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ORAL ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Comparison of Response and Survival Outcomes in Standard- and High-Risk Newly Diagnosed Transplant-Eligible Multiple Myeloma (NDMM) Patients Treated with Lenalidomide, Bortezomib and Dexamethasone (RVD) Versus Daratumumab, Lenalidomide, Bortezomib and Dexamethasone (D-RVD)

Nisha S. Joseph, MD[1], *Jonathan L. Kaufman, MD*[2], *Sara Dicamillo*[3], *Danielle Roberts*[3], *Vikas A. Gupta, MD PhD*[3], *Craig C. Hofmeister, MD*[3], *Madhav V. Dhodapkar, MD PhD*[3], *Lawrence H. Boise*[3], *Sagar Lonial, MD*[2], *Ajay K. Nooka, MDMPH*[2]

[1] Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta
[2] Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA
[3] Winship Cancer Institute of Emory University, Atlanta

Introduction: The combination of lenalidomide, bortezomib, and dexamethasone (RVD) is highly effective for newly diagnosed myeloma (NDMM) patients. However, the addition of daratumumab to RVD (D-RVD) has shown improved depth of response and trend towards PFS benefit. Here, we present a real-world comparison of the largest cohort of patients consecutively treated with either D-RVD or RVD induction therapy in terms of response and long-term outcomes for both standard- and high-risk patients.
Methods: 1000 consecutive NDMM patients treated with RVD between January 2007- August 2016, and 326 NDMM patients treated with D-RVD induction therapy from April 2018 - August 2022 were included in this analysis. Daratumumab was dosed either IV or subcutaneously weekly throughout induction; lenalidomide was started at 25 mg on days 1-14, bortezomib 1.3 mg/m2 on days 1,4,8,11 and dexamethasone 40 mg on days 1,8,15 all on a 21-day cycle. Of note, in contrast to GRIFFIN, no consolidative cycles were administered in either DRVD or RVD cohorts, and maintenance therapy for standard risk patients with lenalidomide alone while high-risk MM patients were managed with a triplet induction regimen for 3 years (Nooka et al, Leuk 2014). Demographic and clinical characteristics and outcomes data were obtained from our institutional review board-approved myeloma database and with manual abstraction. Responses and progression were evaluated per International Myeloma Working Group Uniform Response Criteria.
Results: Patient characteristics for DRVD vs RVD are found in Table 1. Of note, for DRVD vs RVD, 13.8% vs 15.8% had HR disease, and 16% vs 23.3% had ISS 3 and 4.6% vs 11.5% with RISS 3 disease. 98.6% and 99.7% of patients in the RVD vs D-RVD cohorts underwent ASCT. High-risk disease was defined as presence of del(17p), t(4;14), t(4;16), and complex karyotype.
Post-induction overall response rate (ORR) was 99.6% in D-RVD versus 97.1% in RVD, with ≥VGPR rates of 86.5% vs 67.6%, respectively. Post-transplant ORR was 99.3% vs 98.5%, with ≥VGPR rates of 95.6% vs 86.8%, respectively. Though the median follow-up for the Dara-RVD cohort is significantly shorter (19.1 months) compared to the RVD cohort (88.4 months), there is already a PFS benefit demonstrated with quadruplet induction for both standard- and high-risk patients. For all patients, the 2-year PFS and OS for D-RVD vs RVD is 93% and 94% compared to 82% and 91%, respectively. For standard risk patients, the 2-year PFS for D-RVD vs RVD is 94% vs 84%, and for high risk patients, 83% vs 69%, respectively. 2-year OS for standard risk patients was 96% in D-RVD vs 93% in RVD, and 94% vs 79% in HR patients, respectively. OS estimates for HR patients also favored D-RVD, though this is more likely than PFS to be impacted by changes in treatment patterns over the past decade.
Conclusions: D-RVD is a highly effective induction regimen that can improve upon outcomes in a historical NDMM population treated with RVD in terms of depth of response and PFS benefit. In the absence of phase 3 data supporting D-RVD vs RVD as standard of care induction, this analysis provides evidence of benefit with the addition of daratumumab to RVD in increasing depth of response, and provides an early glimpse of the promising PFS and OS benefit not only in standard risk patients, but also in patients with high-risk cytogenetic and disease features.

