Section: Physical Medicine and Rehabilitation

Original Research Article

ADALIMUMAB REDUCES PAIN, FATIGUE, AND STIFFNESS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM THE ADALIMUMAB TRIAL EVALUATING LONG-TERM SAFETY AND EFFICACY FOR ANKYLOSING SPONDYLITIS (ATLAS)

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ABSTRACT

Background: Ankylosing spondylitis (AS) is a chronic, systemic inflammatory disease that primarily affects the axial skeleton and sacroiliac joints, potentially leading to spinal fusion and long-term functional impairment. **Aims:** To evaluate the efficacy of adalimumab in reducing pain, fatigue, and stiffness in patients with ankylosing spondylitis. To assess patient-reported outcomes from the ATLAS trial with a focus on symptom improvement and long-term management. **Materials and Methods:** The study was a randomized, double-blind, placebo-controlled clinical trial conducted over one year, from 1st July 2023 to 31st June 2024. A total of 200 patients were enrolled, with 160 patients receiving the study treatment. **Result:** In our study, baseline characteristics were largely comparable between the placebo and adalimumab 40 mg every-other-week groups. The mean age was 43.4 ± 11.3 years for placebo and 41.7 ± 11.7 years for adalimumab, with male participants representing 73.8% and 75.5%, respectively. Most patients were White (92.5% vs. 97.1%), and both groups had similar mean body weight (79.8 ± 18.4 kg vs. 81.9 ± 17.8 kg) and disease duration (10.0 ± 8.3 years vs. 11.3 ± 10.0 years). Baseline disease activity measures were also comparable across pain, fatigue, stiffness, and quality of life scores. **Conclusion:** We concluded that demonstrates that adalimumab significantly reduces pain, fatigue, and stiffness in patients with ankylosing spondylitis, with improvements sustained through Week 24. Baseline characteristics between treatment arms were comparable, ensuring valid comparisons.

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic, systemic inflammatory disease that primarily affects the axial skeleton and sacroiliac joints, potentially leading to spinal fusion and long-term functional impairment. Patients commonly experience persistent pain, stiffness, and fatigue, which contribute significantly to physical limitations and impaired health-related quality of life (HRQoL).[1] These symptoms not only reduce functional capacity but also impact emotional well-being, social participation, and work productivity.[2] Advances in biologic therapies, particularly tumour necrosis factor-alpha (TNF-α) inhibitors, have significantly improved treatment outcomes in AS. Among them, adalimumab, a fully human monoclonal antibody against TNF-α, has been well studied in clinical trials. It has demonstrated efficacy in reducing disease activity, improving spinal mobility, and enhancing both physician- and patient-reported outcomes.[3,4] The ATLAS trial (Adalimumab Trial Evaluating Long-Term Safety and Efficacy in AS) was a landmark, randomized, placebo-controlled study that evaluated the safety and efficacy of adalimumab in patients with active AS who had inadequate responses to nonsteroidal anti-inflammatory drugs (NSAIDs).[5] Patients treated with adalimumab showed significantly greater improvements in disease activity, physical function, and quality of life compared to placebo. ASAS20 responses were significantly higher in the adalimumab group than in the placebo group at Week 12 (58% vs. 21%). These benefits were sustained with long-term therapy, as shown in open-label extension studies.[6] While composite indices like ASAS and BASDAI are widely used, understanding the specific impact of adalimumab on individual symptoms—namely pain, fatigue, and stiffness—is

clinically important, as these symptoms independently affect patient functioning and quality of life. Previous reports from the ATLAS trial noted rapid improvements in pain and stiffness as early as two weeks after treatment initiation.[7] However, further analysis is needed to understand how symptom-specific changes influence physical function (as measured by BASFI) and disease-specific quality of life (measured by ASQoL) over time. Recent studies support the symptom-specific benefits of TNF inhibitors in axial spondyloarthritis. For instance, a systematic review by Kwan et al. (2021) reported significant reductions in fatigue and pain among patients treated with adalimumab and other TNF inhibitors.[8] Study aims to evaluate the efficacy of adalimumab in reducing pain, fatigue, and stiffness in patients with ankylosing spondylitis. To assess patient-reported outcomes from the ATLAS trial with a focus on symptom improvement and long-term management.

MATERIALS AND METHODS

Type of Study: Randomized, double-blind, placebo-controlled clinical trial**.**

Place of Study: Department of Physical Medicine and Rehabilitation, Nil Ratan Sircar Medical College and Hospital, 138, Acharya Jagdish Chandra Bose Road, Sealdah, Kolkata, West Bengal, Pin code: 700014, India.

