

Efficacy and safety of lenalidomide and dexamethasone in patients with relapsed/refractory multiple myeloma: a real-life experience

Nur SOYER^{1*}, Püsem PATIR¹, Ayşe UYSAL¹, Mustafa DURAN¹, Hatice Demet ÜNAL², Raika DURUSOY³,
Murat TOMBULOĞLU¹, Fahri ŞAHİN¹, Mahmut TÖBÜ¹, Filiz VURAL¹, Güray SAYDAM¹

¹Department of Hematology, Faculty of Medicine, Ege University, İzmir, Turkey

²Department of Hematology, Atatürk Research and Training Hospital, İzmir, Turkey

³Department of Public Health, Faculty of Medicine, Ege University, İzmir, Turkey

Received: 22.12.2017 • Accepted/Published Online: 08.07.2018 • Final Version: 16.08.2018

Background/aim: In Turkey, lenalidomide plus dexamethasone (RD) has been used to treat relapsed/refractory multiple myeloma (RRMM) since 2010. This retrospective, single-center study evaluated the efficacy and tolerability of RD in patients with RRMM between October 2010 and June 2016.

Materials and methods: Patients' records were reviewed, and overall (OS) and progression-free survival (PFS) were assessed.

Results: One hundred and twenty patients (71 males; 59.2%) were included in the study. The median number of prior lines of treatment was one (1–4); 72 patients (60.0%) received RD as second-line therapy and 51 patients (42.5%) had previously undergone autologous stem cell transplantation (ASCT). The overall response rate was 72.5%, with 19% of these patients achieving a complete response. The median length of follow-up and duration of response to RD was 14 months and 19 months, respectively. Median OS and PFS were 32 and 21 months, respectively. Prior ASCT, an overall response, and treatment with RD for >12 cycles were identified as independent prognostic factors for OS and PFS. Adverse events (AEs) occurred in 69 (57.5%) and 14 patients (11.7%) discontinued treatment due to AEs.

Conclusions: We found RD to be safe, well tolerated, and effective in RRMM in everyday clinical practice in Turkey.

Key words: Lenalidomide, dexamethasone, multiple myeloma, efficacy, safety

1. Introduction

Multiple myeloma (MM) is a clonal plasma cell disorder that, in symptomatic patients, is characterized by bone lesions, renal impairment, anemia, and hypercalcemia (1). Over the past 15–20 years, overall survival (OS) in MM has increased significantly with the introduction of novel agents such as proteasome inhibitors and immunomodulatory drugs (2). A Mayo Clinic study reported a median OS of 2.5 years in patients diagnosed before 2001, increasing to 4.6 and 6.1 years in patients diagnosed in 2001–2005 and 2006–2010, respectively (3). Improvement in OS was seen in patients aged >65 years, as well as in younger patients.

The immunomodulatory agent lenalidomide was evaluated in two large, multicenter, randomized, placebo-controlled phase III trials: MM-009 in North America and MM-010 in Europe, Australia, and Israel (4,5). These trials demonstrated the superiority of lenalidomide plus dexamethasone (RD) versus dexamethasone alone in patients with relapsed/refractory multiple myeloma

(RRMM), with the overall response rate (ORR) and OS being significantly increased with RD. The most common adverse events (AEs) were hematologic events, thromboembolic complications, and pneumonia (6). On the basis of the results of MM-009 and -010, lenalidomide was approved by the US Food and Drug Administration and the European Medicines Agency for the treatment of RRMM.

While clinical trials remain the gold standard for drug approval, more information is needed about the performance of specific drugs in patients with unstudied comorbid conditions, and when combined with different concomitant medications in the real world. Some real-life efficacy and safety data are available for RD in patients with RRMM. A Greek study reported an ORR of 74.4%, and median times to first and best response of 2 and 5 months, respectively (7,8). The median duration of response (DOR) was 34.4 months, and it was higher in patients who received RD until progression versus those

* Correspondence: drakadnur@yahoo.com

who received fixed-duration therapy. AEs were reported in 68.9% of the study population. In a study in Portugal, the ORR was 68% and the median DOR was 13.6 months (8). The best outcomes were achieved by patients who were treated at first relapse, and those who received RD for longer than 1 year.

