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P886 EFFICACY, SURVIVAL AND SAFETY OF SELINEXOR, BORTEZOMIB AND DEXAMETHASONE (SVD) IN PATIENTS WITH LENALIDOMIDE-REFRACTORY MULTIPLE MYELOMA: SUBGROUP DATA FROM THE BOSTON TRIAL

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background:

Lenalidomide (LEN) is commonly used in frontline therapy for newly diagnosed MM, and there is a need for effective treatment options for patients (pts) with MM refractory to LEN. 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 in adults with relapsed and refractory MM (RRMM) who have received at least one prior therapy. Initial results of the BOSTON phase 3 trial demonstrated significant improvements in median progression-free survival (mPFS) and overall response rate (ORR) with SVd vs bortezomib and dexamethasone (Vd) in previously treated MM (Grosicki et al. Lancet 2020).

Aims:

We analyzed data from the phase 3 BOSTON trial (NCT03110562) to determine the impact of refractoriness to LEN on SVd efficacy (both PFS and overall survival [OS]) and safety.

Methods:

Eligible pts with RRMM and 1-3 prior therapies were randomized to SVd (selinexor 100 mg QW, bortezomib 1.3 mg/m^2 QW and dexamethasone 20 mg BIW) or standard Vd BIW. We performed a post-hoc stratified analysis of PFS, OS (with crossover adjustment using the two-stage method), response rates and safety in subgroups by refractory status to LEN.

Results:

Of 402 pts, 106 were classified as LEN-refractory (SVd=53, Vd=53). Sixteen pts (30.2%) in the SVd arm became LEN-refractory after 1 prior line of therapy (LOT) and 69.8% after 2 or more LOT; in the Vd group 26.4% became LEN-refractory after 1 prior LOT; 73.6% after 2 or more LOT. Median age was 65 years (range 40-87) in the SVd arm and 66 years (range 45-85) in the Vd arm. At the time of the analyses, median follow-up was 28.7 mo for SVd arm and 28.6 mo for Vd arm. mPFS was 10.2 mo (95% CI 5.8-NR) with SVd vs 7.1 mo (95% CI 3.5-9.8) with Vd (HR 0.52; 95% CI 0.31-0.88, two-sided p=0.012). mOS was 26.7 mo (95% CI 19.9-NR) with SVd vs 18.6 mo (95% CI 13.9-29.0) with Vd, resulting in a statistically significant and clinically meaningful improvement in OS (HR 0.53; 95% CI 0.30-0.95, two-sided p=0.03). Response rates for SVd and Vd were as follows: ORR 67.9% vs 47.2% and VGPR or better 35.8% vs 24.5%, respectively. The most common (≥25%) treatment-emergent adverse

events with SVd vs Vd in 105 LEN-refractory pts included in the safety population were thrombocytopenia (71.7% vs 40.4%), nausea (50.9% vs 11.5%), fatigue (45.3% vs 21.1%), diarrhea (43.4% vs 19.2%), anemia (39.6% vs 25.0%), and peripheral neuropathy (30.2% vs 38.5%).

Summary/Conclusion:

Subgroup data from the BOSTON trial show a statistically significant and clinically meaningful improvement in OS and PFS and higher ORR and VGPR or better with SVd vs Vd in LEN-refractory RRMM pts. The safety profile in the subgroups was similar to that observed in the overall BOSTON population. The statistically significant 47% reduction in risk of death with SVd vs Vd shows an advantage of having a regimen built on two drugs with different mechanisms of action in the difficult-to-treat population of LEN-refractory RRMM pts.