

# Serial sample analysis of 3 IgA multiple myeloma patients using a novel immunoassay measuring IgA kappa and IgA lambda

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## Background

The standard for measuring paraprotein in patients with multiple myeloma (MM) to assess tumour burden is the quantification of protein bands by serum protein electrophoresis (SPE). There are several limitations with this method, such as a large proportion of IgA monoclonal proteins migrate into the  $\beta$  region where they can be obscured by other proteins making quantification subjective. A novel nephelometric immunoassay relies on the specific identification of epitopes spanning the junction of the heavy and light chains on the immunoglobulin molecule. Measurement of the involved and uninvolved heavy-light chains in serum may provide an accurate and quantifiable measurement of residual disease. The aim of this study is to perform retrospective analysis of tumour burden in patients with IgA multiple myeloma using this novel nephelometric assay.

## Method

Samples from MRC MM trial were collected and analysed, results were compared to total IgA and SPE densitometry. 35 presentation sera were analysed and 3 patients were followed throughout the course of their disease. Normal ranges for IgA $\kappa$ /IgA $\lambda$  ratios were derived from 191 blood donor sera.

## Results

In 35 IgA MM patient samples analysed at presentation, 14.3% (5/35) did not have a quantifiable SPE band, whereas IgA $\kappa$ /IgA $\lambda$  ratios were reported in each case.

Patient A was treated with conventional chemotherapy (CVAMP) and received an autologous stem cell transplant resulting in a complete response. Relapse was reported using hevyliite IgA $\kappa$ /IgA $\lambda$  ratio 596 days prior to conventional SPE and IFE methods. In sera from patient B quantification of IgA monoclonal protein by SPE densitometry was difficult due to other proteins in the  $\beta$  region throughout the course of the disease. IgA $\kappa$ /IgA $\lambda$  ratio did not normalise until 518 days after IFE became negative. Patient C received conventional chemotherapy (ABCM) and complete response was reported after 175 days, relapse occurred after 491 days. SPE and IFE became negative with IgA concentration falling into the normal range after treatment. However, the IgA $\kappa$ /IgA $\lambda$  ratio remained abnormal throughout.

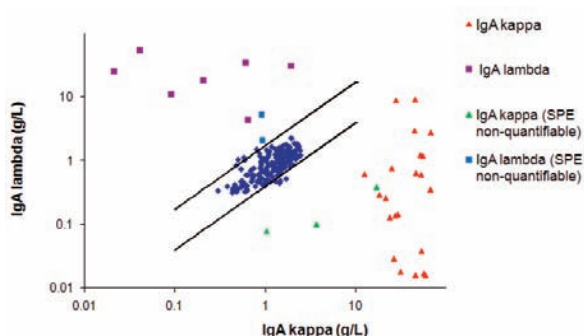


Figure 1: Plot of IgA $\lambda$  v IgA $\kappa$  for 191 blood donor sera and 35 presentation sera from the MRC Myeloma trial. The parallel lines indicate the 95%ile range for the IgA $\kappa$  / IgA $\lambda$  ratio.

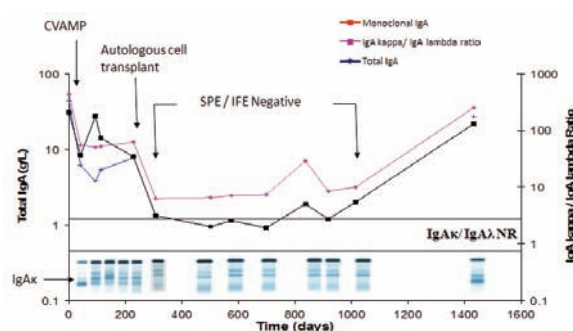


Figure 2: Patient A presented with 66g/L of IgA $\kappa$  and responded well to CVAMP. After autologous cell transplant IgA fell into normal range (0.8g/L – 4.0g/L), however IgA $\kappa$  / IgA $\lambda$  ratio did not normalise until 194 days after total IgA. The IgA $\kappa$  / IgA $\lambda$  ratio became abnormal before a band was quantifiable by SPE (596 days).

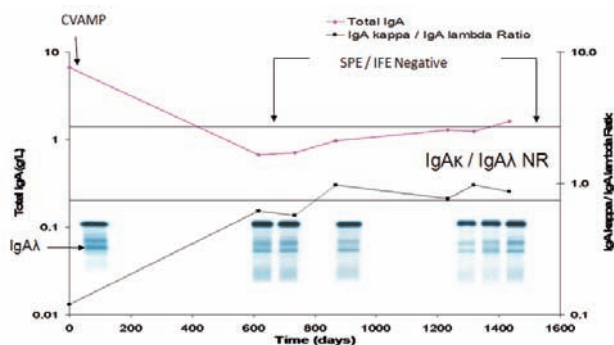


Figure 3: Serial analysis of sera for Patient B comparing total IgA and the IgA $\kappa$  / IgA $\lambda$  ratio. The mono-clonal protein migrated into the  $\beta$  region of SPE and was obscured at presentation and throughout the course of the disease, making accurate quantification by SPE densitometry impossible.

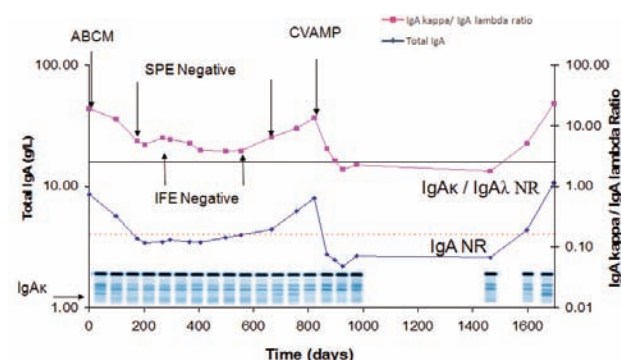


Figure 4: Patient C was followed throughout the course of their treatment and presented with 8.4g/L of IgA $\kappa$ . Patient responded well to treatment and complete response was recorded after 175 days. Patient remained at plateau for 491 days at which point the patient started to relapse. During this time IgA $\kappa$  / IgA $\lambda$  ratio remained abnormal and increasing IgA $\kappa$  / IgA $\lambda$  ratio reported relapse earlier than SPE / IFE.

## Conclusion

The use of IgA $\kappa$ /IgA $\lambda$  ratios correctly identified 35/35 patients tested, including patients where the SPE was ambiguous. Furthermore, analysis of IgA $\kappa$ /IgA $\lambda$  ratios in 3 IgA MM patients followed through the course of their disease proved a more sensitive marker of tumour burden resulting in a significantly earlier detection of residual disease when compared to traditional methods.