Neoplasma 2022; 69(6): 1474–1479

doi:10.4149/neo_2022_220813N827

Real-world evidence of efficacy and safety of pomalidomide and dexamethasone in relapsed/refractory multiple myeloma patients: Czech registry data

Viera SANDECKA[1,2,*], Luděk POUR[1,2], Ivan ŠPIČKA[3], Jiří MINAŘÍK[4], Jakub RADOCHA[5], Tomáš JELÍNEK[6,7], Petr PAVLÍČEK[8], Alexandra JUNGOVÁ[9], Petr KESSLER[10], Marek WRÓBEL[11], Martin ŠTORK[1,2], Jan ŠTRAUB[3], Tomáš PIKA[4], Lenka ČÁPKOVÁ[12], Sabina ŠEVČÍKOVÁ[13], Vladimír MAISNAR[5], Roman HÁJEK[6,7]

[1]Department of Internal Medicine, Hematology and Oncology, University Hospital, Brno, Czech Republic; [2]Faculty of Medicine, Masaryk University, Brno, Czech Republic; [3]1st Department of Medicine-Department of Hematology, First Faculty of Medicine, Charles University and General Hospital, Prague, Czech Republic; [4]Department of Hemato-Oncology, Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital Olomouc, Olomouc, Czech Republic; [5]4th Department of Internal Medicine-Hematology, University Hospital and Faculty of Medicine, Hradec Kralove, Czech Republic; [6]Department of Hematooncology, University Hospital, Ostrava, Czech Republic; [7]Department of Hematooncology, Faculty of Medicine, University of Ostrava, Ostrava, Czech Republic; [8]Department of Internal Medicine and Hematology, 3rd Faculty of Medicine, Charles University and Faculty Hospital Kralovske Vinohrady, Prague, Czech Republic; [9]Hematology and Oncology Department, Charles University Hospital Pilsen, Pilsen, Czech Republic; [10]Department of Hematology and Transfusion Medicine, Hospital Pelhrimov, Pelhrimov, Czech Republic; [11]Department of Clinical Hematology, Hospital Novy Jicin, Novy Jicin, Czech Republic; [12]Institute of Biostatistics and Analyses, Faculty of Medicine, Masaryk University, Brno, Czech Republic; [13]Babak Myeloma Group, Department of Pathological Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic

**Correspondence: vierkabj@yahoo.com*

Received August 13, 2022 / Accepted November 29, 2022

We assessed the outcomes of pomalidomide and dexamethasone treatment in relapsed/refractory multiple myeloma (RRMM) patients with ≥1 prior line of therapy. We analyzed the data of all RRMM patients treated with pomalidomide and dexamethasone at nine Czech centers between 2013 and 2018. The source of the data was the Registry of Monoclonal Gammopathies of the Czech Republic. Primary endpoints included response rates based on International Myeloma Working Group criteria and survival measures, including progression-free survival (PFS) and overall survival (OS). Secondary endpoints were toxicities and previous treatment patterns, including refractory to lenalidomide, and their impact on final outcomes. The overall response rate was 51.8% and the clinical benefit rate (including patients with minimal response) was 67.1%, with 0.6% of complete responses, 8.5% of very good partial responses, and 42.1% of partial responses (PR). Overall, 16.5% of patients had a minimal response, and 32.3% had stable disease /progression. Median PFS was 8.8 months and the median OS was 14.2 months. In patients who achieved ≥PR, the median PFS and OS were significantly longer compared to non-responders (median PFS (12.1 vs. 4.5 months, p≤0.001 respectively), median OS (22.1 vs. 7.7 months, p≤0.001, respectively). The most frequent adverse events (AEs) were neutropenia (29.9%) and anemia (18.9%), non-hematological AEs included infections (14.6%) and fatigue (7.3%). Our analysis confirmed the effectiveness of pomalidomide and dexamethasone in a real-world setting. This therapy achieved reasonable outcomes comparable to the data from clinical trials even though this was an unbiased cohort of patients.

Key words: multiple myeloma, pomalidomide, treatment, relapse

The introduction of novel drugs, such as bortezomib, lenalidomide, or pomalidomide, and recently the more extensive use of monoclonal antibodies, has helped to change the course of multiple myeloma (MM) from a devastating malignancy with an average survival of 3 years into a chronic disease with an increasing number of patients achieving more than 10 years of overall survival (OS) [1]. Nevertheless, the large use of lenalidomide and bortezomib in frontline therapies has increased the proportion of the patients' refractory to one agent or both [2]. The prognosis of double refractory patients is poor [3]. Before the introduction of monoclonal antibodies (MoAbs), substantial change was brought by the next oral immunomodulatory agent with strong direct antimyeloma activity- pomalidomide (POM) [4].

