



Etanercept is Effective and Halts Radiographic Progression in Rheumatoid Arthritis and Psoriatic Arthritis: Final Results from a German Non-interventional Study (PRERA)

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ABSTRACT

Introduction: Etanercept (ETN) has been shown to slow radiographic progression of rheumatoid arthritis (RA) and psoriatic arthritis (PsA) in clinical trials. This real-world, non-interventional study assessed radiographic progression in patients with RA or PsA treated with ETN for ≤ 36 months in outpatient care in Germany (NCT01623752).

Methods: Patients with RA or PsA attended ≤ 10 visits across two study phases (phase 1: seven visits, baseline to month 18; phase 2: three visits until month 36). Radiographs were

taken at baseline (Rx1), months 12–18 (Rx2), and/or months 30–36 (Rx3). Historic radiographs (Rx0) taken 12–48 months pre-baseline were also evaluated (if available). The primary endpoint was the change in modified total Sharp score (mTSS). The erosion score (ES) and joint space narrowing score (JSN) were also evaluated.

Results: Overall, 1821 patients were enrolled (RA: $n = 1378$; PsA: $n = 440$). In patients with Rx1 and Rx2 (RA: $n = 511$; PsA: $n = 167$), the mean mTSS remained stable for both disease groups, and the annualized median change in mTSS was 0. In patients with Rx0, Rx1, and Rx2 (RA: $n = 180$; PsA: $n = 47$), annualized radiographic progression in mTSS, ES, and JSN was larger in the pre-ETN treatment phase than during ETN treatment in both disease groups. The percentage of patients with radiographic non-progression was higher during ETN treatment versus pre-ETN. Improvement in clinical disease activity and patient-reported outcomes was also observed.

Conclusions: This was the first real-world, non-interventional study to report systematically collected radiographic data in a large cohort of patients with RA or PsA under treatment with a biologic. In patients with available radiographic data, mean radiographic progression was lower and the proportion of patients without progression was greater during ETN treatment than in the pre-ETN period.

The affiliation shown for Peter-Andreas Löschmann was his affiliation when the study was conducted.

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PLAIN LANGUAGE SUMMARY

Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are diseases in which inflammation can lead to damage in the joints. X-ray images can show whether the disease gets worse; this is called radiographic progression. Etanercept is a drug that acts on the body's immune system and can reduce inflammation in the joints. In clinical studies, radiographic progression was slower in people with RA or PsA who received etanercept compared with people who received another drug called methotrexate.

In this study, we wanted to know how radiographic progression changes in people in Germany who receive etanercept as part of their routine treatment. A total of 1378 people with RA and 440 people with PsA received etanercept for up to 36 months. We observed little to no radiographic progression for most people during the study. Radiographic progression was worse before people started taking etanercept. More people had no radiographic progression while taking etanercept compared with before they started treatment. The proportion of people who responded to treatment with etanercept as measured by the number of painful joints increased throughout the study. Overall, people felt that their health improved after they started taking etanercept.

This was the first large study in which we investigated how radiographic progression changes when people with RA or PsA start taking etanercept as part of their routine treatment. We observed a slowing or halting of radiographic progression in most people and an improvement in their overall health.

Keywords: Auto-injector; IL-6, IL-6R α ; Patient preference; Pen, Prefilled syringe; Rheumatoid arthritis; Sarilumab

Key Summary Points

Reducing radiographic progression is an important goal in the treatment of rheumatoid arthritis (RA) and psoriatic arthritis (PsA)

Etanercept (ETN) has been shown to slow radiographic progression in patients with RA and PsA in randomized prospective clinical trials

PRERA was a real-world, non-interventional study reporting radiographic data collected over 36 months from a large cohort of patients with RA or PsA treated with ETN in routine clinical practice

Radiographic progression slowed or halted in the majority of patients with RA and PsA during ETN treatment compared with the pre-ETN period

INTRODUCTION

Rheumatoid arthritis (RA) is associated with rapid functional loss [1] and reduced life expectancy [2]. Disease remission and prevention of structural damage as documented by radiographic non-progression are major goals of RA treatment [3]. In several randomized, double-blind clinical trials (COMET [4], TEMPO [5, 6]), the tumor necrosis factor alpha (TNF- α) inhibitor etanercept (ETN) in combination with methotrexate (MTX) has been shown to reduce disease activity, slow radiographic progression, and improve function. It is unclear, however, what proportion of patients with RA achieve remission and radiographic non-progression under the conditions of routine rheumatologic care.

Psoriatic arthritis (PsA) is another chronic inflammatory disorder that causes joint pain and disability and leads to joint destruction, which can be measured and quantified radiologically [7]. Several studies have demonstrated the efficacy of ETN in reducing the signs and

symptoms of PsA and psoriasis, as well as in inhibiting radiological progression [7, 8].

There is evidence to suggest that radiographic progression may continue in patients receiving conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), even when clinical remission is achieved—the so-called silent progressors [9–11]. In contrast, radiographic progression was found to be stopped in patients being treated with TNF blocking agents, even if they were not in clinical remission [12]. The question of whether radiographic progression can be halted in patients treated with TNF blockers and its correlation to clinical response in routine clinical practice are therefore of particular relevance.

Although clinical trials are paramount for investigating the efficacy and safety of treatments in a controlled manner, real-world studies offer insight into outcomes of patients treated in daily practice who would not be selected for clinical trials due to strict inclusion and exclusion criteria [13, 14]. This non-interventional study assessed radiographic progression and disease activity in patients with RA or PsA treated with ETN for up to 36 months as part of routine outpatient care in German hospitals and private practices.

