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Rituximab Therapy Effective for ANCA-associated Vasculitis

Immune Tolerance Network researchers demonstrate rituximab is as effective as the standard treatment protocol in ANCA-associated vasculitis.

WA, Seattle (July 26th, 2013) – In an article published today in the New England Journal of Medicine, Immune Tolerance Network (ITN) researchers demonstrated that a single course of rituximab therapy (anti-CD20; Rituxan, Genentech, Inc.) is as effective as the current standard of care regimen of drugs for remission induction and maintenance in patients with ANCA-associated Vasculitis (AAV). AAV is an autoimmune disease marked by the presence of antibodies that attack neutrophils and cause inflammation of the blood vessels, leading to organ damage and sometimes death. The standard of care for this disease was cyclophosphamide, a potent immunosuppressant that although effective is very toxic when used long-term. Rituximab has a shorter and simpler treatment course compared to standard therapy, thus offering significant treatment advancement for patients with AAV.

The RAVE study is a 197-patient randomized, double-blind, placebo-controlled trial comparing rituximab against cyclophosphamide for remission induction in patients with severe AAV. This clinical trial is led by John Stone, MD (Massachusetts General Hospital) and Ulrich Specks, MD (Mayo Clinic), and is sponsored by the ITN, a clinical trial network funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. The FDA approved a label extension for rituximab for use in AAV after the initial 6-month results of the RAVE study demonstrated that rituximab in combination with glucocorticoids was non-inferior to cyclophosphamide in combination with glucocorticoids for inducing complete remission in patients with severe AAV (reported in the *New England Journal of Medicine* in 2010; www.nejm.org/doi/full/10.1056/NEJMoa0909905). This represented the first approved therapy for AAV in over 40 years. Today's publication reports safety and relapse rates among the two treatment groups out to month 18. Patients in the rituximab arm received only one, short course of therapy over 4 weeks, and those in remission received *only* placebo therapy through month 18. Alternately, patients in the standard therapy arm received 3-6 months of cyclophosphamide followed by azathioprine through the length of the study. Patients who achieved remission had glucocorticoids discontinued before month 6 and did not take any glucocorticoids through month 18 if they remained in remission.

At 18 months, 39% of patients in the rituximab arm were relapse-free (n=39), compared to 33% in the standard therapy arm (n=32). There were no significant differences in overall adverse events between the two groups, although there were fewer cases of pneumonia and leukopenia in the rituximab arm. These results suggest that a short course of rituximab (four once weekly infusion) is as effective for the induction and maintenance of remission in severe AAV patients as continuous treatment over 18 months with standard immunosuppressive drugs that require ongoing monitoring for toxicities.

"The RAVE study is remarkable for several reasons", said Ulrich Specks. "First, its results have provided patients who suffer from these chronically relapsing diseases with access to a very effective alternative to cyclophosphamide to induce remission. Second, the study has shown that a short course of 4 infusions of rituximab is as effective as 18 months of ongoing daily oral therapy with immunosuppressive drugs that require frequent blood test monitoring to assure their safe use. Third, the RAVE study is a model for successful partnerships of federal funding agencies, federally funded research organizations and industry for the study of rare diseases. Last not least, today's publication illustrates how complete transparency between published study analyses and all raw study data can be provided to the public".

Data sets and statistical analyses from the RAVE study are available to the public through ITN TrialShare, www.ITNTrialShare.org, a new clinical trials research portal. This publication is the first to provide public access to the raw study data via direct links from the publication and its figures to the data sets in ITN TrialShare. This represents a big step forward in the general quest for complete transparency of all data accumulated during the conduct of clinical trials.

About The Immune Tolerance Network

The Immune Tolerance Network (ITN) is a research consortium sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. The ITN develops and conducts clinical and mechanistic studies of immune tolerance therapies designed to prevent disease-causing immune responses, without compromising the natural protective properties of the immune system. Visit www.immunetolerance.org for more information.

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