In the registration clinical trial, pomalidomide plus dexamethasone had superior efficacy compared to dexameth-

asone alone in all pre-specified endpoints, including progression-free survival (PFS), time to progression (TTP), and overall survival (OS) [5–7]. This treatment is of special interest in the patient's refractory to both lenalidomide and bortezomib with a response rate of approximately 30% [6].

Pomalidomide-based triplets doubled the response rates compared to pomalidomide plus dexamethasone, and they demonstrated significant activity in advanced MM in several clinical trials, in particular with bortezomib in OPTIMISMM trial [8]; with elotuzumab in ELOQUENT-3 trial [9]; with isatuximab in ICARIA- trial [10]; with carfilzomib [11] and with daratumumab in APOLLO trial [12].

The aim of the present paper was to assess pomalidomide and dexamethasone therapy in relapsed and refractory multiple myeloma (RRMM) patients before the use of triplets with pomalidomide in an unselected real-world population to offer an overview of our registry-based treatment results, and to compare them with clinical trials outcomes as well as other real-world evidence.

Patients and methods

Patients. In total, we analyzed a cohort of 164 RRMM patients on pomalidomide and dexamethasone treatment between December 2013 and November 2018 in one of the nine hematologic centers in the Czech Republic. All patients provided written informed consent with the inclusion of their data in the Registry of Monoclonal Gammopathies (RMG) and with their assessment. The written consent was approved by the Ethics committees of all hematological centers.

The diagnosis, clinical staging, and prognostic score of MM were based on the Durie and Salmon staging system [13] and the International Staging System (ISS) [14]. Patients must be aged ≥18 years. Patients have received at least one prior line of antimyeloma therapy, including proteasome inhibitors and an immunomodulatory drug and had disease progression on or after their last line of therapy. Refractory patients to previous treatment (excluding pomalidomide) were eligible. Patients treated with pomalidomide in clinical trials were not included in our analysis. Disease response and progression were defined according to consensus criteria published by the International Myeloma Working Group (MWG) [15]. Adverse events (AEs) were assessed according to the National Cancer Institute (NCI) common terminology criteria for adverse events (CTCAE, v3.0) [16].

The data for this study were recorded in the RMG of the Czech Myeloma Group (CMG), which is a large monitored multicenter registry covering patients with monoclonal gammopathies dominantly from Central Europe [17].

Treatment. Patients were treated in 28-day cycles until disease progression or intolerance. The median duration of pomalidomide treatment was 4.7 months (range, 0.3–32.4). Pomalidomide was administered in standard dosing of 4 mg daily, on days 1–21 in 28-day cycles. In 94.5% (155/164) of patients, pomalidomide was administered with dexamethasone. Dexamethasone at a dose of 20–40 mg/day was given on days 1, 8, 15, and 22 of each 28-day cycle. In 5.5% (9/164) of patients, who had known dexamethasone intolerance, an equivalent prednisone dose was used. Reduction of any of the drugs due to the patient's age, creatinine clearance, hepatic values, initial hematological toxicities, and other factors was allowed at the discretion of the physician. All patients were required to use thromboprophylaxis per national guidelines [18]. Pomalidomide-based triplets were not included as neither combination was approved or reimbursed at the time of the analysis outside of clinical trials.

Primary endpoints included response rates based on criteria and survival measures including progression-free survival (PFS) and overall survival (OS). OS was measured from the time of pomalidomide-based treatment initiation. Secondary endpoints were toxicities and previous treatment patterns including refractoriness to lenalidomide, and their impact on final outcomes. In order to assess the safety and toxicity of pomalidomide therapy, the occurrence and cause of death during treatment and follow-up periods were analyzed.

Statistical analysis. Data were described by absolute and relative frequencies of categorical variables and median (min–max) for quantitative variables. Survival analysis for different endpoints- OS and PFS, was conducted using the Kaplan-Meier method complemented by the 95% Greenwood confidence interval for estimates of probability survival. The statistical significance of differences in survival among subgroups was assessed using the log-rank test. All statistical tests were performed at a significance level of α=0.05 (all tests two-sided). Analysis was performed in the SPSS software (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0.0.1 Armonk, NY: IBM Corp.) and software R version 3.4.2. (www.r-project.org).

