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Roche Group

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ACTEMRA inhibits progression of joint destruction in RA patients by over 80% compared to methotrexate alone

Long-term data also demonstrate unprecedented remission rates that increase over time

Two-year data from the LITHE study, being presented at the American College of Rheumatology, show that, with long-term use, patients with rheumatoid arthritis treated with ACTEMRA (tocilizumab, known as RoACTEMRA within the EU) plus methotrexate (MTX) suffered 81% less damage to their joints compared to those treated with MTX, the current standard therapy, alone[1]. For patients, this means that their joint damage is significantly reduced, and that they can therefore continue to enjoy their lives without the evolving disability usually associated with the disease.

Furthermore, data from two long-term extension studies[2] also being presented at the meeting demonstrate that the percentage of ACTEMRA patients achieving remission from their disease (DAS28<2.6) increased steadily over a 3-year period, from 27% at 24 weeks to 62% at 180 weeks (3.4 years).

The unprecedented remission rates seen with ACTEMRA were primarily the result of the profound effect on swollen and tender joints across a range of patient populations:

- Patients with no previous biologic therapy: After 96 weeks (1.8 years) of treatment with ACTEMRA, close to 50% of the patients had one or less swollen joint
- Patients with inadequate response to one or more tumour necrosis factor (TNF) inhibitors: Among those patients 34% had one or less swollen joint after treatment with ACTEMRA
- Patients who were MTX-naive and were treated with ACTEMRA as monotherapy: 55% had one or less swollen joint and 35% had one or less tender joints after 96 weeks.

"These data confirm that tocilizumab is very effective at inhibiting the damage to joints which is characteristic of rheumatoid arthritis," says Professor Josef Smolen, University of Vienna, Austria. "This impressive effect on joints, coupled with the previously shown ability of tocilizumab to provide relief from the signs and symptoms of RA gives it an important role within clinical practice. Successful remission with tocilizumab may help to restore a patient's sense of freedom, without painful flare-ups or fear of long-term disability."

The long-term safety profile of ACTEMRA is well characterised in 2.4 year data[3], being presented at the ACR, from the most comprehensive registration trial programme for any RA biologic, with almost 4,000 patients participating in the programme. Analysis from the Phase III programme (including five pivotal trials and two long-term extension studies) show that adverse events and severe adverse events remained stable over extended periods of time.

About the studies

About the LITHE study

The LITHE study, a randomised, double-blind, placebo-controlled trial was designed to evaluate the efficacy of TCZ plus MTX in preventing structural joint damage and improving physical function over two years. LITHE was an international study, including 15 countries and 1196 patients with moderate to severe RA who had an inadequate response to MTX. In this randomised study, patients received either ACTEMRA (4 mg/kg or 8 mg/kg, one infusion every four weeks) in combination with MTX or MTX alone. Results from the 24-month analysis showed that at 104 weeks, total Genant-modified Sharp Score change from baseline for the ACTEMRA 8mg + MTX, 4mg +MTX, and MTX alone groups were: 0.37, 0.58 and 1.96 respectively.

About the long-term extension studies

Patients participating in the most comprehensive trial programme for any biologic in RA including four pivotal studies (OPTION, TOWARD, RADIATE, AMBITION), were entered into two long-term extension studies (GROWTH95, GROWTH96), which examined safety and efficacy of ACTEMRA across a number of different patient populations: DMARD insufficient response (IR), anti-TNF-IR and monotherapy. Over 3,986 patients were included in the 2.4 year safety, and 3.5 year efficacy analyses. Long-term extension studies have shown low discontinuation rates due to side-effects (5.8/100 patient years).

About ACTEMRA

ACTEMRA is the result of research collaboration by Chugai and is being co-developed globally with Chugai. ACTEMRA is the first humanised interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. An extensive clinical development programme of five Phase III trials was designed to evaluate clinical findings of ACTEMRA, all of which met their primary endpoints. ACTEMRA was first approved in Japan, and launched by Chugai in June 2005 as a therapy for Castleman's disease; in April 2008, additional indications for RA, juvenile idiopathic arthritis and systemic-onset juvenile idiopathic arthritis were also approved in Japan. ACTEMRA was approved in the European Union in January 2009 for the treatment of RA in patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or TNF inhibitors. It is also approved for use in several other countries, including India, Brazil, Switzerland and Australia.

The overall safety profile of ACTEMRA is consistent across all global clinical studies. The serious adverse reactions reported in ACTEMRA clinical studies include serious infections, gastrointestinal perforations and hypersensitivity reactions including anaphylaxis. The most common adverse reactions reported in clinical studies were upper respiratory tract infection,

nasopharyngitis, headache, hypertension and increased ALT. Increases in liver enzymes (ALT and AST) were seen in some patients; these increases were generally mild and reversible, with no evidence of hepatic injuries or any observed impact on liver function. Laboratory changes, including increases in lipids (total cholesterol, LDL, HDL, triglycerides) and decreases in neutrophils and platelets, were seen in some patients without association with clinical outcomes. Treatments that suppress the immune system, such as ACTEMRA, may cause an increase in the risk of malignancies.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2008, Roche had over 80,000 employees worldwide and invested almost 9 billion Swiss francs in R&D. The Group posted sales of 45.6 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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