# Kids With Lupus Get Little Benefit From Statins

BY HEIDI SPLETE

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF RHEUMATOLOGY

ATLANTA – Atorvastatin did not prevent early atherosclerosis in children and adolescents with lupus, based on data from 221 patients aged 10-21 years.

"This is a landmark study in the pediatric rheumatology community," said Dr. Laura Schanberg, co-chief of the division of pediatric rheumatology at Duke University Medical Center in Durham, N.C.

To assess the risk of cardiovascular problems, the researchers used an accepted surrogate marker: an ultrasound measurement of the thickening of the carotid arteries. The study participants underwent ultrasound examinations seven times during the 3-year study period.

Overall, progression of thickening in the arteries was not significantly different between the statin and placebo groups.

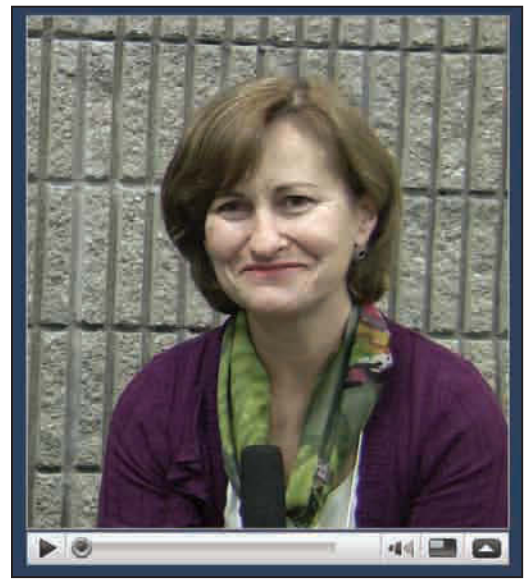
"This was a surprise to us," Dr. Schanberg said. The researchers had expected significantly less carotid intima-media thickening (CIMT) in the statin group.

The data were trending toward a positive effect, but the findings did not show enough benefit to recommend routine statin treatment for most children and adolescents with lupus. The difference in CIMT was 0.0010 mm/year in the statin group, vs. 0.0024 mm/year in the placebo group ($P = .24$).

The statin group did achieve statistically significant reductions in high-sensitivity C-reactive protein levels, total cholesterol, and low-density lipoprotein. Changes in lupus disease activity and damage, quality of life measures, and measures of muscle, liver, and neurotoxicity were similar between the two groups.

Previous studies have shown that lupus is a strong risk factor for cardiovascular problems. Pediatric lupus patients are considered at increased risk because they typically live with the disease for a longer period of time. Statins have not previously been studied as a way to reduce cardiovascular risk in children with lupus, but some clinicians already prescribe statins to children with lupus at especially high risk from factors such as high cholesterol, Dr. Schanberg said.

"We wanted to see whether there was a way to decrease the long-term risk" of cardiovascular problems in children with lupus, she said. In this study, the researchers enrolled patients from 21 sites through the Childhood Arthritis and Rheumatology Research Alliance.



HEIDI SPLETE/ELSEVIER GLOBAL MEDICAL NEWS

**Less carotid intima-media thickening was expected in the statin group, notes Dr. Laura Schanberg at www.rheumatologynews.com.**

All the children received standard lupus care including aspirin, a multivitamin, hydroxychloroquine, and counseling about a low-cholesterol diet and other cardiovascular risk factors. They were randomized to receive atorvastatin or a placebo.

Of note, the study did not include children at especially high risk for cardiovascular problems, such as those with high cholesterol, she said. In fact, a subgroup analysis may reveal certain groups that would benefit from statin use in childhood and adolescence, she said.

Despite the lack of clinical significance, the results showed that atorvastatin was safe and well tolerated in the study population, and Dr. Schanberg advised clinicians to continue prescribing statins for pediatric lupus patients with abnormal cholesterol or lipid levels.

Dr. Schanberg has served on the advisory board for Bristol-Myers Squibb, and Pfizer provided the drugs used in the study. ■

# Protocol Effective for Primary Angiitis of CNS

BY SHARON WORCESTER

FROM THE LANCET

An immunosuppressive treatment regimen was effective for reversing neurological deficits and controlling severe neurologic manifestations of small-vessel childhood primary angiitis of the central nervous system in a relatively large cohort study of the rare inflammatory brain disease.

