Early treatment of psoriatic arthritis is associated with improved patient-reported outcomes: findings from the etanercept PRESTA trial

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Abstract

Objective

The present paper aims to investigate the effect of psoriatic arthritis (PsA) disease duration on the outcome of treatment with etanercept (ETN) in patients with PsA who also have moderate-to-severe psoriasis.

Methods

Patients from the PRESTA trial who received ≥1 ETN 50 mg once weekly (QW) dose and had ≥1 post-baseline value were evaluated. Baseline and after-treatment changes were compared between patients with PsA ≤2 years versus PsA >2 years in efficacy measures (physician global assessment [PGA] arthritis, swollen joint count and Psoriasis Area and Severity Index [PASI]) and patient reported outcomes (PROs; joint pain, arthritis activity, Euro-Qol [EQ-5D] utility and visual analogue score [VAS]) using linear regression analysis.

Results

Baseline efficacy measures were similar between the PsA ≤2 years (n=103) and PsA >2 years (n=269) groups, with the exception of PGA arthritis (p=0.006). At week 24, improvements in efficacy measures were observed in both groups but were significantly greater for PGA arthritis in the PsA ≤2 years group (p=0.03). Quality of life (QoL), measured using PROs, was generally lower at baseline in patients with PsA >2 years. Clinically meaningful improvements were seen in QoL with ETN treatment in both groups, but the change from baseline scores at week 24 were significantly higher in PsA ≤2 years group for joint pain (p=0.007), arthritis activity (p=0.01), EQ-5D utility (p=0.046) and EQ-5D VAS (p=0.04) responses.

Conclusion

PsA patients responded to ETN 50 mg QW treatment irrespective of disease duration; however, patients with shorter PsA duration had greater improvements in arthritis scores and several PRO measures.

Key words

psoriatic arthritis, etanercept, disease duration

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W. Li was an employee of Quintiles, who were paid contractors to Pfizer during the development of this manuscript;
R. Boggs and H. Nab were employees of Pfizer during the PRESTA study and development of this manuscript.
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Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory disorder of the peripheral synovial joints, axial skeleton and entheses (1). Joint disease in PsA can lead to irreversible bone damage, which increases progressively over time (2), resulting in compromised physical functioning and a reduced quality of life (QoL) (3, 4). The presence of PsA is often associated with psoriasis and is estimated to be prevalent in up to 30% of patients who have the skin disease (5). A large proportion of patients with both conditions have a lower QoL than patients with psoriasis alone (6).

Diagnosing and treating patients with PsA and psoriasis can be challenging (7). The majority of patients have psoriasis for a number of years before PsA symptoms arise which can make the initial diagnosis difficult (8). In addition, some patients with joint symptoms may not develop skin disease, it can be hidden in difficult places or may have disappeared (9, 10). Some patients may not realise that their joint symptoms are linked to their psoriasis, and therefore may fail to mention joint issues to their dermatologist. Thus the link between joint pain and psoriasis may take a while to be inferred and, as a result, PsA is often under-diagnosed (1, 8, 11). Treating both PsA and psoriasis can be complicated as therapies need to effectively address 2 diseases simultaneously (12). Traditional non-biologic disease-modifying anti-rheumatic drugs (DMARDs) have been the standard initial treatment (7), however, evidence of their effectiveness in PsA is limited (13). The presence of elevated tumour necrosis factor (TNF) levels in both the psoriatic skin lesions (14) and synovial fluid (15) of PsA joints has recently led to the use of anti-TNF biologics to treat both skin and joint manifestations (16-19). Current treatment recommendations depend on the subject's level of disease with anti-TNFs usually recommended for subjects who have failed ≥1 DMARD or who have a poor prognosis (12).

In patients with other inflammatory conditions such as rheumatoid arthritis (RA), early detection of disease and rapid therapeutic intervention reduces disease activity, halts joint damage and improves physical function and QoL (20). Logically, the benefits of early RA treatment could extend to patients with early PsA as joint damage can occur early in the disease course and can be extensive even in patients with early PsA (21-23). Nevertheless, studies of the effect of disease duration on treatment response in PsA are limited. One study reported that anti-TNF therapy was effective in treating patients with shorter PsA duration (24). However, the patients had minimal skin involvement and their results were not compared with patients with longer disease duration. To date, no study has investigated the effect of shorter *versus* longer disease duration of PsA on the efficacy of anti-TNF treatment responses on skin and joint symptoms as well as functional outcomes in patients with PsA plus moderate-to-severe psoriasis. The role of biologics in the management of early PsA is therefore still unclear (25, 26).