In Turkey, RD has been used in the treatment of RRMM since 2010. We designed the present study to retrospectively evaluate the efficacy and safety of RD in Turkish patients with RRMM in real-life clinical practice.

2. Materials and methods

2.1. Study design and patient selection

This was a retrospective, single-center, noninterventional study designed to assess the efficacy and tolerability of RD treatment in patients with RRMM who had been treated according to standard clinical practice in Turkey. The study was approved by the Local Ethics Committee of Ege University (07.03.2016/16-2.1/13).

The following data were collected from the medical records of patients with RRMM treated with RD at the Ege University Medical Faculty Hospital in İzmir, Turkey, between October 2010 and June 2016: age at diagnosis and at initiation of RD; sex; date of diagnosis; cytogenetic characteristics; disease stage; prior treatments, including prior transplantation; date of initiation of RD; lenalidomide dose reductions; treatment outcome; any AEs; and the date of initiation of any subsequent treatment. Response to treatment was assessed according to International Myeloma Working Group uniform response criteria (9). Initial dose of lenalidomide and dexamethasone was related to physician preference and creatinine clearance of patients.

2.2. Definition of outcomes

OS was measured from the start of RD treatment until either death from any cause or the last date of patient follow-up. Progression-free survival (PFS) was measured from the date of initiation of RD until either disease progression or death from any cause. DOR was evaluated in patients achieving at least a partial response (PR) and was defined as the time from the initiation of RD until disease progression.

2.3. Statistical analysis

Statistical analyses were performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). Variables were first assessed by Kolmogorov–Smirnov/Shapiro–Wilk tests in terms of normal distribution. Results were provided as mean \pm standard deviation for normally distributed variables and as median (range) for nonnormally distributed parameters. All P-values were two-sided and statistical significance was set at the level of $P < 0.05$.

OS and PFS were estimated using Kaplan–Meier methodology. The log-rank test was used to evaluate

the variables affecting OS and PFS (univariate analysis). Independent variables affecting PFS and OS were analyzed using Cox proportional hazards regression for multivariate analysis.

Second primary malignancies (SPMs) were defined using the Medical Dictionary for Regulatory Activities terms found under the System Organ Class ‘Neoplasms’. Incidence rates (IRs; events per 100 patient-years) and their confidence intervals (CIs) were calculated. Patient-years were defined as the time in years from the first dose of lenalidomide to SPM onset in patients with a SPM, and the time from the first to the last dose of lenalidomide in patients without a SPM. Overall IRs include invasive and noninvasive SPMs and nonmelanoma skin carcinomas.

3. Results

3.1. Patients

In total, 120 patients (71 males; 59.2%) were included in the study. Baseline patient characteristics are presented in Table 1. Patients’ median age at diagnosis and at the start of RD was 61 years (range: 29–84 years) and 64 years (range: 30–85 years), respectively. The median number of prior lines of therapy was one (range: 1–4). Cytogenetic data, obtained by fluorescent in situ hybridization (FISH) and/or conventional cytogenetics, were available for only 43 patients; four of these patients had deletion of chromosome 13 [del(13q)]. Metaphase chromosomes were not obtained for 3 of the patients but FISH analysis was normal in these patients.

Seventy-two patients (60%) received RD as second-line therapy, 40 (33.3%) as the third line, seven (5.8%) as the fourth line, and one (0.9%) as the fifth line. Among patients who received RD as second-line therapy ($n = 72$), 5.6% had previously received conventional chemotherapeutic regimens consisting of vincristine, doxorubicin, and dexamethasone (VAD); 41.6% bortezomib-based therapies (VCD, VD, and VMP); 48.6% VAD plus bortezomib-based therapies (VCD, VD, and VTD); and 4.2% melphalan-containing regimens (MP, MPT). Sixteen patients (13.3%) had received thalidomide induction [MPT ($n = 2$), VTD ($n = 1$)] or maintenance ($n = 15$) treatment prior to RD.

