Simultaneous Response in Several Domains in Patients with Psoriatic Disease Treated with Etanercept as Monotherapy or in Combination with Conventional Synthetic Disease-modifying Antirheumatic Drugs

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ABSTRACT. ***Objective.*** To evaluate patients with psoriatic arthritis (PsA) receiving etanercept (ETN) monotherapy or ETN plus conventional synthetic disease-modifying antirheumatic drugs (csDMARD) to determine the proportion achieving a clinically meaningful response in arthritis, psoriasis, and quality of life simultaneously.

Methods. A prospective, multicenter, 52-week observational study in patients with active PsA evaluated treatment with ETN in clinical practice (ClinicalTrials.gov: NCT00293722). This analysis assessed simultaneous achievement of 3 treatment targets: low disease activity (LDA) based on 28-joint count Disease Activity Score (DAS28); body surface area (BSA) involvement ≤ 3%; and a score > 45 on the Medical Outcomes Study Short Form-12 (SF-12) physical component summary.

Results. Of 579 patients, 380 received ETN monotherapy and 199 received combination ETN plus csDMARD. At 52 weeks, data for all 3 disease domains were available for 251 patients receiving monotherapy and 151 receiving combination therapy. In the monotherapy and combination therapy groups, 61 (24.3%) and 37 (24.5%) patients, respectively, achieved all 3 treatment targets simultaneously. A significantly greater proportion of patients receiving monotherapy versus combination therapy achieved SF-12 > 45 (43.0% vs 31.8%; $p < 0.05$) and DAS28 LDA (72.5% vs 62.3%; $p < 0.05$). Conversely, BSA ≤ 3% was reached by a significantly greater proportion receiving combination therapy (75.5% vs 56.6%; $p < 0.001$). However, baseline BSA involvement was higher for the monotherapy group.

Conclusion. While nearly half the patients achieved arthritis and psoriasis treatment targets simultaneously and one-fourth reached all 3 treatment targets, combining ETN and csDMARD did not substantially improve clinical response compared with ETN monotherapy in this real-world PsA patient population. (First Release April 1 2018; J Rheumatol 2018;45:802–10; doi:10.3899/jrheum.170932)

Key Indexing Terms:
PSORIATIC ARTHRITIS MUSCULOSKELETAL DISEASE
DERMATOLOGY QUALITY OF LIFE ETANERCEPT

Psoriatic arthritis (PsA) is a chronic, progressive inflammatory musculoskeletal disease associated with cutaneous manifestations of psoriasis. Prevalence of inflammatory arthritis among patients with psoriasis has been estimated to vary from 6% to 42%, whereas in the general population it is as low as 2–3%[1].

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This study was funded by Pfizer. Medical writing support was provided by Samantha Forster and Jennica Lewis of Engage Scientific Solutions and was funded by Pfizer.

Dr. Behrens has received honoraria, speaker's fees, compensation for consultancies, board memberships, or study documentation from Pfizer, Abbvie, Chugai, Roche, UCB, Lilly, Celgene, MSD, Novartis, and Janssen-Cilag. Dr. Lorenz has received honoraria for talks and consultation from Pfizer. J. Jobst, Dr. Lippe, and Dr. Löschmann are employees of Pfizer.

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Accepted for publication December 27, 2017.

Clinical assessment and treatment of PsA is complex because of the multifaceted character of the disease. The core domains of skin and joint involvement are heterogeneous among patients but will overlap considerably to manifest in reductions in quality of life (QoL) and functional ability[2]. If left untreated, PsA can cause longterm joint damage and progressive disability[3]. Response to treatment with tumor necrosis factor inhibitors (anti-TNF) for the domains of arthritis, skin psoriasis, and QoL has been quantified in randomized clinical trials and observational studies[4,5,6,7,8]. However, limited information is available on what percentage of patients achieves significant improvement in all domains simultaneously[9]. The effectiveness of anti-TNF under real-world settings may differ from that observed in clinical trials for various reasons, such as poor adherence to treatment in daily practice[10] or the presence of medical conditions excluded in prospective clinical studies.

