CONCISE REPORT

Similar response rates in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis after 1 year of treatment with etanercept: results from the ESTHER trial

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ABSTRACT

Objective We assessed whether there is a difference to etanercept (ETA) treatment in patients with ankylosing spondylitis (AS) compared with non-radiographic axial SpA (nr-axSpA) patients with a disease duration <5 years.

Method AS (n=20) and nr-axSpA (n=20) patients who were treated with ETA for 1 year were compared for differences in baseline data and treatment effect. Clinical, laboratory and MRI of sacroiliac joints (SI-joints) and spine were analysed.

Results At baseline, there were no significant differences between the 20 AS and the 20 nr-axSpA patients regarding age, disease duration, gender, HLA-B27 and clinical disease activity in terms of Bath AS Disease Activity Index (BASDAI), C-reactive protein and MRI SI-joint and spine scores in the AS compared with the nr-axSpA group. After 1 year of treatment with ETA the treatment effect was similarly good in AS and nr-axSpA (reduction of BASDAI by 3.3 (95% CI 2.2 to 3.8) vs 3.6 (95% CI 2.7 to 4.4) and reduction of AS Disease Activity Score by 1.8 (95% CI 1.5 to 2.2) vs 1.8 (95% CI 1.5 to 2.1), respectively.

Conclusions The response rate to TNF-blockers does not differ between AS and nr-axSpA if the baseline data regarding symptom duration and disease activity are similar for the two groups.

INTRODUCTION

The recently published Assessment of SpondyloArthritis International Society (ASAS) classification on axial spondyloarthritides (SpA) includes patients with ankylosing spondylitis (AS) who have sacroilitis on conventional radiographs according to the modified New York criteria,1 and patients with non-radiographic axial SpA (nr-axSpA) without definite sacroilitis on x-rays.2 A similar level of clinical disease activity has been shown on AS patients compared with nr-axSpA patients, as measured by the Bath AS Disease Activity Index (BASDAI) or patient pain.3,4 However, it has been reported that nr-axSpA patients might have lower C-reactive protein (CRP)-levels,3,4 and less MRI-inflammation in the spine.4

Regarding response rates to tumour necrosis factor α (TNFα)-blocker therapy, several studies have shown that nr-axSpA patients respond at least as good as, or even better than, AS patients. However, these findings are only based on comparing different studies not comparing these groups inside the same trial.5–7

We recently reported about a good efficacy of etanercept (ETA) treatment in axial SpA patients treated with the TNF-blocker ETA over 1 year in comparison with treatment with sulfasalazine.5 One important criterion for inclusion into the study was symptom duration not exceeding 5 years, independently of whether the patients already had radiographic sacroilitis or not, plus subchondral bone marrow oedema on MRI. In the current analysis, we took advantage of the fact that the patients had radiographic and nr-axSpA in about 50% each allowing a direct comparison of the response between the two groups in the same study.

PATIENTS AND METHODS

Study design

Patients with early axial SpA with a disease duration of <5 years, and with active inflammation on whole-body MRI (wb-MRI) in the spine and/or sacroiliac joints (SI-joints) at baseline were treated with ETA (n=40) or sulfasalazine (n=36) over 48 weeks.5 For this analysis, we analysed the ETA patient population (n=40) from year 1 (20 AS vs 20 nr-axSpA patients).

Outcome parameters

The following efficacy parameters were calculated: response of the ASAS response criteria for 40% improvement in disease activity (ASAS40),8 ASAS criteria for partial remission,9 Bath AS Disease Activity Index criteria for 50% improvement (BASDAI50), AS Disease Activity Score (ASDAS) for inactive disease, ASDAS clinically important change and ASDAS major improvement.10 Other clinical and laboratory outcome assessments included the BASDAI, Bath AS Functional Index (BASFI), patient’s and physician’s global assessments of disease activity and CRP5 11
MRI
Wb-MRIs, short-time inversion recovery (STIR) and T1 images, were performed at weeks 0, 24 and 48 on a 1.5 T scanner (Avanto TIM, Siemens, Germany), as previously described. STIR sequences of wB-MRIs were scored for active inflammation according to a recently described protocol5 using the STIR sequences by two radiologists (KGH, CA), blinded for treatment arm and MRI time point.