Among patients who received RD as third-line therapy ($n = 40$), 72.5% had received VAD chemotherapy, 12.5% bortezomib-based therapies (VD, VMP), and 15% melphalan-containing regimens (MP, MPT) in first-line therapy. In second-line therapy, 77.5% had received bortezomib-based therapies (VD, VMP, and VCD), 5% thalidomide-based therapy (TD), and 2.5% melphalan-containing regimen (MP).

Among patients who received RD as fourth- or fifth-line therapy ($n = 8$), 87.5% had received VAD chemotherapy and 12.5% melphalan-containing regimens (MP) in first-line therapy. In second-line therapy, 12.5% had received

Table 1. Baseline clinical and demographic characteristics.

Characteristic	All patients (n = 120)	Prior ASCT (n = 51)	No prior ASCT (n = 69)	P-value
Median age at diagnosis, years (range)	60.5 (29–84)	56 (29–67)	67 (59–84)	<0.001
Median age at start of RD, years (range)	64 (29–84)	59 (29–74)	70 (59–84)	<0.001
Sex (male/female)	71/49	31/20	40/29	0.75
ECOG PS, n (%)				
0–2	103 (85.8)	41 (80.4)	62 (89.9)	
3–4	8 (6.7)	2 (3.9)	6 (8.7)	
NA	9 (7.5)	8 (15.7)	1 (1.4)	
Type of myeloma, n (%)				0.15
IgG kappa	46 (38.3)	19 (37.3)	27 (39.1)	
IgG lambda	25 (20.8)	12 (23.5)	13 (18.8)	
IgA kappa	19 (15.8)	9 (17.7)	10 (14.5)	
IgA lambda	13 (10.8)	2 (3.9)	11 (15.9)	
Kappa	7 (5.8)	2 (3.9)	5 (7.3)	
Lambda	10 (8.3)	7 (13.7)	3 (4.4)	
ISS disease stage, n (%)				0.22
I	39 (32.5)	16 (31.4)	23 (33.3)	
II	27 (22.5)	9 (17.6)	18 (26.1)	
III	33 (27.5)	13 (25.5)	20 (29.0)	
NA	21 (17.5)	13 (25.5)	8 (11.6)	
Durie–Salmon disease stage, n (%)				0.75
I	5 (4.2)	3 (5.9)	2 (2.9)	
II	21 (17.5)	8 (15.7)	13 (18.8)	
III	94 (78.3)	40 (78.4)	54 (78.2)	
Cytogenetic data available, n (%)	43 (35.8)	14 (27.5)	29 (42.0)	0.1
Lytic lesion(s), n (%)	84 (70.0)	38 (74.5)	46 (66.7)	0.35
Renal disease, n (%)	17 (14.2)	7 (13.7)	10 (14.5)	0.83
Mean creatinine level, mg/dL (SD)	1.5 (1.7)	1.3 (1.0)	1.6 (2.0)	0.39
Mean albumin, g/dL (SD)	3.6 (0.7)	3.6 (0.8)	3.6 (0.6)	0.96
Mean calcium level, mg/dL	9.4 (1.0)	9.5 (1.2)	9.3 (0.8)	0.3
Number of prior lines of therapy, n (%)				0.28
1	72 (60.0)	27 (52.9)	45 (65.2)	
≥2	48 (40.0)	24 (47.1)	24 (34.8)	
Median number of cycles of RD received (range)	8 (2–32)	8 (3–32)	8 (1–30)	0.8

ASCT, Autologous stem cell transplantation; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; NA, not available; RD, lenalidomide and dexamethasone; SD, standard deviation.

VAD chemotherapy, 62.5% had received bortezomib-based therapies (VD, VCD), and 25% thalidomide-based therapy (TD). In third-line therapy, 50% had received bortezomib-based therapies (VD, VCD), 37.5% thalidomide-based therapy (TD), and 12.5% melphalan-containing regimens

(MP). In fourth-line therapy, 1 patient had received VD before RD therapy.

