OncoTargets and Therapy

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ORIGINAL RESEARCH

Lowering the Selinexor Dose within the Pomalidomide and Dexamethasone Combination Regimen Elicits Fewer Side Effects While Comparable Efficacy Against Relapsed/Refractory Multiple Myeloma

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Background: As a novel oral Exportin 1 (XPO1) inhibitor, selinexor at 80 or 100 mg has demonstrated efficacy in treating relapsed/refractory multiple myeloma (RRMM), nonetheless, this dosage has shown poor tolerability.

Objective: To explore the optimal dosage of selinexor, we evaluated the efficacy and safety of 60 vs 40 mg selinexor, combine with regimen comprising pomalidomide and dexamethasone in RRMM.

Design: 21 patients with RRMM were enrolled to receive selinexor (60 or 40 mg once weekly), together with pomalidomide (4 mg/day on days 1–21) and dexamethasone (40 mg once weekly); the SPD-60 group (6 patients) vs SPD-40 group (15 patients).

Methods: The clinical response and efficacy of the two groups were continuously followed up, and statistical analysis was carried out to screen out the dose group with fewer side effects and better efficacy. The primary endpoint was (objective response rates) ORR. The secondary endpoints included treatment safety and tolerability, progression-free survival (PFS) and overall survival (OS).

Results: The ORR of the SPD-60 and SPD-40 groups were 33.3% and 46.7% respectively (P=0.773). With a median follow-up of 20.9 months, the median PFS was 6.2 months and the median OS was not achieved across all treated patients. The median PFS for SPD-60 group was 4.3 months, while for SPD-40 was 8.0 months (P=0.618). The 1-year OS rate were 66.7% for SPD-60 group and 85.1% for the SPD-40 group (P=0.308). The most common hematological adverse events were neutropenia (SPD-60 group 50% vs SPD-40 group 53.3%) and thrombocytopenia (50% vs 46.7%). Fatigue (83.3% vs 40%), infection (50% vs 53.3%), and nausea (83.3% vs 40%) were the most common non-hematologic adverse effects.

Conclusion: The SPD-40 regimen may be more clinically applicable than SPD-60, as it elicited fewer adverse effects while demonstrating equivalent efficacy.

Trial Registration: *ClinicalTrials.gov*: NCT04941937.

Keywords: relapsed/refractory multiple myeloma, selinexor, pomalidomide, dexamethasone

Introduction

Multiple myeloma (MM) is a hematologic malignancy characterized by the abnormal proliferation of plasma cells.[1] Although significant advancements have been made in the treatment of MM over the past two decades, it remains incurable, as a considerable proportion of MM patients treated with the latest therapeutic regimens still develop

Received: 13 January 2025
Accepted: 28 May 2025
Published: 6 June 2025

resistance. Thus, relapsed/refractory MM (RRMM) remains challenging to treat and is associated with high rates of mortality.[2,3]

