Infliximab to Etanercept Switch in Patients with Spondyloarthropathies and Psoriatic Arthritis: Preliminary Data

CAROLINE DELAUNAY, VALÉRIE FARRENQ, ANDRÉ MARINI-PORTUGAL, JEAN-DAVID COHEN, XAVIER CHEVALIER, and PASCAL CLAUDEPIERRE

ABSTRACT. ***Objective.*** To report early experience of switching anti-tumor necrosis factor-α (TNF-α) therapy from infliximab to etanercept in patients with spondyloarthropathy (SpA) and psoriatic arthritis (PsA).
Methods. Thirteen patients with various SpA (7 with ankylosing spondylitis and 6 with undifferentiated SpA) and 2 patients with PsA were receiving infliximab. Because they were experiencing inadequate response or adverse events, therapy was changed to etanercept. Patients were evaluated for response to the change in anti-TNF-α therapy at baseline, after 3 months, and then every 6 months.
Results. During the mean 10-month followup after the change in therapy, 9 of 13 patients with SpA and both patients with PsA responded to etanercept and none experienced intolerance to this agent.
Conclusion. These data suggest that switching between anti-TNF-α drugs may be useful for patients with SpA who are unresponsive or intolerant to a first anti-TNF-α agent. (J Rheumatol 2005;32:2183–5)

Key Indexing Terms:
SPONDYLOARTHROPATHY PSORIATIC ARTHRITIS ETANERCEPT
INFLIXIMAB SWITCH TREATMENT ANTI-TUMOR NECROSIS FACTOR

Although infliximab can provide dramatic clinical improvements in patients with active spondyloarthropathies (SpA) and psoriatic arthritis (PsA), inadequate efficacy or unacceptable side effects may occur, requiring treatment discontinuation. Little is known about potential benefits in this situation of switching to etanercept, another agent targeting tumor necrosis factor-α (TNF-α). Data from patients with rheumatoid arthritis (RA) suggest that changing from one anti-TNF-α agent to another may be helpful[1-5]. We report on our experience with switching from infliximab to etanercept in patients with various SpA and PsA who were unresponsive or intolerant to infliximab.

MATERIALS AND METHODS

Patients with ankylosing spondylitis (AS) or other SpA or peripheral PsA treated with infliximab (5 mg/kg every 6 to 8 weeks) during the last 2 years were switched to etanercept if they failed to achieve or maintain a clinical response (defined below) or if they experienced unacceptable side effects. Etanercept was started at a dosage of 25 mg subcutaneously twice a week with no change in ongoing symptomatic drug therapy. Response to anti-TNF-α was defined as at least a 50% or 20 mm decrease in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) after 6 to 12 weeks' treatment in patients with AS or axial SpA, as recommended by the Assessments in AS (ASAS) working group[6]. We used American College of Rheumatology 20% response (ACR20)[7] and Psoriatic Arthritis Response Criteria (PsARC)[8] in patients with PsA, both of which have been widely used in PsA clinical trials. Patients were evaluated at baseline, after 3 months, then every 6 months in the event of a response to etanercept. In addition, laboratory data (full blood cell counts and liver function tests) and clinical side effects were recorded.

RESULTS

Fifteen patients were switched from infliximab to etanercept therapy. Seven fulfilled the modified New York criteria[9] for AS, 6 met modified European Spondylarthropathy Study Group criteria[10] for undifferentiated SpA and had predominant axial involvement (including 3 patients with cutaneous psoriasis), and 2 met Moll and Wright criteria[11] for PsA and had predominant peripheral involvement. There were 11 women and 4 men, with mean age of 43 (± standard deviation, SD, 30) years, mean disease duration of 15 (± 47) years, and mean time receiving infliximab of 11 (± 19) months. Reasons for infliximab discontinuation included inadequate efficacy in 10 patients; adverse events in 4 patients (2 with infusion-related reactions and one each with leukopenia and vertigo with asthenia); and one patient with both inadequate efficacy and infusion-related symptoms. In 4 patients (Patients 3, 4, 11, 13, see Table 1), loss of efficacy was observed before etanercept was available for SpA in France; as a result, infliximab treatment was maintained for a few weeks more when the patient had estimated that he felt "a significant global improvement," until etanercept became

From the Department of Rheumatology, Henri Mondor Teaching Hospital, Créteil, France.

C. Delaunay, MD; V. Farrenq, MD; A. Marini-Portugal, MD; J-D. Cohen, MD; X. Chevalier, MD, PhD; P. Claudepierre, MD.

Address reprint requests to Dr. P. Claudepierre, Service de Rhumatologie, Hôpital Henri Mondor, 51 Avenue du Maréchal de Lattre de Tassigny, 94010 Créteil Cédex, France.
E-mail: pascal.claudepierre@hmn.ap-hop-paris.fr

Accepted for publication June 27, 2005.

Table 1. Responses of 15 patients with SpA who switched from infliximab to etanercept therapy.