The PRESTA (Psoriasis Randomised Etanercept Study in Patients with Psoriatic Arthritis) trial (Clinicaltrials.gov Identifier: NCT00245960) investigated the efficacy, safety and QoL responses to the anti-TNF biologic etanercept (ETN) in patients with both active PsA and moderate-to-severe psoriasis (27-29). In PRESTA, 2 dose regimens of ETN were evaluated (ETN 50 mg twice weekly [BIW] for 12 weeks followed by ETN 50 mg once weekly [QW] or ETN 50 mg QW for 24 weeks). Both dose groups showed significant improvements in efficacy and QoL measures with no new safety signals (27-29).

The objective of this *post hoc* analysis of PRESTA trial data was to examine the influence of PsA disease duration on the response to ETN 50 mg QW treatment, the licensed dose for PsA, in patients with PsA plus moderate-to-severe psoriasis.

Methods

Study group

PRESTA was a randomised, blinded, 24-week, multicentre study enrolling adult (≥18 years of age) patients diagnosed with active but stable plaque psoriasis involving at least 10% of body surface area (BSA) and a physician's global assessment (PGA) of psoriasis as

moderate-to-severe at baseline. In addition, all patients had active PsA defined as ≥2 swollen joints, ≥2 tender joints, joint pain for ≥3 months and a negative serum rheumatoid factor within 6 months prior to baseline. Details of additional inclusion and exclusion criteria have previously been published (27). This study was conducted in compliance with all ethical principles of the Declaration of Helsinki and an independent ethics committee or institutional review board reviewed and approved the protocol and its amendments before the start of the study.

For this *post hoc* analysis, only patients who received ETN 50 mg QW for 24 weeks (the dose indicated for PsA) were included. The modified intention-to-treat (mITT) population was all patients who had received ≥1 dose of ETN and had ≥1 post-baseline evaluation. Last observation carried forward (LOCF) was used for missing data. Patients were stratified into 2 categories based on their PsA disease duration at baseline (≤2 years and >2 years; Fig. 1). The 2-year disease-duration cut-off was chosen and based on the results of previous early PsA studies (21, 26) and in order to have sufficient numbers for a *post hoc* analysis.

Efficacy assessments

Efficacy assessments included the psoriasis area and severity index (PASI) (30, 31) scores at baseline and weeks 3, 6, 12, 18 and 24. Changes from baseline at week 24 were assessed for the swollen joint count and PGA of arthritis visual analogue scale (VAS). In addition, the proportions of patients achieving the American College of Rheumatology (ACR) 20/50/70 response criteria (32) and the proportions of patients achieving minimal disease activity (MDA) of PsA (33) at week 24 were calculated. Further details of each of these measures and their respective minimum important differences (MIDs) are listed in Table I. The newly developed MDA incorporates measures for both skin and joint symptoms and is the first tool specifically designed to identify a state of disease activity in PsA. In order to achieve MDA, patients must achieve low disease activity targets in 5 of 6 endpoints: a tender joint count of ≤1; a swollen joint count of ≤1; either a PASI score ≤1 or BSA of ≤3%; pain VAS of ≤15; patient global disease activity VAS ≤20; a health assessment questionnaire (HAQ) score of ≤0.5. A previous study, which included an entheseal count with a range of 0–13, included the criterion of tender entheseal points ≤1 for MDA (33). However, this criterion is excluded from our analyses because the PRESTA study featured a smaller range of entheseal counts (0–4), thus making the MDA incomparable to previous work. Excluding this criterion was a conservative approach. The proportions of patients with enthesitis, as well as the mean number of tender entheseal points in these patients, were calculated at baseline and at week 24.

Patient reported outcomes

Patient reported outcomes (PROs) used to assess QoL included patient-reported joint pain VAS, EuroQol 5D (EQ-5D) utility score and its components (patient's mobility, self-care, usual activities, pain/discomfort and anxiety/depression) (34), EQ-5D VAS (34), HAQ score (35, 36), Hospital Anxiety and Depression Scale (HADS) anxiety and HADS depression scale (37), duration of morning stiffness (in minutes), proportions of patients in employment and the number of sick days the patient had taken during the previous month. All PROs were assessed at baseline and week 24 and are reported as the mean improvement from baseline at week 24. Patient-reported joint pain was also reported at weeks 3, 6, 12 and 18. Further details on the PRO measures and score ranges are listed in Table I.