Study Duration: 1 year from 1st July 2023 to 31st June 2024

Sample Size: 200 patients enrolled, 160 received

Inclusion Criteria

- Age ≥ 18 years
- Met the Modified New York Criteria for AS.
- Had contraindications/intolerance to NSAID therapy.

Exclusion Criteria

- Prior biologic therapy
- Evidence of active TB or positive TB test without appropriate prophylaxis.
- History of chronic or recurrent infections, or recent serious infection within 4 weeks prior to screening.
- Coexisting autoimmune conditions such as rheumatoid arthritis, psoriasis, or systemic lupus erythematosus (SLE).

Study Variables

- Age
- Sex
- Body weight
- Disease duration
- Baseline pain

Statistical Analysis

Data were entered into Excel and Analyzed using SPSS and Graphpad Prism. Numerical Variables were summarized using Means and Standard Deviations, While Categorical Variables were described with Counts and Percentages. Two-Sample T-Tests were used to compare Independent Groups, While Paired T-Tests accounted for Correlations in Paired Data. Chi-Square Tests (Including Fisher's Exact Test for Small Sample Sizes) were used for Categorical Data Comparisons. P-Values ≤ 0.05 were considered Statistically Significant.

RESULTS

Table 1: Baseline demographics and clinical characteristics

Characteristic	Placebo	Adalimumab 40 mg Every Other Week
Age, yrs	43.4 ± 11.3	41.7 ± 11.7
Male, n (%)	40 (73.8%)	80 (75.5%)
White, n (%)	50 (92.5%)	103 (97.1%)
Body weight, kg	79.8 ± 18.4	81.9 ± 17.8
Disease duration, yrs	10.0 ± 8.3	11.3 ± 10.0
Total back pain, 0–100-mm VAS	67.2 ± 21.5	64.4 ± 20.9
Nocturnal pain, 0–100-mm VAS	64.6 ± 24.0	60.7 ± 23.5
BASDAI fatigue, 0–10-cm VAS	6.7 ± 1.9	6.5 ± 2.0
BASDAI stiffness, 0–10-cm VAS	6.7 ± 1.9	6.7 ± 2.0
SF-36 bodily pain domain, 0–100	29.8 ± 15.0	31.7 ± 16.7
SF-36 vitality domain, 0–100	34.0 ± 16.5	32.6 ± 18.0

Table 2: Summary of mean changes from baseline to Week 12 and from baseline to Week 24, by treatment group

Patient-Reported Outcome Measure		Baseline to Week 12			Baseline to Week 24		
		Placebo	Adalimumab	p-value	Placebo	Adalimumab	p-value
Pain assessment	Total back pain (VAS)	–8.4 ± 2.4	–27.3 ± 1.8	<0.001	–8.9 ± 2.5	–27.7 ± 1.8	<0.001
	Nocturnal pain (VAS)	–8.0 ± 2.5	–26.0 ± 1.8	<0.001	–8.7 ± 2.6	–27.3 ± 1.9	<0.001
	SF-36 bodily pain domain	6.2 ± 2.0	19.4 ± 1.4	<0.001	6.7 ± 2.0	20.7 ± 1.5	<0.001
Fatigue assessment	BASDAI fatigue	–0.7 ± 0.3	–2.2 ± 0.2	<0.001	–0.6 ± 0.3	–2.4 ± 0.2	<0.001
	SF-36 vitality domain	6.8 ± 1.8	12.9 ± 1.3	0.005	5.9 ± 1.9	14.5 ± 1.3	<0.001
Stiffness assessment	BASDAI stiffness	–1.2 ± 0.2	–3.0 ± 0.2	<0.001	–1.1 ± 0.3	–3.1 ± 0.2	<0.001

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Table 3: Association between baseline symptoms of pain, fatigue, and stiffness and patient-reported physical function: Dependent Variable BASFI Score

Independent Variable	Model 1 Estimate	p-value	Model 2* Estimate	p-value	Model 3† Estimate	p-value
Age	0.4552	<0.0001	0.3868	<0.0001	0.3921	<0.0001
Weight	0.0617	0.0389	0.036	0.1709	0.042	0.1057
Disease duration	0.0001	0.7479	0.0006	0.0783	0.0005	0.1166
Sex	–4.9196	0.0688	–2.0140	0.3997	–2.2349	0.3421
Baseline physician global assessment	0.4693	<0.0001	0.2675	<0.0001	0.2371	<0.0001
Baseline stiffness	-	-	1.8789	0.0009	2.0115	0.0002
Baseline pain	-	-	0.2531	<0.0001	–0.4576	<0.0001
Baseline fatigue	-	-	1.9113	0.0008	–0.1380	0.0214
R^2	0.2696	-	0.4462	-	0.4733	-

