

Original article

ASAS40 and ASDAS clinical responses in the ABILITY-1 clinical trial translate to meaningful improvements in physical function, health-related quality of life and work productivity in patients with non-radiographic axial spondyloarthritis

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Abstract

Objective. To assess the impact of achieving Assessment in SpondyloArthritis international Society 40% (ASAS40) response or an Ankylosing Spondylitis Disease Activity Score inactive disease (ASDAS-ID) state on patient-reported outcomes (PROs) among patients with non-radiographic axial SpA (nr-axSpA).

Methods. Data are from ABILITY-1, a phase 3 trial of adalimumab vs placebo in nr-axSpA patients. PROs included the HAQ for Spondyloarthropathies (HAQ-S), 36-item Short Form Health Survey (SF-36) physical component summary (PCS) score and Work Productivity and Activity Impairment Questionnaire. Patients were grouped by clinical response using ASAS40 response and ASDAS disease states at week 12. Changes in PROs from baseline to week 12 were compared between groups using analysis of covariance with adjustment for baseline scores.

Results. At week 12, 47 of 179 patients were ASAS40 responders and 26 of 176 patients achieved ASDAS-ID (ASDAS <1.3). Compared with non-responders ($n=132$), ASAS40 responders ($n=47$) had a significantly greater improvement in mean HAQ-S (-0.65 vs -0.05 , $P < 0.0001$), SF-36 PCS (12.4 vs 0.7 , $P < 0.0001$), presenteeism (-24.7 vs -2.2 , $P < 0.0001$), overall work impairment (-23.9 vs -2.5 , $P < 0.0001$) and activity impairment (-33.5 vs -0.9 , $P < 0.0001$) at week 12. Similarly, ASDAS-ID, ASDAS clinically important improvement (ASDAS-CII; improvement >1.1) and major improvement (ASDAS-MI; improvement >2.0) were associated with significantly greater improvements from baseline in the majority of the PROs.

Conclusion. Among nr-axSpA patients, ASAS40, ASDAS-CII and ASDAS-MI response and achievement of ASDAS-ID were associated with statistically significant and clinically meaningful improvements in physical function, health-related quality of life and work productivity in a higher percentage of patients.

Key words: axial spondyloarthritis, ankylosis, sacroiliitis, magnetic resonance imaging, adalimumab, health-related quality of life, activities of daily living, work productivity.

Rheumatology key messages

- ASAS40 and ASDAS responses translate to clinically relevant improvements in outcomes among patients with axial SpA.
- Achieving ASDAS inactive disease supports remission as a valid treatment target in patients with axial SpA.
- Achievement of ASAS40 and ASDAS responses confirms the utility of these measures in monitoring axial SpA.

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Submitted 2 October 2014; revised version accepted 23 June 2015

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Introduction

Axial SpA (axSpA) is a chronic inflammatory disease that includes AS and non-radiographic axSpA (nr-axSpA). Patients with nr-axSpA may have spinal inflammation that can be visualized by MRI, but unlike patients with AS, they have no evidence of structural damage on X-rays sufficient to fulfil the modified New York criteria [1, 2]. However, clinical trial and observational cohort data have shown that disease activity and burden in nr-axSpA are comparable to those in patients with AS [3, 4].

Appropriate clinical measures of disease activity and treatment response are important tools for the management of patients with nr-axSpA and are used to assess the efficacy of treatments in clinical trials. The Assessment in SpondyloArthritis international Society 40% (ASAS40) response has been used as a primary endpoint in clinical trials of patients with nr-axSpA [5–7], and the Ankylosing Spondylitis Disease Activity Score (ASDAS) has been used to assess treatment outcomes in clinical trials and to monitor disease activity in patients with nr-axSpA [6, 8].

ASDAS is a validated composite index that combines patient-oriented measures (back pain, duration of morning stiffness, patient global assessment of disease activity and peripheral pain or swelling) with a laboratory measure of inflammation (CRP level or ESR) [9–13]. Unlike ASAS40, ASDAS may be used to monitor the actual level of disease activity, to define a state of remission or low disease activity and to measure response to treatment [9, 12, 13].

Patient-reported outcomes (PROs) provide important assessments of function and the ability to perform daily activities as well as general well-being from the patient's perspective [14]. PROs reflect outcomes with a more tangible impact on the patient's life, hence adding more value to a treatment response in addition to physician-assessed clinical measures [15, 16]. PROs that are most relevant to axSpA patients are those that reflect physical function, health-related quality of life (HRQL) and work-related outcomes.