Statistical analysis

The software package used for the statistical analyses was SAS 9.2. Linear regression of change from baseline at week 24 on PsA duration was performed for each of the variables, to compare PsA duration groups (≤2 years *vs*. >2 years). Baseline values, age and gender were included in the model as potential confounding factors. The baseline values used were of the corresponding predicted variable. Improvements from baseline at week 24 for each group are represented as least squares (LS) means. For each of the ACR responses (ACR 20, 50 and 70), logistic regression was performed to compare the 2 PsA duration groups controlling for age and gender. The *p*-values for the percentages of patients achieving MDA in the PsA ≤2 years *versus* PsA >2 years at baseline were calculated using Fisher's exact test (due to the small sample size) and at week 24 using Pearson's chi-square test, as were the percentages of patients in employment. Statistical differences between the 2 disease duration groups for the proportion of patients with enthesitis were examined by Cochran-Mantel-Haenszel test controlling for pooled site (geographic region) and the mean number of tender entheseal points was examined by *t*-test.

Results

Baseline demographics

Of the 373 patients randomised to the ETN 50 mg QW/QW arm of PRESTA, 372 (PsA ≤2 years, n=103; PsA >2 years, n=269) were included in this analysis (Fig. 1). One patient had an incomplete diagnostic history and was excluded from the dataset. A total of 28 patients discontinued the PRESTA study (27). No major between group differences were observed in the age (p=0.40) or sex (p=0.26) of the patients (Table II). Mean body mass index (BMI) was significantly higher in the patients with PsA ≤2 years (29.4) than the PsA >2 years group (28.0; p=0.04). The median PsA disease duration was 0.5 years for patients in the PsA ≤2 years group and 7.7 years for patients in the PsA >2 years group. Psoriasis duration was significantly shorter in the PsA ≤2 years group (16.3 years; p=0.02) than the PsA >2 years group (19.4 years).

Efficacy assessments

Despite the difference in disease duration, the BSA affected by psoriasis at baseline was similar in both groups (p=0.39). PASI scores were also similar between the 2 groups (p=0.90), as were the number of swollen joints (p=0.62). The mean PGA arthritis score was significantly lower in the PsA ≤2 years

Table I. Outcomes evaluated in the PRESTA trial.

Measures	Scoring
Efficacy measures	
PASI	0–72; 72=worst possible plaques covering 100% of the body. Different sources cite scores of 10 to 20 as constituting severe psoriasis
Swollen joint count	0–76
PGA arthritis	VAS 0–100 mm; lower score=less disease activity
ACR 20/50/70	20%/50%/70% improvement from baseline in tender and swollen joint counts and improvement in 3 out of 5 of the following: acute phase reactants; patient global assessment; physician global assessment; pain VAS; HAQ score
MDA	Achieving 5 of the 6 following criteria: tender joint count ≤1; swollen joint count ≤1; PASI ≤1 or BSA ≤3; pain VAS ≤15; patient global disease activity VAS ≤20; HAQ ≤0.5 (33). The criterion tender entheseal points ≤1 is excluded (see Methods).
Tender entheseal points	0–4 (left and right Achilles tendon and left and right plantar fascia)
PROs	
Joint pain (patient-reported)	VAS 0–100 mm; lower score=less joint pain
Arthritis activity (patient-reported)	VAS 0–100 mm; lower score=less disease activity
EQ-5D utility	Components of EQ-5D: mobility, self-care, usual activities, pain/discomfort and anxiety/depression are scored 1–3 with higher scores representing worse health state. From these, an overall utility score is determined, range 0–1; 0=death, 1=perfect health; MID=Δ ≥0.05 (45).
EQ-5D VAS	VAS 0–100 mm; 0=worst imaginable health state, 100=best imaginable health state; MID=4–8 (46)
HAQ	0–3; lower score=better physical function; MID=Δ ≥0.30 (47) or MID=Δ ≥0.35 (48)
HADS anxiety	0–21; <8=no symptoms, 8–10=mild symptoms, 11–14=moderate symptoms, >14=severe symptoms
HADS depression	0–21; <8=no symptoms, 8–10=mild symptoms, 11–14=moderate symptoms, >14=severe symptoms
Morning stiffness	Duration reported in minutes

ACR: American College of Rheumatology; BSA: body surface area; EQ-5D: EuroQoL-5D; HADS: hospital anxiety and depression scale; HAQ: Health Assessment Questionnaire; MDA: minimal disease activity; MID: minimally important differences; PASI: psoriasis area and severity index; PGA: physician global assessment; PRO: patient reported outcomes; VAS: visual analogue score.