To our knowledge, no randomized controlled trial to date has been designed to compare the effect of concomitant conventional synthetic disease-modifying antirheumatic drugs (csDMARD) and anti-TNF therapy to anti-TNF monotherapy for PsA[11,12]. In this open observational trial, we investigated whether the addition of csDMARD to the anti-TNF etanercept (ETN) is beneficial in a real-world setting by comparing the outcomes of monotherapy versus combination therapy in patients with PsA. Among other factors, response in all disease domains is important for treatment success, treatment persistence, and patient satisfaction in PsA. The primary objective of this posthoc analysis was to assess the proportion and characteristics of patients with PsA who achieve treatment targets in arthritis, skin psoriasis, and QoL simultaneously. A secondary objective was to compare the efficacy of open-label ETN monotherapy versus ETN plus csDMARD combination therapy in patients with PsA.

MATERIALS AND METHODS

A large, prospective, noncontrolled, multicenter, observational study of patients with active PsA was conducted to assess the safety and efficacy of ETN in daily clinical practice (ClinicalTrials.gov identifier: NCT00293722). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and local regulations. According to local German law, ethics committee approval for a noninterventional, observational study was not required. The study enrolled patients aged ≥ 18 years who were receiving treatment with ETN at 251 rheumatology centers in Germany. All patients were under the care of a rheumatologist and treatment was chosen by the physician, based on clinical judgment. Patients received subcutaneous ETN 25 mg twice weekly or 50 mg once weekly, for up to 52 weeks, either as monotherapy or in combination with csDMARD. Dosages were permitted to change during the observation period.

In the full cohort, patients were required to have documentation for at least 5 of 7 visits during the 52-week observation period to be included in the ETN monotherapy or ETN plus csDMARD group. In this posthoc analysis, patients with documentation for at least 5 of 7 visits (inclusive of visit 1 and 7) were included in the efficacy population. In addition, the effect of concomitant use of csDMARD on treatment success was analyzed in all patients and in a subgroup with only peripheral joint disease.

We determined the proportion of patients who achieved treatment targets in 3 different disease domains simultaneously: arthritis, skin psoriasis, and QoL. These were measured using the 28-joint count Disease Activity Score (DAS28), body surface area (BSA) involvement, and the physical component summary of the Medical Outcomes Study Short Form-12 (SF-12), respectively. Treatment targets were established based on achieving a clinically meaningful response, defined as DAS28 low disease activity (LDA; DAS28 < 3.2), BSA ≤ 3%, and SF-12 > 45.

We also evaluated the proportion of patients who attained modified minimal disease activity (mMDA). This outcome measure required patients to meet 5 of 6 of the following criteria: tender joint count 0 or 1, swollen joint count 0 or 1, BSA ≤ 3%, patient pain visual analog scale (VAS) ≤ 15, patient disease activity VAS ≤ 20, and SF-12 > 45. Additionally, standard clinical and safety outcomes were assessed at baseline and at 6 visits over 52 weeks. Persistence with treatment over the study period was evaluated by asking patients at each visit if they were continuing with ETN therapy. If patients answered "no" during ≥ 1 visit, they were classified as nonpersistent.

Statistical analysis. Analyses of baseline demographics and proportions of responders at months 3, 6, and 12 were descriptive; p values were generated posthoc and should be considered descriptive. Summary statistics (arithmetic mean, SD, and percentiles) were generated for numerical data, and frequency statistics were generated for categorical data. Differences in baseline characteristics, clinical outcomes, and nonpersistence between treatment groups were analyzed posthoc using the chi-squared test. For estimation of treatment persistence, Kaplan–Meier analysis was used to estimate time to cessation of ETN treatment.

Observed case analysis was conducted to consider all values that were documented at a given visit. Differences from baseline were only calculated for patients with documentation of both a baseline value and the respective postbaseline value. For categorical variables, analyses with adjusted relative frequencies (i.e., without consideration of patients with missing values in the percentage base) were calculated, if deemed appropriate.

RESULTS

Patient and baseline characteristics. The safety and efficacy populations of the whole cohort comprised 1285 and 1282 patients, respectively, who were treated by rheumatologists. In this analysis, the efficacy population comprised 579 patients receiving ETN monotherapy or ETN plus csDMARD combination therapy who had sufficient documentation for at least 5 of 7 visits (inclusive of visits 1 and 7). Patients had axial and/or peripheral joint involvement. Of these 579 patients, 380 were treated with ETN monotherapy and 199 were treated with ETN plus csDMARD [primarily methotrexate (MTX)]. A total of 464 patients with peripheral arthritis and no axial involvement were included in the analysis; of these, 299 were treated with monotherapy and 165 with combination therapy.

