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RoActemra Could Change the Current Standard of Treatment for People Living with Rheumatoid Arthritis

New study confirms RoActemra is effective when used on its own for people who do not respond to methotrexate

Roche today announced new data from the ACT-RAY study, presented at the European League Against Rheumatism congress. The results demonstrated that in people with rheumatoid arthritis (RA), RoACTEMRA (tocilizumab, known as ACTEMRA outside Europe) alone had comparable clinical efficacy to RoACTEMRA plus methotrexate (MTX). The safety profile of RoACTEMRA was consistent with previous clinical trials.¹

Methotrexate, a disease modifying anti-rheumatic drug (DMARD), is widely prescribed for people with RA. However, up to 40% of people given MTX do not adequately respond to treatment or experience adverse events and require other drugs to help control their inflammation.² Data from the ACT-RAY study demonstrated that RoACTEMRA provided clinical benefit, regardless of whether it was given in combination with MTX or as a monotherapy.¹

“The findings of the ACT-RAY study provide further evidence of the meaningful benefits of RoActemra monotherapy. RoActemra is approved for people with rheumatoid arthritis who do not respond to, or are unable to tolerate the side effects associated with methotrexate, a commonly used treatment for the disease,” said Hal Barron, M.D., Head of Global Development and Chief Medical Officer for Roche.

RA is a chronic, progressive inflammatory disease of the joints and surrounding tissues that is associated with intense pain, irreversible joint destruction and systemic complications such as fatigue and anaemia. RoACTEMRA is the first in a new class of treatments for rheumatoid arthritis which target interleukin-6 receptors. It is currently approved in Europe for the treatment of RA in people who have either responded inadequately to, or who were intolerant to, previous therapy with one or more DMARDs or tumour necrosis factor (TNF) inhibitors. Results from the ACT-RAY study build on a previous Phase III study (AMBITION) which showed that compared to MTX, patients receiving RoACTEMRA alone achieved a greater reduction of signs and symptoms of RA (e.g. swollen and tender joints) at six months and nearly three times as many patients achieved DAS28 disease remission.³ RoACTEMRA is the first and only biologic to have demonstrated superiority as monotherapy treatment over MTX.³

About ACT-RAY

ACT-RAY is a Phase IIIb double-blind two year study designed to evaluate the efficacy and safety of adding RoACTEMRA to MTX versus switching from MTX to RoACTEMRA monotherapy in MTX inadequate responder (IR), biologic naïve, adult patients with moderate to severe active RA. ¹

556 patients with inadequate response to MTX received RoACTEMRA (8mg/kg every four weeks) and were randomised to either remain on stable dose of MTX (combination therapy, n=279), or receive a matching dose of placebo (monotherapy, n=277) with 92 percent (n=512) completing the initial 24 week period. The primary endpoint of this study was to achieve DAS28 remission (DAS28<2.6) at week 24. ¹

Results (at week 24) showed that RoACTEMRA monotherapy had comparable clinical efficacy to RoACTEMRA with MTX in RA patients who had an inadequate response to MTX. ¹

- Remission rates were consistent with previous clinical studies. ¹ DAS28 remission rate was 35 percent for RoACTEMRA plus placebo and 40 percent for RoACTEMRA plus MTX (p=0.19; 95% CI -2.4%, 13.7%). ¹
- The fast onset of action of RoACTEMRA was maintained. ¹ 18.1 percent and 15.2 percent of patients achieved remission at week eight in the combination and monotherapy groups respectively. ¹
- No overt differences in the safety profile were observed between the two treatments. ¹ Rates of adverse events, serious adverse events and serious infections per 100 patient years were 491, 21 and 6 for RoACTEMRA plus MTX and 467, 18 and 6 for RoACTEMRA plus placebo. ¹

About RoACTEMRA / ACTEMRA

RoACTEMRA (tocilizumab, known as ACTEMRA outside Europe) is the result of research collaboration by Chugai and is also being co-developed globally with Chugai. RoACTEMRA is the first humanised interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. 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 rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA) and systemic-onset juvenile idiopathic arthritis (sJIA) were also approved in Japan. RoACTEMRA 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 tumour necrosis factor (TNF) inhibitors. It is also approved for use in over 90 other countries, including India, Brazil, Switzerland, and Australia. ACTEMRA was approved in the United States in January 2010 for the treatment of adult patients with moderately to severely active RA who have had an inadequate response to one or more TNF inhibitors. In addition, ACTEMRA is now approved in the United States and Mexico for the treatment of active SJA in patients two years of age and older.

The safety and efficacy of RoACTEMRA in RA has been established in an extensive clinical development program including five Phase III clinical studies that enrolled more than 4,000 people with RA in 41 countries, including the United States. The overall safety profile of RoACTEMRA is consistent across all global clinical studies. The serious adverse events reported

in RoACTEMRA clinical studies include serious infections, gastrointestinal perforations and hypersensitivity reactions including anaphylaxis. The most common adverse events 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. Laboratory changes, including increases in lipids (total cholesterol, LDL, HDL, triglycerides) and decreases in neutrophils and platelets, were seen in some patients. Treatments that suppress the immune system, such as RoACTEMRA, 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 2010, Roche had over 80,000 employees worldwide and invested over 9 billion Swiss francs in R&D. The Group posted sales of 47.5 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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¹ Dougados *et al.* Abstract presented at EULAR 2011

² Pincus T, *et al.* *Clin Exp Rheumatol* 2010; 28(Suppl. 61):S68–S79.

³ Jones G, *et al.* *Ann Rheum Dis* 2010; 69:88–96.