Tocilizumab improves disease activity in patients with RA

Maini and colleagues have shown that tocilizumab (a monoclonal antibody against the interleukin-6 receptor) results in dose-related improvements in disease activity for patients with rheumatoid arthritis (RA). The efficacy of tumor necrosis factor inhibitors is increased by concomitant methotrexate, but the investigators found that the benefits of tocilizumab were similar with and without concomitant methotrexate.

This randomized, double-blind, 16-week trial included 359 patients with RA who had not responded adequately to ≥4 weeks of methotrexate. Patients received four infusions of tocilizumab 2, 4, or 8 mg/kg at monthly intervals plus either methotrexate or placebo once weekly, or four placebo infusions at monthly intervals plus methotrexate once weekly.

Improvements in RA activity were scored by the American College of Rheumatology (ACR) criteria. A 20% improvement (an ACR20 response) was achieved by 61% and 63% of patients who received 4 and 8 mg/kg of tocilizumab monotherapy, respectively, and by 63% and 74% of patients who received 4 and 8 mg/kg of tocilizumab plus methotrexate, respectively. A surprisingly high proportion (41%) of patients who received methotrexate without tocilizumab achieved an ACR20 response, however, which indicated that they had not yet fully responded to methotrexate at enrolment.

Tocilizumab was generally well tolerated: ~50% of patients experienced an adverse event, although most were mild or moderate. Some tocilizumab-treated individuals experienced clinically significant increases in transaminase levels, which seemed to be exacerbated by methotrexate. Dose-dependent increases in bilirubin, cholesterol, and in neutrophils were also observed.

Original article Maini RN *et al.* (2006) Double-blind randomized controlled clinical trial of the interleukin-6 receptor antagonist, tocilizumab, in European patients with rheumatoid arthritis who had an incomplete response to methotrexate. *Arthritis Rheum* **54:** 2817–2829

Treatment of amyloid A amyloidosis with tocilizumab

Tocilizumab has been successfully used to treat a 26-year-old, female, Japanese patient with amyloid A (AA) amyloidosis—a severe complication of inflammatory rheumatic disease—secondary to juvenile idiopathic arthritis. Immunosuppressants such as azathioprine, cyclophosphamide and moderate-dose prednisolone are used to treat AA amyloidosis, but suppression of serum AA levels is not always achieved.

The patient developed juvenile idiopathic arthritis at the age of 14 years. In September 2001 she had severe gastrointestinal symptoms and deposits of AA protein, and in January 2003 she had proteinuria, renal dysfunction, and AA protein deposits in renal small-vessel walls and the mesangial matrix. She later developed steroid-induced glaucoma. Before tocilizumab therapy began, the patient received methotrexate 15 mg per week and prednisolone 10 mg daily, but despite these treatments her serum AA concentration was 242.7 μg/ml (normal <8 μg/ml).

The patient began treatment with intravenous tocilizumab 8 mg/kg every 3–4 weeks, in addition to her previous treatment, in March 2003. Her serum AA concentration decreased after the first dose to within normal levels. As of December 2005, the patient had received 42 doses of tocilizumab and her serum AA concentrations had remained below 10 μg/ml except on one occasion. Gastrointestinal symptoms resolved within 1 month and proteinuria within 2 months. Methotrexate was tapered to 6 mg per week after 6 months and prednisolone to 5 mg daily after 2 months. Her AA protein deposits markedly regressed.

The authors conclude that tocilizumab could be an important therapy for the treatment of AA amyloidosis secondary to rheumatic disease.

Original article Okuda Y and Takasugi K (2006) Successful use of a humanized anti-interleukin-6 receptor antibody, tocilizumab, to treat amyloid A amyloidosis complicating juvenile idiopathic arthritis. *Arthritis Rheum* **54:** 2997–3000

Imatinib mesylate shows promise as a treatment for RA

Imatinib mesylate has anti-inflammatory properties, because it is a specific and potent inhibitor of several protein tyrosine kinases. Paniagua *et al.* have investigated imatinib's mechanism of action *in vitro*, and have evaluated its efficacy in the collagen-induced arthritis (CIA) mouse model of rheumatoid arthritis (RA).