Abstract: P943

Title: ORAL IXAZOMIB MAINTENANCE FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANT (ASCT) IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): FINAL OVERALL SURVIVAL (OS) ANALYSIS FROM THE TOURMALINE-MM3 STUDY

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

The double-blind TOURMALINE-MM3 study (NCT02181413) included patients (pts) with NDMM who had achieved at least a partial response (PR) following induction therapy, high-dose melphalan conditioning, and single ASCT within 12 months of diagnosis (*Dimopoulos, Lancet 2019*). This study previously demonstrated a statistically significant and clinically meaningful improvement in its primary endpoint of progression-free survival (PFS) for ixazomib (ixa) maintenance vs placebo (pbo; median PFS: 26.5 vs 21.3 months; *P*=0.0023). An interim analysis showed no statistically significant difference in the key secondary endpoint of OS (*Dimopoulos, ASH 2021*).

Aims:

To report the final OS analysis in the TOURMALINE-MM3 intent-to-treat population and pt subgroups of interest.

Methods:

Full methods have been published previously (*Dimopoulos, Lancet 2019*). Eligible pts were randomized 3:2 to receive single-agent ixa maintenance (3 mg for cycles 1–4, and if tolerated, 4 mg from cycle 5; n=395) or matching pbo (n=261) on days 1, 8, and 15 in 28-day cycles for up to 26 cycles, or until progressive disease (PD) or unacceptable toxicity, whichever came first.

Results:

At data cutoff (Sep 08, 2023), in the ixa vs pbo arms, 49% vs 58% of pts had discontinued treatment prior to completion of 26 cycles; 36% vs 46% of discontinuations were due to PD and 6% vs 3% due to adverse events. Median follow-up for ixa vs pbo was 94.4 vs 94.5 months, OS events had occurred in 36% vs 36% of pts, and median OS was not reached (NR) vs NR (hazard ratio [HR], 1.025; 95% confidence interval [CI]: 0.789–1.332;** *P*=0.850). There were no significant differences in median OS for ixa vs pbo among pts: with baseline high-risk cytogenetics [del(17p) and/or t(4;14) and/or t(14;16)] (64.2 vs 69.0 months; HR, 0.970; 95% CI: 0.583–1.613); with minimal residual disease (MRD) at study entry (105.0 months vs NR; HR, 0.966; 95% CI: 0.682–1.368); who were MRD negative at study entry (NR vs NR; HR, 0.700; 95% CI: 0.414–1.184); aged <60 years (NR vs NR; HR, 1.295; 95% CI: 0.862–1.944); aged between ≥60 and <75 years (105.0 vs 94.2 months; HR, 0.907; 95% CI: 0.629–1.307); who received a proteasome inhibitor (PI) as part of next-line therapy (NR vs 94.2 months; HR, 0.794; 95% CI: 0.523–1.206); or whose next-line therapy did not include a PI (74.9 vs 90.3 months; HR, 1.310; 95% CI: 0.901–1.904). In ixa vs pbo arms, 73% vs 73% of pts received ≥1 subsequent anti-myeloma therapy, including: corticosteroids (91% vs 89%); immunomodulatory drugs (89% vs 85%); PIs (63% vs 74%); and monoclonal antibodies (48% vs 39%). Median PFS2 (PFS on next-line therapy) for ixa vs pbo was 84.0 vs 80.4 months (HR, 1.015; 95% CI: 0.795–1.298). Incidences of new primary malignancies (NPMs) in the ixa vs pbo arms were 7% vs 8%; incidences of hematological NPMs were 2% vs 3%. Pt global health quality of life (QoL) score was maintained in both arms over the course of treatment.

Summary/Conclusion:

Although the study met its primary endpoint of PFS, the final OS analysis for TOURMALINE-MM3 showed no

statistically significant difference between ixa maintenance for up to 26 cycles and matching pbo in pts with NDMM who had achieved ≥PR post-ASCT. Despite nearly 8 years of follow-up, median OS had not been reached in either arm, supporting the concept that the growing number of available, highly effective salvage treatments with novel mechanisms of action make demonstrating an OS advantage in front-line myeloma studies increasingly challenging. Ixa maintenance did not appear to have an adverse effect on subsequent therapies. NPM incidence remained low in both treatment arms, and pt QoL was maintained.

Keywords: Maintenance, Proteasome inhibitor, Multiple myeloma, Post-transplant