Response assessment in WM.

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The assessment of response to treatment in patients with WM relies heavily upon documenting changes in serum IgM concentration. Sequential assessment of IgM can however be suboptimal and misleading because of the following phenomena –

- Variability in the presenting IgM levels and additional clinical parameters between patients
- Changes in IgM do not always result in the improvement of symptoms
- IgM flare
- Kinetics of IgM reduction and the effect of the treatment regimen used. Responses to alkylating agents, purine analogues and monoclonal antibodies are typically slow. Whereas responses to bortezomib containing regimens are rapid.

Studies in our laboratory and others have demonstrated that there may be a discrepancy between IgM and BM responses. For instance in the context of purine analogue and monoclonal antibody therapy high quality bone marrow responses may be seen in patients not attaining adequate reductions in IgM. This phenomenon appears to be due to the selective depletion of B cells and persistence of the plasma cell component of the disease. Whereas in bortezomib treated patients prompt serological response may be associated with suboptimal bone marrow and lymph node response in some patients. Recent studies in myeloma have demonstrated that assessment of residual bone marrow disease by flow cytometry is a highly effective way to define response independent of M protein concentration. Indeed in some studies achievement of a flow cytometric remission appears a better predictor of outcome than the achievement of immunofixation negativity. The challenge in WM lies principally in the following areas –

- The identification of early response such that refractory patients can be identified early and the treatment continued in those patients destined to achieve a good IgM response with further follow up.
- Defining CR or a response category which is associated with improved progression free and overall survival.

Detailed sequential bone marrow studies should be performed in all clinical trials.