Cimzia® (certolizumab pegol) data showed rapid improvement in signs and symptoms predicted better long-term outcomes in rheumatoid arthritis patients

- **Patients who achieved a clinical response at week 12 had a much greater probability of achieving a low disease activity state and had less radiographic progression at one year compared to non responders at week 12[1]**
- **Within the group of week-12 responders, the majority had achieved a clinical response by week 6 and these patients had better long-term improvements in both clinical and patient-reported outcome measures compared to later responders[1]**

BRUSSELS, BELGIUM, 3rd May, 13:00 (CET) – UCB announced today results from a post hoc analysis of the RAPID 1 study published in the *Journal of Rheumatology.* The results suggest moderate to severe rheumatoid arthritis (RA) patients treated with Cimzia® (certolizumab pegol), the only approved PEGylated anti-TNF, together with methotrexate (MTX), achieved a rapid response associated with improved long-term outcomes one year after treatment began.[1]

"These results are consistent with a growing body of clinical evidence that suggest a potential for healthcare professionals to predict clinical success as early as week 12 when treating rheumatoid arthritis patients with certolizumab pegol," said lead investigator Edward Keystone, M.D., The Rebecca MacDonald Center for Arthritis, Mount Sinai Hospital, The University of Toronto. "The data supports the importance of monitoring for a rapid response, in line with recently published EULAR recommendations, and the need to consider treatment adjustments in those patients who have not achieved a clinical response at 12 weeks regardless of their treatment."

Rapid response rates following treatment with certolizumab pegol were achieved across various clinical response measures, including good/moderate EULAR response rates at weeks 6 and 12 (67.4% and 77.6% respectively versus 27.0% and 29.1% for placebo) based on this post hoc analysis. Similarly, ACR20 rates were 51.3% and 63.8% in patients treated with certolizumab pegol versus 18.2% and 18.3% for placebo at week 6 and 12 respectively.[1]

Using the disease activity score, DAS28[ESR] ≥ 1.2 responder definition, a higher proportion of patients treated with certolizumab pegol (75.8%) responded at week 12 compared to placebo (27.5%). Results suggest that a higher proportion of patients treated with certolizumab pegol who responded at week 12, achieved DAS28 low disease activity (LDA) at 52 weeks compared with patients who did not (37.2% versus 6.1%). Patients who responded at week 12 also experienced less radiographic progression than those who did not. The majority of patients (approximately 75%) who responded at week 12 had a clinical response at week 6. These patients reported further improved outcomes such as pain, physical function and fatigue, a significantly greater response in terms of ACR20, 50 and 70 measures as well as higher rates of DAS28 LDA and remission, relative to those who showed response at week 12.[1]

The data published were from the RAPID 1 study[1] - a Phase III double-blind placebo-controlled trial. The trial was designed to establish the efficacy and tolerability of certolizumab pegol together with MTX, in the treatment of moderate to severely active RA in patients who did not adequately respond to conventional treatment. The co-primary end points were ACR20 score at week 24 and change in mTSS (modified Total Sharp Score) at week 52. The post hoc analysis focused on patients who received MTX and either 200mg subcutaneously or placebo every 2 weeks for 52 weeks accounting for 393 patients in the ITT population (30 patients were excluded due to nonimputable data).[1]

Patients participating in the trial all met the ACR classification for RA, and had active disease at screening and an inadequate response to MTX treatment (≥ 6 months with a stable dose of ≥ 10 mg weekly for ≥ 2 months prior to baseline).[1]

For the purpose of this post hoc analysis, patients were classified as responders or non-responders based on DAS 28 > 1.2 and ACR20 response at week 6 and 12 respectively. Low disease activity was defined as DAS28 ≤ 3.2. Remission was defined as DAS28 ≤ 2.6. Improvement in disease activity, as measured by DAS28, was classified according to the EULAR response criteria.[1]

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Cimzia® (certolizumab pegol) in European Union / EEA important safety information
Cimzia® was studied in 2367 patients with RA in controlled and open label trials for up to 57 months. The commonly reported adverse reactions (1-10%) in clinical trials with Cimzia® and post-marketing were viral infections (includes herpes, papillomavirus, influenza), bacterial infections (including abscess), rash, headache (including migraine), asthenia, leukopaenia (including lymphopaenia, neutropaenia), eosinophilic disorder, pain (any sites), pyrexia, sensory abnormalities, hypertension, pruritis (any sites), hepatitis (including hepatic enzyme increase), injection site reactions. Serious adverse reactions include sepsis, opportunistic infections, tuberculosis, herpes zoster, lymphoma, leukaemia, solid organ tumours, angioneurotic edema, cardiomyopathies (includes heart failure), ischemic coronary artery disorders, pancytopaenia, hypercoagulation (including thrombophlebitis, pulmonary embolism), cerebrovascular accident, vasculitis, hepatitis/hepatopathy (includes cirrhosis), and renal impairment/nephropathy (includes nephritis). In RA controlled clinical trials, 5% of patients discontinued taking Cimzia® due to adverse events vs. 2.5% for placebo.

