Positive results from Phase 3 study evaluating CIMZIA® (certolizumab pegol) in DMARD-naïve rheumatoid arthritis patients

UCB presented results of the C-EARLY study for the first time at the European League Against Rheumatism Annual Congress (EULAR 2015) in Rome, Italy (10th – 13th June 2015)

Brussels, Belgium – 13 June, 10:00 CET – UCB announced data that advances potential care options for rheumatoid arthritis (RA) patients who have not been treated with disease-modifying anti-rheumatic drugs (DMARD-naïve) and who are at risk for highly progressive disease. The Phase 3 C-EARLY™ study showed the substantial benefits, at 52 weeks, of adding Cimzia® to optimized methotrexate treatment.

"The C-EARLY™ study found that adding Cimzia to optimized methotrexate achieved sustained remission and low disease activity in this at risk patient population. These findings demonstrate the importance of quickly identifying RA patients who will benefit from combination therapy following RA diagnosis. The study raises the bar for long-term treatment strategies for people living with RA," said lead study author Professor Paul Emery, Professor of Rheumatology, University of Leeds, UK.

The study was designed to evaluate the efficacy and safety of certolizumab pegol (CZP) in combination with optimized methotrexate (MTX) for the treatment of DMARD-naïve adult patients with early, active RA.[1,2] Optimized MTX was the highest dose the patient could tolerate up to a maximum of 25mg weekly. For all patients in the study, MTX therapy was initiated with 10mg weekly and increased to 25mg after 6-8 weeks, if well tolerated. At least 15mg weekly of MTX had to be taken to remain in the study.

The study showed that, after 52 weeks, treatment with CZP plus optimized MTX resulted in more patients in sustained remission and low disease activity, greater improvements in the signs and symptoms of rheumatoid arthritis including physical function, and inhibition of structural damage compared with optimized MTX treatment alone. No new safety signals for CZP were reported.[1]

Secondary results from the C-EARLY™ study were also presented at EULAR 2015 and showed that patients treated with CZP plus MTX had greater improvements at one year in pain, disease activity, fatigue and health related quality of life, improved workplace and household productivity, and reduced need for assistance with regular activities compared to patients receiving placebo and MTX.[2]

Based on the results of this study, UCB has submitted a regulatory application to the European Medicines Agency for an extension of the Cimzia® indication in RA to include treatment in combination with MTX for adult patients with severe active and progressive RA not previously treated with MTX or other DMARDs.

A second phase of the study is ongoing for another year to evaluate the potential of reducing CZP

maintenance dosing frequency or withdrawing CZP in subjects who achieve sustained low disease activity in period one of the study.

Key Primary and Key Secondary Outcomes

At Week 52, treatment with CZP plus optimized MTX compared with placebo plus optimized MTX (full analysis set: n=655 CZP and 213 MTX; radiographic analysis set: n=528 CZP and 163 PBO) resulted in significantly more patients with:

- sustained remission (28.9% vs. 15.0%; p<0.001) [1]
- sustained low disease activity (43.8% vs. 28.6%; p<0.001) [1]
- inhibition of structural damage (change from baseline in van der Heijde modified total Sharp score [mTSS]: 0.2 vs. 1.9; p<0.001)[1]

Significant secondary endpoints for patients receiving CZP with optimized MTX, compared to those taking placebo with optimized MTX, included improvements in:

- patient-reported outcomes (CZP plus MTX: n=655; placebo plus MTX: n=213; -1.0 vs. - 0.8; p<0.001 for HAQ-DI) [2]
- household productivity (CZP plus MTX: n=640; placebo plus MTX: n=206; 3.0 vs. 1.9; p<0.01 for household work days missed per month)[2]

Additionally, patients receiving CZP plus optimized MTX reported a reduced need for assistance with their usual daily activities, and employed patients taking CZP with optimized MTX (n=351) stated greater reductions in absenteeism and presenteeism after 52 weeks.[2]

About the study

The C-EARLY™ study is a phase 3, multi-center, randomized, double-blind, placebo-controlled trial.[3] In the study, 879 patients with early, active RA (<1 year since diagnosis; fulfilling the 2010 ACR/EULAR classification criteria) who were DMARD-naïve and had at least moderate disease activity (DAS28[ESR] ≥3.2) were randomized to either CZP plus MTX (n=660) or placebo plus optimized MTX (n=219) for 52 weeks.[1]

The primary endpoint of the study was sustained remission (DAS28[ESR] <2.6 at both Weeks 40 and 52). The key secondary endpoint was sustained low disease activity (DAS28[ESR] ≤3.2 at both Weeks 40 and 52). Other key secondary endpoints included proportion of patients with ACR50 response, change from baseline in HAQ-DI and inhibition of radiographic progression (change from baseline in van der Heijde modified total Sharp score) at Week 52.[1]

NOTES TO EDITORS

About CIMZIA®

CIMZIA® is the only Fc-free, PEGylated anti-TNF (Tumor Necrosis Factor). CIMZIA® has a high affinity for human TNF-alpha, selectively neutralizing the pathophysiological effects of TNF-alpha.

About CIMZIA® in the EU/EEA[4]

CIMZIA® in combination with methotrexate (MTX) is approved in the EU for the treatment of moderate-to-severe active RA in adult patients inadequately responsive to disease-modifying anti-rheumatic drugs (DMARDs) including MTX. CIMZIA® can be given as monotherapy in case of

intolerance to MTX or when continued treatment with MTX is inappropriate. CIMZIA®, in combination with MTX, is indicated for the treatment of active psoriatic arthritis in adults when the response to previous DMARD therapy has been inadequate.

