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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ABSTRACT/POSTER P982

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.

• There are limited data on the effectiveness of pomalidomide + dexamethasone (PD) triplet-based triplets in the evolving post-anti-CD38 mAb treatment landscape, in which there is no standard of care. 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.

• STOMP (NCT02343042) is an ongoing Phase 1b/2 study evaluating selinexor in various triplet/quadrplet combinations in patients with newly diagnosed and relapsed/refractory MM (R/RMM). 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 (OW) in combination with pomalidomide 2 mg QD 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 R/RMM.

• 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 higher dose of SPd 60 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.

Safety, 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

<table>
<thead>
<tr>
<th>Age (years), median (range)</th>
<th>Sex, N (%)</th>
<th>Duration from initial diagnosis to first dose of study treatment (years), median (range)</th>
<th>Baseline ECOG performance status, N (%)</th>
<th>Refractory to, N (%)</th>
<th>Imid (thalidomide, lenalidomide, or pomalidomide) mAb, N (%)</th>
<th>oCd38 mAb (dubatumab or isatuximab), N (%)</th>
<th>SS stage at initial diagnosis, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>67 (54-89) vs 65 (43-76)</td>
<td>Male 17 (60.7) vs 7 (35.0)</td>
<td>4.27 (0.8-23.0) vs 3.41 (1.1-9.2)</td>
<td>2 (100.0) vs 2 (100.0)</td>
<td>26 (92.9) vs 17 (75.0)</td>
<td>21 (75.0) vs 17 (75.0)</td>
<td>12 (41.9) vs 6 (29.0)</td>
<td>7 (25.0) vs 7 (35.0)</td>
</tr>
<tr>
<td>67 (54-89) vs 65 (43-76)</td>
<td>Female 11 (39.3) vs 13 (65.0)</td>
<td>4 (14.3) vs 4 (20.0)</td>
<td>16 (57.1) vs 14 (70.0)</td>
<td>16 (57.1) vs 17 (75.0)</td>
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<td>12 (41.9) vs 6 (29.0)</td>
<td>7 (25.0) vs 7 (35.0)</td>
</tr>
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</table>

• 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, 7.6-NE] after median follow-up of 12.2 months vs 8.3 months [95% CI, 7.6-NE]).

• There were no TEAEs leading to death reported.

Table 4. Treatment-emergent adverse events

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Table 3. Efficacy

<table>
<thead>
<tr>
<th>ORR, n (%) [95% CI]</th>
<th>SPD 40 (N = 28)</th>
<th>SPD 60 (N = 20)</th>
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<tbody>
<tr>
<td>Overall response rate</td>
<td>14 (50.0) [30.6, 69.4]</td>
<td>13 (65.0) [40.8, 84.5]</td>
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<tr>
<td>VGPR</td>
<td>7 (25.0) [10.7, 44.9]</td>
<td>6 (30.0) [11.9, 54.3]</td>
</tr>
<tr>
<td>Median follow-up (months)</td>
<td>12.2 (8.3)</td>
<td>58.6 (40.6, 84.5)</td>
</tr>
<tr>
<td>12-month survival rate, % [95% CI]</td>
<td>76.5 (61.5, 95.3)</td>
<td>76.0 (62.4, 87.8)</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• The all-oral combination of selinexor + PD in patients with R/RMM 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 R/RMM in the EMM29 Phase 3 study (NCT05028348).

REFERENCES