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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Using Mass Spectrometry to Assess Disease Status in Treated Multiple Myeloma Patients

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Introduction

As multiple myeloma (MM) is a bone-marrow based disease, the majority of MRD studies have focused on sensitive bone-marrow based assays. However, to effectively monitor patients this would require sequential invasive procedures at semi-frequent intervals. Sensitive, non-invasive, blood-based assays which can detect the presence of MRD are needed to optimize the management of MM patients.

Mass spectrometry (MS) is currently being investigated for its clinical utility at different points in the monoclonal gammopathy pathway, from screening to MRD detection. This study aimed to compare the sensitivity and prognostic utility of MS with other blood-based M-protein detection methods and bone marrow flow cytometry at active disease, best response and MRD timepoints.

Methods

MS analysis took place at The Binding Site laboratory (The Binding Site, UK) using a pre-commercial quantitative immuno-precipitation (QIP-MS) system. Mass spectra was acquired over an *m/z* range of 10,000 to 30,000 and analysis was performed by two independent readers.

Both transplant eligible and non-transplant chemotherapy only patients were recruited at varying stages of disease and treatments. Median follow up was 18 months. A total of 190 serum samples from 87 individual patients were tested for the presence of M-protein by conventional methods (serum electrophoresis (SPEP), immunofixation (IFE), free light chain (FLC)) and MS. A bone marrow flow cytometry (NGF) assay was performed up to a sensitivity of 10^{-6} at pre- and post-transplant for a subset of patients. Disease response was determined according to the IMWG criteria.

Results and Discussion

When compared to conventional techniques MS showed increased sensitivity over SPEP, IFE and FLC (Table 1). The 1 M-protein detected by SPEP and IFE but not by MS was a post-transplant sample which showed multiple oligoclonal peaks by MS where the original M-protein could not be determined due to not having a diagnostic MS result available. When evaluating the 37 samples from 19 individual patients which were MS positive and IFE negative it was found that 7/19 (37%) patients in this group relapsed during the course of the study.

As SPEP, IFE and FLC analyses are often performed together, the utility of using MS alone was compared to an algorithm of SPEP/IFE/FLC tests, where if any of the conventional tests showed abnormality this was considered positive. Using this scenario, MS outperforms the conventional tests in the 190 samples evaluated - with 7 samples being MS positive only and 1 sample (discussed above) being negative by MS but positive by all SPEP/IFE/FLC.

As expected, upon analysing the percentage of samples within each IMWG clinical response group which had a positive or negative MS results the percentage of samples with a negative MS result increased with greater depth of response whilst those in partial response or worse had no negative MS samples. However, even in the deepest response group, complete response, 77% of samples were MS positive, showing how MS outperforms the IMWG criteria. Progression free survival (PFS) analysis at the best response time point showed a significant survival advantage of having a MS negative result (p=0.007).

When comparing MS against NGF results at bone marrow testing time points agreement at pre-transplant was 88%, with all samples being NGF positive but 22/25 being MS positive and 1 of these 3 discordant patients relapsing during the study. At post-transplant agreement was only 56%. However, evaluating PFS at the post-transplant time point showed that MS status had a significant effect on survival (p=0.02) (Figure 1) where IFE (p=0.44) did not and NGF only approached significance (p=0.051).

Conclusion

This study aimed to evaluate the viability of using MS to identify M-proteins in treated MM patients. In this study the MS method had a higher number of positive results than any of the conventional methods, and outcompeted the algorithm of SPEP/IFE/FLC in detecting the presence of M-protein.

This study has shown a survival benefit of being MS negative at both post-ASCT and best response time points across a range of treatments. There were a high number of patients who were MS positive throughout monitoring and it will be important to determine how such a sensitive method can be used to provide clinically useful information to clinicians to give the best balance between treatment and quality of life for patients.

Table 1: Agreement between conventional methods and MS results for detecting M-protein in 190 samples

	MS DETECTED	MS UNDETECTED	Concordance
SPEP DETECTED	105	1	69%
SPEP UNDETECTED	58	26	
IFE DETECTED	126	1	80%
IFE UNDETECTED	37	26	
FLCr ABNORMAL	133	13	80%
FLCr NORMAL	26	18	

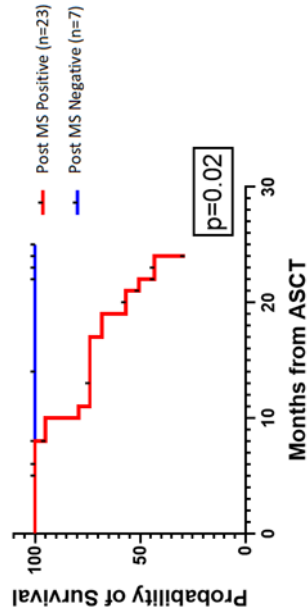**Progression free survival by post-ASCT MS status**

Figure 1:
(HR, 4.6; 95% CI, 1.3-17.5; p=0.02) Median survival is 22 months vs undefined

Figure 1