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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone (DVRd) and Daratumumab, Carfilzomib, Lenalidomide and Dexamethasone (DKRd) As Induction Therapy in Newly Diagnosed Multiple Myeloma

Carlyn Tan, MD[1], *Kylee H Maclachlan, PhDBSc,FRACP,FRCPA*[1], *David Nemirovsky, MS*[2], *Andriy Derkach, PhD*[2], *Malin Hultcrantz, MDPhD*[1], *Hani Hassoun, MD*[1], *Sham Mailankody, MBBS*[1], *Urvi A Shah, MD*[1], *Sridevi Rajeeve, MD*[1], *Dhwani Patel, MD*[1], *Tala Shekarkhand, MS*[1], *Colin Rueda*[1], *Oscar Boutros Lahoud*[3], *Gunjan L. Shah*[3], *Michael Scordo*[3], *David Chung, MDPhD*[3], *Heather Landau, MD*[3], *Sergio A. Giralt, MD FACP*[3], *Alexander Lesokhin, MD*[1], *Saad Z Usmani, MD*[1], *Neha Korde, MD*[1]

[1] Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
[2] Department of Biostatistics and Epidemiology, Memorial Sloan Kettering Cancer Center, New York, NY
[3] Adult Bone Marrow Transplant Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Background: Daratumumab, bortezomib, lenalidomide, dexamethasone (DVRd) and daratumumab, carfilzomib, lenalidomide, dexamethasone (DKRd) are promising induction regimens for newly diagnosed multiple myeloma (NDMM), resulting in deep responses and high minimal residual disease (MRD) negativity rates. Our prior work demonstrated progression-free survival (PFS) benefit in patients with high-risk (HR) NDMM receiving KRd versus VRd. Herein, we examined early outcomes associated with DVRd and DKRd induction in the management of patients with NDMM.
Methods: We conducted a chart review study with NDMM patients treated with DVRd (N=107) and compared outcomes with patients treated with DKRd (N=82), of which 68 were on study (NCT03290950) at Memorial Sloan Kettering (MSK) from 10/5/2017 to 5/1/23. Cutoff date for analysis was 7/19/23. Patients who received ≤1 prior cycle of another regimen for MM were included (N=29). Patients who have not completed induction and received <4 cycles of a quadruplet regimen or who received the majority of their quadruplet induction outside of MSK were excluded. Bone marrow biopsies (BMBx) were typically performed for MRD evaluation prior to stem cell collection or at the end of cycle 8. MRD negativity was evaluated by flow cytometry at 10^{-5} sensitivity threshold. Discrete patient characteristics were summarized by frequency (percentage) and continuous characteristics were summarized by median (Interquartile Range, IQR). PFS and overall survival (OS) were evaluated by Kaplan-Meier method. Logistic regression was used to estimate odds ratios (ORs) with 95% confidence intervals (CIs).
Results: Median age was 66 (IQR, 60-70) for DVRd- and 59 (50-65) for DKRd-treated patients (P<0.001). In the DVRd group, 72% were White and 15% Black while the DKRd group had 79% were White and 9% Black. Most of the patients in both groups had RISS Stage 2 disease (DVRd RISS 1/2/3: 33%/61%/7%; DKRd: 35%/60%/5%). With HR cytogenetic abnormality (HRCA) defined as +1q, del(1p), t(4;14), t(14;16), t(14;20), and/or del(17p), 43/100 (43%) in DVRd group and 46/81 (57%) in the DKRd group had cytogenetic abnormalities that met HR criteria (P=0.065). Among the DVRd patients, 57, 28, and 15 had 0, 1, 2+ HRCA, respectively, while in the DKRd group, 35, 30, and 16 had 0, 1, 2+ HRCA, respectively (P=0.2). Median number of cycles was 6 (IQR, 4-6) for DVRd and 8 (IQR, 6-8) for DKRd (P<0.001). At data cutoff, 72 DVRd and 74 DKRd patients completed stem cell collection; among these patients, 41 (57%) DVRd- and 25 (34%) DKRd-treated patients received upfront ASCT.
Best overall response rate (ORR) was 98% and 100% for DVRd and DKRd (P=0.5), respectively. Within 8 cycles of therapy, 21 (20%) and 28 (34%) patients achieved a ≥complete response (CR) in the DVRd and DKRd groups, respectively (P=0.024). Additionally, 83 (78%) patients were in ≥VGPR in the DVRd group and 74 (90%) in the DKRd group (P=0.021). There were 2 pts with best response as stable disease in the DVRd group. 86 DVRd pts and 73 DKRd patients had a BMBx within 8 cycles of induction therapy and were evaluable for MRD. Among these patients, 20 (23%) and 38 (52%) achieved MRD negativity for DVRd and DKRd, respectively. Multivariable analysis with clinical variables including type of quadruplet therapy, age, gender, race, R-ISS stage, cytogenetic risk, and number of cycles, demonstrated no significant association with achievement of CR (DKRd [ref] vs DVRd, OR 0.46, 95%CI 0.19-1.04; P=0.064). After a median follow-up of 13 (95%CI, 11-15) months for DVRd and 53 (48-55) months for DKRd, 1-year estimated PFS was 92% (95%CI, 86%-99%) and 94% (89%-99%) for DVRd and DKRd, respectively (P=0.5).
Conclusion: In this single-center chart review study, DVRd was compared to DKRd as induction therapy for patients with NDMM. Importantly, DKRd patients were primarily comprised of patients from a clinical trial (NCT03290950), perhaps affecting

