



## **Remicade<sup>®</sup> Study Results Show Greater Steroid-Free Remission and Mucosal Healing Compared With Conventional Immunomodulator Azathioprine in Treatment of Crohn's Disease**

### **Findings Published in Today's New England Journal of Medicine**

HORSHAM, PA, April 15, 2010 - Findings published today in The New England Journal of Medicine from a first-of-its-kind comparator trial evaluating the anti-tumor necrosis factor (TNF)-alpha biologic treatment REMICADE (infliximab) in the treatment of moderately to severely active Crohn's disease in patients who were naïve to immunomodulator and biologic therapy, showed that a significantly greater proportion of patients receiving REMICADE achieved steroid-free remission and mucosal healing compared with patients receiving azathioprine.

The results of the Phase 4 Study of Biologic and Immunomodulator Naïve Patients in Crohn's (SONIC) clinical trial published in today's New England Journal of Medicine is the first of its kind to compare REMICADE, an anti-TNF-alpha therapy, with an immunomodulator (azathioprine) in patients with moderate to severe Crohn's disease. Azathioprine (AZA) is not approved by the United States Food and Drug Administration (FDA) for the treatment of Crohn's disease; however, it is widely used by gastroenterologists and other physicians in the U.S. to treat patients with Crohn's disease. Azathioprine is approved for the treatment of Crohn's disease in some countries outside the U.S.

Crohn's disease is a chronic inflammatory disease of the gastrointestinal tract that affects approximately 500,000 Americans. Symptoms of the disease can vary but often include abdominal pain and tenderness, frequent diarrhea, rectal bleeding, weight loss and fever. The cause of Crohn's disease is not known.

"As the first trial to compare an anti-TNF therapy with an immunomodulator in patients who have failed 5-ASA and/or steroids, the SONIC trial has the potential to change how we currently treat patients with moderate to severe Crohn's disease," said Dr. Jean-Frédéric Colombel, Professor of Hepatogastroenterology, Centre Hospitalier Universitaire de Lille (France) and principal investigator. "The results provide new insights into the benefits of starting REMICADE alone or in combination with azathioprine - earlier in the treatment of moderate to severe Crohn's disease."

Investigators reported that at the week 26 primary endpoint of the trial, 57 percent of patients receiving REMICADE combination therapy (REMICADE and azathioprine together) and 44 percent of patients receiving REMICADE monotherapy achieved steroid-free remission compared with 30 percent of patients receiving azathioprine alone (P<0.001 REMICADE with azathioprine vs. azathioprine monotherapy; P=0.006 REMICADE monotherapy vs. azathioprine monotherapy; P=0.02 REMICADE with azathioprine vs. REMICADE monotherapy).

In addition to improved rates of steroid-free remission in patients receiving REMICADE, the data showed that a greater proportion of patients receiving REMICADE achieved mucosal healing (i.e. complete absence of mucosal ulceration at week 26 in patients with mucosal ulcerations at baseline) a secondary endpoint of the study. Forty-four percent of patients receiving REMICADE combination therapy and 30 percent receiving REMICADE monotherapy achieved mucosal healing compared with 17 percent of patients receiving azathioprine alone (P<0.001 REMICADE with azathioprine vs. azathioprine monotherapy; P=0.02 REMICADE monotherapy vs. azathioprine monotherapy; P=0.06 REMICADE with azathioprine vs. REMICADE monotherapy). The P values for all secondary endpoints should be considered nominal since no adjustments were made for multiple comparisons.

Patients participating in the SONIC study through 30 weeks were given the option of continuing in a blinded study extension through 50 weeks. At week 50, REMICADE showed similar significant therapeutic benefit over azathioprine monotherapy.

The data also showed that the safety profile of REMICADE in combination or as monotherapy was similar to that of azathioprine monotherapy in the study. Through week 30, 24 percent of patients receiving azathioprine monotherapy experienced one or more serious adverse events compared with 16 and 14 percent of patients receiving REMICADE monotherapy and REMICADE with azathioprine, respectively. This includes two patients receiving azathioprine monotherapy who developed colon cancer, one patient receiving azathioprine monotherapy who died following a colectomy and one patient receiving REMICADE combination therapy who was diagnosed with tuberculosis. Serious infections were reported in 6 percent of patients in the azathioprine monotherapy group, 5 percent in the REMICADE monotherapy group and 4 percent in the REMICADE combination therapy group.

