UCB News

UCB announces four-year imaging results demonstrating low disease progression and long-term efficacy of CIMZIA® (certolizumab pegol) in patients with axial spondyloarthritis (axSpA)

- RAPID-axSpA was the first study to investigate imaging results across both ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) subpopulations when treated with a TNF-inhibitor
- Magnetic Resonance Imaging (MRI) assessments demonstrated a rapid and sustained reduction of inflammation in the spine and sacroiliac joints (SIJ), while X-ray results revealed a low rate of disease progression
- Long-term control of disease, through suppression of inflammation and prevention or slowing of new bone formation, is a major goal of the treatment of axSpA, including AS and nr-axSpA. These findings demonstrate long-term value for this broad axSpA population

Brussels, Belgium – 14 June, 00:20 CEST – Today, UCB presented the four-year imaging results from an extension study of RAPID-axSpA, a long-term Phase 3 trial evaluating efficacy and safety of CIMZIA® (certolizumab pegol) in a broad spectrum of patients with active axial spondyloarthritis (axSpA), with both ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA). The study found limited spinal radiographic progression in CIMZIA-treated patients, especially between weeks 96 and 204, limited change in radiographic sacroiliitis, and maintenance of early reductions of inflammation of the spine and sacroiliac joints (SIJ) using Magnetic Resonance Imaging (MRI) through the duration of the study. These results were reported in an oral presentation today at the Annual European Congress of Rheumatology (EULAR) 2017 in Madrid, Spain. The results were also published in the journal *Rheumatology* in May.

“These findings provide important information on the long-term efficacy of certolizumab pegol for patients across a broad spectrum of axial spondyloarthritis,” said Professor Désirée van der Heijde, MD, PhD at Leiden University Medical Center, Leiden, Netherlands, and lead investigator of the study. “MRI and X-ray results are measures of inflammation and structural damage, respectively, in the sacroiliac joints and the spine. These four-year data show that there is minimal progression in structural damage and the reduction in inflammation is sustained. This supports the good long-term clinical outcome of treatment with certolizumab in patients with axial spondyloarthritis.”

Axial spondyloarthritis is a chronic inflammatory rheumatic disease that mostly affects the spine and SIJ. The disease can be further divided into AS and nr-axSpA, depending on the presence or absence of definitive changes on X-ray in the SIJ. Ankylosing spondylitis is a chronic inflammatory rheumatic disease of the spine and is the most well-recognized subset of axSpA.[1] The disease usually first develops in young adults[2] and has a prevalence rate similar to rheumatoid arthritis (RA).[3]

Some patients develop syndesmophytes (new bone formations) in the spine which considerably contribute to the restriction of spinal mobility and function, especially later in the course of the disease. Therefore, in addition to an effective suppression of inflammation, the prevention of structural damage is an important target in these patients.[4]

“Helping to define the fullest extent yet of CIMZIA’s value for patients living with axSpA, many of whom are struck in the prime of their lives, is just part of the ongoing contributions made by UCB’s RAPID-axSpA clinical trial, which also became the first international study in 2012 to investigate a TNF-inhibitor in the broad axSpA population,[5]” said Emmanuel Caeymaex, Head of Immunology and Executive Vice President, Immunology Patient Value Unit at UCB. “UCB has several ongoing studies in axSpA to improve our understanding of the best treatment strategies for this population. We are committed to this kind of sustained and focused research for diseases as complex as axSpA because it is the only way to reach the most patients with appropriate therapies that meaningfully improve their lives for as long as possible.”

RAPID-axSpA (NCT01087762) evaluated 315 CIMZIA-treated patients at multiple doses (200mg Q2W/400mg Q4W) and was double-blind and placebo-controlled to week 24, dose-blind to week 48, and open-label to week 204.[6] Patients fulfilling the Assessment of SpondyloArthritis International Society (ASAS) axSpA criteria were stratified according to presence/absence of radiographic sacroiliitis (AS/nr-axSpA) at randomization and had active disease.[6] Centrally-read lateral X-rays of cervical/lumbar spine at baseline, week 96 and week 204 were assessed using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). SIJ X-rays were scored for radiographic damage at baseline and week 204. MRI scans performed at baseline, weeks 12, 48, 96 and 204 in a subset of patients, were assessed using Spondyloarthritis Research Consortium of Canada (SPARCC) score for SIJ and Berlin score for spine.[6]

In AS patients, mean mSASSS change between baseline and week 204 was 0.98; 0.67 from baseline to week 96, and 0.31 from week 96 to week 204 (0.06, -0.01, and 0.07 respectively for nr-axSpA patients). Limited changes in SIJ X-ray grading were observed to week 204: only 4.5% of patients progressed from nr-axSpA classification to AS and 4.3% changed from an AS classification to nr-axSpA in four years. MRI assessments of the spine and SIJ showed sustained improvement in both subpopulations of axSpA patients.[6] No new safety signals were reported in this study.

About CIMZIA® in the EU/EEA
In the EU, CIMZIA® in combination with methotrexate (MTX) is indicated 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 also indicated for the treatment of severe, active and progressive RA in adults not previously treated with MTX or other DMARDs.

CIMZIA® has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function, when given in combination with MTX.

CIMZIA®, in combination with MTX, is also 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 MTX or when continued treatment with MTX is inappropriate.

CIMZIA® is also indicated in the EU for the treatment of adult patients with severe active axial spondyloarthritis (axSpA), comprising:

- 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 204 weeks and in 409 patients with psoriatic arthritis (PsA) in a placebo-controlled clinical trial for up to 204 weeks .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 May 2017.
http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf.

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