

UCB announces initial clinical trial results involving patients taking certolizumab pegol for moderate to severe Crohn's disease

BRUSSELS, Belgium – December 21, 2009 – 07:00 (CET) - regulated information - UCB, a global biopharmaceutical company, announced the preliminary results of a recently completed Phase IIIb, multinational, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of certolizumab pegol, a pegylated fab' fragment of a humanized anti-TNF alpha monoclonal antibody in patients with moderately to severely active Crohn's disease. The study randomized more than 400 adult patients from March 2008 through August 2009 at 104 medical facilities around the world.

The primary objective of the study was to evaluate the efficacy of certolizumab pegol in inducing clinical remission in patients with moderate to severe Crohn's disease as compared with standard of care based on a CDAI score at week 6.

The results showed that 32% of patients in the study taking certolizumab pegol achieved remission as early as week 6. The study also showed that 25% of patients in the study taking a placebo achieved remission at week 6. Certolizumab pegol results were numerically superior at all time points, but were not statistically significant in the overall population meaning the primary end point was not achieved. Certolizumab pegol showed statistical significance in induction of remission in the more severe patient population as defined by inflammation levels and CDAI scores at baseline, as demonstrated by additional exploratory analyses.

UCB remains committed to certolizumab pegol for Crohn's patients and their unmet needs.

About Crohn's disease

Crohn's disease is a chronic, progressive, destructive disorder that causes inflammation of the gastrointestinal (GI) tract, most commonly at the end of the small intestine (the ileum) and beginning of the large intestine (the colon). If not effectively treated, it may result in the need for surgery and hospitalization. Crohn's disease has been estimated to affect as many as half a million Americans. People with Crohn's can experience an ongoing cycle of flare-up and remission throughout their lives. Together with ulcerative colitis, Crohn's disease is an inflammatory bowel disease (IBD).

About certolizumab pegol

Certolizumab pegol is the only PEGylated anti-TNF (Tumor Necrosis Factor). It has a high affinity for human TNF-alpha, selectively neutralising 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 certolizumab pegol for reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderate to severe active disease who have had an inadequate response to conventional therapy. It is also approved for the treatment of adults with moderately to severely active rheumatoid arthritis. Certolizumab pegol was approved in Switzerland



for induction of a clinical response and for the maintenance of a clinical response and remission in patients with active Crohn's disease who have not responded adequately to conventional treatment in September 2007.

Important safety information

Risk of Serious Infections and Malignancy

Patients treated with certolizumab pegol are at an increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Certolizumab pegol should be discontinued if a patient develops a serious infection or sepsis. Reported infections include:

- **Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before certolizumab pegol use and during therapy. Treatment for latent infection should be initiated prior to certolizumab pegol use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral and other infections due to opportunistic pathogens.**

The risks and benefits of treatment with certolizumab pegol should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with certolizumab pegol, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which certolizumab pegol is a member. Certolizumab pegol is not indicated for use in pediatric patients.

Serious and sometimes fatal infection due to bacterial, mycobacterial, invasive fungal, viral or other opportunistic pathogens has been reported in patients receiving TNF-blocking agents. Among opportunistic infections, tuberculosis, histoplasmosis, aspergillosis, candidiasis, coccidioidomycosis, listeriosis, and pneumocystosis were the most common. Treatment with certolizumab pegol should not be initiated in patients with an active infection, including clinically important localized infections. Certolizumab pegol should be discontinued if a patient develops a serious infection or sepsis. Patients who develop a new infection during treatment with certolizumab pegol should be closely monitored, undergo a prompt and complete diagnostic workup appropriate for immunocompromised patients, and appropriate antimicrobial therapy should be initiated. Appropriate empiric antifungal therapy should also be considered while a diagnostic workup is performed for patients who develop a serious systemic illness and reside or travel in regions where mycoses are endemic.

Malignancies

During controlled and open-labeled portions of certolizumab pegol studies of Crohn's disease and other diseases, malignancies (excluding non-melanoma skin cancer) were observed at a rate of 0.5 per 100 patient-years among 4,650 certolizumab pegol-treated patients versus a rate of 0.6 per 100 patient-years among 1,319 placebo-treated patients. In studies of certolizumab pegol for Crohn's disease and other investigational uses, there was one case of lymphoma among 2,657 certolizumab pegol-treated patients and one case of Hodgkin lymphoma among 1,319 placebo-treated patients. In certolizumab pegol RA clinical trials (placebo-controlled and open label) a total of three cases of lymphoma were observed among 2,367 patients. This is approximately 2-fold higher than expected in the general population. Patients with RA, particularly those with highly active disease, are at a higher risk for the development of lymphoma. The potential role of TNF blocker therapy in the development of malignancies is not known.

Malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blocking agents (initiation of therapy ≤ 18 years of age), of which certolizumab pegol is a member. Approximately half of the cases were lymphoma (including Hodgkin's and non-Hodgkin's lymphoma), while the other cases represented a variety of different malignancies and included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents. Most of the patients were receiving concomitant immunosuppressants.

Cases of acute and chronic leukemia have been reported with TNF-blocker use. Even in the absence of TNF-blocker therapy, patients with RA may be at a higher risk (approximately 2-fold) than the general population for developing leukemia.



