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Roche Roche Group

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RoACTEMRA: New Hope for Children with Systemic Juvenile Idiopathic Arthritis

First presentation of TENDER study demonstrates RoACTEMRA's strong efficacy in this severe childhood condition with no currently licensed treatment

Roche today announced that new data being presented at the European League Against Rheumatism (EULAR) congress demonstrates that RoACTEMRA (known as ACTEMRA outside Europe) is highly effective in improving the signs and symptoms of systemic Juvenile Idiopathic Arthritis (sJIA), a severe childhood arthritis, where there are no currently licensed treatments. RoACTEMRA is also well tolerated in children with sJIA having a safety profile similar to adults with RA.

Data from the phase III TENDER study[i] showed that, following three months' treatment with RoACTEMRA, 85 percent of patients achieved 30 percent improvement (JIA ACR30[1]) in the signs and symptoms of sJIA and absence of fever, a primary characteristic of sJIA, compared to 24 percent of patients receiving placebo. Further data showed 70 percent achieved JIA ACR70 and 37 percent achieved ACR90. In addition to the significant improvement in JIA ACR response nearly two thirds were free of rash after three months.

"There is a critical need for new therapies for children suffering from the debilitating and life-threatening effects of sJIA, and these data represent an exciting breakthrough", commented Hal Barron, M.D, Head of Global Development and Chief Medical Officer for Roche. "RoACTEMRA's striking efficacy confirms a major advance in the treatment of this disease. It promises to have a significant impact in the life of these young children."

sJIA is characterised by chronic arthritis accompanied by intermittent fever, skin rash, anaemia, enlargement of the liver and/or spleen and inflammation of the lining of the heart and/or lungs.[ii] The peak age of onset of sJIA is between 18 months and two years[iii,iv] although persistence of the disease into adulthood does occur.

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[1] JIA ACR30 response is defined as 3 of the 6 core components improving (from the Baseline assessments) by ≥ 30%, with no more than 1 of the remaining components worsening by > 30%. Core components include Physician global assessment of disease activity VAS; Parent/patient global assessment of overall well-being VAS; Number of joints with active arthritis; Number of joints with limitation of movement; Erythrocyte Sedimentation Rate (ESR); Functional ability – Childhood Health Assessment Questionnaire (CHAQ)

Its disease course is variable and in the most severe cases, up to two thirds of patients have chronic and persistent arthritis and approximately half of these will develop significant disability.[5,6] It has the worst long term prognosis of all childhood arthritis subtypes, accounting for almost two-thirds of all deaths among children with arthritis, with an overall mortality rate estimated to be between two to four percent.[7] There are no approved therapies for sJIA and current treatment consists of high dose corticosteroids to control systemic symptoms. However, these do not improve the long-term prognosis and their use is accompanied by severe side effects.[ii]

The TENDER study findings reflect previous Japanese studies[8,9] which demonstrated that RoACTEMRA is well tolerated and effective in children with sJIA who could not tolerate, or showed inadequate response to systemic corticosteroids and immunosuppressants. No new major safety signals were observed and the adverse event profile was similar to adult RA studies and as expected for this patient population.

RoACTEMRA inhibits the activity of interleukin-6 (IL-6), a contributor to the major features of sJIA including chronic synovial inflammation, articular cartilage damage, fever, anaemia, growth impairment and osteoporosis.[10] Commenting on IL-6 as a treatment approach, Hal Barron said: "RoACTEMRA's efficacy in treating these symptoms provides further evidence of the pivotal role of IL-6 in mediating joint inflammation and the detrimental systemic effects of chronic inflammatory diseases."

RoACTEMRA is already approved in the EU, US and other countries for adult RA, a disease also associated with elevated levels of IL-6 and systemic symptoms such as fatigue, anaemia and fever. Studies in RA have demonstrated RoACTEMRA's strong efficacy and safety, with consistently high remission rates across all patient types[11] and inhibition of structural joint damage.[12] In addition it is the only product to have proven superiority to methotrexate in monotherapy in ACR20, ACR50 and ACR70 responses at six months, in adult RA.[13]

About the TENDER Study

The TENDER study is an international study, including approximately 70 centres in 20 countries. The study aimed to assess efficacy for signs and symptoms and short term safety of RoACTEMRA versus placebo in 112 patients with active sJIA. Additional aims were efficacy for the common systemic features of sJIA, steroid reduction, other concomitant drug reductions, safety with chronic administration and biomarkers.

In this randomised study, patients received RoACTEMRA 8 mg/kg (if weight ≥ 30 kg) and 12 mg/kg (if weight < 30 kg), every 2 weeks versus placebo infusions for 12 weeks. Patients were also given the option to enroll for long-term, open label follow-up. The study was performed in close collaboration with the PRINTO (Paediatric Rheumatology International Trials Organisation) and PRCSG (Paediatric Rheumatology Collaborative Study) groups.

About RoACTEMRA/ACTEMRA

RoACTEMRA/ACTEMRA is the result of research collaboration by Chugai and is also being co-developed globally with Chugai. RoACTEMRA/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 RoACTEMRA/ACTEMRA, all of which met their primary endpoints. RoACTEMRA/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 and systemic-onset juvenile idiopathic arthritis were also approved in Japan. RoACTEMRA/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 tumour necrosis factor (TNF) inhibitors. It is also approved for use in several other countries, including India, Brazil, Switzerland, and Australia. RoACTEMRA/ACTEMRA was most recently (January 2010) approved in the United States for the treatment of adult patients with moderately to severely active RA who have had an inadequate response to one or more TNF inhibitors.

The overall safety profile of RoACTEMRA/ACTEMRA is consistent across all global clinical studies. The serious adverse events reported in RoACTEMRA/ACTEMRA 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, 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 RoACTEMRA/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 2009, Roche had over 80’000 employees worldwide and invested almost 10 billion Swiss francs in R&D. The Group posted sales of 49.1 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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[11] Long-term efficacy of tocilizumab in rheumatoid arthritis for up to 3.5 years. Smolen J et al. Oral presentation at ACR, 18th October 2009

[12] LITHE: Tocilizumab inhibits radiographic progression and improves physical function in rheumatoid arthritis (RA) patients (Pts) at 2 years with increasing clinical efficacy over time. Fleischmann, R et al. Oral presentation at ACR, 18th October 2009

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