Rituximab Benefit Seen in Childhood Lupus

BY JANE SALODOF MACNEIL
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VERSAILLES, FRANCE — A small retrospective study found the monoclonal antibody rituximab benefited 7 of 11 French children with severe systemic lupus erythematosus.

The wide variation in regimens used at different French centers does not allow any firm conclusions to be drawn, investigator Marjolaine Willems, M.D., said in a presentation at the 12th European Pediatric Rheumatology Congress.

Dr. Willems of Hôpital de Bicêtre, Kremlin-Bicêtre, France, called for prospective trials to assess long-term safety and efficacy of rituximab in comparison with cyclophosphamide. "It needs to be investigated in future prospective studies," she said.

The patients, all girls, were nearly 14 years old on average when they started rituximab treatment. Eight patients had class IV or V nephritis, and two had autoimmune cytopenia. One girl had hypoprothrombinemia, class II nephritis, and pulmonary hypertension.

Nine patients had a prior history of nephritis, and all were on immunosuppressive regimens previously. Two were also treated with cyclophosphamide. The average follow-up was 13 months.

Dr. Willems and her coauthors reported that 9 out of 12 courses of rituximab resulted in complete or partial remissions. Treatment failed in two patients, and was not tolerated in another.

Six of the eight patients with renal involvement achieved complete or partial remissions. Antiphosphoid antibodies became negative in three of four patients. Normalization of CD3 and/or CD4 was reported in four of eight patients.

Five children had mild side effects, such as rash, mild neutropenia, and benign infections. Five others had severe hematologic toxicity, including septicemia, thrombopenia, neutropenia, and lymphopenia.

B-cell depletion appeared to parallel clinical remissions but was not consistent in all patients, according to Dr. Willems. She advocated monitoring B-cell depletion in children treated with rituximab.

Issues that still need to be addressed in pediatric randomized trials include the optimal regimen of rituximab, cotreatment with cyclophosphamide, maintenance of immunosuppression, and long-term effects.

"We've got so much heterogeneity in the rituximab regimens and confounding factors that cannot lead us to a good conclusion," she said in an interview.

The most that can be said is that "some patients who did not respond to cyclophosphamide alone had a good response with rituximab," and some patients who had been taking maintenance therapies without rituximab had a relapse and then did well after adding rituximab to their maintenance therapy. ■

Diagnostic Criteria Drafted For Juvenile Systemic Sclerosis

BY JANE SALODOF MACNEIL
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VERSAILLES, FRANCE — The presence of sclerosis/induration is the cornerstone criterion for confirming the diagnosis of juvenile systemic sclerosis, according to conclusions drawn from an international consensus conference.

In addition, Francesco Zulian, M.D., explained at the 12th European Pediatric Rheumatology Congress, that the diagnosis also requires that patients have at least two of the following minor criteria:

Skin: Sclerodactyly.

Vascular: Raynaud's phenomenon, digital ulcers, nailfold capillary changes.

Gastrointestinal: Gastrointestinal reflux, dysphasia.

Respiratory: Lung fibrosis, pulmonary hypertension, diffuse lung capacity for carbon monoxide.

Renal: Renal crisis, new-onset hypertension.

Cardiac: Heart failure, arrhythmias.

Neurologic: Carpal tunnel syndrome, peripheral neuropathy.

Musculoskeletal: Arthritis, myositis, tendon friction rubs.

Serology: Antinuclear antibodies, systemic sclerosis-selective autoantibodies.

Dr. Zulian of the University of Padua (Italy) emphasized that these criteria are in the draft stage. The next step will be to validate the classification with trials in adult and juvenile patients. Although the system is based on childhood cases, he suggested it might also improve the rate of diagnosing the disease accurately in adults.

'This is a very rare disease, and we need cooperation between different countries. It is a devastating disease, and the mortality is high.'

An added benefit of the project is that "we [now] have an international database we are going to open up and use for future research," he told this newspaper in an interview. "This is a very rare disease, and we need cooperation between different countries. It is a devastating disease, and the mortality is high."

Fifty-five centers in 24 countries contributed data on 205 patients. The cases included 153 patients with systemic sclerosis, 26 patients with overlap syndrome, and another 26 patients with mixed connective tissue disease.

The project, which began in 2002, initially identified 86 preliminary classification criteria, including the three major criteria: sclerosis/induration, Raynaud's phenomenon, and sclerodactyly.

A group of 16 adult and pediatric rheumatologist experts then used the criteria to diagnose 160 patients from records presented at a consensus conference. The case files included children with systemic sclerosis and the confounding diseases.

The experts were able to reach consensus on 127 patients (79%): 70 with juvenile systemic sclerosis and 57 without the condition. They were unable to reach a consensus on 33 patients (21%), Dr. Zulian reported.

As a result of that concensus process, the 86 possible diagnostic factors were narrowed down to a short list. The objectives were "to propose classification criteria that mimic as much as possible the evaluation of physicians attending the consensus conference," and to evaluate how well the criteria distinguish patients who have juvenile systemic sclerosis from those who do not, he said. ■