METHODS

Study Design

The PRospective Evaluation of The RADIOgraphic Efficacy of Etanercept in Patients With Rheumatoid Arthritis or Psoriatic Arthritis (PRERA) trial was a non-interventional, prospective, multicenter study (NCT01623752). Up to 10 visits took place during the two phases of the study: phase 1 comprised visit 1 at baseline and visits 2–7 every 3 months until month 18. Enrollment in phase 2 was optional and comprised visits 8–10 every 6 months until month 36. Mandatory radiographs of hands and feet were taken at baseline (\pm 3 months with respect to the start of ETN treatment), and optional radiographs were taken at months 12–18 (towards the end of phase 1) and/or at months 30–36 (towards the end of phase 2); if

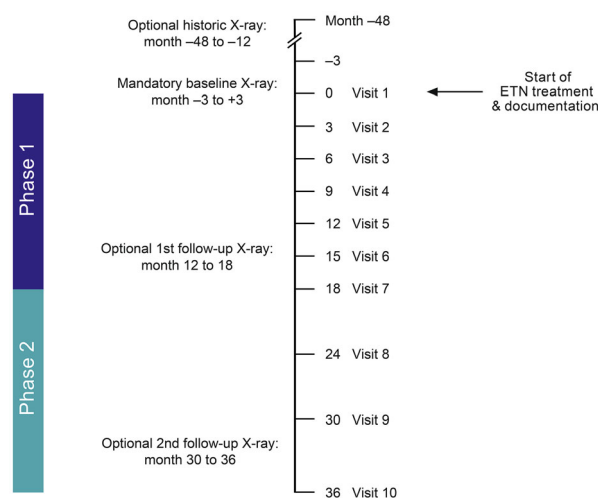


Fig. 1 Study design

available, historic radiographs taken 12–48 months prior to study start were also collected at baseline and assessed (Fig. 1).

Inclusion and Exclusion Criteria

Adult patients with a diagnosis of RA or PsA (confirmed by their rheumatologists) who were naïve to treatment with ETN, eligible for treatment with ETN according to the summary of product characteristics (SmPC), and for whom there were plain radiographs of hands and feet within 3 months prior to or after the initiation of treatment with ETN were included in the study. Patients who previously received ETN or any investigational drug within 3 months of study inclusion, or who were ineligible for ETN treatment according to the SmPC, were excluded from the study.

Effectiveness and Safety Endpoints

The primary effectiveness endpoint was the change (absolute and annualized) in van der Heijde modified total Sharp score for RA patients ($mTSS^{RA}$) [15] or van der Heijde modified total Sharp score adapted for PsA patients ($mTSS^{PsA}$) [16] as assessed by two blinded assessors (SW, RR). Radiographic non-progression was defined as a change in $mTSS^{RA/PsA}$ of < 0.5 .

Secondary efficacy parameters included the change in disease activity score in 28 joints (DAS28) [17]. The DAS28 included information from the Patient's Global Assessment, the number of swollen and tender joints as determined by the physician, and the laboratory values for erythrocyte sedimentation rate and/or C-reactive protein.

Additional secondary efficacy endpoints included the erosion score (ES) and joint space narrowing (JSN) score, separately. Patient-reported outcomes included the pain visual analog scale (VAS), the Hannover Functional Ability Questionnaire (FFbH) [18], comprising 18 questions on functional ability in activities of daily living, and the Euro Quality of Life-5 Dimensions (EQ-5D) [19], comprising health-related quality of life questions in which patients were asked if they have "extreme problems," "some problems," or "no problems" within five sub-categories: "mobility," "self-care," "usual activities," "pain/discomfort," and "anxiety/depression."

Safety endpoints included incidence of adverse events (AE) and serious adverse events (SAE). All AEs reported during the course of the study were collected and coded using version 17 of the Medical Dictionary for Regulatory Activities (MedDRA).

Statistical Analyses

Data were reported descriptively and presented as sample size, mean, or median values for continuous variables as appropriate, and as frequencies for categorical variables. A paired *t*-test was performed for the comparison of normalized radiographic progression. Missing data were generally not imputed; however, for mTSS calculations, missing scores for individual joints were imputed using the mean scores of the remaining joints for that patient, but only X-ray assessments that were performed were included in the analysis.

The relationship of risk factors and baseline disease characteristics (disease duration, concomitant or previous medication, including csDMARD and biologic DMARD [bDMARD] use, anti-citrullinated protein antibodies,

rheumatoid factor, baseline DAS28, and radiographic progression) were evaluated using either a linear regression model or an analysis of (co)variance model.

Ethical Conduct of the Study

The study was conducted in accordance with the Declaration of Helsinki and local legal and regulatory requirements. Written informed consent was obtained prior to patients entering the study (before the initiation of study-protocol-specified procedures) by the treating physician. The final observational plan, any amendments, and informed consent documentation were reviewed and approved by the Ethics Committee of the Berlin Chamber of Physicians, Germany.

Patient and Public Involvement Statement

The patients and the public were not involved in the design, conduct, reporting, or dissemination plans of the data obtained from the PRERA study.

RESULTS

Patient Disposition and Baseline Characteristics

Mean age among patients with RA and PsA was 58 and 52 years, respectively (Table 1), and the proportion of patients ≥ 65 years of age was 29% and 11%, respectively. Mean disease duration was 8.0 years in the RA group and 6.4 years in the PsA group. The vast majority of patients received systemic therapy for RA or PsA prior to starting ETN treatment (RA: 97%; PsA: 93%), with MTX being the most common treatment used in each group (RA: 88%; PsA: 87%).

Around half of the patients completed phase 1, and 20.5% and 25.9% of patients with RA and PsA, respectively, entered the optional phase 2. Supplementary Fig. 1 shows the number of patients with data recorded at each visit.

