Comparative response assessment by total serum IgM and IgM M-component in Waldenstrom's macroglobulinemia.

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Background: Changes in total IgM and the electrophoretically determined IgM M-component are used as surrogate serum response markers in Waldenstrom's Macroglobulinemia (WM). Their ability to reflect underlying disease burden changes have not been compared.

Methods: 73 rituximab-naïve patients were studied who underwent rituximab-based therapy on a study, and for whom serial total serum IgM levels, IgM M-component, and bone marrow (BM) assessments were available. Baseline: Median age 61 years; serum IgM 3,960 mg/dL; IgM M-component 2.55 g/dL; BM disease by core biopsy 60%. 5 patients had serum IgM levels <1,000 mg/dL, and 23 > 5,000 mg/dL. 39 patients had adenopathy and/or splenomegaly by baseline CT scans. Post-therapy, serum IgM declined from 3,960 to 1,800 mg/dL ($p<0.0001$); IgM M-component from 2.55 to 1.28 g/dL ($p<0.0001$); and BM involvement from 60% to 10% ($p<0.0001$). Among 39 patients with extramedullary disease, post-therapy CT scans were improved for 18, unchanged for 14, and worse for 7.

Results: By linear regression analysis, reductions in serum total IgM and IgM M-component correlated with decreased BM disease involvement, though were relatively moderate ($r=0.4490$, $p<0.0001$; and $r=0.4051$; $p=0.0004$, respectively). To assess the difference between serum IgM and IgM M-component for correlation with BM response, an r to z transformation was performed. Serum IgM and IgM M-component were not significantly different as predictors for BM response ($p=0.3745$). Moreover, total serum IgM and the IgM M-component were poor estimators of BM response in patients with IgM levels <1,000 mg/dL ($r=0.3635$, $p=0.2815$ for serum IgM; $r=0.1869$, $p=0.4672$ for IgM M-component) or >5,000 mg/dL ($r=0.0762$, $p=0.2022$ for serum IgM; $r=0.0306$, $p=0.4246$ for IgM M-component). Extramedullary disease presence had no impact on serum IgM or IgM M-component correlations with BM disease involvement.

Conclusions: Serum IgM levels and IgM M-component show similar correlations to changes in BM disease burden following therapy in WM patients, though overall the strength of these correlations are moderate, and particularly poor among patients with either low (<1,000 mg/dL) or high (>5,000 mg/dL) serum IgM levels.