Results of a phase-I/II randomized, masked, placebo-controlled trial of recombinant human interleukin-11 (rhIL-11) in the treatment of subjects with active rheumatoid arthritis

ABSTRACT

The trial showed rhIL-11 to be safe and well tolerated at a variety of doses and schedules over a 12-week treatment period in patients with active RA. The only adverse event clearly associated with rhIL-11 administration was reaction at the injection site.

INTRODUCTION

Introduction Recombinant human interleukin-11 (rhIL-11) is a pleiotropic cytokine that regulates the growth and development of hematopoietic stem cells and decreases the proinflammatory mediators of cytokine and nitric oxide production. Treatment with rhIL-11 decreases the production of proinflammatory cytokines, including tumor necrosis factor (TNF)-α and interleukin (IL)-1β, and inhibits NF-κB binding activity. In animal models both of collagen-induced and adjuvant-induced arthritis, rhIL-11 reduced both the level of synovitis and the histologic lesion score in the joints. Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology. Its worldwide prevalence is approximately 1%. There appears to be no single therapeutic regimen or combination of therapies that has consistently been associated with sustained improvement (i.e. remission). A number of disease-modifying drugs (e.g. methotrexate) are available to treat RA but are limited by significant toxicity requiring adjunct therapy, or are of variable efficacy. There are currently a number of anticytokine and other immune-modulating therapies in clinical trials. The proinflammatory cytokine TNF has been shown to play a role in the pathogenesis of RA. Etanercept (sTNFR:Fc) and infliximab (chimeric anti-TNF monoclonal antibody) have been shown to be efficacious in the treatment of patients with RA for whom treatment with at least one disease-modifying antirheumatic drug had previously failed; both of these biologicals have been approved by regulatory agencies for the treatment of patients with RA. rhIL-11 has previously been assessed in a Phase-I/II, masked, placebo-controlled trial in patients with active Crohn's disease. The data suggested clinical benefit as assessed from the mean change from baseline in the Crohn's Disease Severity Index after 21 days at doses of 16 and 40 μg/kg per week ($P < 0.05$). The researchers concluded that rhIL-11 was safe at the doses and schedules used and had a therapeutic effect. The findings supported the initiation of a phase-I/II clinical trial in patients with RA.

CONCLUSION

These preliminary data suggest that rhIL-11 may be safely administered to patients with active RA at a variety of doses and schedules. No dose-limiting adverse event was observed. The dose of 15 μg/kg of rhIL-11 once per week suggested a minimal therapeutic effect, an improvement in tender-joint counts. Further studies are warranted to find out if higher or more frequent doses of rhIL-11 may be safe and efficacious in treating RA.