Articles, Abstracts, and Reports

1-1-2017

Prediction and benefits of minimal disease activity in patients with psoriatic arthritis and active skin disease in the ADEPT trial.

Philip Mease
Swedish Medical Center and University of Washington, Seattle, Washington, USA

Arthur Kavanaugh

Laura C Coates

Iain B McInnes

Maja Hojnik

See next page for additional authors

Recommended Citation

Authors

Philip Mease, Arthur Kavanaugh, Laura C Coates, Iain B McInnes, Maja Hojnik, Ying Zhang, Jaclyn K Anderson, Alexander P Dorr, and Dafna D Gladman

ORIGINAL ARTICLE

Prediction and benefits of minimal disease activity in patients with psoriatic arthritis and active skin disease in the ADEPT trial

Philip J Mease,[1] Arthur Kavanaugh,[2] Laura C Coates,[3] Iain B McInnes,[4] Maja Hojnik,[5] Ying Zhang,[6] Jaclyn K Anderson,[6] Alexander P Dorr,[6] Dafna D Gladman[7]

ABSTRACT

Objectives To determine the proportion of patients with psoriatic arthritis in the Adalimumab Effectiveness in Psoriatic Arthritis trial achieving minimal disease activity (MDA) and its individual components at 1 or more visits over 144 weeks, identify baseline predictors of MDA achievement, and evaluate the association of MDA status with independent quality of life (QoL)-related patient-reported outcomes (PROs).

Methods Univariate and multivariate analyses were used to identify the baseline characteristics that predicted achievement of MDA at individual time points (weeks 12 through 144) or sustained MDA (achievement of MDA at 2 consecutive time points 12 weeks apart). The association of independent QoL-related PROs with MDA achievement was evaluated at weeks 24 and 144.

Results In univariate analyses, higher baseline patient assessment of pain, tender joint count (TJC), enthesitis and Health Assessment Questionnaire-Disability Index (HAQ-DI) score were significantly associated with lower likelihood of achieving MDA at later time points. Multivariate analyses confirmed higher baseline HAQ-DI as a significant predictor for failure to achieve MDA at later time points. Achievement of sustained MDA was associated with lower baseline TJC and HAQ-DI score. Achievement of different MDA components appeared to be treatment dependent. MDA achievers had significantly better QoL-related PROs and greater improvements in PROs from baseline to week 24 compared with non-achievers.

Conclusions Higher HAQ-DI score was the most consistent baseline factor that decreased the likelihood of achieving MDA and sustained MDA at later time points. Achieving MDA was associated with better independent QoL-related PROs.

Key messages

What is already known about this subject?
► There is limited understanding of patient and disease characteristics that predict long-term minimal disease activity (MDA) achievement and potential benefits associated with achievement of MDA.

What does this study add?
► The present study provides further insights into the achievement, prediction and benefits of MDA status in patients treated with adalimumab.
► It further confirms higher baseline Health Assessment Questionnaire-Disability Index as a significant negative predictor for MDA achievement.
► MDA achievement was associated with significantly better quality of life-related patient-reported outcomes (PROs) and greater improvements in PROs from baseline.

How might this impact on clinical practice?
► Our data provide further support for MDA as a valid treatment target in psoriatic arthritis, since its achievement is associated with meaningful benefits in PROs other than those included in the MDA calculation.

For numbered affiliations see end of article.

Correspondence to
Dr Dafna D Gladman; dafna.gladman@utoronto.ca

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic systemic inflammatory disease that affects the synovium, tendons, entheses and bone, and is associated with varied tissue pathology.[1][2] PsA is thus characterised clinically by arthritis, enthesitis and dactylitis in addition to skin and nail psoriasis.[3][4] Approximately 30% of patients with psoriasis develop PsA.[2] Joint damage and functional impairment may result from uncontrolled disease.[1] The European League Against Rheumatism, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis, and a PsA treat-to-target task force recommend remission or low/minimal disease activity (MDA) as treatment targets for patients with PsA.[5–7] The criteria for MDA in PsA were developed[8] and validated as a clinically meaningful and comprehensive treatment target for PsA,[9][10] which encompasses skin, joints and entheses. MDA corresponds to a state of low disease

activity or remission in PsA,[9 11] and patients who achieve MDA have less radiographic progression and functional impairment than patients who fail to reach this target.[10 12]

In the Adalimumab Effectiveness in Psoriatic Arthritis (ADEPT[13]) trial, a significantly higher number of patients treated with adalimumab achieved MDA compared with those treated with placebo at week 24 (39% vs 7%, respectively).[14] However, the attainment of individual MDA components in MDA achievers has not been extensively evaluated.[15] Identification of MDA components that are difficult to achieve may ascertain clinical or pathological factors that merit future attention in disease management strategies. Additionally, there is limited understanding of patient and disease characteristics that predict MDA achievement over longer term and of other potential benefits associated with achievement of MDA.[16] The aim of the present analysis was to determine which baseline clinical and/or patient demographic characteristics predict the achievement of MDA over 144 weeks in patients with PsA included in the ADEPT trial and to evaluate the achievement of individual MDA components, as well as the association of MDA status with independent quality of life (QoL)-related patient-reported outcomes (PROs) (not included in MDA criteria).

METHODS
Patients and study
The methods and primary results of the phase 3, double-blind, placebo-controlled ADEPT trial (NCT00646386) of adalimumab in patients with moderately to severely active PsA are published.[13] Briefly, ADEPT patients were ≥18 years of age, had active PsA (≥3 tender and ≥3 swollen joints) and an inadequate response or intolerance to non-steroidal anti-inflammatory drugs. Patients were randomised 1:1 to receive adalimumab 40 mg or placebo every other week for 24 weeks, after which they were eligible to enter an extension study in which they received open-label adalimumab for up to 144 weeks. The present analysis included a subset of ADEPT patients randomised to adalimumab (n=66) and placebo (n=69) who had active skin disease at baseline (body surface area ≥3%) and in whom MDA could be calculated (at least 5/7 MDA components available).