Limitations in physical function are a major consequence of axSpA that affects patients' abilities to perform typical daily activities [17, 18]. AxSpA has also been noted to affect both the physical and mental aspects of patients HRQL, with the level of impairment being as high as that seen in other musculoskeletal diseases [19]. Work limitations are important to consider in the treatment of axSpA because the disease affects patients at a young age, with age of onset in the 20s and 30s, when patients are in their most productive years [3, 20].

The relationship between the ASAS40 response or ASDAS and PROs of physical function, HRQL and work productivity has not been established for patients with nr-axSpA. The objective of this study was to assess the impact of achieving ASAS40 response, ASDAS clinically important improvement (ASDAS-CII), ASDAS major improvement (ASDAS-MI) or ASDAS inactive disease (ASDAS-ID) state on patient-reported measures of physical function, HRQL and work productivity among patients with nr-axSpA.

Methods

Patients and study design

Study patients were from the ABILITY-1 trial, a multicentre, phase 3, randomized, double-blind, placebo-controlled study with an open-label phase that was designed to evaluate the efficacy and safety of adalimumab (ADA) in patients with nr-axSpA. Details about selection of the patient population, inclusion/exclusion criteria and study methodology for ABILITY-1 are published elsewhere [6]. Adults ≥ 18 years of age were eligible to participate in the ABILITY-1 trial if they fulfilled the ASAS axSpA criteria but not the modified New York criteria for AS (nr-axSpA), had active disease and an inadequate or intolerant response to one or more NSAIDs or had a contraindication for NSAIDs. The trial protocol of the ABILITY-1 study was approved by the institutional review boards or ethics committees of the participating centres. All patients gave their written informed consent before participating in the ABILITY-1 trial. The analysis presented here was a post hoc analysis that did not need ethics approval.

Patients were randomly assigned (in a 1:1 ratio) to receive a s.c. injection of either ADA 40 mg every other week or placebo for 12 weeks during the double-blind period of the study. Following the double-blind period, all ongoing patients entered the open-label phase of the study in which they received a s.c. injection of ADA 40 mg every other week for up to an additional 144 weeks. The primary efficacy endpoint of ABILITY-1 was the ASAS40 response at week 12. ASDAS, physical function, HRQL and work productivity measures were additional efficacy endpoints in ABILITY-1.

Study variables

Outcome measures

ASAS40 response. An ASAS40 response was defined as a $\geq 40\%$ improvement and an absolute improvement from baseline of ≥ 20 U (range 0–100) in \geq three of the following four domains: back pain [10 cm visual analogue scale (VAS)], patient global assessment of disease activity (10 cm VAS), physical function (BASFI; range 0–100) and inflammation (mean score of items 5 and 6 of the BASDAI; both 10 cm VAS) without any worsening in the remaining domain [21, 22].

ASDAS response. The ASDAS is a composite index that assesses disease activity. The ASDAS incorporates three items from the BASDAI: back pain (10 cm VAS), duration of morning stiffness (10 cm VAS) and pain/swelling of peripheral joints (10 cm VAS), as well as patient global assessment of disease activity (10 cm VAS) and a laboratory measure of inflammation [CRP level (in mg/l) or ESR (in mm/h)] [12, 13]. Four disease activity states have been defined: inactive (ASDAS < 1.3), moderate (≥ 1.3 to < 2.1), high (≥ 2.1 to ≤ 3.5) and very high (> 3.5) [9, 10]. ASDAS-CII is defined as a decrease from baseline in the ASDAS score ≥ 1.1 , and ASDAS-MI is defined as a decrease from baseline in ASDAS ≥ 2.0 [9, 10].

HAQ modified for the spondyloarthropathies

The HAQ modified for the spondyloarthropathies (HAQ-S) is a self-reported outcome measure that assesses the physical function of patients with SpA [23]. The HAQ-S total score was calculated as the mean of the following eight category scores: dressing and grooming, rising, eating, walking, hygiene, reach, grip and activities. The functional status measure also included scores for carrying heavy packages, sitting for long periods, ability to work at a flat-topped table and (if the patient had a driver's licence or a car) ability to look in the rear-view mirror and turn head to drive in reverse. Scores ranged from 0 to 3, with a higher score reflecting greater disability. A decrease in the HAQ-S score of 0.26 for an individual patient is considered the minimal clinically important difference (MCID) [24].