Results

The median age at diagnosis was 67 years (range 37.0–84.0); 72% of patients were ≥65 years at the time of treatment initiation. The median number of prior therapies was 4 (range 1–9). All patients prior to pomalidomide treatment had received antimyeloma therapy including a proteasome inhibitor (bortezomib in 97%, carfilzomib in 11.6%, ixazomib in 3.7%); immunomodulatory drug (lenalidomide in 96.3%, thalidomide in 64.6%) and 64.6% of patients had undergone autologous stem cell transplantation (ASCT). Altogether, 48.2% of patients (79/164) patients were refractory to bortezomib, 57.3% (94/164) patients were refractory to lenalidomide, and 23.8% (39/164) of patients were refractory to both lenalidomide and bortezomib. Baseline characteristics and prior therapies are presented in Table 1.

The median study follow-up was 9.9 months as of the data cutoff; 21.3% (35/164) of patients remain on pomalidomide treatment. The most frequent reason for treatment discontinuation was PG (58.8%); additional causes of treat-

ment discontinuations were death (16%), lack of efficacy (8.4%), the physician's decision (4.2%), AEs (3.4%), and other reasons including the patient decision of withdrawal (9.2%).

ORR was 51.8% (85/164) and clinical benefit rate (CBR, including patients with a minimal response) was 67.1% (110/164), with 0.6% (1/164) of complete responses (CR), 8.5% (14/164) of very good partial responses (VGPR), and 42.1% (69/164) of partial responses (PR). Overall, 16.5% (27/164) of patients had minimal response (MR) and 32.3% (53/164) had stable disease (SD)/progression (PD). Median PFS was 8.8 months (range, 6.2–1.4) and OS was 14.2 months (range, 10.7–17.7).

Median PFS and OS correlated with the depth of response. In patients who achieved at least PR, the median PFS and OS interval was significantly longer compared to patients with minimal or no response, median PFS (12.1 vs. 4.5 months, $p<0.001$, respectively); median OS (22.1 vs. 7.7 months, $p<0.001$, respectively) (Figures 1, 2). Patients with ≥VGPR had better outcomes compared to patients who achieved PR, MR, SD, or PD. The medians PFS were as follows: in VGPR+ 19.6 months, in PR 11.4 months, in MR 7.1 months, in SD 2.7 months, and in PD 3.9 months, $p<0.001$, respectively and median OS was decreasing accordingly: not reached vs. 21.5 vs. 14.9 vs. 3.3 vs. 5.4 months, $p<0.001$, VGPR vs. PR vs. MR vs. SD, vs. PD, respectively; (Figures 3, 4).

No other factors were found to significantly influence PFS and OS (gender, age, refractoriness, or previous treatment).

Treatment-related toxicity. AEs associated with pomalidomide treatment are shown in Table 2. The most frequent grade 3/4 hematological toxicities were neutropenia (41.2%), anemia (25.8%), and thrombocytopenia (25.0%). The most frequent grade 3/4 non-hematological AEs were infections (20.3%) and fatigue (10.2%). The incidence of any grade deep-vein thrombosis was 1.2%. Other non-hematological AEs were generally mild to moderate, interestingly, three of the patients developed grade 3/4 peripheral neuropathy. With appropriate management, the rates of discontinuations due to AEs were low (3.4%).

Discussion

Despite multiple novel therapeutic options, most MM patients ultimately relapse. In order to select the optimal treatment strategy for each RRMM patient, it is important to consider the patient, the course of the disease, and treatment-related factors [19]. For the treatment of RRMM patients, even in patients failing lenalidomide, the recommended treatment option is pomalidomide [20].

So far, two studies MM-003 and MM-010 found that pomalidomide plus low-dose dexamethasone significantly improved PFS, OS, and ORR vs. high-dose dexamethasone alone in RRMM patients [5, 7]. At present, great emphasis is placed on real-world evidence data, because clinical trials data do not always reflect real-world clinical practice and

Table 1. Characteristics at pomalidomide treatment initiation and prior treatment history in 164 MM patients.