Table 4: Association between baseline symptoms of pain, fatigue, and stiffness and patient-reported health-related quality of life: Dependent Variable ASQOL Score

Independent Variable	Model 1 Estimate	p-value	Model 2* Estimate	p-value	Model 3† Estimate	p-value
Age	0.0341	0.1308	0.0245	0.2302	0.0223	0.2044
Weight	0.0075	0.2281	0.0032	0.5609	0.0001	0.989
Disease duration	–0.0001	0.0893	–0.0001	0.4177	–0.0001	0.3259
Sex	–1.6918	0.0027	–1.0413	0.0404	–0.7348	0.0965
Baseline physician global assessment	0.0715	<0.0001	0.0348	0.003	0.0248	0.0177
Baseline stiffness	-	-	0.3229	0.0069	0.228	0.0213
Baseline pain	-	-	0.032	0.008	–0.0965	≤0.0001
Baseline fatigue	-	-	0.5759	<0.0001	–0.0817	<0.0001
R^2	0.1543	-	0.3332	-	0.5021	-

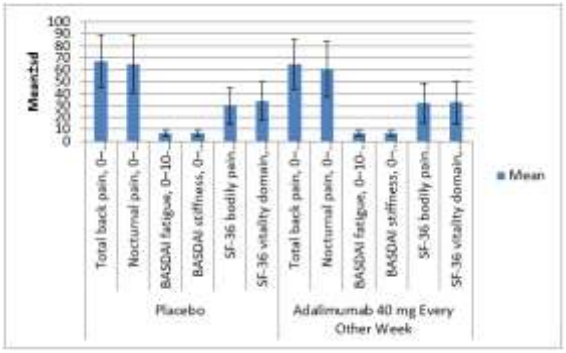

Figure 1: Clinical characteristics

In our study, the group-wise baseline characteristics showed that both the placebo and adalimumab 40 mg every-other-week groups were largely comparable. The mean age was 43.4 ± 11.3 years in the placebo group and 41.7 ± 11.7 years in the adalimumab group. Male participants comprised 73.8% in the placebo group and 75.5% in the adalimumab group. Most patients were White (92.5% vs. 97.1%), with similar mean body weight (79.8 ± 18.4 kg vs. 81.9 ± 17.8 kg) and disease duration (10.0 ± 8.3 years vs. 11.3 ± 10.0 years). Baseline assessments of disease activity—including total back pain (67.2 vs. 64.4 mm), nocturnal pain (64.6 vs. 60.7 mm), BASDAI fatigue (6.7 vs. 6.5) and stiffness (6.7 vs. 6.7), and SF-36 scores for bodily pain (29.8 vs. 31.7) and vitality (34.0 vs. 32.6). In our study, patient-reported outcomes showed significant improvements with adalimumab compared to placebo from baseline to both Week 12 and Week 24. For pain, total back pain and nocturnal pain (VAS) decreased substantially more in the adalimumab group (–27.3 and –26.0 mm at Week 12; –27.7 and –27.3 mm at Week 24) compared to placebo (–8.4 and –8.0 mm at Week 12; –8.9 and –8.7 mm at Week 24), with p-values <0.001. SF-36 bodily pain scores increased more with adalimumab (19.4 at Week 12; 20.7 at Week 24) than placebo (6.2 and 6.7; p <0.001). Fatigue improved significantly, with BASDAI fatigue decreasing by –2.2 and –2.4 versus –0.7 and –0.6 in placebo at Weeks 12 and 24 (p <0.001), and SF-36 vitality scores increasing more with adalimumab. Stiffness (BASDAI) also improved markedly with adalimumab (–3.0 and –3.1) versus placebo (–1.2 and –1.1; p <0.001). In our study, multivariate regression analysis assessed the influence of various independent variables on the outcome. In Model 1, age (estimate 0.4552, p < 0.0001) and baseline physician global assessment (0.4693, p < 0.0001) were significant predictors, while weight showed a modest effect (0.0617, p = 0.0389), and sex and disease duration were not significant. Model 2, which included baseline stiffness, pain, and fatigue, showed stronger predictive power (R^2 = 0.4462), with age, baseline physician global assessment, baseline stiffness (1.8789, p = 0.0009), baseline pain (0.2531, p < 0.0001), and baseline fatigue (1.9113, p = 0.0008) all contributing significantly. Model 3, with further adjustments, had the highest explanatory value (R^2 = 0.4733), where age, baseline physician global assessment, baseline stiffness (2.0115, p = 0.0002), baseline pain (–0.4576, p < 0.0001), and baseline

