

Interleukin-6 (IL-6)

The role of interleukin 6 (IL-6) in rheumatoid arthritis (RA)

IL-6 is a chemical messenger in the body, known as a cytokine, which contributes to the painful and persistent joint damage and chronic inflammation that people with RA suffer.^{i,ii} In people with RA, excess levels of IL-6 are produced in the joints,ⁱ particularly in the thin tissue layer covering the joint.²

Wider effects of IL-6

It is thought that excess IL-6 levels also lead to a range of complications in patients with RA, including anaemia, fatigue, weight loss, increased risk of cardiovascular disease and osteoporosis.^{i,2,iii,iv}

Excess levels of IL-6 can be associated with systemic inflammation, which has been linked to a higher risk of cardiovascular disease. The increased production of a protein in the blood, called C-reactive protein (CRP), may serve as a potential marker for this increased cardiovascular risk and can be measured.^v

Excess IL-6 may also cause anaemia, a condition in which the body lacks red blood cells.^{vi,vii} This lowers the capacity of the blood to carry oxygen around the body, which can result in tiredness and fatigue.^{viii}

IL-6 may also cause permanent damage of bone and cartilage, as it encourages the body to break down bones and blocks the formation of bones.^{1,ix,x,xi}

Targeting IL-6

ACTEMRA (tocilizumab, RoACTEMRA within the EU) is the first treatment for RA which targets IL-6. It blocks the activity of IL-6, reducing its impact and preventing the progression of RA both in the joints and throughout the body.^{xii} Clinical trials evaluating the efficacy and safety of ACTEMRA demonstrate rapid improvements in disease signs and symptoms plus effective control of inflammation in the joints and throughout the body.^{xiii,xiv,xv,xvi,xvii,xviii}

References:

- ⁱ Yoshizaki K, Nishimoto N, Mihara M, Kishimoto T. Therapy of rheumatoid arthritis by blocking IL-6 signal transduction with a humanized anti-IL-6 receptor antibody. *Springer Semin Immunopathol* 1998;20:247-259
- ⁱⁱ Lipsky PE. Interleukin-6 and rheumatic diseases. *Arthritis Res Ther* 2006; 8 (Suppl 2):S4
- ⁱⁱⁱ Maggio M, Guralnik JM, Longo DL, Ferrucci L. Interleukin-6 in Aging and Chronic Disease: A Magnificent Pathway. *Journal of Gerontology* 2006;61A(6):575-584
- ^{iv} Arthritis Care: Osteoarthritis <http://www.arthritiscare.org.uk/AboutArthritis/Conditions/Osteoarthritis> Last accessed 21st May 2009
- ^v American Heart Association. Inflammation, Heart Disease and Stroke: The Role of C-Reactive Protein. <http://www.americanheart.org/presenter.jhtml?identifier=4648> Last accessed 21st May 2009
- ^{vi} Mihara M, Hashizume M. IL-6-induced hepcidin is involved in the development of anemia in a monkey arthritis model. Program and abstracts of EULAR 2008: The European League Against Rheumatism Annual Congress; June 11-14, 2008; Paris, France. Abstract SAT0048
- ^{vii} Smolen JS, Chester Wasko M, Ramos-Remus CR, et al. Tocilizumab improves hemoglobin levels and FACIT-fatigue scores in patients with rheumatoid arthritis. Program and abstracts of EULAR 2008: The European League Against Rheumatism Annual Congress; June 11-14, 2008; Paris, France. Abstract THU0168
- ^{viii} National Heart Lung and Blood Institute: Anemia. http://www.nhlbi.nih.gov/health/dci/Diseases/anemia/anemia_what.html Last accessed 21st May 2009
- ^{ix} National Rheumatoid Arthritis Society Website: What is RA? http://www.rheumatoid.org.uk/article.php?article_id=224 Last accessed 21st May 2009
- ^x Arthritis Care: Osteoarthritis <http://www.arthritiscare.org.uk/AboutArthritis/Conditions/Osteoarthritis> Last accessed 21st May 2009
- ^{xi} Katagiri T, Takahashi N. Regulatory mechanisms of osteoblast and osteoclast differentiation. *Oral Diseases* 2002;8(3):147-159
- ^{xii} Sebba A. Tocilizumab: The first interleukin-6-receptor inhibitor. *American Journal of Health-System Pharmacy* 2008;65(15):1413-1418
- ^{xiii} Smolen JS, Beaulieu A, Rubbert-Roth A *et al.* Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis (OPTION study): a double-blind, placebo-controlled, randomised trial. *The Lancet* 2008;371(9617):987-997
- ^{xiv} Genovese MC, McKay JD, Nasonov EL *et al.* Interleukin-6 receptor inhibition with tocilizumab reduces disease activity in rheumatoid arthritis with inadequate response to disease-modifying antirheumatic drugs: The tocilizumab in combination with traditional disease-modifying antirheumatic drug therapy (TOWARD) study. *Arthritis & Rheumatism* 2008;58(10):2968-2980
- ^{xv} Emery P, Keystone E, Tony H *et al.* Tocilizumab significantly improves disease outcomes in patients with rheumatoid arthritis whose anti-TNF therapy failed: The RADIATE study. Presented at the European League Against Rheumatism (EULAR) congress, 11-14 June 2008, Paris
- ^{xvi} Jones, G. *et al.* Comparison of tocilizumab monotherapy versus methotrexate monotherapy in patients with moderate to severe rheumatoid arthritis: The AMBITION study. *ARD Online First*, published March 17, 2009
- ^{xvii} Kremer, J. *et al.* Tocilizumab inhibits structural joint damage, improves physical function, and increases DAS28 remission rates in RA patients who respond inadequately to methotrexate: The LITHE Study. Abstract presented at EULAR 2009
- ^{xviii} Smolen, J. *et al.* Efficacy of Tocilizumab (TCZ) in Rheumatoid Arthritis (RA): Interim analysis of long-term extension trials of up to 2.5 years. Abstract presented at EULAR 2009