36-item Short Form Health Survey

The 36-item Short Form Health Survey (SF-36) is a generic HRQL measure that assesses the patient's view of his/her health and consists of two components: physical and mental. For each component, a transformed summary score was calculated using eight subdomains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. Scores range from 0 to 100, with higher scores reflecting better health status [25–27]. For the purpose of these analyses, the focus was on the physical component summary (PCS) scores of the SF-36. The PCS scores of the SF-36 include the physical functioning scale, which assesses a patient's ability to perform all physical activities including bathing or dressing; the role-physical scale, which assesses whether a patient has problems with work or other daily activities as a result of physical health, and the bodily pain scale, which assesses whether there are any limitations of physical activities because of pain. A ≥ 3 point increase in the SF-36 PCS for an individual patient is considered the minimal clinically important improvement [28, 29].

Work Productivity and Activity Impairment questionnaire: specific health problem

The Work Productivity and Activity Impairment questionnaire (WPAI) was developed to measure the effect of overall health and specific symptoms on productivity at work and outside of work [30]. The WPAI: Specific Health Problem is designed such that it can be modified for any health problem by specifying the disease/condition of interest in the questions. Four outcomes were measured: absenteeism (disease-related work time missed), presenteeism (disease-related impairment while working), overall work impairment (composite of absenteeism and presenteeism) and total activity impairment (disease-related impairment of daily non-work activities). These four outcomes were expressed as a percentage of impairment (range 0–100% impairment), with higher numbers indicating greater impairment and less productivity. For each WPAI outcome, an improvement of ≥ 7 points from baseline for an individual patient is considered the minimal clinically important improvement [31].

Statistical analyses

For analysis, patients were grouped according to clinical response (ASAS40, ASDAS-CII or ASDAS-MI responders vs non-responders) at week 12 and disease activity state (ASDAS-ID, moderate, high and very high) at week 12, regardless of treatment group assignment.

Changes in the least square (LS) mean for each outcome (HAQ-S, SF-36 PCS and WPAI domain scores) from baseline to week 12 were compared between groups using analysis of covariance with adjustment for baseline scores. Missing data were not imputed and all categorical and continuous variables were analysed using observed-case analysis. All statistical comparisons were made at an α level of 0.05.

Results

Patient characteristics

A total of 192 patients were enrolled in ABILITY-1. Because of investigator non-compliance at a single site, all seven patients from that site were excluded from efficacy analyses. Therefore 185 patients (91 in the ADA group and 94 in the placebo group) were included in the efficacy data analyses [6]. In the present analyses, data were analysed for 179 patients with non-missing week 12 ASAS40 data, 176 patients with non-missing ASDAS data and 169 patients with non-missing data to determine achievement of ASDAS-CII and ASDAS-MI. Baseline demographic and clinical disease characteristics are reported for patients achieving an outcome at week 12, i.e. ASAS40 response and ASDAS-ID (Table 1).

Outcomes as a function of clinical improvement

ASAS40 responders

Of 179 study participants with non-missing ASAS40 data, 47 (26%) were ASAS40 responders at week 12 and 132 (74%) were non-responders (ADA and placebo patients combined). Significantly greater improvements were observed in the LS mean for HAQ-S (-0.65 vs -0.05 , $P < 0.0001$) and SF-36 PCS scores (12.4 vs 0.7 , $P < 0.0001$) among ASAS40 responders vs non-responders (Fig. 1). Further analysis revealed that these changes were clinically meaningful improvements in physical function, as significantly more ASAS40 responders achieved MCID for the HAQ-S (72.3% vs 23.7%, $P < 0.0001$) and SF-36 PCS (91.5% vs 28.8%, $P < 0.0001$) compared with non-responders.