Minimal disease activity
MDA was defined as achieving ≥5 of the following seven criteria[8]: tender joint count of 78 joints (TJC) ≤1; swollen joint count of 76 joints (SJC) ≤1; Psoriasis Area and Severity Index (PASI) ≤1; patient assessment of pain (patient pain) ≤15 on a 0–100 mm visual analogue scale (VAS); Patient Global Assessment of disease activity (PtGA) ≤20 on a 0–100 mm VAS; Health Assessment Questionnaire-Disability Index (HAQ-DI) ≤0.5; and tender entheseal points (assessed bilaterally at two sites) ≤1. Patients who met MDA criteria were termed 'achievers' and those who did not were termed 'non-achievers.' Sustained MDA was defined as MDA achievement at two

consecutive time points 12 weeks apart, except for week 144, where the previous visit was 16 weeks earlier.

Baseline variables tested as predictors of MDA included age (years), sex, weight (kg), duration of psoriasis or PsA since diagnosis (years), structural damage measured by modified total Sharp score, TJC, SJC, PASI (range, 0–72), C-reactive protein (mg/dL), patient pain, PtGA, HAQ-DI, enthesitis (absent vs present at two bilateral sites (proximal insertion of Achilles tendon, insertion of plantar fascia)), Physician Global Assessment of disease activity (PhGA, 0–100 mm VAS) and Physician Global Assessment of psoriasis (PhGA-P) on a 7-point scale ranging from severe (very marked plaque elevation, scaling and/or erythema) to clear (no sign of psoriasis).

Patient-reported outcomes
Health-related QoL was assessed using the Short Form 36 (SF-36) Health Survey questionnaire (total score, physical component summary score (PCS) and mental component summary score (MCS)) and Dermatology Life Quality Index (DLQI). Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score.

Statistical analysis
The percentage of patients achieving MDA over time was assessed using observed data and non-responder imputation. Baseline characteristics that predicted the achievement of MDA or sustained MDA at weeks 12, 24, 48, 96 and 144 were identified using univariate and multivariate analyses. For multivariate analyses, the least absolute shrinkage and selection operator method was used to refine baseline variable selection. Penalties were added to constrain regression coefficients in the presence of correlated data. The positive predictive value (PPV) or negative predictive value (NPV) of week 12 MDA status to determine MDA status at week 24 or 144 was determined using a two-way contingency table. Analyses of PROs at week 24 (and for completers at week 144) were based on observed data, with each analysis conducted on the available data at a particular time point.

RESULTS
Achievement of MDA and sustained MDA through week 144
At the end of the 24-week double-blind period, 36.4% (24/66) of patients randomised to receive adalimumab achieved MDA compared with 5.8% (4/69) receiving placebo while sustained MDA was achieved by 34.8% (23/66) and 5.8% (4/69) of patients receiving adalimumab and placebo, respectively. At week 24, very low disease activity, defined as achieving MDA score of 7/7, was attained by 15.4% (10/65) and 0% (0/61) of patients treated with adalimumab and placebo, respectively. During the open-label period, MDA rate was either maintained or higher in patients initially randomised to adalimumab whereas MDA rate was numerically lower throughout the follow-up in patients switching to open-label adalimumab after receiving placebo for 24 weeks
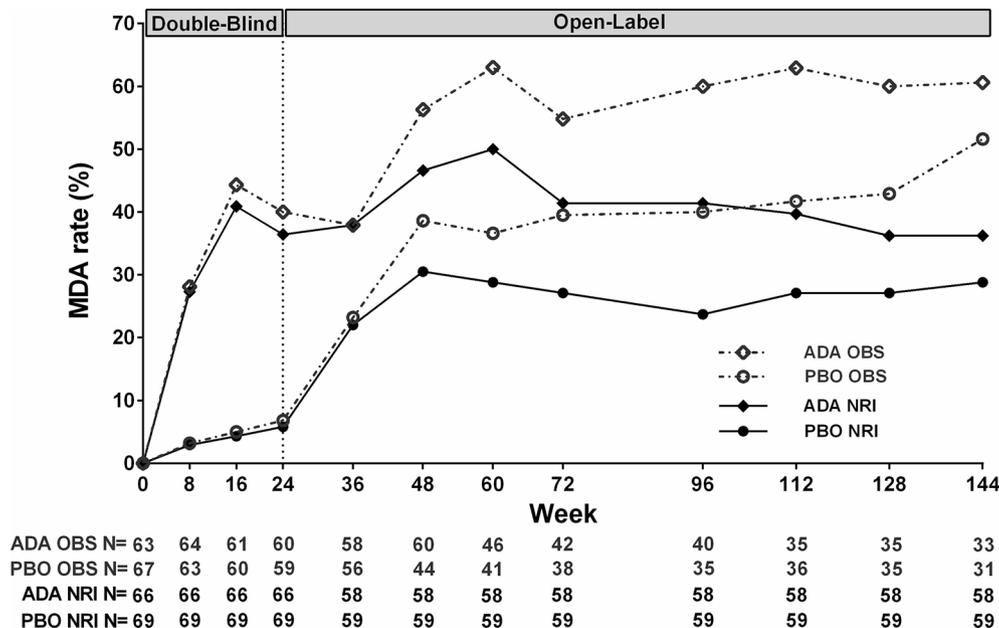
ADA OBS N=	63	64	61	60	58	60	46	42	40	35	35	33
PBO OBS N=	67	63	60	59	56	44	41	38	35	36	35	31
ADA NRI N=	66	66	66	66	58	58	58	58	58	58	58	58
PBO NRI N=	69	69	69	69	59	59	59	59	59	59	59	59

Figure 1 Achievement of MDA over 144 weeks in patients initially receiving adalimumab or placebo during the double-blind period. Data are presented as observed (solid lines) and using NRI (dashed lines). Patients who escalated to weekly dosing on or after week 36 were counted as non-responders. Numbers of patients at each study visit are presented below the graph. ADA, adalimumab; MDA, minimal disease activity; NRI, non-responder imputation; OBS, as observed; PBO, placebo.

