Acute myeloid leukemia and myelodysplastic syndromes in patients with multiple myeloma: assessment of risk factors

Gudbjorg Jonsdottir,[1,2] Magnus Björkholm,[3] Ingemar Turesson,[4] Malin Hultcrantz,[3,5] Anna Porwit,[6]
Yogesh S. Jethava,[2] Ola Landgren,[5] and Sigurdur Y. Kristinsson[1,3]
[1]University of Iceland; [2]University of Iowa Hospitals and Clinics; [3]Karolinska University Hospital and Karolinska Institutet;
[4]Skane University Hospital; [5]Memorial Sloan Kettering Cancer Center; [6]Lund University

Introduction

- Risk factors for acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) in patients with multiple myeloma (MM) are not well understood.
- The excess risk of AML/MDS in Lenalidomide treated patients has been most prominent in patients that also receive alkylating agents.
- Delayed autologous transplant found to have the same overall survival as upfront autologous transplant with high dose Melphalan at 3 years of follow-up.
- Minimal residual disease (MRD) negativity found to have similar progression free survival independent of therapy.
- Define the role of alkylating therapy in relation to subsequent risk of secondary malignancies.

Results

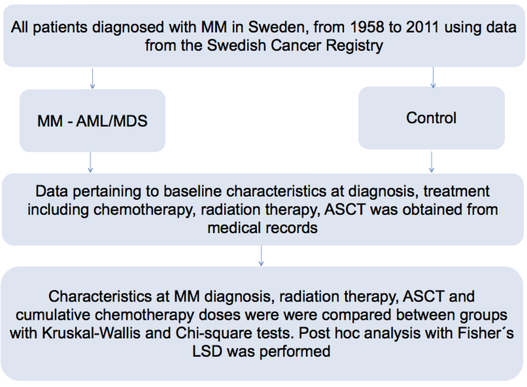
General characteristics	MM-AML/MDS (n = 87)	Controls (n = 69)	P values
Age at MM diagnosis, median (IQR)	73 (63-78)	70 (60-77)	0.189
Gender (M), n (%)	49 (56)	38 (55)	1.000
Year of MM diagnosis, n			
1958-1970	3	1	
1971-1980	15	9	
1981-1990	31	22	
1991-2000	24	23	
2001-2011	14	14	
Time to secondary malignancy, median years (IQR)	3.8 (2.8-5.58)	*NA*	
Diagnostic factors, median (IQR)			
Plasma cells in BM (%)	23 (13-30)	22 (10-35)	0.868
B2M concentration (mg/L)	4.1 (2.8-5.3)	5.1 (2.3-7.6)	0.643
Albumin (g/L)	34 (30-39)	34 (29-39)	0.470
M protein concentration (g/L)	31 (18-45)	32 (22-49)	0.544
Type of M spike, n			
IgG (κ or λ)	39	42	
IgA (κ or λ)	23	20	
Light chain disease	5	1	
Unknown	21	7	

Table 1. Label in 18pt Calibri.

Treatment	MM-AML/MDS n=87		Control n=69		P values
Chemotherapy, cumulative dose	**M ± SD**	**n (%)**	**M ± SD**	**n (%)**	
Melphalan, mg	1321 ± 1165	86 (98)	709 ± 565	66 (96)	<0.001
Cyclophosphamide, mg	9684 ± 13674	27 (31)	10983 ± 18043	23 (33)	0.747
Carmustine, mg	217 ± 117	11 (12)	360 (NA)	1 (1)	-
Doxorubicin, mg	239 ± 263	18 (20)	322 ± 341	14 (20)	0.444
Vincristine, mg	76 ± 142	19 (22)	18 ± 24	20 (29)	0.077
Interferon, million units	977 ± 1279	11 (13)	195 ± 149	6 (9)	0.162
Etoposide, mg	1902 ± 1845	4 (5)	4140 (NA)	1 (1)	-
Lomustine, mg	540 ± 368	2 (2)	100 (NA)	1 (1)	-
Thalidomide, mg	81257 ± 81240	7 (8)	6650 ± 7019	4 (6)	0.515
Bortezomib, mg	-	-	21 (NA)	1 (1)	-
Lenolidomide, mg	-	-	945 (NA)	1 (1)	-
Other types of therapy					
Radiation therapy received, n (%)	21 (24.1)		16 (23)		0.689
ASCT, n (%)	5 (5.7)		6 (8.7)		1.000
Response to treatment, PR or better, n (%)					
Yes	42 (48)		18 (26)		0.071
No	20 (23)		20 (29)		-
Unknown	25 (29)		31 (45)		-

Table 2. Label in 18pt Calibri.

Methods and Materials



Conclusions

- The preliminary results from this large nationwide population based study including almost 27,000 MM patients in Sweden over >50 years shows the mean cumulative dose of Melphalan was higher in MM patients who developed AML/MDS compared to MM patients who did not.
- Strategies to avoid secondary complications is becoming more important.
- Our results showing that Melphalan is associated with an increased risk of AML/MDS, call for studies using response driven (i.e. MRD based) therapy in myeloma; were high dose Melphalan is rather offered to patients who are MRD positive.

UNIVERSITY OF IOWA HOSPITALS & CLINICS
University of Iowa Health Care

Contact:
Gudbjorg Jonsdottir, MD
University of Iowa hospitals and clinics
Gudbjorg-jonsdottir@uiowa.edu