Fifty-one patients (42.5%) received autologous stem cell transplantation (ASCT) conditioned with high-dose melphalan prior to RD treatment; the median

interval between ASCT and the initiation of RD was 24 months (range: 1–148 months). In one patient, a new plasmacytoma was detected at 1 month after ASCT. RD treatment was started as second-line treatment. Baseline characteristics did not differ among the prior ASCT versus no prior ASCT groups, with the exception of median age at diagnosis and at the start of RD, as shown in Table 1.

3.2. Treatment

All 120 patients were treated with RD. Eighty-two patients (68.3%) received lenalidomide at the full recommended dose of 25 mg/day on days 1–21 of every 28-day cycle for the duration of treatment; the daily dose was reduced to 15 mg in 17 patients (14.2%), 10 mg in nine patients (7.5%), and 5 mg in 12 patients (10%). Reductions in the initial lenalidomide dose were required for renal insufficiency (grade 2; $n = 13$), cytopenias (grade 3–4; $n = 16$), and other AEs (grade 3; $n = 9$). Dexamethasone was administered at a dose of 40 mg/week in 67 patients (55.8%); the remaining patients ($n = 53$) received a dose of 20–32 mg/week. Patients received a median of eight cycles of RD (range: 2–32 cycles). Dexamethasone dose reductions were required by 28 (23.3%) patients. Eighty-five patients (70.8%) discontinued RD: 30 (25%) due to disease progression, 14 (11.7%) due to toxicity, 25 (20.8%) due to completion of the prescribed number of treatment cycles, and 16 (13.3%) for other reasons (patients' preference, insurance problems). Twenty-nine (24.2%) of the 85 patients who discontinued RD received subsequent treatment protocols; the median treatment-free interval following RD was 3 months (range: 1.2–4.7 months). One hundred and eleven patients (92.5%) received antithrombotic prophylaxis with low-dose aspirin ($n = 100$; 83.3%), warfarin ($n = 3$; 2.5%), low-molecular-weight heparin ($n = 7$; 5.8%), or clopidogrel ($n = 1$; 0.8%). There was no prior thromboembolic disease in all patients. Thromboembolic events were not reported in any of the patients who did not receive any antithrombotic prophylaxis.

3.3. Efficacy

Overall, 87 patients (72.5%) achieved an objective response (\geq PR) and 23 (19.2%) of them achieved a complete response (CR). Thirty patients (25%) progressed while on therapy. The median time to first observed clinical improvement and to best response was 3 (range: 1–15) and 4 (range: 1–20) months, respectively. The median length of follow-up and median DOR was 14 months (range: 1–72 months) and 19 months (range: 12.4–25.6 months), respectively.

Median OS and PFS were 32 months (95% CI: 15.8–48.1) and 21 months (95% CI: 15.8–26.1 months), respectively. OS was significantly prolonged in patients who received >12 cycles versus ≤ 12 cycles of RD, who had undergone prior ASCT versus no prior ASCT ($P = 0.007$), or who achieved \geq PR versus $<$ PR as a best response to

RD ($P < 0.001$), as shown in Table 2. PFS was significantly prolonged in patients who achieved \geq PR versus $<$ PR as a best response to RD ($P < 0.001$) or received >12 versus ≤ 12 cycles of RD ($P < 0.001$), as shown in Table 2. There were not response differences between patients using different dose of lenalidomide (25 mg vs. <25 mg, $P = 0.119$). On multivariate analysis, achievement of \geq PR as a best response to RD, prior ASCT, and receipt of >12 cycles of RD were confirmed as independent prognostic factors for OS and PFS, as shown in Figures 1 and 2. The results of the univariate and multivariate analyses are summarized in Tables 2 and 3.

3.4. Safety

AEs were reported in 69 patients (57.5%). Rates of hematologic and nonhematologic AEs were identical ($n = 47$; 39.2%). Neutropenia was the most common hematologic AE, occurring in 34 patients (28.3%). Twenty-six patients (21.7%) received granulocyte-colony stimulating factors (G-CSFs) for the prevention or treatment of neutropenia. Pneumonia was the most common nonhematologic AE, occurring in 19 patients (15.8%); one of these cases was fatal. In our center, patients did not receive antibiotic prophylaxis at the beginning of RD treatment. Rates of lenalidomide-related peripheral neuropathy and deep-vein thrombosis were 2.5% and 1.6%, respectively. A summary of treatment-related AEs is presented in Table 4.

