SKEWED RATIOS OF HEAVY CHAINS IGM-KAPPA /IGM-LAMBDA AS MEASURED BY HEVYLITE™ CHARACTERIZE REMISSION DEPTH BETTER AS IMMUNOFIXATION AND FREE LIGHT CHAIN RATIOS

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BACKGROUND:
HevyliteTM, a novel immunoassay is designed for analysis of immunoglobulin heavy chain/light chain pairs. These assays can identify, separately, the different light chain types of each immunoglobulin class i.e. IgG kappa, IgG lambda, IgA kappa, IgA lambda, IgM kappa and IgM lambda. The molecules are then measured in pairs e.g. IgG kappa/IgG lambda to produce ratios of monoclonal immunoglobulin/background polyclonal immunoglobulin concentrations (HLR).

HYPOTHESIS:
Hevylite Ratios (HLR) may serve as a parameter for plasma cell dyscrasia induced immunoparesis and serve as a new biomarker for validating remission depth and relapse probabilities, as well as guidance of therapy.

METHODS:
The IgM kappa/IgM lambda pair of assays (The Bindingsite) was tested in patients supposed to be in remission or responding to specific treatment during routine surveillance visits for IgM parapotein secreting diseases [NHL, IgM MGUS, Waldenstroems macroglobulinaemia (MW), and IgM Myeloma (IgM MM)] in comparison to measurements of total immunoglobulins, free light chains as well as immunofixation. Results were correlated to the patients further clinical course in the framework of informed consent to the local clinical registry and BioBank .

RESULTS:
28 pts. with IgM MGUS (6 pts.), MW (19 pts.), IgM MM (1 pt.), and IgM positive NHL (2 pts.), were analyzed using 53 distinct samples. In comparison to standard immunofixation (IFT), and freelight ratios (FLR), Accuracy of cumulative measurements of IgM kappa and IgM lambda

compared to a standard IgM assay was within +/- 10mg/l in 72%, +/- 100mg/l in 86% and within +/- 500mg/l in 90% of cases.
HLR proved to be more sensitive, detecting residual disease in 76% of cases compared to IFT (37%) and FLR (43%). Pts. exposing positivity in HLR only later showed a rapid clinical deterioration in some cases and pts. with the most pathological HLR were also prone to infectious complications.

CONCLUSION & DISCUSSION:
As this case series illustrates HLR may serve as a sensitive new diagnostic tool for rational treatment allocation, especially with respect to maintenance and consolidation strategies. An update comprising data on IgA and IgG excreting diseases, mainly focused on myeloma, will be presented, as well as the outline of a cooperative European project (OPTATIO) in the 7th EC framework program (FP7) to further validate this putative biomarker will be introduced. In the future HLR should be validated against techniques using sCR, flow-CR and molCR. Furthermore the effect of proven immunoparesis on complication frequencies especially respective to infections should be evaluated.