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# EFFICACY AND SAFETY OF WEEKLY SELINEXOR, IN COMBINATION WITH POMALIDOMIDE, AND DEXAMETHASONE (SPd) FOR TREATMENT OF PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA (RRMM): UPDATES FROM THE STOMP TRIAL

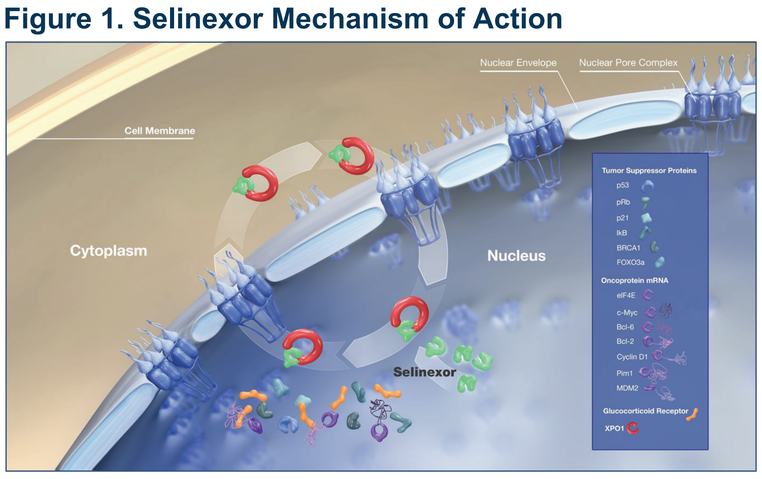
Muhamed Baljevic[1], Nizar Bahlis[2], Rami Kotb[3], Gary Schiller[4], Brea Lipe[5], Sumit Madan[6], Heather Sutherland[7], Suzanne Lentzsch[8], Natalie Callander[9], Noa Biran[10], Dane Van Domelen[11], Tomer Mark[11], Darrell White[12]

[1]Vanderbilt University Medical Center, Nashville, TN, USA; [2]University of Calgary, Charbonneau Cancer Research Institute, Calgary, AB, Canada; [3]CancerCare Manitoba, Winnipeg, MB, Canada; [4]David Geffen School of Medicine, University of California, Los Angeles, CA, USA; [5]University of Rochester, Rochester, NY, USA; [6]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [7]Vancouver General Hospital, Vancouver, BC, Canada; [8]Columbia University, New York, NY, USA; [9]University of Wisconsin, Carbone Cancer Center, Madison, WI, USA; [10]Hackensack University Medical Center, Hackensack, NJ, USA; [11]Karyopharm Therapeutics, Newton, MA, USA; [12]Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada

## INTRODUCTION

- Multiple myeloma (MM) remains incurable[1]; despite the promise of T-cell–engaging therapies, no standard of care has been established for patients with relapsed/refractory multiple myeloma (RRMM) after treatment with immunomodulatory drugs (IMiD), proteasome inhibitors (PIs), or anti-CD38 (αCD38) monoclonal antibodies (mAbs)[1-4]
- Large observational studies, such as LocoMMotion, have reported short median progression-free survival (PFS) of approximately 4.6 months in triple-class-exposed (TCE) RRMM with commonly used anti-MM agents; however, the vast majority of these patients did not receive selinexor[5]
- Selinexor, an oral, selective inhibitor of XPO1-mediated nuclear export (**Figure 1**) approved in combination with dexamethasone in penta-refractory MM and with dexamethasone and bortezomib in RRMM after ≥1 prior therapy,[6] is being evaluated with pomalidomide (selinexor + pomalidomide + dexamethasone [SPd]) for the treatment of RRMM in the phase 1b/2 STOMP trial (NCT02343042)

### Figure 1. Selinexor Mechanism of Action




- Updated clinical and safety data for the cohorts that received SPd regimens with selinexor 40 mg or 60 mg once weekly (QW) or 60/80 twice weekly (BIW; SPd-60/80 BIW) are presented