Dose reductions owing to AEs were reported in 24 patients, while the dose of lenalidomide was increased in four patients whose starting dose was <25 mg daily. Fourteen patients (11.7%) discontinued treatment prematurely owing to AEs. Only one noninvasive SPM (basal cell carcinoma) was reported. The overall IR of SPMs was 0.93 (95% CI: 0.04–4.60).

4. Discussion

In this study, we retrospectively evaluated the efficacy and safety of RD treatment in Turkish patients with RRMM in a clinical practice setting. Randomized controlled trials remain the gold standard for drug approval, as they include patient populations selected specifically to evaluate the efficacy of the investigational drug. In contrast, real-life studies include all types of patients who require treatment in everyday clinical practice, some of whom have comorbidities that would preclude their participation in randomized clinical trials. Additionally, real-life studies enable the collection of longer-term efficacy and safety data than can be obtained in a controlled clinical trial setting. Nevertheless, real-life studies are limited by factors such as insufficient data, inadequate data quality, study design, and patient selection and assessment bias (10,11).

In the present study, patients' median age at the start of RD was similar to that reported in the literature

Table 2. Factors associated with PFS and OS (univariate analysis).

Factor	PFS		OS	
	median [95% CI], months	P-value	median [95% CI], months	P-value
Best response to RD				
≥PR	29 [16.0–41.9]	<0.001	44 [25.5–62.4]	<0.001
<PR	10 [8.5–11.4]		14 [9.9–18.0]	
Number of earlier therapies				
1	25 [15.7–34.3]	0.199	45 [14.3–75.7]	0.731
≥2	16 [11.2–20.7]		28 [10.2–5.8]	
Age in years at start of RD				
<65	23 [0–46.0]	0.28	59 [30.6–87.3]	0.005
≥65	21 [14.7–27.2]		22 [19.4–24.5]	
Previous ASCT				
Yes	29 [6.8–51.1]	0.07	59 [33.2–84.7]	0.007
No	20 [13.4–26.5]		22 [19.4–24.5]	
Number of cycles of RD received				
1–12	12 [8.9–15.0]	<0.001	16 [10.5–21.4]	<0.001
>12	38 [32.4–43.5]		Not reached	

ASCT, Autologous stem cell transplant; CI, confidence interval; OS, overall survival; PFS, progression-free survival; PR, partial response; RD, lenalidomide plus dexamethasone.