Variable	
Age (years)	
median	67 (range: 37-84)
ECOG performance status	
0–1	129 (78.7%)
2	28 (17.0%)
3–4	7 (4.3%)
Number of prior lines	
median	4 (range: 1-9)
1	2 (1.2%)
2	21 (12.8%)
3	49 (29.9%)
4	44(26.8%)
>5	48 (29.3%)
Prior ASCT	
yes	106 (64.6%)
Prior PI	
Bortezomib	159 (97.0%)
Carfilzomib	19 (11.6%)
Ixazomib	6 (3.7%)
Prior IMiD	
Lenalidomide	158 (96.3%)
Thalidomide	106 (64.6%)
Pomalidomide	2 (2.4%)
Refractory* to prior	
Bortezomib	79 (48.2%)
Lenalidomide	94 (57.3%)
Bortezomib+Lenalidomide	39 (23.8%)

Abbreviations: N-number of total cases; n-number of valid cases; ASCT-autologous stem cell transplantation; PI-proteasome inhibitor; IMiD-immunomodulatory drugs. Notes: unless otherwise noted, data presented in absolute and relative (to valid cases) frequency; *refractority was based on the most recent prior medication

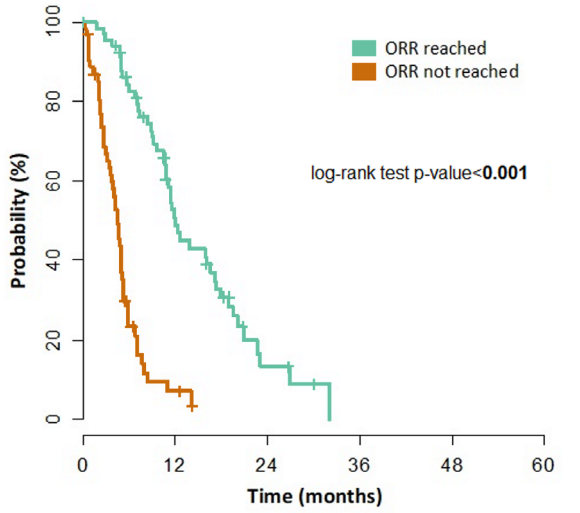
Table 2. Most frequent (> 10%) adverse events (AEs).

Variable	Overall (N=164)	
AEs, n (%)*	Any Grade	Grade 3/4
Hematological AEs		
Anemia	106 (64.6)	31 (18.9)
Neutropenia	102 (62.2)	49 (29.9)
Thrombocytopenia	87 (53.0)	30 (18.3)
Non-hematological AEs		
Fatigue	85 (51.8)	12 (7.3)
Infection	80 (48.8)	24 (14.6)
Nausea/Vomiting	21 (12.8)	1 (0.6)
AEs of special interest		
Peripheral sensory neuropathy before treatment	43 (26.2)	1 (0.6)
Peripheral sensory neuropathy after treatment	43 (26.2)	3 (1.8)

Abbreviations: N-number of total cases; n-number of valid cases; AE-adverse event. Notes: *AE severity was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events v 4.03

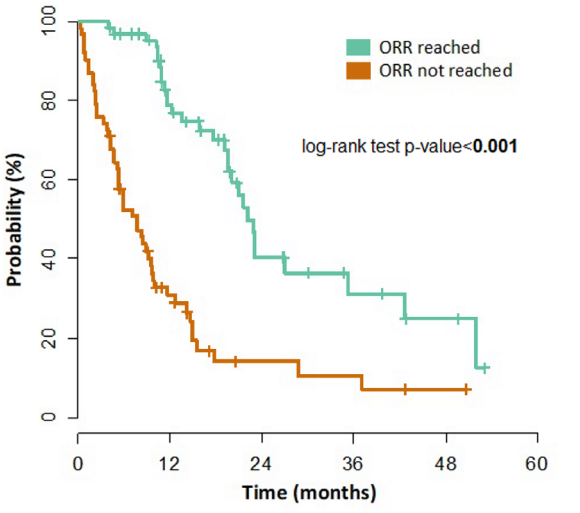
outcomes. Particularly when dealing with a cohort of patients with such advanced stage of the disease, many of whom have significant co-morbidities, makes delivery of recommended treatment challenging. Several myeloma groups published real-world evidence data to describe the outcomes as well as the tolerability of pomalidomide in RRMM patients. The ORR rate varied from 32.3% to 52.9%; the median PFS varied from 5.2 to 11.8 months [21–25].

