



Arthritis News

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**Embargoed for Release at
6:15 PM ET, Sunday Oct. 17, 2004**

INFLIXIMAB RISK OF SERIOUS INFECTION IN CLINICAL PRACTICE EQUAL TO METHOTREXATE WHEN USED IN RECOMMENDED DOSE

SAN ANTONIO, TEXAS—Rheumatoid arthritis patients receiving the recommended starting dose (3mg/kg) of infliximab (REMICADE®) have no more serious rate of infections than do patients taking methotrexate alone; however, patients undergoing induction and treatment with a high dose have more problems with infections, according to research presented this week at the American College of Rheumatology Annual Scientific Meeting in San Antonio, Texas.

Biologic disease-modifying anti-rheumatic drugs (DMARDs), like infliximab, have been given to more than 700,000 people worldwide since their introduction in 1998. These drugs, designed to suppress the inflammation associated with rheumatoid arthritis, have been shown to reduce the signs and symptoms of rheumatoid arthritis, improve physical function and inhibit the progression of joint damage to the joints. But, as is true of any medication that affects the immune system, a concern with this class of medications is that they may increase the risk of infections.

To evaluate the risk of serious infections associated with the use of infliximab plus methotrexate relative to placebo, researchers conducted a year-long multinational double-blind study on 1,082 patients in 12 countries.

Patients were randomized into one of three groups using a 1:1:1 ratio (placebo/methotrexate n=363; 3 mg/kg infliximab plus methotrexate arm n=360; 10 mg/kg infliximab plus methotrexate arm n=361). Group one received placebo for the first 22 weeks, crossing over to 3mg/kg every eight weeks of infliximab up through week 54. Group two was given a dose of 3mg/kg of infliximab at the outset and weeks two and six, followed by every eight weeks until week 22. The dose was then increased by increments of 1.5mg/kg every eight weeks if needed. Group three received a dose of 10mg/kg (outset, weeks two and six, followed by every eight weeks) throughout the duration of the study. All patients also received methotrexate through the course of the study.

Findings demonstrated that over the course of a year, the relative risk of serious infection with infliximab given at the recommended induction and maintenance regimen of 3mg/kg was similar to placebo, even though some patients had their dose escalated in the second half of the study. However, infliximab given at the higher induction and maintenance regimen of 10mg/kg was associated with an increased risk of serious infections.

“This study underscores the relative safety of infliximab, when used properly,” said David Yocum, MD, University of Arizona, Tucson, and an investigator in the study. “With careful monitoring, more rheumatoid arthritis patients can safely realize the significant benefits of biologic anti-rheumatic therapy.”

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.

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Editor’s Notes: Dr. Yocum will present this research during a scientific session at the ACR Annual Scientific Meeting from 2:30–2:45 PM CT (3:30–3:45 PM ET) on Wednesday, October 20, in Ballroom A of the Henry B. González Convention Center. He will be available for media questions during a briefing at 8:30 AM CT (9:30 AM ET) on Tuesday, October 19, in the on-site Press Conference Room, Room 218.

The Safety and Efficacy of Infliximab in RA: 1-year Results of a Large, Randomized, Placebo-Controlled Trial in Patients with Various Comorbidities and Background Treatments As Encountered in Clinical Practice

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Objectives: Patients diagnosed with rheumatoid arthritis (RA) with various comorbidities and background treatments as encountered in clinical practice were assessed for the relative risk of serious infection after treatment with infliximab (IFX).

Methods: Patients with active RA, despite concomitant methotrexate (MTX), were randomly assigned to receive placebo (Group 1) or IFX 3 mg/kg (Group 2) or 10 mg/kg (Group 3) at wks 0, 2, 6, and 14. Patients initially assigned to placebo (ie, Group 1) crossed over to receive IFX 3 mg/kg at wks 22, 26, 30, 38, and 46. Patients in Group 2 had their dose increased, beginning at wk 22, in increments of 1.5 mg/kg every 8 weeks if specific criteria were met. Patients in Group 3 continued to receive 10 mg/kg through wk 46. All patients received concomitant MTX (<25 mg/week). The primary endpoint of the study was the proportion of patients who developed serious infections (ie, serious adverse events that the investigator reported as infections) through wk 22.

Results: Overall, 1082 patients in 12 countries were treated (361 [Group 1], 360 [Group 2], 361 [Group 3]). During the first 22 wks, 1.7%, 1.7%, and 5.3% of patients in Group 1, Group 2, and Group 3, respectively, reported serious infections, rates that were lower than those reported in previous clinical trials. The relative risk (95% CI) of serious infection was 1.00 (0.32, 3.14) (p=0.99), 3.29 (1.30, 8.35) (p=0.008), and 2.13 (0.86, 5.23) (p=0.09) in the 3 mg/kg, 10 mg/kg, and combined IFX groups, respectively, relative to placebo. Through wk 54, 3.6% of patients in Group 1, 3.6% of patients in Group 2, and 8.3% of patients in Group 3 reported serious infections. Serious infections through week 54 included pneumonia (5, 5, and 7 patients, respectively), active TB (1, 2, and 4), abscess (2, 0, and 5), pyelonephritis (3, 0, and 1), and sepsis (0, 0, and 2). All cases of TB occurred either in Europe or South America. The incidences of other adverse events were comparable among the three groups. At wk 22, 26%, 58%, and 61% of patients in Groups 1, 2, and 3, respectively, achieved ACR 20 response (p<0.001) and the efficacy was maintained through wk 54.

Conclusion: The relative risk of serious infections in patients receiving IFX 3 mg/kg was similar to that of placebo. However, subjects receiving the unlabeled induction and maintenance regimen of 10 mg/kg experienced a higher incidence of serious infections, including TB. The efficacy of IFX and types of serious infections observed in this study were similar to those reported in previous clinical trials.

Disclosure: D. Yocum, Centocor, Inc. 2, 5, 8; F. Wolfe, Centocor, Inc. 2; M.U. Rahman, Centocor, Inc. 1, 3; J. Han, Centocor, Inc. 1, 3; A. Berman, Centocor, Inc. 2; I. Strusberg, Centocor, Inc. 2; P. Geusens, None; R. Westhovens, Centocor, Inc. 5

Author disclosure legend—Authors' disclosures of third-party relationships are listed in numeric format according to the following listing:

None—Nothing to disclose; 1—Stock options or bond holdings in a for-profit corporation or self-directed pension plan; 2—Research grants; 3—Employment (full or part-time); 4—Ownership or partnership; 5—Consulting fees or other remuneration (payment); 6—Non-remunerative positions of influence such as officer, board member, trustee or public spokesperson; 7—Receipt of royalties; 8—Speakers bureau.