ASAS40 responders were more engaged and productive on the job and better able to perform daily non-work-related activities than non-responders, as shown by significant ($P < 0.0001$) mean decreases from baseline in the WPAI outcomes of presenteeism (-24.7 vs -2.2), overall work impairment (-23.9 vs -2.5) and activity impairment (-33.5 vs -0.9) (Fig. 1). No significant difference was seen for absenteeism. The improvements in presenteeism, overall work impairment and activity impairment were found to be clinically relevant, as demonstrated by the fact that significantly more ASAS40

TABLE 1 Baseline demographics and clinical characteristics

Characteristic	Week 12 ASAS40 responder		Week 12 ASDAS-ID	
	Yes (n = 47)	No (n = 132)	Yes (n = 26)	No (n = 150)
Age, mean (s.d.), years	35.0 (11.0)	38.8 (10.5)	32.7 (10.0)	38.7 (10.7)
Females, n (%)	16 (34.0)	83 (62.9)	7 (26.9)	91 (60.7)
Duration since diagnosis, mean (s.d.), years	3.1 (3.8)	2.6 (3.8)	2.7 (3.3)	2.7 (3.9)
Symptom duration, mean (s.d.), years	8.2 (7.1)	10.4 (9.1)	8.2 (7.6)	10.1 (8.9)
BASDAI, mean (s.d.), cm	6.1 (1.5)	6.6 (1.5)	5.8 (1.5)	6.6 (1.5)
Patient Global Assessment, mean (s.d.), cm	62.8 (18.0)	68.9 (18.3)	60.0 (18.0)	68.6 (18.4)
BASFI, mean (s.d.)	42.8 (20.1)	48.0 (21.7)	36.8 (18.3)	48.9 (21.3)
Back pain, mean (s.d.), cm	63.5 (16.3)	71.3 (17.8)	60.7 (18.6)	70.7 (17.2)
Inflammation/morning stiffness, ^a mean (s.d.), cm	6.2 (1.8)	6.8 (2.1)	5.8 (1.7)	6.7 (2.0)
HAQ-S, mean (s.d.)	0.9 (0.6)	1.0 (0.5)	0.9 (0.4)	1.0 (0.6)
SF-36 PCS, mean (s.d.)	35.1 (7.3)	33.3 (8.0)	35.0 (7.1)	33.4 (7.9)
Employed, n (%)	34 (72.3)	87 (65.9)	19 (73.1)	99 (66.0)
WPAI, mean (s.d.), %				
Absenteeism ^b	6.1 (13.7)	11.4 (23.3)	16.1 (26.8)	8.9 (19.9)
Presenteeism ^b	38.5 (25.0)	45.8 (25.8)	39.4 (26.0)	44.7 (25.6)
Overall work impairment ^b	40.6 (26.0)	50.9 (28.1)	47.0 (29.0)	48.4 (27.7)
Activity impairment ^b	48.9 (23.7)	59.6 (25.0)	50.4 (21.1)	58.0 (25.4)

^aInflammation/morning stiffness, mean of BASDAI questions 5 and 6. ^bWPAI domains were assessed for employed patients only (n = 122). BASDAI: 10 cm visual analogue scale (VAS); Patient Global Assessment: 10 cm VAS; BASFI: range 0–100; back pain: 10 cm VAS; inflammation/morning stiffness: 10 cm VAS; HAQ-S: range 0–3; SF-36 PCS: range 0–100; WPAI: range 0–100%. ASAS40: Assessment in SpondyloArthritis international Society 40% response; ASDAS-ID: Ankylosing Spondylitis Disease Activity Score inactive disease; HAQ-S: Health Assessment Questionnaire modified for spondyloarthropathies; PCS: physical component summary; SF-36: 36-item Short Form Health Survey; WPAI: work productivity and activity impairment.

responders achieved the MCID for presenteeism (75.0% vs 42.5%, $P=0.002$), overall work impairment (69.0% vs 40.3%, $P=0.01$) and activity impairment (82.6% vs 45.0%, $P<0.0001$) compared with non-responders.

ASDAS

ASDAS disease activity states at week 12 were reported for 176 patients; of these, 26 (15%) were classified with ASDAS inactive disease at week 12 and 35 (20%), 79 (45%) and 36 (20%) were classified as moderate, high and very high, respectively (ADA and placebo patients combined). Decreasing disease activity as measured by these ASDAS categories was associated with increasing improvement in the LS mean scores for each outcome assessed (HAQ-S and SF-36 PCS, Fig. 2; WPAI domain scores, Fig. 3). Improvements in the HAQ-S (−0.65 vs 0.09), SF-36 PCS (13.5 vs −2.0), presenteeism (−27.4 vs 0.7), overall work impairment (−30.9 vs 1.8) and activity impairment (−36.9 vs 8.4) were significantly greater (all $P<0.05$) among patients classified as ASDAS inactive vs ASDAS very high. Improvement in absenteeism was not significantly different between ASDAS inactive and ASDAS very high.