(44.9) than the PsA >2 years group (51.8; p=0.006). No patients achieved MDA criteria at baseline. The proportions of patients presenting with enthesitis were similar across both groups (p=0.71) as were the mean number of tender entheseal joints in patients with enthesitis (p=0.88).

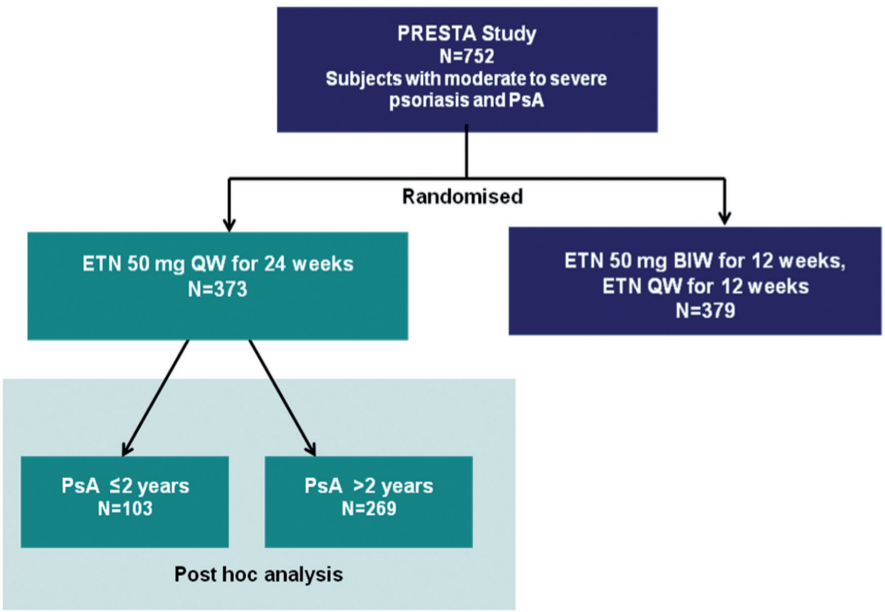

Fig. 1. Study design. Patients from the ETN 50 mg QW arm of the PRESTA trial were divided into 2 groups based on their PsA disease duration at baseline.
BIW: twice weekly; ETN: etanercept; PsA: psoriatic arthritis; QW: once weekly.

After 24 weeks of ETN 50 mg QW treatment, patients on average showed improvements in efficacy measures, regardless of their disease duration (Table III, Fig. 2-3). Improvements from baseline in PASI were similar between the PsA ≤2 years and PsA >2 years groups across all time points (Fig. 3A) with scores of 5.3 and 4.9 at week 24, respectively (p=0.56). In terms of improvements in joint disease, the change from baseline at week 24 in the PGA arthritis score was significantly greater in the PsA ≤2 years group (-39.8) *versus* the PsA >2 years group (-35.7; p=0.03; Fig. 2). The mean number of swollen joints improved from baseline at week 24 was not significantly different between the 2 groups (p=0.31). No significant between group differences were observed in the percentages of patients achieving the ACR20 (p=0.12), ACR50 (p=0.43) and ACR70 (p=0.89) responses. The numbers of patients achieving MDA were not significantly different between the PsA ≤2 years (38.9%) and PsA >2 years (29.4%; p=0.08) groups. Of the patients presenting with enthesi-

Table II. Baseline demographics and disease characteristics by PsA disease duration.

Parameter	PsA ≤2 years (n=103)	PsA >2 years (n=269)	*p*-value
Baseline demographics			
Age, years	46.1 (12.0)	47.2 (11.2)	0.40
Female gender, %	42.7	36.4	0.26
BMI, kg/m^2	29.4 (5.9)	28.0 (5.6)	0.04
Duration of PsA, median, years	0.5	7.7	-
Duration of psoriasis, years	16.3 (11.9)	19.4 (11.1)	0.02
BSA affected by psoriasis, %	32.0 (23.3)	29.8 (21.8)	0.39
Efficacy measures			
PASI	19.1 (9.9)	19.0 (9.8)	0.90
Swollen joint count	12.4 (15.1)	13.3 (15.3)	0.62
PGA arthritis	44.9 (22.1)	51.8 (20.0)	0.006
MDA, %	0.0	0.0	NA*
Patients with enthesitis, n/N (%)	33/103 (32)	92/269 (34)	0.71†
no. of tender entheseal points in patients with enthesitis	2.2	2.2	0.88‡
PROs			
Joint pain	58.0 (27.7)	63.3 (24.1)	0.07
Arthritis activity	57.7 (27.1)	63.1 (23.7)	0.06
EQ-5D utility	0.55 (0.31)	0.47 (0.33)	0.046
Mobility	1.69 (0.49)	1.74 (0.44)	0.31
Self-care	1.30 (0.50)	1.43 (0.53)	0.03
Usual activity	1.67 (0.59)	1.79 (0.55)	0.06
Pain/discomfort	2.09 (0.49)	2.18 (0.49)	0.11
Anxiety/depression	1.67 (0.62)	1.75 (0.68)	0.30
EQ-5D VAS	58.6 (21.1)	54.7 (20.3)	0.11
HAQ	0.77 (0.67)	0.98 (0.70)	0.01
HADS anxiety	7.3 (4.1)	8.2 (4.4)	0.07
HADS depression	6.2 (4.2)	6.6 (3.8)	0.36
Morning stiffness	117.5 (299.3)	151.0 (341.8)	0.39
Employed, % of patients	60.8%	59.3%	0.80§
Sick days	3.6 (7.8)	1.6 (4.3)	0.02

