



New long-term data on Cimzia[®] (certolizumab pegol) presented at EULAR 2014 shows sustained outcomes in patients with spondyloarthritis

For the attention of European journalists only

- New 96-week interim data cut from the RAPID[™]-PsA and -axSpA studies showed that improvements in disease activity at 24 weeks in Cimzia[®]-treated psoriatic arthritis and axial spondyloarthritis patients were sustained over this two year period^{1,2}
- Post-hoc analyses suggested that disease activity state and clinical response level to Cimzia[®] during first 12 weeks of treatment may predict outcomes at week 48^{3,4}

Brussels (Belgium), June 12th, 2014 – 0700 (CEST) – UCB announced today new long-term data on Cimzia[®] (certolizumab pegol) in the treatment of spondyloarthritis including patients with psoriatic arthritis (PsA) and patients with axial spondyloarthritis (axSpA). Results from the 96-week open-label periods of the RAPID[™]-PsA and RAPID[™]-axSpA studies, along with post-hoc analyses, are presented this week at the European League Against Rheumatism (EULAR) 2014 Annual Congress in Paris, France.

“The new long-term data from the RAPID[™]-PsA and -axSpA studies presented at EULAR 2014 showed that the 24-week outcomes observed in Cimzia[®]-treated PsA and axSpA patients were sustained over two years,” said Dr. Philip J. Mease, Director Rheumatology Research, Swedish Medical Center and Clinical Professor, University of Washington School of Medicine, Seattle, WA, U.S. “Post-hoc analyses suggested that disease activity and clinical response during the first 12 weeks of treatment with Cimzia[®] may predict 48-week outcomes. This approach may enable physicians to determine early on when to change treatment in patients not responding to Cimzia[®].”

Previous reports from the RAPID[™]-PsA and -axSpA studies demonstrated that the efficacy and safety of Cimzia[®] to 24 weeks^{5,6} were sustained to 48 weeks^{7,8} in patients with PsA and patients with axSpA, including those with ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA). The new data presented at EULAR, based on an additional 48 weeks of open-label data, showed that improvements in clinical efficacy and patient-reported outcomes observed over 24 weeks were sustained throughout the dose-blind and open-label periods to week 96, with no new safety signals reported.^{1,2} In patients with PsA, clinical efficacy was maintained in patients with or without prior anti-tumour necrosis factor (TNF) exposure.¹ In patients with axSpA, similar sustained improvements were observed in both AS and nr-axSpA sub-populations.²

New data were also presented from post-hoc analyses of the RAPID™-PsA and -axSpA studies, evaluating the association between disease activity and clinical response during the first 12 weeks of Cimzia® treatment, and the achievement of treatment goals at week 48. The results suggested that using disease activity state and the level of clinical response at week 12 of Cimzia® treatment made it possible to selectively identify a subset of patients who were unlikely to achieve treatment targets.^{3,4}

Cimzia®, in combination with methotrexate (MTX), is approved in the EU for the treatment of moderate to severe active rheumatoid arthritis (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 PsA 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 axSpA, comprising:

Ankylosing spondylitis - 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.⁹

Abstract title: Long-Term Safety and Efficacy of Certolizumab Pegol in Patients with Psoriatic Arthritis With and Without Prior Anti-Tumor Necrosis Factor Exposure: 96-week Outcomes from the RAPID-PsA Trial¹

This analysis of open-label data from the RAPID-PsA trial assessed clinical efficacy and safety up to 96 weeks in PsA patients receiving certolizumab pegol.

American College of Rheumatology (ACR)20/50/70 and Minimal Disease Activity (MDA) responses were sustained in both dosing regimens from week 24 to week 96. ACR responses at week 96 were similar in patients with or without prior anti-TNF exposure (ACR20: 63.0% vs. 64.4%, ACR50: 50.0% vs. 49.8%, ACR70: 35.2% vs. 33.3%). Improvements in skin disease (for patients with ≥3% surface area skin involvement at baseline) were also maintained up to week 96, including Psoriasis Area and Severity Index (PASI)75 and PASI90 measures (61.4% at week 24 vs. 53.0% at week 96 and 41.6% at week 24 vs. 44.0% at week 96 respectively). Certolizumab pegol also improved patient reported outcomes such as pain, physical function and health-related quality of life.

