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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Impact of Revised International Staging System 2 (R2-ISS) Risk Stratification on Outcomes of Patients with Multiple Myeloma Receiving Autologous Hematopoietic Stem Cell Transplantation

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Background: The second revision of the International Staging System (R2-ISS) is a new and simple tool to risk stratify newly diagnosed multiple myeloma (NDMM) patients. Our aim in this study was to evaluate the utility of R2-ISS in NDMM patients who received upfront autologous hematopoietic stem cell transplantation (auto-HCT).
Methods: We conducted a retrospective analysis of all NDMM patients who underwent upfront auto-HCT between 1988 and 2021 at MD Anderson Cancer Center and had available data for calculation of R2-ISS, including albumin, β-2 microglobulin, LDH, and fluorescence in-situ hybridization (FISH) analysis at diagnosis. High-risk cytogenetic abnormalities (HRCA) were t(4;14), del(17p), and 1q21 gain or amplification, as detected by FISH. The primary endpoints were progression-free survival (PFS) and overall survival (OS), and the secondary endpoint was hematological response after auto-HCT.
Results: A total of 1291 patients were included, with a median age of 62 years (range 29 - 83) and 60% were male. Four hundred-and-nineteen patients (32%) had HRCA. Most patients received either bortezomib, lenalidomide, and dexamethasone (VRD) (34%) or carfilzomib, lenalidomide, and dexamethasone (KRD) (25%) induction regimens, and most patients (95%) received melphalan based conditioning. The distribution of R2-ISS stages in our cohort was as follows: 123 (10%) stage I, 471 (36%) stage II, 566 (44%) stage III, and 131 (10%) stage IV. A total of 1027 (80%) patients received post auto-HCT maintenance, mostly lenalidomide with or without dexamethasone (n = 785, 61%) **(Table 1).**
With a median follow-up of 42.2 months (range 0.3 - 181.0) for the entire cohort, the median PFS was 73.0, 65.2, 44.0, and 24.8 months ($P < .001$) and the median OS was 130.8, 128.5, 94.2, and 61.4 months ($P < .001$) for patients with R2-ISS stages I, II, III, and IV, respectively **(Figure 1)**. On multivariable analysis (MVA) for PFS, using R2-ISS stage I as the reference group, there was no significant difference for R2-ISS stage II (hazard ratio [95% CI], 1.11 [0.76-1.63]; $P = .59$), but there was a significant worsening in PFS for R2-ISS stage III (1.55 [1.05-2.29]; $P = .028$) and R2-ISS stage IV (2.04 [1.24-3.36]; $P = .005$). On MVA for OS, again using R2-ISS stage I as the reference group, there was no significant difference for R2-ISS stage II (1.33 [0.74-2.40]; $P = .34$) or R2-ISS stage III (1.75 [0.97-3.17]; $P = .06$), but there was a significant worsening in OS for R2-ISS stage IV (2.43 [1.18-5.01]; $P = .017$).
On MVA, other measures significantly associated with worsening PFS were year of auto-HCT < 2010, lambda light chain disease subtype, presence of HRCA, prior MRD/response other than negative/≥CR, and not achieving MRD negative/≥ CR post auto-HCT. For OS, other measures significantly associated with worsening survival on MVA were presence of HRCA, HCT-CI > 3, having at least one bone lesion, not achieving CR at best response, and not receiving post auto-HCT maintenance therapy.

Conclusion: Our study demonstrates that R2-ISS is a reliable prognostic tool for NDMM in a large cohort of patients who received standard anti-myeloma treatment, including modern induction regimens, upfront auto-HCT, and post-transplant maintenance.

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Table 1. Summary of Patients and Clinical Characteristics

Measures	All (N=1291)
Age at auto-HCT, years	
Median (range)	61.8 (29.0 - 83.0)
Gender, n (%)	
Male	771 (60)
Female	520 (40)
Race, n (%)	
Black	207 (16)
Non-black	1068 (83)
Unknown	16 (1)
Year of auto-HCT, n (%)	
< 2010	63 (5)
≥ 2010	1228 (95)
Light chain type, n (%)	
Kappa	857 (66)
Lambda	426 (33)
Biclonal	3 (<1)
Unknown	5 (<1)
Cytogenetic risk, n (%)	
High-risk	419 (32)
Standard-risk	871 (67)
Unknown	1 (<1)
R2-ISS, n (%)	
I	123 (10)
II	471 (36)
III	566 (44)
IV	131 (10)
R-ISS, n (%)	
I	444 (34)
II	614 (48)
III	123 (10)
Unknown	110 (9)
ISS, n (%)	
I	618 (48)
II	353 (27)
III	320 (25)
HCT-CI, n (%)	
≤ 3	955 (74)
> 3	335 (26)
Unknown	1 (<1)
LDH, n (%)	
Normal	1014 (79)
> ULN	205 (16)
Unknown	72 (6)
Creatinine, n (%)	
≤2 mg/dL	1129 (87)
>2 mg/dL	160 (12)
Unknown	2 (<1)
β2 microglobulin	
Median (range)	3.3 (0.3 - 81.4)
Bone lesions, n (%)	
0	263 (20)
1-3	503 (40)
> 3	509 (39)
Unknown	16 (1)
Induction treatment, n (%)	
IMiD+Dexa	61 (5)
KRD	327 (25)
VCD	167 (13)
VD	123 (10)
VRD	440 (34)
Other	172 (13)
Unknown	1 (<1)

Measures	All (N=1291)
Hematologic response prior to transplant, n (%)	
sCR/CR	172 (13)
VGPR	597 (46)
PR	500 (39)
SD	22 (2)
Conditioning regimen, n (%)	
Mel	1018 (79)
BuMel based	203 (16)
Other	70 (5)
Post-auto-HCT maintenance, n (%)	
No	264 (20)
Yes	1027 (80)
Rev with or without Dexa	785 (61)
PI with or without Dexa	78 (6)
Rev/Elo	69 (5)
IMID+PI	65 (5)
Other	30 (2)

Abbreviations: auto-HCT, autologous hematopoietic stem cell transplantation; BuMel, busulfan+melphalan; CR, complete response; Dexa, dexamethasone; Elo, elotuzumab; HCT-CI, hematopoietic cell transplant comorbidity index; IMiD, immunomodulatory drug; ISS, international Staging System; KRD, carfilzomib-lenalidomide-dexamethasone; LDH, lactate dehydrogenase; Mel, melphalan; PI, proteasome inhibitor; PR, partial response; Rev, lenalidomide; R-ISS, revised international staging system; R2-ISS, second revision of the international staging system; sCR, stringent complete response; SD, stable disease; VCD, bortezomib-cyclophosphamide-dexamethasone; VD, bortezomib-dexamethasone; VGPR, very good partial response; VRD, bortezomib-lenalidomide-dexamethasone; ULN, upper limit of normal.

Figure 1. Overall Survival-by R2-ISS

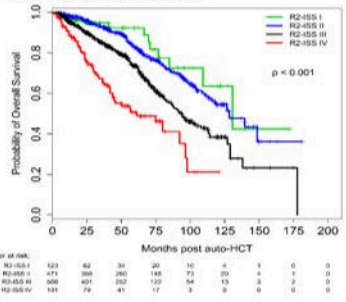

Figure 1

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