(figure 1). Similarly, throughout the open-label period, the rate of sustained MDA was higher among patients initially randomised to adalimumab compared with placebo: week 48, 43.1% (25/58) vs 32.2% (19/59); week 96, 37.9% (22/58) vs 27.1% (16/59); and week 144, 34.5% (20/58) vs 22.0% (13/59). Of the 88 patients who completed the 144-week open-label period, 15 (17.1%) achieved MDA at every time point from week 24 through week 144.

Univariate analysis of factors associated with achievement of long-term and sustained MDA

In the univariate analysis, higher scores at baseline for TJC, patient pain and HAQ-DI were significantly associated with lower odds of achieving MDA at every time point. Higher SJC and higher enthesitis scores or presence of enthesitis at baseline were associated with lower odds of achieving MDA at most time points (figure 2). At every time point, lower baseline TJC, SJC and HAQ-DI scores were associated with higher odds of achieving sustained MDA (data not shown).

Multivariate analysis of factors associated with achievement of long-term and sustained MDA

Multivariate analysis confirmed higher baseline HAQ-DI score as a significant predictor for failure to achieve MDA at later time points (figure 3). A 1-unit increase in baseline HAQ-DI reduced the odds of achieving MDA at later time points by 64%–77%. Lower age, TJC and HAQ-DI at baseline were associated with sustained MDA at week 48, and lower enthesitis at baseline was associated with sustained MDA at week 144 (online supplementary figure 1).

Prediction of MDA at later time points based on MDA status at week 12

MDA status at week 12 had a 100% PPV, 95.7% NPV, 100% specificity and 85.2% sensitivity for predicting MDA status at week 24. MDA status at week 12 had 100% PPV, 64.7% NPV, 100% specificity and 40.0% sensitivity for predicting MDA status at week 144. The high NPV (95.7%) for prediction of week 24 MDA status indicated a good ability of week-12 MDA non-achievement to predict MDA non-achievement at week 24. However, the moderate NPV (64.7%) for prediction of week-144 MDA status indicated a poor ability of week-12 MDA non-achievement to predict MDA non-achievement at week 144.

Achievement of individual MDA components

The comparison of individual MDA components at baseline between MDA achievers and non-achievers at week 24 is presented in online supplementary table 1. MDA achievers, especially those receiving placebo, trended towards lower mean scores for the individual MDA components at baseline.

At week 24, in adalimumab-treated patients regardless of their MDA status, SJC≤1 (MDA achievers, 58.3% (14/24); MDA non-achievers, 13.5% (5/37)) and TJC≤1 (MDA achievers, 83.3% (20/24); MDA non-achievers, 10.8% (4/37)) were achieved by the smallest number of patients; whereas in patients treated with placebo, PASI was achieved by the lowest number of patients (MDA achievers, 0% (0/4); MDA non-achievers, 3.6% (2/55), table 1). Although a high proportion of MDA achievers and non-achievers satisfied the enthesitis
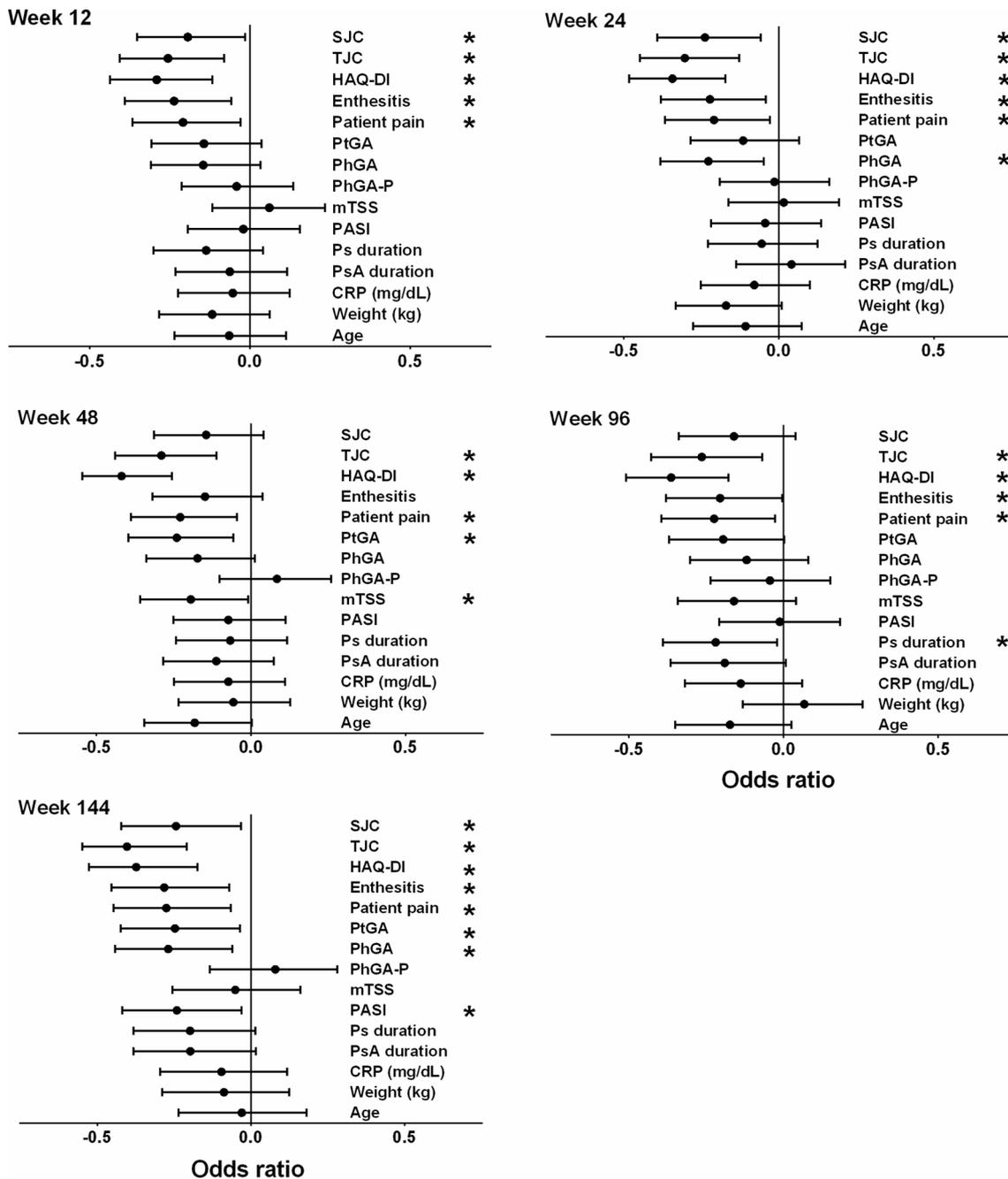
Figure 2 OR for baseline predictors of MDA at weeks 12, 24, 48, 96 and 144 by univariate analysis of observed data. CRP, C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; mTSS, modified total Sharp score; PASI, Psoriasis Area and Severity Index; PhGA, Physician Global Assessment of disease activity; PhGA-P, Physician Global Assessment of psoriasis; Ps, psoriasis; PsA, psoriatic arthritis; PtGA, Patient Global Assessment of disease activity; SJC, swollen joint count of 76 joints; TJC, tender joint count of 78 joints. *Statistically significant predictor of MDA.