A final safety analysis for the entire study included data through week 54. The proportion of patients with one or more serious

adverse events during the study was 27 percent (n=43) in the AZA monotherapy treatment group, 24 percent (n=39) in the REMICADE monotherapy treatment group and 15 percent (n=27) in the combined REMICADE and AZA treatment group. No new serious adverse events, such as opportunistic infections, malignancies or death, were reported between weeks 30 and 54.

In 1998, REMICADE became the first anti-TNF-alpha therapy approved by the FDA for the treatment of moderately to severely active Crohn's disease for the reduction of the signs and symptoms in patients who have an inadequate response to conventional therapy. During the past decade, REMICADE has also become the first and only anti-TNF-alpha therapy approved by the FDA for the treatment of moderately to severely active ulcerative colitis, in patients with an inadequate response to conventional therapy, a related inflammatory bowel disease. REMICADE is also approved for the treatment of pediatric patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapies.

The SONIC study was supported by Centocor Ortho Biotech Inc.

### **About SONIC**

SONIC was a multicenter, Phase 4, randomized, double-blind, controlled clinical trial designed to compare the efficacy and safety of REMICADE monotherapy, azathioprine monotherapy and combination therapy with the 2 drugs in patients with moderately to severely active Crohn's disease who were naive to immunomodulator and biologic therapy. A total of 508 patients from the U.S., Europe and Israel were enrolled in the study and were randomized into three groups; 170 patients received azathioprine 2.5 mg/kg/day and placebo infusions, 169 patients received REMICADE 5 mg/kg infusions at weeks 0, 2, 6 and every 8 weeks thereafter with placebo capsules and 169 patients received REMICADE 5 mg/kg at weeks 0, 2, 6 and every 8 weeks thereafter and azathioprine 2.5 mg/kg/day. The primary endpoint of SONIC was to assess the induction of steroid-free remission at week 26. Fifty-two percent of patients enrolled in SONIC were male and patients had a median age of 34-years-old, median weight of 70 kg, median disease duration of 2.3 years and median baseline Crohn's Disease Activity Index (CDAI) score of 275. Patients completing treatment through week 30, and who, in the opinion of the investigator, may benefit from continued treatment, entered into the study extension beginning at week 30 through week 50.

For more information regarding the safety profile for REMICADE, please see "Important Safety Information" below.

### **About Crohn's Disease**

Crohn's disease, a chronic inflammatory disease of the gastrointestinal tract, affects approximately 500,000 Americans, including approximately 150,000 pediatric patients. The cause of Crohn's disease is not known, but the disease is associated with abnormalities of the immune system that could be triggered by a genetic predisposition or diet and other environmental factors. Symptoms of Crohn's disease can vary but often include abdominal pain and tenderness, frequent diarrhea, rectal bleeding, weight loss and fever. There is currently no cure for Crohn's disease.

### **About REMICADE**

REMICADE was the first anti-TNF-alpha treatment to be approved in three different therapeutic areas: gastroenterology, rheumatology and dermatology. REMICADE has demonstrated broad clinical utility with indications in Crohn's disease (CD), rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), ulcerative colitis (UC), pediatric Crohn's disease (PCD) and psoriasis (PsO). The safety and efficacy of REMICADE have been well established in clinical trials over the past 17 years and through commercial experience with more than one million patients treated worldwide.

In the U.S., REMICADE is approved for the following indications:

- Reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in patients with moderately to severely active RA, when administered in combination with methotrexate.
- Reducing signs and symptoms in patients with active AS.
- Reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients with moderately to severely active CD who have had an inadequate response to conventional therapy.
- Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD.
- Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in patients with moderately to severely active UC who have had an inadequate response to conventional therapy.
- Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage and improving physical function in patients with PsA.
- Treatment of adult patients with chronic severe plaque PsO who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

REMICADE is unique among available anti-TNF biologic therapies. It is the only anti-TNF biologic administered directly by caregivers in the clinic or office setting. REMICADE is a two-hour infusion administered every 4 or 8 weeks (indication-dependent), following a standard induction regimen that requires treatment at weeks 0, 2 and 6. As a result, REMICADE patients may require as few as six treatments each year as maintenance therapy.

## **Important Safety Information**

Only a doctor can recommend a course of treatment after checking a patient's health condition. REMICADE<sup>®</sup> (infliximab) can cause serious side effects such as lowering your ability to fight infections. There are reports of serious infections caused by viruses, fungi or bacteria that have spread throughout the body, including tuberculosis (TB) and histoplasmosis. Some of these infections have been fatal. Your doctor should monitor you closely for signs and symptoms of TB during treatment with REMICADE<sup>®</sup>.