The safety profile was in line with that previously reported from the RAPID-PsA trial, with no new safety signals observed with increased exposure.

Abstract title: Disease Activity and Clinical Response Early in the Course of Treatment Predict Long-Term Outcomes in Psoriatic Arthritis Patients Treated with Certolizumab Pegol³

Post-hoc analysis of the RAPID-PsA study assessed the association between disease activity and clinical response during the first 12 weeks of treatment and the achievement of a treatment target at

week 48 in PsA patients receiving certolizumab pegol.

A relationship between DAS28 disease activity state at week 2 and Minimal Disease Activity (minDA) at week 48 was observed, with 68% (17/25) of patients who were in remission at week 2 achieving minDA at week 48, in comparison to 10% (5/52) of patients with high disease activity at week 2 achieving minDA at week 48. This trend was maintained at week 12, with 73% (57/78) of patients in remission at week 12 achieving minDA at week 48 whereas 0% (0/26) of patients with high disease activity at week 12 achieved minDA at week 48.

Abstract title: Long-Term Safety and Efficacy of Certolizumab Pegol in Patients with Axial Spondyloarthritis, including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis: 96-Week Outcomes of the RAPID-axSpA Trial²

Open-label data from the RAPID-axSpA trial were analysed to assess the clinical efficacy and safety of certolizumab pegol in axSpA patients up to 96 weeks.

Assessment of SpondyloArthritis international Society (ASAS)20/40 and partial remission (PR) responses were sustained in patients on both certolizumab pegol dosing regimens from week 24 through to week 96 (ASAS20, combined doses: 67.4% vs. 62.8%, ASAS40: 50.9% vs. 50.5%, ASAS PR: 30.3% vs. 28.4%). Improvements in disease activity scores including Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI)-linear were also maintained from week 24 through to week 96. Similar sustained improvements were seen in both AS and nr-axSpA subpopulations.

The safety profile was in line with that previously reported from the RAPID-axSpA trial, with no new safety signals observed with increased exposure.

Abstract title: Disease Activity and Clinical Response Early in the Course of Treatment Predict Long-Term Outcomes in Axial Spondyloarthritis Patients Treated with Certolizumab Pegol⁴

The aim of this post-hoc analysis of the RAPID-axSpA study was to assess the association between disease activity and clinical response during the first 12 weeks of treatment and the achievement of a treatment target at week 48 in axSpA patients, including AS and nr-axSpA patients, receiving certolizumab pegol.

A relationship between disease activity at week 2 and clinical response (ASDAS inactive disease [ID]) at week 48 was observed, with 71% (22/31) of patients with ASDAS ID at week 2 achieving ASDAS ID at week 48, compared to 0% (0/27) of patients with very high disease activity achieving ASDAS ID at week 48. This trend was maintained at week 12, with 68% (34/50) of patients in remission (ASDAS ID) at week 12 achieving ASDAS ID at week 48 whereas 0% (0/21) of patients with very high disease activity achieved ASDAS ID at week 48. Furthermore, the magnitude of clinical response at week 12 was associated with the likelihood of attaining ASDAS ID at week 48. Similar trends were observed in the AS and nr-axSpA sub-populations.

Notes to editors

About the RAPID™-PsA study⁵

The RAPID™-PsA study is a Phase 3, multicenter, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of certolizumab pegol in patients with active PsA. Patients (n=409) were randomized 1:1:1 to placebo or 400 mg loading dose certolizumab pegol at week 0, 2 and 4 followed by either 200 mg certolizumab pegol every two weeks or 400 mg certolizumab pegol every four weeks. RAPID™-PsA is a double-blind and placebo-controlled to week 24, dose-blind to week 48 and open-label to week 216.