Patient	Diagnosis	Infliximab Duration, mo	Infliximab MTX	Infliximab Reason for Discontinuation	Etanercept Duration, mo	Etanercept MTX	Etanercept Response*	Etanercept Continuation
1	AS	11	No	IE	3	No	No	No
2	AS	21	No	IE	7	No	Yes	Yes
3	AS	20	Yes	IE	12	No	No	Yes
4	AS	21	Yes	IE	8	No	No	Yes
5	AS	8	No	IE	3	No	Yes	Yes
6	AS	11	No	IE	4	No	Yes	Yes
7	AS	6	No	Infusion-related reaction	17	No	No	No
8	SpA, psoriasis	4	No	IE	6	No	Yes	Yes
9	SpA, psoriasis	2	No	Leukopenia	19	Yes	Yes	Yes
10	SpA, psoriasis	8	No	Infusion-related reaction	12	No	Yes	Yes
11	SpA, undifferentiated	7	No	IE	13	No	Yes	Yes
12	SpA, undifferentiated	9	No	Vertigo, asthenia	5	No	Yes	Yes
13	SpA, undifferentiated	12	No	IE	14	No	Yes	Yes
14	PsA	17	Yes	IE	6	Yes	Yes	Yes
15	PsA	13	No	IE, infusion-related reaction	17	No	Yes	Yes

* At last followup. AS: ankylosing spondylitis; SpA: spondyloarthropathy; PsA: psoriatic arthritis; MTX: methotrexate; IE: inadequate efficacy.

available. As shown in Table 1, a few patients received methotrexate (MTX) in combination with anti TNF-α therapy. Etanercept therapy was initiated instead of, or within a few weeks after, a scheduled infliximab infusion, except in Patients 9 and 12 (initiation 8 and 10 months after the last infliximab infusion, respectively). For the 13 patients with predominant axial involvement, the mean BASDAI score at the time of starting etanercept was 71 (± 36). Mean time on etanercept at study completion was 10 (± 16) months.

A clinical response was achieved in 3 of 7 patients with AS (Table 1). In 2 of the 4 nonresponders (Patients 3 and 4), global self-evaluation indicated an improvement, explaining why etanercept therapy was continued after the first 3 months despite failure to strictly meet response criteria. All 8 patients with undifferentiated axial SpA or PsA met response criteria after 3 months and at last followup. For the 13 patients with predominant axial involvement, the mean BASDAI score at the time of last followup was 41 (± 73).

No patient required etanercept discontinuation because of side effects. No serious adverse events such as severe infections or allergies were recorded.

DISCUSSION

Published data on switching anti-TNF-α therapies have been compiled primarily from open studies of patients with RA and suggest a beneficial effect[1-5]. To our knowledge, this is the first study addressing anti-TNF-α switching, specifically from infliximab to etanercept, in patients with SpA. In a study of 31 patients switching from one anti-TNF-α agent to another, van Vollenhoven, *et al* included 3 patients with SpA: 2 could not tolerate infliximab and one failed to respond to etanercept, and all 3 patients improved after the switch[4]. In our group of patients with immediate or delayed unresponsiveness to infliximab, the clinical response rate to etanercept was 73% (8/11). Further, all patients who responded to infliximab but had to stop the medication because of side effects achieved a clinical response to etanercept without experiencing treatment-limiting adverse effects.

These results must be interpreted with caution because of the sample size and the study design (pragmatic retrospective cross-sectional study with heterogenous subtypes and followup durations). However, they suggest that switching to another anti-TNF-α agent may be appropriate in patients with SpA and PsA with lack of response or intolerance to their current agent. Larger studies including various patterns of switching need to be undertaken before a definite conclusion can be drawn.

REFERENCES

1. Sanmarti R, Gomez-Puerta JA, Rodriguez-Cros JR, Albaladejo C, Munoz-Gomez J, Canete JD. Etanercept in rheumatoid arthritis patients with a poor therapeutic response in infliximab. Med Clin (Barc) 2004;122:321-4.
2. Hansen KE, Hildebrand JP, Genovese MC, et al. The efficacy of switching from etanercept to infliximab in patients with rheumatoid arthritis. J Rheumatol 2004;31:1098-102.
3. Yazici Y, Erkan D. Do etanercept-naive patients with rheumatoid arthritis respond better to infliximab than patients for whom etanercept has failed? Ann Rheum Dis 2004;63:607-8.
4. van Vollenhoven R, Harju A, Brannemark S, Klareskog L. Treatment with infliximab (Remicade) when etanercept (Enbrel) has failed or vice versa: data from the STURE registry showing that switching tumour necrosis factor alpha blockers can make sense. Ann Rheum Dis 2003;62:1195-8.
5. Brocq O, Plubel Y, Breuil V, et al. Etanercept–infliximab switch in rheumatoid arthritis 14 out of 131 patients treated with anti TNF-alpha. Presse Med 2002;31:1836-9.
6. Braun J, Pham T, Sieper J, et al. International ASAS consensus statement for the use of anti-tumour necrosis factor agents in

patients with ankylosing spondylitis. Ann Rheum Dis 2003;62:817-24.
7. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum 1995;38:727-35.
8. Clegg DO, Reda DJ, Mejias E, et al. Comparison of sulfasalazine and placebo in the treatment of psoriatic arthritis. Arthritis Rheum 1996;39:2013–20.
9. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361-8.
10. Dougados M, van der Linden S, Juhlin R, et al. The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. Arthritis Rheum 1991;34:1218-27.
11. Moll JM, Wright V. Psoriatic arthritis. Semin Arthritis Rheum 1973;3:55-78.