All values shown are means (SD) unless otherwise stated. *p*-values calculated from: *Fisher's exact test, †Cochran-Mantel-Haenszel test controlling for pooled site, ‡un-paired *t*-test; §Pearson's Chi-square test. BMI: body mass index; BSA: body surface area; EQ-5D: EuroQoL-5D; HADS: hospital anxiety and depression scale; MDA: minimal disease activity; PASI: psoriasis area and severity index; PGA: physician global assessment; PRO: patient reported outcome; PsA: psoriatic arthritis; SD: standard deviation; VAS: visual analogue score.

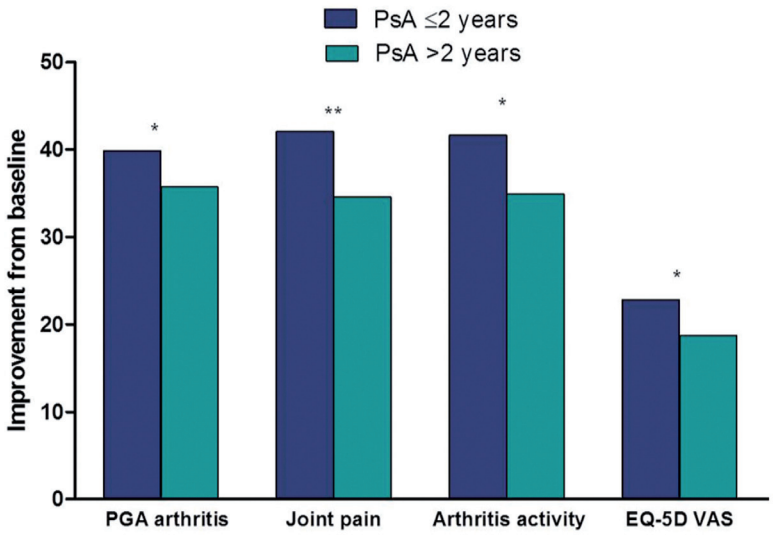

Fig. 2. The effect of PsA disease duration on the improvement from baseline at week 24 in efficacy and PRO scores.
*p<0.05; **p<0.01 for the between group comparison. LS means controlling for baseline values, age and sex. EQ-5D VAS: EuroQol 5D visual analogue scale; PGA: physician global assessment; PsA: psoriatic arthritis.

tis at baseline, only 25% in the PsA ≤2 years group and 22% in the PsA >2 years group still had enthesitis at week 24 (p=0.78), with a mean number of tender entheseal points of 1.9 and 2.8, respectively (p=0.06).

Patient reported outcomes

At baseline, although patient-reported joint pain and arthritis activity were lower in the PsA ≤2 years group than the PsA >2 years group, the differences were not statistically significant (p=0.07 and p=0.06, respectively; Table II). The EQ-5D utility score was significantly higher in the PsA ≤2 years group than the PsA >2 years group (p=0.046) indicating better health in the former. Specifically, the self-care dimension of the EQ-5D utility score was significantly lower in the PsA ≤2 years group suggesting better self-care ability than patients with PsA >2 years (p=0.03). EQ-5D VAS scores were similar between disease duration groups (p=0.11). At baseline, the HAQ score was significantly lower in the PsA ≤2 years group than the PsA >2 years group (0.77 *vs*. 0.98; p=0.01), indicating better physical function in the shorter duration group. For both HADS anxiety and depression, scores were similar for both disease duration groups (p=0.07 and p=0.36, respectively) at baseline. Employment levels were also similar between groups (p=0.80), although patients with shorter PsA duration took more time off work than patients with PsA >2 years (p=0.02).

