

Direct Comparison of Certolizumab Pegol versus Adalimumab in Rheumatoid Arthritis: 2-Year Efficacy and Safety Results from the Randomized EXXELERATE Study

Technical Title: A Multicenter, Single-Blind, Randomized Parallel-Group Study To Assess The Short - And Long-Term Efficacy Of Certolizumab Pegol Plus Methotrexate Compared With Adalimumab Plus Methotrexate In Subjects With Moderate To Severe Rheumatoid Arthritis Responding Inadequately To Methotrexate – EXXELERATE

Thank you	UCB would like to thank all of the participants of this clinical study. Patient participation in clinical studies like this one directly contributes towards better management of patients for conditions like rheumatoid arthritis.
Background	<p>Rheumatoid arthritis is a <u>chronic systemic</u> disorder that causes the immune system to rapidly attack the joints.^{1, 2} Patients' most common signs and symptoms result in pain, joint swelling, fatigue, and potential subsequent joint damage that can lead to disability.² If the disease remains uncontrolled, it can affect the patients' activities such as work and/or other components of social activities, as a result of loss of <u>functioning</u> and mobility.³</p> <p>Until a cure is found for rheumatoid arthritis, researchers continue to evaluate available treatment options to improve use of the current therapies to better manage patients' disease.</p>
Purpose of the study⁴	<ul style="list-style-type: none">• To evaluate if certolizumab pegol (Cimzia[®]) was more effective than adalimumab (Humira[®]) (both <u>tumor necrosis factor inhibitors</u> [TNFi]) in combination with methotrexate in improving patients' symptoms of rheumatoid arthritis after 12 weeks and 2 years of treatment.• To evaluate how effective and safe it was to change from Cimzia[®] to Humira[®] or vice versa in patients where the first treatment administered had not been effective.
Study participants⁴	The study included 915 adult patients aged 18 years or more with rheumatoid arthritis whose symptoms had not improved with methotrexate treatment alone.
Key findings⁴	<ul style="list-style-type: none">• The study showed that Cimzia[®] was not more effective than Humira[®]. The treatments were no different to one another in terms of how well they worked in the short term (at 12 weeks) and long term (at 2 years).<ul style="list-style-type: none">○ For the majority of patients, both treatments improved the patients' symptoms and reduced the number of tender and swollen joints*.• Among the patients who did not respond initially to either Cimzia[®] or Humira[®], more than half did respond when they changed to the other drug**.• The type and number of side effects was similar between both drugs during the 2 year period of the study, including when changing treatment from Cimzia[®] to Humira[®] or vice versa.• The most common side effects reported in at least 5% of patients (i.e., 5 patients out of every 100 treated) were:⁵<ul style="list-style-type: none">○ headache,○ nasopharyngitis (an infection of the upper respiratory system)○ upper respiratory tract infection (an infection affecting the nose, sinuses and throat)○ urinary tract infection (an infection of the bladder, kidneys, ureters or urethra)

Study design and research methodology⁴

- sinusitis (inflammation of the sinuses)
- bronchitis (inflammation of the breathing tubes within the lungs)
- latent tuberculosis (a TB infection in which the TB bacteria are dormant (“sleeping”) and are not infectious or causing symptoms)
- cough
- high blood pressure
- diarrhoea

Most side effects were mild to moderate in intensity.

- The study was conducted at 151 centers in Europe (Austria, Bulgaria, Czech Republic, France, Germany, Hungary, Ireland, Italy, Poland, Portugal, Romania, Spain, and Switzerland), Australia, and North America (Canada, Mexico and USA)⁶ between December 2011 and November 2013.
- Patients took part in the study for a maximum of 2 years.
- The study participants were randomly divided into 2 groups. One group was given Cimzia[®] and the other Humira[®], as an injection under the skin every 2 weeks for 12 weeks at first.
- All patients continued taking methotrexate throughout the study.
- Patients did not know which treatment they were taking up to Week 12. After Week 12 patients knew which treatment they were taking. The physicians did not know which treatment the patients were taking during the entire period of the study.
- After 12 weeks the patients’ response to treatment was assessed. If the treatment improved a patient’s symptoms of disease to a level considered to be a clinical response, that patient remained on the same treatment until the end of the study.
- If patients’ symptoms did not improve enough, they were given the other medicine and their response to this new treatment measured after another 12 weeks (24 weeks from the start of the first treatment). If patients’ symptoms improved after treatment with the second medicine, they remained on this treatment until the end of the study; if not, they could leave the study.
- During the study, the patients were regularly seen to measure changes in their symptoms and physical function (such as their ability to carry out day to day activities like walking, eating, dressing, and grooming).
- The patients’ response to treatment was assessed once more at the end of the study (at 2 years).
- Unwanted effects (side effects) of both treatments were also studied.