Overall, 36% of patients with RA and 39% of patients with PsA discontinued treatment with

Table 1 Patient demographics

	RA (<i>n</i> = 1378)	PsA (<i>n</i> = 440)	Total (<i>N</i> = 1821) ^a
Sex, <i>n</i> (%)			
Female	1062 (77.1)	259 (58.9)	1323 (72.7)
Age, years			
<i>n</i>	1372	436	1810
Mean ± SD	57.5 ± 12.7	51.5 ± 11.5	56.0 ± 12.7
BMI, kg/m ²			
<i>n</i>	1357	433	1791
Mean ± SD	27.3 ± 5.6	28.8 ± 5.7	27.7 ± 5.6
Duration of disease, years			
<i>n</i>	1365	431	1797
Mean ± SD	8.0 ± 8.7	6.4 ± 7.1	7.6 ± 8.4
ACPA			
<i>n</i>	978	241	n/a
ACPA positive, <i>n</i> (%)	634 (64.8)	13 (5.4)	n/a
RF			
<i>n</i>	1096	287	n/a
RF positive, <i>n</i> (%)	651 (59.4)	28 (9.8)	n/a
DAS28			
<i>n</i>	1014	327	n/a
Mean ± SD	4.63 ± 1.2	4.2 ± 1.1	n/a
mTSS			
<i>n</i>	504	166	n/a
Mean ± SD	25.1 ± 42.4	14.7 ± 25.7	n/a
FFbH			
<i>n</i>	1271	409	n/a
Mean ± SD	65.0 (22.7)	68.7 (22.1)	n/a
Pain, VAS total score, mm			
<i>n</i>	1074	356	n/a
Mean ± SD	55.9 ± 26.3	57.7 ± 25.1	n/a
Medication prior to starting ETN, ^b <i>n</i> (%)			
<i>n</i>	1375	440	1816
MTX	1212 (88.1)	382 (86.8)	1594 (87.8)

Table 1 continued

Total(<i>N</i> = 1821) ^a	RA (<i>n</i> = 1378)	PsA (<i>n</i> = 440)	
	Ciclosporin	48 (3.5)	42 (9.5)
90 (5.0)			
Sulfasalazine	388 (28.2)	105 (23.9)	493 (27.1)
Leflunomide	845 (61.5)	179 (40.7)	1024 (56.4)
Gold	82 (6.0)	5 (1.1)	87 (4.8)
Antimalarials	177 (12.9)	3 (0.7)	180 (9.9)
Other (azathioprine)	31 (2.3)	4 (0.9)	35 (1.9)
Biologic therapy ^c	338 (24.7)	113 (25.7)	452 (25.0)
Glucocorticoids ^d	1206 (88.3)	245 (56.8)	1451 (80.7)
Mean (SD) daily dose, mg	6.4 (4.5)	6.2 (4.4)	6.4 (4.5)
MTX use at visit 1/baseline, <i>n</i> (%)	558 (42.7)	159 (36.1)	747 (41.1)

ACPA anti-citrullinated protein antibody, *BMI* body mass index, *DAS28* disease activity score in 28 joints, *ETN* etanercept, *FFbH* Hannover Functional Ability Questionnaire, *MTX* methotrexate, *mTSS* modified total Sharp score, *n/a* not available, *RF* rheumatoid factor, *SD* standard deviation, *VAS* visual analog scale

^aIncludes three patients with an unconfirmed diagnosis

^bData represent the cumulative occurrence, so the total may be more than 100%

^c*n* = 1370 for RA, *n* = 439 for PsA, and *N* = 1811 for total

^d*n* = 1370 for RA, *n* = 439 for PsA, and *N* = 1811 for total

ETN before the end of the study. The main reasons for treatment discontinuation were lack of efficacy (RA: 20%; PsA: 22%) and AEs (RA: 10%; PsA: 10%) (Fig. 2). Patients who discontinued ETN treatment had similar baseline characteristics compared with those who continued ETN treatment (Supplementary Table 1).

Effectiveness

Mean *mTSS* remained stable across all subpopulations in both RA and PsA, and was consistently highest in patients who completed both phase 1 and 2 (Fig. 3A, B). Median change in *mTSS* was 0 during both phase 1 and phase 2 in both disease groups.

In both disease groups, the times between the baseline X-ray and the historic, first, and second follow-up X-rays varied considerably between individual patients. Therefore, annualized radiographic progression was calculated to facilitate comparison. Annualized

radiographic progression (*mTSS*, *ES*, and *JSN*) for patients with RA and PsA is shown in Fig. 4A, B, respectively. In general, mean annualized progression in *mTSS*, *ES*, and *JSN* before the start of ETN treatment was significantly higher than that during ETN treatment in phase 1 in patients with historic, baseline, and first follow-up X-rays in both disease groups. Cumulative annualized progression (*mTSS*) for patients with RA and PsA with historic, baseline, and first follow-up X-rays was lower during ETN treatment in phase 1 than before the start of ETN treatment (Fig. 4C, D). No statistical difference in annualized progression was seen between patients with RA receiving ETN monotherapy and those receiving ETN + MTX combination therapy (data on file).

In patients with historic, baseline, and first follow-up X-rays, the percentage of patients with radiographic non-progression was higher during ETN treatment in phase 1 compared

