority of cases these consisted of anti‐BCMA agents, due to restricted regulatory approval during the study period. In an era of earlier exposure to antiCD38 and lenalidomide, and increasingly aggressive disease biology at relapse, the role of PVd appears limited. Data on other approved regimens in antiCD38-len-refractory patients are also scarce. In real-world cohorts of RRMM enriched for antiCD38 exposed or refractory patients, the median PFS with either Kd56 or EloPD did not exceed 10 months, whereas SVd achieved a PFS of 12.2 months in a subgroup analysis of BOSTON trial with similar characteristics.[11–13] Conversely, targeting BCMA represents a promising treatment

strategy in antiCD38-len-refractory patients. The most favorable outcomes were observed with anti-BCMA CAR-T. Among 386 RRMM patients (95% antiCD38-refractory, 73% lenalidomide-refractory), ide-cel achieved a median PFS of 13.3 months vs 4.4 with standard regimens (HR 0.49; p<0.001).[14] In the CARTITUDE-4 trial that enrolled 419 lenalidomide-refractory patients (24% antiCD38-len-refractory), the median PFS with cilta-cel was not reached vs 11.8 months with standard regimens at 33.6 months of follow up (HR 0.29; p<0.001).[9] In the DREAMM-8 study that enrolled 305 RRMM with prior lenalidomide exposure (22% antiCD38 refractory), Bela-Pd achieved longer median PFS compared to PVd (not reached vs 12.7 months; HR 0.52, p<0.001).[7] Notably, the efficacy of PVd in this trial aligned closely with results in our cohort, underscoring that antiCD38-len-refractory patients represent a distinct and challenging population.[7] Ultimately, bispecific antibodies targeting either BCMA or GPRC5D have shown significant efficacy in heavily-pretreated RRMM, whereas their use in earlier LOTs is still under investigation.[15] Interestingly, PVd still represents the control arms in many ongoing phase 3 trials involving bispecific antibodies-based combinations in RRMM patients with antiCD38-len-refractory disease. The retrospective design, lack of a comparator arm, and limited cohort size are acknowledged limitations. Nonetheless, the multicenter design and homogeneity of antiCD38-len-refractory population provide valuable real-world evidence and a benchmark for future prospective trials.

In a real-world setting, the PVd regimen showed meaningful effectiveness in RRMM patients with antiCD38-len-refractory disease. Although the safety profile was manageable, long-term survival remained suboptimal, underscoring the need for earlier and broader access to innovative strategies, such as anti-BCMA therapies, that may contribute to reshaping treatment paradigms in this challenging and expanding population.

References

1. Wang Y, Zhang L, He D, et al. Addition of anti-CD38 mAb in newly diagnosed multiple myeloma: advancing toward quadruplet induction regimens. Blood Neoplasia. 2026;18;3(1):100189.

2. Mina R, Mangiacavalli S, Rossini B, et al. Multiple Myeloma in Italy: An Epidemiological Model by Treatment Line and Refractoriness Status. Clin Lymphoma Myeloma Leuk. 2025;25(5):e253-e261.

3. Hansen DK, Gautam S, Lafeuille M-H, et al. Comparison of Time to Next Treatment or Death between Front-Line Daratumumab, Lenalidomide, and Dexamethasone (DRd) and Bortezomib, Lenalidomide, and Dexamethasone (VRd) in Transplant Ineligible Patients with Multiple Myeloma. Cancer Med. 2024;13(21):e70308.

4. Gandhi UH, Cornell RF, Lakshman A, et al. Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. Leukemia. 2019;33(9):2266-2275.

5. Mateos MV, Weisel K, De Stefano V, et al. LocoMMotion: a prospective, non-interventional, multinational study of real-life current standards of care in patients with relapsed and/or refractory multiple myeloma. Leukemia. 2022;36(5):1371-1376.

