COMy
The 7th World Congress on Controversies in Multiple Myeloma (COMy)

Safety and Efficacy of Weekly Selinexor, Bortezomib, and Dexamethasone (XVd) Versus Standard Vd in European Patients With Previously Treated Multiple Myeloma (MM)

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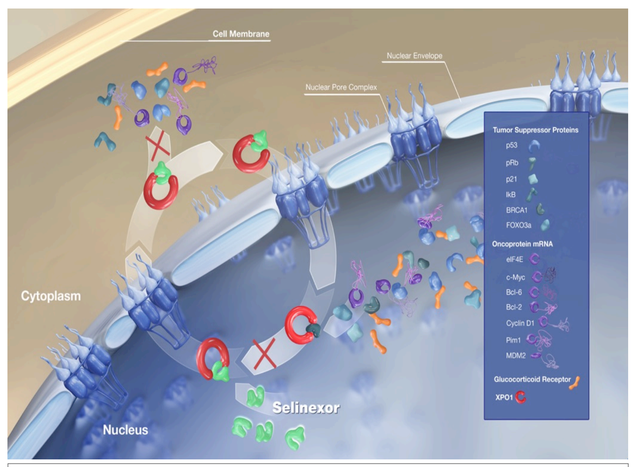
Selinexor: First-in-Class, Oral Selective Inhibitor of Nuclear Export



1. Gupta A, et al. Therapeutic targeting of nuclear export inhibition in lung cancer. J Thorac Oncol. 2017;12(9):1446-1450. 2. Sun Q, et al. Inhibiting cancer cell hallmark features through nuclear export inhibition. Signal Transduct Target Ther. 2016;1:16010. 3. Gandhi UH, et al. Clinical implications of targeting XPO1-mediated nuclear export in multiple myeloma. Clin Lymphoma Myeloma Leuk. 2018;18(5):335-345. 4. Gravina GL, et al. Nucleo-cytoplasmic transport as a therapeutic target of cancer. J Hematol Oncol. 2014;7:85. 5. Chari NEJM 2019, 6. Gavriatopoulou IMW 2019

Exportin 1 (XPO1)[1-6] is overexpressed in MM; its levels correlate with poor prognosis and drug resistance

XPO1 Overexpression Causes:

- Tumor suppressor proteins (e.g., p53, IκB and FOXO) and glucocorticoid receptor inactivation and enhanced oncoprotein (e.g., c-Myc, Bcl-xL, cyclins) translation

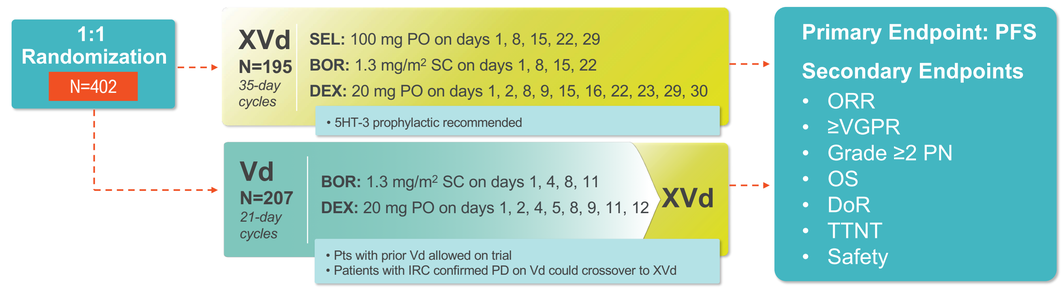
Selinexor (XPOVIO, X) is an oral selective XPO1 inhibitor that reactivates multiple TSPs and inhibits oncoprotein translation

Phase 3 BOSTON Trial: Velcade-dex ± X (XVd vs Vd):

- Once weekly XVd significantly prolongs PFS (HR 0.70, *p*=0.0075) vs standard twice weekly Vd, and was superior to Vd on ORR, TTNT, DoR with a trend to improved overall survival

The BOSTON Trial Design: XVd *vs*. Vd

BOSTON Trial[7]: Phase 3, Global, Randomized, Open Label Study in Patients with MM who had Received 1–3 Prior Therapies



The XVd regimen requires ~**40% less bortezomib and ~25% less dexamethasone** than standard Vd, with **37% fewer clinic visits** over the first 6 months of treatment

[7]Grosicki *et al*, The Lancet 2020;396(10262):1563-1573

Methods

We performed post-hoc analyses to compare the outcomes on European patients, including those from Austria, Belgium, Bulgaria, Czech Republic, France, Germany, Greece, Hungary, Italy, Poland, Romania, Russia, Serbia, Spain, UK, and Ukraine