Cimzia® is contraindicated in patients with hypersensitivity to the active substance or any of the excipients, active tuberculosis or other severe infections such as sepsis or opportunistic infections, moderate to severe heart failure.

Before initiation of Cimzia®, evaluate patients for both active or inactive (latent) tuberculosis infection. Monitor patients for the development of signs and symptoms of infection during and after treatment with Cimzia®. If an infection develops, monitor carefully, and stop Cimzia® if infection becomes serious.

TNF blockers including Cimzia® may increase the risk: of reactivation of Hepatitis B Virus (HBV) in patients who are chronic carriers of the virus; of new onset or exacerbation of clinical symptoms and/or radiographic evidence of demyelinating disease; of formation of autoantibodies and uncommonly of the development of a lupus-like syndrome; of severe hypersensitivity reactions. If a patient develops any of these adverse reactions, Cimzia® should be discontinued and appropriate therapy instituted.

With the current knowledge, a possible risk for the development of lymphomas, leukaemia or other malignancies in patients treated with a TNF antagonist cannot be excluded. Rare cases of neurological disorders, including seizure disorder, neuritis and peripheral neuropathy, have been reported in patients treated with Cimzia®.

Adverse reactions of the hematologic system, including medically significant cytopenia, have been infrequently reported with Cimzia®. Advise all patients to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever, bruising, bleeding, pallor) while on Cimzia®. Consider discontinuation of Cimzia® therapy in patients with confirmed significant haematological abnormalities.

The use of Cimzia® in combination with anakinra or abatacept is not recommended due to a potential increased risk of serious infections. As no data are available, Cimzia® should not be administered concurrently with live vaccines or attenuated vaccines. The 14-day half-life of Cimzia® should be taken into consideration if a surgical procedure is planned. A patient who requires surgery while on Cimzia® should be closely monitored for infections.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision February 2011.

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf

About CIMZIA®

Cimzia® is the only PEGylated anti-TNF (Tumor Necrosis Factor). Cimzia® has a high affinity for human TNF-alpha, selectively neutralizing the pathophysiological effects of TNF-alpha. Over the past decade, TNF-alpha has emerged as a major target of basic research and clinical investigation. This cytokine plays a key role in mediating pathological inflammation, and excess TNF-alpha production has been directly implicated in a wide variety of diseases. The U.S. Food and Drug Administration (FDA) has approved Cimzia® for reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy and for the treatment of adults with moderately to severely active rheumatoid arthritis. Cimzia® in combination with MTX, is approved in the EU for the treatment of moderate to severe active RA in adult patients inadequately responsive to disease-modifying antirheumatic drugs (DMARDs) including MTX. Cimzia® can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. UCB is also developing Cimzia® in other autoimmune disease indications. Cimzia® is a registered trademark of UCB PHARMA S.A.

About UCB

UCB, Brussels, Belgium (www.ucb.com) is a biopharmaceutical company dedicated to the research, development and commercialization of innovative medicines with a focus on the fields of central nervous system and immunology disorders. Employing more than 9000 people in over 40 countries, UCB produced revenue of EUR 3.22 billion in 2010. UCB is listed on Euronext Brussels (symbol: UCB).

Forward-looking statements

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. Such statements are subject to risks and uncertainties that may cause actual results to be materially different from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, effects of future judicial decisions, changes in regulation, exchange rate fluctuations and hiring and retention of its employees.

References

1. *Keystone, EC. et al. Rapid Improvement in the Signs and Symptoms of Rheumatoid Arthritis Following Certolizumab Pegol Treatment Predicts Better Longterm Outcomes: Post-hoc Analysis of a Randomized Controlled Trial; The Journal of Rheumatology; DOI: 10.3899/jrheum.100935; http://www.jrheum.org/content/early/2011/02/24/jrheum.100935*