6. Dimopoulos MA, Terpos E, Boccadoro M, et al. EHA–EMN Evidence-Based Guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma. Nat Rev Clin Oncol. 2025;22(9):680-700.

7. Dimopoulos MA, Beksac M, Pour L, et al. Belantamab Mafodotin, Pomalidomide, and Dexamethasone in Multiple Myeloma. N Eng J Med. 2024;391(5):408-421.

8. Hungria V, Robak P, Hus M, et al. Belantamab Mafodotin, Bortezomib, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2024; 91(5):393-407.

9. Einsele H, San-Miguel J, Dhakal B, et al. Cilta-cel in lenalidomide-refractory multiple myeloma (CARTITUDE-4): an updated analysis including overall survival from an open-label, multicentre, randomised, phase 3 trial. Lancet Oncol. 2026; 27(2):254-268.

10. Richardson PG, Oriol A, Beksac M, et al. Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial. Lancet Oncol. 2019;20(6):781-794.

11. Del Giudice ML, Gozzetti A, Antonioli E, et al. Carfilzomib plus dexamethasone in patients with relapsed and refractory multiple myeloma: A retro-prospective observational study. Eur J Haematol. 2022;109(4):373-380.

12. Gentile M, Vigna E, Palmieri S, et al. Elotuzumab plus pomalidomide and dexamethasone in relapsed/refractory multiple myeloma: a multicenter, retrospective, real-world experience with 200 cases outside of controlled clinical trials. Haematologica. 2024;109(1):245-255.

13. Grosicki S, Simonova M, Spicka I, et al. Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. Lancet. 2020;396(10262):1563-1573.

14. Rodriguez-Otero P, Ailawadhi S, Arnulf B, et al. Ide-cel or Standard Regimens in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2023;388(11):1002-1014.

15. Dima D, Banerjee R, Hansen DK. CAR T-cell therapy and bispecific antibodies in the management of multiple myeloma. Hematology Am Soc Hematol Educ Program. 2025;2025(1):324-333.

Table 1. Baseline characteristics of real-world patients compared with the lenalidomide-refractory population treated with PVd in the OPTIMISMM trial.

Characteristic	Real-world PVd patients (N=77)	LEN-refractory PVd patients OPTIMISMM (N=67)
Median follow-up, years (IQR)	2.7 (2.1–3.8)	NE
Median age at PVd initiation, years (IQR)	75 (70–77)	68 (38–87)
Sex, n (%)		
· male	37 (47.4)	37 (57.8)
· female	40 (52.6)	27 (42.2)
Cytogenetic profile by FISH#, n (%)	45 (58)	
· high risk	31 (68.9)	13 (20.3)
ISS stage, n (%)	61 (79)	NE
· I	9 (14.8)	-
· II	20 (32.8)	-
· III	32 (52.5)	-
R-ISS stage, n (%)	40 (52)	NE
· I	4 (10.0)	-
· II	19 (47.5)	-
· III	17 (42.5)	-
Soft tissue plasmacytoma, n (%)	10 (13)	NE
· paraskeletal	9 (11)	
· extramedullary	1 (2)	
Median time from diagnosis to PVd, months (IQR)	21.4 (11.5–34.0)	32.4 (2.4–129.6)
Prior lines of therapy, median (IQR)	1 (1–2)	1 (1–1)
· 1 prior LOT, n (%)	56 (72.7)	67 (100)
· ≥2 prior LOT, n (%)	21 (27.3)	0 (0)
Previous treatment exposure, n (%)		
Lenalidomide · in first LOT	77 (100) 58 (75.3)	64 (100) 64 (100)
Daratumumab · in first LOT	77 (100) 59 (76.6)	0 (0)