criterion throughout the study, fewer than half of the patients (adalimumab, 41.7% (25/60); placebo, 39.0% (23/59)) had baseline entheseal involvement in ≥1 of the two enthesial sites assessed. The differences between the rates of achieving individual MDA components were less pronounced during the open-label period (online supplementary file 3). At week 144, in patients initially treated with placebo, patient pain ≤15 and TJC≤1 were the two MDA components that were consistently met by the lowest number of patients and could therefore be

considered the limiting components for achieving MDA after delayed adalimumab introduction (online supplementary file 3).

To evaluate the contribution of each individual MDA component to MDA achievement at the group level, individual MDA components were omitted separately from the MDA calculation (MDA 5/6, defined as achievement of ≥5 of 6 criteria). Exclusion of SJC did not impact the MDA 5/6 rate at week 24 in patients treated with adalimumab, whereas exclusion of TJC or PASI decreased MDA
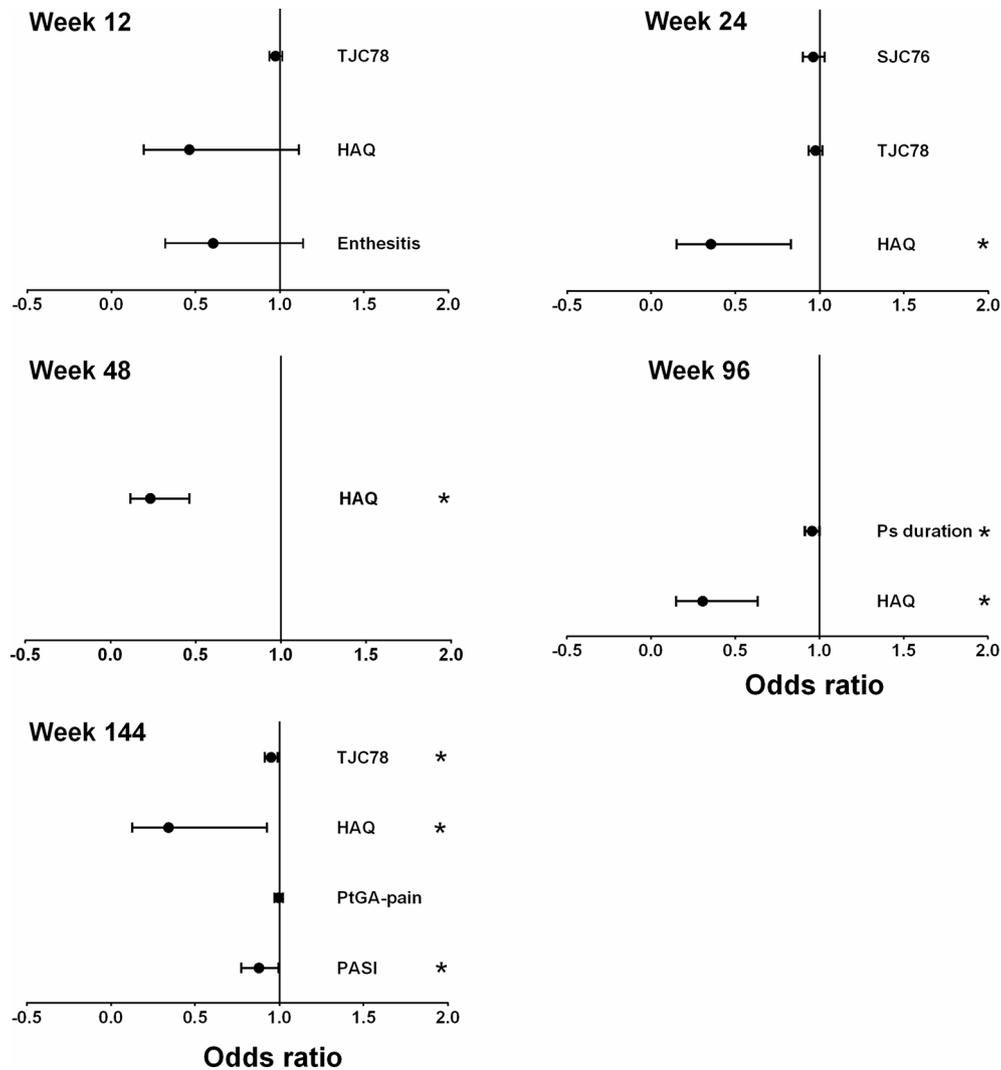
Figure 3 OR for selected baseline predictors of MDA at weeks 12, 24, 48, 96 and 144 by multivariate analysis of observed data. Statistically significant variables in the univariate analysis were further selected with LASSO to adjust for confounding factors and collinearity. HAQ-DI, Health Assessment Questionnaire-Disability Index; LASSO, least absolute shrinkage and selection operator method; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; Ps, psoriasis; SJC, swollen joint count of 76 joints; TJC, tender joint count of 78 joints. *Statistically significant predictor of MDA.

