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906O Phase 3 randomised study of daratumumab, bortezomib and dexamethasone (DVd) vs bortezomib and dexamethasone (Vd) in patients (pts) with relapsed or refractory multiple myeloma (RRMM): CASTOR

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Background: Daratumumab (D), a human CD38 IgGκ monoclonal antibody, induces deep and durable responses with a favorable safety profile in RRMM pts. We report a pre-specified interim analysis of the first randomised, controlled study of D (CASTOR; NCT02136134).

Methods: Pts with ≥1 prior line of therapy were randomised (1:1) to 8 cycles q3w of bortezomib (V)/dexamethasone (d) (V: 1.3 mg/m2 sc on Days 1, 4, 8, 11; d: 20 mg po on Days 1, 2, 4, 5, 8, 9, 11, 12) ± D (16 mg/kg iv qw in Cycles 1-3, Day 1 of Cycles 4-8, then q4w until progression). Primary endpoint was PFS.

Results: 498 pts (DVd, 251; Vd, 247) were randomised. Baseline demographics and disease characteristics were well balanced. Pts received a median of 2 prior lines of therapy (range 1-10). 76% received prior IMiD; 66% received prior V; 48% received prior PI and IMiD; 33% were IMiD-refractory; 32% were refractory to last line of prior therapy. With a median follow-up of 7.4 months, D significantly improved PFS (61% reduction in risk of progression), ORR, rates of ≥VGPR, rates of ≥CR, and delayed time to next therapy (Table). Median OS was NR in both groups. Most common (>25%) AEs (DVd/Vd) were thrombocytopenia (59%/44%), peripheral sensory neuropathy (47%/ 38%), diarrhea (32%/22%) and anemia (26%/31%). Most common grade 3/4 AEs (>10%) were thrombocytopenia (45%/33%), anaemia (14%/16%), neutropenia (13%/4%). 7%/9% of pts discontinued due to a TEAE. D-associated infusion-related reactions (45% of pts) mostly occurred during the first infusion; most were grade 1/2 (grade 3/4, 9%/0%). Additional subgroup analyses will be presented.

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	DVd	Vd
PFS		
Median, mo	NR	7.2
HR (95% CI)	0.39 (0.28-0.53)	
P	<0.0001	
ORR, %	83	63
P	<0.0001	
≥VGPR, %	59	29
P	<0.0001	
≥CR, %	19	9
P	0.0012	
Time to next therapy		
Median, mo	NR	9.8
HR (95% CI)	0.30 (0.20-0.45)	
P	<0.0001	

Conclusions: D in combination with Vd significantly improved PFS and ORR and delayed time to next therapy vs Vd alone. DVd doubled both VGPR and sCR/CR rates vs Vd alone. Safety of DVd is consistent with the known safety profile of D and Vd. The addition of D to Vd should be considered a new standard of care for RRMM pts currently receiving Vd alone.

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