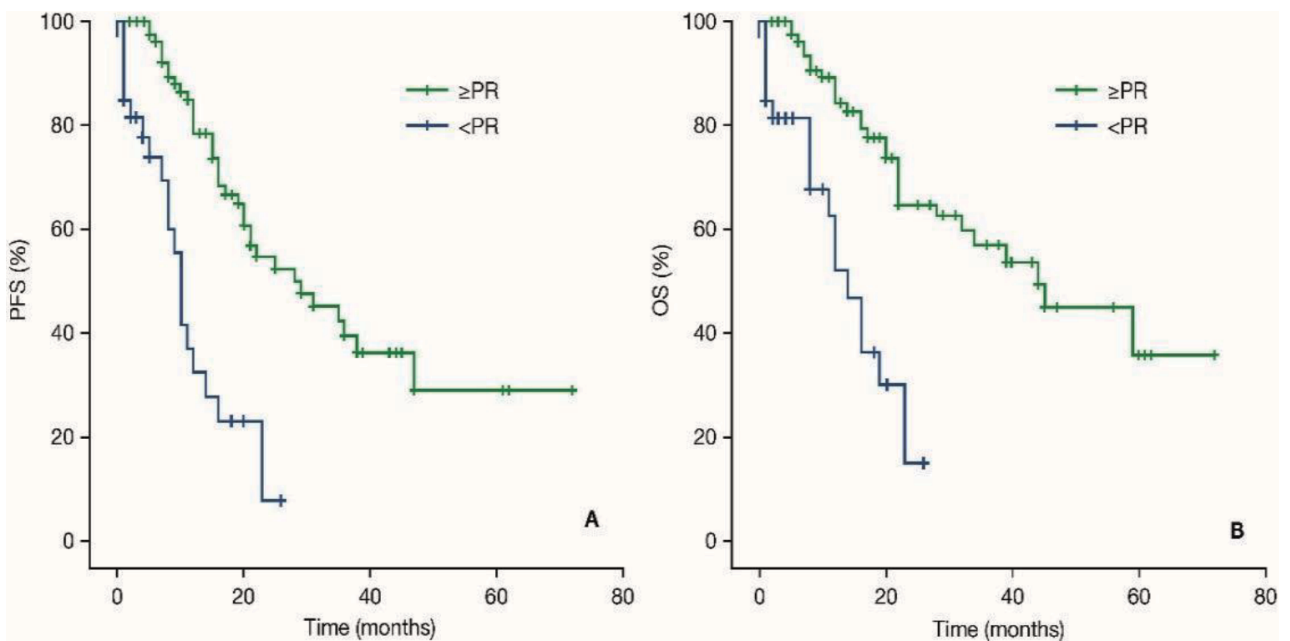


Figure 1. Kaplan–Meier estimates of A) PFS and B) OS, according to best response to RD treatment. OS, Overall survival; PFS, progression-free survival; PR, partial response; RD, lenalidomide plus dexamethasone.

(4,5,8,12–14). Overall, 60% of patients received RD as second-line therapy, a higher rate than that reported in previous clinical trials and real-life studies (4,5,7,8,14).

This observation could reflect an influence of publications demonstrating that the greatest benefits are obtained when RD is administered early in RRMM (6,15). Approximately

