POOLED ANALYSIS OF PROGRESSION-FREE SURVIVAL (PFS) ACCORDING TO CYTOGENETIC ABNORMALITY (CA) STATUS IN PATIENTS WITH MULTIPLE MYELOMA (MM) TREATED WITH IXAZOMIB- VS PLACEBO-BASED THERAPY IN THE TOURMALINE PHASE 3 STUDIES

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Introduction: The presence of adverse CAs is associated with poorer prognosis of MM. This pooled analysis of the TOURMALINE-MM1, MM2, MM3, and MM4 phase 3 studies evaluated PFS according to specific adverse CAs in patients receiving ixazomib- vs placebo-based therapy.

Material and methods: In TOURMALINE-MM1 (N=722) and MM2 (N=705), patients received ixazomib plus lenalidomide-dexamethasone (Rd) vs placebo-Rd (1:1). In TOURMALINE-MM3 (N=656) and MM4 (N=706), patients received ixazomib vs placebo (3:2) as maintenance therapy. CAs were assessed centrally (MM1/MM2; at screening) or locally (MM3/MM4) by fluorescence *in situ* hybridization for the presence of del(17p), t(4;14), t(14;16), and/or amp1q21.

Results: 22% vs 22% of patients receiving ixazomib- (N=1227) vs placebo-based (N=1019) therapy had high-risk CAs [≥1 of del(17p), t(4;14), t(14;16)]; 78% vs 78% had complementary standard-risk CAs. 49% vs 50% of patients receiving ixazomib- (N=1142) vs placebo-based (N=955) therapy had expanded high-risk CAs (high-risk ±amp1q21); 51% vs 50% had complementary standard-risk CAs. After a median follow-up of 25.6 months, the hazard ratio for PFS (PFS-HR) with ixazomib- vs placebo-based therapy was 0.74 (95% confidence interval [CI] 0.59–0.93, median PFS [mPFS] 17.8 vs 13.2 months) in patients with high-risk CAs and 0.70 (95% CI 0.62–0.80, mPFS 26.3 vs 17.6 months) among patients with complimentary standard-risk CAs. PFS-HR with ixazomib- vs placebo-based therapy was 0.75 (95% CI 0.64–0.87, mPFS 18.1 vs 14.1 months) in the expanded high-risk subgroup and 0.71 (95% CI 0.59–0.85, mPFS 36.1 vs 21.4 months) in the complementary standard-risk subgroup. Analyses regarding individual CAs showed different magnitudes of PFS benefit.

Conclusions: PFS benefit with ixazomib-Rd/ixazomib vs placebo-Rd/placebo was found regardless of CA status; the magnitude of benefit was similar between the (expanded) high-risk and respective complementary standard-risk subgroups. Due to differing patient populations, ixazomib-based therapy may not abrogate the negative impact of high-risk CAs, warranting further analysis.