achievement by 3.2%; exclusion of patient pain, PtGA, HAQ-DI or enthesitis decreased MDA achievement by 6.5%. This suggested a relatively equal contribution of individual MDA components to achieving MDA at the population level.

Relationship between disease duration and HAQ-DI
We next explored the relationship between HAQ-DI, a negative predictor of MDA achievement, and disease duration. Generally, HAQ-DI increased with longer PsA duration both at baseline as well as at various study time points (figure 4), but the correlation between PsA duration and HAQ-DI was weak (correlation coefficient <0.3). The mean HAQ-DI score exceeded 0.5 at weeks 96 and 144 in patients with PsA duration of >8 years (figure 4), suggesting that in a substantial proportion of patients with long-standing PsA, the impairment in physical function related to irreversible damage could prevent

achievement of this MDA criterion even with effective control of inflammation.

QoL-related PROs associated with MDA achievement
At week 24, independent QoL-related PROs (those not included in the MDA criteria) were significantly better in MDA achievers than MDA non-achievers (figure 5A,B), including higher mean SF-36 total (p<0.001), PCS (p<0.001) and MCS (p<0.01) scores, higher FACIT-F score (p<0.001) and lower DLQI score (p<0.001). MDA achievers at week 24 had favourable mean (±SD) PRO scores at baseline compared with MDA non-achievers for SF-36 total (58.0±19.0 vs 46.5±19.7; p<0.01) and PCS (37.7±12.0 vs 31.6±9.1; p<0.01) scores, as well as FACIT-F (34.9±10.9 vs 29.2±12.2; p<0.05) scores, but not SF-36 MCS (48.2±11.0 vs 45.6±12.1; p=0.314) and DLQI (7.9±5.6 vs 9.7±7.4; p=0.243) scores. Age, sex, PsA duration and methotrexate use did not influence

Table 1 Attainment of individual MDA components in MDA achievers and non-achievers at week 24 by randomised treatment

MDA component	MDA achievers			MDA non-achievers		
	Patients meeting criterion, n (%)			Patients meeting criterion, n (%)		
	Adalimumab (n=24)	Placebo (n=4)	Response difference (95% CI)	Adalimumab (n=37)	Placebo (n=55)	Response difference (95% CI)
TJC≤1	20 (83.3)	3 (75.0)	8.3 (–36.6 to 53.3)	4 (10.8)	3 (5.5)	5.4 (–6.3 to 17.0)
SJC≤1	14 (58.3)	2 (50.0)	8.3 (–44.9 to 61.2)	5 (13.5)	6 (10.9)	2.6 (–11.2 to 16.4)
PASI≤1	21 (87.5)	0	87.5 (74.3 to 100)*	15 (40.5)	2 (3.6)	36.9 (20.3 to 53.5)**
Patient pain ≤15	24 (100)	4 (100)	0	6 (16.2)	3 (5.5)	10.8 (–2.6 to 24.1)
PtGA≤20	24 (100)	4 (100)	0	6 (16.2)	7 (12.7)	3.5 (–11.3 to 18.3)
HAQ-DI≤0.5	23 (95.8)	4 (100)	–4.2 (–12.2 to 3.8)	8 (21.6)	17 (30.9)	–9.3 (–27.3 to 8.7)
Tender entheseal points ≤1	24 (100)	4 (100)	0	26 (70.3)	35 (63.6)	6.6 (–12.8 to 26.1)

**p<0.001; *p<0.01.

HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PtGA, Patient Global Assessment of disease activity; SJC, swollen joint count of 76 joints; TJC, tender joint count of 78 joints.

results for SF-36, FACIT-F or DLQI in MDA achievers versus MDA non-achievers (data not shown).

Furthermore, MDA achievers experienced larger mean changes from baseline for the evaluated PROs than MDA non-achievers (figure 5C,D); these changes reached the established minimal clinically important difference (MCID) for all the evaluated PROs.[17] Although the mean change from baseline in SF-36 total and PCS scores for MDA non-achievers reached the MCID, these changes were of a lower magnitude compared with MDA achievers. For patients who completed 144 weeks, no significant differences in PRO scores were observed between MDA achievers and non-achievers at the end of follow-up (data not shown).

DISCUSSION

MDA has been established as a validated composite outcome measure in PsA that is discriminative and has prognostic value in terms of structural damage. Further,

its use as a treatment target in the first treat-to-target trial in PsA (TIght COntrol of Psoriatic Arthritis; TICOPA) resulted in improved joint, skin and PROs compared with standard care following no treatment target.[18 19] With the trend for increased use of MDA as a clinical trial endpoint, as well as its adoption into clinical practice,[5 6] it is important to fully understand predictors of MDA and the contribution of individual MDA components to the overall MDA achievement, as well as potential associations of MDA status with other outcomes. The current analysis provided insights into the achievement, prediction and benefits of MDA that were obtained within the randomised, placebo-controlled ADEPT trial of adalimumab, including its open-label extension through week 144.

