Abstract: PB2106

Title: REAL-WORLD SAFETY AND EFFECTIVENESS OF SELINEXOR-BASED REGIMENS IN PATIENTS WITH RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA AND DIALYSIS-DEPENDENT RENAL IMPAIRMENT

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Background:

Renal impairment (RI) is common in patients (pts) with multiple myeloma (MM), often worsening as pts progress through therapies, limiting use of renally metabolized or potentially nephrotoxic therapies. Selinexor, a first-in-class oral selective inhibitor of nuclear exportin 1 approved in combination with dexamethasone (Xd) and dexamethasone + bortezomib (XVd, approved in relapsed/refractory MM [RRMM] after ≥1 prior therapy), is metabolized primarily via hepatic routes, urinary excretion isn't a major elimination pathway, it doesn't affect creatinine clearance, and no dose adjustments are needed for mild to severe RI not requiring hemodialysis (HD). A prior analysis of a subset of pts with MM and RI from BOSTON (NCT03110562) found once-weekly XVd compared to twice-weekly Vd led to increased progression free survival (PFS) and overall response rate (ORR) and was generally well tolerated. However, the safety of selinexor in HD-dependent pts is unknown.

Aims:

We present data from pts with RRMM and HD-dependent RI treated with selinexor regimens in the real-world setting of the Karyopharm Expanded Access Program (KEAP), providing selinexor to eligible pts with no other treatment options.

Methods:

We retrospectively reviewed data from pts with RRMM and HD-dependent RI prior to initiation of selinexor who received ≥1 dose of selinexor under KEAP. Dual antiemetic prophylaxis was recommended to all pts. Pt details were obtained via a validated portal system and treating physicians.

Results:

From March 2020 to December 2022, 15 pts with HD-dependent RI received selinexor-based regimens, including Xd, XVd, Xd + pomalidomide (XPd), and Xd + carfilzomib (XKd) (Table 1). The majority (80.0%) were male, median age was 66 years, median prior lines of therapy was 5, and median time from first therapy to first selinexor dose was 4.2 years. As of 19 December 2022, 1 pt remains on treatment. A total of 86.7% (13/15) had triple-class treated (TCT) and 66.7% (10/15) had penta-treated (PT) MM. Median duration of treatment was 4.1 months (mos) (range, 0.1 – 15.4) in the full cohort and 4.3 and 4.8 mos in TCT and PT MM, respectively. In the full cohort, 12/15 (80%) completed at least 1 treatment cycle. Reported adverse events (AEs) included thrombocytopenia (33.3%), nausea (20.0%), and fatigue (20.0%). No cardiac AEs, fluid overload, electrolyte abnormalities or uremia events were reported. There were no deaths related to treatment toxicity. In pts treated with selinexor-based triplets, ORR was 37.5% (95% CI, 8.5, 75.5), including 1 very good partial response, 42.9% in TCT and 60% in PT MM. In the Xd group, ORR was 42.9% (95% CI, 9.9, 81.6), 50% in TCT and 60% in PT MM (Table 1). Median PFS was 4.3 mos (95% CI, 2.3-not evaluable [NE]) in the full cohort, 4.8 mos (95% CI, 3.7-NE) in TCT MM and 5.2 mos (95% CI 4.1-NE) in PT MM.

Summary/Conclusion:

These results from a real-world cohort suggest selinexor regimens are generally tolerable, safe and effective in pts with RRMM and HD-dependent RI. No new safety signals or concerns were reported in this vulnerable pt group. Inherent limitations of real-world outcomes include variability in enrollment and methodologies of collecting data, primarily missing data relating to etiology of RI, renal response, and refractoriness to prior therapies. Despite

these limitations, evidence of clinical benefit was observed with a PFS of more than 4 mos and ORR of 40% despite a median of 5 prior lines of therapy with 86.7% of pts having TCT MM. These results suggest real-world effectiveness and tolerability of selinexor regimens in a challenging-to-treat pt population.