Of 169 patients with baseline and week 12 ASDAS data, 46 (27%) achieved ASDAS-CII and 20 (12%) met ASDAS-MI criteria, regardless of treatment group assignment (Table 2). Significantly greater improvements were observed in each outcome among ASDAS-CII responders vs non-responders. Also, ASDAS-MI was associated with significantly greater improvements from baseline in the majority of the PROs.

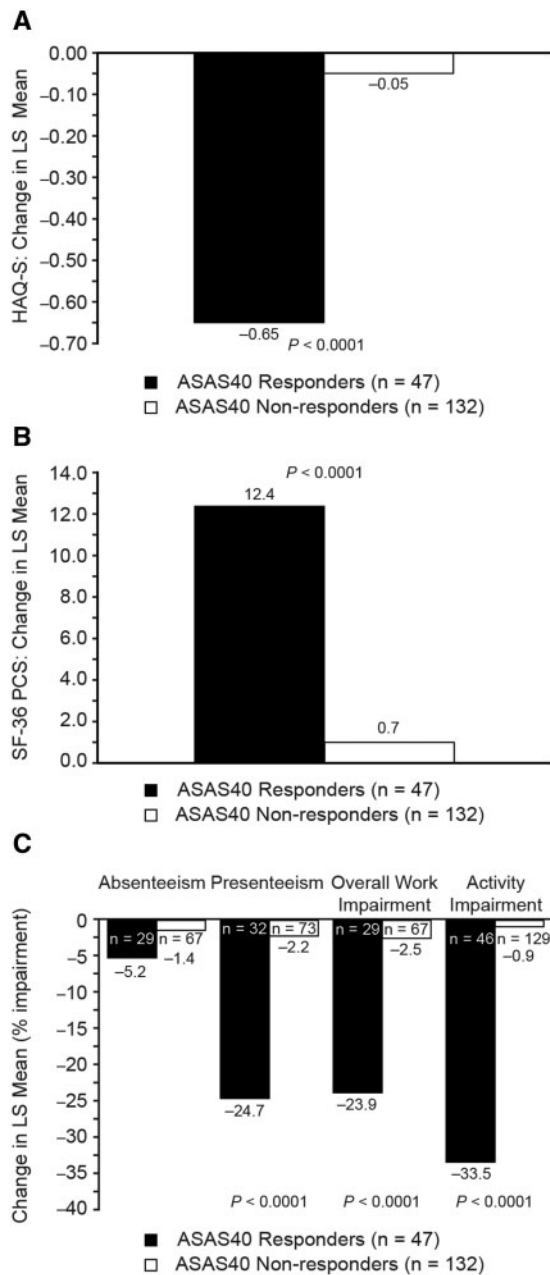
Patients achieving ASDAS-ID had a mean HAQ-S score of 0.26, which represents normal function [32], and a mean SF-36 PCS of 47.9, indicative of nearly normal physical health [33] (Table 3). Significantly more patients who achieved ASDAS-ID (vs those who did not) achieved nearly normal physical function (61.5% vs 14.7%, $P<0.0001$) and nearly normal physical health (38.5% vs 6%, $P<0.0001$). Also, significantly more patients who attained ASDAS-ID (vs those who did not) achieved an MCID for HAQ-S (69.2% vs 30.2%, $P=0.0001$), SF-36 PCS (92.3% vs 37.3%; $P<0.0001$) and the WPAI outcomes of presenteeism (81.3% vs 47.1%, $P=0.01$), overall work impairment (81.3% vs 42.3%, $P=0.005$) and activity impairment (92.0% vs 48.3%, $P<0.0001$). Similar results were observed for patients who attained ASDAS-CII and ASDAS-MI.

Supplementary Tables S1 and S2, available at *Rheumatology* Online, show the ASAS40 and ASDAS responder analysis stratified by treatment groups. Results signify that response differences between responders and non-responders follow the same pattern regardless of treatment group.