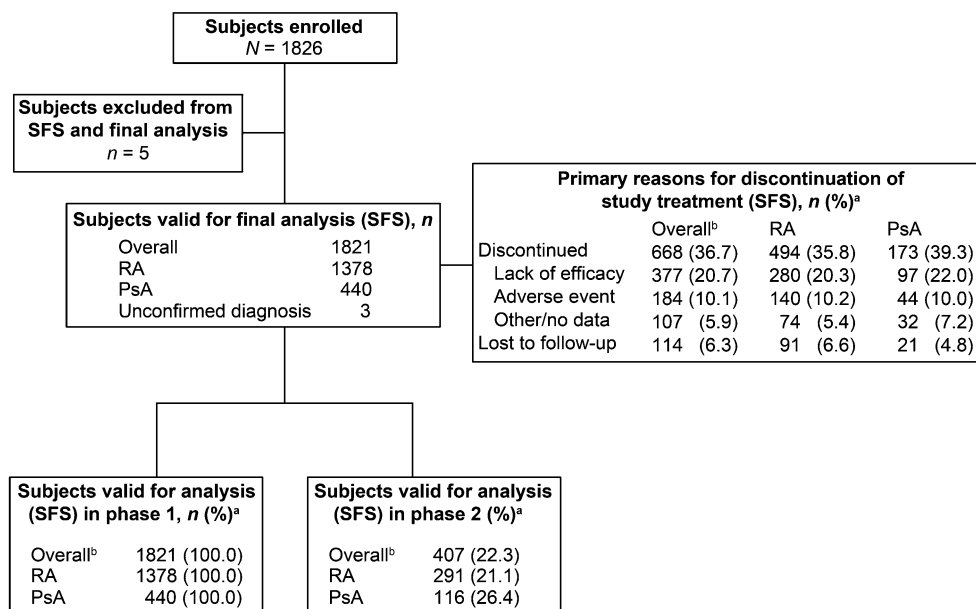


Fig. 2 Patient disposition

with pre-ETN treatment for both the RA and PsA groups (Fig. 5A, B).

DAS28 Response

Mean DAS28 decreased from baseline to the end of phase 2 in all patients and in all subpopulations for both RA and PsA groups (Fig. 6A, B). The proportion of patients in DAS28 remission (DAS28 < 2.6) increased steadily from baseline in both the RA (6–62%) and the PsA (10–65%) groups (Fig. 6C, D).

Patient-Reported Outcomes

Mean FFbH scores were 65% for patients with RA and 69% for patients with PsA at visit 1 (baseline) and increased to 73% and 75%, respectively, at month 18 (visit 7, end of phase 1) (Fig. 7A, B). Scores remained stable during phase 2. In the RA group, 27% of patients reported functional remission (FFbH scores of > 83%) at baseline (data on file), which increased to 45% by the end of phase 1. This proportion remained largely stable until the end of phase 2 (42%). In the PsA group, 30% of patients reported functional remission at

baseline, which increased to 48% by the end of phase 1. This proportion also remained stable until the end of phase 2 (48%).

In general, the proportion of patients reporting “no problems” increased across all EQ-5D dimensions until the end of phase 1 in both disease groups. This remained stable until the end of phase 2 (Fig. 7C, D). The number of patients with “extreme problems” in “pain/discomfort” declined from baseline until visit 7/month 18 (end of phase 1) in both disease groups (RA: 30–8%; PsA: 30–9%). Proportions remained largely stable until visit 10/month 36 (end of phase 2; RA: 7%; PsA: 11%). The greatest change was seen in the domain of “usual activities:” at visit 1, 26% of patients with RA and 28% of patients with PsA reported “no problems” with “usual activities,” but, by visit 2, 39% of patients with RA and 41% of patients with PsA had “no problems” with “usual activities.” Frequencies further increased until visit 7 (end of phase 1; RA: 51%; PsA: 54%) and remained stable until visit 10 (end of phase 2; RA: 53%; PsA: 58%).

Mean pain VAS at baseline was 56 mm and 58 mm for patients with RA and PsA, respectively, and decreased until the end of phase 1 to

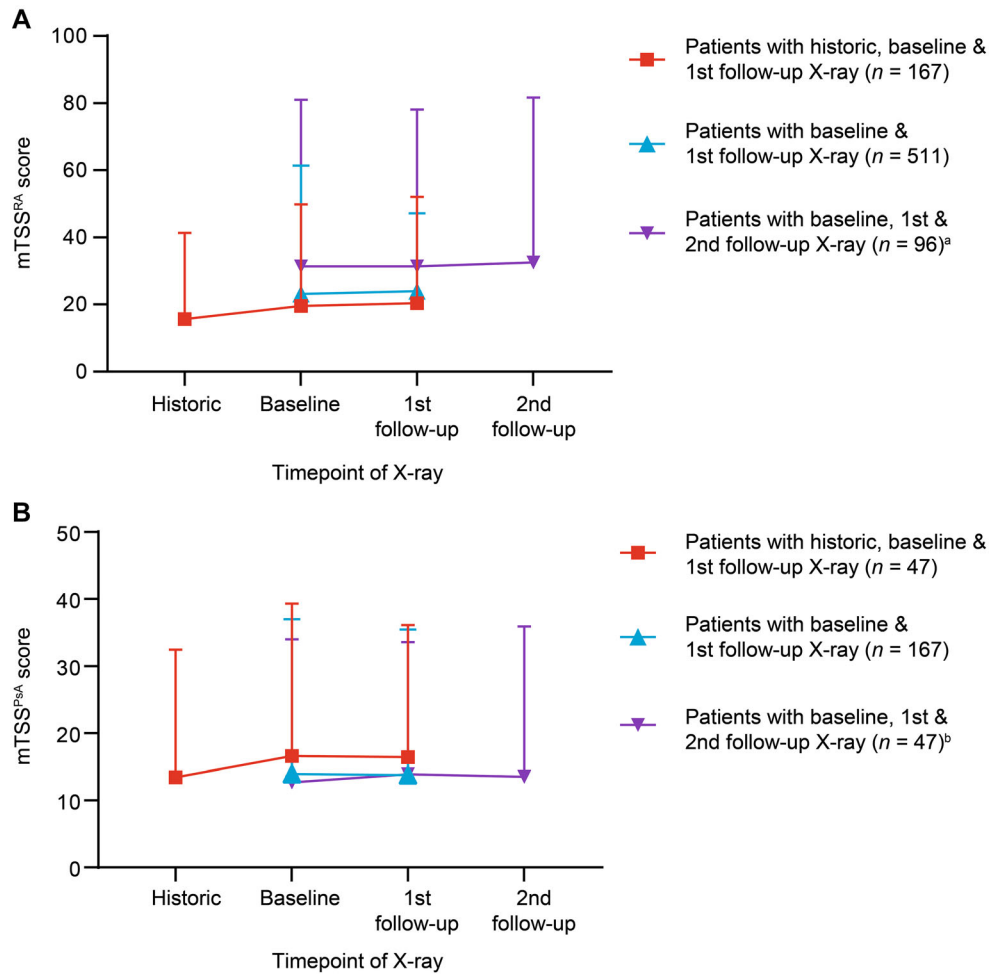


Fig. 3 Mean mTSS during the course of the study for different subpopulations: **A** RA and **B** PsA

32 mm in both disease groups (Fig. 7E, F). Pain VAS scores remained stable during phase 2.

