Daratumumab, Bortezomib and Dexamethasone (DVd) vs Bortezomib and Dexamethasone (Vd) in Relapsed or Refractory Multiple Myeloma (RRMM): Efficacy and Safety Update (CASTOR)

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Introduction: Daratumumab (D), a human, CD38-targeting mAb, is well tolerated and induces deep and durable responses in patients (pts) with RRMM. We provide an update of CASTOR (NCT02136134), a multicenter, phase 3, randomized study of DVd vs Vd in RRMM.

Methods: All pts received ≥1 prior line of therapy (LOT) and were administered 8 cycles (Q3W) of Vd (1.3 mg/m^2 SC bortezomib on days 1, 4, 8, and 11; 20 mg PO/IV dexamethasone on days 1-2, 4-5, 8-9, and 11-12) ± D (16 mg/kg IV once weekly in Cycles 1-3, every 3 weeks for Cycles 4-8, then every 4 weeks until progression). Bortezomib-refractory pts were ineligible. Minimal residual disease (MRD) was assessed upon suspected CR and at 6 and 12 months following the first dose at sensitivities of 10^{-4}, 10^{-5}, and 10^{-6} using the clonoSEQ™ assay (Adaptive Biotechnologies, Seattle, WA).

Results: Pts received a median (range) of 2 (1-10) prior LOTs. 66% were previously treated with bortezomib and 21% were refractory to lenalidomide in their last prior LOT. After a median follow-up of 13.0 months, PFS was significantly prolonged with DVd vs Vd (median: not reached vs 7.1 months; HR, 0.33; 95% CI, 0.26-0.43; P<0.0001). This PFS benefit was seen regardless of number of prior LOTs received, with greatest benefit observed in 1 prior line pts (median: not reached vs 7.9 months; HR, 0.22; 95% CI, 0.14-0.34; P<0.0001). ORR was also significantly higher for DVd vs Vd (84% vs 63%), along with ≥VGPR (62% vs 29%) and ≥CR (26% vs 10%; P<0.0001 for all). MRD-negative rates were ≥4-fold higher at all three sensitivity thresholds with DVd vs Vd (10% vs 2% at 10^{-5} threshold). Pts who achieved MRD negativity demonstrated prolonged PFS compared with MRD-positive pts. 37 (15%) and 58 (24%) deaths

were observed in DVd vs Vd, respectively, and follow up is ongoing. The most common grade 3/4 TEAE was thrombocytopenia (45% vs 33%). Updated efficacy and safety data will be presented.

Conclusions: DVd provided significant benefits with respect to PFS, ORR, depth of response, and MRD-negative rate vs Vd. No new safety signals were reported. These data continue to support the use of DVd in RRMM pts and indicate that pts with 1 prior LOT will derive the most benefit.

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