Over the course of ETN 50 mg QW treatment, patient-reported joint pain scores were similar (Fig. 3B), however, by week 24 the improvements from baseline were significantly larger in the PsA ≤2 years group compared with the PsA >2 years group (-42.1 *vs*. -34.6; p=0.007; Fig. 2). A significant difference favouring the PsA ≤2 years group was also observed in the improvements from baseline in patient-reported arthritis activity (PsA ≤2 years, -41.7; PsA >2 years, -34.9; p=0.01). Mean improvements in EQ-5D utility and EQ-5D VAS in both disease duration groups were larger than the MIDs of ≥0.05 and between 4–8, respectively (Tables I and III). Improvements from

Table III. The effect of PsA disease duration on the mean change from baseline at week 24 on efficacy and PRO measures.

	PsA ≤2 years (n=103)	PsA >2 years (n=269)	*p*-value
Efficacy measures			
Mean change from baseline at week 24[*,†]			
PASI	-13.7	-14.1	0.56
Swollen joint count	-10.6	-9.8	0.31
PGA arthritis	-39.8	-35.7	0.03
% of patients at week 24			
ACR20	77.6	69.3	0.12[‡]
ACR50	57.1	52.5	0.43[‡]
ACR70	37.8	36.4	0.89[‡]
MDA	38.9	29.4	0.08[§]
Enthesitis, n/N (%)[#]	8/32 (25)	20/90 (22)	0.78[‖]
no. of tender entheseal points in patients with enthesitis	1.9	2.8	0.06[¶]
PROs			
Mean change from baseline at week 24[*,†]			
Joint pain	-42.1	-34.6	0.007
Arthritis activity	-41.7	-34.9	0.01
EQ-5D utility	+0.30	+0.24	0.046
Mobility	-0.48	-0.39	0.07
Self-care	-0.23	-0.21	0.67
Usual activity	-0.46	-0.42	0.52
Pain/discomfort	-0.65	-0.47	0.003
Anxiety/depression	-0.30	-0.24	0.29
EQ-5D VAS	+22.8	+18.7	0.04
HAQ	-0.52	-0.49	0.56
HADS anxiety	-2.1	-2.0	0.60
HADS depression	-1.6	-1.6	0.95
Morning stiffness	-103.8	-95.0	0.67
Sick days	-0.9	-1.0	0.90
% of patients at week 24			
Employed	59.8%	59.7%	0.99[§]

[*]LS means controlling for baseline values, age and sex. *p*-values from: [†]linear regression analysis controlling for baseline values, age and sex; [‡]logistic regression analysis controlling for age and sex; [§]Pearson's Chi-square test; [‖]Cochran-Mantel-Haenszel test controlling for pooled site; [¶]un-paired *t*-test. [#]Percentages are based on population of those who had baseline assessment and enthesitis present at baseline.
ACR: American College of Rheumatology; EQ-5D: EuroQoL-5D; HADS: hospital anxiety and depression scale; HAQ: Health Assessment Questionnaire; MDA: minimal disease activity; PASI: psoriasis area and severity index; PGA: physician global assessment; PROs: patient-reported outcomes; PsA: psoriatic arthritis; VAS: visual analogue scale.

baseline at week 24 in the EQ-5D utility score were significantly and meaningfully higher for patients with PsA ≤2 years (+0.3; greater than the MID) *versus* PsA >2 years (+0.24; p=0.046; Table III). Specifically, the pain/discomfort dimension of the EQ-5D utility questionnaire showed a significant difference between disease duration groups (p=0.003). A difference was also observed for the VAS component of the EQ-5D (PsA ≤2 years, +22.8; PsA >2 years +18.7; p=0.04; Fig. 2), however, this difference was less than the MID. Although the HAQ score was significantly lower in the PsA ≤2 years group than the PsA >2 years group at baseline, after 3 weeks of treatment they reached similar levels (Fig. 3C) that continued to week 24 (0.41 in PsA ≤2 years group *vs*. 0.44 in PsA >2 years; p=0.56) with LS mean changes from baseline of -0.52 and -0.49 in the PsA ≤2 years and PsA >2 years groups, respectively (Table III). The mean improvement in HAQ in both groups at week 24 was larger than the MID of ≥0.35. HADS anxiety and HADS depression symptom scores both improved on treatment with no significant difference between the disease duration groups observed (p=0.60 and p=0.95, respectively). After 24 weeks of treatment, the duration of morning stiffness also improved similarly in both disease duration groups (PsA ≤2 years, 104 minutes *vs*. PsA >2 years, 95 minutes; p=0.67). The percentages of patients in employment were similar at week 24 in both PsA ≤2 years (59.8%) and PsA >2 years (59.7%; p=0.99). The number of sick days taken by patients was lower in each disease duration group than at baseline; the reduction was similar between groups (0.9 days *vs*. 1.0 days; p=0.90).