Safety

A total of 48% and 43% of patients experienced AEs in the RA and PsA groups, respectively (Supplementary Table 2). General disorders and administration-site conditions (RA: 16%; PsA: 16%) and infections and infestations (RA: 16%; PsA 14%) were most common. Twelve percent of patients in the RA and PsA groups, respectively, experienced SAEs (Supplementary Table 3). Overall, 25.0% and 22.7% of patients, respectively, experienced treatment-related AEs, and 2.6% and 2.5%, respectively, experienced serious treatment-related AEs, none of which

resulted in death. Of the six deaths that occurred during the study, five were considered unrelated to the study drug by the investigator (causes of death: endocarditis, sepsis, malignant lung neoplasm, bronchial carcinoma, and myocardial infarction). For one death (cause of death unknown), the relationship to ETN was not determined.

DISCUSSION

This was the first real-world, prospective, non-interventional study evaluating radiographic progression before and during treatment with ETN in adult patients with RA and PsA. Treatment of patients with RA or PsA with ETN in

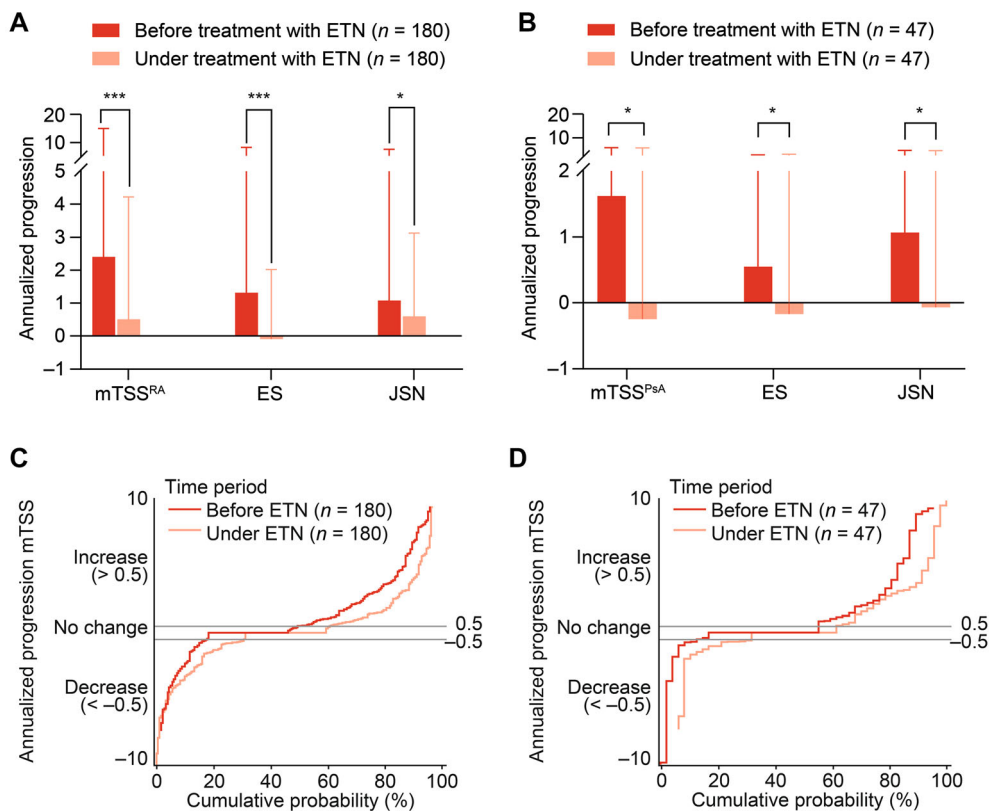


Fig. 4 Mean annualized radiographic progression in mTSS, ES, and JSN before and during ETN treatment in patients with **A** RA and **B** PsA with historic, baseline, and first follow-up X-rays, and cumulative probability plots

of progression in patients with **C** RA and **D** PsA with historic, baseline, and first follow-up X-rays

routine clinical practice in Germany resulted in an increasing proportion of patients with radiographic non-progression and with disease remission over a period of up to 36 months. In patients who had a historic X-ray available, annualized radiographic progression during the first 18 months (phase 1) of the study was significantly lower than during the pre-ETN treatment period in both RA and PsA. *P*-values for non-progression as measured by ES were highly significant ($p < 0.005$), indicating a slowing down in joint erosion during ETN treatment.

These findings are consistent with those from other observational studies which included historic X-rays. While one study from a Swiss longitudinal cohort from the Swiss Clinical Quality Management in Rheumatoid Arthritis (SCQM-RA) registry of patients with RA demonstrated a decrease in radiographic

progression once treatment was started, treatments included both chemical as well as biologic DMARDs [20]. However, in another study of patients with RA from the Danish Biologics Registry (DANBIO) who were treated with TNF- α inhibitors, significantly reduced radiographic progression was observed during treatment compared with the pre-treatment period: the median radiographic progression rate decreased from 0.7 total Sharp score units/year to 0 units/year ($p < 0.0001$) [21]. A British study of patients with PsA treated with TNF- α inhibitors showed that the median modified Sharp/van der Heijde score decreased from 8.5 to 2.1 per year [22].

