

Results of a Randomised, Double-Blind Study to Evaluate the Efficacy and Safety of Etanercept in Patients With Psoriasis and Psoriatic Arthritis: The PRESTA Trial

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INTRODUCTION

- The prevalence of psoriatic arthritis (PsA) in patients with psoriasis is estimated to be as high as 30%, contrasted with an occurrence of <1% in the general population.^{1,3}
- Dermatologists and other practitioners treating patients with moderate-to-severe plaque psoriasis are in an ideal position to screen for PsA and provide therapeutic management or referral in order to prevent progression, joint damage and pain. The severe manifestations of PsA require systemic therapy.

- Etanercept (ETN), a fully human tumor necrosis factor soluble receptor, is approved for treatment of moderate to severe plaque psoriasis and active psoriatic arthritis. ETN is efficacious in treating both skin and joint symptoms.
- The aim of this study was to determine the efficacy of two different dose regimens of ETN (50 mg twice weekly [BiW] vs 50 mg once weekly [QW]) over 12 weeks for patients who have both psoriasis and PsA.

METHODS

This clinical study is registered in the ClinicalTrials.gov (NCT00195507) registry.

Patients

Key Eligibility Criteria Included:

- Age: 18 years or older
- Moderate-to-severe plaque psoriasis with body surface area involvement $\geq 10\%$
- Physician Global Assessment (PGA) moderate or worse (≥ 3)
- Active PsA, defined as:
 - Two or more swollen/tender joints at screening and baseline
 - Patient-reported joint pain for at least 3 months prior to screening
 - Negative serum rheumatoid factor within 6 months of screening

Key Exclusion Criteria Were:

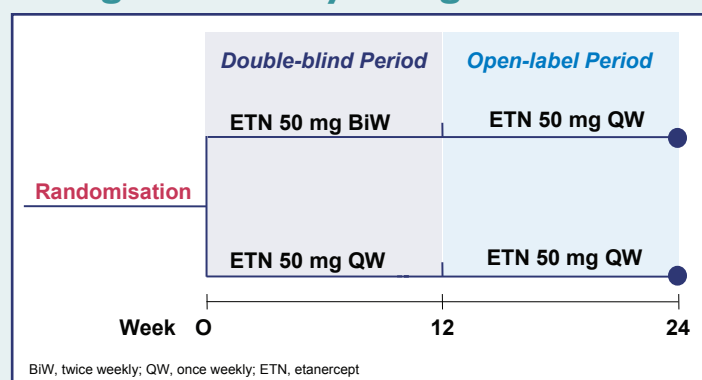
- Serious infection within 1 month of test article administration or active infection at screening
- Known human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), or hepatitis C virus (HCV) positive
- Tuberculosis infection
- Demyelinating disease
- Exposure to PUVA within 28 days
- Exposure to UV light B, topical steroids, topical vitamin A or D analog preparations, or anthralin within 14 days
- Pregnancy

Study Design

- This randomised, multicentre study enrolled patients with both psoriasis and psoriatic arthritis from 110 global sites.

- In the double-blind period, patients received either ETN 50 mg BiW or 50 mg QW for 12 weeks; in the subsequent open-label period, patients received 50 mg QW for 12 weeks (Figure 1).

Figure 1. Study Design Schema



Primary Endpoint

- The primary endpoint was the proportion of patients achieving a status on the PGA of psoriasis of clear or almost clear at Week 12.

	Rating	Clinical Response
Primary Endpoint	0	Clear
	1	Almost clear
	2	Mild
	3	Moderate
	4	Marked
	5	Severe

PGA of psoriasis

- PGA is a subjective physician-reported instrument designed to assess severity of psoriasis on a 6-point skin assessment rating scale.
- PGA was assessed at baseline and at Weeks 3, 6, 12, 18 and 24.

Secondary Endpoints

- Proportion of patients achieving PGA of clear or almost clear at Week 24
- Proportion of patients achieving Psoriasis Area and Severity Index (PASI) improvement $\geq 50\%$, $\geq 75\%$, and $\geq 90\%$ at Weeks 12 and 24; assessed at baseline and at Weeks 3, 6, 12, 18 and 24.

PASI is a clinical measure of the average redness, thickness, and scaliness of the psoriasis lesions		
Each lesion is graded on a 0 to 4 scale and weighted by the area of involvement.	Recorded on a scale of 0 to 72, where 0 represents no psoriasis lesions and 72 represents 100% body coverage of the worst possible lesions.	Scores ≥ 10 represent severe psoriasis.

