



Cimzia® (certolizumab pegol) shows sustained clinical improvements over three years and inhibition of joint progression in patients with rheumatoid arthritis

- **In adult patients with moderate to severely active rheumatoid arthritis, Cimzia® provided rapid and sustained improvements in ACR responses, DAS 28 scores, HAQ-DI scores and in pain VAS over three years¹**
- **Sustained inhibition of progression of structural joint damage was observed in patients treated with Cimzia® up to 2.5 years¹**

ROME June 16th, 2010, 08.30 CET — UCB today announced data showing that rapid improvements in ACR20, physical function, pain and fatigue of rheumatoid arthritis (RA) as early as Week 1, following treatment with Cimzia® (certolizumab pegol), together with methotrexate (MTX), was sustained up to 148 weeks.¹ Inhibition of progression of structural joint damage (seen at Week 24) was sustained up to the last x-ray evaluation at 2.5 years.¹ Cimzia® was well tolerated with no new safety signals across three years.¹

"These data have shown certolizumab pegol as an effective and well tolerated therapy in patients treated for a sustained period of time," said lead investigator Josef Smolen, M.D., and Chairman of the Department of Rheumatology, Internal Medicine III, Medical University of Vienna, "As a chronic condition, it is critical patients and physicians are confident that treatments deliver a rapid response and are effective in the longer term to help maintain overall quality of life."

The data presented were from an open label extension (OLE) to the phase III, Rheumatoid Arthritis Prevention of Structural Damage (RAPID 2) study.¹ The OLE was designed to investigate the long-term efficacy and safety of Cimzia® and methotrexate (MTX) over three years (148 weeks).¹ Patients receiving Cimzia® 200mg or 400mg + MTX who completed RAPID 2 initially received Cimzia® 400mg + MTX every other week (EOW) in the OLE; this Cimzia® dose was decreased from 400mg to 200mg EOW per protocol (after ≥6 months in the OLE).^{1*}

Efficacy was measured by ACR 20/50/70 responder rates, DAS28[ESR]. Patient-reported outcomes included physical function (assessed using the Health Assessment Questionnaire-Disability Index [HAQ-DI]) and pain (assessed on a 0–100-mm visual analogue scale [VAS]).

At 148 weeks, ACR responses in Cimzia® 200mg completers were sustained.¹ Sixty-three percent of Cimzia® 200mg completers who entered the OLE had an ACR50 response.¹ ACR20/50/70 response rates were similar in CZP 400mg completers.¹ Low disease activity (DAS28[ESR]≤3.2) was reported in 39% of patients with 36% of patients originally



treated with 200mg Cimzia® and 42% originally treated with 400mg Cimzia®. Twenty percent of patients had remission at week 148¹ (19% of patients originally treated with 200mg Cimzia® and 20% originally treated with 400 mg Cimzia®).¹

Improvements in HAQ-DI scores were sustained over 3 years in Cimzia® 200mg completers,¹ as were improvements in pain VAS.¹ Results were similar in Cimzia® 400mg completers.¹

Inhibition of radiographic progression observed during the double-blind phase (weeks 0-24) was sustained up to the last x-ray evaluation at 2.5 years.¹ The mean change from baseline in modified total Sharp score (mTSS) for the combined Cimzia® dose groups at Week 128 was 0.75.¹

There was no increase in incidence of AEs in the OLE, nor were any new safety signals observed.¹

In Cimzia®'s pivotal clinical trials reported serious adverse reactions included infections (including tuberculosis) and malignancies (including lymphoma). The most common adverse reactions belonged to the system organ classes Infections and Infestations, reported in 15.5% of patients on Cimzia® and 7.6% of patients on placebo, and General disorders and administration site conditions, reported in 10.0% of patients on Cimzia® and 9.7% of patients on placebo. A pooled analysis of the safety data showed there was a low incidence of injection site pain (1.5%) and a low level of discontinuations due to adverse events (5%). Cimzia® demonstrated a favorable risk-benefit profile in patients with at least up to two years of drug exposure.