In addition, several observational studies have shown that radiographic progression can slow down or halt during treatment with ETN and other bDMARDs compared with baseline

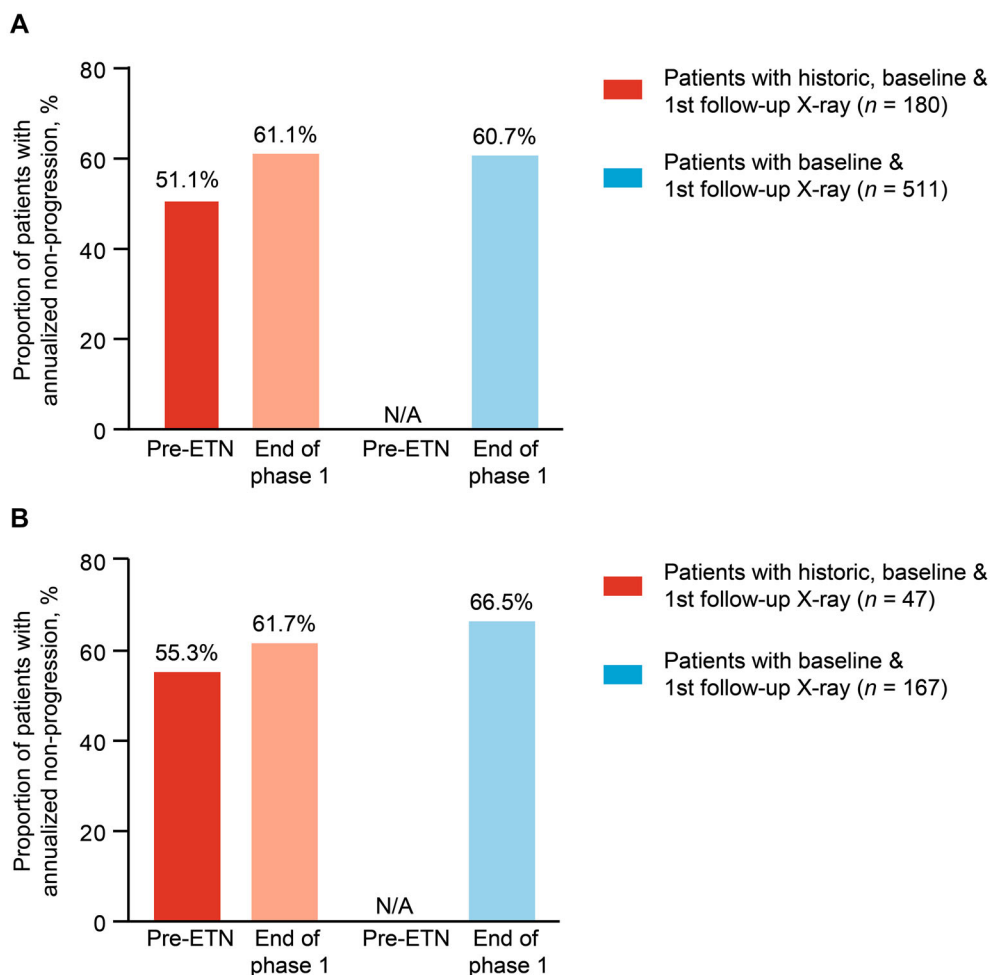


Fig. 5 Percentage of patients with historic, baseline, and first follow-up X-rays with radiographic non-progression: **A** RA and **B** PsA

scores. An earlier study of patients from the SCQM-RA registry showed that radiographic progression halted during treatment with rituximab (an anti-CD20 bDMARD) as well as anti-TNF- α inhibitors [23], as measured using the Ratingen erosion score [24]. In a Dutch study of patients with RA treated with the TNF- α inhibitor adalimumab, 53% and 42% of patients had no radiographic progression (as measured by the original Sharp/van der Heijde score [25]) after 1 and 2 years, respectively [26], compared with 61% after 18 months in this study.

Differences in the methodology used to rate radiographic progression, patient populations, and treatment regimens can make it difficult to compare results from different observational

trials. We would welcome the publishing of more data from observational studies, particularly of patients with PsA.

While data from observational trials cannot be compared directly to results from randomized clinical trials, data from the latter can inform real-life treatment practices. Overall, results from this non-interventional trial were similar to those observed in randomized clinical trials with TNF- α inhibitors and other bDMARDs and targeted synthetic DMARDs for the treatment of both RA and PsA [10, 27–49]. In patients with RA, treatment with ETN, infliximab, adalimumab, golimumab or certolizumab, abatacept, tocilizumab [40–42], sarilumab, rituximab, tofacitinib, baricitinib,