Although new drugs are under development, there are presently limited drug options for patients with RRMM. The treatment regimen based on immunomodulators is still one mainstay of MM therapies. Pomalidomide plays an important role in the treatment phases of MM induction, consolidation and maintenance. And as a third-generation IMiDs, it has no cross-resistance to thalidomide and lenalidomide. Many studies have shown that pomalidomide-based regimens have significant efficacy and safety in the treatment of MM.[4,5] Exportin 1 (*XPO1*) is a well characterized nuclear export protein of tumor suppressor protein (TSP) and glucocorticoid receptor (GCR). Unbiased high-throughput short interfering RNA screening revealed *XPO1* to be a selected survival gene,[6] which is frequent overexpressed in MM.[7] Selinexor is a novel, oral, slow-reversible, and highly selective nuclear export inhibitor; it functions by selectively binding to *XPO1* and inhibiting the nuclear export of TSP and GCR.[8] The Phase III study BOSTON study, compared the efficacy of selinexor in combination with once-weekly bortezomib and low-dose dexamethasone (SVd) against the standard therapy of twice-weekly bortezomib and low-dose dexamethasone (Vd), in 400 patients with RRMM who had received 1–3 prior lines of therapy.[9] In the SVd regimen, the recommended dose of selinexor was 100 mg once weekly. The results showed that RRMM patients belonging to the SVd group had a significantly longer progression-free survival (PFS) than that those in the Vd group (13.93 vs 9.46 months, respectively). The phase I/II study KCP-330-017 (STOMP) evaluated the efficacy of selinexor, alongside other drugs, such as bortezomib, lenalidomide, pomalidomide, and carfilzomib, in combination with a backbone protocol in the treatment of MM and RRMM.[10] All of the combination regimens achieved good levels of efficacy and safety, among which the objective response rate (ORR) of RRMM patients who had previously received fourth-line therapy with pomalidomide in the selinexor, pomalidomide, dexamethasone (SPD) regimen reached 56%. Earlier studies have typically used selinexor at 80 or 100 mg,[9,11] nonetheless, this dosage has shown poor tolerability.[12–14] Our previous Phase II, single-arm MARCH study, demonstrated the efficacy of selinexor 80 mg combined with low-dose dexamethasone in RRMM patients in China, as evidenced by a 29.3% ORR; however serious adverse events (AEs) were reported in 54.9% of patients, The most frequent grade 3/4 AEs included anemia (57.3%), thrombocytopenia (51.2%), lymphopenia (42.7%), neutropenia (40.2%), hyponatremia (29.3%), and lung infection (26.8%).[15] Furthermore, limited research has been conducted on exploring a lower dosage of selinexor, and there is a lack of relevant data.

Given that selinexor-associated AEs are dose-dependent, its incorporation into combination therapies may not only improve overall therapeutic efficacy but also enable it to be used at lower doses, improving its tolerability. Hence, we conducted a prospective study (NCT04941937) to compare the safety and effectiveness of two relatively low, once-weekly doses (60 vs 40 mg) of selinexor in combination with standard dosages of pomalidomide and dexamethasone in the treatment of RRMM, with the aim of investigating an optimal dosage of selinexor.

Methods

Patients and Study Design

As of December 19, 2022, 21 patients with RRMM, who had previously received at least one line of therapy, were admitted to the Shanghai Changzheng Hospital as part of this open-label study. The cut-off date for follow-up was May 31, 2024. The study was conducted in accordance with the International Conference on Harmonization guidelines for Good Clinical Practice and the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee at each study center. Written informed consent was obtained from each patient. Eligible patients had histologically or cytologically confirmed MM and met the International Myeloma Working Group (IMWG) diagnostic criteria for RRMM,[16,17] had an Eastern Cooperative Oncology Group (ECOG) performance status of 0–3, had a life expectancy of at least 12 weeks, and had adequate organ function.

Depending on patient compliance and early safety findings, all patients were randomly divided into two selinexor dose groups: 60 mg or 40 mg (SPD-60 and SPD-40, respectively). The following types of data were gathered from the participants: sex, age, the time of the initial diagnosis, the International Staging System (ISS) stage and the Revised ISS (R-ISS) stage at initial diagnosis, cytogenetic risk factors, the number of prior lines of treatment, and the medications

used in the previous lines of treatment. The International Myeloma Working Group consensus defines the presence of t (4;14), t(14;16), del(17p), t(14;20) and amplification of 1q (copy number≥3)[18] as high cytogenetic risk.[19] Based on the data collected and expert consensus, the number of prior treatment lines and extent of drug resistance were identified.[20]

Treatment

The two regimens differed only in the concentration of their selinexor component. SPD-60: selinexor 60 mg, once weekly, while SPD-40: selinexor 40 mg, once weekly. The following pomalidomide and dexamethasone treatment regimens were used in this study with pomalidomide 4 mg/day, on days 1–21; dexamethasone 40 mg, once weekly.

Outcomes

Outcomes were evaluated according to the standard IMWG criteria.[16] The primary endpoint was ORR, defined as a response equal to or greater than a partial response (PR). The secondary endpoints included treatment safety and tolerability, which were evaluated according to the National Cancer Institute (NCI) Common Terminology Standard for Adverse Event Evaluation (CTCAE, v5.0). In addition, PFS was defined as the duration from the first dose of study treatment to the first confirmation of progressive disease (PD) or death. Overall survival (OS) was defined as the period from the initiation of treatment to death from any cause.

