



Its the Response that matters: Real world data of Multiple myeloma patients treated without upfront stem cell transplant

L. Rohit Reddy¹, Raja Mounika Velagapudi², Sreenivas Konda³, Shalabh Arora¹, Lalit Kumar¹

1. Department of Medical Oncology, Dr.B.R.A. IRCH, All India Institute of Medical Sciences, New Delhi, India
2. Department of Internal Medicine, Pandit Madan Mohan Malviya Hospital, New Delhi, India
3. Department of Epidemiology and Biostatistics, University of Illinois, Chicago, United States of America



Background

Treatment paradigm of Newly diagnosed multiple myeloma (NDMM) has changed in the last decade.(1) We report treatment outcomes among NDMM patients in the era of proteasome inhibitors (PI) and newer immunomodulatory drugs (IMiDs) in an Indian cohort who were not planned for upfront stem cell transplant.

Objective

The primary objective was to determine the progression free survival (PFS) of NDMM patients. Secondary objectives included objective response rates (ORR), (≥ partial response (PR)), and factors for relapse.

Materials & Methods

Its a single center retrospective study of NDMM patients diagnosed between January 2014 to December 2019 and followed till May 2021 for outcomes.

The study was conducted at a North Indian tertiary cancer referral center. Records of 650 NDMM patients were screened for the study. All of them received initial induction therapy followed by maintenance treatment. 248 (39.2%) patients with incomplete induction therapy and significant missing data were excluded. 402 patients were included in study.

Statistical analysis

Categorical variables were compared using chi square test or Fischer's exact test and noncategorical normal variables were compared using student t-test and Wilcoxon's rank sum test. PFS and OS were analysed using Kaplan-Meier survival curve estimates and the difference between groups was compared using stratified log-rank tests. Multivariate Cox regression analysis was done to identify independent predictors. Analysis was performed using SPSS software 20.0.

Results

Median age was 59.4 years (range; 23 to 84 years), male: female ratio was 1.9:1. 225 (56%) patients had an IgG subtype. 248 (61.7%) patients had ISS stage III.

323 (80.3%) patients received triplet-based induction regimen and 79 (19.7%) with doublets. VRd was commonest regimen, used in 123(32.1%) patients.

Following induction, 222(52.2%) patients were treated with bortezomib and 142(35.3%) received IMiDs, 12% received no maintenance.

ORR was 84.9% (67/79) with doublets and 95.2% (302/323) with triplets.

Complete response was observed in 31.4% (103/323) patients on triplets and 29.1% (23/79) patients on doublets.

After a median follow up of 32.9 months (range; 0-102 months), median PFS did not differ by type of induction (22.8 vs 28.5 months in doublets; hazard ratio [HR] 1.06, 95% C.I 0.71 – 1.58; p-value 0.8).

Multivariate cox proportion analysis suggested that response to induction (<PR), [HR] 3.86, 95% C. I 2.34-6.38; p-value <0.001) and IgA subtype predicted a poor PFS.

Maintenance with IMiDs predicted a better PFS as compared to maintenance with PI or no maintenance

All grade adverse events were noted in 140 patients (34.8%) with commonest being thrombocytopenia in 18.4% of patients and most common grade 3-4 adverse event was anemia noted in 7.5% of patients

Baseline characteristics	Number (N) =402	Range/percentage
Median age (years)	59.5	51- 65
Age		
≤ 60 years	230	57.2%
> 60 years	172	42.8%
Sex		
Male	264	65.7%
Female	138	34.3%
Type of myeloma		
Light chain disease (LCD)	106	26.4%
IgA	62	15.4%
IgG	227	56.5%
Non secretory	2	0.5%
Missing	5	1.2%
ISS		
Stage I	48	11.9%
Stage II	89	22.1%
Stage III	248	61.7%
Missing	17	4.2%
Cytogenetics		
Standard risk	81	20.1%
High risk	20	5%
Missing	301	74.9%
LDH		
>ULN	44	10.9%
<ULN	289	71.9%
Missing	69	17.2%
Extra medullary disease		
Present	20	5%
Absent	382	95%

Treatment details/ Response	Number (N=402)	Percentage(%)
1st line induction		
Bortezomib	136	33.8%
Bortezomib+IMiD	167	41.5%
Doublets	80	19.9%
Others	19	4.7%
Response to 1st line induction		
Complete response	133	33.1%
Very good partial response	96	23.9%
Partial response	141	35.1%
Minor response	20	5%
Stable disease	12	2.9%
Maintenance		
Bortezomib	221	55%
IMiDs	140	34.8%
Others	5	1.2%
No maintenance	36	9%

Predictors of PFS	Non Relapsed (N=184)(%)	Attained PFS 1 (N=218)(%)	Hazard ratio (95% CI)	Log rank p-value	
				Univariate	Multivariate
Subtype IgG IgA LCD	104 (56.5%) 26 (14.1%) 51 (27.7%)	121 (55.5%) 37 (17.0%) 59 (27.1%)	- 1.61 (1.05-2.5) 1.05 (0.72-1.55)	- 0.017 0.29	- 0.028 0.8
1 st line induction Doublet Triplet	27 (14.7%) 157 (85.3%)	52 (23.9%) 166 (76.1%)	1.06 (0.71-1.58)	0.005	0.8
Maintenance Bortezomib IMiD None	106 (57.6%) 60 (32.6%) 17 (9.2%)	116 (53.2%) 82 (37.6%) 19 (8.7%)	1.36 (0.94-1.59) - 1.7 (0.95-1.95)	<0.001 - <0.001	0.1 - 0.074
Response CR, VGPR, PR MR SD	179 (97.3%) 5 (2.7%)	192 (88.1%) 26 (11.9%)	3.86 (2.34-6.38)	<0.001	<0.001

Summary

In NDMM patients we suggest that depth of response, irrespective of induction and treatment with IMiDs predict a better PFS. However, these findings require validation by a randomized control trial

Discussion

Median age of our retrospective cohort is almost a decade earlier as compared to Western literature.(2) Response to induction is definitely a major driving factor for better PFS as proved in major RCTs.(3) Interestingly we also noticed that following induction maintenance with IMiDs predict a better PFS. These findings require confirmation in a RCT.

Limitations of our studies include its retrospective nature and missing data

References

1. Rajkumar SV, Kumar S. Multiple myeloma current treatment algorithms. Blood cancer journal. 2020 Sep 28;10(9):1-0.
2. <https://seer.cancer.gov/statfacts/html/mulmy.html>
3. Paul B, Lipe B, Ocio EM, Usmani SZ. Induction therapy for newly diagnosed multiple myeloma. American Society of Clinical Oncology Educational Book. 2019 May 17;39:e176-86.