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Actemra inhibits joint damage and improves physical function of patients with Rheumatoid Arthritis

Fifth phase III study for Actemra adds to body of evidence that Actemra is an important breakthrough in the treatment of rheumatoid arthritis

Roche announced today that Actemra (tocilizumab) can significantly inhibit structural damage to joints in patients with rheumatoid arthritis (RA), a critical measure of effectiveness of an RA treatment. Actemra also improved the patients' physical function after one year of therapy, leading to a better quality of life.

Results from the LITHE (1) trial showed that a greater proportion of patients treated with Actemra in combination with a commonly used RA drug called methotrexate (MTX) benefited from a significant inhibition of structural damage during 12 months of therapy, compared to patients treated with MTX alone. This is critical to patients because damage in the joints caused by the disease leads to the disability and pain associated with RA. Additionally, Actemra improved the patients' ability to perform normal daily activities, as assessed by Health Assessment Questionnaire (HAQ) scores (2).

In the LITHE study, Actemra was generally well tolerated and the overall safety profile after 12 months of treatment was consistent with previously reported 6 month trial data.

The outcome of this study is good news for RA patients as presently many either fail to achieve an adequate response or cannot tolerate therapies currently available. New treatment options are needed, particularly those that can target different pathways to bring relief and inhibit joint damage in patients suffering from RA.

“The LITHE data further shows the potential of Actemra as an effective and well tolerated treatment for patients suffering from the debilitating effects of RA” said William M. Burns, CEO Roche Pharmaceuticals Division. “By demonstrating an inhibition of joint damage and improving physical function, Actemra not only positively impacts the disease, but also helps patients to improve the quality of their lives.”

The LITHE study is the fifth global phase III trial on Actemra to successfully meet its primary endpoints in patients with moderate to severe RA. First-year data from this two-year trial will be submitted for presentation at upcoming international scientific meetings.

Actemra is the first of a new class of drug with a novel mechanism of action that brings new hope to RA patients. It is a humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody which works by suppressing the activity of IL-6, an important trigger of the inflammatory process. This novel mode of action reduces inflammation of the joints and relieves the systemic effects of RA.

Rheumatoid Arthritis - A High Unmet Medical Need

Rheumatoid arthritis is thought to affect over 21 million people worldwide. It is a progressive autoimmune disease characterized by inflammation of the membrane lining in the joints throughout the body. This inflammation causes distortion of the joint and impaired function accompanied by pain, stiffness and swelling and ultimately leading to irreversible joint destruction and disability. In addition, the systemic symptoms of RA include fatigue, anaemia, osteoporosis and may contribute to shortening life expectancy by affecting major organ systems. After 10 years, less than 50% of patients can continue to work or function normally on a daily basis.

About the LITHE study

The LITHE study is an international study, including 15 countries and 1196 patients with moderate to severe RA who had an inadequate response to MTX. In this randomized study, patients received either Actemra (4 mg/kg or 8 mg/kg, one infusion every four weeks) in combination with methotrexate or methotrexate alone. The study aimed to show the inhibition of structural damage at the joints, as demonstrated by changes in validated radiographic parameters. The study also examined the improvement in physical function in patients, as demonstrated by HAQ scores.

About Actemra

Actemra is the result of research collaboration by Chugai and is being co-developed globally with Chugai. Actemra is the first humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. An extensive clinical development program of five Phase III trials was designed to evaluate clinical findings of Actemra. The five studies have reported meeting their primary endpoints. Actemra is awaiting approval in the United States and Europe. In Japan, Actemra was launched by Chugai in June 2005 as a therapy for Castleman's disease; in April 2008, additional indications for rheumatoid arthritis, juvenile idiopathic arthritis and systemic-onset juvenile idiopathic arthritis were also approved in Japan.

Actemra is generally well tolerated. The overall safety profile of Actemra is consistent across all global clinical studies. The most common, non-serious, adverse events reported are upper respiratory tract infection, nasopharyngitis, headache and hypertension. As with other biological disease modifying anti-rheumatic drugs (DMARDs), serious infections and hypersensitivity reactions including a few cases of anaphylaxis, have been reported in some patients treated with Actemra. Increases in liver transaminases (ALT and AST) were seen in some patients; these increases were generally mild and reversible, with no hepatic injuries or any observed impact on liver function.

About Roche in rheumatoid arthritis

One of the most important drivers for growth at Roche over the next few years is expected to be the company's emerging franchise in autoimmune diseases with rheumatoid arthritis as the first indication. Following the launch of MabThera (rituximab) there are a number of projects in development, potentially allowing Roche to build on further opportunities. MabThera is the first and only selective B-cell therapy for RA, providing a fundamentally different treatment approach by targeting B cells, one of the key players in the pathogenesis of RA. Actemra is Roche's second novel medicine and is a humanised monoclonal antibody to the interleukin-6 (IL-6) receptor, inhibiting the activity of IL-6, a protein that plays a major role in the RA inflammation process. Additional projects creating a rich pipeline include compounds in Phase I, II and III clinical trials. Notably, ocrelizumab, a humanised anti-CD20 antibody, has entered phase III development for RA.

About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As the world's biggest biotech company and an innovator of products and services for the early detection, prevention, diagnosis and treatment of diseases, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is the world leader in in-vitro diagnostics and drugs for cancer and transplantation, and is a market leader in virology. It is also active in other major therapeutic areas such as autoimmune diseases, inflammatory and metabolic disorders and diseases of the central nervous system. In 2007 sales by the Pharmaceuticals Division totalled 36.8 billion Swiss francs, and the Diagnostics Division posted sales of 9.3 billion francs. Roche has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai, and invested over 8 billion Swiss francs in R&D in 2007. Worldwide, the Group employs about 79,000 people. Additional information is available on the Internet at www.roche.com.

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- Roche & Autoimmune diseases: www.roche.com/med_events_mb1106
- Chugai: www.chugai-pharm.co.jp

Roche Group Media Relations

Telephone: +41 61 688 8888 / Email: basel.mediaoffice@roche.com

- Daniel Piller (Head)
- Alexander Klauser
- Claudia Schmitt
- Martina Rupp
- Nina Schwab-Hautzinger

References:

- (1) LITHE refers to the Tocilizumab safety and **THE** prevention of structural joint damage trial
- (2) HAQ, or the Health Assessment Questionnaire Disability Index, is a patient self-report functional status (disability) measurement used to assess the patient's functional ability and discomfort during the past week. It is a commonly used instrument in many disease areas, including RA