We describe a real-world experience in our registry-based cohort of 164 patients receiving pomalidomide for RRMM in the Czech Republic. Our study confirmed pomalidomide and dexamethasone is an effective regimen that confers



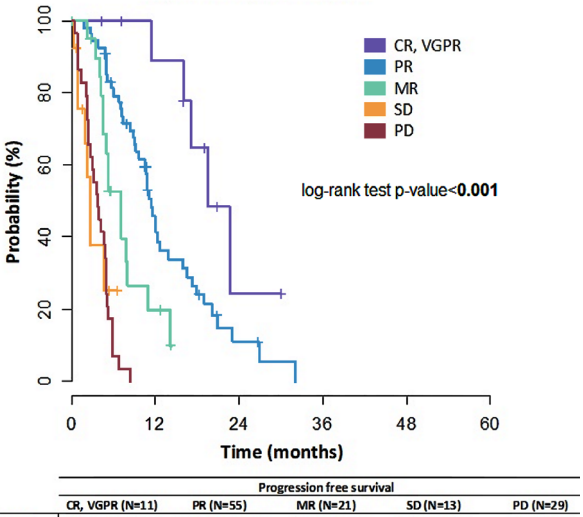
	Progression free survival	
	ORR not reached (N=63)	ORR reached (N=66)
median (95% CI)	4.5 (3.8–5.1)	12.1 (10.7–13.5)
12 m. % (95% CI)	7.0 (1.9–16.8)	50.7 (37.2–62.8)
24 m. % (95% CI)	–	13.3 (4.8–26.2)
36 m. % (95% CI)	–	–

Figure 1. Progression-free survival (PFS) by the overall response (ORR).



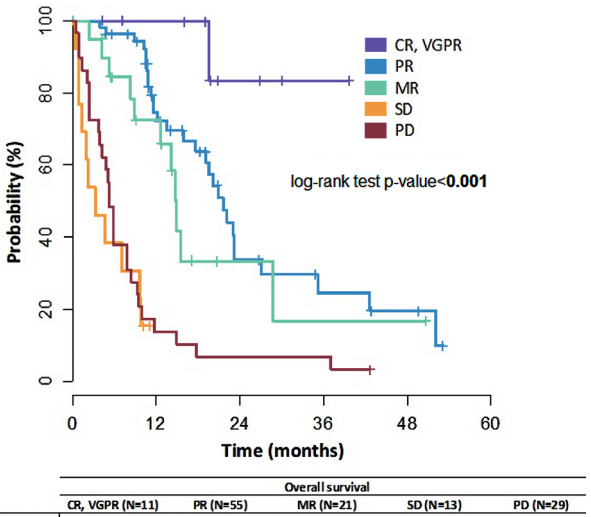
	Overall survival	
	ORR not reached (N=63)	ORR reached (N=66)
median (95% CI)	7.7 (5.0–10.4)	22.1 (19.4–24.8)
12 m. % (95% CI)	30.8 (19.4–43.0)	78.7 (65.5–87.4)
24 m. % (95% CI)	14.1 (5.9–25.8)	40.5 (24.9–55.6)
36 m. % (95% CI)	10.6 (3.4–22.4)	31.3 (15.8–48.0)

Figure 2. Overall survival (OS) by the overall response (ORR).



	Progression free survival				
	CR, VGPR (N=11)	PR (N=55)	MR (N=21)	SD (N=13)	PD (N=29)
median (95% CI)	19.6 (14.6–24.6)	11.4 (10.0–12.8)	7.1 (4.8–9.3)	2.7 (1.9–3.6)	3.9 (2.4–5.3)
12 m. % (95% CI)	88.9 (43.3–98.4)	43.5 (29.2–56.9)	19.8 (5.1–41.5)	–	–
24 m. % (95% CI)	24.3 (1.3–62.9)	11.0 (3.3–24.1)	–	–	–
36 m. % (95% CI)	–	–	–	–	–

Figure 3. Progression-free survival (PFS) by maximal treatment response.



