Peripheral neuropathy is a well-recognized complication of IgM paraproteinaemia associated with both underlying NHL, usually Lymphoplasmacytic Lymphoma (LPL) and IgM MGUS. In 60% of cases the M protein shows reactivity to myelin-associated glycoprotein (MAG). Anti-MAG antibodies have been shown to be neuropathic and the natural history of the neuropathy is of persistent functional decline with poor response to immunomodulatory agents. We postulated that the neuropathic component may respond better to combination therapy than to chemotherapy or immunotherapy alone as seen in LPL.

### RESULTS

All patients with underlying NHL achieved at least a partial remission at 3 months. The treatment was well tolerated. IgM paraprotein levels fell from a baseline median level of 4.7g/l to 2.25g/l at 3 months, p=0.000 and to 1.95g/l at 2 years, p=0.000.

In patients with Anti-MAG antibody, levels fell from a baseline median of 38,956 to 14,783 units by 2 years post treatment p=0.002.

### CONCLUSIONS

In patients with IgM paraproteinaemic neuropathy, a disease with poor outcomes and response to conventional treatment, R-CP chemoimmunotherapy is well tolerated and capable of inducing sustained significant improvement for at least 2 years in nerve conduction studies, overall neuropathy limitation, motor scores and patient reported symptoms and is associated with significant reductions in both IgM paraprotein and Anti-MAG antibody.

### References


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Poster presented at: Printing supported by: 


doi: 10.1007/s12046-016-0531-z

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### METHODS

25 patients (16 IgM MGUS and 9 NHL) were treated with 6 cycles every 21 days of Rituximab 375mg/m2 and Cyclophosphamide 750mg/m2 i/v on day 1 and 5 days of oral Prednisolone 50mg/m2. Assessments carried out at baseline and then at 3 months, 1 and 2 years post-treatment were serum paraprotein and Anti-MAG titres, standardised neurological functional scores - Overall Neuropathy Limitation Score (ONLS), MRC Sum Score for muscle power, Sensory Sum Score and standard nerve conduction studies (NCS) as well as patient reported outcome measures (PROMS). BM biopsy and CT scans were performed at baseline and at 3 months post treatment to assess remission status. Statistical analysis was by Wilcoxon signed ranks.

### INTRODUCTION AND OBJECTIVES

Peripheral neuropathy is a well-recognized complication of IgM paraproteinaemia associated with both underlying NHL, usually Lymphoplasmacytic Lymphoma (LPL) and IgM MGUS. In 60% of cases the M protein shows reactivity to myelin-associated glycoprotein (MAG). Anti-MAG antibodies have been shown to be neuropathic and the natural history of the neuropathy is of persistent functional decline with poor response to immunomodulatory agents. We postulated that the neuropathic component may respond better to combination therapy than to chemotherapy or immunotherapy alone as seen in LPL.

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