



Use of Tocilizumab in

## Adult-Onset Still's Disease

Evidence Based Medicine

Official recommendations

Expert opinion

### Rationale for targeting IL-6 in Still's disease

In patients with adult-onset Still's disease, serum IL-6 levels increase during the flares and correlate with disease activity<sup>(121-125)</sup>. IL-6 overproduction may explain the main symptoms, as IL-6 can induce a fever, leukocytosis, thrombocytosis, elevations in protein markers for inflammation, and bone resorption.

A prospective controlled study has established that tocilizumab is effective in systemic juvenile idiopathic arthritis<sup>(94)</sup>.

### IL-6 antagonist therapy in adult-onset Still's disease: data from the literature

The only published data on tocilizumab therapy for adult-onset Still's disease come from anecdotal case-reports<sup>(55, 118-120)</sup> and a French retrospective study of 10 patients with adult-onset Still's disease refractory to conventional treatments including methotrexate, anakinra, and TNF antagonists.

No dose-finding studies in patients with adult-onset Still's disease are available and, consequently, the modalities of tocilizumab administration in this indication remain to be determined.

In the French retrospective study, half the 14 patients given tocilizumab 8 mg/kg monthly had a good EULAR joint response within 3 months and a joint remission (EULAR criteria) within 6 months<sup>(121)</sup> with resolution of the systemic signs in the vast majority of patients. In some patients, however, the joint manifestations failed to improve. The rate of improvement in the systemic manifestations was even higher. Escape phenomenon affecting both the joint and the systemic manifestations occurred in some patients. These results were obtained in patients with refractory adult-onset Still's disease who failed methotrexate, anakinra, and at least two TNF antagonists.

Tocilizumab has been used in a dosage of 4 to 8 mg/kg every 15 days from the outset in some patients with adult-onset Still's disease<sup>(55, 118-120)</sup>, although no proof has been obtained that twice monthly infusions confer additional benefits. Increasing the interval between the infusions was successful in some patients<sup>(55, 119)</sup> but led to a relapse of the joint and systemic manifestations in others<sup>(55, 118)</sup>.

The safety profile of tocilizumab in adult-onset Still's disease seems similar to that described in rheumatoid arthritis or systemic juvenile idiopathic arthritis. A case of macrophage activation syndrome, a well-known complication of Still's disease, occurred during cytomegalovirus infection in a tocilizumab-treated patient, although there is no proof of a causal link with the drug<sup>(55)</sup>. Bolus methylprednisolone therapy combined with cyclosporine ensured a favourable outcome, and re-treatment with tocilizumab in the same dosage

produced a good therapeutic effect with no relapse of the macrophage activation syndrome<sup>(55)</sup>.

The optimal duration of tocilizumab therapy remains to be determined. Tocilizumab therapy seems to suspend the symptoms in the overwhelming majority of cases. Nevertheless, a prolonged remission (up to 7 years without treatment) was reported after 18 months of tocilizumab therapy in one patient with adult-onset Still's disease<sup>(118, 120)</sup>.