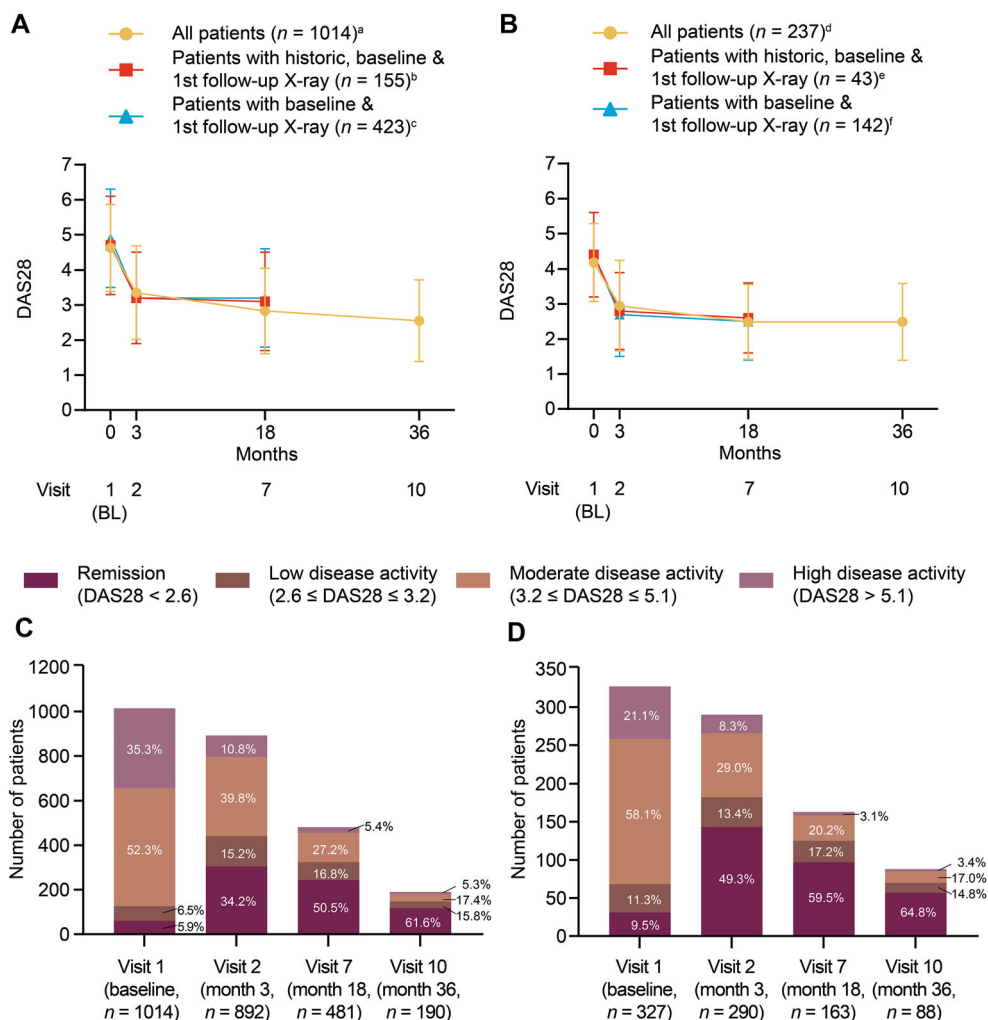


Fig. 6 Mean DAS28 during phase 1 and phase 2: **A** RA and **B** PsA; and the level of disease activity as measured by DAS28: **C** RA and **D** PsA

upadacitinib, or filgotinib reduced radiographic progression in addition to improving clinical outcomes compared to MTX. Similarly, ETN, infliximab, adalimumab, certolizumab, golimumab, and the JAK inhibitors tofacitinib and upadacitinib were proven to be superior to MTX or other csDMARDs in terms of radiographic progression and clinical outcomes in controlled trials in patients with PsA.

There is some evidence that combined treatment with ETN and MTX may be clinically more efficacious than treatment for RA with ETN alone [5, 6, 50]. In a Canadian open-label study of patients with RA, progression in joint space narrowing and ES was consistently higher

after 12 and 24 months for patients receiving ETN monotherapy compared with combination therapy [51]. In contrast, an analysis of factors that influenced radiographic progression in patients included in the DANBIO registry did not identify concomitant MTX therapy as being related to less progression [52]. In this study, we did not observe a statistically significant difference in annualized progression between patients with RA receiving ETN monotherapy and those receiving ETN + MTX combination therapy. This was consistent across subgroups and indicates that combination therapy does not necessarily provide better outcomes than monotherapy. As this was a non-interventional