## METHODS

- The SPd arm of the multi-arm STOMP study evaluated selinexor at multiple doses and schedules in combination with Pd (P dose of 2, 3, or 4 mg once daily; d dose of 20 mg BIW or 40 mg QW)
- Key inclusion criteria included age ≥18 years, confirmed RRMM, and Eastern Cooperative Oncology Group (ECOG) performance status ≤2. Exclusion criteria included any anticancer therapy within 2 weeks of start of study drug (6 weeks for radioimmunotherapy) and unresolved grade >2 nonhematological toxicity from prior therapy
- Study objectives were to determine the maximum tolerated dose (MTD) and the recommended phase 2 dose (RP2D) to assess safety and to examine the efficacy of the SPd regimen
- QW selinexor 60 mg (SPd-60) was determined to be the RP2D for SPd based on the MTD; 20 patients were enrolled at that dose
- An additional expansion cohort in which patients received a lower dose of QW selinexor 40 mg (SPd-40) was opened in line with the shift away from the MTD paradigm and evolving dose-optimization paradigms in clinical development
- Efficacy, safety, and exposure of the regimens were analyzed and compared by dose
- Response assessments were investigator-determined per International Myeloma Working Group criteria

## RESULTS

### Patient Demographics

- As of October 1, 2024, 81 patients had been enrolled in the SPd arm of STOMP; results for the SPd-40, SPd-60, and pooled SPd-60/80 BIW cohorts are presented (**Table 1**)
- Of all patients treated with SPd, 53.1% were male, the median age (range) was 65 years (37–85), and patients had a median (range) of 3 (1–10) prior lines of therapy

### Table 1. Patient Characteristics and Demographics

| | SPd-40 (n=16) | SPd-60 (n=20) | SPd-60/80 BIW (n=18) |
|---|---|---|---|
| **Age, years, median (range)** | 67.5 (48-78) | 65.5 (37-85) | 60.5 (43-83) |
| **Sex, n (%)** | | | |
| Male | 10 (62.5) | 7 (35.0) | 7 (38.9) |
| Female | 6 (37.5) | 13 (65.0) | 11 (61.1) |
| **Duration from initial diagnosis to first dose of study treatment, years, median (range)** | 3.7 (0.8-25.0) | 3.4 (1.1-9.2) | 6.3 (0.9-22.8) |
| **Baseline ECOG performance status, n (%)** | | | |
| 0 | 2 (12.5) | 2 (10.0) | 5 (27.8) |
| 1 | 10 (62.5) | 14 (70.0) | 11 (61.1) |
| 2 | 4 (25.0) | 4 (20.0) | 2 (11.1) |
| **Number of prior lines of therapy, median (range)** | 2.5 (1-5) | 2.0 (1-9) | 4.0 (2-7) |
| **Previously exposed to αCD38, n (%)** | 8 (50.0) | 6 (30.0) | 4 (22.2) |
| **Refractory to, n (%)** | | | |
| PI (bortezomib, carfilzomib, or ixazomib) | 15 (93.8) | 16 (80.0) | 14 (77.8) |
| IMiD (thalidomide, lenalidomide, or pomalidomide) | 10 (62.5) | 18 (90.0) | 17 (94.4) |
| αCD38 (daratumumab or isatuximab) | 7 (43.8) | 5 (25.0) | 4 (22.2) |
| αCD38, PI, and IMiD | 5 (31.3) | 5 (25.0) | 4 (22.2) |
| **ISS stage at initial diagnosis, n (%)** | | | |
| I | 2 (12.5) | 7 (35.0) | 6 (33.3) |
| II | 2 (12.5) | 3 (15.0) | 1 (5.6) |
| III | 5 (31.3) | 3 (15.0) | 4 (22.2) |
| Missing | 7 (43.8) | 7 (35.0) | 7 (38.9) |
| **Genetic abnormalities at initial diagnosis or screening, n (%)** | | | |
| del(17p) | 2 (12.5) | 5 (25.0) | 5 (27.8) |
| t(4;14) | 2 (12.5) | 6 (30.0) | 1 (5.6) |
| t(14;16) | 0 | 2 (10.0) | 0 |
| gain/amp 1q | 6 (37.5) | 7 (35.0) | 1 (5.6) |
| Any of del(17p), t(4;14), t(14;16), or gain/amp 1q | 7 (43.8) | 13 (65.0) | 7 (38.9) |
| Missing | 5 (31.3) | 4 (20.0) | 8 (55.6) |