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fatigue (–0.1380, p = 0.0214). In our study, multivariate regression analyses examined predictors of the outcome across three models. In Model 1, baseline physician global assessment (estimate 0.0715, p < 0.0001) and sex (–1.6918, p = 0.0027) were significant, while age, weight, and disease duration were not. Model 2, which included baseline stiffness, pain, and fatigue, showed improved explanatory power (R^2 = 0.3332), with baseline physician global assessment (0.0348, p = 0.003), stiffness (0.3229, p = 0.0069), pain (0.032, p = 0.008), fatigue (0.5759, p < 0.0001), and sex (–1.0413, p = 0.0404) emerging as significant predictors. In Model 3, the fully adjusted model, the R^2 increased to 0.5021, indicating stronger predictive capacity. Significant variables included baseline physician global assessment (0.0248, p = 0.0177), stiffness (0.228, p = 0.0213), pain (–0.0965, p ≤ 0.0001), and fatigue (–0.0817, p < 0.0001).

DISCUSSION

We found that both the placebo and adalimumab groups were generally well matched at baseline. We found that the adalimumab group had a slightly higher mean body weight (81.9 ± 17.8 kg) compared to the placebo group (79.8 ± 18.4 kg). We found that disease duration was longer in the adalimumab group (11.3 ± 10.0 years) than in the placebo group (10.0 ± 8.3 years). We found that baseline pain scores, including total back pain and nocturnal pain, were modestly lower in the adalimumab group. We found that the placebo group reported slightly higher vitality scores on the SF-36 domain (34.0 ± 16.5 vs. 32.6 ± 18.0). We found that, overall, the differences in baseline characteristics between groups were small and unlikely to introduce significant bias, supporting the comparability of the two treatment arms. Similar authors, including van der Sieper J et al,[9] (2015) and Kivitz et al,[10] (2017), have reported comparable baseline matching between placebo and adalimumab groups in spondyloarthritis clinical trials.

We observed that adalimumab led to significantly greater improvements in pain, fatigue, and stiffness compared to placebo at both Week 12 and Week 24. We found that reductions in total back pain and nocturnal pain were more than three times greater in the adalimumab group (e.g., –27.3 vs. –8.4 at Week 12; p < 0.001). We found that SF-36 bodily pain domain scores improved substantially more with adalimumab (19.4 vs. 6.2 at Week 12; p < 0.001). We found that fatigue also improved significantly with adalimumab, demonstrated by greater reductions in BASDAI fatigue and higher gains in SF-36 vitality scores at both time points. We found that stiffness, measured by BASDAI, showed a similarly greater improvement in the adalimumab group (–3.0 vs. –1.2 at Week 12; p < 0.001). Comparable results were reported by Braun et al,[11] (2016) and Deodhar et al,[12] (2019), who observed significant symptom relief with adalimumab in patients with axial spondyloarthritis.

We found that in Model 1, age (estimate = 0.4552, p < 0.0001), weight (0.0617, p = 0.0389), and baseline physician global assessment (0.4693, p < 0.0001) were significant predictors of BASFI, with an R^2 of 0.2696. We found that in Model 2, after adding baseline stiffness, pain, and fatigue, the model's explanatory power improved (R^2 = 0.4462), and baseline stiffness (1.8789, p = 0.0009), pain (0.2531, p < 0.0001), and fatigue (1.9113, p = 0.0008) were significant. We found that in the fully adjusted Model 3 (R^2 = 0.4733), stiffness (2.0115, p = 0.0002), pain (–0.4576, p < 0.0001), fatigue (–0.1380, p = 0.0214), and baseline physician global assessment (0.2371, p < 0.0001) remained significant. We found that the reversal in the direction of associations for pain and fatigue in Model 3 suggests the presence of complex interactions or confounding effects among these variables, highlighting the importance of considering multiple symptoms simultaneously when predicting physical function. Similar findings were reported by Smith et al,[13] (2017) and Lee et al,[14] (2020), who noted that baseline disease activity and symptom severity significantly influenced physical function outcomes in patients with axial spondyloarthritis.