demographics of the groups (DVRd group had older patients and more Black patients; DKRd group had more cycles of therapy due to trial design). DVRd and DKRd are both associated with high ORR. Although the ≥CR rate was greater with DKRd, on multivariable analysis there was no statistically significant difference between DKRd and DVRd after adjusting for various clinical variables. Data with follow-up outcomes will be presented at the meeting.

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Table 1. Best response to induction

	DVRd (n=107)	DKRd (n=82)	P-value
Best overall response rate – no. (%)	100 (98)	82 (100)	0.5
sCR/CR – no. (%)	21 (20)	28 (34)	0.024
VGPR – no. (%)	62 (58)	46 (56)	
PR – no. (%)	22 (21)	8 (10)	
SD – no. (%)	2 (2)	0 (0)	

Figure 1. Kaplan-Meier Curve for Progression-free Survival

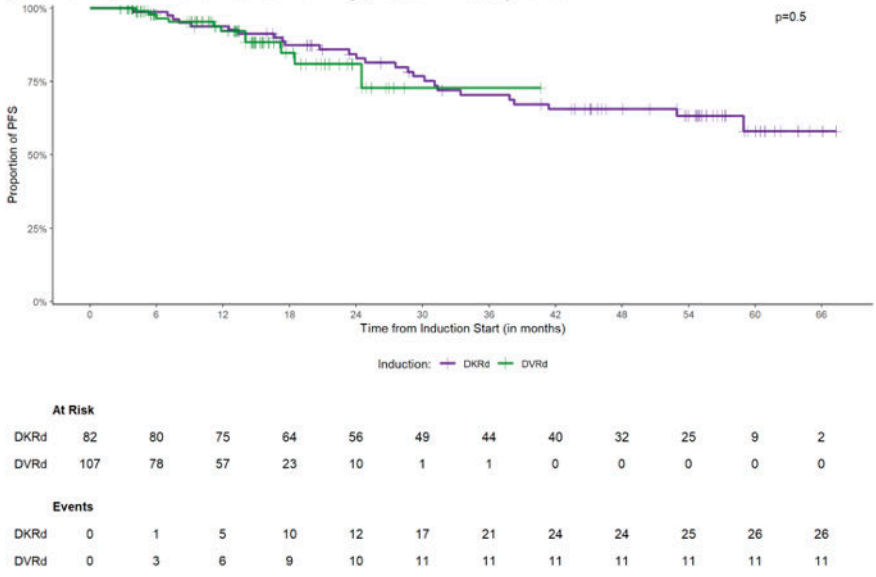

Figure 1

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