Total Patients Enrolled	XVd (n=195)	Vd (n=207)
European Patients	**71%** (n=139)	**76%** (n=158)

Baseline and Disease Characteristics

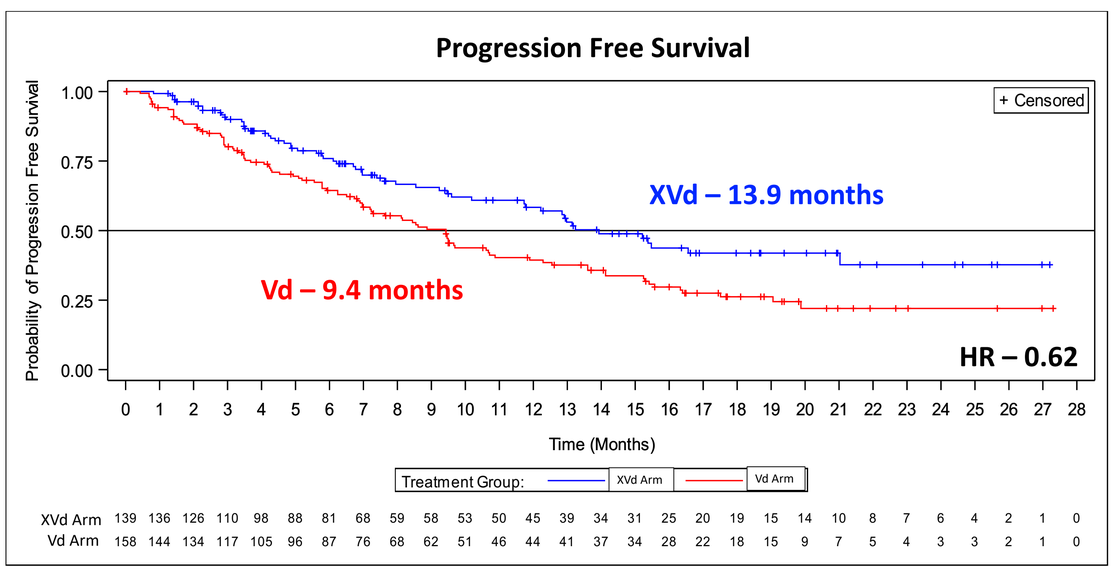
Age Categories	XVd (n=139)	Vd (n=158)
Median Age, Years (range)	**66** (43, 84)	**68** (43, 90)
Males, n (%)	**80** (57.6)	**81** (51.3)
Females, n (%)	**59** (42.4)	**77** (48.7)
Number of Prior Treatment Regimens, n (%)		
1	**73** (52.5)	**76** (48.1)
2	**44** (31.7)	**49** (31.0)
3	**22** (15.8)	**33** (20.9)

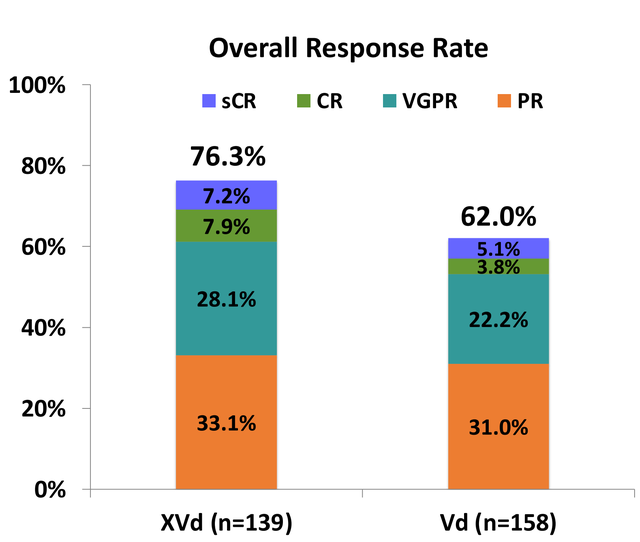
Treatment Emergent Adverse Events, All Grades, ≥10% Overall