## RESULTS (continued)

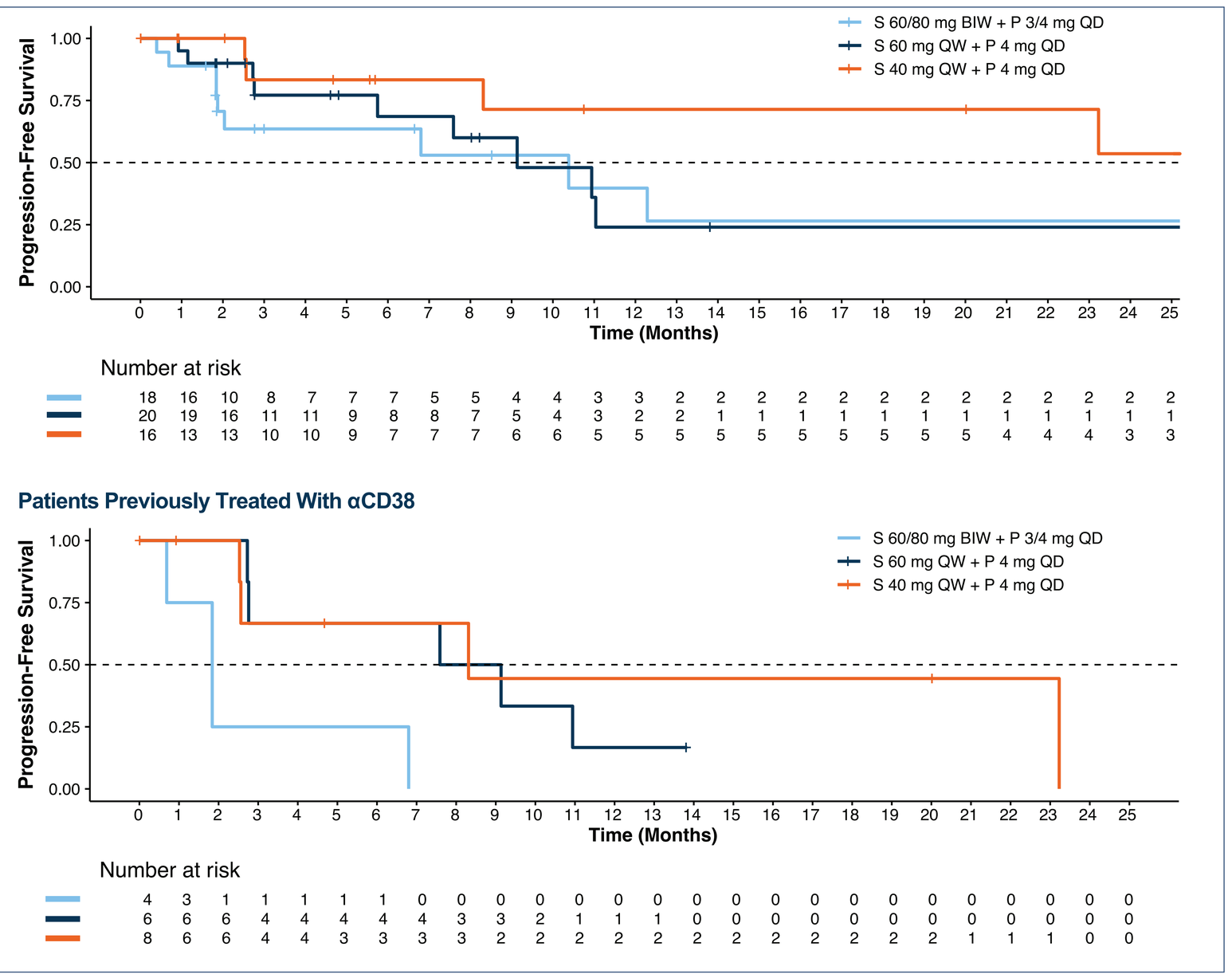
### Efficacy

- Median PFS in the SPd-40 cohort was not reached, compared with 9.1 months in SPd-60 and 10.4 months in SPd-60/80 BIW (**Table 2** and **Figure 2**)

