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P917 SELINEXOR, BORTEZOMIB, AND DEXAMETHASONE IN PATIENTS WITH PREVIOUSLY TREATED MULTIPLE MYELOMA: UPDATED RESULTS OF BOSTON TRIAL BY PRIOR THERAPIES

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background:

Increasing use of daratumumab + lenalidomide + dexamethasone (DRd) in the frontline setting for multiple myeloma (MM) has led to more patients (pts) with proteasome inhibitor (PI)-naïve early relapse. ESMO Guidelines endorse the use of a PI-based combination including selinexor, bortezomib, and dexamethasone (SVd) in MM pts with PI-naïve early relapse. Selinexor is a first-in-class, orally bioavailable XPO1 inhibitor with a unique mechanism of action that results in nuclear retention and functional activation of tumour suppressor proteins ultimately impacting cellular proliferation and tumour growth rate. SVd is indicated for relapsed and refractory MM (RRMM) in adults who have received at least one prior therapy.

Aims:

We analyzed longer follow-up data from the phase 3 BOSTON trial (NCT03110562) to determine the impact of prior therapies, including PI, on SVd efficacy and safety.

Methods:

Eligible pts with RRMM and 1-3 prior therapies (including bortezomib, carfilzomib, ixazomib, daratumumab, lenalidomide, or pomalidomide) were randomized to selinexor QW (100 mg), bortezomib QW (1.3 mg/m^2) and dexamethasone BIW (20 mg) (Vd) or standard BIW Vd. A stratified efficacy analysis and safety analysis were performed in subgroups by prior PI therapy and number of prior regimens. Efficacy analyses were based on Feb 2021 data cut and safety analyses on Jun 2022 data cut.

Results:

Of 402 pts, 198 received 1 prior line of treatment (LOT) (SVd=99; Vd=99; median ages 67 and 69 y, respectively); 95 pts were PI-naïve (SVd=47; Vd=48; median ages 68 and 67.5, respectively); and 123 were not previously exposed to bortezomib (SVd=61; Vd=62; median ages 68 y both arms). In pts with 1 prior LOT, SVd reduced the risk of disease progression or death by 38% vs Vd (HR 0.62; 95% CI 0.41-0.95, two-sided p=0.028; table). Similarly, in both patients with PI-naïve and bortezomib naïve disease, SVd reduced the risk of disease progression or death (see table). Overall response rate (ORR) and very good partial response (VGPR) or better rates were longer with SVd vs Vd in all subgroups (see table).

	1 Prior LOT Pts		PI-Naïve Pts		Bortezomib-Naïve Pts	
	SVd (n=99)	Vd (n=99)	SVd (n=47)	Vd (n=48)	SVd (n=61)	Vd (n=62)
Median PFS, mo (95% CI)	**21.0** (13.2-NR)	**10.7** (7.3-16.4)	**29.5** (27.5-NR)	**9.7** (8.4-23.7)	**29.5** (24.8-NR)	**9.7** (8.4-17.5)
HR (95% CI); two-sided p-value	**0.62** (0.41-0.95); 0.028		**0.29** (0.14-0.63); <0.001		**0.35** (0.18-0.68); 0.002	
ORR, %	80.8	66.7	76.6	70.8	75.4	69.4
VGPR, %	52.5	29.3	53.2	41.7	49.2	41.9

The most common (≥25%) treatment-emergent adverse events (AEs) with SVd vs Vd in pts with 1 prior LOT were thrombocytopenia (61.6% vs 28.6%), nausea (52.5% vs 11.2%), fatigue (45.4% vs 17.3%), peripheral neuropathy (38.4% vs 52.0%), diarrhea (34.3% vs 24.5%), and anemia (30.3% vs 26.5%). Safety findings were similar in the PI naïve and bortezomib naïve subgroups.

Summary/Conclusion:

Stratified subgroup data from longer follow-up in the BOSTON trial confirm the PFS benefit of SVd over Vd in pts without prior PI or bortezomib exposure as well as pts who have received 1 prior LOT. There is a statistically significant and clinically meaningful ~20 mo median PFS improvement of SVd over Vd in RRMM pts that had no prior exposure to PI and bortezomib, as well as a significant ~10 mo PFS improvement in pts with 1 prior LOT. These outcomes coupled with generally manageable AE profile emphasize the synergy between selinexor and bortezomib and the importance of a double mode of action switch, further supporting SVd use in 1) PI-naïve RRMM pts, 2) bortezomib-naïve RRMM pts, and 3) pts at first relapse.