The BOSTON Trial Design: XVd vs. Vd

The BOSTON trial was a Phase 3, global, randomized, open-label study in patients with multiple myeloma who had received 1–3 prior therapies. The primary endpoint was progression-free survival (PFS), and secondary endpoints included overall survival (OS), objective response rate (ORR), time to next treatment (TTNT), and duration of response (DoR).

Methods

The study enrolled 396 patients from 90 centers in 25 countries. Patients were randomized to receive either dexamethasone (XVd) or standard dexamethasone (Vd). The treatment regimen for XVd was 10 mg PO on days 1, 2, 4, 5, 8, 9, 11, 12, and 15, and for Vd, 40 mg PO on days 1, 2, 4, 5.

Efficacy

The ORR was significantly higher with XVd vs. Vd (43.2% vs. 31.0%; p=0.02). The 76.3% of patients in the XVd arm achieved a very good partial response (VGPR) or better, compared to 62.0% in the Vd arm (p=0.001). The 35.1% of patients in the XVd arm achieved a partial response (PR) or better, compared to 21.0% in the Vd arm (p=0.004).

Conclusions

- 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).
- The OBR was significantly higher with XVd vs. Vd (76.3% vs 62.0%; p=0.004).
- The pVGPR rate was also significantly higher in XVd compared to Vd (43.2% vs. 31.0%; p<0.002).
- 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 PN (58% vs 27%), nausea (42% vs 10%), anemia (37% vs 22%), fatigue (35% vs 17%), and decreased appetite (30% vs 3%).
- 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.

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

Selinexor (XPOVIO, X) is an oral selective XPO1 inhibitor that reactivates multiple TSPs and inhibits oncoprotein translation. This is overexpressed in MM; its levels correlate with poor prognosis and drug resistance.

XPO1 Overexpression Causes:
- Tumor suppressor proteins (e.g., p53, hnRNP and FDC1) and pluricellular receptor interaction and enhanced oncoprotein (e.g., c-Myc, Bcl-XL) cycling translation.

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.