AE Term	XVd (n=139)	Vd (n=157)
Thrombocytopenia	80 (57.6)	43 (27.4)
Peripheral Neuropathy (PN)	49 (35.3)	73 (46.5)
Anemia	52 (37.4)	35 (22.3)
Fatigue	48 (34.5)	26 (16.6)
Nausea	59 (42.4)	15 (9.6)
Diarrhoea	38 (27.3)	33 (21.0)
Asthenia	36 (25.9)	17 (10.8)
Upper Respiratory Tract Infection	27 (19.4)	24 (15.3)
Weight Decreased	32 (23.0)	17 (10.8)
Pneumonia	22 (15.8)	24 (15.3)
Decreased Appetite	41 (29.5)	4 (2.5)
Constipation	17 (12.2)	22 (14.0)
Bronchitis	20 (14.4)	19 (12.1)

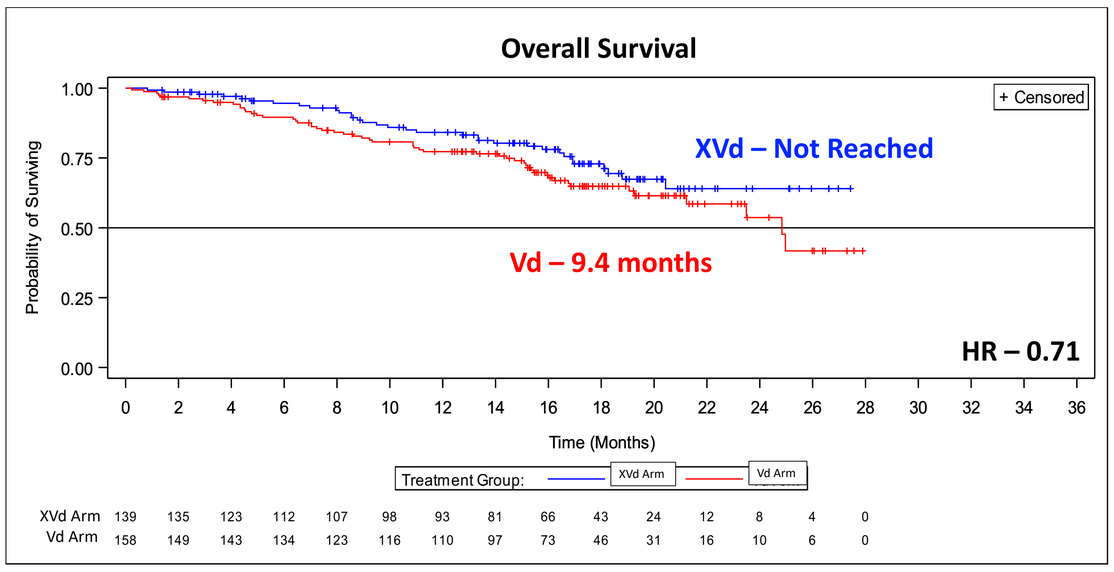
- Similar to the overall population, the most common AEs were thrombocytopenia, peripheral neuropathy (PN), anemia, and fatigue.
- As compared to the Vd arm, the XVd arm had a higher incidence of thrombocytopenia (58% vs 27%), nausea (42% vs. 10%), anemia (37% vs. 22%), fatigue (35% vs. 17%), and decreased appetite (30% vs. 3%)
- ≥Grade 2 PN was significantly higher (*p=0.04*) in the Vd arm (34%) compared to the XVd arm (25%); overall PN was also higher (p=0.03)
  - In the total population, PN as a cause of dropout: 2.6% on XVd and 3.4% on Vd
- Serious AEs occurred in 50% of patients on the XVd arm compared to 39% of patients on the Vd arm
- There were more deaths in Vd arm (13, 8.3%) compared with XVd arm (9, 6.5%)

Efficacy





- The median PFS benefit of XVd was sustained in the European population compared to Vd: 13.9 vs 9.4 months (HR, 0.62; 95% CI, 0.45-0.86; p=0.001)
- Median OS was not reached in the XVd arm compared to 24.8 months in the Vd arm (HR, 0.71; 95% CI, 0.46-1.09; p=0.05)
- The ORR was significantly higher with XVd vs. Vd (76.3% vs 62.0%; p=0.004)
- The ≥VGPR rate was also significantly higher in XVd compared to Vd (43.2% vs. 31.0%; p=0.02)



Conclusions

- **Activity of weekly XVd was consistent in European patients as compared with the entire population: mPFS of 13.9 months, PFS HR of 0.62 (p=0.001)**
- **In the European population XVd showed significantly higher response rates including ≥VGPR and lower rates of PN compared to standard twice weekly Vd**
- **Non-PN AEs were higher with in XVd than Vd therapy, but most of the AEs were reversible and treatable; there was no maximal duration of therapy**
- **Once weekly XVd is a highly active and tolerable option for patients with previously treated MM, including European patients**