Bortezomib · in first LOT	21 (27.3) 20 (26.0)	36 (56.3) 0 (0)
ASCT	12 (15.6)	26 (40.6)
Refractory status, n (%)		
· Lenalidomide	77 (100)	64 (100)
· Daratumumab	77 (100)	0 (0)
· Bortezomib	1 (1.3)	6 (9.4)
Time to antiCD38-len-refractoriness, n (%)		
· ≤12 months	25 (35.1)	27 (36.5)
· ≤18 months	37 (46.8)	36 (48.7)
· ≤24 months	49 (58.4)	45 (60.8)
Best response rate, n (%)		
· ORR[+]	53 (75.7)	55 (85.9)
· ≥VGPR	33 (47.2)	36 (56.3)
Median PFS, months (95% CI)	9.4 (7.0–13.6)	17.84 (12.02–NE)
Median OS, months (95% CI)	22.6 (14.4–NR)	NE

Abbreviations: PVd (pomalidomide, bortezomib, dexamethasone); n (number); IQR (interquartile range); FISH (fluorescence in situ hybridization); NE (not evaluable); LOT (line of therapy); ASCT (autologous stem cell transplantation); antiCD38-len-refractory (anti-CD38 monoclonal antibodies and lenalidomide refractory); ORR (overall response rate); VGPR (very good partial response); PFS (progression-free survival); CI (confidence Interval); OS (overall survival).

[#] Chng WJ, Dispenzieri A, Chim CS, Fonseca R, Goldschmidt H, Lentzsch S, et al. International Myeloma Working Group. IMWG consensus on risk stratification in multiple myeloma. Leukemia. 2014 Feb;28(2):269-77.

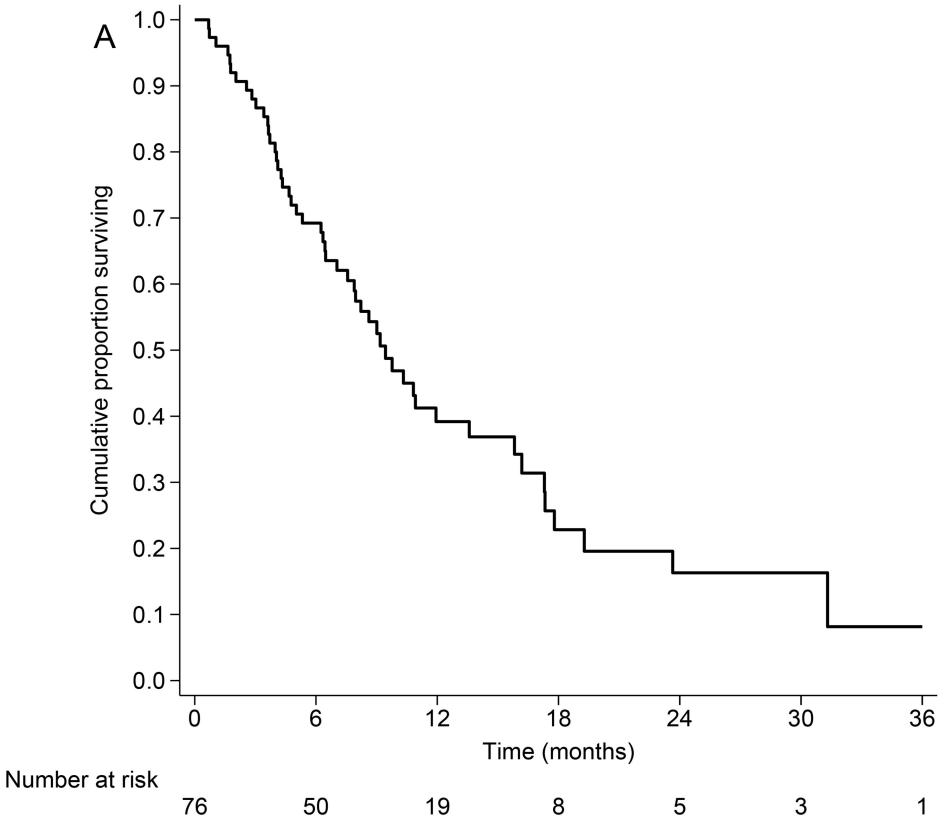
Table 2. Adverse events.

