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Letter to the Editor

Exploratory study of adalimumab in twelve patients with chronic low back pain associated with Modic I changes

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Non-specific chronic low back pain (NS-CLBP) is the leading musculoskeletal disorder, and its treatment remains a challenge for clinicians [1]. Patients with Modic I changes (i.e., bone oedema within the endplate) are an NS-CLBP subgroup showing a number of clinical, biological, and magnetic resonance imaging (MRI) similarities with patients suffering from axial spondyloarthropathy (SpA) [2–6]. Increased expression of TNF-α in these endplate lesions has also been reported [7]. We hypothesized that TNF inhibitors (TNFi) could be effective in NS-CLBP patients presenting with inflammatory back pain and Modic I on MRI. We therefore conducted this preliminary, proof of concept-type study to evaluate the potential role of adalimuab (ADA) in this subgroup of NS-CLBP patients. Twelve patients fulfilling the inclusion criteria (inflammatory back pain for more than 3 months and Modic I on MRI) were recruited in the rheumatology departments of Geneva University Hospitals and Fribourg Hospital (Switzerland). They were naive to any biological therapy and not using corticosteroids. Every two weeks, one subcutaneous injection of 40 mg ADA was given for a total of six injections

Table 1
Baseline characteristics.

	n = 10
Sex (male, %)	40
Age	41.0 [40.0–48.5]
BMI	22.4 ± 3.0 22.6 [20.6–23.6]
Type of employment (%)	
Sedentary	50
Physical	20
Mixed	30
Age at 1st pain, years	36.5 [31.8–42.8]
Duration of back pain, years	2.5 [1.3–5.3]
Pain (VAS 0 to10)	6.5 [6.0–7.8]
RMDQ (0 to 24)	16.0 [11.0–18.0]
BASDAI (0 to 10)	5.1 [4.4–5.3]
Quality of sleep (0–10)	5.3 [4.3–6.0]
Duration of morning stiffness, minutes	45 [45–60]
hs CRP (mg/L)	0.72 [0–1.3][a]
HLA-B27 negative	8/10 patients

When not specified, scores are median [interquartile range].
VAS: visual analogue scale; RMDQ: Roland and Morris disability questionnaire; BASDAI: bath ankylosing spondylitis disease activity index. 0–3; 0–3; 0–3.
[a] 2 patients had CRP level superior to 5.0. Respectively 5.1 and 7.8.

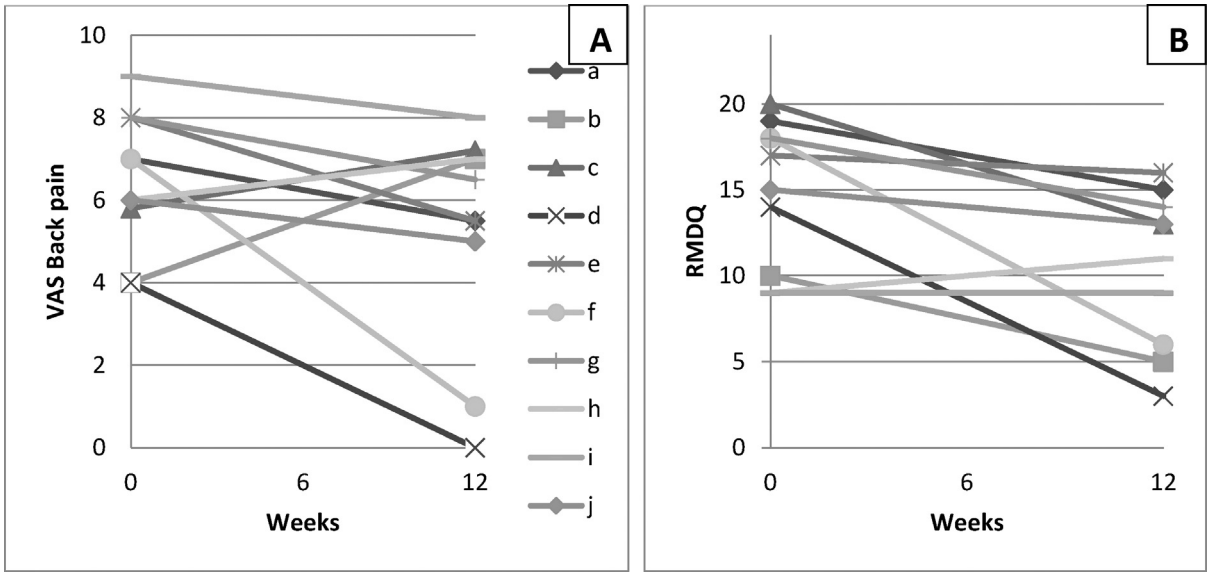

Fig. 1. Individual back pain (Visual Analogue Scale/VAS) (A) and disability Score (RMDQ Roland–Morris disability questionnaire) (B) changes over the 3-month study.

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over 3 months. Answers to the Roland–Morris disability questionnaire (RMDQ), co-medication, and side effects were recorded at each injection. MRI was repeated at the final assessment, scheduled at 3 months (i.e., 2 weeks after the last injection). MRI scans were anonymized and randomly assessed by an experienced radiologist. Modic I changes were quantitatively assessed according to a published method [8]. The primary outcome was a state of low clinical activity, defined as a composite index of low pain (a visual analogue scale/VAS Score ≤ 2) and low disability (RMDQ Score ≤ 4). Secondary outcomes were improvements in back and leg pain (VAS), RMDQ Score, and a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score. Ethical approval was obtained from the competent local bodies, and the study was registered with the Swiss Agency for Therapeutic Products (Swissmedic, # 2011DR2213). Two patients withdrew after the first injection, one for personal reasons and one due to a cutaneous allergic reaction. Baseline characteristics are displayed in Table 1. At 3 months, two patients had reached a VAS Pain Score ≤ 2, but only one of them had an RMDQ Score ≤ 4. As seen in Fig. 1, almost no changes were observed for all the other patients.

To the best of our knowledge, this is the first study to explore the potential effects of a biological therapy in a subgroup of NS-CLBP patients. The stringent primary endpoint was not reached. Most importantly, no significant clinical effects were observed, for the large majority of patients, in any of the secondary outcomes. A partial response was observed in 2 patients, none of them had increased CRP levels or any clinical or imaging features corresponding to spondyloarthropathy. This could be related to a spontaneous clinical evolution or a placebo effect.

The present study's results should be analyzed keeping in mind the typical limitations related to a pilot study design. Strict eligibility criteria were established to maximize the potential effects of the experimental treatment. Hence a control group was not deemed necessary at this stage. Furthermore, with the aim of observing a large effect supporting TNF's key role in this pathology, only a small number of patients were included. Although this study cannot rule out a small effect of ADA, the lack of clinically relevant improvements in any of the outcomes, for most of the participants, suggests that ADA have no potential therapeutic effects among this specific patient group.

As the role of anti-inflammatory treatment in this pathology has recently been confirmed [9] whereas the effect of antibiotic treatment was not confirmed [10], future studies exploring promising alternative inflammatory pathways (e.g., IL-1 or IL-6) [7] or the osteoclast activation pathway [11] should be promoted.

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