	Overall survival				
	CR, VGPR (N=11)	PR (N=55)	MR (N=21)	SD (N=13)	PD (N=29)
median (95% CI)	not reached	21.5 (18.4–24.7)	14.9 (13.8–16.0)	3.3 (0.2–6.5)	5.4 (4.2–6.5)
12 m. % (95% CI)	100.0 (–)	74.5 (59.3–84.7)	72.4 (45.6–87.6)	–	13.8 (4.4–28.6)
24 m. % (95% CI)	83.3 (27.3–97.5)	33.9 (18.5–49.9)	33.4 (11.1–57.9)	–	6.9 (1.2–19.8)
36 m. % (95% CI)	83.3 (27.3–97.5)	24.7 (10.8–41.7)	16.7 (1.3–47.8)	–	6.9 (1.2–19.8)

Figure 4. Overall survival (OS) by maximal treatment response.

disease stabilization or regression in 67.1% of pretreated Czech patients with RRMM, including disease refractory to lenalidomide, bortezomib, or both. The characteristics of the patients and treatment (including age, number of prior therapies, number of pomalidomide cycles, and treatment duration) are broadly similar to those in published clinical trials [5, 7]. However, it is important to emphasize that this is an unbiased group of patients with a number of different comorbidities.

Despite real-world data, our results were surprisingly favorable compared to study results. Survival outcomes were analyzed for the entire cohort of 164 patients in our study. Disease response was 51.9% compared to 31.4% in MM-003 and 32.6% in MM-010.

In our cohort, the median PFS was 8.8 months, OS was 14.2 months. In MM-003 and MM-010 trials [5, 7] PFS was 4.0 and 4.6 months, respectively, with OS of 13.1 and 11.9 months, respectively. With the aim to find an explanation for the better treatment responses achieved in our conditions, we focused on the patient's refractory to previous treatment. In MM-003 and MM-010, patient cohorts were heavily pre-treated compared to our cohort: 75% vs. 72.9% vs. 25% were refractory to both an IMiD and bortezomib, respectively. Further, the studies had different inclusion criteria, including lenalidomide pretreatment. Until 2016, in the Czech Republic, lenalidomide was available for the treatment of RRMM but only to a maximum dose of 4200 mg, not until progression. The correction took place in December 2016, when the treatment of RRMM by lenalidomide became available until progression or unacceptable toxicity [18]. It could be a partial explanation for better treatment responses in our analysis. The important factor of survival benefit in our cohort was the depth of response. Achievement of ORR, especially VGPR or better, was associated with a PFS and OS benefit (Figures 3, 4).

The adverse events reported in our study were consistent with established toxicity profiles for pomalidomide [5, 6]. The most common grade 3/4 hematological AEs were neutropenia (29.9%), anemia (18.9%), and thrombocytopenia (18.3%). The most common grade 3/4 non-hematological AEs were infections (14.6%) and fatigue (7.3%). The results of our analysis support previous clinical trials [5, 6]. The incidence of deep-vein thrombosis which is generally increased when lenalidomide or thalidomide are combined with dexamethasone [26] was low (1.2%), with relatively standard thromboprophylaxis consisting mainly of oral aspirin (100 mg/day) or subcutaneous low molecular weight heparin (100 IU/kg/day). Importantly, only 1.8% of the patients developed grade 3–4 peripheral neuropathy, and other nonhematologic AEs were generally mild to moderate, overall, under 10%.

In summary, we report real-world experience data of patients receiving pomalidomide and dexamethasone for relapsed/refractory myeloma, with outcomes (response, survival, tolerability). Our results confirmed the effectiveness of pomalidomide and dexamethasone in a real-world setting. Despite being an unbiased cohort of patients, the therapy achieved reasonable outcomes comparable to the data from clinical trials. The response rate in severely pretreated RRMM patients (including 23.8% of double refractory patients) was approximately 52%; the clinical benefit rate was 67.1% Patients who achieved therapeutic responses, the response results began to be clinically significant, especially in patients with VGPR and better.

Based on the already mentioned real-world evidence results, we can conclude that pomalidomide and dexamethasone is an effective and safe treatment option for pretreated RRMM patients.

Our results confirmed the effectiveness of pomalidomide and dexamethasone in a real-world setting. Despite being an unbiased cohort of patients, the therapy achieved reasonable outcomes comparable to the data from clinical trials. The response rate in severely pre-treated RRMM patients (including 23.8% of double refractory patients) was approximately 52%; the clinical benefit rate was 67.1% Patients who achieved therapeutic responses, the response results began to be clinically significant, especially in patients with VGPR and better. Based on the already mentioned results, we can conclude that pomalidomide and dexamethasone have modest efficacy and good safety profile. This doublet could be a suitable treatment option for pretreated RRMM patients.

