UCB News

First phase 3 study evaluating Cimzia® (certolizumab pegol) in early rheumatoid arthritis presented at EULAR 2014

For the attention of European Medical Journalists

- Positive results from study in Japanese patients with early rheumatoid arthritis

Brussels (Belgium), June 13th, 2014 – 0700 (CEST) – Results of a phase 3 study evaluating the efficacy and safety of Cimzia® (certolizumab pegol) in the treatment of Japanese patients with early rheumatoid arthritis (RA) are presented this week at the European League Against Rheumatism (EULAR) 2014 Annual Congress in Paris, France (11th-14th June 2014).[1] The study showed that combination treatment of certolizumab pegol with methotrexate (MTX) was significantly more effective than placebo with MTX in inhibiting structural disease progression, as well as achieving clinical remission in MTX-naïve Japanese patients with early RA and poor prognostic factors.[1]

In Japan, Astellas Pharma Inc. (TSE:4503) and UCB Japan are jointly developing and commercializing certolizumab pegol. Cimzia® (certolizumab pegol) 200 mg Syringe for s.c. injection is currently approved in Japan for the treatment of adult patients with RA who have had an inadequate response to conventional treatment.

“We are committed to improving the lives of patients at all stages of RA and are encouraged by the first Phase 3 study evaluating certolizumab pegol in the treatment of early RA. Data from this study suggested that Japanese patients with early RA and poor prognostic factors experienced meaningful clinical improvement when treated with a combination of certolizumab pegol with MTX. ” said Professor Dr. Iris Loew-Friedrich, Chief Medical Officer and Executive Vice President, UCB.

In the study reported at EULAR 2014, 316 Japanese patients with early RA (<12 months from onset of persistent RA symptoms), who fulfilled the 2010 ACR/EULAR Classification Criteria, had at least moderate disease activity (DAS28[ESR]≥3.2), poor prognostic factors,* and who were MTX-naïve, were randomized either to certolizumab pegol and MTX or to MTX and placebo.[1,2] The primary endpoint of the study was inhibition of radiographic progression (change from baseline in modified Total Sharp Score) at week 52. Secondary endpoints were inhibition of radiographic progression at week 24, and clinical remission rates (DAS28[ESR], ACR/EULAR [SDAI], and ACR/EULAR [Boolean]) at weeks 24 and 52.[1]

Patients in the certolizumab pegol with MTX group (n=159) showed significantly greater inhibition of radiographic progression relative to the placebo with MTX group (n=157) at week 52 (p<0.001) and week 24 (p=0.003). Clinical remission rates for the certolizumab pegol with MTX group were higher than those in the placebo with MTX group, across all parameters, at week 24 and at week 52. For example, at week 52, 45.3% of patients taking certolizumab pegol with MTX achieved ACR/EULAR [Boolean] remission compared to 28.0% of patients taking placebo with MTX (p=0.002). The

ACR/EULAR [Boolean] definition of remission requires that a patient has little, if any, active disease.[3] Almost half (45.3%) of the early RA patients receiving certolizumab pegol with MTX in this study achieved clinical remission using the stringent Boolean-based definition.[1] No new or unexpected safety signals were observed.[1]

An additional multi-center, randomized, double-blind, placebo-controlled study is currently evaluating certolizumab pegol in combination with methotrexate in the treatment of disease modifying antirheumatic Drugs (DMARD)-naïve adults with early active rheumatoid arthritis. Top-line results of this global study are expected in 2016.[4]

In the European Union, Cimzia®, in combination with MTX, is approved 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. 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 MTX or when continued treatment with MTX is inappropriate. Cimzia® is also approved in the EU for the treatment of adult patients with severe active axial spondyloarthritis (axSpA), comprising:[5]

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 without radiographic evidence of AS - adults with severe active axSpA without radiographic evidence of AS but with objective signs of inflammation by elevated CRP and/or MRI, who have had an inadequate response to, or are intolerant to NSAIDs.[5]

** high-positive anti-CCP, and either positive rheumatoid factor or erosion on radiographs*

About CIMZIA® in the EU/EEA

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. 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. Cimzia® is a registered trademark of UCB PHARMA S.A.

Cimzia® (certolizumab pegol) EU/EEA Important Safety Information[5]
Cimzia® was studied in 4,049 patients with 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 May 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.[6] RA is more common in women than men and although it can occur at any age, it usually begins after the age of 40.[6]

References

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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 € 3.4 billion in 2013. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

About Astellas Pharma Inc.

Astellas Pharma Inc., based in Tokyo, Japan, is a pharmaceutical company dedicated to improving the health of people around the world by providing innovative and reliable pharmaceutical products. Astellas has approximately 17,000 employees worldwide. The organization is committed to becoming a global category leader in Urology, Immunology (including Transplantation) and Infectious diseases, Oncology, Neuroscience and DM Complications and Kidney diseases. For more information on Astellas Pharma Inc., please visit the company's Website at www.astellas.com/en.

Forward looking statements

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially 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, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, product liability claims, challenges to patent protection for products or product candidates, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws and hiring and retention of its employees. UCB is providing this information as of the date of this press release and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.
There is no guarantee that new product candidates in the pipeline will progress to product approval or that new indications for existing products will be developed and approved. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be

subject to differences between the partners. Also, UCB or others could discover safety, side effects or manufacturing problems with its products after they are marketed.
Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.