Statistics
Statistical analysis was performed according to the intention-to-treat principle. To compare the outcome parameters between AS and nr-axSpA patients after adjustment for baseline, a mixed-model approach was applied. This statistical method allows the inclusion of dropouts (n=3) in the analysis. The Blyth-Still-Casella method was used to calculate 95% CIs (figure 1). The clinical trials performed so far in the field of early axial SpA did not offer the opportunity to evaluate whether AS versus nr-axSpA patients respond differently to TNFα-inhibition. The first clinical trial in axial SpA only included nr-axSpA patients. In another axSpA study, all 40 patients showed active inflammation in the SIJ on MRI, among these patients, X-rays were available only in 34 patients, 11.8% (4/34) of whom fulfilled the modified New York criteria. The most recent study also included only patients with nr-axSpA.

The current analysis was a posthoc analysis, and the study was originally not designed to address the question whether there is a different treatment response between the two groups. This can be seen as a limitation of the current investigation, although the number of patients and the baseline data were similar in the two groups.

The data presented here underline the concept of axial SpA being the same disease with different stages, and nicely demonstrate that the presence or absence of radiographic sacroiliitis is not important if the other baseline parameters are similar. Thus, even if nr-axSpA patients on the group level show somehow less objective signs of inflammation as measured by CRP and/or MRI-inflammation compared with AS patients, the response rate to TNF-blockade seems to be similar if the treated patients have similar CRP-score and MRI-score levels.

Table 2 BASDAI, ASAS and ASDAS response rates in patients with ankylosing spondylitis (AS) and patients with non-radiographic axial spondyloarthritis (nr-axSpA) after 1 year of treatment with etanercept

<table>
<thead>
<tr>
<th>Parameter at week 48</th>
<th>ETA, AS, (n=20)</th>
<th>ETA, nr-axSpA (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI20, % (95% CI)</td>
<td>80 (59 to 93)</td>
<td>85 (65 to 96)</td>
</tr>
<tr>
<td>BASDAI50, % (95% CI)</td>
<td>55 (34 to 75)</td>
<td>75 (54 to 90)</td>
</tr>
<tr>
<td>ASAS40, % (95% CI)</td>
<td>75 (54 to 90)</td>
<td>65 (43 to 83)</td>
</tr>
<tr>
<td>ASAS partial remission, % (95% CI)</td>
<td>40 (21 to 62)</td>
<td>60 (38 to 79)</td>
</tr>
<tr>
<td>ASAS clinically important improvement, %*</td>
<td>55 (34 to 75)</td>
<td>75 (54 to 90)</td>
</tr>
<tr>
<td>ASAS major improvement, %†</td>
<td>30 (14 to 52)</td>
<td>25 (10 to 46)</td>
</tr>
<tr>
<td>ASAS inactive disease (&lt;1.3), % (95% CI)</td>
<td>40 (21 to 62)</td>
<td>40 (21 to 62)</td>
</tr>
</tbody>
</table>

Results shown as percentage (%) and 95% CI. No statistical differences between patients with AS versus nr-axSpA were found for any of the parameters (p>0.05).

*ASAS clinically important improvement: change of ASAS between baseline and follow-up ≥1.1.
†ASAS major improvement: change of ASAS between baseline and follow-up ≥2.0.

AS, ankylosing spondylitis; ASAS, Ankylosing Spondylitis Disease Activity Score; ASAS40/partial remission, response of the Assessment of SpondyloArthritis international society (ASAS) criteria for 40% improvement in disease activity; ASAS criteria for partial remission; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASDAI20/50, Bath Ankylosing Spondylitis Disease Activity Index criteria for 20% and 50% improvement at week 48; CRP, C-reactive protein; ETA, etanercept; n, number of patients; nr-axSpA, nonradiographic axial spondyloarthritis.
REFERENCES


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