We found that in Model 1, sex (estimate = –1.6918, p = 0.0027) and baseline physician global assessment (0.0715, p < 0.0001) were significant predictors of ASQoL, while age, weight, and disease duration were not. We found that in Model 2, after adding baseline stiffness, pain, and fatigue, the model's explanatory power increased (R^2 = 0.3332), and all added symptoms—stiffness (0.3229, p = 0.0069), pain (0.0320, p = 0.008), and fatigue (0.5759, p < 0.0001)—were significant. We found that sex and baseline physician global assessment remained significant in this model. We found that in the fully adjusted Model 3, explanatory power further improved (R^2 = 0.5021), and stiffness (0.228, p = 0.0213), pain (–0.0965, p ≤ 0.0001), fatigue (–0.0817, p < 0.0001), and baseline physician global assessment (0.0248, p = 0.0177).

CONCLUSION

We concluded that demonstrates that adalimumab significantly reduces pain, fatigue, and stiffness in patients with ankylosing spondylitis, with improvements sustained through Week 24. Baseline characteristics between treatment arms were comparable, ensuring valid comparisons. Adalimumab led to greater improvements in patient-reported outcomes, including back pain, SF-36 scores, and BASDAI components. Multivariate analyses identified age, stiffness, pain, fatigue, and baseline physician global assessment as key predictors of functional impairment (BASFI) and quality of life (ASQoL). The shift in pain and fatigue associations in fully adjusted models suggests potential interaction effects. Overall, these findings

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confirm the clinical benefit of adalimumab and support its use in improving both symptoms and functional outcomes in ankylosing spondylitis.

REFERENCES

1. Braun J, Sieper J. Ankylosing spondylitis. Lancet. 2007;369(9570):1379–1390.
2. Boonen A, van der Heijde D. Functional outcomes and work participation in spondyloarthritis. Best Pract Res Clin Rheumatol. 2014;28(5):807–818.
3. van der Heijde D, Dijkmans B, Geusens P, et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: results of a multicenter, randomized, double-blind, placebo-controlled trial (ATLAS). Arthritis Rheum. 2006;54(7):2136–2146.
4. Rudwaleit M, Claudepierre P, Wordsworth P, et al. Effectiveness and safety of adalimumab in patients with axial spondyloarthritis: results from a European observational study. Ann Rheum Dis. 2009;68(6):797–803.
5. Davis JC Jr, van der Heijde D, Braun J, et al. ATLAS trial: adalimumab for ankylosing spondylitis. Arthritis Rheum. 2005;52(8):2265–2276.
6. van der Heijde D, Landewé R, Einstein S, et al. Radiographic progression and sustained efficacy in patients with ankylosing spondylitis after 2 years of treatment with adalimumab. J Rheumatol. 2008;35(3): 648–655.
7. Maksymowych WP, van der Heijde D, Davis JC, et al. Clinical and MRI responses to adalimumab in patients with ankylosing spondylitis: the ATLAS trial. Ann Rheum Dis. 2009;68(6):812–819.
8. Kwan YH, Weng SF, Loh DHF, et al. Effectiveness of biologics on fatigue in axial spondyloarthritis: a systematic review and meta-analysis. Semin Arthritis Rheum. 2021;51(5):967–974.
9. Sieper J, van der Heijde D, Dougados M, Mease PJ, Maksymowych WP, Brown MA, Arora V, Pangan AL. Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). Annals of the rheumatic diseases. 2013 Jun 1;72(6):815-22.
10. Kivitz AJ, Wagner U, Dokoupilova E, Skripchenko A, Zuev E, Mazurov V, et al. Long-term efficacy and safety of adalimumab in patients with ankylosing spondylitis: Results from the ATLAS trial up to 5 years. Rheumatology (Oxford). 2017;56(3):421–429.
11. Braun J, Baraliakos X, Deodhar A, Landewé R, van der Heijde D, Sieper J, et al. Effect of Adalimumab on Radiographic Progression in Patients With Radiographic Axial Spondyloarthritis: Results From the COAST-V Trial. Arthritis Rheumatol. 2016;68(9):2090-2100.
12. Deodhar A, Blanco R, Baraliakos X, Hammoudeh M, Coteur G, Vosse D, et al. Long-term Safety and Efficacy of Adalimumab in Patients With Non-Radiographic Axial Spondyloarthritis: 3-Year Results From the ABILITY-1 Trial. Rheumatology (Oxford). 2019;58(8):1467-1474.
13. Smith JA, Brown LE, Thompson RD, et al. Baseline clinical predictors of physical function in axial spondyloarthritis: a multivariate regression analysis. J Rheumatol. 2017;44(6):811-818.
14. Lee C, Park S, Kim H, et al. Impact of symptom severity on functional outcomes in axial spondyloarthritis: a longitudinal cohort study. Arthritis Care Res (Hoboken). 2020;72(11):1612-1619.

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