Statistical Analysis

Baseline characteristics were summarized using descriptive statistics. The ORR of the two groups was compared using the Fisher's exact test. The median follow-up time was determined using the reverse Kaplan–Meier method. Survival probabilities were illustrated using Kaplan–Meier curves and compared using the Log rank test. SPSS version 25 (IBM, Chicago, IL, USA) was used for all statistical analyses. Every statistical test was carried out using a two-sided test. Differences with a P-value ≤ 0.05 were considered as statistically significant and were examined within a 95% confidence interval (CI).

Results

Baseline Demographics and Clinical Characteristics

At the data collection cutoff date (May, 31, 2024), a total of 21 RRMM patients with a median age of 65 (50–74) years were enrolled in this study, which the baseline characteristics are outlined in Table 1. The median time to initial diagnosis was 47 (13–118) months. The follow-up time after enrollment was 20.9 (1.4–28.5) months. The median time to previous treatment was 4 (1–7) months. Of the patients, 85.7% (18/21) had ISS stage II/III disease, while 95.2% (20/21) had R-ISS stage II/III disease. The results indicated that 57.1% (12/21) of the patients were at high cytogenetic risk, and 50% (3/6) in the SPD-60

Table 1 Baseline Data Collected from the 21 Patients Enrolled in the Study

Clinical Characteristic	All Patients (N=21)	SPD-40 (n=15)	SPD-60 (n=6)
Median age, years (range)	65 (50–74)	63 (50–69)	67 (63–74)
Sex, n (%)			
Male	12 (57.1%)	8 (53.3%)	4 (66.7%)
Female	9 (42.9%)	7 (46.7%)	2 (33.3%)
Initial ISS stage, n (%)			
I	3 (14.3%)	3 (20.0%)	0 (0.0%)
II	11 (52.4%)	6 (40.0%)	5 (83.3%)
III	7 (33.3%)	6 (40.0%)	1 (16.7%)
Initial R-ISS stage, n (%)			
I	1 (4.8%)	1 (6.7%)	0 (0.0%)
II	14 (66.7%)	9 (60.0%)	5 (83.3%)
III	6 (28.6%)	5 (33.3%)	1 (16.7%)

(*Continued*)

https://doi.org/10.2147/OTT.S516486

Table 1 (Continued).

Clinical Characteristic	All Patients (N=21)	SPD-40 (n=15)	SPD-60 (n=6)
Median time since initial diagnosis, months (range)	47 (13–118)	46 (13–117)	85 (19–118)
At high cytogenetic risk, n (%)	12 (57.1%)	9 (60.0%)	3 (50.0%)
Received autologous stem cell transplantation, n (%)	7 (33.3%)	5 (33.3%)	2 (33.3%)
Median number prior lines of therapy, n (range)	4 (1–7)	2 (1–6)	4.5 (3–7)
PIs exposed: refractory, n (%)	21 (100%): 15 (71.4%)	15 (100%): 9 (60.0%)	6 (100%): 6 (100%)
Immunomodulator exposed: refractory, n (%)	18 (85.7%): 18 (85.7%)	12 (80.0%): 12 (80.0%)	6 (100%): 6 (100%)
Double class exposed: refractory, n (%)	18 (85.7%): 13 (61.9%)	12 (80.0%): 7 (46.7%)	6 (100%): 6 (100%)
Anti-CD38 antibody exposed: refractory, n (%)	4 (19.0%): 3 (14.3%)	3 (20.0%): 2 (13.3%)	1 (16.7%): 1(16.7%)
Cyclophosphamide/doxorubicin exposed, n (%)	17 (81.0%)	13 (86.7%)	4 (66.7%)

Abbreviations: SPD-40, selinexor 40 mg, qw; pomalidomide 4 mg qd, days 1–21; dexamethasone 40 mg, qw; SPD-60, selinexor 60 mg, qw; pomalidomide 4 mg qd, days 1–21, dexamethasone 40 mg, qw; PI, proteasome inhibitors; PIs exposed: refractory, n (%), number and proportion of patients exposed to PIs and refractory to PIs.

