ABSTRACT/
POSTER
P982

EFFICACY AND SAFETY OF 40 MG VS 60 MG OF ONCE WEEKLY SELINEXOR IN COMBINATION WITH POMALIDOMIDE AND DEXAMETHASONE IN RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA

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INTRODUCTION

- Selinexor is an oral, selective inhibitor of XPO1-mediated nuclear export approved in combination with low-dose dexamethasone + bortezomib for adult patients with multiple myeloma (MM) who have received ≥ 1 prior therapy.[1]

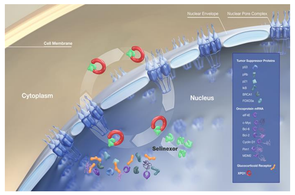


Figure 1. Selinexor mechanism of action.

- There are limited data on the effectiveness of pomalidomide + low-dose dexamethasone (Pd)-based triplets in the evolving post-anti CD38 mAb treatment landscape, in which there is no standard of care.[2,3] Prior studies have reported an overall response rate (ORR) of 28% and a median progression free survival (mPFS) of 3.7 months to Pd in patients with MM refractory to both bortezomib and lenalidomide.[4]
- STOMP (NCT02343042) is an ongoing Phase 1b/2 study evaluating selinexor in various triplet/quadruplet combinations in patients with newly diagnosed and relapsed/refractory MM (RRMM). In the selinexor + Pd (SPd) arm, selinexor was evaluated at doses of 60-80 mg twice weekly (BIW; weeks 1-3 only) or 40-100 mg once weekly (QW) in combination with pomalidomide 2-4 mg once daily (QD, days 1-21) and dexamethasone 40 mg weekly in 28-day treatment cycles. In Phase 2, two once-weekly selinexor regimens with pomalidomide 4 mg QD were tested: 60 mg QW (SPd-60) and 40 mg QW (SPd-40).
- XPORT-MM-028 (NCT04414475) is a parallel ongoing Phase 2b trial with similar objectives and eligibility criteria, evaluating selinexor in various combinations including SPd-40 in patients with RRMM.
- The aim of this analysis was to identify the optimal dose of SPd by comparing the safety and efficacy of SPd-60 (from STOMP Phase 1/2) vs. SPd-40 (from STOMP Phase 2 and XPORT-MM-028).

METHODS

- We retrospectively analyzed data from patients with RRMM treated with SPd-60 in the STOMP trial and SPd-40 in the XPORT-MM-028 trial.
- SPd-60 was determined to be the recommended phase 2 dose in phase 1 of the STOMP trial based on the maximum tolerated dose and 20 patients were enrolled at that dose.
- An additional expansion cohort in which patients received an even lower dose of SPd-40 was opened in line with the shift away from the maximum tolerated dose paradigm and evolving dose optimization paradigms in clinical development. To expedite enrollment, XPORT-MM-028 was also utilized for SPd-40.
- Efficacy, safety, and exposure of the regimens were analyzed and compared by dose.

RESULTS

- Results as of Sept 6, 2022. Median follow-up time: 13.6 months for SPd-40, 17.5 months for SPd-60.

Table 1. Patient characteristics and demographics

	SPd-40 (N = 28)	SPd-60 (N = 20)
Age (years)[a], median (range)	67.5 (48-79)	65.5 (37-85)
Sex, N (%)		
Male	17 (60.7)	7 (35.0)
Female	11 (39.3)	13 (65.0)
Duration from initial diagnosis to first dose of study treatment (years), median (range)	4.27 (0.8-25.0)	3.41 (1.1-9.2)
Baseline ECOG performance status, N (%)		
0	8 (28.6)	2 (10.0)
1	16 (57.1)	14 (70.0)
2	4 (14.3)	4 (20.0)
Number of prior lines of therapy, median (range)	2.0 (1-5)	2.5 (1-9)
Previously exposed to αCD38 mAb (daratumumab or isatuximab), n (%)	16 (57.1)	6 (30.0)
Refractory to, n (%):		
PI (bortezomib, carfilzomib, or ixazomib)	26 (92.9)	15 (75.0)
IMiD (thalidomide, lenalidomide, or pomalidomide)	21 (75.0)	17 (85.0)
αCD38 mAb (daratumumab or isatuximab)	16 (57.1)	4 (20.0)
αCD38 mAb, PI, and IMiD	12 (42.9)	4 (20.0)
ISS stage at initial diagnosis, n (%)		
I	7 (25.0)	7 (35.0)
II	6 (21.4)	3 (15.0)
III	8 (28.6)	3 (15.0)
Missing	7 (25.0)	7 (35.0)
Genetic abnormalities at initial diagnosis, n (%)		
del(17p)	0	1 (5.0)
t(4;14)	3 (10.7)	1 (5.0)
t(14;16)	1 (3.6)	1 (5.0)
Any of del(17p), t(4;14), or t(14;16)	4 (14.3)	3 (15.0)

Abbreviations: αCD38 mAb=anti-CD38 monoclonal antibody; ECOG=Eastern Cooperative Oncology Group; IMiD=immunomodulatory drug; PI=proteasome inhibitor; POM=pomalidomide; SEL=selinexor.
[a] Age at screening.