Table 1. Demographics, baseline characteristics, and effectiveness of selinexor regimens

	All Regimens[1] (N = 15)	Xd (N = 7)	XVd, XPd, or XKd (N = 8)	XVd (N = 4)
End of Treatment Disposition, n (%)				
On Treatment	1 (6.7)	0	1 (12.5)	0
Discontinued Treatment and Reasons	14 (93.3)	7 (100.0)	7 (87.5)	4 (100.0)
COVID-19 infection	1 (6.7)	1 (14.3)	0	0
Disease progression	12 (80.0)	5 (71.4)	7 (87.5)	4 (100.0)
Patient choice to stop all treatments (including dialysis)	1 (6.7)	1 (14.3)	0	0
Treatment Regimen, n (%)				
Xd	7 (46.7)	7 (100.0)	0	0
XVd	4 (26.7)	0	4 (50.0)	4 (100.0)
XPd	3 (20.0)	0	3 (37.5)	0
XKd	1 (6.7)	0	1 (12.5)	0
Age at Time of Joining KEAP (Years)				
Median (range)	66.0 (52, 87)	67.0 (52, 87)	64.0 (57, 76)	66.0 (57, 76)
Gender, n (%)				
Male	12 (80.0)	6 (85.7)	6 (75.0)	3 (75.0)
Female	3 (20.0)	1 (14.3)	2 (25.0)	1 (25.0)
Duration from First Therapy to KEAP Day 1 (Years)				
N	13	6	7	3
Median (range)	4.2 (1.1, 21.1)	6.2 (1.1, 12.8)	3.8 (1.2, 21.1)	2.6 (2.5, 21.1)
Number of Prior Lines of Therapy				
Median (range)	5.0 (3, 10)	6.0 (4, 10)	4.5 (3, 7)	4.5 (4, 7)
Prior therapies, n (%)				
PI (bortezomib, carfilzomib, ixazomib)	15 (100.0)	7 (100.0)	8 (100.0)	4 (100.0)
IMiD (lenalidomide, pomalidomide, thalidomide)	15 (100.0)	7 (100.0)	8 (100.0)	4 (100.0)
Anti-CD38 mAb (daratumumab, isatuximab)	13 (86.7)	6 (85.7)	7 (87.5)	4 (100.0)
Triple-class treated (PI, IMiD, αCD38 mAb)	13 (86.7)	6 (85.7)	7 (87.5)	4 (100.0)
Penta-treated (≥2 PIs, ≥2 IMiDs, 1 αCD38 mAb)	10 (66.7)	5 (71.4)	5 (62.5)	3 (75.0)
Duration of Treatment (Months)				
Median (range)	4.1 (0.1, 15.4)	2.2 (0.1, 4.3)	6.3 (0.9, 15.4)	6.3 (0.9, 8.5)
Overall Response Rate[2], n (%)	6 (40.0)	3 (42.9)	3 (37.5)	2 (50.0)
[95% CI]	[16.3-67.7]	[9.9-81.6]	[8.5-75.5]	[6.8-93.2]
Best Overall Response, n (%)				
Very Good Partial Response	1 (6.7)	0	1 (12.5)	1 (25.0)
Partial Response	5 (33.3)	3 (42.9)	2 (25.0)	1 (25.0)
Stable Disease	5 (33.3)	1 (14.3)	4 (50.0)	1 (25.0)
Progressive Disease	2 (13.3)	1 (14.3)	1 (12.5)	1 (25.0)
Not Evaluable	2 (13.3)	2 (28.6)	0	0
Progression-Free Survival (Months)				
Median (95% CI)	4.3 (2.3, NE)	3.7 (2.2, NE)	6.3 (5.2, NE)	6.3 (0.9, NE)

Abbreviations: IMiD = immunomodulatory drug; KEAP = Karyopharm Expanded Access Program; mAb = monoclonal antibody; NE = not evaluable/reached; PI = proteasome inhibitor; Xd = selinexor + dexamethasone; XVd = selinexor+bortezomib+dexamethasone; XPd = selinexor+pomalidomide+dexamethasone; XKd = selinexor+carfilzomib+dexamethasone.

[1] Xd is FDA-approved at a selinexor dose of 80 mg BIW, XVd is FDA-approved at a selinexor dose of 100 mg QW. The recommended phase 2 dose of selinexor in additional combinations is 60 mg QW (XPd) and 80 mg QW (XKd).

[2] Overall response rate is the percentage of patients who achieved partial response or better before disease progression or initiating a new treatment.

Keywords: Renal impairment, Multiple myeloma, relapsed/refractory