Peer-reviewed publication

[Smolen JS, Burmester GR, Combe B, et al, Head-to-head comparison of certolizumab pegol versus adalimumab in rheumatoid arthritis: 2-year efficacy and safety results from the randomised EXXELERATE study. Lancet, 2016, Epublication ahead of print.](#)

* around 70 out of every 100 treated patients achieved an [ACR20](#) response at 12 weeks.

** around 60 out of every 100 treated of patients had a meaningful improvement in [Disease Activity Score \(DAS\)](#), 12 weeks after changing to the other medicine.

Glossary

Single blind	Physicians were not aware of the drug the patients were taking during the entire period of the study ⁴
Chronic	A disease or condition that persists throughout a person's life and must be managed because it cannot be cured ⁷
Systemic	A systemic disease is one that affects a number of organs and tissues, or affects the body as a whole ⁷
Functioning	Ability to carry out day to day activities like walking, eating, dressing, and grooming ³
Tumor necrosis factor (TNF) inhibitor	A TNFi is a medicine that blocks TNF, a protein that promotes inflammation ⁸
ACR20 response	20% improvement in tender and swollen joints plus 20% improvement in 3 out of the 5 following criteria: ⁹ <ul style="list-style-type: none"> • physician's overall assessment of patient's arthritis • patient's overall assessment of arthritis • patient's overall assessment of pain • patient's overall assessment of physical function • laboratory values of blood markers of inflammation (ESR or CRP)
Disease Activity Score (DAS) improvement	Patients had to either: ⁴ <ul style="list-style-type: none"> • have a meaningful improvement based on this scoring of disease activity, or • be in low disease activity according to the same scoring

References

1. Choy E. Understanding the dynamics: pathways involved in the pathogenesis of rheumatoid arthritis. *Rheumatology* 2012;51:v3-v11.
2. National Rheumatoid Arthritis Society. What is RA? Available at: <http://www.nras.org.uk/what-is-ra-article> [Accessed 13/10/16].
3. Hazes JM, Taylor P, Strand V, et al. Physical function improvements and relief from fatigue and pain are associated with increased productivity at work and at home in rheumatoid arthritis patients treated with certolizumab pegol. *Rheumatology* 2010;49:1900-1910.
4. Smolen J, Burmester G, Combe B, et al. Head-to-Head Comparison of Certolizumab Pegol versus Adalimumab in Rheumatoid Arthritis: 2-Year Efficacy and Safety Results from the Randomised EXXELERATE Study. *Lancet* 2016:Epublication ahead of print.
5. UCB Data on file: EXXELERATE RA0077 TFL 9.1.11, 2016
6. ClinicalTrials.gov. Study to Assess the Short- and Long-term Efficacy of Certolizumab Pegol Plus Methotrexate Compared to Adalimumab Plus Methotrexate in Subjects With Moderate to Severe Rheumatoid Arthritis (RA) Inadequately Responding to Methotrexate. Available online at <https://clinicaltrials.gov/ct2/show/NCT01500278>. [Accessed: 14/10/16].
7. Arthritis Research UK. Glossary. Available at: <http://www.arthritisresearchuk.org/arthritis-information/inflammatory-arthritis-pathway/glossary.aspx> [Accessed 14/10/16].
8. Arthritis Research UK. What is certolizumab pegol and why is it prescribed? Available at: <http://www.arthritisresearchuk.org/arthritis-information/drugs/certolizumab-pegol/what-it-is.aspx> [Accessed 14/10/16].
9. Felson DT, Anderson JJ, Boers M, et al. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. *Arthritis & Rheumatism* 1993;36:729-740.

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