XIX CONGRESSO NAZIONALE SIES2026
Firenze | 4-6 marzo 2026 Palazzo degli Affari

XIX Congress of the Italian Society of Experimental Hematology ABSTRACT N. P107

Monoclonal Gammopathies & Multiple Myeloma

KARYOTYPE EVALUATION ACCORDING TO PATIENT AGE IN MULTIPLE MYELOMA

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Introduction: Multiple Myeloma (MM) is a genetically complex disease with several chromosomal alterations, divided into primary, observed at diagnosis, and secondary, due to an accumulation of genomic defects in clone subsets that provide an advantage in disease progression. However, these data generally refer to a younger population, in which karyotype is currently evaluated: in elderly MM patients, karyotype is not routinarily assessed. The aim of this study was to evaluate the existence of significant age-related differences in the cytogenetic and clinical characteristics of patients at disease onset, in order to identify age-dependent specificities.

Methods: The cohort analyzed included a total of 105 consecutive newly diagnosed MM patients from 1/2018 to 12/2023 with an available cytogenetic characterization, performed at our Center in all cases; the entire cohort was divided into two subgroups according to age at diagnosis (< 70 years versus 70 years or older) and evaluating for each group the clinical and biological features and the overall survival (OS). Statistical data analysis was performed using SPSS software.

Results: The main clinical features of the entire cohort and according to age are reported in Table 1. The only clinical feature with a significant different distribution in the age groups was the light chain type [k chain in 36/54 (66.6%) patients < 70 years compared to 22/49 (44.9%) in patients ≥ 70 years, p=0.026]. Numerical distribution of karyotypic abnormalities at FISH analysis as well as cytogenetic risk categories were similar in the two group (Table 1). As to the most frequent karyotypic abnormalities reported, no difference was observed for del 13q, ampl 1q, ampl 11q and ampl 14q between the two age group: the frequence of t(11;14), on the contrary, was significantly higher in the younger age group [15/53 patients < 70 years (28.3%) versus 6/49 (12.2%) in patients ≥ 70 years, p=0.045]. Five-year cumulative OS of the entire cohort was 54.8% (95%CI 40.6 – 69.0), without difference according to age group [5-year cumulative OS in patients aged < 70 years 51.6% (95%CI 32.3 – 70.9) versus 60.5% (95%CI 41.8 – 79.2) in patients ≥ 70 years, p=0.997]. At univariate analysis on the entire cohort, the karyotypic features with significant poor impact on OS were the high risk cytogenetic group (p<0.001), presence of ≥ 3 alterations at FISH analysis (p=0.001), presence of ampl-1q (p<0.001) and presence of t(11;14) (p=0.03).

Conclusions: Present data showed no difference in the distribution of karyotypic alterations in patients with MM according to age from a quantitative and qualitative point of view, with the exception of a higher rate of t(11::14) in younger subjects. It is worth of note that in our cohort OS was similar in the two age groups. Considering the strong prognostic value of karyotype, a larger use of cytogenetic evaluation also in elderly patients should be encouraged.

Table – Clinical and karyotypic features according to age group

	All pts (105)	Pts < 70 years (55)	Pts ≥ 70 years (50)	p
Gender, M/F (%)	55/50 (52.4/47.6)	28/27 (50.9/49.1)	27/23 (54.0/46.0)	0.751
Median age (years) (IQR)	69.2 (60.8 – 76.2)	62.2 (56.7 – 66.4)	76.5 (73.3 – 80.1)	**<0.001**
Hb, g/dl (IQR)	12.2 (10.2 – 13.6)	12.1 (10.7 – 13.6)	12.2 (10.0 – 13.6)	0.622
Previous MGUS, n° evaluable (%):	105	55	49	
No	57 (54.8)	33 (60.0)	24 (48.9)	0.260
Yes	48 (45.2)	22 (40.0)	25 (51.1)	
ISS, n° evaluable (%):	87	47	40	
Stage 1°	40 (46.0)	22 (46.8)	18 (45.0)	
Stage 2°	25 (28.7)	12 (25.5)	13 (32.5)	0.738
Stage 3°	22 (25.3)	13 (27.7)	9 (22.5)	
CRAB, n° evaluable (%):	101	52	49	
No	41 (40.6)	19 (36.5)	22 (44.9)	0.393
Yes	60 (59.4)	33 (63.5)	27 (55.1)	
Type of monoclonal component, n° evaluable(%):	102	54	48	
IgG-k	34 (33.3)	19 (35.2)	15 (31.2)	
IgG-λ	31 (30.4)	12 (22.2)	19 (39.6)	
IgA-k	11 (10.9)	8 (14.8)	3 (6.3)	0.119
IgA-λ	9 (8.8)	3 (5.5)	6 (12.5)	
Light chain k	13 (12.7)	10 (18.6)	3 (6.3)	
Light chain λ	4 (3.9)	2 (3.7)	2 (4.1)	
Type of light chain, n° evaluable (%):	103	54	49	
Kappa	58 (56.3)	36 (66.6)	22 (44.9)	**0.026**
Lambda	45 (43.7)	18 (33.4)	27 (55.1)	
FISH alterations, n° evaluable (%)	103	55	48	
Negative	28 (27.2)	13 (23.7)	15 (31.3)	
1 alteration	16 (15.5)	10 (18.1)	6 (12.5)	0.475
2 alterations	20 (19.4)	13 (23.7)	7 (14.5)	
≥ 3 alterations	39 (37.9)	19 (34.5)	20 (41.7)	
Cytogenetic risk, n° evaluable (%)	105	55	50	
Standard risk	69 (65.7)	38 (69.0)	31 (62.0)	0.445
High risk	36 (34.3)	17 (31.0)	19 (38.0)	
Del 13q, n° evaluable (%):	103	54	49	
No	72 (69.9)	38 (70.3)	34 (69.4)	0.914
Yes	31 (30.1)	16 (29.7)	15 (30.6)	
t(11;14), n° evaluable (%):	102	53	49	
No	82 (79.4)	38 (71.7)	43 (87.8)	**0.045**
Yes	21 (20.6)	15 (28.3)	6 (12.2)	
Ampl 1q, n° evaluable (%):	103	54	49	
No	82 (79.6)	44 (81.5)	38 (77.5)	0.621
Yes	21 (20.4)	10 (18.5)	11 (22.5)	
Ampl 11q, n° evaluable (%):	103	54	49	
No	94 (91.3)	47 (87.0)	43 (87.7	0.913
Yes	9 (8.7)	7 (13.0)	6 (12.3)	
Ampl 14q, n° evaluable (%):	103	54	49	
No	90 (87.4)	48 (88.9)	46 (93.8)	0.371
Yes	13 (12.6)	6 (11.1)	3 (6.2)	