Discussion

Outcome measures in clinical trials and monitoring tools used in clinical practice are often primarily focused on measures of disease activity and clinical response. However, it is also important to take into account improvements in other aspects of the disease that affect

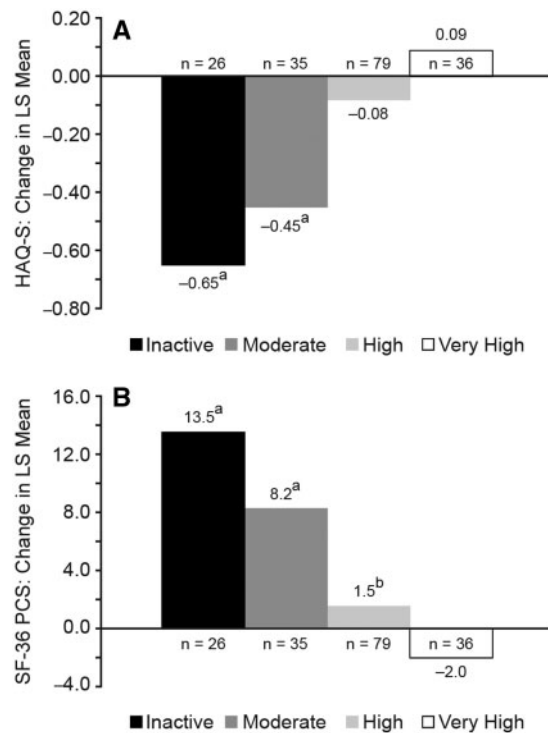
Fig. 1 Change in patient-reported outcomes by ASAS40 response



Change in least square (LS) mean from baseline to week 12 for (A) HAQ-S, (B) SF-36 PCS and (C) WPAI domain scores. ASAS40: Assessment in SpondyloArthritis international Society 40% response; HAQ-S: Health Assessment Questionnaire modified for spondyloarthropathies; PCS: physical component summary; WPAI: work productivity and activity impairment.

function and quality of life and to allow patients to continue to be productive members of society. To this end, the purpose of the present study was to determine if the improvements in composite clinical measures, ASAS40

