Maintenance therapy with carfilzomib, pomalidomide, and dexamethasone (KPd) in high-risk myeloma patients (pts): A phase 2 study with a safety run-in.

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Background: High-risk pts derive survival benefit from combination maintenance (PI and IMiD) strategies. We have evaluated the safety and efficacy of the next generation PI (carfilzomib) and IMiD (pomalidomide) in combination with dexamethasone in high-risk myeloma (NCT03756896). Methods: Newly diagnosed high-risk myeloma pts that have achieved \( \geq PR \) post-ASCT were included. High-risk myeloma was defined by the presence of t(4;14) in 27.6%, t(14;16) in 17.2%, del17p in 58.6% pts by FISH or CTG or presence of \( \geq 20\% \) circulating cells (pPCL) in 6.9%. Double-hit myeloma (as defined by presence of \( \geq 2 \) high-risk cytogenetic abnormalities including gain of 1q) was seen in 58.6% of pts. Each cycle is 28 days. Carfilzomib 20/56 mg/m2 IV was given on days 1, 8, 15 and pomalidomide 2 mg PO on days 1 to 21 and dexamethasone 40 mg PO was administered on days of carfilzomib. Statistical analysis was conducted using SAS Version 9.4. Results: After the safety run in the first 3 pts, 26 additional pts were enrolled. Median age was 60 years (range, 46–75); 58.6% male and 58.6% black. At diagnosis, 65.5% had RISS stage 3 disease. 54.5% of whites and 64.7% of blacks had double-hit disease. Median time from diagnosis and from transplant to study entry was 9.3 (range, 6.08-12.42) and 2.89 (range, 2-8.51) months, respectively. At study entry, \( \geq CR \) and \( \geq VGPR \) rates were 24.1% and 68.9%, respectively, which deepened to 79.3% and 100% while on study. The median time to best response was 2.07 months (range, 1.22-14.26). Of the 15 pts with available MRD data, MRD \( (10^{-5}) \) and \( (10^{-6}) \) were achieved in 80% and 53.3%, respectively. After a median follow-up of 25.8 months, 36 month PFS was 63.2% (95% CI 38.3-80.3%) and 36 month OS was 72.4% (95% CI 54.2-88.0%). Double-hit disease was an independent predictor for progression and death. Among these high risk patients, RISS did not show any statistical significance. While there is no PFS difference by race, the 36 month OS for black pts was inferior compared to whites (61.1% [23.1-84.7%] vs 85.7% [53.4%-97.9%], log rank 0.05). At data cut-off, 37.9% of pts were still receiving treatment; most common reason for permanent treatment discontinuation was progressive disease (27.6%). Among the 6 pt deaths, the most common cause of death was progressive disease (83.3%). Most common (\( \geq 20\% \)) TEAEs were fever (37.9%), fatigue (34.5%), diarrhea (27.6% [G3/4, 3.4%]), nausea (24.1%), cough (20.7%), muscle cramps (20.1%), acneiform rash (20.1%). TEAEs of interest were cardiac (10.3% [G3/4, 3.4%]), cataracts (17.2% [G3/4, 17.2%]), neutropenia (6.9% [G3/4, 6.9%]) and anemia (10.3% [G3/4, 0%]). Conclusions: In pts with high-risk myeloma, KPd maintenance deepened responses. MRD negativity \( (10^{-5}) \) was attained in 80% of pts. Despite the encouraging results in this cohort of high-risk patients, PFS and OS among double-hit pts remains poor, warranting newer strategies aimed at remission sustenance. Clinical trial information: NCT03756896. Research Sponsor: Amgen.