Disclosures Joseph: *Janssen Oncology:* Consultancy; *BMS:* Honoraria. **Kaufman:** *Sanofi:* Consultancy; *BMS:* Consultancy; *Incyte:* Consultancy; *Abbvie:* Consultancy. **Hofmeister:** *BMS:* Research Funding; *AbbVie:* Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Research Funding; *Sanofi:* Research Funding. **Dhodapkar:** *Sanofi:* Membership on an entity's Board of Directors or advisory

committees; *Lava Therapeutics:* Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Membership on an entity's Board of Directors or advisory committees. **Boise:** *Abbvie:* Consultancy; *Astra Zeneca:* Consultancy, Honoraria. **Lonial:** *AbbVie Inc, Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Genentech, a member of the Roche Group, GlaxoSmithKline, Janssen Biotech Inc, Novartis, Pfizer Inc, Takeda Pharmaceuticals USA Inc:* Consultancy, Other: Advisory Committee; *TG Therapeutics Inc:* Other: Board of Directors with Stock; *Janssen:* Research Funding; *Bristol-Myers Squibb Company, Janssen Biotech Inc, Novartis, Takeda Pharmaceuticals USA Inc.:* Other: Contracted Research, Research Funding; *Novartis:* Research Funding. **Nooka:** *Aduro Biotech, Amgen, Arch Oncology, Bristol Myers Squibb, Cellectis, Genentech, GlaxoSmithKline, Janssen, Karyopharm, Kite Pharma, Merck, Pfizer, Takeda:* Honoraria, Research Funding; *Adaptive Biotechnologies, Amgen, BeyondSpring, Bristol Myers Squibb, Cellectar Biosciences, GlaxoSmithKline, Janssen, Karyopharm, Oncopeptides, ONK therapeutics, Pfizer, Sanofi, Secura Bio, Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees.

Table 1. Patient Characteristics

		DRVD (n=326)	RVD (n=1000)
Sex	Male	181 (55.5%)	546 (54.6%)
	Female	145 (44.5%)	454 (45.4%)
Age		62.1 (23.5-79.3)	61.2 (16.3-83)
Race	White	179 (55.1%)	618 (63.2%)
	Black	133 (40.9%)	360 (36.8%)
	Asian	9 (2.8%)	0 (0%)
	American Indian/Alaskan Native	1 (0.3%)	0 (0%)
	Other	3 (0.9%)	0 (0%)
Ethnicity	Hispanic	12 (3.7%)	24 (2.4%)
	Non-Hispanic	313 (96.3%)	973 (97.3%)
ISS	1	128(49.6%)	344 (45.8%)
	2	78(30.2%)	231 (30.8%)
	3	52 (20.2%)	176 (23.45)
R-ISS	1	114 (46.3%)	163 (39.9%)
	2	117 (47.6%)	199 (48.7%)
	3	246 (6.1%)	409 (11.5%)
Risk Status	SR	259 (86.2%)	633 (63.3%)
	HR	42 (13.8%)	251 (25.1%)
	Missing	25 (.07%)	116 (11.6%)

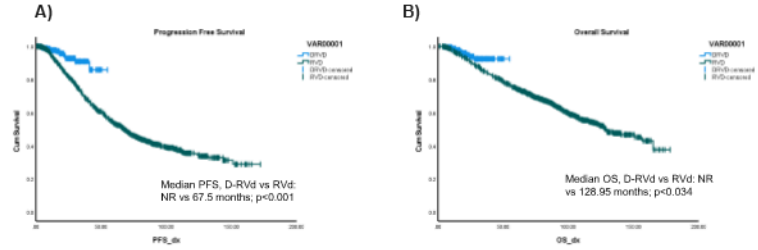

Figure 1. (A) Median PFS and (B) OS for D-RVD vs RVD

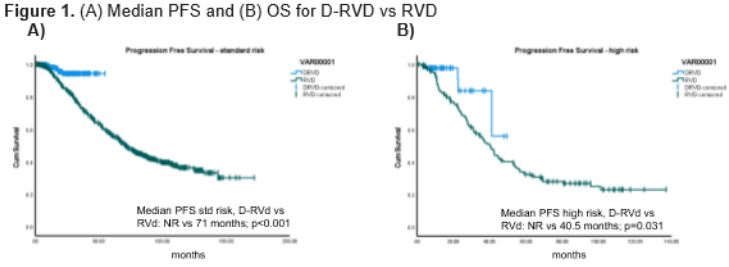

Figure 2. (A) Median PFS for standard-risk patients treated with D-RVD vs RVD and (B) Median PFS for high risk patients treated with D-RVD vs RVD

Figure 1

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