

# PROGNOSTIC VALUE OF FREE AND HEAVY/LIGHT CHAIN ANALYSIS

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## Introduction

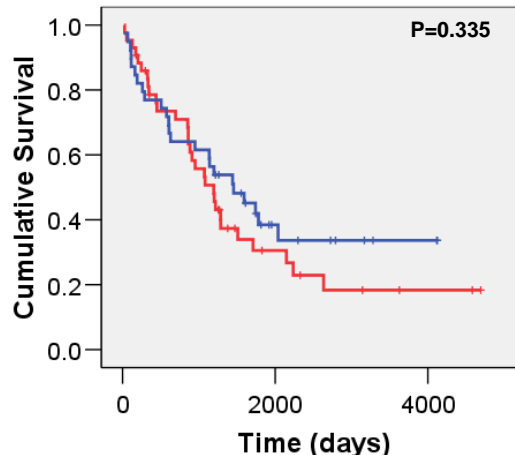
The serum free light chain (sFLC) ratio at presentation has been shown to be an independent prognostic marker in multiple myeloma (MM). Antibodies recognising conformational, junctional epitopes between the heavy and light chain have now been produced which make it possible to measure Ig $\kappa$  and Ig $\lambda$  ratios. Here we describe the use of sFLC and heavy/light chain (HLC) ratios to predict survival in MM patients.

## Materials and Methods

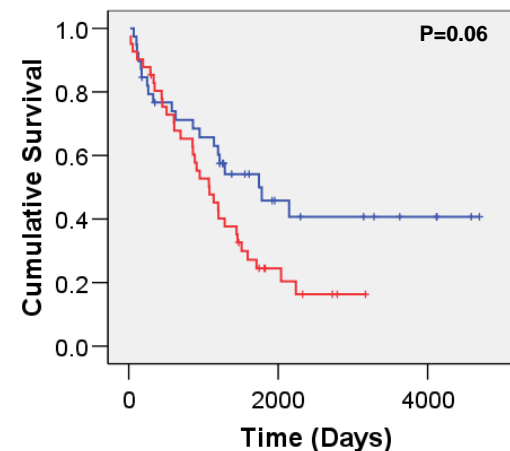
Archived sera from Medical Research Council MM trials were utilised. 86 presentation sera (24 IgA $\kappa$ , 9 IgA $\lambda$ , 45 IgG $\kappa$ , 8 IgG $\lambda$ ) were analysed retrospectively using sFLC and HLC (The Binding Site) nephelometric assays. Kaplan Meier survival curves were constructed to compare patients above or below the median value for sFLC and/or HLC ratio (either  $\kappa/\lambda$  or  $\lambda/\kappa$ ) and paraprotein concentration (analysis using SPSS v14.0 and Mantle-Cox test to determine significance).

## Results and Discussion

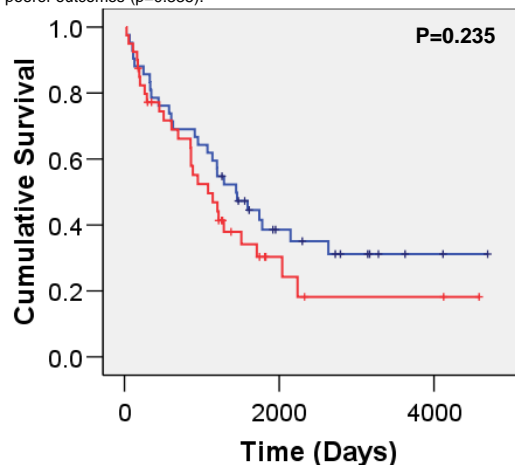
There was no significant difference in survival when analysing intact monoclonal protein concentrations ( $p=0.335$ , Fig 1), sFLC concentrations ( $p=0.103$ , data not shown), FLC ratios ( $p=0.06$ , Fig 2) or HLC ratios ( $p=0.235$ , Fig 3) individually. When adding sFLC and HLC ratios together there was a significantly shorter survival for those patients with greater than median values (50% survival 949 days vs 1592 days,  $p=0.02$ , Fig 4). The sFLC ratio is likely to be more predictive of outcome than the concentration of the tumour sFLC because it includes a measure of immunoparesis as well as tumour production. Use of the HLC ratio also incorporates a measure of immunoparesis but additionally, it will compensate for any reduction in the concentration of monoclonal immunoglobulin due to increased catabolism (IgG) and/or increased plasma volume. It is probable the use of the summated sFLC and HLC ratios was more predictive of outcome because there were some patients with very low monoclonal intact immunoglobulin production for whom the sFLC ratio was the most appropriate prognostic marker and visa versa for patients with low sFLC production.



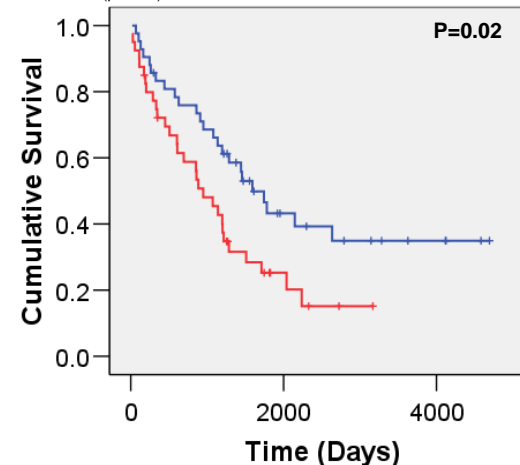
**Figure 1:** Kaplan Meier survival curve for 86 MM patients (33 IgA and 53 IgG) comparing paraprotein measurements above (red line) and below (blue line) the median value (median value=41.6g/L; Range 1.71-104). Paraprotein concentrations above the median value were not associated with significantly poorer outcomes ( $p=0.335$ ).



**Figure 2:** Kaplan Meier survival curve for 86 MM patients (33 IgA and 53 IgG) comparing serum free light chain ratios ( $\kappa/\lambda$  or  $\lambda/\kappa$ ) above (red line) and below (blue line) the median value (median value =23.9; Range 1.63-33700). Free light chain ratios above the median value were not associated with significantly poorer outcomes ( $p=0.06$ ).



**Figure 3:** Kaplan Meier survival curve for 86 MM patients (33 IgA and 53 IgG) comparing heavy /light chain ratios (Ilg $\kappa$ /Igl $\lambda$  or Igl $\lambda$ /Ilg $\kappa$ ) above (red line) and below (blue line) the median value (median value =80.85; Range 2.26-3675). Heavy /light chains ratios above the median value were not associated with significantly poorer outcomes ( $p=0.235$ ).



**Figure 4:** Kaplan Meier survival curve for 86 MM patients (33 IgA and 53 IgG) comparing summated free light chain + heavy /light chain ratios ( $\kappa/\lambda$  or  $\lambda/\kappa$ ) above (red line) and below (blue line) the median value (median value =148.98; Range 5.61-33708.6). Summated ratios were associated with significantly poorer outcomes ( $p=0.02$ ).

## Conclusion

In this preliminary investigation, summated sFLC and HLC ratios were found to be predictive of overall survival for myeloma patients. Further studies with larger patient numbers and comparison with other prognostic markers are needed.