

**Rituximab in the treatment of systemic sclerosis-associated
interstitial lung disease. Comment on the article by Yoo**

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Abstract

Several lines of evidence from basic research indicate that B cells may contribute to the pathogenesis of systemic sclerosis. Clinical studies as well, have provided preliminary data pointing to the direction that B cell depletion with rituximab might be a therapeutic option for patients with this debilitating disease.

Key words: systemic sclerosis; scleroderma; rituximab; interstitial lung disease; B cells; fibrosis; skin thickening; rheumatic diseases

Dear Sir

We read with interest the article by Yoo which reported a case of successful treatment of systemic sclerosis (SSc)-associated interstitial lung disease (ILD) with rituximab (RTX) in a patient resistant to steroid and cyclophosphamide (CYC) therapy. The author mentions that there is only one case report of improvement of SSc-associated ILD with RTX so far. This is incorrect. We have previously shown that RTX may improve lung function in patients with SSc-associated ILD, in a randomized, controlled, proof of principle study, of one year duration. (1) This study was available online (Epub ahead of print) since May 2009, six months prior of the date this article was submitted. This is why we were surprised to notice that our study was not included in the references even though the author has performed an exhaustive literature search and has included all the articles regarding the use of rituximab in SSc, including two in abstract form.

Three studies so far have explored the potential clinical efficacy of RTX in SSc. (1-3) Our study, however, was the only one specifically designed to test the effect of RTX on SSc-associated ILD, since the presence of ILD was an inclusion criterion and most patients had severe ILD. On the contrary the other two studies excluded patients with severe ILD and only a fraction of patients had evidence of mild ILD. We evaluated 14 patients with SSc. Eight patients were randomized to receive 2 courses of RTX at baseline and 24 weeks, whereas 6 patients (control group) received standard treatment alone. The median percentage of improvement of FVC in the RTX group was 10.25% whereas that of deterioration in the controls was 5.04% ($p=0.002$). The median percentage of improvement of DLco in the RTX group was 19.46% whereas that of deterioration in the control group was 7.5% ($p=0.023$). We also found evidence of skin remodelling with reduction of collagen deposition in most patients

treated with RTX which correlated with skin B cell depletion. We have also published a case report describing dramatic improvement of lung function and skin fibrosis in a patient with severe, diffuse scleroderma following long term treatment with RTX. (4) Our data indicate a possible disease modifying role of RTX in SSc, particularly in SSc-associated lung disease. (5)

The case report by Yoo is in agreement with our data and suggests that RTX may have beneficial effects on SSc-associated ILD. It is worth mentioning that this particular patient showed a dramatic improvement in HRCT findings something that was not observed in our cohort, probably due to the longer disease duration of our patients which had more established fibrosis.

SSc is a multisystem disease with poor prognosis since no disease modifying drugs exist so far. Cyclophosphamide has shown modest results, however its toxicity restricts its long term use. Clinical, as well as basic research data indicate that targeting B cells with RTX may be a promising therapeutic approach in SSc. We propose that further exploration of the clinical efficacy of RTX in SSc-associated ILD is highly needed. A direct comparison of RTX versus cyclophosphamide, the gold standard of care so far, in a large, multicentre, randomized, double blind study, would seem a reasonable approach.

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