group, 60% (9/15) in the SPD-40 group, respectively, which had no differences between them. 18 (85.7%) patients exhibited resistance to immunomodulators (IMiDs) and 15 (71.4%) to protease inhibitor (PIs). Moreover, 13 (61.9%) patients exhibited dual resistance to PIs and IMiDs. A third of patients had received prior autologous hematopoietic stem cell transplantation therapy. Initially, there were 11 patients in the SPD-60 group and 10 patients in the SPD-40 group; however, after a brief period of therapy, five patients in the SPD-60 group became treatment-intolerant and had to be moved to the SPD-40 group. Consequently, we ended up with 6 patients in SPD-60 group and 15 patients in SPD-40 group (Figure 1). There was no significant difference in baseline characteristics between the two final groups. The patients in the SPD-60 and SPD-40 groups had a median age of 67 (63–74) and 63 (50–69) years, respectively; moreover, 100% (6/6) vs 80% (12/15) of the patients had ISS II/III, 100% (6/6) vs 93.3% (14/15) of the patients had ISS II/III, and 50% (3/6) vs 60% (9/15) were at high cytogenetic risk. In the SPD-60 group, all were resistant to PIs and IMiDs. Meanwhile, in the SPD-40

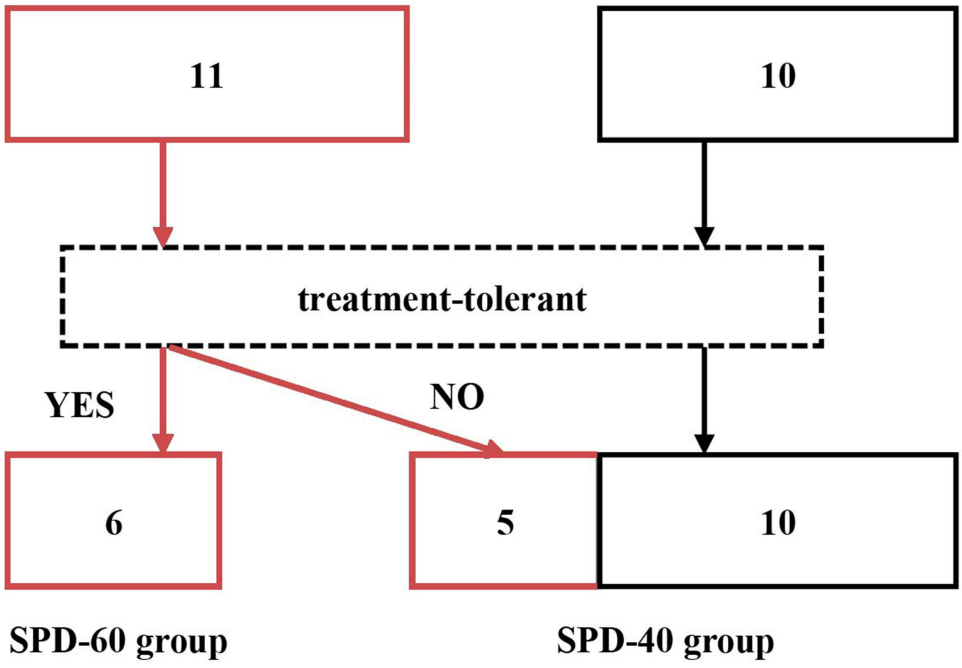

Figure 1 Groups. After a brief period of therapy, 5 patients in the SPD-60 group moved to the SPD-40 group because of treatment-intolerance.

 https://doi.org/10.2147/OTT.S516486

Table 2 Evaluation of Outcomes in Patients After a Median of 4 Cycles of Treatment