At a median follow-up of 33 months in the single-center, open-label study, 9 of 19 children studied had a good neurologic outcome based on the pediatric stroke outcome measure (PSOM) after treatment with steroid- and cyclophosphamide-based induction therapy, followed by maintenance therapy with azathioprine or mycophenolate mofetil.

Four of the children remained in remission after as long as 57 months off treatment, reported Dr. Clare Hutchinson and her colleagues at the Hospital for Sick Children, Toronto.

This cohort is the largest to date to prospectively follow children with this recently recognized disease, and it is the first to demonstrate the potential efficacy of immunosuppressive treatment, they wrote (Lancet 2010 Oct. 4 [doi:10.1016/S1474-4422(10)70243-X]).

**VITALS**

**Major Finding:** At a median follow-up of 33 months, 9 of 19 children studied had a good neurologic outcome based on the PSOM after treatment with steroid- and cyclophosphamide-based induction therapy, followed by maintenance therapy with azathioprine or mycophenolate mofetil.

**Data Source:** A single-center, open-label cohort study of 19 children with small-vessel childhood primary angiitis of the CNS.

**Disclosures:** The study authors had no disclosures to report.

To date, a variety of treatments have been tried, but no standardized protocol or documentation of neurologic outcomes have been described.

The 6-month induction phase used in the current study included seven pulses of 500-750 mg/m$^2$ intravenous cyclophosphamide every 4 weeks for 6 months, along with cotrimoxazole prophylaxis. Patients also received 2 mg/kg of prednisone daily (up to 60 mg), weaned every 4 weeks to 50, 40, 30, 25, and 20 mg daily, and then by 2.5 mg every 4 weeks until completed. Calcium and vitamin D supplementation was given during prednisone treatment, and anticonvulsants and antipsychotics were given as needed.

The 18-month maintenance phase included 800-1,200 mg/m$^2$ of mycophenolate mofetil daily up to 2,000 mg, or 2-3 mg/kg azathioprine daily up to 150 mg. Calcium and vitamin D supplementation continued until prednisone weaning was completed; anticonvulsants and antipsychotics were continued as needed.

The regimen was well tolerated; two infections requiring hospitalization occurred, including one during induction, and one during maintenance, but there were no deaths. However, a high proportion of patients experienced a flare of neurologic symptoms or significant adverse events such as lymphopenia, pancytopenia, and infection while on azathioprine. All of these events resolved after the patients were switched to mycophenolate mofetil, prompting the investigators to recommend that mycophenolate mofetil be used during the maintenance phase of this protocol rather than azathioprine.

This immunosuppressive therapy regimen has the potential for improving long-term neurologic outcomes. "We therefore recommend this protocol for treatment of patients with small-vessel childhood primary angiitis of the CNS," they wrote.

Children in the study were aged 5-17 years, with a median age of 9.8 years. Patients were assessed using clinical, neurologic, and quality of life measures, and laboratory markers were done at baseline, and at 3, 6, 9, 12, 18, and 24 months, and then yearly for the duration of follow-up. Brain imaging was done at baseline and then every 6 months for 24 months.

The number of patients in the study was small largely because of the requirement of a brain biopsy to confirm the diagnosis, the investigators said.

Another limitation is that the PSOM, although a useful measure of neurologic deficits on the basis of clinical findings, does not measure quality of life or account for other neurologic sequelae such as academic impairments, psychiatric manifestations, and ongoing seizure disorder. ■

**VIEW ON THE NEWS**

## A Useful Framework

These promising findings are "a crucial and necessary first step in identifying the optimum treatment for children with small-vessel childhood primary angiitis of the CNS and will provide a useful reference for future studies of similar or alternative treatment options," according to Dr. Neil. R. Friedman.

In fact, the study will undoubtedly serve as the basis for ongoing and future studies of this disease, he added, noting that although the small sample size precludes the recommended treatment regimen from being considered the standard of care in patients with small-vessel primary angiitis of the CNS, the study does provide a useful framework for managing and treating childhood stroke.

Questions that remain unanswered about the disease, according to Dr. Friedman, include whether it is homogenous, which potential risk factors at presentation affect disease course and outcome, and whether thrombosis contributes to stroke risk because of vascular inflammation.

DR. FRIEDMAN *is with the Center for Pediatric Neurology at the Cleveland Clinic. His comments are derived from an accompanying editorial (Lancet 2010 Oct. 4 [doi:10.1016/S1474-4422(10)70244-1]). He has served as a speaker for Genzyme.*