Session V: Prognostic, Predictive and Response Markers in WM

Abstract 128

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Complexities of assessing response in WM. Roger Owen, HMDS Laboratory, The Leeds Teaching Hospitals NHS Trust, Leeds, UNITED KINGDOM.

Standard clinical response assessment in WM patients principally rely upon changes in the serum concentration of monoclonal IgM. However IgM levels are a poor surrogate of overall tumour bulk and the kinetics of clearance are such that maximum responses are frequently not achieved until at least 6 months following the completion of therapy. WM is characterised by morphologically and immunophenotypically distinct B-cell and plasma cell components. The B-cell component dominates in the majority of patients and is typically sIgM+ CD20+ sCD79+ CD52+ CD138- MUM1/IRF4- COX2- while the plasma cell component is cIgM+ CD20- cCD79+ CD52- CD138+ MUM1/IRF4+ COX2+. It is clear therefore that the expression of key therapeutic targets differs between the proliferative B-cell component and the immunosecretory plasma cell components of WM. Indeed we have previously demonstrated that monoclonal antibody therapy with either alemtuzumab or rituximab results in the depletion of the B-cell component but does not appear to deplete monoclonal plasma cells. This phenomenon is also seen in patients treated with purine analogues although the mechanism is clearly different. These are highly relevant clinical observations particularly given the kinetics of M protein response in many patients. We have observed that patients treated with fludarabine show an apparent selective depletion of B-cells at interim and end of treatment marrow assessments. Many of these patients would be considered to have non-responsive disease with respect to their M-protein concentration but subsequently show excellent serological responses with a further 6-12 months of observation. This phenomenon highlights the limitations of conventional serological assays as well as the value of repeat marrow assessment in patients treated with monoclonal antibodies and purine analogues. Additional markers of early response are clearly required. The serum free light chain assay is an attractive option as the majority of patients with symptomatic WM have abnormal ratios. Data from myeloma trials has shown the SFLC assay to be a good indicator of early response but not an indicator of complete (immunofixation negative) response. Sensitive multi-parameter flow cytometry assays that detect low levels of circulating tumour cells may also have a role in the early assessment of response.