



## Arthritis News

**Media Contact:** Tammy McCoy  
(404) 633-3777 (until Oct. 15)  
(210) 582-7010 (Oct. 16–Oct. 21)  
[tmccoy@rheumatology.org](mailto:tmccoy@rheumatology.org)

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### **DMARDS SHOW ON-GOING BENEFIT IN JUVENILE ARTHRITIS PATIENTS**

SAN ANTONIO, TEXAS—Children with juvenile arthritis have long-term improvement in joint pain and swelling when treated with leflunomide or methotrexate, drugs commonly used to treat rheumatoid arthritis in adults, according to research presented this week at the American College of Rheumatology Annual Scientific Meeting in San Antonio, Texas.

One in every 1,000 children will develop juvenile rheumatoid arthritis (also referred to as JRA or juvenile chronic arthritis). The resulting joint inflammation can last from several months to many years, sometimes extending into adulthood. These patients are often treated with disease-modifying antirheumatic drugs (DMARDS) such as methotrexate and leflunomide to reduce or prevent joint damage, and preserve joint integrity and function. In a trial being conducted to assess the on-going efficacy, safety and tolerance to leflunomide and methotrexate in children with juvenile rheumatoid arthritis, researchers studied 94 patients between the ages of three and 17 in a 16-week randomized controlled trial. Patients were given either leflunomide or methotrexate, at a dose based on body weight, and assessed every four weeks for improvement in arthritis signs and symptoms including physical function. Seventy of the 94 patient were then enrolled in a 32-week blinded extension study, and re-assessed every eight weeks for efficacy and safety.

Results showed that both drugs were well tolerated and that the improvements patients had in their arthritis during the first 16 weeks, including physical function, were maintained throughout the 48-week test period. Physical function was measured by the Childhood Health Assessment Questionnaire which assesses ability to perform daily activities such as walking, dressing, and eating.

“Not every child with juvenile arthritis responds to treatment with methotrexate, and it is important to have other treatment alternatives,” said Earl Silverman, MD, Hospital for Sick Children, Toronto, Canada, and an investigator in the study. “Leflunomide, a tablet taken orally, is an effective and well-tolerated alternative to methotrexate for these patients.”

The American College of Rheumatology is the professional organization for rheumatologists and health professionals who share a dedication to healing, preventing disability and curing arthritis and related rheumatic and musculoskeletal diseases. For more information on the ACR’s annual meeting, see [www.rheumatology.org/annual](http://www.rheumatology.org/annual).

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*Editor’s Notes: Dr. Silverman will present this research during a scientific session at the ACR Annual Scientific Meeting from 12:15–2:00 PM CT (1:15–3:00 PM ET) Monday, October 18, in Exhibit Hall C–D of the Henry B. González Convention Center. He will be available for media questions during a briefing at 1:30 PM CT (2:30 PM ET) on Tuesday, October 19, in the on-site Press Conference Room, Room 218.*

## Durability of Efficacy, Safety, and Tolerability of Leflunomide (LEF) or Methotrexate (MTX) Over 48 Weeks of Treatment in Pediatric Patients With Juvenile Rheumatoid Arthritis (JRA)

Earl Silverman<sup>1</sup>, Richard Mouy<sup>2</sup>, Lynn Spiegel<sup>1</sup>, Lawrence Jung<sup>3</sup>, Rotraud Saurenmann<sup>4</sup>, Pekka Lahdenne<sup>5</sup>, Ilona Szer<sup>6</sup>, Karen Simpson<sup>7</sup>, John A. Stewart<sup>8</sup>, Vibeke Strand<sup>9</sup>. <sup>1</sup>Hospital for Sick Children, Toronto, ON, Canada; <sup>2</sup>Hopital des Enfants Malades, Paris, France; <sup>3</sup>Creighton University Medical Center, Omaha, NE; <sup>4</sup>University Children's Hospital, Zurich, Switzerland; <sup>5</sup>Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland; <sup>6</sup>Children's Hospital San Diego, San Diego, CA; <sup>7</sup>Aventis Pharmaceuticals, Bridgewater, NJ; <sup>8</sup>Aventis Pharma Canada, Laval, PQ, Canada; <sup>9</sup>Stanford University, Palo Alto, CA

**Purpose:** To evaluate durability of efficacy, continued safety, and tolerability of LEF or MTX treatment in subjects with polyarticular course JRA who enrolled in a 32-week extension after completing 16 weeks of treatment.

