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New data reinforces long-term efficacy of ACTEMRA in rheumatoid arthritis across all patient population types

Patients treated with ACTEMRA achieve consistently high remission rates which increase over time

Up to 56% of patients with active rheumatoid arthritis (RA) treated with ACTEMRA (tocilizumab, known as RoACTEMRA within the EU) for over two years, will achieve disease remission, according to new data presented today at the European League Against Rheumatism (EULAR) congress¹. Remission, as defined by DAS28 <2.6², provides real-life benefits to people living with RA by meaningfully improving disease symptoms which help them to continue or regain normal day-to-day functioning.

Commenting on the data, Professor Josef Smolen, University of Vienna, Austria, said, "Consistently high levels of remission such as these are really significant for both doctors and patients – firstly, in demonstrating that very low disease activity and remission is possible in large numbers and in all types of patients, and secondly, by confirming that tocilizumab offers us an effective long-term treatment which can make a dramatic difference to a patient's life."

These long-term data add to the wealth of evidence supporting the efficacy of ACTEMRA in achieving consistently high remission rates. The safety profile from the long-term extension studies is consistent with that previously reported and the most common adverse events reported were upper respiratory tract infection, nasopharyngitis, headache and hypertension.

In addition to disease remission, ACTEMRA has also demonstrated efficacy in preventing the progression of joint destruction. One year results from the LITHE study³, also presented at EULAR, demonstrate that patients treated with ACTEMRA had three times less progression of joint damage (measured by Total Sharp Score) compared to those treated with methotrexate (MTX) alone. Inhibiting the structural damage to joints in people living with RA is a critical measure of the effectiveness of an RA treatment.

Significantly more patients treated with ACTEMRA 8mg/kg in the LITHE study achieved remission at 6 months compared to those treated with MTX alone (33% vs 4%), and these rates continued to increase over

time to 1 year (47% vs. 8%). Recently announced top-line results from LITHE demonstrate that these benefits are maintained or improved at 2 years. ACTEMRA also improved the patients' ability to perform normal daily activities, as assessed by the Health Assessment Questionnaire (HAQ)⁴.

Results from the Phase III AMBITION study demonstrated that ACTEMRA is the only product to have proven superiority to MTX, the current standard therapy, in monotherapy in ACR20, ACR50 and ACR70 responses (at 6 months)⁵, and 40% of patients who had no prior treatment with DMARDs achieved DAS28 remission at week 24⁵.

About the studies

Over 2,500 people with RA participating in the Phase III OPTION, TOWARD, RADIATE and AMBITION trials entered the long-term extension studies (GROWTH95; GROWTH96), which assessed the use of ACTEMRA 8mg/kg every four weeks across following patient populations: DMARD-IR, anti-TNF-IR and without prior failure to MTX. Measures included ACR20/50/70, DAS28 and other efficacy scores.

The LITHE study, a randomized, double-blind, placebo-controlled trial, was designed to evaluate the efficacy of ACTEMRA plus MTX in inhibiting structural joint damage and improving physical function over 2 years. LITHE is an international study, including 15 countries and 1196 patients with moderate to severe RA who had an inadequate response to MTX. In this study, patients received either ACTEMRA (4 mg/kg or 8 mg/kg, one infusion every four weeks) in combination with MTX or MTX alone.

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 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 rheumatoid arthritis, juvenile idiopathic arthritis and systemic-onset juvenile idiopathic arthritis 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 TNF inhibitors. It is also approved for use in several other countries, including India, Brazil, Switzerland and Australia.

ACTEMRA is generally well tolerated and the overall safety profile is consistent across all global clinical studies. As with other biological 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.

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1. Smolen, J. *et al.* Efficacy of Tocilizumab (TCZ) in Rheumatoid Arthritis (RA): Interim analysis of long-term extension trials of up to 2.5 years. Abstract presented on 12th June 2009 at EULAR
2. National Rheumatoid Arthritis Society, The DAS28 score http://www.rheumatoid.org.uk/article.php?article_id=475 Last accessed 19 May 2009
3. Kremer, J. *et al.* Tocilizumab inhibits structural joint damage, improves physical function, and increases DAS28 remission rates in RA patients who respond inadequately to methotrexate: The LITHE Study. Presented on 12th June 2009 at EULAR

4. 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
5. Jones G, et al. Efficacy of Tocilizumab (TCZ) VS Methotrexate (MTX) Monotherapy in Patients with Rheumatoid Arthritis (RA) with No Prior MTX or DMARD Exposure. Abstract presented on 12th June at EULAR.