Management of biochemical relapse during lenalidomide maintenance therapy post ASCT in multiple myeloma: a descriptive observational study of a single institution

• Rola El Sayed¹, Yolla Haibe ¹, Nour Moukalled¹, Radwan Massoud¹, Basel Haffar¹, Charbel Matar¹, Ammar Zahreddine¹, Ali Bazarbach¹ and Jean El-Cheikh¹

¹Bone Marrow Transplantation Program and Division of Hematology and oncology, Department of Internal Medicine, Beirut, Lebanon

BACKGROUND

Patients with multiple myeloma (MM) who underwent autologous stem cell transplantation (ASCT), are known to benefit from maintenance therapy post-transplant. With signs of early relapse, physicians can either optimize maintenance therapy or use a new therapeutic regimen.

OBJECTIVE

The purpose of this study is to analyze the clinical outcomes beyond biochemical relapse of patients with MM on maintenance therapy. Time to next treatment (TNT), progression free survival (PFS) and overall survival (OS) are assessed. Different approaches for treatment of relapse such as increase in lenalidomide (R) dose, addition of dexamethasone (D) or Bortezomib (V) or shift to different lines of treatment are possible.

METHODS

Between January 2011 and May 2017, we included 51 patients with MM who underwent ASCT and received Bortezomib/Lenalidomide/Dexamethasone (VRD) consolidation and maintenance therapy, mainly lenalidomide(R) 10mg/day for 21 days every 28 days.

Results

Variable	No of Patients N (%)	
Number of patients included in the study	51	
Gender	Male	30 (59)
	Female	21 (41)
Median age at diagnosis (years)	54 [35-74]	
Median age at transplant (years)	55[46-75]	
Staging (Salmon and Durie)	A	B
I	2(4)	1(2)
II	17(33)	1(2)
III	16(31)	6(12)
NA	8(16)	
Staging (ISS)		
I	26(51)	
II	15(29)	
III	6(12)	
NA	4(8)	
High-risk features	25(49)	
Cytogenetic abnormality	7(14)	
17p deletion only	2(4)	
t(4;14) only	3(6)	
17p13q deletion	1(2)	
13q deletion only	1(2)	
Stage III (S&D)	22(43)	
Stage III (ISS)	6(11)	
Diagnosed outside AUBMC		
Yes	19(37)	
No	32(63)	
Type of MM		
IgG K	23(45)	
IgG L	9(17)	
IgA K	3(6)	
IgA L	7(14)	
IgD L	2(4)	
Light chain disease K	2(4)	
Light chain disease L	3(6)	
Mixed component	2(4)	
Progression/Relapse	29(57)	
Lines of therapy post progression post transplant ⁴		
None	11(22)	
1	12(23)	
2	1(2)	
3 or more	5(10)	
Second Transplant		
Yes	10(20)	
No	41(80)	
Received Zometa		
Yes	35(68)	
No	16(31)	
Induction therapy		
TD	2(4)	
VD	11(21)	
VTD	8(15)	
VCD	3(6)	
VRD	15(29)	
MTP	1(2)	
Combination	11(21)	

Results

Variable	No of Patients N (%)
Conditioning regimen	
Melphalan 140 mg/m2	1(2)
Melphalan 200 mg/m2	47(92)
Melphalan -velcade	3(6)
Maintenance post transplant	
Lenalidomide	46 (90)
Thalidomide ¹	2(4)
VRD	3(6)
Disease status post transplant	
CR	17(33)
PR	4(8)
VGPR	5(10)
SD	23(45)
NA	2(4)
Toxicity with maintenance ³	
Hematologic ²	9(17)
GI	2(4)
Neurologic	11(21)
Infectious	3(6)
Thrombosis	2(4)
Skin	1(2)
Changes with biochemical relapse	
Observation	6(11)
Lenalidomide increased/Dexamethasone added	10(20)
Treatment changed	13(25)
Patient status with biochemical relapse requiring only observation or alteration of maintenance	
Progressed	3(6)
CR	10(20)
SD	2(4)
Patients with signs of biochemical relapse requiring change of treatment	19(37)
Dose reduction/Dose interruption	
Yes	17(33)
Dose reduction	4(8)
Dose interruption	13(25)
No	34(67)
Last disease status	
CR	27(53)
VGPR	2(4)
PR	2(4)
MR	1(2)
SD	8(15)
PD	11(22)
Death ⁵	3(6)
Lost to follow up	4(8)

Table 1: Patient Characteristics

¹ Patient received Lenalidomide maintenance post second transplant
² Only one hematologic complication was grade III.
³ All other toxicities were grade I-II.
⁴ Treatment beyond progression included: VRD, VTD, PCD, KRd, DRd
⁵ Death, 2 due to disease relapse and 1 due to disease progression

PATIENTS

The median age at transplant was 55 years (46-75). Forty-six (90%) of patients received R maintenance, 3 patients received VRD maintenance for higher risk features. Median duration of R maintenance was 22 months (3-62). R dose was changed for toxicity (grade I-II) in 17 (33%) patients. Twenty-nine (57%) patients relapsed: 13 (25%) patients were shifted to different treatment protocols (treatment change). 6 patients (11%) were kept on the same R maintenance (observation group) and 10 (20%) patients had increased lenalidomide dose with dexamethasone (R/ D group). 6 patients (37%) of the last 2 groups required change of treatment later. The median follow up was 38 months (1-85). Median TNT was 32 months (7-62). At 2 years, the estimated PFS and OS were 39% and 97.5% respectively. The median OS and PFS2 (from change of therapy) were 54 and 29 months for patients in the observation group, versus 52 and 27 months in the R/D group, and 45 and 33 months with treatment change, respectively. No statistically significant difference was noted.

CONCLUSION:

Our small monocentric study is limited by its retrospective design and small sample size. However, it suggests that increasing lenalidomide dose as well as adding dexamethasone in selected patients can postpone change to different lines of treatment without affecting survival.