Efficacy, n(%)	All (N=21)	SPD-40 (N=15)	SPD-60 (N=6)	P-value	Proteasome Inhibitors Refactory (N=15)	Immunomodulators Refactory (N=18)
ORR	9 (42.9%)	7 (46.7%)	2 (33.3%)	0.773	5 (33.3%)	8 (44.4%)
sCR	2 (9.5%)	1 (6.7%)	1 (16.7%)		2 (13.3%)	2 (11.1%)
CR	1 (4.8%)	1 (6.7%)	0 (0.0%)		0 (0.0%)	0 (0.0%)
PR	6 (28.6%)	5 (33.3%)	1 (16.7%)		3 (20.0%)	6 (33.3%)
MR	2 (9.5%)	2 (13.3%)	0 (0.0%)		1 (6.7%)	1 (5.6%)
SD	4 (19.0%)	2 (13.3%)	2 (33.3%)		3 (20.0%)	4 (22.2%)
PD	2 (9.5%)	1 (6.7%)	1 (16.7%)		2 (13.3%)	2 (11.1%)

Abbreviations: CR, Complete Response; MR, Minimal Response; ORR, Objective Response Rate; PD, Progressive Disease; PR, Partial Response; SD, Stable Disease; SPD-40, selinexor 40 mg, qw; pomalidomide 4 mg qd, days 1–21; dexamethasone 40 mg, qw; SPD-60, selinexor 60 mg, qw; pomalidomide 4 mg qd, days 1–21, dexamethasone 40 mg, qw.

group, 60% (9/15) of patients were resistant to PIs and 80% (12/15) were resistant to IMiDs. The efficacy and safety were assessed based on the final group assignment.

Efficacy of Treatment

The patient outcomes at the time of the data cutoff are summarized in Table 2. The ORR after a median of five treatment cycles was 42.9%; the ORR of the 18 patients who were refractory to immunomodulators was 44.4%, while that of the 15 patients who were refractory to PIs was 33.3%. The ORRs of the SPD-60 and SPD-40 groups were 33.3% and 46.7%, respectively (P = 0.773). In the SPD-60 group, 16.7% patient achieved CR or better. Meanwhile, in the SPD-40 group, 13.4% patient achieved CR or better.

Prognosis

With a median follow-up time of 20.9 months, the median PFS was 6.2 months across all treated patients. The median PFS for the SPD-60 group was 4.3 months (95% CI: 0.8–7.8), while for the SPD-40 group, the median PFS was 8.0 months (95% CI: 3.3–12.7, P=0.681, Figure 2 and Table 3). The median OS was not achieved across all treated patients.

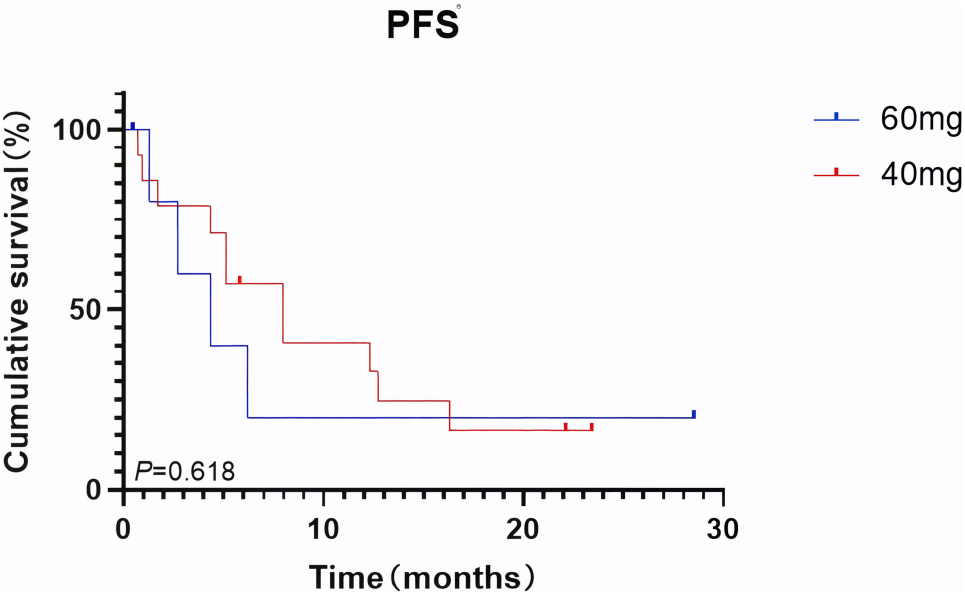

Figure 2 Kaplan–Meier curves comparing progression-free survival of patients who received SPD-60 versus that of patients who received SPD-40.

