

Immune responses to tetanus vaccine unchanged for RA patients on rituximab

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Researchers from Johns Hopkins University determined that immune responses to the tetanus vaccine were not changed when rituximab in combination with methotrexate (MTX) was compared with MTX alone in patients with rheumatoid arthritis (RA). Responses to a pneumococcal vaccination (Pneumovax® pneumonia vaccine), however, were reduced in RA patients with rituximab. Complete findings of this study are published in the January 2010 issue of *Arthritis & Rheumatism*.

According to the Centers for Disease Control and Prevention (CDC), RA affects 1.3 million adults in the U.S. (2005). RA patients may be at an increased risk of infection because of impaired immune function due to the disease as well as from the use of immunosuppressive medications. As a result, vaccinations against infections are an essential part of rheumatic disease management. How immunosuppressive agents alter the effectiveness of vaccines in RA patients was the focus of the clinical trial led by Clifton O. Bingham III, M.D.

The controlled study enrolled 103 RA patients from 26 centers in the U.S. between January 2006 and December 2007. Patients treated with a stable dose (10-25 mg/week) of MTX were randomly allocated to two groups: placebo and treatment with rituximab (2 x 1000 mg given two weeks apart). Both groups were immunized with the tetanus and pneumococcal vaccines along with keyhole limpet hemocyanin (KLH) to evaluate humoral immunity and skin tested with *Candida albicans* to evaluate the cellular immune response.

Results indicate that 39.1% of patients in the rituximab+MTX group and 42.3% of MTX-only patients demonstrated a 4-fold rise in the anti-tetanus IgG titer. A 2-fold rise was confirmed in 54.7% of rituximab-treated patients and 61.5% of subjects on MTX alone. The research demonstrates that RA patients given a tetanus vaccine responded the same to tetanus vaccination regardless of whether they received MTX alone or rituximab in combination with MTX.

Patients treated only with MTX had a greater response to the [pneumonia](#) vaccine compared with those also receiving rituximab. Researchers found that only 57% of patients treated with rituximab had a response to one type of pneumococcal vaccine (Pneumovax®) compared with 82% of MTX-only patients.

The ability to maintain a positive delayed-type hypersensitivity (DTH) response to the *Candida albicans* skin test was comparable in both groups with 77.4% of rituximab-treated patients and 70% of MTX-only patients responding. "Our study, the first to examine DTH responses, confirmed that rituximab had no incremental effect on the patient's ability to mount a DTH response," said Dr. Bingham.

Treatment with rituximab produces a rapid depletion of B cells from the circulation, impacting the body's immune function. This depleted B cell pool begins to recover approximately 6-9 months after the initial treatment with rituximab. In his editorial also published in [Arthritis & Rheumatism](#), E. William St. Clair, M.D. from Duke University Medical Center highlighted the need for further research into the effects of rituximab treatment.

"Further studies similar to Bingham et al are necessary to understand the complex effects of rituximab therapy on immune responses," noted Dr. St. Clair. "This study only evaluated immunization responses approximately 6 months after rituximab was administered; the responses

at earlier time points, based on animal studies and its mechanism of action, may have been further attenuated," St. Clair added.

More information: "Immunization Responses in Rheumatoid Arthritis Patients Treated With Rituximab." Clifton O. Bingham III, R. John Looney, Atul Deodhar, Neal Halsey, Maria Greenwald, Christine Coddling, Benjamin Trzaskoma, Flavius Martin, Sunil Agarwal, and Ariella Kelman. *Arthritis & Rheumatism*; Published Online: December 28, 2009 ([DOI: 10.1002/art.25034](https://doi.org/10.1002/art.25034)); Print Issue Date: January 2010.

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