Nearly 40% of patients treated with adalimumab were previously reported to have achieved MDA by the end of the 24-week, double-blind period of ADEPT.[14] The present analysis showed that the proportion of patients
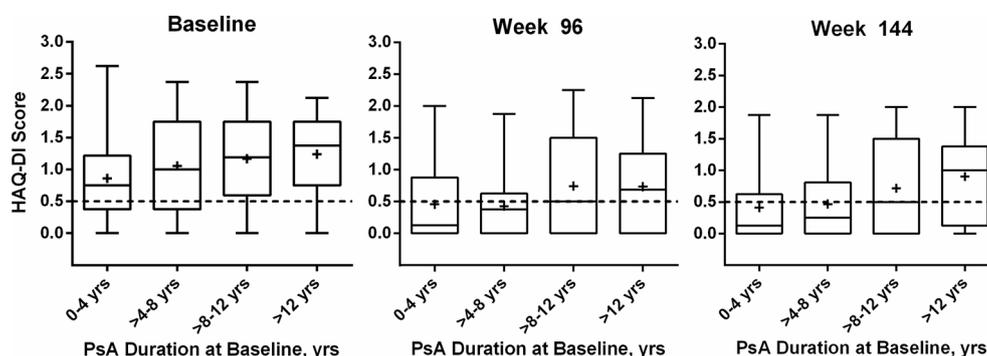

Figure 4 Box plot of HAQ-DI scores at baseline, week 96 and week 144 categorised by baseline PsA duration. The horizontal lines indicate the median, boxes mark the interval between the 25th and 75th percentiles, vertical lines indicate the maximum and minimum values, and + represents the mean. The dashed line represents HAQ-DI=0.5, which is the cut-off point for the MDA component. HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; PsA, psoriatic arthritis.
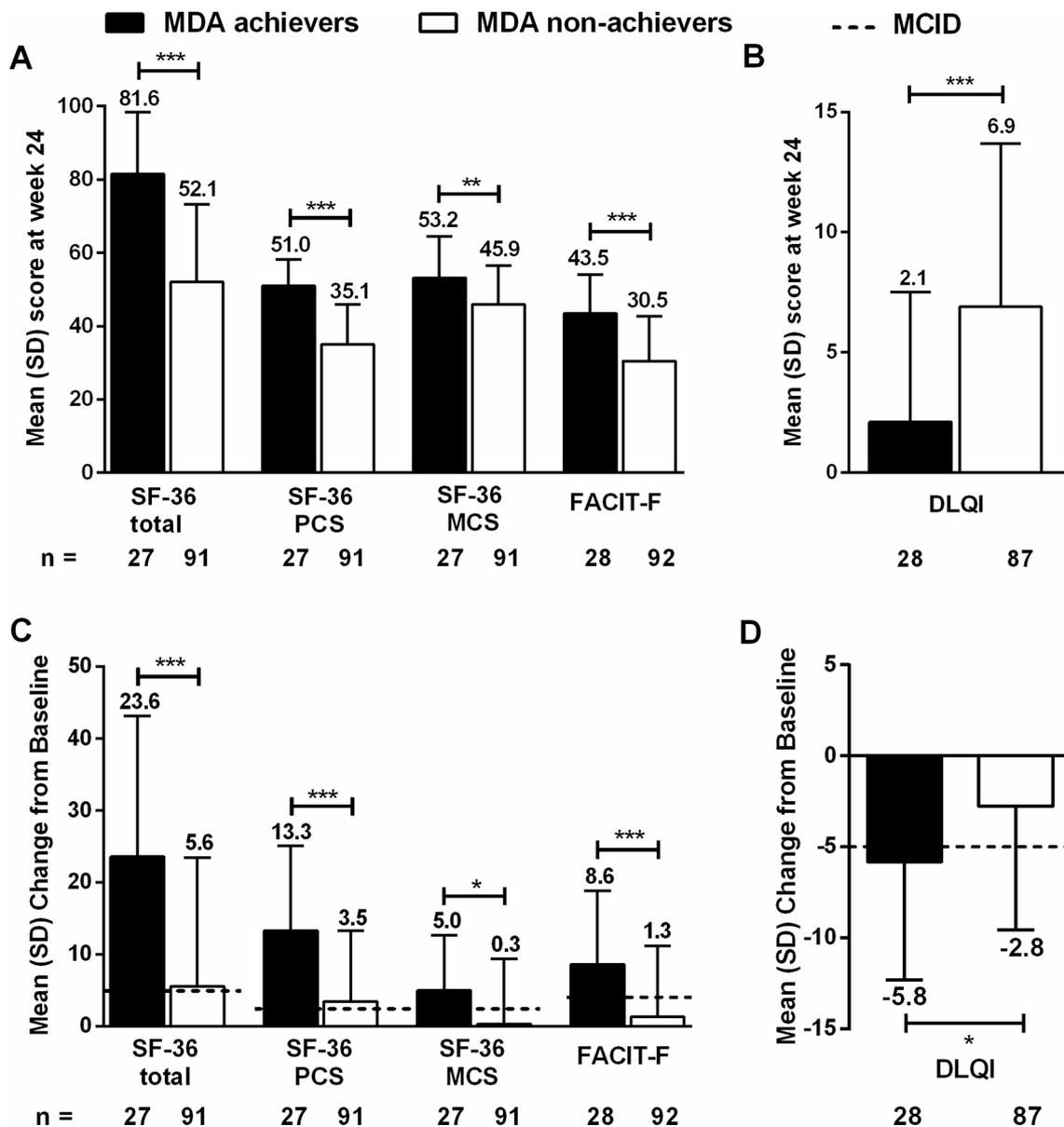
Figure 5 Mean of SF-36 and FACIT-F (A) and DLQI (B) scores at week 24 and mean change from baseline to week 24 in SF-36 and FACIT-F (C) and DLQI (D) scores in MDA achievers and MDA non-achievers. Data are presented as observed. Dashed lines represent MCID. *p<0.01; **p<0.01; ***p<0.001. DLQI, Dermatology Life Quality Index; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; MCID, minimal clinically important difference; MCS, mental component score; MDA, minimal disease activity; PCS, physical component score; SF-36, Short Form 36 Health Survey.