### Table 2. Efficacy

| | SPd-40 (n=16) | SPd-60 (n=20) | SPd-60/80 BIW (n=18) |
|---|---|---|---|
| **ORR, n (%) [95% CI]** | 7 (43.8) [19.8, 70.1] | 11 (55.0) [31.5, 76.9] | 7 (38.9) [17.3, 64.3] |
| ≥VGPR | 5 (31.3) [11.0, 58.7] | 6 (30.0) [11.9, 54.3] | 3 (16.7) [3.6, 41.4] |
| **PFS, months, median (95% CI)** | NE (8.3, NE) | 9.1 (5.7, NE) | 10.4 (2.0, NE) |
| Median follow-up, months | 10.8 | 8.1 | 8.5 |
| 12-month survival probability, % (95% CI) | 71.4 (48.2, 100.0) | 24.0 (7.5, 76.4) | 39.7 (18.5, 85.4) |
| **PFS in patients with previous αCD38** | n=8 | n=6 | n=4 |
| PFS, months, median (95% CI) | 8.3 (2.6, NE) | 8.4 (2.8, NE) | 1.8 (0.7, NE) |
| Median follow-up, months | 20.0 | 13.8 | NE |
| 12-month survival probability, % (95% CI) | 44.4 (16.7, 100.0) | 16.7 (2.8, 99.7) | 0 (NE, NE) |
| **Time to response, months, median (95% CI)** | 1.2 (1.0, NE) | 1.0 (1.0, NE) | 1.2 (1.0, NE) |
| **Duration of response, months, median (95% CI)** | NE (22.3, NE) | 10.0 (3.9, NE) | 40.8 (9.5, NE) |
| **OS, months, median (95% CI)** | 27.3 (12.3, NE) | NE (9.3, NE) | 11.9 (7.6, NE) |
| Median follow-up, months | 33.8 | 17.5 | 56.4 |
| Patients with event, n (%) | 7 (43.8) | 7 (35.0) | 14 (77.8) |
| 12-month survival probability, % (95% CI) | 74.0 (55.0, 99.6) | 61.4 (41.1, 91.6) | 48.1 (29.4, 78.8) |

### Figure 2. Progression-Free Survival




### Safety

- The most common treatment-emergent adverse events were neutropenia, fatigue, and nausea (**Table 3**)

### Table 3. Treatment-Emergent Adverse Events

| | SPd-40 (n=16) | SPd-60 (n=20) | SPd-60/80 BIW (n=18) |
|---|---|---|---|
| **Anemia, all grades, n (%)** | 5 (31.3) | 13 (65.0) | 11 (61.1) |
| Grade 3/4, n (%) | 3 (18.8) | 5 (25.0) | 10 (55.6) |
| **Neutropenia, all grades, n (%)** | 12 (75.0) | 15 (75.0) | 9 (50.0) |
| Grade 3/4, n (%) | 11 (68.8) | 12 (60.0) | 9 (50.0) |
| **Thrombocytopenia, all grades, n (%)** | 4 (25.0) | 9 (45.0) | 11 (61.1) |
| Grade 3/4, n (%) | 3 (18.8) | 5 (25.0) | 9 (50.0) |
| **Fatigue, all grades, n (%)** | 11 (68.8) | 15 (75.0) | 12 (66.7) |
| Grade 3/4, n (%) | 1 (6.3) | 3 (15.0) | 2 (11.1) |
| **Nausea, all grades, n (%)** | 8 (50.0) | 14 (70.0) | 12 (66.7) |
| Grade 3/4, n (%) | 0 | 0 | 0 |
| **Diarrhea, all grades, n (%)** | 6 (37.5) | 7 (35.0) | 8 (44.4) |
| Grade 3/4, n (%) | 0 | 0 | 1 (5.6) |
| **Infection, all grades, n (%)** | 0 | 0 | 1 (5.6) |
| Grade 3/4, n (%) | 0 | 0 | 1 (5.6) |
| **Weight loss, all grades, n (%)** | 4 (25.0) | 5 (25.0) | 8 (44.4) |
| Grade 3/4, n (%) | 0 | 0 | 0 |

- Median duration of exposure in weeks was 19.0 (range 1, 260) in the entire cohort, 28.0 (4, 201) in SPd-40, 22.0 (7, 114) in SPd-60, and 16.0 (1, 260) in SPd-60/80 BIW
- Median relative selinexor dose intensity was 86.4% (57.5 mg/week) for the entire cohort, 91.3% (36.5 mg/week) for SPd-40, 77.5% (46.5 mg/week) for SPd-60, and 95.8% (92.8 mg/week) for SPd-60/80 BIW