https://doi.org/10.2147/OTT.S516486

Table 3 The Prognostic Survival Analysis of Patients with the SPD-40 and SPD-60 Groups

	N	Median PFS, Months (95% CI)	Median OS, Months (95% CI)	OS Rate (%)
				1-Year
All patients	21	6.2 (2.5–9.9)	NR	79.6 (54.3–91.8)
SPD-40	15	8.0 (3.3–12.7)	NR	85.1 (52.3–96.1)
SPD-60	6	4.3 (0.8–7.8)	NR	66.7 (19.5–90.4)

Abbreviations: CI, confidence interval; OS, Overall survival; PFS, progression-free survival; SPD-40, selinexor 40 mg, qw; pomalidomide 4 mg qd, days 1–21; dexamethasone 40 mg, qw; SPD-60, selinexor 60 mg, qw; pomalidomide 4 mg qd, days 1–21, dexamethasone 40 mg, qw.

The 1-year OS rate for SPD-60 was 66.7% (95% CI: 19.5–90.4%) for SPD-60 group, and 85.1% (95% CI: 52.3–96.1%) for the SPD-40 group (P=0.308, Figure 3 and Table 4).

Safety and Tolerability

We next evaluated the AEs associated with SPD treatment (Table 4). In the comparison of the SPD-60 vs SPD-40 groups, the most common hematological AEs observed were neutropenia (50% vs 53.3%) and thrombocytopenia (50% vs 46.7%). In addition, some cases of ≥ grade 3 neutropenia (16.7% vs 40%) and ≥ grade 3 thrombocytopenia (16.7% vs 33.3%) were reported. In both groups, the most common nonhematologic AEs were fatigue (83.3% vs 53.3%), infection (50% vs 53.3%), and nausea (83.3% vs 40%). Hematological AEs were treated with G-CSF or TPO, while nonhematological AEs were managed by preventing vomiting and inhibiting acid reflux. When none of these treatments provided relief or patients achieved grade 2 or higher dose-limiting toxicities, we reduced the selinexor dose or interrupted the selinexor treatment. Notably, most AEs were resolved after discontinuing selinexor or reducing its dosage.

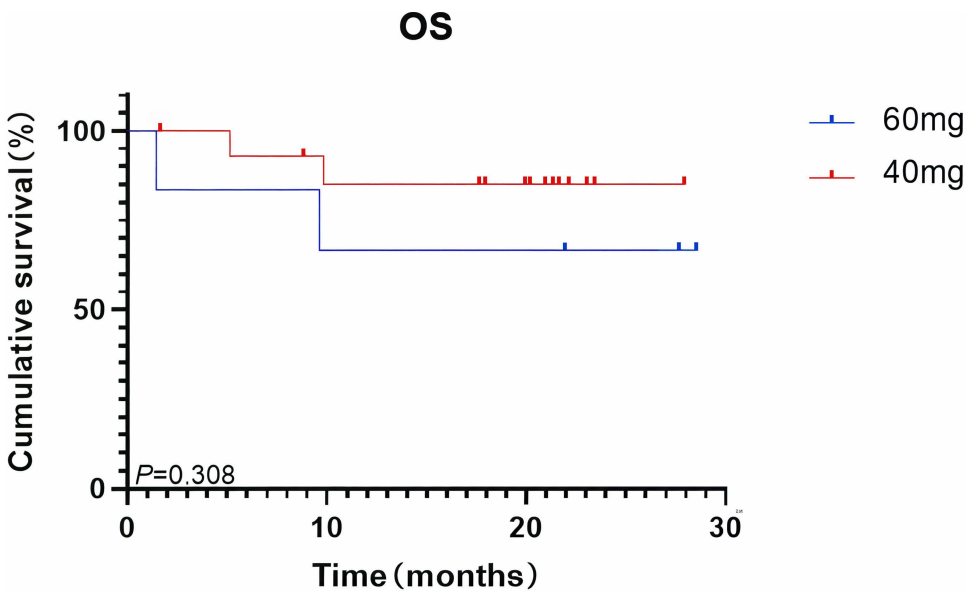

Figure 3 Kaplan–Meier curves comparing the overall survival of patients who received SPD-60 versus that of patients who received SPD-40.