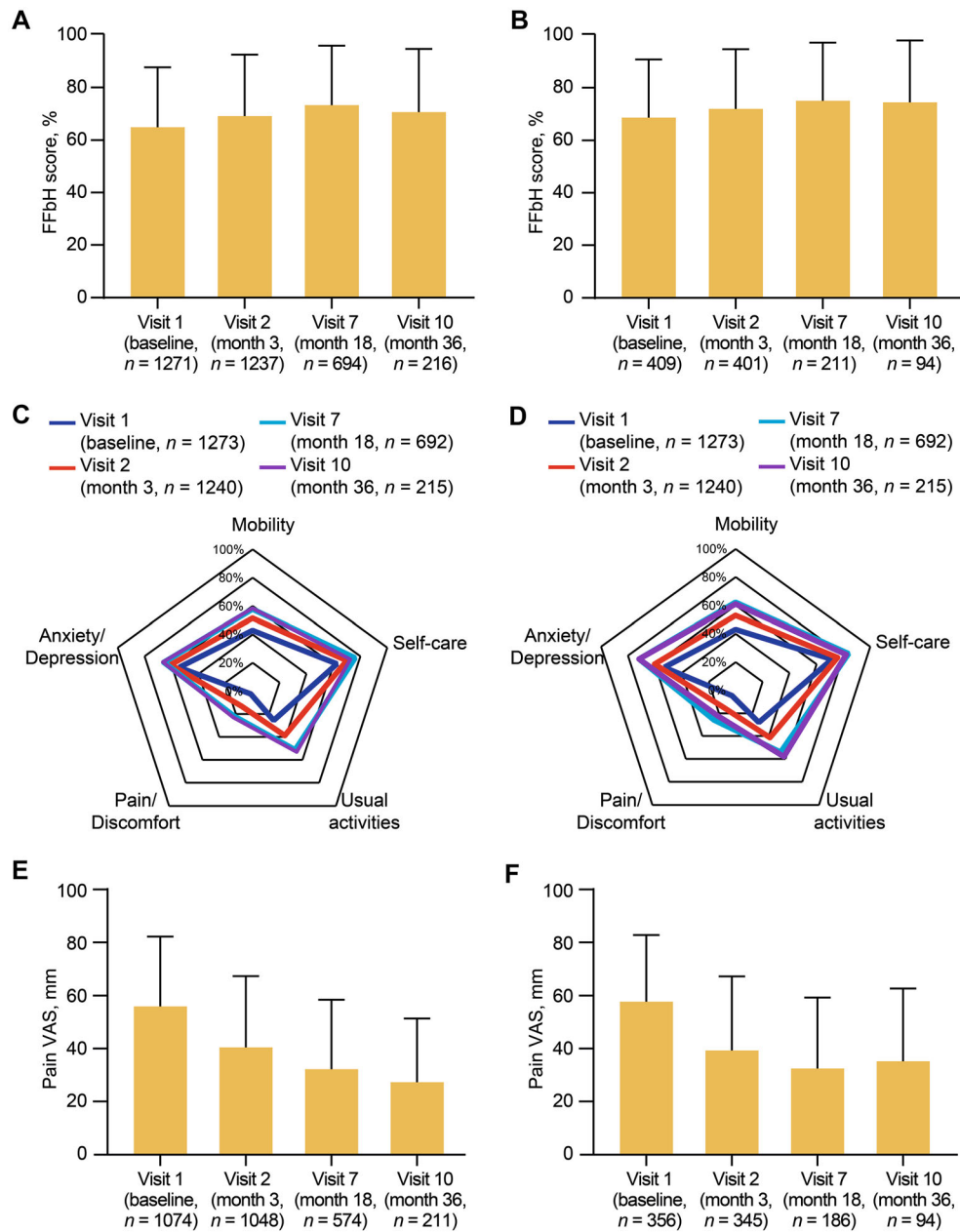


Fig. 7 FFbH scores reported by patients with **A** RA and **B** PsA; proportion of patients reporting “no problems” by EQ-5D dimension: **C** RA and **D** PsA; pain VAS scores reported by patients with **E** RA and **F** PsA

study, MTX therapy was prescribed at the discretion of the investigator, who may have opted for combination therapy in patients with a more complicated or refractory course of disease.

We also observed a steady increase in the percentage of patients with DAS28 remission. In addition, we observed improvements in patient-

reported outcomes, including increased quality of life (QoL) and functional status and reduced pain. Reducing radiographic progression and improving functional status can improve patients’ QoL as well as their ability to participate in everyday activities. Both should be considered when reviewing treatment outcomes.

Limitations of this study included the relatively low number of patients completing both phase 1 and 2; however, this was addressed by analyzing subpopulations within each disease population. The PRERA study initially comprised only phase 1; however, the enrollment period was extended to meet recruitment targets and phase 2 was added later. Study centers had to sign a separate contract and patients needed to sign an additional consent form to enter phase 2, which might explain the low number of patients entering phase 2. Long-term follow-up of patients in a non-investigational study (NIS) setting can be difficult, as demonstrated by the relatively low number of patients completing both phases. A further limitation of this NIS was that only baseline X-ray images were mandatory (and a requirement for study participation) while all other X-rays were voluntary, thereby explaining the lower number of follow-up X-rays. Conclusions regarding radiographic progression are therefore only valid for a smaller subgroup with available data. Missing data may have led to bias, with overestimation of results. Selection criteria for this study were relatively unconstricted, reflecting the variability of the “real world.” However, standardized measurements were taken to ensure the quality and integrity of the data. Regarding the inclusion criteria, the RA or PsA diagnosis was confirmed by the patients’ rheumatologists; however, almost 10% of the patients with PsA were RF positive, even though classification criteria require patients with PsA to be RF negative. As the frequency of RF-positive individuals in the general population increases with age reaching a proportion of around 10% at the age of 60, this finding may not indicate diagnostic mistakes by physicians; it may hint that our data better represent the whole spectrum of patients with PsA in the real world than interventional trials that impose strict classification criteria.

CONCLUSIONS

Overall, this study suggests that patients with RA and PsA treated with ETN in a real-world setting experience a slowing of radiographic

progression during treatment compared with the pre-treatment period. In patients with available radiographic data, a large proportion of the patients were treated with ETN for up to 3 years without radiographic progression. The treatment with ETN was well tolerated and no new safety signals were reported. Furthermore, disease activity was reduced during ETN treatment, and increased functional remission and improvements in patients’ QoL were observed.

DECLARATIONS

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Authors’ Contributions. All authors were involved in the writing and reviewing process and have read and approved this manuscript. Additional contributions to this body of work were as follows: Siegfried Wassenberg and Rolf Rau: conception/design of the study, acquisition and interpretation of data. Thilo Klopsch: acquisition of data. Anja Plenke, Jürgen Jobst, Thomas Meng, and Peter-Andreas Löschmann: conception/design of the study and interpretation of data. Pascal Klaus: interpretation of data.

List of Investigators. Please see full list of investigators in Supplementary Table 4.

Prior Presentation. Data included in this manuscript have partially been presented at congresses:

Wassenberg S, Rau R, Klopsch T, Plenske A, Jobst J, Klaus P, Meng T, Löschmann P-A. Effektivität von Etanercept auf die radiologische Progression bei erwachsenen Patienten mit Rheumatoider Arthritis oder Psoriasis-Arthritis (PRERA). Poster presented at the Congress of the German Society for Rheumatology (DGRh) 2019

Wassenberg S, Rau R, Klopsch T, Plenske A, Jobst J, Klaus P, Meng T, Löschmann P-A. Effectiveness of etanercept on radiographic progression in adult patients with rheumatoid arthritis or psoriatic arthritis: final results from a German non-interventional, prospective, multi-center study (PRERA). Poster presented at the Annual Meeting of the American College of Rheumatology 2019.

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Compliance with Ethics Guidelines. The final protocol and subject information and informed consent documentation were reviewed and approved by the Ethics Committee of the Berlin Chamber of Physicians, Germany. This study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients by the treating physician or a

designated person prior to patients entering the study.

Data Availability. Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions, and exceptions, Pfizer may also provide access to the related individual de-identified participant data. See <https://www.pfizer.com/science/clinical-trials/trial-data-and-results> for more information.

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