Discussion

Until now, the effect of early *versus* late treatment had not been extensively investigated in subjects with PsA who also have psoriasis. We have shown improvements in measures related to PROs and QoL were generally superior in patients with shorter PsA duration after 24 weeks of ETN treatment. Notably, the PROs that specifically measure joint symptoms showed a significantly greater improvement with ETN treatment in patients with shorter PsA *versus* longer PsA duration. Interestingly, the similar HAQ improvements shown in the two disease duration groups contrasts with previous analyses performed in patients with RA that found a reduced HAQ response to therapy in subjects with longer RA disease duration (38, 39). This reduced HAQ response with increased disease duration in RA occurred in the context of similar disease activity responses to therapy and is thought to relate to joint damage. Radiographs were not included in the PRESTA study, but one possible explanation for these differences could be that the group with longer disease duration did not have significant joint damage to prevent improvements of function in response to improved inflammatory joint disease. Moreover, it could be that once a patient reaches a certain HAQ score it is very difficult to have further improvement.

Evidence on the effect of treatment in patients with early PsA is limited. A prospective study of patients with PsA duration of 9.9 months at baseline found 47% had radiological damage 2 years later, despite receiving DMARDs and showing clinical improvement (21). This accumulation of irreversible joint damage highlights the potential severity of PsA, even in patients with early disease. The first study into the ef-

fect of biologics in early PsA involved Italian patients with an unsatisfactory response to previous treatments and PsA <12 months. Patients showed major improvements in both joint symptoms and HAQ score within 24 weeks of anti-TNF biologics (ETN, infliximab or adalimumab) (24). However, these patients had minimal skin involvement (median PASI at baseline was 0.6) compared with our study. A recent prospective study investigated patients who presented with early *versus* late PsA disease to a specialised PsA clinic (40). Patients receiving therapy in the specialised clinic earlier did better than those who presented late. However, the late presenting group had previously received a variety of therapies (DMARDs, non-steroidal anti-inflammatory drugs and biologic agents) prior to presentation. In our study, we did not fully know the treatment history for patients with long PsA duration; some may have been treated for PsA but were refractory to treatment. Ideally, to address our research question, a comparison between early and late PsA using only patients that had not previously received treatment would need to be performed.

In RA, treat-to-target guidelines focus on treating the disease earlier and more aggressively rather than waiting for the disease to worsen. These include adding a biologic within 3–6 months if DMARD therapy is not working (41, 42). The success of these guidelines in RA has led to interest in transferring the treat-to-target concept to PsA (43, 44) and the results presented here support this. However, PsA comes with its own distinct symptoms and more disease-specific treat-to-target guidelines need to be developed for PsA.

The main limitation of our study is this was a *post hoc* analysis and the original trial was not designed to explore the effect of early treatment *versus* later treatment in patients with PsA and moderate-to-severe psoriasis. Because this study used trial data, the inclusion/exclusion criteria forced homogeneity on the patient population that is not found in routine clinical practice. They did, however, receive a standard treatment regimen which allows comparison of effects such as disease duration on outcomes. The >2 years group had a median disease duration of 7.7 years. To ensure our results were robust and not depend-

