

## **B-Lymphocyte Depletion with Rituximab and Beta-Cell Function: Two-Year Results.**

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### **Abstract**

**Objective**We previously reported that selective depletion of B-lymphocytes with rituximab, an anti-CD20 monoclonal antibody, slowed decline of beta-cell function in recent-onset type 1 diabetes mellitus (T1DM) at one year. Subjects were followed further to determine whether there was persistence of effect.  
**Research Design and Methods**Eighty-seven subjects (ages 8-40) were randomly assigned to, and 81 received, infusions of rituximab or placebo on days 1, 8, 15, and 22. The primary outcome - baseline-adjusted mean 2-hour area under the curve (AUC) serum C-peptide during a mixed meal tolerance test (MMTT) at one year - showed higher C-peptide AUC with rituximab versus placebo. Subjects were further followed with additional MMTTs every 6 months.  
**Results**The rate of decline of C-peptide was parallel between groups, but shifted by 8.2 months in rituximab treated subjects. Over 30 months, AUC, insulin dose, and HbA1c were similar for rituximab and placebo. However, in evaluating change in C-peptide over the entire follow-up period, the rituximab group means were significantly larger as compared within assessment times to the placebo group means using a global test ( $p = 0.03$ ). Odds ratio for loss of C-peptide to  $< 0.2$  nmol/L following rituximab was 0.565 ( $p = 0.064$ ). B-lymphocytes recovered to baseline values by 18 months. Serum IgG levels were maintained in the normal range but IgM levels were depressed.  
**Conclusions**Like several other immunotherapeutic approaches tested, in recent-onset T1DM, rituximab delays the fall in C-peptide, but does not appear to fundamentally alter the underlying pathophysiology of the disease