

Cancer rate 4 times higher in children with juvenile arthritis

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New research reports that incident malignancy among children with juvenile idiopathic arthritis (JIA) is four times higher than in those without the disease. Findings now available in *Arthritis & Rheumatism*, a journal published by Wiley-Blackwell on behalf of the American College of Rheumatology (ACR), suggest JIA treatment, such as tumor necrosis factor (TNF) inhibitors, does not necessarily explain the development of cancer in this pediatric population.

Children with JIA experience symptoms similar to adults with [arthritis](#) including joint pain, swelling, tenderness and stiffness. JIA is a general term used to describe the various chronic arthritis diseases in [children](#) and affects roughly 294,000 under the age of 17 in the U.S. according to a 2008 report from the National Arthritis Data Workgroup.

One of the drug types used to treat childhood and adult arthritis, along with a number of other rheumatic conditions, is TNF inhibitors. Studies have reported that more than 600,000 people worldwide have received anti-TNF therapy since their introduction 15 years ago. However, possible cancer risk has been associated with treatment, prompting the U.S. Food and Drug Administration (FDA) to place "black box" warnings of the potential malignancy risk on TNF inhibitors labels.

In the present study Dr. Timothy Beukelman from the University of Alabama at Birmingham and colleagues conducted one of the largest investigations into the rates of incident malignancy among JIA pediatric patients relative to their treatment. Using data from the U.S. Medicaid

records from 2000 through 2005, researchers identified 7,812 children with JIA and two comparator groups without JIA; one group with asthma (652,234 children) and the second with attention-deficit hyperactivity disorder (ADHD; 321,821 children).

The team categorized patients' treatment with methotrexate and TNF inhibitors as "ever" or "never" used, though many children with JIA did not receive either of these treatments during the study. The research team did not have access to detailed medical records, and therefore categorized the identified incident malignancies as "possible," "probable," or "highly probable."

Children diagnosed with JIA had a total follow-up time of 12,614 person-years with 1,484 children in this group contributing 2,922 person-years of anti-TNF exposure. The team determined that among all children with JIA compared to those without JIA, the incidence rate was 4.4 times higher for probable and highly probable malignancies. Pediatric JIA patients treated with methotrexate without TNF inhibitors had a similarly increased incidence of cancer, which was 3.9 times higher than children without JIA. No probable or highly probable malignancies were identified in patients following any use of anti-TNF during the study period.

In a related editorial published today in *Arthritis & Rheumatism*, Dr. Karen B. Onel and Dr. Kenan Onel from the University of Chicago state that the Beukelman et al. study indicates that children with JIA may be at increased cancer risk from the disease, but suggests that anti-TNF therapy may not be associated with a further increased cancer risk. Dr. Kenan Onel cautions, "Larger studies in different populations and with longer follow up are required to confirm Dr. Beukelman's findings."

The editorial authors point out that most patients in this study were treated with etanercept, a soluble TNF receptor blocker, and the

investigation of other anti-TNF agents working by different mechanisms may yield different results. Nonetheless, Dr. Onel argues, "By focusing on the possible cancer risk associated with the use of TNF inhibitors, the underlying [cancer risk](#) associated with JIA may have been understated, and it is important to make patients, families, and physicians aware of the possible late consequences of this disease."

Dr. Beukelman concludes, "While our findings show children with JIA have a higher incidence of cancer compared to peers without JIA, the greater frequency of [malignancy](#) does not appear to be necessarily associated with treatment, including use of TNF inhibitors. This highlights the critical importance of appropriate comparator groups when evaluating the safety of new medications. Further confirmation of our findings with large-scale and long-term investigation of the association between cancer and JIA, and its treatment is needed."

More information: "Rates of Malignancy Associated with Juvenile Idiopathic Arthritis and Its Treatment." Timothy Beukelman, Kevin Haynes, Jeffrey R Curtis, Fenglong Xie, Lang Chen, Christina J. Bemrich-Stolz, Elizabeth Delzell, Kenneth G Saag, Daniel H Solomon, James D Lewis on behalf of the Safety Assessment of Biological thERapeutics (SABER) Collaboration. *Arthritis & Rheumatism*; Published Online: February 13, 2012 ([DOI: 10.1002/art.34348](#)).

Editorial: "TNF inhibitors and Cancer in JIA: Disentangling the Web." Karen B Onel and Kenan Onel. *Arthritis & Rheumatism*; Published Online: February 13, 2012 ([DOI: 10.1002/art.34349](#)).

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