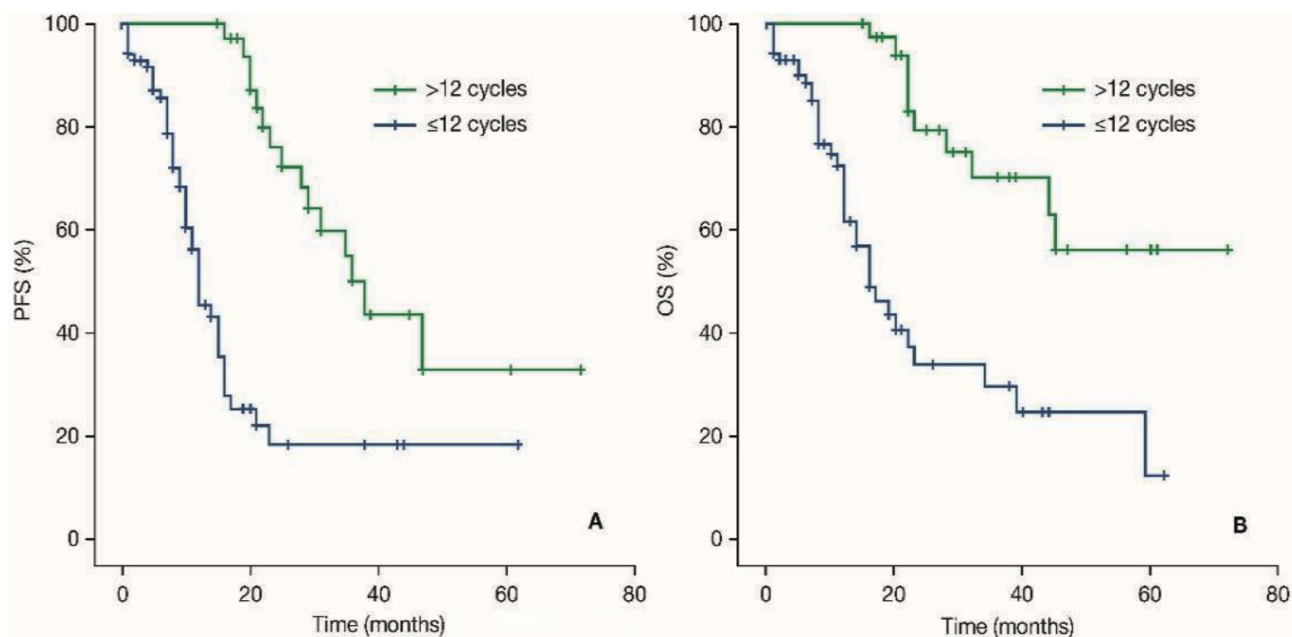


Figure 2. Kaplan–Meier estimates of A) PFS and B) OS, according to duration of RD treatment. OS, Overall survival; PFS, progression-free survival; RD, lenalidomide plus dexamethasone.

Table 3. Factors associated with PFS and OS (multivariate analysis).

	Hazard ratio	95% CI	P-value
OS			
Age at start of RD, years			
<65 vs. ≥65	1.7	0.84–3.46	0.139
Previous ASCT			
Yes vs. no	2.92	1.33–6.42	0.007
Best response to RD			
≥PR vs. <PR	2.30	1.18–4.47	0.014
Treatment duration, cycles			
1–12 vs. >12	6.02	2.70–13.4	<0.001
PFS			
Age at start of RD, years			
<65 vs. ≥65	0.96	0.53–1.74	0.91
Previous ASCT			
Yes vs. no	2.37	1.3–4.6	0.008
Best response to RD			
≥PR vs. <PR	2.51	1.4–4.6	0.002
Treatment duration, cycles			
1–12 vs. >12	4.64	2.4–9.1	<0.001

ASCT, Autologous stem cell transplant; CI, confidence interval; OS, overall survival; PFS, progression-free survival; PR, partial response; RD, lenalidomide plus dexamethasone.

Table 4. Adverse events in patients treated with RD.

Adverse event, n (%)	All grades	Grade 3–4
Hematologic		
Anemia	15 (12.5)	5 (4.2)
Thrombocytopenia	11 (9.2)	2 (1.7)
Neutropenia	34 (28.3)	10 (8.3)
Pancytopenia	3 (2.5)	2 (1.7)
Nonhematologic		
Pneumonia	19 (15.8)	5 (4.2)
Fatigue	17 (14.2)	2 (1.7)
Herpes zoster	1 (0.8)	0 (0)
Cutaneous reaction	2 (1.7)	1 (0.8)
Neuropathy	3 (2.5)	0 (0)
Renal failure	2 (1.7)	2 (1.7)
Diarrhea	3 (2.5)	1 (0.8)
Deep-vein thrombosis	2 (1.7)	0 (0)
Nausea	1 (0.8)	0 (0)
Urinary tract infection	3 (2.5)	0 (0)

RD, Lenalidomide plus dexamethasone.

92% of patients who received RD as a second-line regimen had previously been treated with bortezomib-based regimens either alone or following VAD chemotherapy. This reflects the fact that, in Turkey, reimbursement is provided with bortezomib treatment following two cycles of conventional chemotherapy in patients with newly diagnosed MM under the age of 65. Another difference versus other studies was the lower usage of thalidomide: 13% in our study versus 23%–64% in previous reports (4,5,8). This again can be attributed to reimbursement considerations, in addition to concerns regarding the risk of thalidomide-induced neuropathy. Nearly 50% of patients in our study had previously undergone ASCT, a rate that is consistent with the range of 49%–62% reported previously in the literature (4,5,8,14).

In our study, the ORR was 73%, with a CR rate of 19%; these rates are comparable with those reported in the literature (61%–78% and 6%–21%, respectively) (6–8,12,13). In a Dutch compassionate-use study, in which patients had received a median of three previous lines of treatment, the ORR and CR + very good partial response (VGPR) rate were 69% and 25%, respectively (13). Stadtmayer et al., who analyzed data from two phase III trials on RRMM, found that the ORR was higher (67% vs. 57%; $P = 0.06$) and the CR+VGPR rate was significantly higher (40% vs. 28%; $P = 0.025$) in patients treated with RD at first relapse versus later in the course of the disease (14).