with MDA was maintained or increased through the end of the 144-week open-label extension period, reaching up to 50% in patients initially treated with adalimumab. This observed MDA rate is consistent with findings in the open-label extension of a randomised controlled trial with golimumab[12] and observational studies with antitumour necrosis factors (TNFs) in clinical practice settings.[9 16 20 21] A fairly consistent proportion of patients (37%–40%) had sustained MDA, which was also in accordance with previous data.[9 12] This adds to the body of evidence that long-term sustained MDA is achievable with anti-TNF therapy in up to 50% of patients with established PsA.[9 12 16 20] In a recent study, <20% of patients treated with methotrexate achieved MDA

at 6 months, providing further evidence in support of early introduction of anti-TNF therapy.[22] At week 24, 15.4% of patients treated with adalimumab achieved an MDA score of 7/7, which was recently proposed as very low disease activity.[23] This MDA 7/7 rate is consistent with the rates reported in patients receiving anti-TNF therapy.[24]

Patients initially randomised to placebo arm were slow to attain MDA following treatment with open-label adalimumab. Interestingly, the MDA rate among patients initially treated with placebo remained consistently lower compared with patients who initially received adalimumab through 144 weeks. Although the differences did not reach statistical significance at any time point,

this may indicate that delay in introduction of effective therapy could negatively impact MDA achievement, even in patients with long-standing PsA.

Higher scores at baseline for TJC, SJC, patient pain, enthesitis and HAQ-DI were significantly associated with lower odds of achieving MDA at most time points, including sustained MDA, by univariate analysis. Multivariate analysis confirmed high baseline HAQ-DI score as the most consistent predictor for failure to achieve MDA. A 1-unit increase in baseline HAQ-DI reduced the odds of achieving MDA at later time points by 64%–77%. Consistent with our results, worse physical function (measured by HAQ-DI) was most commonly identified as a negative predictor of MDA in prior studies,[9 12 16 21 25] whereas other predictive factors varied across studies.[9 12 16 20 21 25 26] In patients with longer disease duration, the mean HAQ-DI scores remained high even after long-term adalimumab treatment. This suggests that in patients with effective control of inflammation, higher HAQ-DI was most likely due to irreversible structural damage. Previous studies have shown that the onset of disease symptoms of less than 6 or 12 months prior to starting treatment is associated with better long-term function outcomes.[27 28] This analysis, where higher baseline HAQ-DI scores were observed in established disease and associated with lower MDA achievement, further supports the need for early and effective treatment in PsA.

In patients who achieved MDA at week 24, the baseline scores for individual MDA components were lower, suggesting that patients with milder disease achieve MDA more easily. Achieving MDA early (at week 12) was a strong predictor of MDA response at weeks 24 and 144. Although not achieving MDA early remained a good predictor of non-MDA status at week 24, the ability of week-12 MDA non-response to predict non-response at week 144 was relatively poor. Therefore, not achieving MDA at week 12 should not result in an immediate change to another therapy.

The joint responses (TJC and SJC criteria) appeared to limit MDA achievement in patients treated with adalimumab at the end of the double-blind period, whereas fewer differences in the attainment of individual MDA components were observed during prolonged adalimumab therapy. This could indicate more equivalent long-term adalimumab effectiveness across different MDA components, but could also be biased by the observed analysis in the open-label period. By contrast, patients treated with placebo had difficulty meeting the PASI criterion, which was not fulfilled by any of the MDA achievers and also not met by the highest percentage of MDA non-achievers at week 24. These findings suggest that fulfilment of individual MDA components may be treatment dependent. A previous study reported a highly active skin component still present in patients otherwise meeting MDA criteria; however, details of PsA therapy were not presented.[15]

Patients who achieved MDA at week 24 had significantly better PROs reflecting improved QoL and fatigue.

Furthermore, the MDA achievers experienced larger improvements from baseline than non-achievers in all PROs measured. The mean change from baseline reached MCID for all PROs in MDA achievers but not MDA non-achievers. Previous studies demonstrated lower radiographic progression and improvements in PROs which were included in the MDA criteria in MDA achievers compared with non-achievers.[6 8] Our data provide further support for MDA as a valid treatment target in PsA that is associated with meaningful benefits as measured by PROs beyond those included in the MDA calculation.

The limitations of our analyses include the low patient numbers and the fact that ADEPT was not specifically designed to assess MDA achievement a priori. However, these limitations exist for most other studies of MDA[9 12 16 20 21 25 26] and, along with different patient populations and treatments, may explain inconsistent findings on MDA predictors other than HAQ-DI. A recent study reported that patients with PsA and with fibromyalgia had lower likelihood of achieving MDA.[29] Given that fibromyalgia was not an exclusion criterion in the ADEPT study and systematic assessment for fibromyalgia was not performed, the impact of comorbid fibromyalgia cannot be assessed. Strengths of our post hoc analyses include a 24-week placebo-controlled period, enabling a comparison that is lacking in observational studies, and the relatively long open-label extension period with adalimumab treatment.

In summary, the present study provides further insights into the long-term achievement of MDA in patients treated with adalimumab and confirms higher baseline HAQ-DI as a negative predictor for the achievement of MDA, supporting the necessity for early and effective treatment in PsA before irreversible functional impairment occurs. Finally, it demonstrates that improvements in QoL-related PROs are associated with MDA achievement, which lends further support to MDA as a meaningful treatment target in PsA.