- Proportion of patients meeting Psoriatic Arthritis Response Criteria (PsARC) at Weeks 12 and 24.

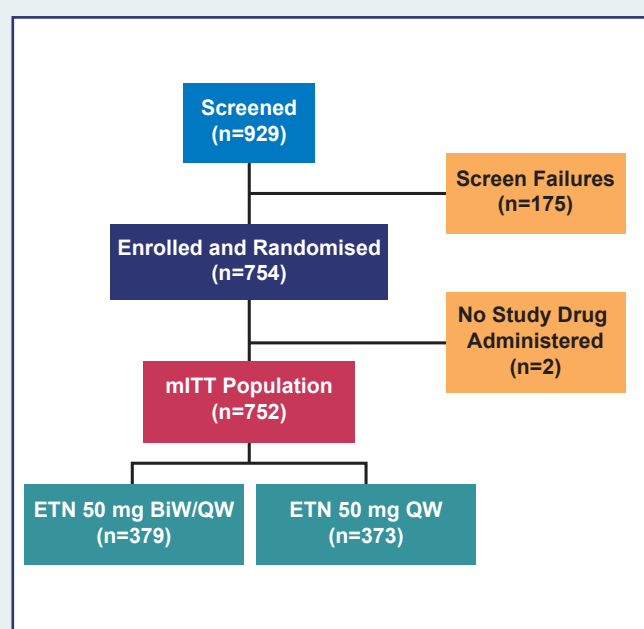
PsARC consists of 4 clinical improvement criteria:	To achieve a clinical response, the patient must:
≥ 1 unit (0 to 5 Likert scale) improvement on the PGA	Improve in 2 of the 4 PsARC criteria (1 of which is the number of tender or swollen joints)
$\geq 20\%$ (0 to 100 scale) improvement on the Subject Assessments	Not worsen on scores of any of the 4 clinical improvement criteria
$\geq 30\%$ reduction in the number of tender joints	
$\geq 30\%$ reduction in the number of swollen joints	

Statistical Analysis

- The primary endpoint and other response endpoints were analyzed using 2-sided Mantel-Haenszel chi-square tests, stratified by region (Europe, Latin America, Asia-Pacific).
- The modified intention-to-treat population (mITT) was used for all efficacy analyses. All patients in this population were randomised, received at least one dose of ETN and had at least one on-therapy evaluation.
- Last-observation-carried-forward was used for imputation of missing values.

Disposition

Figure 2. Patient Flow Diagram



Patients

Demographics and Baseline Clinical Data

Baseline values are presented in Table 1. The groups are balanced except for the greater percentage of patients in the ETN 50 mg QW group with prior MTX use.

Table 1. Demographics and Baseline Clinical Data		
	ETN 50 mg BiW/QW (n=379)	ETN 50 mg QW (n=373)
Age, y	46	47
Gender, %	Male	64
	Female	36
Race, %	White	88
	Other	12
BMI	28	28
PsO Disease Duration, y	19	19
PsA Disease Duration, y	7	7
PGA-psoriasis	3.6	3.6
PASI	20	19
Affected Body Surface Area	31	30
Swollen Joints, n	12	13
Tender Joints, n	19	19
Prior MTX use [†]	32	40

Data represent mean values, unless otherwise specified
*P<0.05, Fisher exact test, 2-tail.
[†]Refers to use within six months prior to screening

Concomitant Therapies

- No statistical difference between the treatment groups was detected for administration of concomitant therapies.

Safety

- Rates of serious adverse events (4% vs 3%) and serious infections (0.5% vs 0.8%) were similar between the BiW/QW and QW groups at end of study (Table 2).

Table 2. Tolerability and Safety

	ETN 50 mg BiW/QW (n=379) n (%)	ETN 50 mg QW (n=373) n (%)	Total (n=752) n (%)
Patients with an AE of >5% incidence	213 (56)	190 (51)	403 (54)
SAE	15 (4)	11 (3)	26 (3.5)
Death	0	0	0
Malignancy	3 (0.8) [*]	1 (0.3) [†]	4 (0.5)
Serious infection	2 (0.5)	3 (0.8)	5 (0.7)
Opportunistic infection			
Histoplasmosis	0	0	0
Tuberculosis	0	0	0
AE of special interest			
Demyelination	0	0	0

