Relationship between the clinical response to adalimumab treatment and serum levels of adalimumab and anti-adalimumab antibodies in patients with psoriatic arthritis
van Kuijk, A.W.R.; de Groot, M.; Stapel, S.O.; Dijkmans, B.A.C.; Wolbink, G.J.; Tak, P.P.

Published in:
Annals of the Rheumatic Diseases

DOI:
10.1136/ard.2009.108787

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Relationship between the clinical response to adalimumab treatment and serum levels of adalimumab and anti-adalimumab antibodies in patients with psoriatic arthritis

While the majority of patients with psoriatic arthritis (PsA) respond well to treatment with adalimumab, some patients lose response. An explanation might be the development of anti-adalimumab antibodies, which has been reported in rheumatoid arthritis. Therefore, we studied the incidence of anti-adalimumab antibodies in PsA, and the relationship with serum adalimumab concentration and clinical response.

Twenty-two patients with active PsA, fulfilling CASPAR classification criteria, started adalimumab treatment (Table 1). The patients met the requirements of the Dutch consensus on initiation of tumour necrosis factor blocking therapy in PsA and were seen at baseline, and after 3 and 12 months. Serum samples were collected just before the next injection with adalimumab. The Disease Activity Score in 28 joints (DAS28), which has been shown to discriminate between active drug and placebo in clinical trials in PsA, was chosen to monitor clinical disease activity, and EULAR response criteria were applied. All patients continued to receive adalimumab 40 mg every other week for 12 months.

Trough serum adalimumab concentrations were measured by ELISA, and anti-adalimumab antibodies were detected by radioimmunoassay. The antibody test was considered positive when antibody concentrations exceeded 12 AU/ml and adalimumab concentration was <5 mg/l.

Mean (SEM) DAS28 decreased from 4.9 (0.3) at baseline to 2.9 (0.3) after 3 months, and 2.9 (0.3) after 12 months (p<0.001 for both). At 3 months there were 12 moderate and 10 good responders. At 12 months there were four non-responders, eight moderate and 10 good responders.

In four patients (18%) anti-adalimumab antibodies were detected at any time point. After 3 months, three patients had low concentrations of anti-adalimumab antibodies (<100 AU/ml), two of those developed high concentrations (>100 AU/ml) at 12 months. In the third patient the antibodies had disappeared at 12 months, but a fourth patient demonstrated a low concentration of antibodies at 12 months.

The median adalimumab concentration at 3 months was 7.8 mg/l (range 0.9–16.7), and 7.0 mg/l (undetectable–21.8) at 12 months. Patients with anti-adalimumab antibodies had lower median adalimumab concentrations than those without such antibodies. The patients without anti-adalimumab antibodies (n = 19) showed sustained clinical improvement, while the patients with such antibodies (n = 3) lost the initial good response to adalimumab. After 12 months the mean (SEM) DAS28 was higher in the anti-adalimumab positive patients than in the anti-adalimumab negative patients: 5.05 (0.84) vs 2.58 (0.32) (p = 0.01).

In the three patients with anti-adalimumab antibodies at 12 months, demonstrating a loss of the initial clinical response to adalimumab treatment. At 3 months these patients were moderate (n = 1) or good (n = 2) responders, at 12 months they were non-responders (n = 2), or a moderate responder (n = 1).

Table 1 Basic and clinical characteristics at baseline of the 22 patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>14/8</td>
</tr>
<tr>
<td>Age (years), mean (range)</td>
<td>43.3 (21–61)</td>
</tr>
<tr>
<td>Disease duration psoriasis (years), median (range)</td>
<td>12.7 (1–53)</td>
</tr>
<tr>
<td>Disease duration PsA (years), median (range)</td>
<td>6.3 (1–18)</td>
</tr>
<tr>
<td>Clinical phenotype: PA/OA/DIP</td>
<td>15/6/1</td>
</tr>
<tr>
<td>Concomitant MTX use, n (%)</td>
<td>12 (55)</td>
</tr>
<tr>
<td>MTX dose (mg/week), median (range)</td>
<td>17.5 (10–25)</td>
</tr>
<tr>
<td>DAS28, mean (SEM)</td>
<td>4.92 (0.25)</td>
</tr>
<tr>
<td>PASI, median (IQR)</td>
<td>5.7 (1.5–7.0)</td>
</tr>
<tr>
<td>ESR (mm/h), median (IQR)</td>
<td>17.5 (7.8–31)</td>
</tr>
<tr>
<td>CRP (mg/l), median (IQR)</td>
<td>6.2 (2.6–25.7)</td>
</tr>
</tbody>
</table>

C-reactive protein; DAS28, Disease Activity Score in 28 joints; DIP, distal interphalangeal joint; ESR, erythrocyte sedimentation rate; IQR, interquartile range; MTX, methotrexate; OA, oligoarticular; PA, polyarticular; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis.
Patients with antibodies appeared to lose their initial good response (fig 1). Our study was not designed to examine whether concomitant methotrexate treatment could reduce the formation of anti-adalimumab antibodies.

In conclusion, anti-adalimumab antibodies develop in a minority of patients with PsA, and are associated with lower serum levels of adalimumab and diminished clinical response to treatment.

**A W R van Kuijk,1,2 M de Groot,3 S O Stapel,4 B A C Dijkmans,2,5 G J Wolbink,2,4 P P Tak1**

1 Division of Clinical Immunology and Rheumatology, Academic Medical Centre/University of Amsterdam, Amsterdam, The Netherlands; 2 Jan van Breemen Institute, Amsterdam, The Netherlands; 3 Department of Dermatology, Academic Medical Centre/University of Amsterdam, Amsterdam, The Netherlands; 4 Sanquin Research, Amsterdam, The Netherlands; 5 Department of Rheumatology, VU University Medical Centre, Amsterdam, The Netherlands

**Correspondence to** Professor P P Tak, Division of Clinical Immunology and Rheumatology, F4-105, Academic Medical Centre/University of Amsterdam, Meibergdreef 9, NL-1105 AZ Amsterdam, The Netherlands; p.p.tak@amc.uva.nl

**Competing interests** BACD is a member of the advisory board of Abbott and has received honoraria for lectures. PPT has served as a consultant to Abbott, Schering-Plough, UCB and Wyeth.

**Ethics approval** Ethics committee approval from Academic Medical Centre/University of Amsterdam.

**Patient consent** Patient consent received.

**Provenance and peer review** Not commissioned; externally peer reviewed. Accepted 21 April 2009


**REFERENCES**


Relationship between the clinical response to adalimumab treatment and serum levels of adalimumab and anti-adalimumab antibodies in patients with psoriatic arthritis


Ann Rheum Dis 2010 69: 624-625
doi: 10.1136/ard.2009.108787