

Medical Update Memo

June 23, 2010

Rituximab add-on therapy for breakthrough relapsing multiple sclerosis: A 52-week phase II trial

Summary

Recent studies have demonstrated a potential role of Rituximab in inflammatory suppression in autoimmune diseases. The aim of this study was to evaluate the efficacy, safety and tolerability of the combination of rituximab with standard injectable therapies in people with relapsing Multiple Sclerosis (MS). Naismith RT, Piccio L, Lyons JA, Lauber J, Tutlam NT, Parks BJ, Trinkaus K, Song SK, Cross AH.

Neurology. 2010 Jun 8; 74(23):1860-1867.

Details

B cells and the humoral immune system have been implicated in the pathogenesis of multiple sclerosis (MS). This study sought to evaluate the efficacy, safety, and tolerability of add-on therapy with rituximab, a monoclonal antibody that depletes circulating B cells, in subjects with relapsing MS with breakthrough disease defined by clinical and MRI activity (Class III evidence).

Thirty subjects with a relapse within the past 18 months despite use of an injectable disease-modifying agent, and with at least 1 gadolinium-enhancing (GdE) lesion on any of 3 pretreatment MRIs, received rituximab administered at 375 mg/m² weekly x 4 doses. Three monthly post treatment brain MRI scans were obtained beginning 12 weeks after the first infusion. Multiple Sclerosis Functional Composite (MSFC) and Expanded Disability Status Scale (EDSS) were obtained at baseline and throughout the posttreatment follow-up.

GdE lesions were reduced after treatment with rituximab, with 74% of post treatment MRI scans being free of GdE activity compared with 26% free of GdE activity at baseline ($p < 0.0001$). Median GdE lesions were reduced from 1.0 to 0, and mean number was reduced from 2.81 per month to 0.33 after treatment (88% reduction). MSFC improved as well ($p = 0.02$). EDSS remained stable.

CONCLUSION: Rituximab add-on therapy was effective based upon blinded radiologic endpoints in this phase II study. In combination with standard injectable therapies, rituximab was well-tolerated with no serious adverse events. B-cell-modulating therapy remains a potential option for treatment of patients with relapsing MS with an inadequate response to standard injectable therapies.

CLASSIFICATION of EVIDENCE: This study provides Class III evidence that add-on rituximab reduces gadolinium-enhancing brain lesions in multiple sclerosis.

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