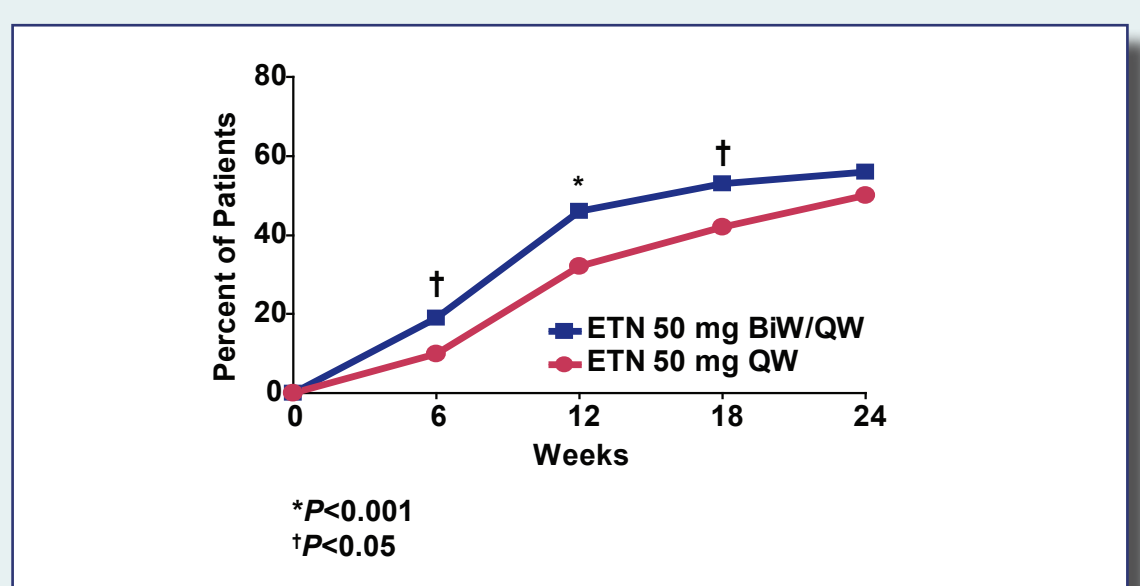
*2 skin carcinomas, 1 breast carcinoma; [†]1 skin carcinoma

RESULTS

Efficacy

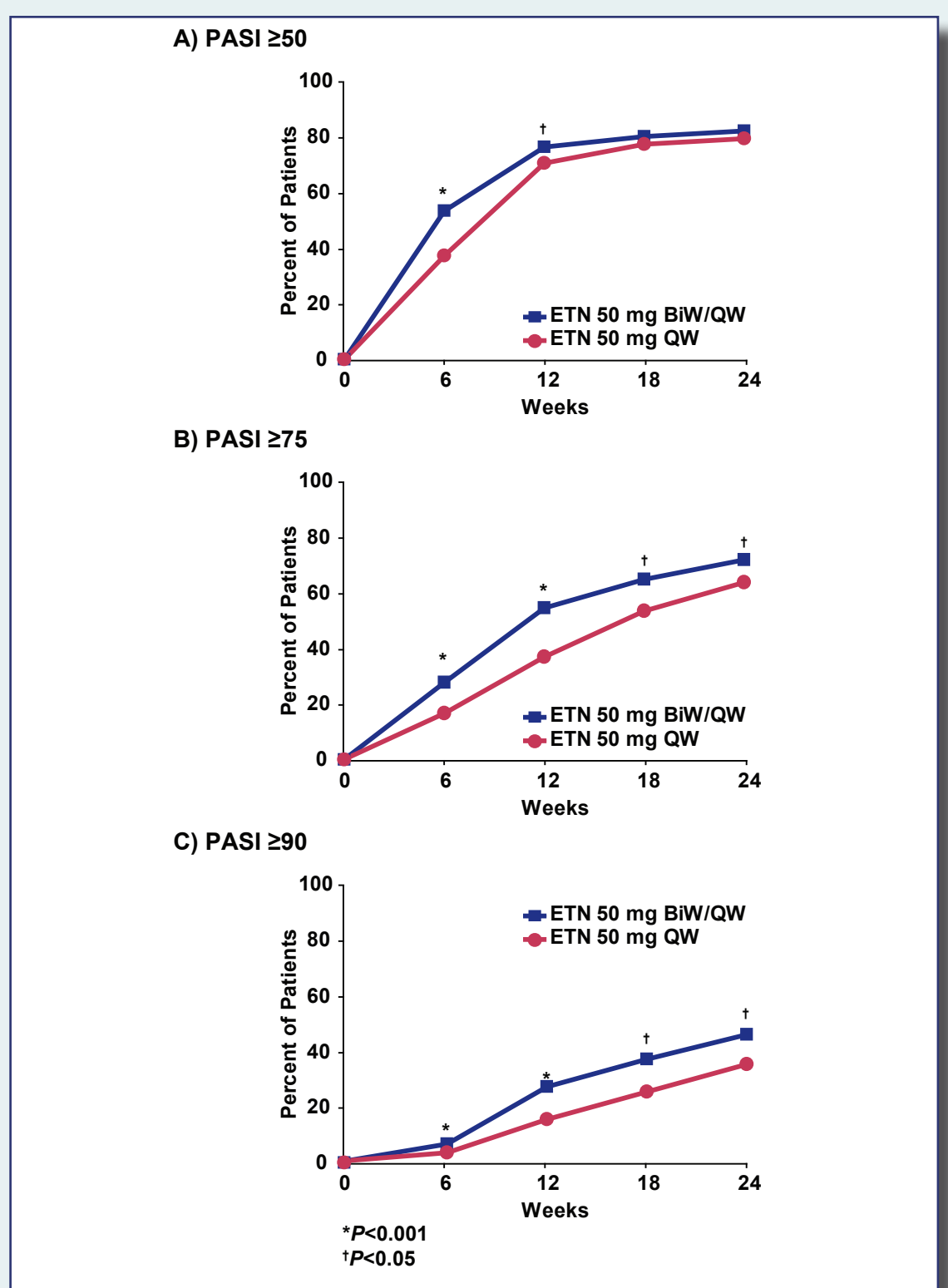
- At Week 12, 46% of the ETN 50 mg BiW/QW group achieved a PGA response of 0 or 1 (clear or almost clear) compared with 32% of the ETN 50 mg QW group (P<0.001) (Figure 3).
- At Week 24, 56% of patients in the ETN 50 mg BiW/QW group achieved PGA response of 0 or 1 (clear or almost clear) compared with 50% in the ETN 50 mg QW group (P=NS).