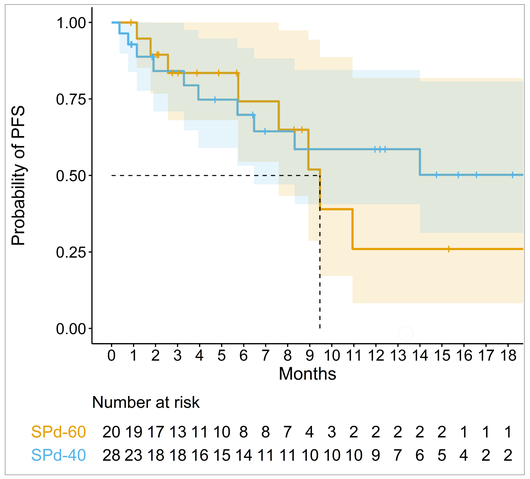
Table 2. Selinexor exposure

	SPd-40 (N = 28)	SPd-60 (N = 20)
Patients with selinexor dose modification, n (%)	18 (64.3)	15 (75.0)
Duration of exposure, median (weeks) (range)	28.0 (2, 93)	22.0 (7, 111)
Weekly selinexor dose, median (mg/week) (range)	37.9 (9.3, 45.7)	46.6 (28.3, 60.0)
Relative selinexor dose intensity, (%), median (range)	94.8 (23, 114)	77.6 (47, 100)

Efficacy

- Numerically lower ORR and rate of patients with ≥very good partial response (VGPR) were observed for SPd-40 vs SPd-60 (ORR: 50% vs 65%; ≥VGPR: 25% vs 30%).
- PFS was longer for SPd-40 vs SPd-60 (mPFS in months: not reached [95% CI, 6.5-NE] after median follow-up of 12.2 months vs 8.3 months [95% CI, 7.6-NE).

Figure 1. Progression-free survival in patients who received SPd-40 vs those who received SPd-60.



Safety

- Hematologic toxicities primarily consisted of changes in blood count with no cases of high grade bleeding and one case of febrile neutropenia in each dose level.
- Rates of nausea, fatigue, and diarrhea were numerically lower with SPd-40.
- There were no TEAEs leading to death reported.

Table 4. Treatment-emergent adverse events[a]

	SPd-40 (N = 28) n (%)	SPd-60 (N = 20) n (%)
Anemia, all grades	11 (39.3)	13 (65.0)
Grade 3/4	3 (10.7)	5 (25.0)
Neutropenia, all grades	19 (67.9)	15 (75.0)
Grade 3/4	17 (60.7)	12 (60.0)
Thrombocytopenia, all grades	12 (42.9)	9 (45.0)
Grade 3/4	7 (25.0)	5 (25.0)
Fatigue, all grades	12 (42.9)	15 (75.0)
Grade 3/4	1 (3.6)	3 (15.0)
Nausea, all grades	9 (32.1)	14 (70.0)
Grade 3/4	2 (7.1)	0
Diarrhea, all grades	7 (25.0)	7 (35.0)
Grade 3/4[b]	0	0

[a] Occurring in >25% of patients. [b] 1 TEAE in the SPd 40 group was missing grade.

Table 3. Efficacy

	SPd-40 (N = 28)	SPd-60 (N = 20)
ORR, n (%) [95% CI]	14 (50.0) [30.6, 69.4]	13 (65.0) [40.8, 84.6]
≥VGPR	7 (25.0) [10.7, 44.9]	6 (30.0) [11.9, 54.3]
PFS, median (months) (95% CI)	NR (6.5, NR)	9.5 (7.6, NR)
Median follow-up (months)	12.2	8.3
12-month survival rate, % (95% CI)	58.6 (40.6, 84.5)	26.0 (8.2, 81.8)
PFS in patients with previous αCD38 mAb		
N	16	6
Median (months) (95% CI)	11.2 (3.3, NR)	8.9 (7.6, NR)
Median follow-up (months)	13.5	15.3
12-month survival rate, % (95% CI)	50.0 (27.7, 90.3)	20.8 (3.7, 100.0)
Time to response		
Median (months) (95% CI)	1.0 (1.0, 6.0)	1.0 (0.9, NR)
Duration of response		
Median (months) (95% CI)	NR (12.2, NR)	8.6 (3.9, NR)
Overall survival, median (months) (95% CI)	NR (NR, NR)	NR (9.3, NR)
Patients with events, n (%)	6 (21.4)	7 (35.0)
12-month survival rate, % (95% CI)	76.5 (61.5, 95.3)	61.4 (41.1, 91.6)

CONCLUSIONS

- **The all-oral combination of selinexor + Pd in patients with RRMM showed signs of preliminary efficacy and was generally tolerable in these cohorts.**
- **Most non-hematologic TEAEs, including nausea, occurred at lower frequency in the 40 mg cohort and were generally transient and reversible. The SPd-40 group had a better AE profile than the SPd-60 group, which could explain the higher relative dose intensity and longer duration of therapy.**
- **ORR was greater in the SPd-60 cohort, but both PFS and duration of treatment were longer in the SPd-40 group despite a higher rate of triple-class refractory disease at baseline, with the overall risk-benefit profile favoring the SPd-40 regimen.**
- **SPd-40 is being further evaluated in patients with triple-class exposed RRMM in the EMN29 Phase 3 study (NCT05028348).**

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