Fig. 2 Change in HAQ-S and SF-36 PCS by ASDAS classification

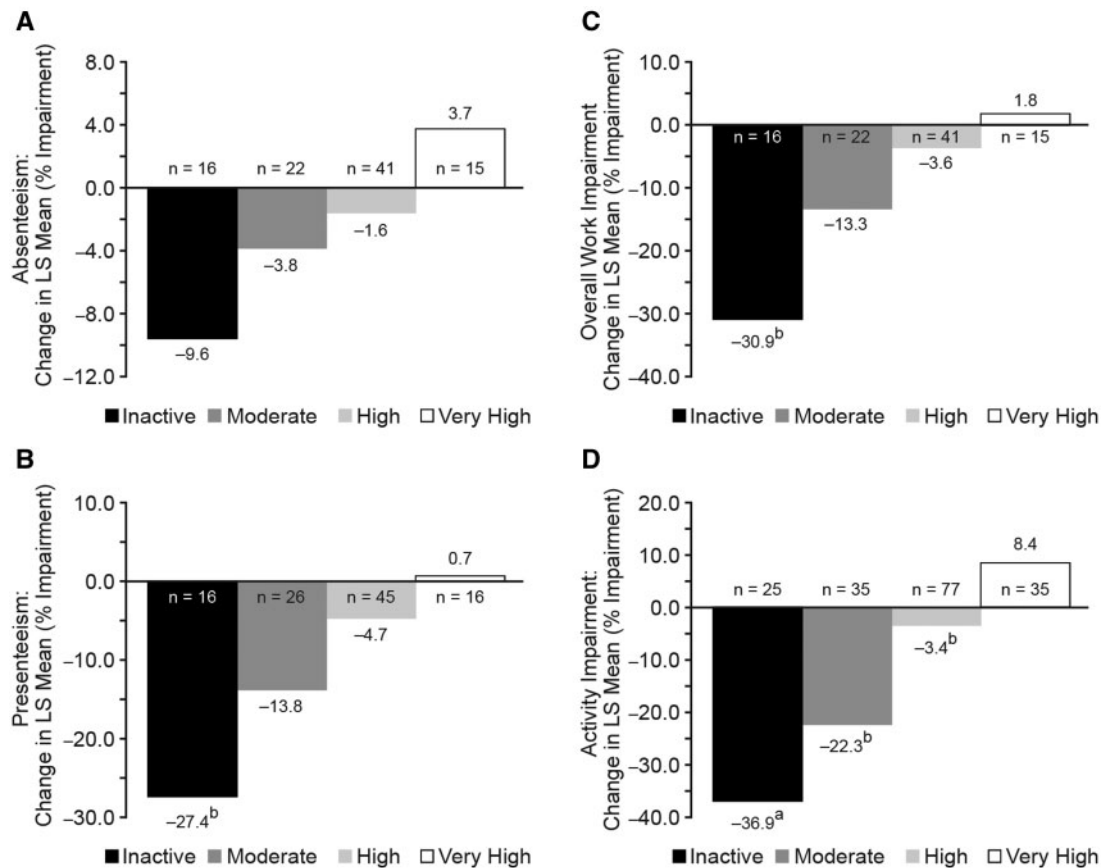


Change in least square (LS) mean from baseline to week 12 for (A) HAQ-S and (B) SF-PCS. ^a $P < 0.0001$. ^b $P < 0.05$ relative to ASDAS very high. ASDAS: Ankylosing Spondylitis Disease Activity Score; HAQ-S: Health Assessment Questionnaire modified for spondyloarthropathies; PCS: physical component summary; SF-36: 36-item Short Form Health Survey.

and ASDAS, translate into improvements in function, HRQL and work productivity.

In this study, patients with nr-axSpA who achieved ASAS40, ASDAS-CII and ASDAS-MI response at week 12 had better HRQL, performed daily activities with greater ease, had more substantially improved physical function and were more engaged and productive at work than non-responders. Assuming a 40 h work week, ASAS40 responders gained 9.6 h/week of improved productivity at work compared with only 1 h/week in non-responders. Also, ASAS40 responders had a 33.5% improvement in social participation and in their ability to perform daily household activities compared with only 1% improvement in non-responders, as reflected in the activity impairment score at week 12.

Patients in remission at week 12, as reflected by achievement of ASDAS-ID, experienced clinically relevant improvements in HRQL and physical function, greater ease in performing daily activities and greater productivity at work. In fact, achievement of ASDAS-ID led to normalization of physical function in 61.5% of patients and of physical health in 38.5% of the patients. Assuming a

Fig. 3 Change in WPAI domain scores by ASDAS classification

Change in least square (LS) mean from baseline to week 12 for (A) absenteeism, (B) presenteeism, (C) overall work impairment and (D) activity impairment. ^a $P < 0.0001$. ^b $P < 0.05$ relative to ASDAS very high. ASDAS: Ankylosing Spondylitis Disease Activity Score; WPAI: work productivity and activity impairment.

TABLE 2 Change from baseline to week 12 in patient-reported outcomes by ASDAS improvement

Outcome, LS mean (s.e.)	ASDAS improvement (week 12)			
	Clinically important improvement (ASDAS improvement ≥ 1.1)		Major improvement (ASDAS improvement ≥ 2.0)	
	Responder (n = 46)	Non-responder (n = 123)	Responder (n = 20)	Non-responder (n = 149)
HAQ-S	-0.62 (0.05)	-0.05 (0.03)	-0.84 (0.09) ^a	-0.12 (0.03)
SF-36 PCS	10.6 (1.0) ^a	1.3 (0.6)	14.9 (1.5) ^a	2.3 (0.5)
Absenteeism ^c	-8.4 (2.3) ^b	-1.8 (1.5)	-10.0 (3.7)	-2.9 (1.4)
Presenteeism ^c	-23.4 (4.1) ^b	-4.3 (2.6)	-26.9 (6.5) ^b	-7.3 (2.4)
Overall work impairment ^c	-25.4 (4.1) ^a	-3.8 (2.7)	-29.1 (6.8) ^b	-7.7 (2.5)
Activity impairment ^c	-30.8 (2.9) ^a	-1.8 (1.8)	-35.9 (4.8) ^a	-6.3 (1.8)

^a $P < 0.0001$, ASDAS responders vs non-responders. ^b $P < 0.05$, ASDAS responders vs non-responders. ^cWPAI domains were assessed for employed patients only ($n = 122$). ASDAS: Ankylosing Spondylitis Disease Activity Score; HAQ-S: Health Assessment Questionnaire for spondyloarthropathies; LS: least square; PCS: physical component summary; SF-36: 36-item Short Form Health Survey; WPAI: work productivity and activity impairment.