 https://doi.org/10.2147/OTT.S516486

Table 4 The Severity of Adverse Events Will Be Graded According to the NCI-CTCAE 5.0 Standard

Adverse Events	All (N=21)	SPD-40 (N=15)	SPD-60 (N=6)
Thrombocytopenia, n (%)	10 (47.6%)	7 (46.7%)	3 (50.0%)
≥ Grade 3 thrombocytopenia, n (%)	6 (33.3%)	5 (33.3%)	1 (16.7%)
Neutropenia, n (%)	11 (52.4%)	8 (53.3%)	3 (50.0%)
≥ Grade 3 neutropenia, n (%)	7 (33.3%)	6 (40.0%)	1 (16.7%)
Nausea, n (%)	11 (52.4%)	6 (40.0%)	5 (83.3%)
Fatigue, n (%)	13 (61.9%)	8 (53.3%)	5 (83.3%)
Infections, n (%)	11 (23.8%)	8 (53.3%)	3 (50.0%)

Abbreviations: SPD-40, selinexor 40 mg, qw; pomalidomide 4 mg qd, days 1–21; dexamethasone 40 mg, qw; SPD-60, selinexor 60 mg, qw; pomalidomide 4 mg qd, days 1–21, dexamethasone 40 mg, qw.

Discussion

In the present study, we assessed the effectiveness and safety of selinexor combined with pomalidomide and dexamethasone in patients with RRMM who had previously received at least one line of therapy. The ORR was 42.9% in all treated patients, with a median PFS of 6.2 months and no achieved OS at clinical cutoff. Several trends emerged in efficacy and survival analysis. Although the differences did not each statistical significance, patients in the SPD-60 group showed a tendency towards lower ORR (33.3% vs 46.7%) and median PFS (4.3 months vs 8.0 months) compared to those in the SPD-40 group. Moreover, the incidence of AEs was higher in the SPD-60 group. These findings suggest that the combination of selinexor, pomalidomide, and dexamethasone may be an effective and safe option for RRMM patients, especially if the selinexor dose is kept below 60 mg; however, the full clinical value of this regimen should be explored in large cohort further.

Selinexor, as a novel oral *XPO1* inhibitor, is a new therapy with a novel mechanism of action for RRMM. Selinexor has demonstrated high effective in treating MM by inhibiting nuclear factor κB, limiting the translation of oncoprotein mRNA, block the output of *XPO1*, and promoting the nuclear accumulation and activation of tumor suppressor proteins.[6,21] Moreover, the anti-inflammatory qualities of *XPO1* inhibitors can be exploited to create a favorable immune microenvironment for helper T cells, which are key to preventing the growth and development of myeloma tumors. In the STORM phase III clinical trial,[11] selinexor (80 mg) and dexamethasone (20 mg) were administered orally twice weekly to 122 patients with RRMM who had previously received a median of seven lines of treatment. The study demonstrated that the median duration of response (DOR) was 4.4 months, the median PFS was 3.7 months, and the median OS was 8.6 months, indicating that patients with RRMM can derive benefit from a combination therapy involving selinexor and dexamethasone.

In recent studies, selinexor is typically used at doses of 80 or 100 mg, with the caveat that while these doses have demonstrated favorable efficacy in patients with RRMM, they are also associated with a high incidence of intolerable side effects.[9,11,22] The STOMP multi-arm clinical trial, which treated 32 patients with a combination of selinexor, carfilzomib, and dexamethasone (XKD), reported a 78% ORR in RRMM patients who had received four lines of prior treatment.[22] In this study, the dose of selinexor was 80 or 100 mg, and among these patients, common AEs included thrombocytopenia (72%), which was higher than both SPD-60 and SPD-40 groups in our study (50% vs 46.7%), and nausea (72%), which was higher than SPD-40 group (40%) and lower than SPD-60 (83.3%) in our study.[22] Salcedo et al evaluated the combination of selinexor, ixazomib, and dexamethasone (XID) in 18 RRMM patients who had received five prior regimens.[12] The reported ORR was 22%, of which 14% had a VGPR. Unfortunately, the gastrointestinal side effects associated with this triple regimen have limited its wider application. And among hematological AEs, thrombocytopenia was the most frequent, with an incidence of 72%, which was also apparently higher than the incidence of the two reduced-dose groups in our study.[12] The open-label, Phase II GEM-SELIBORDARA trial investigated the feasibility of a tetrad of selinexor, daratumumab, bortezomib, and dexamethasone (XVDd) in 57 patients with RRMM. AEs

