

Efficacy and safety of 40 mg vs 60 mg once weekly selinexor in combination with pomalidomide and dexamethasone in relapsed and/or refractory multiple myeloma (RRMM).

Darrell White, Gary J. Schiller, Sumit Madan, Suzanne Lentzsch, Evgeni Chubar, Noa Lavi, Dane R. Van Domelen, Ohad S. Bentur, Muhamed Baljevic; Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada; David Geffen School of Medicine at UCLA, Los Angeles, CA; Banner MD Anderson Cancer Center, Gilbert, AZ; Division of Hematology/Oncology, Columbia University, New York, NY; Clalit Health Services, Ha'Emek Medical Center, Afula, Israel; Department of Hematology and Bone Marrow Transplantation, Rambam Health Care Campus, Haifa, Israel; Karyopharm Therapeutics Inc., Newton, MA; Vanderbilt University Medical Center, Nashville, TN

Background: Selinexor (SEL) is an oral exportin 1 inhibitor approved with low-dose dexamethasone ± bortezomib in patients (pts) with previously treated multiple myeloma (MM). Prior studies have reported an overall response rate (ORR) of 28% and a median progression free survival (mPFS) of 3.7 mos to pomalidomide + low dose dexamethasone (Pd) in pts with MM refractory to both bortezomib and lenalidomide. **Methods:** We analyzed data of pts with RRMM treated with SEL + Pd (SPd) in the Phase 1b/2 STOMP and XPORT-MM-028 clinical trials. SEL 60 mg or 40 mg QW was given with pomalidomide 4 mg QD (days 1-21) and dexamethasone 40 mg weekly in 28-day cycles. Efficacy and safety of the combination were analyzed. **Results:** As of Sept 6, 2022, 28 pts with a median of 2.0 prior treatment lines (mLOT) and 20 pts with 2.5 mLOT were enrolled in the SPd-40 cohort and SPd-60 cohort, respectively. Among pts treated with SPd-40 and SPd-60, 93% and 75% had MM refractory to a proteasome inhibitor (PI), 75% and 85% had MM refractory to an immunomodulatory drug (IMiD), and 43% and 20% had triple-class refractory MM refractory to an anti-CD38 monoclonal antibody (αCD38 mAb), a PI and an IMiD, respectively. Prior exposure to αCD38 mAbs was reported in 57% and 30% of pts in the SPd-40 and SPd-60 cohorts, respectively. Median duration of exposure in the SPd-40 vs SPd-60 cohorts was 28 vs 22 wks, respectively. Higher ORR and rate of pts with ≥very good partial response (VGPR) were observed for SPd-60 vs SPd-40 (ORR: 65% vs 50%; ≥VGPR: 30% vs 25%), but the PFS was numerically longer for SPd-40 vs SPd-60 (mPFS in mos: not reached [95% CI, 6.5-NE] after median follow-up of 1 year vs 9.5 mos [95% CI, 7.6-NE]; 9-mo PFS probability: 0.59 [95% CI, 0.41-0.85] vs 0.52 [95% CI, 0.29-0.94]). Across both doses among patients previously treated with αCD38 mAbs (n = 22), mPFS was 8.9 mos (95% CI, 6.5-NE). For the 27 responders across both doses, median time to response was 1.0 mo (95% CI, 1-2) and median duration of response was 21.8 mos (95% CI, 8.6-NE). Common hematologic treatment-emergent adverse events (TEAEs) included (all grades: SPd-40 vs SPd-60) neutropenia (68% vs 75%, with one case of grade 3 febrile neutropenia in each cohort), anemia (39% vs 65%) and thrombocytopenia (43% vs 45%). No high-grade hemorrhages were observed. Non-hematologic TEAEs were generally transient and reversible, including fatigue (43% vs 75%), nausea (32% vs 70%) and diarrhea (25% vs 35%). **Conclusions:** The all-oral combination of SEL + Pd in pts with RRMM showed signs of preliminary efficacy and was generally tolerable in these cohorts. Most TEAEs, including nausea, occurred at lower frequency in the 40 mg cohort. Although a higher 60 mg QW SEL dose may be associated with a higher ORR, mPFS correlated with longer duration of treatment and is numerically longer for pts treated with the 40 mg dose, suggesting that clinical benefit is optimized at the lower 40 mg dose. Clinical trial information: NCT02343042, NCT04414475. Research Sponsor: Karyopharm Therapeutics.