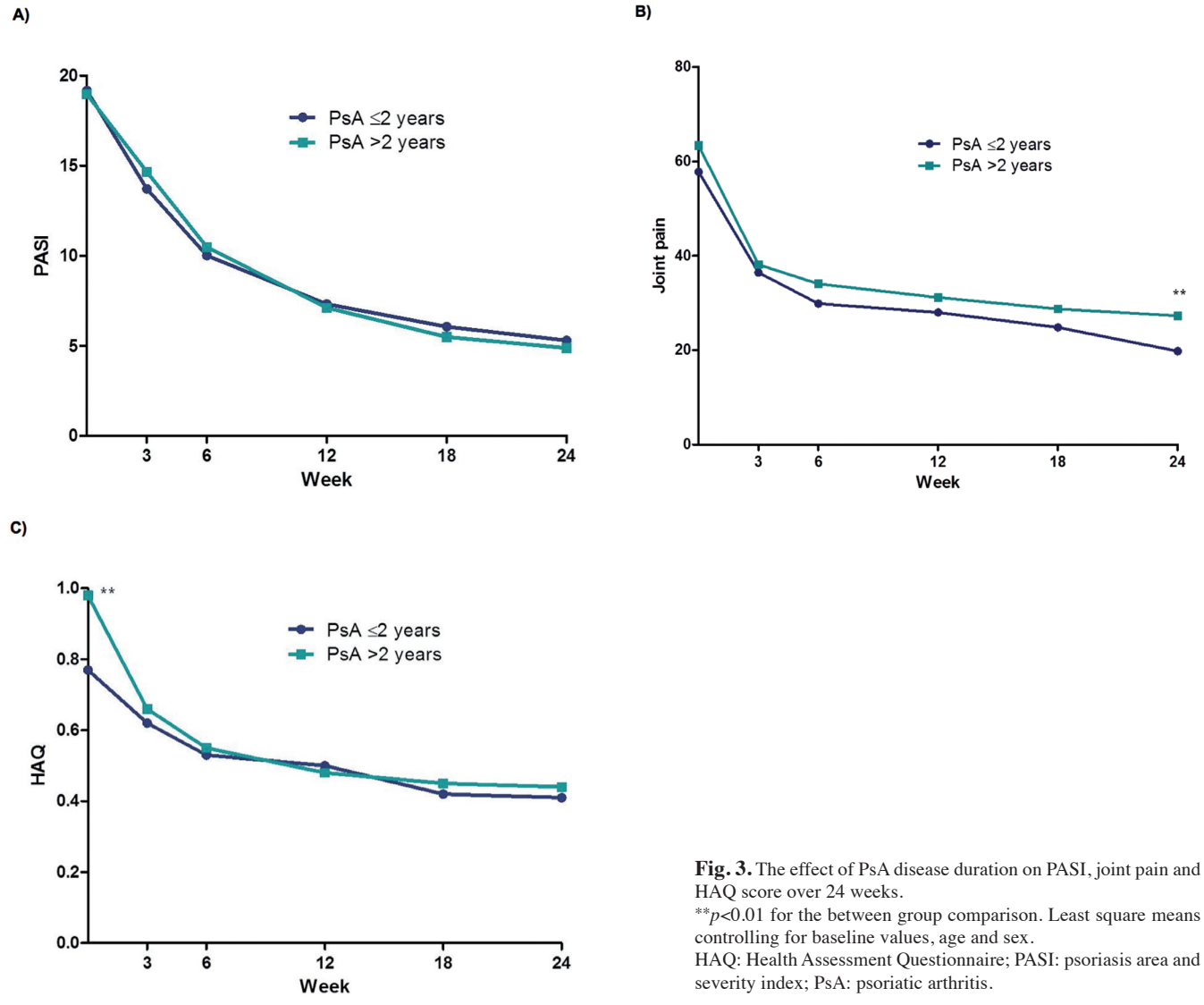

Fig. 3. The effect of PsA disease duration on PASI, joint pain and HAQ score over 24 weeks.
$^{**}p<0.01$ for the between group comparison. Least square means controlling for baseline values, age and sex.
HAQ: Health Assessment Questionnaire; PASI: psoriasis area and severity index; PsA: psoriatic arthritis.

ent on the arbitrary cut-off of 2 years, we divided patients into quartiles based on their PsA disease duration since diagnosis (0–1.57 years, 1.57–5.18 years, 5.18–10.52 years; and >10.52 years) and compared the outcomes. When comparing patients in the lowest quartile (PsA <1.57 years) *versus* all other patients the results were similar to the results presented in the manuscript. When patients in the lower quartile (PsA <1.57) were compared with patients in the highest quartile (PsA >10.52 years), no significant differences in the changes from baseline at week 24 were observed between groups although a trend favouring the early treatment group was seen in joint pain, subject assessment of arthritis activity, and EQ-5D VAS. It appeared that dividing patients into more groups generally did not uncover any other findings, but diluted the statistical power for our tests. Therefore, we concluded that PsA <2 years was an appropriate cut-off to measure outcomes. One other potential limitation of this *post hoc* analysis is that many comparisons have been made and reported *p*-values are not corrected to account for these multiple comparisons. Therefore some differences reported as statistically significant may in fact be due to chance. However, the pattern of improvements in the early PsA group in multiple PRO measures suggests that an improved response was seen which has important implications for QoL.

Conclusion

In conclusion, this *post hoc* analysis found that all patients with PsA responded well to ETN 50 mg QW treatment, but patients with shorter PsA duration had better responses in several efficacy measures and PROs than those with longer PsA duration. Clinicians should consider treating their PsA patients with therapies effective in PsA early rather than late.

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