included thrombocytopenia and nausea, both occurring in 70.6% of the patients, followed by fatigue (61.8%), and anemia (61.8%).[13] Our previous single-arm clinical study enrolled a total of 82 patients with RRMM, who administrating Selinexor 80 mg combined with dexamethasone 20 mg, reported an ORR of 29.3% (95% CI: 19.7–40.4), a median DOR of 4.7 months, and median a PFS and OS of 3.7 and 13.2 months, respectively.[15] Because selinexor was administered at a dose of 80 mg, serious AEs occurred in 54.9% of patients; the grade 3/4 AEs included, thrombocytopenia (51.2%), neutropenia (40.2%), much higher than the incidence in the SPD-60 and SPD-40 groups of this study (16.7% vs 33.3%; 16.7% vs 40%, respectively). Thus, overall, the treatment regimen was poorly tolerated by patients, emphasizing the importance of selinexor dosage optimization in our study.

A recent U.S.-based study investigated the optimal dose of selinexor in combination with pomalidomide and dexamethasone. The results indicated that both SPD-60 and SPD-40 demonstrated comparable efficacy, while the SPD-40 regimen exhibited a more favorable toxicity profile.[14] However, such only data is very limited, and there is no relevant data in Chinese population. Therefore, the present study, we set up a subgroup of patients treated with selinexor at 40 mg once weekly. We found that the ORR of evaluable patients reached more than 40%, while the median PFS reached > 5 months; however, the median OS was not reached.

Crucially, there was no significant difference between the SPD-60 and SPD-40 groups in terms of treatment response. Although patients in the SPD-60 group initially had more hematologic/nonhematologic side effects than patients in the SPD-40 group, the ORR of each group showed that SPD was effective in treating patients with RRMM. We found that patient quality of life was significantly impacted by AEs, such as fatigue and nausea, even though they were mostly grade 1 or grade 2 occurrences. In addition, cytogenetic abnormalities can influence disease course, response to therapy, and prognosis,[18] but there was no significant difference between the two groups in cytogenetic abnormalities in this study.

Our study implies that the SPD-40 regimen may represent a more practical treatment option, which elicits fewer side effects while demonstrating comparable efficacy. Especially if the selinexor dose is kept below 60 mg, we observed comparable efficacy in patients of the SPD-40 group compared to those in the SPD-60 group, along with a reduced occurrence of adverse events. Owing to the small sample size, the transition of patients between treatment groups and potential confounding factors (eg, COVID-19 status) during follow-up, further studies with larger cohorts and longer follow-up durations are warranted.

Conclusion

To summarize, the SPD-40 regimen, which comprised 40 mg rather than the more standard 60 mg dose of selinexor, exhibited preliminary efficacy and was more tolerable to patients with RRMM than the SPD-60 regimen. As such, SPD-40 represents a promising and practical treatment option for RRMM patients, with a better benefit to risk ratio than SPD-60.

Data Sharing Statement

The datasets generated or analyzed during this study are available from the corresponding author on reasonable request.

Ethics Approval

The study was approved by the Ethics Committee of Shanghai Changzheng Hospital (project number: NCT04941937) and was conducted in accordance with the Declaration of Helsinki (and its amendments) and China's clinical trial research norms and regulations. Before enrollment, all patients provided written informed consent.

Consent for Publication

Written informed consent was obtained from the patient for publication of this study.

Disclosure

The authors declare that they have no conflicts of interest.

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