Adverse Event	Any Grade n (%)	Grade 3–4 n (%)
Hematologic toxicity, n (%)		
· neutropenia	9 (14)	3 (33)
· thrombocytopenia	13 (20)	6 (46)
· anemia	5 (8)	2 (40)
Non-hematologic toxicity, n (%)		
· infections	14 (22)	8 (57)
· peripheral neuropathy	16 (25)	4 (25)
· gastrointestinal events	5 (8)	3 (60)
· fatigue	2 (3)	—
· cardiac disorders	1 (2)	1 (100)
· rash	1 (2)	—
Total, n (%)	64 (100)	27 (42)

Figure 1. Kaplan-Meier analysis of survival from PVd initiation.

(A) Kaplan-Meier analysis of progression-free survival from PVd initiation. (B) Kaplan-Meier analysis of overall survival from PVd initiation.

Abbreviations: PVd (pomalidomide, bortezomib, dexamethasone).


A
Cumulative proportion surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
6
12
18
24
30
36
Time (months)
Number at risk
76
50
19
8
5
3
1

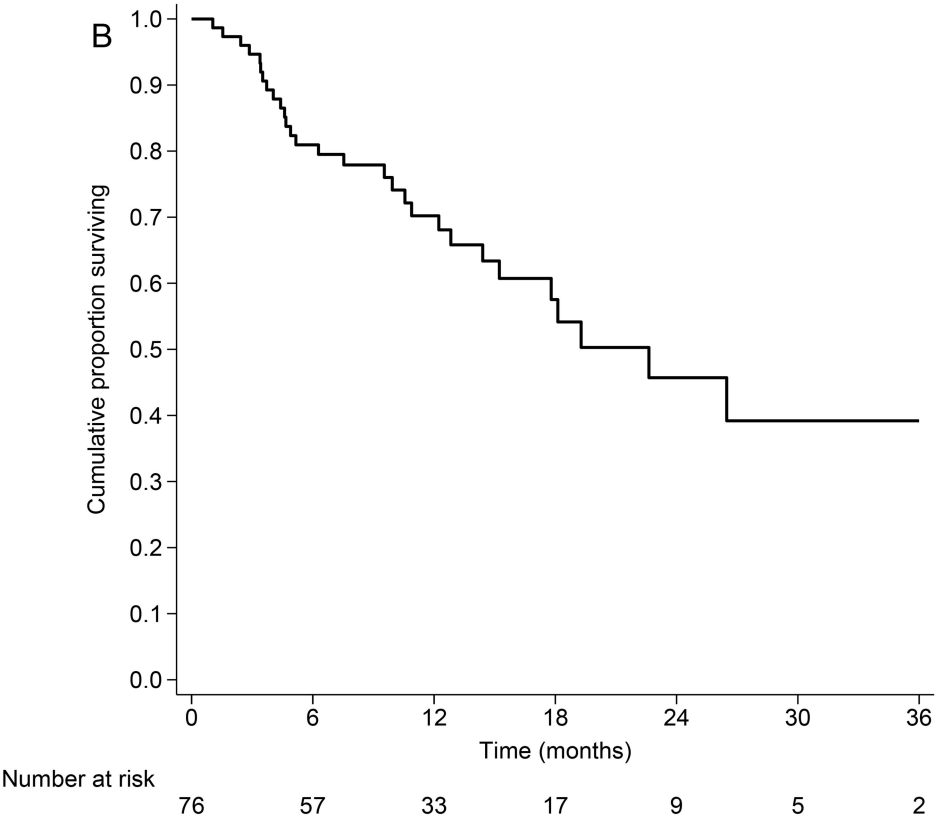

B
Cumulative proportion surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
6
12
18
24
30
36
Time (months)
Number at risk
76
57
33
17
9
5
2

Figure S1. Progression-free survival (PFS) according to depth of response at the 3-month landmark analysis.

