Management of relapse in acute promyelocytic leukemia treated with upfront

Arsenic trioxide based regimens

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INTRODUCTION

The standard of care for patients with acute promyelocytic leukemia (APL) relapsing after frontline treatment with Arsenic trioxide (ATO) based regimens remains to be defined. Available data on response and survival outcomes in patients who had received ATO as part of upfront therapy suggests that there is a high incidence of resistance to ATO and ATRA resulting in inferior response and inferior survival than seen in patients who has not received ATO as part of upfront therapy¹. We present our experience on management of relapse in APL patients treated with frontline ATO based therapy.

PATIENTS AND METHODS

Data on all consecutive patients with relapsed APL diagnosed and treated in the Department of Haematology, Christian Medical College, Vellore, from January, 1998–December, 2015 were included in this retrospective analysis.

RESULTS

104 (29%) of the total 358 APL patients diagnosed during the study period had relapsed. Out of these 73 (70%) patients received upfront ATO based therapy. 6/73 refused treatment; the remaining 67 (91.8%) were included in the analysis

Table : 1 Baseline characteristics of patients (n=67)

Variable	N (%) / Median (Range)
Age (in years)	28 (4-54)
Gender	
Male	44 (65.7)
Female	23 (34.3)
Time to relapse from diagnosis (mths)	19.6 (5.9-128.4)
Sites of relapse	
Isolated molecular	1 (1.5)
Isolated CNS*	6 (9.0)
Marrow + CNS	13 (19.4)
Isolated Marrow	47 (70.1)
Re-induction regimens at relapse	
ATO +Anthra/ATO +Bortezomib	9 (13.4)
ATO+ATRA	10 (14.9)
ATO+ATRA+Anthra**	26 (38.8)
ATO+ATRA+Anthra+Bortezomib	22 (32.8)
Response to re-induction at relapse	
Molecular remission	63 (94.0)
Discontinued treatment	1 (1.5)
Expired	3 (4.5)
Post re-induction Trt at CR2 (n=63)	
Auto- SCT***	35 (55.6)
ATO based maintenance chemotherapy	28 (44.4)
Time to auto-SCT from relapse (mths)	5.8 (1.8-32.2)

*Central Nervous System **Anthracycline ***autologous stem cell transplantation

Table 2: Adjusted Cox regression analysis

Variables	Hazard Ratio	95 % CI for Exp(B)		P value
		Lower	Upper	
Post Relapse Treatment				
AutologousSCT	1.00			
ATO based Chemotherapy	7.576	1.988	28.873	0.003
Duration of CR1	0.999	0.998	1.000	0.143
Total WBC at Relapse	1.017	0.992	1.042	0.187
Age	1.005	0.959	1.053	0.832

REFERENCES

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THE AUTHORS DECLARE NO CONFLICTS OF INTEREST

Fig 1: Kaplan - Meier estimate of survival of relapse APL patients treated with upfront ATO based regimens (A) Overall survival (B) Event free survival

Fig 1: Kaplan - Meier estimate of survival of relapse APL patients treated with upfront ATO based regimens and received autologous stem cell transplantation (ASCT) versus ATO based chemotherapy in CR2 (A) Overall survival (B) Event free survival

CONCLUSIONS

Remission induction with ATO based regimens followed by an autologous SCT in patients with relapsed APL who were treated with frontline ATO based regimens is associated with excellent long term survival and should be considered the standard of care even in this setting.