Lack of efficacy of tocilizumab in severe axial refractory spondyloarthritis: a report of 5 patients

Sirs,

Even though the introduction of anti-tumour necrosis factor (anti-TNF) drugs has been a major advance in the treatment of spondyloarthritis (SpA), high disease activity persists in some patients despite these treatments. Reports of axial SpA treatment with other alternative biological drugs, such as rituximab or abatacept, are disappointing. In the field of SpA, higher serum IL-6 levels have been reported (1-3). There is, thus, a pharmacological background supporting the use of tocilizumab, a monoclonal humanised anti-human IL-6 receptor antibody, in these patients; which is also supported by some recent case reports (4-9).

Thus, our objective was to assess the short-term efficacy and tolerance of tocilizumab in axial SpA patients who were refractory or intolerant to usual treatments, including anti-TNF.

A prospective, non-controlled, open study was performed between March 2010 and March 2011 in one tertiary referral centre. The study was approved by the Cochin ethics committee. Inclusion criteria were axial SpA patients (modified New York criteria) with inadequately controlled disease by anti-TNF, and who received at least one infusion of tocilizumab. The intervention assessed was tocilizumab, at the dose used in rheumatoid arthritis (8mg/kg intravenous every 4 weeks), whatever the concomitant treatments. Patients were followed-up until treatment discontinuation. Clinical efficacy was assessed monthly by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI) and acute phase reactants. Treatment discontinuation and tolerance were also assessed.

In all, 5 patients were treated with tocilizumab for 4–8 months (total follow-up: 30 patient-months). Two patients (n. 2 and 3) had co-medication with methotrexate (20 and 15 mg/week orally respectively). The patients were all male, median age was 43 years, median disease duration was 21 years, with severe axial SpA, previously treated by anti-TNF and in 3 cases, rituximab (Table). Patients n. 1, 3 and 4 had previous peripheral involvement; patients 2 and 5 had previous entheseal involvement; patient 5 had previous episodes of anterior acute uveitis; patients 4 and 5 had psoriasis; none of the patients had inflammatory bowel disease. The indication was severe uncontrolled axial symptoms with elevated acute phase reactants (n=4) or controlled symptoms but with elevated acute phase reactants, while taking high doses of anti-TNF (n=1).

No clinical improvement was noted in 4 patients. At 3rd infusion, only patient 4 showed a decrease in BASDAI (going from 100 to 76mm) but the improvement was considered insufficient by both patient and physician. In the other patients, BASDAI remained stable in 2 patients, and worsened for the other 2. Thus the median relative change of BASDAI from baseline to 3rd infusion was a worsening: +13mm [range: -11 to +49]. BASFI values remained globally stable. Acute phase reactants decreased dramatically in all patients. All 5 patients discontinued treatment for inefficacy after 3–7 infusions. No adverse reactions were noted.Thus, the present study did not show clear evident short-term symptomatic efficacy of tocilizumab in 5 patients with severe refractory axial SpA.

The previous case reports of patients who benefited from tocilizumab were mostly suffering from a peripheral articular involvement of the disease (4-9). The present study focused on patients suffering mainly from axial involvement; and importantly, the recruited patients were not representative since suffering from a long-lasting, particularly refractory and severe disease. Furthermore, the follow-up was short-term and the doses of tocilizumab used in this study might not be optimal in axial SpA. Such data suggest the role of tocilizumab in the management of SpA should be further evaluated in prospective, controlled trials.

L. Gossec, *MD, PhD*
N. Del Castillo-Piñol, *MD*
C. Roux, *MD, PhD*
M. Dougados, *MD*

Faculty of Medicine, Paris Descartes University; APHP, Rheumatology B Department, Cochin Hospital, Paris, France.

Address correspondence to: Dr Laure Gossec, Service de Rhumatologie B, Hôpital Cochin 27, rue du Faubourg Saint-Jacques, 75014 Paris, France.
E-mail: laure.gossec@cch.aphp.fr

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Table I. Characteristics and previous treatments of the 5 patients with axial SpA treated with tocilizumab.

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age, years	40	49	43	55	39
Disease duration, years	21	14	27	26	15
Axial involvement: - Sacroiliitis (modified New York)	Yes	Yes	Yes	Yes	Yes
Occiput-to-wall distance, cm	16	24	11	12	5
HLA B27 positivity	yes	no	yes	yes	yes
Previous anti-TNF with reason for discontinuation	ETA: intolerance (osteosarcoma)	ADA and ETA: intolerance, INF: secondary inefficacy	ETA and ADA: partial efficacy but very elevated acute phase reactants, INF: clinical efficacy with persistent elevated acute phase reactants	ADA, ETA, INF: secondary inefficacy	ADA and INF: intolerance, ETA: primary inefficacy
Previous other biologics with reason for discontinuation	RTX: primary inefficacy	none	RTX: primary inefficacy	RTX: intolerance	none

ETA: etanercept; ADA: adalimumab; INF: infliximab; RTX: rituximab.