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FREE LIGHT CHAIN: A MARKER OF DISEASE AND PROGNOSTIC IN INTACT IMMUNOGLOBULIN MULTIPLE MYELOMA

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INTRODUCTION

In non-pathological conditions, heavy (HC) and light chains (LC) are asynchronously synthesized with a 10-40% excess of LC. The LC excess is secreted to the serum as free LC (FLC). In Multiple Myeloma (MM), the FLC production can vary from within normal range to a great overexpression. Paraprotein isotypes can reflect tumour burden; if FLC to HC ratios are studied, then, we could find intraclonal heterogeneity of the plasma-cell population, resulting in a very interesting biomarker in clinical practice.

It is our aim to understand how and in which intact Ig MM patients can the serum FLC concentration or its excess production, be used as a differential marker of intraclonal heterogeneity in early disease.

METHODS

Intact Ig MM patients diagnosed in 2016 and 2017. We calculated the Monoclonal sFLC to MP ratio for each patient, at diagnosis, and divided the population according to the sFLC excess greater or smaller than the median observed for the whole population. Patients were also studied as a function of monoclonal sFLC concentrations, considering the i) median and ii) the 25% and 75% percentiles.

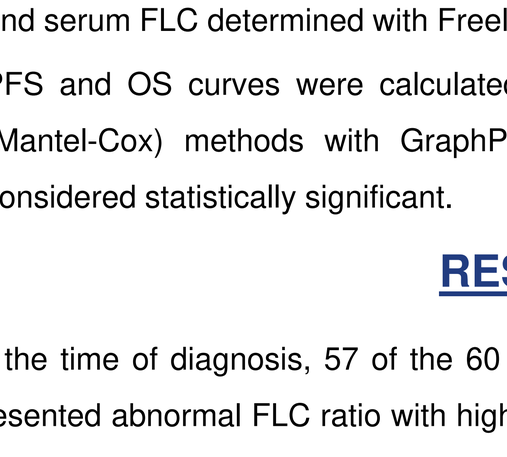
Monoclonal protein (MP) was quantified in a capillary electrophoresis (Sebia) and serum FLC determined with Freelite in a turbidimeter (BindingSite).

PFS and OS curves were calculated using the Kaplan-Meier and Log-rank (Mantel-Cox) methods with GraphPad Prism 8.2.1. A p-value <0.05 was considered statistically significant.

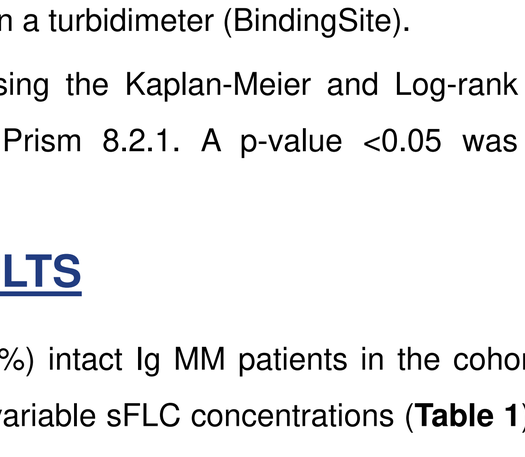
RESULTS

At the time of diagnosis, 57 of the 60 (95%) intact Ig MM patients in the cohort presented abnormal FLC ratio with highly variable sFLC concentrations (**Table 1**). FLC/MP median was used to defined 2 groups: <30% (N=26) and >30% (N=31) FLC excess secretion in relation to MP. OS and PFS did not show statistical differences when analysing all patients. However, analysing only patients non-eligible to transplant shows a statistically significant (p<0.04) worse OS and PFS for patients with a FLC excess > 30% (median: 1028 days vs not-reached and 443 days vs 651 days, respectively) (**Figure 1**). Additionally, the results show a tendency to better prognosis in patients with lower sFLC concentration at diagnosis, median OS and PFS not reached the group <200 (**Figure 2**).

FLC EXCESS PROGNOSTIC VALUE



	>30%	< 30%
Median survival	746	Undefined



	>30%	<30%
Median survival	443	651

Figure 1. Prognostic value at diagnostic of FLC excess in relation to only non-transplanted patients (N=40; >30%=23pts; <30%=17pts).

CONCLUSION

Data is consistent with prognostic relationship between FLC excess >30% and a worse outcome. Further studies are necessary to validate and explain this observation. Furthermore, and despite the short follow-up, the study reinforces the role of FLC as an independent disease biomarker also in intact Ig MM.

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Table 1. sFLC median and range in Intact Ig MM.

	sFLC Kappa (mg/L)	sFLC Lambda (mg/L)
Median (range)	442,6 (7,4 - 7183)	496 (15,4 - 25292)
Reference range	(3,3 - 19,4)	(5,7 - 16,3)

FLC CONCENTRATIONS PROGNOSTIC VALUE

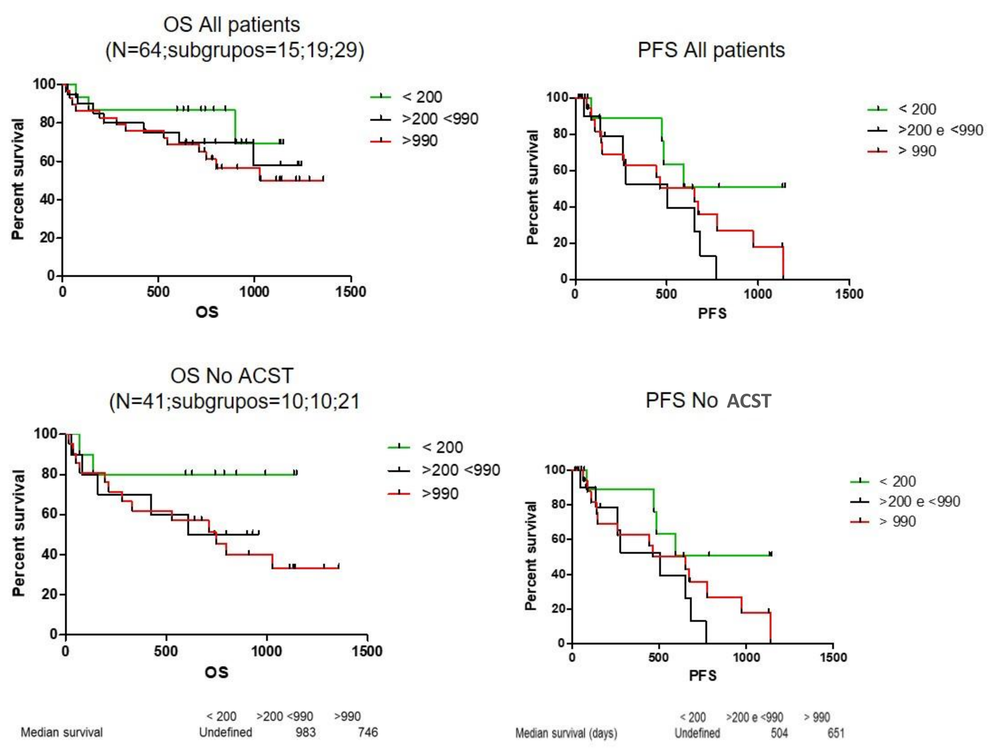

Figure 2. Prognostic value at diagnostic of sFLC concentrations based on the interquartile range of the cohort: patients stratification as follows <200, >200<990, >990 (mg/L), and also divided according to non-transplanted patients.

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