These and other Cimzia® data are available on display during the 2010 Annual Meeting of the European League Against Rheumatism in Rome, Italy, June 16 – 19.

** The recommended starting dose of Cimzia for adult patients with rheumatoid arthritis is 400 mg (as 2 injections of 200 mg each on one day) at weeks 0, 2 and 4, followed by a maintenance dose of 200 mg every 2 weeks. Methotrexate should be continued during treatment with Cimzia where appropriate.*

For further information

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Important safety information

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Cimzia® is contraindicated in patients with active tuberculosis or other severe infections such as sepsis, abscesses and opportunistic infections and in patients with moderate to severe heart failure. Before initiation of Cimzia®, evaluate patients for both active or inactive (latent) tuberculosis infection. Monitor patients for the development of signs and symptoms of infection during and after treatment with Cimzia®. If an infection develops, monitor carefully, and stop Cimzia® if infection becomes serious.

Use of TNF blockers, including Cimzia®, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus, of new onset or exacerbation of clinical symptoms and/or radiographic evidence of demyelinating disease, in the formation of autoantibodies and uncommonly in the development of a lupus-like syndrome or of severe hypersensitivity



reactions following Cimzia administration. If a patient develops any of these adverse reactions, Cimzia[®] should be discontinued and appropriate therapy instituted.

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 biological DMARDs such as anakinra, abatacept and rituximab 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 or attenuated vaccines.

Please see full prescribing information before prescribing. This can be accessed at: www.ema.europa.eu/humandocs/PDFs/EPAR/cimzia/emea-combined-h1037en.pdf

About CIMZIA[®]

Cimzia[®] is the only 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. The U.S. Food and Drug Administration (FDA) has approved Cimzia[®] for reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy and for the treatment of adults with moderately to severely active rheumatoid arthritis. Cimzia[®] in combination with MTX, is approved in the EU** 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. UCB is also developing Cimzia[®] in other autoimmune disease indications. Cimzia[®] is a registered trademark of UCB PHARMA S.A.

About RAPID 2

This Phase III double-blind placebo-controlled trial, involving 619 patients with active adult-onset RA was designed to evaluate the efficacy and tolerability of subcutaneous (SC) liquid certolizumab pegol (200 and 400 mg) together with MTX every 2 weeks compared to placebo together with MTX in patients with active RA despite ≥ 6 months treatment with MTX. * Patients were randomly allocated to receive one of three treatment regimens: 246 patients received certolizumab pegol (liquid formulation) 400 mg and at Weeks 0, 2 and 4, then 200 mg every two weeks; 246 patients received certolizumab pegol (liquid formulation) 400 mg every 2 weeks; * 127 patients received placebo every 2 weeks. RAPID 2 met its primary endpoint ACR20 response rate at Week 24, and secondary endpoints: change from baseline in mTSS, ACR 50 and ACR 70 responses at Week 24. Significantly more patients in the certolizumab pegol 200 and 400 mg groups achieved an ACR20 response versus placebo ($p \leq 0.001$); rates were 57.3%, 57.6%, and 8.7%, respectively. Certolizumab pegol 200 and 400 mg also significantly inhibited radiographic progression; mean changes from baseline in mTSS at Week 24 were 0.2 and -0.4, respectively, versus 1.2 for placebo (rank analysis $p \leq 0.01$). Certolizumab pegol treated patients reported rapid and significant improvements in physical function versus placebo ($p \leq 0.001$).

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 more than 9000 people in over 40 countries, UCB produced revenue of EUR 3.1 billion in 2009. UCB is listed on Euronext Brussels (symbol: UCB).

Forward-looking statements

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.



References

1. Smolen JS et al. Efficacy and Safety of Certolizumab Pegol Plus Methotrexate in patients With Rheumatoid Arthritis: 3-Year Data From the RAPID 2 Study. 2010 Meeting of the European League Against Rheumatism (EULAR). Rome, Italy, June 16 – 19. SAT0127.