TABLE 3 Patient-reported outcomes of patients achieving ASDAS-ID at week 12

Outcomes	ASDAS-ID at week 12, observed, mean (s.d.)	
	Yes (n = 26)	No (n = 150)
HAQ-S	0.26 (0.29)*	0.90 (0.59)
SF-36 PCS	47.91 (6.64)*	35.7 (9.03)
Absenteeism ^a	2.42 (9.20)**	8.26 (18.0)
Presenteeism ^a	15.79 (17.74)*	39.39 (25.96)
Overall work impairment ^a	16.94 (20.55)*	44.25 (27.55)
Activity impairment ^a	16.8 (16.51)*	52.62 (26.52)

* $P < 0.0001$, ASDAS ID responders vs non-responders.

** $P < 0.05$, ASDAS ID responders vs non-responders.

^aWPAI domains were assessed for employed patients only ($n = 122$). ASDAS-ID: Ankylosing Spondylitis Disease Activity Score inactive disease; HAQ-S: Health Assessment Questionnaire for spondyloarthropathies; PCS: physical component summary.

40 h work week, patients who achieved the ASDAS-ID gained 12.4 h/week of improved productivity at work and 37% improvement in social participation and in their ability to perform daily household activities. These results are particularly relevant in light of the recent treatment-target recommendations for SpA that define treatment targets as remission or low disease activity. For axSpA, validated composite measures such as ASDAS or the use of BASDAI plus acute phase reactants are recommended for monitoring disease activity [34]. ASDAS has demonstrated better psychometric properties than BASDAI and CRP, hence making it a desirable measure of disease activity [12, 13]. However, evidence assessing the value of achieving ASDAS-ID as a potential treatment target is limited [35]. This study demonstrated that achieving remission had a beneficial impact on patients' daily functioning, quality of life and ability to work.

In order to assess whether the observed differences between responders and non-responders could be attributed to a treatment effect, the ASAS40 and ASDAS responder analyses were stratified by treatment group. Although there were more responders in the ADA treatment group, a similar pattern of improvement was observed in physical function, HRQL and work productivity among patients who were ASAS40 responders and patients who achieved ASDAS-ID compared with those who were non-responders, regardless of treatment group.

This study has several limitations that should be taken into consideration. It is based on post hoc analyses of the ABILITY-1 clinical trial [6], which was not powered specifically to conduct these responder analyses. Another limitation of the study is the short assessment period. The relationship between ASAS40 response and ASDAS inactive disease state and PROs was evaluated at 12 weeks because that was the length of the double-blind period of the ABILITY-1 trial; however, it is likely that

this estimated relationship exists over the long-term because a sustained effect was observed during the open-label period for both clinical response and PROs [36]. As noted in the Results section, statistically significant improvement was not observed for absenteeism among those who achieved ASAS40 or ASDAS responses. There may be several reasons for this observation. First, WPAI was reported only for patients who were employed (66%), which results in a smaller sample size for this outcome. In addition, the degree of absenteeism was relatively low at baseline (~10%), which would make it difficult to observe a significant improvement in absenteeism over time. Finally, missing data because of attrition and loss to follow-up are potential limitations of clinical trial data.

In summary, the results of this post hoc analysis demonstrate that ASAS40 and ASDAS responses are associated with statistically significant and clinically relevant improvements in the patient reported outcomes of physical function, HRQL and work productivity. In addition, they demonstrate the value of achieving ASDAS-ID as a potential treatment target in nr-axSpA. These findings support the use of these measures in clinical trials of patients with nr-axSpA and in monitoring disease activity in clinical practice.

Acknowledgements

Medical writing services were provided by Joann Hettasch, PhD, of Arbor Communications, Ann Arbor, MI, USA. All authors contributed to the development of this manuscript and reviewed and approved the content.

Funding: The design, study conduct and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review and approval of the publication. AbbVie funded the medical writing support for this publication.

Disclosure statement: D.vdH. received consulting fees, research grants and speaker fees from AbbVie. K.B. is an employee of Analysis Group, which received funding from AbbVie for this study. A.J. is an employee of and shareholder in AbbVie. Y.B. is an employee of AbbVie and receives a salary and stock. M.M. is an employee of and owns stock in AbbVie. N.C. is an employee of and owns stock in AbbVie. A.L.P. is an employee of and owns stocks in AbbVie.

Supplementary data

Supplementary data are available at *Rheumatology Online*.

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