The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Non-Invasive MRD Monitoring in Multiple Myeloma Patients By Heavy/Light Chain Analysis

Lauren Campbell[1], Karthik Ramasamy[2], Ross Sadler[1]

[1] Immunology Laboratory, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom
[2] Department of Haematology, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom

Introduction

The majority of multiple myeloma (MM) patients are now achieving very deep responses. The most sensitive disease detection techniques are currently bone marrow assays. However, as bone marrow sampling is invasive and unpleasant for patients it is important to investigate whether blood-based assays could be equally or more informative of disease status. The heavy/light chain assay (Hevylite ™, The Binding Site, UK) evaluates serum heavy/light chains (HLC) for IgG, IgA and IgM M-proteins. This study assessed whether the HLC assay could act as an effective marker for disease in the bone marrow of treated MM patients and evaluated the prognostic utility of HLC measurements at best response and relapse time points.

Methods

104 IgG and IgA MM patients were recruited either prior to transplant or during chemotherapy. Median follow up was 18 months. Routine M-protein tests were performed alongside HLC testing with parameters including involved HLC (iHLC), uninvolved HLC (uHLC) and kappa/lambda HLC ratio (HLCr). A bone marrow flow cytometry (NGF) assay was performed up to a sensitivity of 10^{-6} and was considered to be the gold standard assay. Disease response was determined according to the IMWG criteria.

Results and Discussion

At pre- and post-transplant time points there was significant agreement between HLC measurements and NGF, with uHLC being the most sensitive measurement (86%) and HLCr the most specific (100%). Both uHLC and HLCr show substantial agreement with the bone marrow NGF method whilst iHLC cannot be used to indicate bone marrow status.

Survival analysis showed significantly inferior progression free survival (PFS) in patients with an abnormal uHLC (p=0.01) (Figure A) or HLCr (p=0.02) result post-transplant but no survival difference based on iHLC status (p=0.78) (Figure B). Interestingly, performing survival analysis on these same samples using serum immunofixation (IFE) status (positive or negative) did not produce a significant PFS difference between participants (p=0.21).

During long term follow up, HLC values showed a correlation with depth of response, with uHLC being abnormal in 60% of complete response (CR) patients. This suggests that those participants currently grouped as CR may be able to be further subdivided according to uHLC level and this could have a prognostic value in the monitoring and treatment of these patients. At best response uHLC was the only HLC or free light chain (FLC) measurement which gave a significant difference in PFS for all patients in partial response (PR) or better (p=0.005), remaining true when analysing patients in ≥CR only (p=0.002). The addition of free light chain measurements into the HLC analysis did not improve the significance of these survival differences. In relapsed patients, paired comparisons of M-protein and disease activity markers at best response vs. prior to clinical relapse were performed. uHLC was the only marker which was significantly different between the two time points in IgG and IgA patients. The significance of this was confirmed by showing that those patients in stable disease did not experience a significant change in uHLC levels. For other M-protein variables such as total immunoglobulin, IFE status and FLC values there was an increase in levels or abnormality between best response and pre-relapse but these were not significant. The paired comparison suggests that monitoring an individual using HLC could help to detect relapse earlier than conventional methods.

In all analyses performed the HLC assay showed increased sensitivity and utility over the IFE technique.

Conclusion

This study suggests that the HLC assay can be used prior to bone marrow analysis to help influence decisions and improve the patient and laboratory experience. These results can be put into practice during patient follow up post initial treatment in the following ways:

At deepest response an abnormal uHLC or HLCr suggests a positive MRD status, meaning a possible reduction or delay in the requirement for bone marrow assessment.

All patients in ≥VGPR should have HLC performed alongside conventional assays during follow up.

If uHLC values become abnormal during follow up then it should be assumed that the patient is about to undergo relapse.

The measurement of HLC values have been shown to be a significant marker in this study, for sensitively detecting the M-protein, giving further clarification of response status and predicting early relapse.

Disclosures Ramasamy: *Amgen, Celgene (BMS), GSK, Janssen, Takeda:* Research Funding; *AbbVie, Adaptive Biotechnologies, Amgen, Celgene (BMS), GSK, Janssen, Karyopharm, Oncopeptides, Pfizer, Sanofi, Takeda, Recordati pharma, Menarini Stemline:* Speakers Bureau; *AbbVie, Adaptive Biotechnologies, Amgen, Celgene (BMS), GSK, Janssen, Karyopharm, Oncopeptides, Pfizer, Sanofi, Takeda Recordati pharma, Menarini Stemline:* Honoraria; *Pfizer, GSK:* Membership on an entity's Board of Directors or advisory committees.
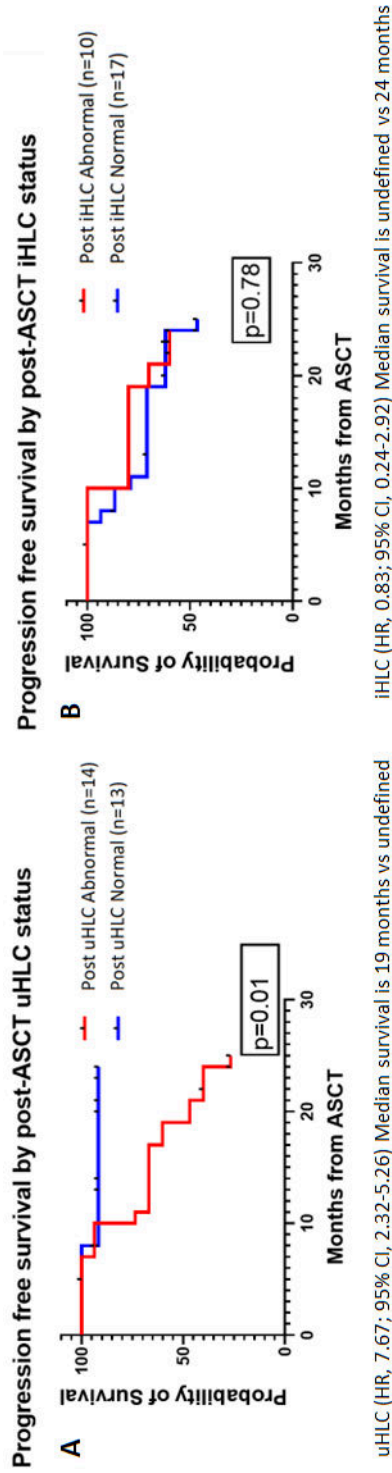
Figure 1