Heart Failure

Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers. Certolizumab pegol has not been formally studied in patients with CHF. Exercise caution when using certolizumab pegol in patients who have heart failure and monitor them carefully.

Hypersensitivity

Symptoms compatible with hypersensitivity reactions, including angioedema, dyspnea, hypotension, rash, serum sickness, and urticaria, have been reported rarely following certolizumab pegol administration. If such reactions occur, discontinue further administration of certolizumab pegol and institute appropriate therapy.

Hepatitis B Reactivation

Use of TNF blockers, including certolizumab pegol, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. Some cases have been fatal. Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating certolizumab pegol therapy. Exercise caution in prescribing certolizumab pegol for patients identified as carriers of HBV, with careful evaluation and monitoring prior to and during treatment. In patients who develop HBV reactivation, discontinue certolizumab pegol and initiate effective anti-viral therapy with appropriate supportive treatment.

Neurologic Reactions

Use of TNF blockers, including certolizumab pegol, has been associated with rare cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of demyelinating disease. Rare cases of neurological disorders, including seizure disorder, optic neuritis, and peripheral neuropathy have been reported in patients treated with certolizumab pegol. Exercise caution in considering the use of certolizumab pegol in patients with these disorders.

Hematologic Reactions

Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia (e.g., leukopenia, pancytopenia, thrombocytopenia) has been infrequently reported with certolizumab pegol. 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 certolizumab pegol. Consider discontinuation of certolizumab pegol therapy in patients with confirmed significant hematologic abnormalities.

Drug Interactions

An increased risk of serious infections has been seen in clinical trials of other TNF blocking agents used in combination with anakinra or abatacept. Formal drug interaction studies have not been performed with rituximab or natalizumab; however because of the nature of the adverse events seen with these combinations with TNF blocker therapy, similar toxicities may also result from the use of certolizumab pegol in these combinations. Therefore, the combination of certolizumab pegol with anakinra, abatacept, rituximab, or natalizumab is not recommended. Interference with certain coagulation assays has been detected in patients treated with certolizumab pegol. There is no evidence that certolizumab pegol therapy has an effect on *in vivo* coagulation. Certolizumab pegol may cause erroneously elevated aPTT assay results in patients without coagulation abnormalities.

Autoimmunity

Treatment with certolizumab pegol may result in the formation of autoantibodies and, rarely, in the development of a lupus-like syndrome. Discontinue treatment if symptoms of lupus-like syndrome develop.

Immunizations

Do not administer live vaccines or attenuated vaccines concurrently with certolizumab pegol.

Adverse Reactions

In controlled Crohn's clinical trials, the most common adverse events that occurred in $\geq 5\%$ of certolizumab pegol patients (n=620) and more frequently than with placebo (n=614) were upper respiratory infection (20% certolizumab pegol, 13% placebo), urinary tract infection (7% certolizumab pegol, 6% placebo), and arthralgia (6% certolizumab pegol, 4% placebo). The proportion of patients who discontinued treatment due to adverse reactions in the controlled clinical studies was 8% for certolizumab pegol and 7% for placebo.

In controlled RA clinical trials, the most common adverse events that occurred in $\geq 3\%$ of patients taking certolizumab pegol 200 mg every other week with concomitant methotrexate (n=640) and more frequently than with placebo with concomitant methotrexate (n=324) were upper respiratory tract infection (6% certolizumab pegol, 2% placebo), headache (5% certolizumab pegol, 4% placebo), hypertension (5% certolizumab pegol, 2% placebo), nasopharyngitis (5% certolizumab pegol, 1% placebo), back pain (4% certolizumab pegol, 1% placebo), pyrexia (3% certolizumab pegol, 2% placebo), pharyngitis (3% certolizumab pegol, 1% placebo), rash (3% certolizumab pegol, 1% placebo), acute bronchitis (3% certolizumab pegol, 1% placebo), fatigue (3% certolizumab pegol, 1% placebo). Hypertensive adverse reactions were observed more frequently in patients receiving certolizumab pegol than in controls. These adverse reactions occurred more frequently among patients with a baseline history of hypertension and among patients receiving concomitant corticosteroids and non-steroidal anti-inflammatory drugs. Patients receiving certolizumab pegol 400mg as monotherapy every 4 weeks



in RA controlled clinical trials had similar adverse reactions to those patients receiving certolizumab pegol 200mg every other week. The proportion of patients who discontinued treatment due to adverse reactions in the controlled clinical studies was 5% for certolizumab pegol and 2.5% for placebo.

Please see full prescribing information at www.cimzia.com before prescribing.

For further information

*Bert Kelly, UCB U.S. Communications & Public Relations, UCB
T +1 770.970.8491, bert.kelly@ucb.com*

*Richard Simpson, Investor Relations, UCB
T+32.2.559.9494, richard.simpson@ucb.com*

*Michael Tuck-Sherman, Investor Relations, UCB
T +32.2.559.9712, michael.tuck-sherman@ucb.com*

*Nancy Nackaerts, External Communications, UCB
T +32.473.864.414, nancy.nackaerts@ucb.com*

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 approximately 10 000 people in over 40 countries, UCB generated revenue of EUR 3.6 billion in 2008. UCB is listed on Euronext Brussels (symbol: UCB).

Forward-looking statement

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.