**Methods:** 94 patients 3–17 years old enrolled in a 16-week randomized controlled trial (RCT). Patients received LEF according to body weight (10 mg every other day, 10 mg/d, or 20 mg/d; loading dose 100 mg/d for 1–3 d, respectively) or MTX 0.5 mg/kg/week up to 25 mg/week. Of the 86 completing the 16-week RCT, 70 subsequently enrolled into a 32-week blinded extension. Percent Improvement Index (PII) and JRA Definition of Improvement  $\geq 30\%$  responses (JRA<sub>30</sub>) were assessed at baseline, every 4 weeks for the RCT, and every 8 weeks for the 32-week extension.

**Results:** Results from the 16-week RCT were presented previously (Silverman et al, ACR 2003; Abstract LB2). Median disease duration was 0.33 y in both randomized groups at baseline. In the extension trial, the PII at week 16 was maintained at week 48 for both LEF (-54.66% and -55.36%,  $P=0.088$ ) and MTX (-57.96% and -65.51%,  $P=0.058$ ). The JRA<sub>30</sub> responder rate was the same at weeks 16 and 48 within each treatment group (LEF 78.8%; MTX 91.4%). JRA<sub>50</sub> and JRA<sub>70</sub> responder rates at week 16 were also maintained at week 48 for both LEF and MTX. Improvement in physical function (Childhood Health Assessment Questionnaire Disability Index) was also maintained between week 16 and 48 in both treatment groups (LEF: -0.49 and -0.51; MTX: -0.45 and -0.55). Both drugs were generally well tolerated; in the extension, 1 LEF subject and 5 MTX subjects withdrew because of an adverse event. As in the initial 16-week RCT, transaminase elevations were more frequent with MTX over the 32-week extension (n=11 vs n=5 for LEF).

**Conclusions:** Both LEF and MTX resulted in clinically meaningful improvements by JRA<sub>30</sub> and PII. At 48 weeks, clinical benefit was maintained in both treatment groups. LEF is an effective and well-tolerated alternative to MTX for polyarticular JRA.

### Within-Group Comparisons Between Week 16 and 48 of Treatment

	Week 16	Week 48	P value
PII, adjusted mean (SE)			
LEF (N=33)	-54.66 (3.17)	-55.36 (3.17)	0.8774
MTX (N=35)	-57.96 (2.72)	-65.51 (2.72)	0.0580
JRA <sub>30</sub> , n (%)			
LEF (N=33)	26 (78.8)	26 (78.8)	1.0000
MTX (N=35)	32 (91.4)	32 (91.4)	1.0000
JRA <sub>50</sub> , n (%)			
LEF (N=33)	24 (72.7)	25 (75.8)	0.7389
MTX (N=35)	30 (85.7)	30 (85.7)	1.0000
JRA <sub>70</sub> , n (%)			
LEF (N=33)	18 (54.5)	23 (69.7)	0.0956
MTX (N=35)	23 (65.7)	29 (82.9)	0.0578

**Disclosure:** E. Silverman, Aventis Pharmaceuticals 5; R. Mouy, None; L. Spiegel, None; L. Jung, None; R. Saurenmann, None; P. Lahdenne, None; I. Szer, None; K. Simpson, Aventis Pharmaceuticals 3; J.A. Stewart, Aventis Pharmaceuticals 3; V. Strand, Aventis 5; Abbott Immunology 5; Centocor 5, 8; Amgen 5, 8; Pfizer 5, 8.

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None—Nothing to disclose; 1—Stock options or bond holdings in a for-profit corporation or self-directed pension plan; 2—Research grants;  
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