

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

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,iii} In people with RA, excess levels of IL-6 are produced,ⁱ particularly in the thin tissue layer covering the joint.ⁱⁱ

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, depression and mood disorders, weight loss, increased risk of cardiovascular disease and osteoporosis.^{i,ii,iii}

Excess levels of IL-6 can be associated with systemic inflammation in the context of uncontrolled active disease, which has been linked to a higher risk of cardiovascular disease in patients with RA. 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.^{iv}

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

High IL-6 levels may also cause permanent damage of bone and cartilage, as it encourages the body to increase bone resorption and blocks new bone tissue formation.^{i,iv,viii,ix}

Targeting IL-6

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

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} American Heart Association. Inflammation, Heart Disease and Stroke: The Role of C-Reactive Protein. <http://www.americanheart.org/presenter.jhtml?identifier=4648> Last accessed 12 April 2011
- ^v Hashizume M et al., Tocilizumab, a humanized anti-interleukin-6 receptor antibody, improved anemia in monkey arthritis by suppressing IL-6-induced hepcidin production. *Rheumatology International*, 2009;Vol. 30, No.7; 917-923
- ^{vi} Smolen JS, 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*, Vol 371, Issue 9617, Pages 987-997
- ^{vii} National Heart Lung and Blood Institute: Anemia. http://www.nhlbi.nih.gov/health/dci/Diseases/anemia/anemia_what.html Last accessed 12 April 2011
- ^{viii} National Rheumatoid Arthritis Society Website: What is RA? http://www.nras.org.uk/about_rheumatoid_arthritis/what_is_ra/what_is_ra.aspx Last accessed 12 April 2011
- ^{ix} Katagiri T, Takahashi N. Regulatory mechanisms of osteoblast and osteoclast differentiation. *Oral Diseases* 2002;8(3):147-159
- ^x Sebba A. Tocilizumab: The first interleukin-6-receptor inhibitor. *American Journal of Health-System Pharmacy* 2008;65(15):1413-1418
- ^{xi} 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
- ^{xii} 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
- ^{xiii} 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
- ^{xiv} 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
- ^{xv} Fleischmann R *et al.* LITHE: Tocilizumab inhibits radiographic progression and improves physical function in rheumatoid arthritis (RA) patients (Pts) at 2 years with increasing clinical efficacy over time. Oral presentation at ACR, 18th October 2009
- ^{xvi} 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