

## **Pediatric Rheumatology Literature Review: An Article No One Should Miss**

Reviewer: Lisabeth V. Scalzi, MD

University Hospitals of Cleveland/Rainbow Babies and Children's Hospital

Editors of Literature Reviews:

Kathleen Haines

Hackensack, NJ

Randy Cron

Childrens Hospital of Philadelphia

**Rituximab Therapy for Multisystem Autoimmune Diseases in Pediatric Patients.** Binstadt BA, Caldas AMC, Turvey, SE, Weinstein HJ, Jackson J, Fuhlbrigge RC, Sundel RP: *J Pediatr* 2003, **143**: 598-604

### **Significance:**

Rituximab is a chimeric murine/ human anti-CD-20 antibody which targets B cells. This paper reviews the authors' experience of four children with multisystem autoimmune diseases who failed initial standard treatment and responded to rituximab therapy. The authors suggest that rituximab may be a therapeutic medication for a variety of autoimmune-mediated diseases. In particular, all of their subjects manifested central nervous system (CNS) disease that responded to the rituximab. Since CD20 is found on immature and mature B cells, but not on plasma cells and T cells, it is less potentially immunosuppressive than other therapeutic agents at the rheumatologist's disposal. It is an extremely promising biologic agent for autoimmune diseases that are triggered by pathogenic autoantibodies or by the presentation of antigens by autoreactive B cells.

Data from the 2003 American College of Rheumatology annual meeting demonstrated its potential and value in a variety of disorders including rheumatoid arthritis, cryoglobulinemia, systemic lupus erythematosus (SLE), and dermatomyositis. Other data from sites in the United States and the United Kingdom, which has not yet been published, is greatly anticipated in order to determine its safety and efficacy in diseases including SLE.

**Findings:** Four patients with autoimmune syndromes responded to treatment with rituximab. The first patient was a 17-year-old male with a SLE-like presentation of pancytopenia, seizures, mononeuritis multiplex, positive autoantibodies including ANA, antiphospholipid antibodies, direct Coombs, anti-neutrophil and anti-platelet antibodies. The second patient was a 15-year-old female with neutropenia, hypothyroidism, bronchiolitis obliterans organizing pneumonia, insulin dependent diabetes (IDDM), demyelinating central nervous system (CNS) disease and hypocomplementemia without autoantibodies. The third patient (the half-brother of the second subject) was a 7-year-old male with a history of IDDM who developed lymphoplasmacytic colitis, hemiplegic migraine, and mediastinal mass with pulmonary nodules that were inaccessible for biopsy and whose autoantibodies were negative except for anti-gliadin antibodies. The fourth patient was a 4-year-old female who had a previous history, at the age of 22 months, of pre-B-cell acute lymphoblastic leukemia treated with chemotherapy for 2 years. She developed a partial complex seizure disorder and choreoathetosis that was believed to be secondary to anti-cardiolipin antibodies; her ANA was negative.

All of these patients failed regimens of immunosuppressive or traditional medications but responded to four weekly infusions of rituximab (375 mg/m<sup>2</sup>). All of the subjects had improvement of their CNS manifestations, but not of their endocrine disease when present. The average time of serum IgG nadir was 4-6 months and 3 of the 4 patients received replacement IVIG.

Although rituximab has been FDA approved only for CD20-positive, B-cell non-Hodgkin's lymphoma, it has also been used for autoimmune disorders including immune thrombocytopenia, autoimmune hemolytic anemia, and SLE.

The authors propose that patients with immune-mediated CNS diseases, such as multiple sclerosis or SLE and other autoantibody associated illnesses, who fail standard immunosuppressant therapy may benefit from treatment with rituximab. Although the data are only representative of 4 patients, rituximab therapy appears promising for children with multisystem autoimmune disorders.