

Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomized placebo-controlled trial (ABILITY-1)

BACKGROUND:

- Although adalimumab and other anti-TNF agents have been approved for ankylosing spondylitis, there is still no alternative to NSAIDs for treatment of non-radiographic axial spondyloarthritis.

OBJECTIVE

- To evaluate the safety and efficacy of adalimumab in patients with non-radiographic axial spondyloarthritis

METHODS

- **Design:** Multicenter, randomized, placebo-controlled, double blind parallel study
- **Inclusion criteria:** At least 18 years of age, fulfilling ASAS classification criteria for axial spondyloarthritis without meeting modified NY criteria for ankylosing spondylitis, active disease demonstrated by total back pain score >3 on a 0-10cm visual analogue scale and a Bath Ankylosing Spondylitis Disease Activity Index score >3, and inadequate response or contraindications to NSAID therapy.
- **Exclusion criteria:** Previous or current diagnosis of psoriasis, psoriatic arthritis, a history of inflammatory arthritis, or previous exposure to biological agents
- **Primary outcome measure:** Percentage of patients achieving ASAS40 (a response criteria for AS in clinical trials) at week 12
- **Secondary outcome measures:** Several rating scales including ASAS20, ASAS partial remission, ASAS5/6, BASDAI, BASDAI50, ASDAS, ASDAS clinically important improvement, ASDAS major improvement, ASDAS inactive disease, Maastricht Ankylosing Spondylitis Enthesitis Score, linear Bath Ankylosing Spondylitis Metrology Index, 36-item Short Form V.2 Health Survey, Health Assessment Questionnaire modified for Spondyloarthropathies, and Spondyloarthritis Research Consortium of Canada MRI scores for sacroiliac joints
- 185 patients (91 adalimumab, 94 placebo) received either
 - Adalimumab 40mg SQ every other week
 - OR
 - Matching placebo SQ every other week
- Power 90% with an alpha level of 0.05 to detect a 20% difference in ASAS40 response rates between treatment groups. This was calculated for a total of 194 patients.
- Data handling method was modified intent-to-treat

RESULTS

- 7 patients (3 placebo, 4 adalimumab) were excluded from efficacy analyses but included in safety analyses due to investigator noncompliance at a single site. One patient from each group discontinued due to adverse events. 4 patients (1 placebo, 3 adalimumab) discontinued for other reasons including pregnancy, lack of efficacy, or violation of entry criteria.
- **Primary outcome measure:** A greater percentage of patients treated with adalimumab achieved ASAS40 response (33/91, 36%) compared with patients in the placebo group (14/94, 15%), $p < 0.001$
- **Secondary outcome measures:** Significantly higher percentages of patients in the adalimumab group achieved improvements as measured by ASAS, ASDAS, BASDAI, CRP, and MRI scores. Improvements were also noted based on HAS-S and SF36 summary scores.
- **Author's conclusion:** The study met its primary endpoint, and adalimumab provided significant clinical improvements in patients with non-radiographic axial spondyloarthritis

and further added evidence that adalimumab controls inflammation with similar safety profile across a range of spondyloarthritides.

STRENGTHS

- Gold standard study design (randomized, double blind, placebo-controlled)
- Measurable endpoints consistent with current AS and nr-aSpA guidelines
- Research methods were consistent with what is already known about ankylosing spondylitis and similar conditions

LIMITATIONS

- Confidence intervals not reported
- Statistical analyses not done on secondary endpoints
- Duration of therapy – no long-term data available
- Possible conflicts of interest – Although it did not seem to affect interpretation of results, many of the authors were employees of or had received funding from the manufacturer and study supporter.

CONCLUSION

- Adalimumab is a reasonable treatment option for patients with non-radiographic axial spondyloarthritis who have failed or have contraindications to NSAIDs.
 - Significantly more patients taking adalimumab had improvement in their ASAS40 scores over the 12 week period compared to placebo.
 - Although not all endpoints were tested for statistical significance, the clinical improvements in those areas is promising. For example, patients with positive HLA-B27 status, elevated CRP values, and greater SI joint inflammation all appeared to respond better to treatment than patients that did not fit into those groups, but those analyses did not reach statistical significance.
 - Studies with appropriate power and statistical analysis that test the effect of HLA-B27 status, CRP, and SI joint inflammation on response rates should be performed.
 - Long-term studies demonstrating safety and efficacy are also needed.

Reference:

Sieper J, van der Heijde D, Dougados M, Mease P, Maksymowych W, Brown M, et al. (2012c) Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). *Ann Rheum Dis.* 2013 Jun;72(6): 815-822.

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