Newly approved oral medication slows rheumatoid arthritis joint damage

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A Phase 3 clinical trial demonstrates that tofacitinib improves disease activity and inhibits progression of joint damage in rheumatoid arthritis (RA) patients who did not respond to methotrexate (MTX). Results of the 12-month interim analysis of the efficacy of tofacitinib appear in *Arthritis & Rheumatism*, a journal published by Wiley on behalf of the American College of Rheumatology (ACR).

RA is a chronic, autoimmune disease that causes inflammation, pain and swelling of the joints. Over time, RA may destroy joints, impair daily function, and lead to significant disability. The World Health Organization (WHO) estimates that RA affects up to one percent of individuals worldwide and 1.3 million of those are Americans according to the ACR.

"Tofacitinib inhibits Janus kinase (JAK) enzymes that are found in white blood cells, and which help to regulate the immune system," explains lead investigator Dr. Désirée van der Heijde from Leiden University Medical Center in The Netherlands. "We are examining the oral JAK inhibitor, tofacitinib, as a disease-modifying anti-inflammatory drug (DMARD) and for its ability to modulate the immune system in those with RA."

In this 24-month, double-blind, placebo-controlled study, 797 participants were randomized (4:4:1:1) to receive 5 mg of tofacitinib twice daily (BID) (n=321); 10 mg of tofacitinib BID (n=316); placebo to tofacitinib 5 mg BID (n=81); or placebo to tofacitinib10 mg BID

(N=79). Participants had a mean age of 53 years, 85% were female, 54% were non-Caucasian, and the mean duration of RA was 9 years. Patients who did not respond to placebo were advanced to tofacitinib at three months and the remaining placebo participants at six months.

Results from a planned 12-month interim analysis from the 24-month, Phase 3 trial show that tofacitinib is effective in preserving joint structure in patients with moderate to severe RA who had an inadequate response to MTX therapy. The difference from placebo in mean change from baseline in the van der Heijde modified total Sharp score was statistically significant for tofacitinib at 10 mg BID but not at 5 mg BID at month 6 (co-primary endpoint) and month 12.

Patients treated with tofacitinib at both 5 and 10 mg BID doses displayed less progression of joint erosion and joint space narrowing compared to placebo at six and twelve months. Change in the joint space narrowing score was statistically significant at month 12 for the tofacitinib groups versus placebo. Researchers also reported that the proportion of patients with no radiographic progression in the tofacitinib groups was significantly greater compared to placebo.

Analysis confirms previous results that tofacitinib is effective in treating RA symptoms and reducing the rate of joint damage. "Our findings provide the first evidence that tofacitinib reduces the progression of structural damage in RA patients with active disease," concludes Dr. van der Heijde.

The U.S. Food and Drug Administration (FDA) approved tofacitinib—the first oral JAK inhibitor for treatment of moderate to severe RA—on November 6, 2012. A twice daily 5 mg dose of tofacitinib was approved by the FDA for RA patients who are unresponsive or intolerant to MTX. The drug is being marketed by Pfizer as Xeljanz®.

More information: "Tofacitinib (CP-690,550) in Patients with Rheumatoid Arthritis on Methotrexate: 12-Month Data from a 24-Month Phase 3 Randomized Radiographic Study." Desiree van der Heijde, Yoshiya Tanaka, Roy Fleischmann, Edward Keystone, Joel Kremer, Cristiano Zerbini, Mario H.Cardiel, Stanley Cohen, Peter Nash, Yeong-Wook Song, Dana Tegzova, Bradley T. Wyman, David Gruben, Birgitta Benda, Gene Wallenstein, Sriram Krishnaswami, Samuel H. Zwillich, John D. Bradley, Carol A. Connel and the ORAL Scan investigators. Arthritis & Rheumatism; January 24, 2013 (DOI: 10.1002/art.37816).

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