Efficacy of Daratumumab in Combination with Lenalidomide Plus Dexamethasone (DRd) or Bortezomib Plus Dexamethasone (DVd) in Relapsed or Refractory Multiple Myeloma (RRMM) Based on Cytogenetic Risk Status

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Introduction: In 2 randomized phase 3 trials of RRMM patients (pts), DRd (POLLUX) or DVd (CASTOR) significantly improved PFS and deepened responses compared with Rd or Vd alone, respectively. The novel mechanism of action of daratumumab (D) may improve the poor prognosis associated with high-risk cytogenetic abnormalities in RRMM. Therefore, we examined the efficacy of DRd and DVd among RRMM pts with standard (std) or high cytogenetic risk status.

Methods: Bone marrow aspirates were collected at screening and assessed centrally via next generation sequencing (NGS). Pts with high-risk cytogenetics included those who had ≥1 of the following abnormalities: t(4;14), t(14;16), or del17p; std-risk pts were defined as those confirmed negative for these abnormalities. Efficacy analyses included PFS and ORR.

Results: Samples from 311/569 pts in POLLUX and 353/498 pts in CASTOR were assessed via NGS. In POLLUX, the median duration of follow-up was 17.3 months. Significantly longer median PFS and numerically higher ORR were observed with DRd vs Rd among high-risk

patients, and significant improvements in these outcomes were observed in std-risk patients (**Table**). In CASTOR, the median duration of follow-up was 13.0 months. Significantly longer median PFS and higher ORR were observed with DVd vs Vd among both high- and std-risk pts (**Table**). Concordance rates for t(4;14), t(14;16), and del17p were high (88%-98%) between NGS and FISH. Updated data, including subgroup analyses, will be presented.

Conclusion: In RRMM pts, the addition of D to standard-of-care regimens improved outcomes regardless of cytogenetic risk status. Targeting CD38 by combining D with Rd or Vd appears to improve the poor outcomes associated with high-risk cytogenetic status.

Table

NGS	**POLLUX**				**CASTOR**			
	High		**Std**		**High**		**Std**	
	DRd (n=28)	**Rd (n=37)**	**DRd (n=133)**	**Rd (n=113)**	**DVd (n=44)**	**Vd (n=51)**	**DVd (n=123)**	**Vd (n=135)**
Median PFS, mo	NR	10.2	NR	17.1	11.2	7.2	NR	7.0
HR (95% CI)	0.44 (0.19-1.03)		0.30 (0.18-0.49)		0.49 (0.27-0.89)		0.29 (0.20-0.43)	
P	0.0475		<0.0001		0.0167		<0.0001	
ORR, %	85	67	95	82	82	62	85	64
P	0.14		0.0020		0.039		0.0003	
≥CR, %	33	6	52	24	30	9	25	8
≥VGPR, %	63	31	84	51	64	34	64	27