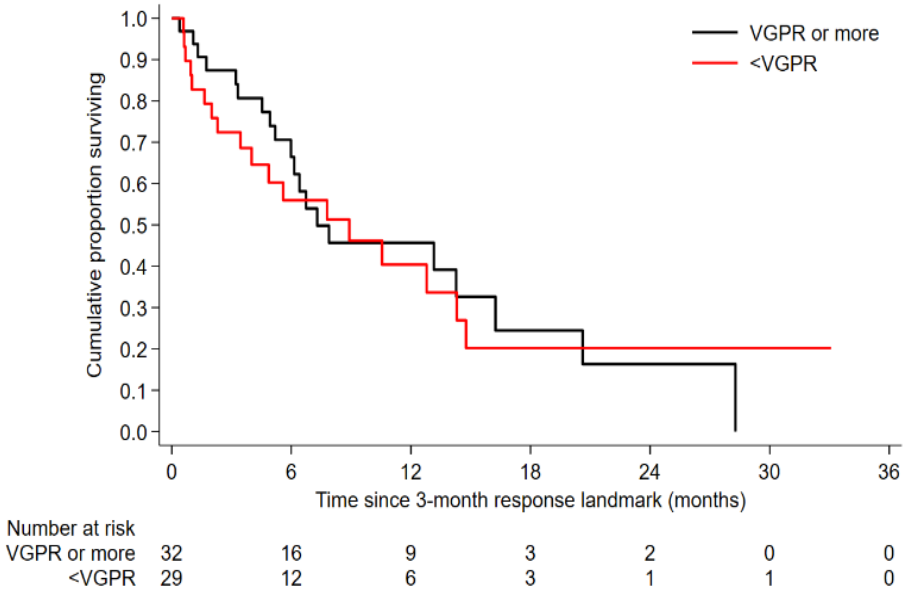
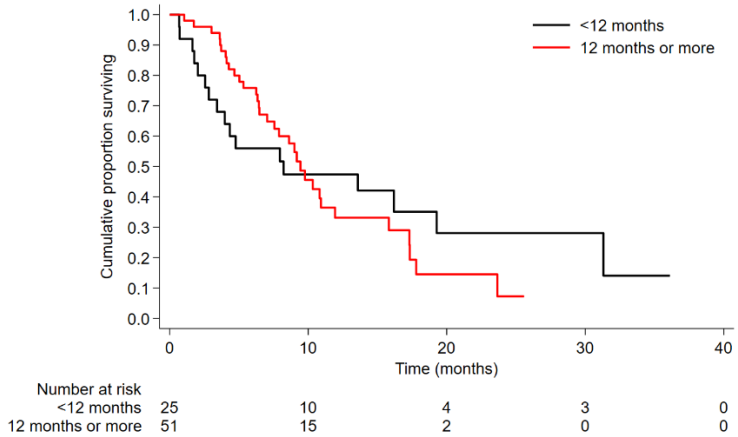
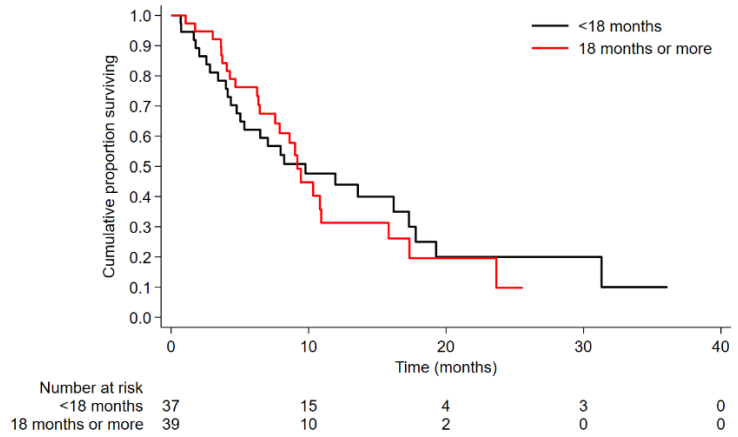