Unusual cancers have been reported in children and teenage patients taking TNF-blocker medicines. A rare form of fatal lymphoma has occurred mostly in teenage or young adult males with Crohn's disease or ulcerative colitis who were taking REMICADE<sup>®</sup> and azathioprine or 6-mercaptopurine. For children and adults taking TNF blockers, including REMICADE<sup>®</sup>, the chances of getting lymphoma or other cancers may increase.

Patients should discuss any concerns about their health and medical care with their doctor.

Patients should let their doctors know if they have or ever had any of the following:

- Tuberculosis (TB) or have been near someone who has TB. Your doctor will check you for TB with a skin test. If you have latent (inactive) TB, you will begin TB treatment before you start REMICADE<sup>®</sup>.
- Lived in a region where certain fungal infections like histoplasmosis or coccidioidomycosis are common.
- Infections that keep coming back, have diabetes or an immune system problem.
- Any type of cancer or a risk factor for developing cancer, for example, chronic obstructive pulmonary disease (COPD) or had phototherapy for psoriasis.
- Heart failure or any heart condition. Many people with heart failure should not take REMICADE<sup>®</sup>.
- Hepatitis B virus (HBV) infection or think you may be a carrier of HBV.
- Nervous system disorders (like multiple sclerosis or Guillain-Barré syndrome).
- Also tell your doctor about any medications you are taking, including vaccines or Kineret (anakinra), and if you are pregnant, plan to become pregnant or are nursing. Adults and children should not receive a live vaccine while taking REMICADE<sup>®</sup>.

The following serious (sometimes fatal) side effects have been reported in people taking REMICADE.

Patients should tell their doctors right away if you have any of the signs listed below:

- Infections (like TB, blood infections, pneumonia)-fever, tiredness, cough, flu, or warm, red or painful skin or any open sores. REMICADE<sup>®</sup> can make you more likely to get an infection or make any infection that you have worse.
- Lymphoma, or any other cancers in adults and children.
- Heart failure-new or worsening symptoms, such as shortness of breath, swelling of your ankles or feet, or sudden weight gain.
- Reactivation of HBV-feeling unwell, poor appetite, tiredness, fever, skin rash and/or joint pain.
- Liver injury-jaundice (yellow skin and eyes), dark brown urine, right-sided abdominal pain, fever, or severe tiredness.
- Blood disorders-fever that doesn't go away, bruising, bleeding or severe paleness.
- Nervous system disorders-numbness, weakness, tingling, changes in your vision or seizures.
- Allergic reactions during or after the infusion-hives, difficulty breathing, chest pain, high or low blood pressure, swelling of face and hands, and fever or chills.
- Lupus-like syndrome-chest discomfort or pain that does not go away, shortness of breath, joint pain, rash on the cheeks or arms that gets worse in the sun. The more common side effects with REMICADE<sup>®</sup> are respiratory infections (that may include sinus infections and sore throat), headache, rash, coughing and stomach pain.
- Psoriasis-new or worsening psoriasis such as red scaly patches or raised bumps on the skin that are filled with pus.

Please read important information about REMICADE, including full U.S. prescribing information and Medication Guide, at [www.remicade.com](http://www.remicade.com).

## **About Centocor Ortho Biotech Inc.**

Centocor Ortho Biotech Inc. redefines the standard of care in immunology, nephrology and oncology. The company was formed when Centocor, Inc. and Ortho Biotech Inc. were consolidated in late 2008, and was renamed Centocor Ortho Biotech Inc. Built upon a pioneering history, Centocor Ortho Biotech Inc. harnesses innovations in large-molecule and small-molecule research to create important new therapeutic options. Beyond its innovative medicines, Centocor Ortho Biotech is at the forefront of developing education and public policy initiatives to ensure patients and their families, caregivers, advocates and healthcare professionals have access to the latest treatment information, support services and quality care. For more information about Centocor Ortho Biotech, visit [www.centocororthobiotech.com](http://www.centocororthobiotech.com).

**Media Contacts:**

Centocor Ortho Biotech, Inc. Craig Stoltz  
215-325-3612 (office)  
215-779-9396 (cell)

**Investor Relations:**

Johnson & Johnson  
Tina Pinto  
732-524-2034