Acknowledgments: This work was supported by the program Cooperatio, research area ONCO, and by the grant NU21-03-00076.

References

[1] HÁJEK R, JARKOVSKY J, MAISNAR V, POUR L, ŠPIČKA I et al. Real-world Outcomes of Multiple Myeloma: Retrospective Analysis of the Czech Registry of Monoclonal Gammopathies. Clin Lymphoma Myeloma Leuk 2018; 18: e219–e240. https://doi.org/10.1016/j.clml.2018.04.003

[2] LAUBACH J, GARDERET L, MAHINDRA A, GAHRTON G, CAERS J et al. Management of relapsed multiple myeloma: recommendations of the International Myeloma Working Group. Leukemia 2016; 30: 1005–1017. https://doi.org/10.1038/leu.2015.356

[3] LEE HC, SHAH JJ, ORLOWSKI RZ. Novel approaches to treatment of double-refractory multiple myeloma. Am Soc Clin Oncol Educ Book 2013; 2013: 302–306. https://doi.org/10.1200/EdBook_AM.2013.33.e302

[4] LACY MQ, MCCURDY AR. Pomalidomide. Blood 2013; 122: 2305–2309. Erratum in: Blood 2014; 123: 4153. https://doi.org/10.1182/blood-2013-05-484782

[5] MIGUEL JS, WEISEL K, MOREAU P, LACY M, SONG K et al. Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for patients with relapsed and refractory multiple myeloma (MM-003): a randomised, open-label, phase 3 trial. Lancet Oncol 2013; 14: 1055–1066. https://doi.org/10.1016/S1470-2045(13)70380-2

[6] RICHARDSON PG, SIEGEL DS, VIJ R, HOFMEISTER CC, BAZ R et al. Pomalidomide alone or in combination with low-dose dexamethasone in relapsed and refractory multiple myeloma: a randomized phase 2 study. Blood 2014; 123: 1826–1832. Erratum in: Blood 2014; 123: 3208–3209. https://doi.org/10.1182/blood-2013-11-538835

[7] DIMOPOULOS MA, PALUMBO A, CORRADINI P, CAVO M, DELFORGE M et al. Safety and efficacy of pomalidomide plus low-dose dexamethasone in STRATUS (MM-010): a phase 3b study in refractory multiple myeloma. Blood 2016; 128: 497–503. https://doi.org/10.1182/blood-2016-02-700872

[8] RICHARDSON PG, ORIOL A, BEKSAC M, LIBERATI AM, GALLI M et al. OPTIMISMM trial investigators. 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: 781–794. https://doi.org/10.1016/S1470-2045(19)30152-4

[9] DIMOPOULOS MA, DYTFELD D, GROSICKI S, MOREAU P, TAKEZAKO N et al. Elotuzumab plus Pomalidomide and Dexamethasone for Multiple Myeloma. N Engl J Med 2018; 379: 1811–1822. https://doi.org/10.1056/NEJMoa1805762

[10] ATTAL M, RICHARDSON PG, RAJKUMAR SV, SAN-MIGUEL J, BEKSAC M et al. ICARIA-MM study group. Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study. Lancet 2019; 394: 2096–2107. Erratum in: Lancet 2019; 394: 2072. https://doi.org/10.1016/S0140-6736(19)32556-5

[11] BRINGHEN S, MINA R, CAFRO AM, LIBERATI AM, SPADA S et al. Once-weekly carfilzomib, pomalidomide, and low-dose dexamethasone for relapsed/refractory myeloma: a phase I/II study. Leukemia 2018; 32: 1803–1807. https://doi.org/10.1038/s41375-018-0024-1

[12] DIMOPOULOS MA, TERPOS E, BOCCADORO M, DELIMPASI S, BEKSAC M et al. APOLLO Trial Investigators. Daratumumab plus pomalidomide and dexamethasone versus pomalidomide and dexamethasone alone in previously treated multiple myeloma (APOLLO): an open-label, randomised, phase 3 trial. Lancet Oncol 2021; 22: 801–812. https://doi.org/10.1016/S1470-2045(21)00128-5

[13] DURIE BG, SALMON SE. A clinical staging system for multiple myeloma. Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival. Cancer 1975 Sep; 36: 842–854. https://doi.org/10.1002/1097-0142(197509)36:3<842::aid-cncr2820360303>3.0.co;2-u

