

## MSG 2010 Abstract

Clinical Improvement and Decreased Peripheral Autoreactivity in Refractory Myasthenia Gravis Treated with Rituximab.

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**Introduction:** Myasthenia gravis (MG) is a prototypical autoimmune disorder characterized by fatigable oculobulbar and limb weakness. Treatment of MG consists of symptomatic therapy with acetylcholinesterase inhibitors and immunotherapy such as corticosteroids, azathioprine, cyclosporine, plasmapheresis and intravenous immunoglobulin (IVIg). Despite current therapies a subset of patients are refractory or have intolerable adverse effects. Our goal was to assess the use of rituximab, a chimeric monoclonal antibody that targets CD20 antigen on B lymphocytes and modulates B cell activation, in treatment of refractory MG.

**Methods:** A retrospective study was performed of MG patients referred to Yale Neuromuscular Clinic. Fourteen patients were identified with refractory disease. Eight muscle specific kinase (MuSK+) and six acetylcholine receptor (AChR+) antibody patients were included. Pre-/post-rituximab therapy was evaluated through clinical exams, measuring the autoantibody titers and determining the frequency of peripheral T cells that react with MG-specific autoantigens via an EliSpot assay.

**Results:** Thirteen patients were identified on oral corticosteroids. A dose reduction was observed after initiation of rituximab therapy. Prednisone dose decreased by an average of 74.9% ( $p=0.0009$ ; standard deviation of 35.5) with six patients being tapered off completely. Clinical improvement was also observed in these patients with reduction of symptoms and abnormal exam findings as compared to pre-rituximab treatment. It is important to note that clinical improvement occurred in the setting of other immunomodulatory agents being tapered down. The number of plasma exchange (PE) sessions was also decreased in twelve patients identified receiving PE therapy prior to rituximab initiation. There was a statistically significant reduction in plasma exchange sessions in the groups analyzed at 6 and 12 months with  $p$  values of 0.0038 and 0.0044 respectively. Nine of the twelve patients no longer required plasma exchange at 6 months following initiation of rituximab. Six AChR+ patients refractory to conventional therapy were identified. Following the final treatment cycle autoantibody titers and the frequency of autoreactive T cells both decreased.

**Conclusion:** Refractory MG patients followed in our clinic respond to rituximab as measured by tapering down immunomodulatory therapy and clinical improvement. Improvement also correlated with decreased peripheral autoreactivity. These findings support the idea that rituximab is an efficacious therapeutic option for refractory disease.

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