Figure 3. PGA Responders Over 12 and 24 Weeks



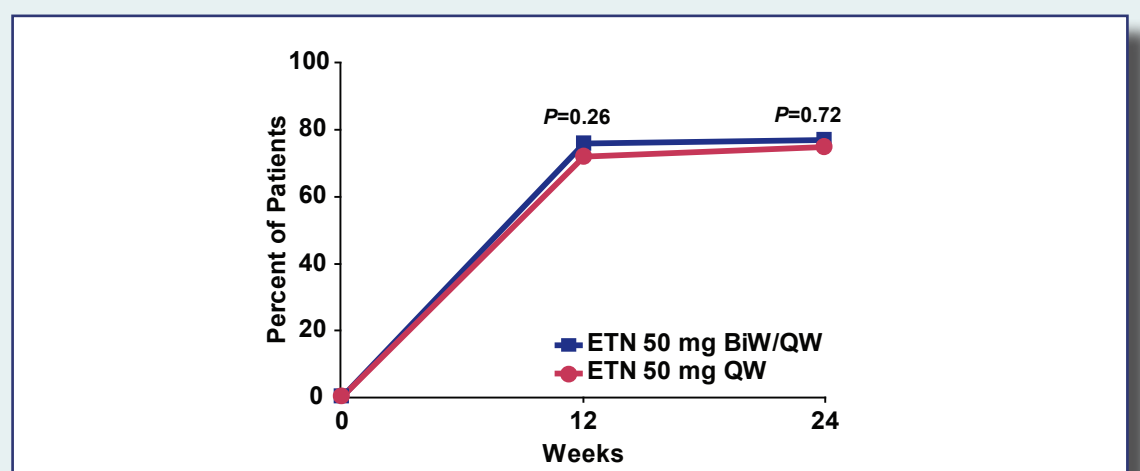
- For patients achieving PASI $\geq 75\%$ improvement, there was a significant difference between the treatment groups at Week 12 (P<0.001) and at Week 24 (P=0.026) (Figure 4).

Figure 4. Percent of Patients Achieving Improvement in PASI Score



- Improvement in joint symptoms was observed in both treatment groups, but there was no significant difference between the groups at any time point (Figure 5).

Figure 5. Percentage of Patients Achieving PsA Response Criteria (PsARC)



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CONCLUSIONS

- For patients who have plaque psoriasis and psoriatic arthritis, benefits from etanercept 50 mg twice weekly for skin manifestations were superior to 50 mg once weekly at Week 12, but similar for joint manifestations.
- Both the step-down and the usual dose regimens for psoriasis were equivalent by Week 24.

- Both etanercept dose regimens were well tolerated up to 24 weeks with no new safety signals noted.
- Either etanercept dose regimen can be used safely and effectively in the treatment of the psoriasis associated with psoriatic arthritis allowing for individualised patient care.