PROBLEMS WITH CURRENT RESPONSE CRITERIA.

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The assessment of the efficacy of treatment regimens in WM relies principally on the serial measurement of the concentration of monoclonal IgM. This has a number of inherent limitations which are detailed below -

- The serum concentration of IgM is not a direct measure of disease bulk
- Responses in IgM are typically slow in patients treated with alkylating agents, purine analogues and monoclonal antibodies
- Complete responses are uncommon with standard therapies and it remains unclear whether the quality of response predicts for overall outcome
- Clinically meaningful responses are not always reflected in changes in IgM concentration and conversely apparently adequate IgM responses do not necessarily imply improvement in symptoms.

These factors provide real difficulties for clinicians and patients. The kinetics of M protein response means that an early assessment of response is frequently not possible which can result in the exposure to unnecessary toxicity in many patients. Recent studies from our laboratory and others have however proven the value of repeat bone marrow assessment particularly in the context of treatment with purine analogues, monoclonal antibodies and bortezomib. Non-invasive methods of determining early response to therapy are clearly needed. In this context prospective evaluation of the serum free light chain assay which appears to be informative in a significant proportion of patients is required. One potential alternative is to look for low levels of circulating tumour cells using multiparameter flow cytometry. Early depletion of such cells may predict for subsequent response which may allow an early change of therapy in suboptimally responding patients.