## CONCLUSIONS

- The all-oral combination of SPd showed signs of preliminary efficacy and was generally tolerable in patients with RRMM, including those previously treated with αCD38 mAb
- Although the ORR was numerically greater in the SPd-60 cohort, the median PFS was longer in the SPd-40 cohort, in which treatment-emergent adverse events were less frequent, duration of exposure was longer, and higher dose intensity was achieved
- These data support the further evaluation of low-dose QW selinexor in the ongoing EMN29 trial (NCT05028348) of SPd-40 versus elotuzumab and Pd in TCE RRMM progressing immediately after an αCD38-containing line of therapy

**REFERENCES:** **1.** Bhatt P, et al. *Curr Oncol.* 2023;30(2):2322-2347. **2.** Kumar S, et al. *Blood Cancer J*. 2022;12(6):98. **3.** Lim SL, et al. *Intern Med J*. 2024;54(5):773-778. **4.** Ribbands A, et al. *Future Oncol*. 2023;19(22):1549-1562. **5.** Mateos MV, et al. *Leukemia*. 2022;36(5):1371-1376. **6**. Xpovio. Package insert. Karyopharm Therapeutics; 2020.

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**ABBREVIATIONS:** αCD38, anti-CD38 monoclonal antibodies; BIW, twice a week; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; IMiD, immunomodulatory agents; ISS, International Staging System; mAbs, monoclonal antibodies; mg, miligrams; MM, multiple myeloma; MTD, maximum tolerated dose; n, number; NE, not estimable; ORR, overall response rate; OS, overall survival; P, pomalidomide; Pd, pomalidomide and dexamethasone; PI, proteasome inhibitor; PFS, progression-free survival; QD, every day; QW, every week; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma; S, selinexor; SPd, selinexor, pomalidomide, and dexamethasone; SPd-40, selinexor 40 mg QW dose; SPd-60, selinexor 60 mg QW dose; SPd-60/80, selinexor 60/80 mg BIW doses; TCE, triple-class-exposed; VGPR, very good partial response; XPO-1, exportin-1.

**DISCLOSURES:** **Baljevic:** Janssen Biotech, BMS/Celgene, Sanofi-Genzyme, Prothena: Other: advisory board; AbbVie, Pfizer: Consultancy; Parexel: Other: IRC. **Bahlis:** Pfizer, Janssen: Research Funding; AbbVie, Amgen, BMS, Celgene, Janssen, GSK, Genentech, Karyopharm, Kyte, Novartis, Pfizer, Roche, Sanofi, Takeda: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees. **Kotb:** Karyopharm: Current holder of stock options in a privately-held company; Akcea, Amgen, Bristol Myers Squibb, Celgene, Janssen, Merck, Pfizer, Sanofi, Takeda: Honoraria; Merck, Sanofi: Research Funding. **Lipe:** Janssen and Amgen: Research Funding; Janssen, Karyopharm, BMS, Sanofi, Pfizer, and AbbVie: Consultancy, Honoraria. **Madan:** Harpoon, Karyopharm: Other: Travel, accommodations, expenses; Karyopharm, Sanofi, Pfizer, Janssen: Consultancy; Karyopharm, Harpoon, Pfizer, Iteos: Research Funding. **Sutherland:** Sanofi: Consultancy; Celgene: Consultancy; Amgen: Consultancy; GSK: Research Funding; Karyopharm: Research Funding; Janssen: Consultancy, Research Funding. **Lentzsch:** Caelum Bioscience: Patents & Royalties; Pfizer, Regeneron, Janssen, GSK, Sanofi, BMS, Karyopharm, Antigia: Consultancy, Membership on an entity's Board of Directors or advisory committees; PeerView, Clinical Care, Options (CCO), RedMed, Aptitude, Bio Ascend: Speakers Bureau. **Biran:** Amgen: Research Funding; AbbVie: Consultancy; Karyopharm: Research Funding; Bristol Myers Squibb: Consultancy, Honoraria, Research Funding, Speakers Bureau; Janssen: Consultancy, Honoraria, Research Funding, Speakers Bureau; Sanofi: Honoraria, Speakers Bureau; Pfizer: Consultancy, Honoraria. **Van Domelen:** Karyopharm Therapeutics: Current Employment. **Mark:** Karyopharm Therapeutics: Current Employment. **White:** GSK: Honoraria; Pfizer: Honoraria; Sanofi: Honoraria; Karyopharm: Honoraria; Janssen: Honoraria; Forus: Honoraria; BMS: Honoraria; Antengene: Honoraria; Amgen: Honoraria.