Spondyloarthritis: From disease phenotypes to novel treatments
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Fast relapse upon discontinuation of tumour necrosis factor blocking therapy in patients with peripheral spondyloarthritis

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Relapse after adalimumab discontinuation

Tumour necrosis factor (TNF) blockade is effective in axial spondyloarthritis (SpA), including both ankylosing spondylitis and non-radiographic axial SpA, as well as peripheral SpA, which comprises psoriatic arthritis (PsA) but also other SpA subtypes. It is well established that anti-TNF therapy discontinuation leads to fast relapse in almost all axial SpA patients. This study aimed to investigate if similar relapses are seen after anti-TNF therapy discontinuation in peripheral SpA.

Twenty-six patients from our randomised clinical trial with adalimumab in peripheral arthritis in non-AS, non-PsA SpA were included. Patients had received either 12 (n=12) or 24 weeks (n=14) of adalimumab before discontinuation of the anti-TNF therapy. After discontinuation, patients were followed for 16 weeks and seen for a relapse visit upon worsening of symptoms. Relapse was defined as increase of ≥1 swollen joint, or ≥2 points in patient’s or physician’s global assessment of disease activity or Bath Ankylosing Spondylitis Disease Activity Index. At the relapse visit, or in absence of relapse at the 16 weeks follow-up visit, disease activity parameters were measured. The study was approved by the local ethics committee.

At the time point of adalimumab discontinuation, the disease activity was low (table 1). In all, 11 patients (42.3%) had reached a 66 swollen joint count (SJC66) of zero and 14 patients (53.8%) Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease. After adalimumab discontinuation, 19 patients (73.1%) relapsed after a mean of 10.0±3.2 weeks. Only four patients (16.0%) maintained a SJC66 of zero or ASDAS inactive disease over 16 weeks. At the group level, there was a significant increase in all disease activity parameters after adalimumab interruption (table 1).

The number of patients with relapse increased over time (figure 1A). Relapse was largely based on an increase in SJC66 (12/19 patients), reflecting the peripheral SpA phenotype of this population, but was also associated with worsening of systemic and axial parameters as most SpA patients depict a combination of different disease manifestations. Univariate analysis

<table>
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<tr>
<th>Table 1. Disease activity upon anti-TNF therapy discontinuation (baseline) and at the follow-up visit (upon relapse or, in absence of relapse, at 16 weeks after discontinuation)</th>
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</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
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<tr>
<td>Patient’s global assessment, 0-100 mm VAS</td>
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<tr>
<td>Physician’s global assessment, 0-100 mm VAS</td>
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<tr>
<td>Swollen joint count, 0-66 joints</td>
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<td>Tender joint count, 0-68 joints</td>
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<tr>
<td>BASDAI</td>
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<td>ASDAS</td>
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<td>CRP, mg/l</td>
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<td>ESR, mm/hour</td>
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<tr>
<td>Swollen joint count = 0, n (%)</td>
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<tr>
<td>ASDAS inactive disease, n (%)</td>
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</table>

Except where indicated otherwise, values are the mean (standard deviation). VAS = visual analogue scale; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; ASDAS = Ankylosing Spondylitis Disease Activity Score; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate. Significance of the comparisons is determined by paired t-tests.
did not identify parameters (including treatment duration, disease activity parameters and
demographic or clinical characteristics) to be significantly associated with the occurrence
of relapse. In particular, longer duration of adalimumab treatment, SJC66 of zero or ASDAS
inactive disease at the time point of adalimumab discontinuation did not result in lower relapse
rates (figure 1B–D). However, time to relapse correlated with the duration of adalimumab
treatment (R=0.722, p<0.001 assessed by Pearson correlation test) and SJC66 at the time point
of adalimumab interruption (R=−0.585, p=0.002).

In conclusion, our data show a rapid relapse in more than 70% of the peripheral SpA patients
within 16 weeks after interruption of TNF blockade. Even patients with complete remission of
arthritis or reaching ASDAS inactive disease did rapidly flare. This is in agreement with findings
in axial SpA3–6 and preliminary findings in combined axial and peripheral undifferentiated SpA.9
We therefore hypothesise that rapid relapse upon anti-TNF therapy discontinuation is a general
SpA feature. It needs to be further investigated whether the patients not flaring within 16 weeks
can maintain a longer drug-free remission.

Figure 1. Cumulative percentage of peripheral spondyloarthritis patients who experienced relapse
upon follow-up after discontinuation of treatment with adalimumab. The panel represents the total
group of patients (A), and the sub-analyses for the duration of adalimumab treatment before anti-TNF
treatment discontinuation (B), the number of swollen joints at week 24 and the achievement of Ankylosing
Spondylitis Disease Activity Score (ASDAS) inactive disease at week 24 (D). SJC = swollen joint count 66; Wk
= week; ASDAS active = ASDAS≥1.3; ASDAS inactive = ASDAS<1.3.
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REFERENCES