CIMZIA® can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.

CIMZIA® is also approved in the EU for the treatment of adult patients with severe active axial spondyloarthritis (axSpA) comprising:[4]

- Ankylosing spondylitis (AS) - adults with severe active AS who have had an inadequate response to, or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs).
- Axial spondyloarthritis (axSpA) without radiographic evidence of AS - adults with severe active axSpA without radiographic evidence of AS but with objective signs of inflammation by elevated C-reactive protein (CRP) and/or Magnetic Resonance Imaging (MRI), who have had an inadequate response to, or are intolerant to NSAIDs.

Important Safety Information about CIMZIA® in the EU/EEA

CIMZIA® was studied in 4,049 patients with rheumatoid arthritis (RA) in controlled and open label trials for up to 92 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), asthaenia, leukopaenia (including lymphopaenia, neutropaenia), eosinophilic disorder, pain (any sites), pyrexia, sensory abnormalities, hypertension, pruritus (any sites), hepatitis (including hepatic enzyme increase), injection site reactions, and nausea. Serious adverse reactions include sepsis, opportunistic infections, tuberculosis, herpes zoster, lymphoma, leukaemia, solid organ tumours, angioneurotic oedema, 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, 4.4% of patients discontinued taking CIMZIA® due to adverse events vs. 2.7% 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 or moderate-to-severe heart failure.

Serious infections including sepsis, tuberculosis and opportunistic infections have been reported in patients receiving CIMZIA®. Some of these events have been fatal. Monitor patients closely for signs and symptoms of infections including tuberculosis before, during and after treatment with CIMZIA®. Treatment with CIMZIA® must not be initiated in patients with a clinically important active infection. If an infection develops, monitor carefully and stop CIMZIA® if infection becomes serious. Before initiation of therapy with CIMZIA®, all patients must be evaluated for both active and inactive (latent) tuberculosis infection. If active tuberculosis is diagnosed prior to or during treatment, CIMZIA® therapy must not be initiated and must be discontinued. If latent tuberculosis is diagnosed, appropriate anti-tuberculosis therapy must be started before initiating treatment with CIMZIA®. Patients should be instructed to seek medical advice if signs/symptoms (e.g. persistent cough,

wasting/weight loss, low grade fever, listlessness) suggestive of tuberculosis occur during or after therapy with CIMZIA®.

Reactivation of hepatitis B has occurred in patients receiving a TNF-antagonist including CIMZIA® who are chronic carriers of the virus (i.e. surface antigen positive). Some cases have had a fatal outcome. Patients should be tested for HBV infection before initiating treatment with CIMZIA®. Carriers of HBV who require treatment with CIMZIA® should be closely monitored and in the case of HBV reactivation CIMZIA® should be stopped and effective anti-viral therapy with appropriate supportive treatment should be initiated.

TNF antagonists including CIMZIA® may increase the risk 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 cytopaenia, 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. 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.

CIMZIA® was studied in 325 patients with active axial spondyloarthritis (axSpA) in a placebo-controlled clinical trial for up to 30 months and in 409 patients with psoriatic arthritis (PsA) in a placebo-controlled clinical trial for up to 30 months. The safety profile for axSpA and PsA patients treated with CIMZIA® was consistent with the safety profile in RA and previous experience with CIMZIA®.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision 16th December 2014.

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

About Rheumatoid Arthritis

RA is a chronic inflammatory disorder that typically affects joints in the hands and feet. In addition to causing joint problems, RA can sometimes affect other organs of the body such as the skin, eyes, lungs and blood vessels.[5] RA is more common in women than men, and although it can occur at any age, it usually begins after the age of 40.[5]

References

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2. Emery, P, Bingham, C, Burmester, G-R et al. Improvements in patient-reported outcomes and workplace and household productivity following 52 weeks of treatment with certolizumab pegol in combination with methotrexate in DMARD-naïve early rheumatoid arthritis patients: results from the C-EARLY randomized, double-blind, controlled phase 3 study. Presented at the European League Against Rheumatism (EULAR) 2015 Congress; abstract # **SAT0165**
3. ClinicalTrials.gov. Accessed 26th February 2015 from https://clinicaltrials.gov/ct2/show/NCT01519791?term=C-EARLY&rank=1
4. CIMZIA® EU Summary of Product Characteristics. Accessed 26th February 2015 from http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf
5. MayoClinic. Diseases and Conditions. Rheumatoid Arthritis. Accessed 26th February 2015 from http://www.mayoclinic.org/diseases-conditions/rheumatoid-arthritis/basics/definition/con-20014868

For further information, UCB:

Corporate Communications	Investor Relations	Brand Communications
France Nivelle, Global Communications, UCB T +32.2.559.9178, france.nivelle@ucb.com Laurent Schots, Media Relations, UCB T+32.2.559.92.64, Laurent.schots@ucb.com	Antje Witte, Investor Relations, UCB T +32.2.559.94.14, antje.witte@ucb.com	Andrea Levin Christopher, Immunology Communications, UCB T +1.404.483.7329 andrea.levin@ucb.com

About UCB

UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 8500 people in approximately 40 countries, the company generated revenue of € 3.3 billion in 2014. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

Forward looking statements - UCB

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