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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Carfilzomib, Lenalidomide and Dexamethasone (KRd) As Induction Therapy in High-Risk Newly Diagnosed Multiple Myeloma

Carlyn Tan, MD[1], Neha Korde, MD[1], Andriy Derkach, PhD[2], Malin Hultcrantz, MDPhD[1], Kylee H Maclachlan, PhDBSc,FRACP,FRCPA[1,1], Hani Hassoun, MD[1], Sham Mailankody, MBBS[1], Urvi A Shah, MD[1], Sridevi Rajeeve, MD[1], Dhwani Patel, MD[1], Alexander Lesokhin, MD[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], Craig C. Hofmeister, MD[4], Jonathan L. Kaufman, MD[4], Ajay K. Nooka, MDMPH[4], Saad Z Usmani, MD[1], Sagar Lonial, MD[4], Nisha S. Joseph, MD[4]

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

Background: Carfilzomib, lenalidomide and dexamethasone (KRd) has been shown to be an effective induction regimen for newly diagnosed myeloma (NDMM), particularly in myeloma with high-risk (HR) features in the FORTE trial (Mina et al, Lancet Onc 2023). Here, we present a retrospective analysis in patients with HR NDMM in a real-world population from two high-volume centers, highlighting efficacy and survival outcomes in high-risk subgroups to gain a better understanding of the utility of this regimen in clinical practice.

Methods: We conducted a retrospective study of patients with HR NDMM treated with KRd at Memorial Sloan Kettering (MSK) and Winship Cancer Institute from 1/1/2015 to 9/30/22. Cutoff date for analysis was 12/31/2022. HR was defined as the presence of high-risk cytogenetic abnormalities (HRCA) including +1q, del(1p), t(4;14), t(14;16), t(14;20), and/or del(17p), circulating plasma cells (cPC) ≥5%, extramedullary disease (EMD), and/or complex cytogenetics by conventional cytogenetics. Patients who received ≤1 prior cycle of a different MM regimen were included. Responses and progression were evaluated per International Myeloma Working Group Uniform Response Criteria. Discrete patient characteristics were summarized by frequency (percentage) and continuous characteristics were summarized by median (Interquartile Range, IQR). Progression-free survival (PFS) and overall survival (OS) were evaluated by Kaplan-Meier method. Association between time to event outcomes and patient's characteristics were determined by log-rank test. Univariate Cox proportional hazard model was used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: We identified 179 consecutive NDMM patients with HR features treated with KRd at MSK (N=106) and Winship Cancer Institute (N=73). Baseline patient characteristics are listed in Table 1. The median age was 62 (IQR, 55-68) and 28% of patients were Black. There were 45 (25%), 76 (42%), 47 (26%), and 11 (6%) patients with 0, 1, 2, 3+ HRCA, respectively. A median of 5 (IQR 4-6) cycles were administered. At data cutoff, 70% of patients received upfront autologous stem cell transplant (ASCT). Best overall response rate (ORR) by the end of KRd induction was 94% for 178 response-evaluable patients, including 39% with ≥complete response (CR) and 78% with ≥very good partial response (VGPR).

After a median follow-up of 41.9 (95% CI 39-45.6) months, the median PFS (mPFS) was 78.2 months (95% CI 52.5-not reached [NR]), and 2-year estimated PFS was 79% (73%-85%). Median OS (mOS) was not reached, and 2-year OS was 92% (95%CI 89%-97%). For HR subgroups based on the number of HRCA present, mPFS was 78.2 (95% CI 40.1-NR), 65.2 (43.4-NR), 55.9 (44.9-NR), and 17.5 (8.78-NR) months for patients with 0, 1, 2, 3+ HRCA, respectively, with 2-year PFS of 83% (95% CI, 73%-95%), 82% (74%-92%), 78% (67%-91%), and 46% (24%-87%), respectively (P=0.35). Median OS was NR for patients with 0, 1, and 2 HRCA and was 58.2 months (95% CI 38.8-NR) for patients with 3+ HRCA with 2-year OS of 93% (95% CI, 86%-100%), 96% (91%-100%), 89% (81%-99%), and 81% (60%-100%), respectively (P=0.13). In univariable analysis, lack of t(14;16) (HR 0.32, 95%CI 0.11-0.95; P=0.03), White race (HR 0.38, 95%CI 0.17-0.84; P=0.02), presence of ≤2 HRCA (HR 0.31, 95%CI 0.11-0.92; P=0.04) were associated with longer OS in this cohort of HR-NDMM patients treated with KRd induction. Multivariable analysis for clinical variables, including specific HRCA, number of HRCA present, age, gender, race, R-ISS stage, presence of EMD, presence of cPCs, cardiac history, and upfront ASCT did not demonstrate any single variable was a significant predictor of progression or death.

Conclusion: For this real-world patient population, KRd induction was associated with high response rates and promising outcomes with best ORR of 94% and mPFS of 6.5 years for patients with high-risk newly diagnosed multiple myeloma consistent with FORTE trial data. PFS did not significantly differ among HR patients with 0, 1, 2, 3+ HRCA although mPFS for patients with 3+ HRCA was only 17.5 months. Data with maintenance therapy and longer follow-up outcomes will be presented at the meeting.

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Table 1. Baseline Patient Characteristics and Response

Characteristic	KRd (n=179)
Median age – yr (IQR)	62 (55 – 68)
Gender: Female/Male %	54/46
Race, n (%)	
White	107 (60)
Black	51 (28)
Asian	7 (4)
Other/unknown	14 (8)
Cardiac history* – n (%)	44 (25)
Stage (R-ISS)[a] – n/total n (%)	
I	29/160 (18)
II	105/160 (66)
III	26/160 (16)
Presence of HRCA – n (%)	134 (75)
del(17p) or monosomy 17 – n (%)	59 (33)
t(4;14) – n (%)	27 (15)
t(14;16) – n (%)	12 (7)
t(14;20) – n (%)	3 (2)
Gain/amp 1q	85 (47)
del(1p)	19 (11)
Number of high-risk abnormalities – n (%)	
0	45 (25)
1	76 (42)
2	47 (26)
3+	11 (6)
Presence of complex cytogenetics – n (%)	102 (57)
Presence of extramedullary disease – n (%)	66 (37%)
Presence of circulating plasma cells ≥5%	12 (7)
Upfront ASCT – n (%)	125 (70)
Best response to KRd induction – n/total n (%)	
sCR/CR	69/178 (39)
VGPR	69/178 (39)
PR	31/178 (17)
MR	2/178 (1)
PD	7/178 (4)

*cardiac history include atrial fibrillation, atrial flutter, coronary artery disease, right bundle branch block, valvular heart disease, aortic aneurysm, sick sinus syndrome, systolic heart failure, non-ischemic cardiomyopathy, heart failure with preserved ejection fraction, heart block

Figure 1. Kaplan-Meier curve for progression-free survival according to presence of HRCA

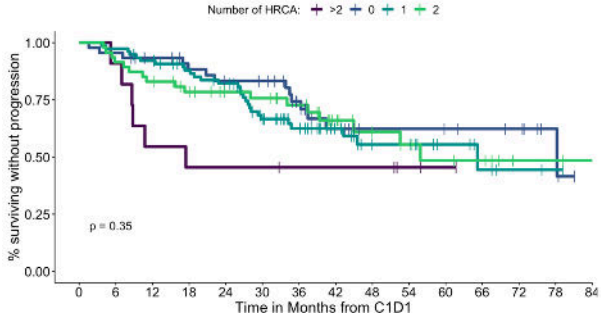

Figure 1

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