These findings suggest that the high ORR and CR rates in our study may be associated with the early administration of RD.

Previous studies of RD in RRMM have reported median times to first observed clinical improvement and to best response of 2–2.8 and 3–5 months, respectively (7,8,12), and a median DOR of 15.8–34.4 months (6–8,12). These values are similar to those in our study.

We observed a median OS of 32 months, which is comparable to values reported in the literature for similar patient populations (29–42 months), while median PFS in our study was notably prolonged versus literature reports: 21 months versus 9–14.1 months (6–8,12,15). These findings contrast with the median OS of 22 months and median PFS of 11 months in the previously discussed Dutch study of heavily pretreated patients (13). The impressive PFS in our study may thus be attributable to several factors, including early use of lenalidomide, less aggressive disease, effective management of AEs, and a high level of patient compliance with the prescribed treatment regimen. Our finding that previous ASCT, the achievement of \geq PR, and receipt of >12 cycles of RD were independent prognostic factors for both PFS and OS appears to support this hypothesis. Previous studies have also demonstrated an association between best response to treatment and length of PFS and OS (8,12), while others have shown that PFS and OS are significantly prolonged in patients who have previously undergone ASCT and those with only one prior line of therapy versus patients with no prior ASCT and who receive RD as a later line of treatment (6,13).

The 58% AE rate in our study is slightly lower than that in the literature (60%–83%) (6–8). Neutropenia and thrombocytopenia occurred in 28% and 9% of our patients, respectively; these rates are comparable with those in other published studies (20%–22.6% and 7.5%–19%, respectively) (7,8). Rates of grade 3–4 neutropenia (8%) and thrombocytopenia (2%) were lower than in the literature (35%–51% and 9%–14%, respectively) (6,12,15), possibly as a result of the early administration of RD and prophylactic use of G-CSF in our study. However, rates of grade 3–4 neutropenia and thrombocytopenia were consistent with the Turkish PASS study (14). Pneumonia was the most common nonhematologic AE; the 16% incidence in our study was slightly higher than the 10%–13% reported with RD treatment in previous real-life studies (7,8). However, the rate of grade 3–4 pneumonia in our study was lower than that in the analysis of the MM-009 and -010 trials: 4% versus 9% (6). The rate of grade 3–4 pneumonia was similar to that of the Turkish PASS study (14). Twelve percent of patients in our study discontinued treatment owing to AEs, compared with literature rates of 10.8%–26% (7,8,12,14,15). The lower

rate in our study could perhaps be explained by the fact that many physicians in real life will try to keep patients on treatment for as long as possible, managing AEs through dose reductions or supportive treatment. The thrombosis rate in our study was very low (1.6%), owing to the extensive use of thromboprophylaxis. This rate was similar to the Turkish PASS study (14). Thrombosis rates in the literature range from 6% to 9% (7,8). The rate of peripheral neuropathy (2.5%) was slightly lower than in previous studies (2.5%–6%) (7,8). The lower rate could be explained by the fact that we only evaluated the rate of lenalidomide-related peripheral neuropathy.

A retrospective pooled analysis of 11 clinical trials including 3846 patients with RRMM found an overall IR of SPMs of 3.62 (16), while an analysis of data from the MM-009 and -010 studies reported an overall IR of 2.3 (17). In our study, the overall IR of SPMs was lower at 0.93,

which could be a result of low patient numbers and the relatively short follow-up.

In conclusion, we found RD to be safe, well tolerated, and effective in the treatment of RRMM in real-life clinical practice in Turkey. A good response (\geq PR) to treatment, previous ASCT, and the receipt of >12 cycles of treatment were all associated with improved survival. Additionally, administration of RD at first relapse versus later in the course of RRMM was associated with prolonged PFS and OS, and a higher ORR. AEs were manageable and less frequent with prophylaxis.

Acknowledgment

Editorial assistance in the preparation of this manuscript was provided by Sandralee Lewis, PhD, of the Investigator Initiated Research Writing Group (an initiative of Ashfield Healthcare Communications, a part of UDG Healthcare plc), and was funded by Celgene Corporation.

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