About the RAPID™-axSpA study⁶

The RAPID™-axSpA study is a Phase 3, multicenter, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of certolizumab pegol in patients with active axSpA. Patients (n=325) were randomized 1:1:1 to placebo or 400 mg loading dose certolizumab pegol at week 0, 2 and 4 followed by either 200 mg certolizumab pegol every two weeks or 400 mg certolizumab pegol every four weeks. RAPID™-axSpA is a double-blind and placebo-controlled to week 24, dose-blind to week 48 and open-label to week 204.

About CIMZIA®⁹

Cimzia® is the only Fc-free, PEGylated anti-TNF (Tumour 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® (certolizumab pegol) EU/EEA Important Safety Information⁹

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, pancytopenia, 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 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. 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 axSpA in a placebo-controlled clinical trial for up to 30 months and in 409 patients with 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 25th November 2013.

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

For further information

- Eimear O'Brien, Brand Communications, UCB
T +32.2.559.9271, eimear.obrien@ucb.com
- Antje Witte, Investor Relations UCB
T +32.2.559.9414, antje.witte@ucb.com

- Alexandra Deschner, Investor Relations, UCB
T +32 2 559 9683, alexandra.deschner@ucb.com
- France Nivelles, Global Communications UCB
T +32.2.559.9178, france.nivelles@ucb.com
- Laurent Schots, Media Relations, UCB
T +32.2.559.9264, laurent.schots@ucb.com

References

1. P. J. Mease, R. Fleischmann, J. Wollenhaupt *et al.* Long-Term Safety and Efficacy of Certolizumab Pegol in Patients with Psoriatic Arthritis with and without Prior Anti-Tumor Necrosis Factor Exposure: 96-Week Outcomes from the RAPID-PsA Trial. Presented at the European League Against Rheumatism (EULAR) 2014 Congress. Abstract #OP0077
2. J. Sieper, M. Rudwaleit, D. van der Heijde *et al.* Long-Term Safety and Efficacy of Certolizumab Pegol in Patients with Axial Spondyloarthritis, including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis: 96-Week Outcomes of the RAPID-axSpA Trial. Presented at the European League Against Rheumatism (EULAR) 2014 Congress. Abstract #SAT0351
3. P. J. Mease, R. Fleischmann, O. Davies *et al.* Disease Activity and Clinical Response Early in the Course of Treatment Predict Long-Term Outcomes in Psoriatic Arthritis Patients Treated with Certolizumab Pegol. Presented at the European League Against Rheumatism (EULAR) 2014 Congress. Abstract #SAT0405
4. D. van der Heijde, A. Deodhar, O. Davies *et al.* Disease Activity and Clinical Response Early in the Course of Treatment Predict Long-Term Outcomes in Axial Spondyloarthritis Patients Treated with Certolizumab Pegol. Presented at the European League Against Rheumatism (EULAR) 2014 Congress. Abstract #SAT0338
5. P. J. Mease, R. Fleischmann, A. Deodhar *et al.* Effect of Certolizumab Pegol on Signs and Symptoms in Patients with Psoriatic Arthritis: 24-Week Results of a Phase 3 Double-Blind Randomised Placebo-Controlled Study (RAPID-PsA). *Ann Rheum Dis* 2014; 73(1): 48-55.
6. R. Landewé, J. Braun, A. Deodhar *et al.* Efficacy of Certolizumab Pegol on Signs and Symptoms of Axial Spondyloarthritis including Ankylosing Spondylitis: 24-Week Results of a Double-Blind Randomised Placebo-Controlled Phase 3 Study. *Ann Rheum Dis* 2014 73(1): 39-47.
7. P. J. Mease, R. Fleischmann, J. Wollenhaupt *et al.* Effect of Certolizumab Pegol over 48 Weeks on Signs and Symptoms in Patients with Psoriatic Arthritis with and without Prior Tumor Necrosis Factor Inhibitor Exposure. *Arthritis Rheum* 2013;65(10):S132-S133
8. R. Landewé, M. Rudwaleit, D. van der Heijde *et al.* Effect of Certolizumab Pegol over 48 Weeks in Patients with Axial Spondyloarthritis, including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis. *Arthritis Rheum.* 2013;65(10):S767
9. Cimzia® EU Summary of Product Characteristics, European Medicines Agency. Accessed 24th April 2014 from http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf

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

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