[14] GREIPP PR, SAN MIGUEL J, DURIE BG, CROWLEY JJ, BARLOGIE B et al. International staging system for multiple myeloma. J Clin Oncol 2005; 23: 3412–3420. Erratum in: J Clin Oncol 2005; 23: 6281. https://doi.org/10.1200/JCO.2005.04.242

[15] RAJKUMAR SV. Multiple myeloma: 2018 update on diagnosis, risk-stratification, and management. Am J Hematol 2018; 93: 981–1114. https://doi.org/10.1002/ajh.25117

[16] TROTTI A, COLEVAS AD, SETSER A, RUSCH V, JAQUES D et al. CTCAE v3.0: development of a comprehensive grading system for the adverse effects of cancer treatment. Semin Radiat Oncol 2003; 13: 176–181. https://doi.org/10.1016/S1053-4296(03)00031-6

[17] RADOCHA J, POUR L, SPICKA I, SCUDLA V, GREGORA E et al. Registry of Monoclonal Gammopathies (RMG) in the Czech Republic. Blood 2015; 126: 4514. https://doi.org/10.1182/blood.V126.23.4514.4514

[18] MAISNAR V, KREJČÍ M, MINAŘÍK J et al. (Eds.) [Diagnosis and treatment of multiple myeloma.] In: [Transfusion and Hematology Today] 2018; 24. Česká lékařská společnost J.E. Purkyně p. 156. ISSN 1805-4587

[19] DURER C, DURER S, LEE S, CHAKRABORTY R, MALIK MN et al. Treatment of relapsed multiple myeloma: Evidence-based recommendations. Blood Rev 2020; 39: 100616. https://doi.org/10.1016/j.blre.2019.100616

[20] LACY MQ, HAYMAN SR, GERTZ MA, SHORT KD, DISPENZIERI A et al. Pomalidomide (CC4047) plus low dose dexamethasone (Pom/dex) is active and well tolerated in lenalidomide refractory multiple myeloma (MM). Leukemia 2010; 24: 1934–1939. https://doi.org/10.1038/leu.2010.190

[21] MACIOCIA N, MELVILLE A, CHEESMAN S, SHARPLEY F, RAMASAMY K et al. Real-world use of pomalidomide and dexamethasone in double refractory multiple myeloma suggests benefit in renal impairment and adverse genetics: a multi-centre UK experience. Br J Haematol 2017; 176: 908–917. https://doi.org/10.1111/bjh.14547

[22] CHARLINSKI G, GRZASKO N, JURCZYSZYN A, JANCZARSKI M, SZEREMET A et al. The efficacy and safety of pomalidomide in relapsed/refractory multiple myeloma in a "real-world" study: Polish Myeloma Group experience. Eur J Haematol 2018; 101: 354–361. https://doi.org/10.1111/ejh.13106

[23] TERPOS E, MIKHAEL J, HAJEK R, CHARI A, ZWEEGMAN S et al. Management of patients with multiple myeloma beyond the clinical-trial setting: understanding the balance between efficacy, safety and tolerability, and quality of life. Blood Cancer J 2021; 11: 40. https://doi.org/10.1038/s41408-021-00432-4

[24] LECHNER D, GREIL R, HARTMANN B, KRAUTH MT, GISSLINGER H et al. Pomalidomide (POM) and Low-Dose Dexamethasone (LoDEX) in Relapsed/Refractory Multiple Myeloma (RRMM): Analysis of Real World Data from an Ongoing, National, Multi-Center, Non-Interventional Study. Blood 2018; 132: 2018. https://doi.org/10.1182/blood-2018-99-116292

[25] MELE G, PASTORE D, DI RENZO N, FRAGASSO A, GUARINI A et al. Real world Italian experience of pomalidomide plus low-dose dexamethasone in the relapsed and refractory myeloma setting: extended follow-up of a retrospective multicenter study by the 'Rete Ematologica Pugliese E Basilicata'. Leuk Lymphoma 2019; 60: 3565–3568. https://doi.org/10.1080/10428194.2019.1636989

[26] PALUMBO A, RAJKUMAR SV, DIMOPOULOS MA, RICHARDSON PG, SAN MIGUEL J et al. Prevention of thalidomide- and lenalidomide-associated thrombosis in myeloma. Leukemia 2008; 22: 414–423. https://doi.org/10.1038/sj.leu.2405062