Author affiliations
[1]Swedish Medical Center and University of Washington, Seattle, Washington, USA
[2]Department of Rheumatology, Allergy and Immunology, University of California San Diego, San Diego, California, USA
[3]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, University of Leeds, Leeds, UK
[4]Glasgow Biomedical Research Centre, University of Glasgow, Glasgow, UK
[5]AbbVie, Ljubljana, Slovenia
[6]AbbVie Inc, North Chicago, Illinois, USA
[7]Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, Ontario, Canada

REFERENCES

1. Gladman DD. Psoriatic arthritis. *Dermatol Ther* 2009;22:40–55.
2. Gladman DD, Antoni C, Mease P, *et al*. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;64(suppl 2):ii14–ii17.
3. Healy PJ, Helliwell PS. Dactylitis: pathogenesis and clinical considerations. *Curr Rheumatol Rep* 2006;8:338–41.
4. Coates LC, Helliwell PS. Classification and categorisation of psoriatic arthritis. *Clin Rheumatol* 2008;27:1211–6.
5. Gossec L, Smolen JS, Ramiro S, *et al*. European League against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis* 2016;75:499–510.
6. Coates LC, Kavanaugh A, Mease PJ, *et al*. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for Psoriatic Arthritis. *Arthritis & rheumatology* 2016;68:n/a–71.
7. Smolen JS, Braun J, Dougados M, *et al*. Treating spondyloarthritis, including ankylosing spondylitis and psoriatic arthritis, to target: recommendations of an international task force. *Ann Rheum Dis* 2014;73:6–16.
8. Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. *Ann Rheum Dis* 2010;69:48–53.
9. Coates LC, Cook R, Lee K-A, *et al*. Frequency, predictors, and prognosis of sustained minimal disease activity in an observational psoriatic arthritis cohort. *Arthritis Care Res* 2010;62:970–6.
10. Coates LC, Helliwell PS. Validation of minimal disease activity criteria for psoriatic arthritis using interventional trial data. *Arthritis Care Res* 2010;62:965–9.
11. Gladman DD, Mease PJ, Strand V, *et al*. Consensus on a core set of domains for psoriatic arthritis. *J Rheumatol* 2007;34:1167–70.
12. Kavanaugh A, van der Heijde D, Beutler A, *et al*. Radiographic progression of patients with Psoriatic Arthritis Who achieve Minimal disease activity in response to Golimumab therapy: results through 5 years of a Randomized, Placebo-Controlled Study. *Arthritis Care Res* 2016;68:267–74.
13. Mease PJ, Gladman DD, Ritchlin CT, *et al*. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2005;52:3279–89.
14. Mease PJ, Heckaman M, Kary S, *et al*. Application and modifications of minimal disease activity measures for patients with psoriatic arthritis treated with adalimumab: subanalyses of ADEPT. *J Rheumatol* 2013;40:647–52.
15. Marin J, Acosta Felquer ML, Ferreyra Garrot L, *et al*. Patients with Psoriatic Arthritis fulfilling the Minimal disease activity criteria do not have Swollen and Tender Joints, but have Active skin. *J Rheumatol* 2016;43:907–10.
16. Lubrano E, Parsons WJ, Perrotta FM. Assessment of response to Treatment, remission, and minimal disease activity in Axial Psoriatic Arthritis treated with tumor necrosis factor inhibitors. *J Rheumatol* 2016;43:918–23.
17. Gladman DD, Mease PJ, Cifaldi MA, *et al*. Adalimumab improves joint-related and skin-related functional impairment in patients with psoriatic arthritis: patient-reported outcomes of the Adalimumab Effectiveness in Psoriatic Arthritis Trial. *Ann Rheum Dis* 2007;66:163–8.
18. Coates LC. Treating to target in psoriatic arthritis. *Curr Opin Rheumatol* 2015;27:107–10.
19. Coates LC, Moverley AR, McParland L, *et al*. Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a UK multicentre, open-label, randomised controlled trial. *Lancet* 2015;386:2489–98.
20. Haddad A, Thavaneswaran A, Ruiz-Arruza I, *et al*. Minimal disease activity and anti-tumor necrosis factor therapy in psoriatic arthritis. *Arthritis Care Res* 2015;67:842–7.
21. Perrotta FM, Marchesoni A, Lubrano E. Minimal disease activity and remission in Psoriatic Arthritis Patients treated with Anti-TNF-α drugs. *J Rheumatol* 2016;43:350–5.
22. Sheane BJ, Thavaneswaran A, Gladman DD, *et al*. Attainment of minimal disease activity Using Methotrexate in Psoriatic Arthritis. *J Rheumatol* 2016;43:1718–23.
23. Coates LC, Helliwell PS. Defining low disease activity States in Psoriatic Arthritis using novel Composite Disease Instruments. *J Rheumatol* 2016;43:371–5.
24. Lubrano E, Perrotta FM. Defining low disease activity States in Psoriatic Arthritis using novel Composite Disease Instruments. *J Rheumatol* 2016;43:1765–6.
25. Theander E, Husmark T, Alenius GM, *et al*. Early psoriatic arthritis: short symptom duration, male gender and preserved physical functioning at presentation predict favourable outcome at 5-year follow-up. results from the swedish early psoriatic Arthritis Register (SwePsA). *Ann Rheum Dis* 2014;73:407–13.
26. Iervolino S, Di Minno MN, Peluso R, *et al*. Predictors of early minimal disease activity in patients with psoriatic arthritis treated with tumor necrosis factor-α blockers. *J Rheumatol* 2012;39:568–73.
27. Haroon M, Gallagher P, FitzGerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. *Ann Rheum Dis* 2015;74:1045–50.
28. Tillett W, Jadon D, Shaddick G, *et al*. Smoking and delay to diagnosis are associated with poorer functional outcome in psoriatic arthritis. *Ann Rheum Dis* 2013;72:1358–61.
29. Brikman S, Furer V, Wollman J, *et al*. The effect of the presence of Fibromyalgia on common clinical disease activity indices in patients with psoriatic Arthritis: a Cross-sectional study. *J Rheumatol* 2016;43:1749–54.