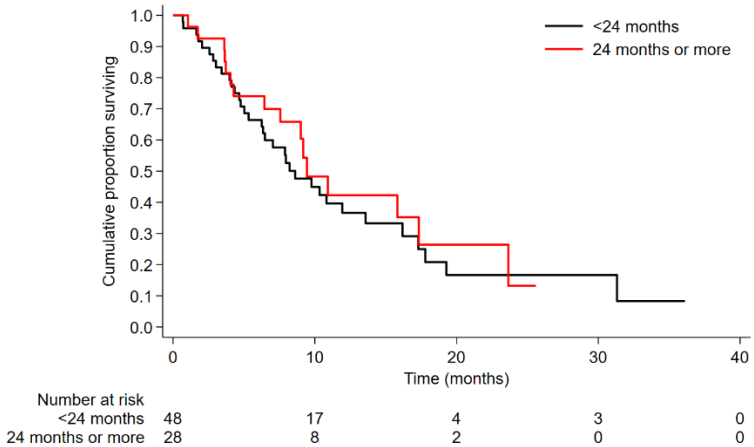
Figure S2. Progression-free survival (PFS) stratified by time to double refractoriness.



Number at risk					
<12 months	25	10	4	3	0
12 months or more	51	15	2	0	0



Number at risk					
<18 months	37	15	4	3	0
18 months or more	39	10	2	0	0



Number at risk					
<24 months	48	17	4	3	0
24 months or more	28	8	2	0	0

Table S1. Univariable Cox proportional hazard models for progression-free survival.

	N (%)	Median PFS (months)	HR (95%CI)	p-value
Age at PVd initiation				
<70 years	18	9.2	-	-
≥70 years	59	9.8	0.99 (0.49-2.00)	0.979
ISS at diagnosis				
I-II	28	16.2	-	-
III	32	8.0	1.92 (1.02-3.61)	0.043
R-ISS at diagnosis				
II	22	9.2	-	-
III	17	10.3	1.22 (0.57-2.64)	0.608
Cytogenetic profile by FISH[#], n (%)				
low risk	13	10.8	-	-
high risk	31	8.2	1.64 (0.72-3.76)	0.239
Prior lines of therapy				
1 LOT	56	9.8	-	-
≥2 LOT	21	9.4	1.00 (0.54-1.84)	0.992
Prior ASCT				
no	65	9.8	-	-
yes	12	9.4	1.04 (0.50-2.14)	0.926
Time from first line to antiCD38-len-refractory				
<12 months	25	8.2	-	-
≥12 months	51	9.4	1.13 (0.61-2.08)	0.701
Time from first line to antiCD38-len-refractory				
<18 months	37	9.8	-	-
≥18 months	39	9.2	1.06 (0.60-1.88)	0.828
Time from first line to antiCD38-len-refractory				
<24 months	48	8.6	-	-
≥24 months	28	9.4	0.83 (0.46-1.51)	0.535
Best response to PVd regimen				
<VGPR	29	8.9	-	-
≥VGPR	32	7.3	1.11 (0.59-2.10)	0.753

Abbreviations: PVd (pomalidomide, bortezomib, dexamethasone); n (number); IQR (interquartile range); FISH (fluorescence in situ hybridization); NE (not evaluable); LOT (line of therapy); ASCT (autologous stem cell transplantation); antiCD38-len-refractory *(anti-CD38 monoclonal antibodies and lenalidomide refractory); ORR (overall response rate); VGPR (very good partial response); PFS (progression-free survival); CI (confidence Interval); OS (overall survival).*

[#] Chng WJ, Dispenzieri A, Chim CS, Fonseca R, Goldschmidt H, Lentzsch S, et al. International Myeloma Working Group. IMWG consensus on risk stratification in multiple myeloma. Leukemia. 2014 Feb;28(2):269-77.