Safety and Efficacy of Daratumumab-based Regimens in Elderly (≥75 y) Patients (Pts) with Relapsed or Refractory Multiple Myeloma (RRMM): Subgroup Analysis of POLLUX and CASTOR

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Introduction: Daratumumab (D) plus lenalidomide and dexamethasone (Rd; POLLUX) or with bortezomib and dexamethasone (Vd; CASTOR) demonstrated prolonged PFS and tolerability compared with Rd and Vd alone, respectively, in RRMM pts. We examined the safety and efficacy profiles of DRd and DVd in elderly (≥75 y) pts from these phase 3 studies.

Methods: Pts with ≥1 prior line of therapy were enrolled. All pts in POLLUX were treated until progression; CASTOR pts received 8 cycles of Vd ± daratumumab. Different D (16 mg/kg) dosing schedules were used in POLLUX (qw for cycles 1-2, q2w for cycles 3-6, and q4w thereafter) and CASTOR (qw in Cycles 1-3, q3w for Cycles 4-8, and q4w thereafter). Elderly pts received a reduced dexamethasone dose (20 mg once weekly).

Results: In POLLUX, 29/286 (DRd) and 35/283 (Rd) were ≥75 y, with 86% and 91% having ECOG status ≤1, respectively. With 17.3 months of median follow up, 10% in DRd and 11% in Rd discontinued due to treatment-emergent adverse events (TEAEs). Common (>10%) grade 3/4 TEAEs for DRd included neutropenia and hypokalemia (**Table**). Twelve (41%) DRd pts experienced infusion-related reactions (IRR) and 4 (14%) experienced grade 3/4 IRR; none discontinued due to IRR. Median PFS was not reached (NR) in DRd vs 11.4 months in Rd (HR 0.19; 95% CI, 0.06-0.55; *P*=0.0007), and ≥CR % was significantly higher with DRd vs Rd (52% vs 9%; P=0.0002).

In CASTOR, 23/251 (DVd) and 35/247 (Vd) were ≥75 y, with 100% and 94% having ECOG status ≤1, respectively. With 13.0 months of median follow up, rates of discontinuation due to TEAEs were similar (15% vs 20%). Thrombocytopenia, fatigue, and pneumonia were common grade 3/4 TEAEs for DVd (**Table**). Thirteen (65%) pts reported IRR (10% grade 3/4) and no pts discontinued due to IRR. Median PFS was NR in DVd vs 8.1 months in Vd (HR 0.27; 95% CI, 0.12-0.61; *P*=0.0007), and significantly higher ≥CR % was observed in DVd vs Vd (25% vs 3%; *P*=0.0154).

Conclusions: The safety and efficacy profiles in elderly pts were generally comparable with the overall population in each study.

% Grade 3/4 TEAEs	**DRd**	**Rd**	**DVd**	**Vd**
Neutropenia	45	31	0	3
Hypokalemia	14	3	0	0
Pneumonia	10	11	15	17
Thrombocytopenia	7	14	45	37
Anemia	3	20	10	11
Fatigue	3	3	15	11