Demographics and baseline disease characteristics are presented in Table 1. Demographics were similar across all cohorts, regardless of treatment group. A total of 212 (36.6%) of 579 patients had BSA involvement ≤ 3%; 345 patients (59.6%) had BSA > 3%, and 22 patients (3.8%) had no BSA information. The mean affected BSA was numerically smaller in the combination therapy group than in the monotherapy group (8.0% vs 12.2%, respectively). Palmoplantar psoriasis was present in a greater proportion of patients in the combination therapy group [n = 24 (12.1%)] than the monotherapy group [n = 20 (5.3%), p < 0.05]. For the musculoskeletal domains of PsA, baseline disease activity

Table 1. Demographics, baseline disease characteristics, and systemic therapies. Data are mean (SD) unless otherwise specified.

Variables	Safety Population, n = 1285	Posthoc Analysis, Efficacy Population*		
		Total Efficacy Population, n = 579	ETN Monotherapy, n = 380	ETN plus csDMARD, n = 199
Age, yrs	50.9 (11.4)	51.4 (11.5)	52.1 (11.5)	50.3 (11.4)
Males, n (%)	571 (44.6)	274 (47.5)	176 (46.6)	98 (49.2)
Weight, m/f, kg	88.8 (16.3) / 76.5 (16.7)	87.9 (15.7) / 77.3 (17.9)	87.6 (16.1) / 76.9 (17.7)	88.5 (15.2) / 78.2 (18.4)
Duration of PsA, yrs	7.3 (7.8)	7.4 (7.9)	7.7 (8.3)	6.8 (7.1)
DAS28	4.8 (1.4)†	4.9 (1.4)	5.0 (1.3)	4.7 (1.4)
Affected BSA, %	9.7 (15.9)†	10.7 (16.2)	12.2 (16.5)	8.0 (15.2)
TJC	8.2 (7.3)†	8.0 (6.8)	8.3 (6.9)	7.6 (6.7)
SJC	4.8 (5.4)†	5.1 (5.3)	5.4 (5.4)	4.5 (5.1)
Duration of psoriasis, yrs	16.6 (13.3)	17.8 (13.4)	18.2 (13.6)	17.0 (12.8)
Type of psoriasis‡, n (%)				
Plaque	718 (55.9)	361 (62.3)	241 (63.4)	120 (60.3)
Palmoplantar	95 (7.4)	44 (7.6)	20 (5.3)	24 (12.1)
Nail	485 (37.7)	234 (40.4)	154 (40.5)	80 (40.2)
Details available for nail psoriasis, n	1044	496	324	172
Only nail psoriasis	127 (12.2)	47 (9.5)	36 (11.1)	11 (6.4)
Both nail and other psoriasis	358 (34.3)	187 (37.7)	118 (36.4)	69 (40.1)
Only other psoriasis, no nail	559 (53.5)	262 (52.8)	170 (52.5)	92 (53.5)
PsA characteristics, n (%)				
Polyarticular symmetric	603 (46.9)	290 (50.1)	187 (49.2)	103 (51.8)
Polyarticular asymmetric	373 (29.0)	160 (27.6)	105 (27.6)	55 (27.6)
Oligoarticular	237 (18.4)	105 (18.1)	68 (17.9)	37 (18.6)
Mutilating arthritis	39 (3.0)	12 (2.1)	8 (2.1)	4 (2.0)
Enthesitis	163 (12.7)	77 (13.3)	50 (13.2)	27 (13.6)
Dactylitis	202 (15.7)	98 (16.9)	68 (17.9)	30 (15.1)
Sacroiliitis	135 (10.5)	58 (10.0)	41 (10.8)	22 (11.1)
Systemic therapies used prior to study start, n (%)				
Any systemic therapy	1219 (95.1)	543 (93.9)	347 (91.3)	196 (99.0)
Methotrexate	1136 (88.4)	508 (87.7)	317 (83.4)	191 (96.0)
Leflunomide	630 (49.0)	271 (46.8)	166 (43.7)	105 (52.8)
Infliximab	61 (4.7)	26 (4.5)	16 (4.2)	10 (5.0)
Adalimumab	287 (22.3)	118 (20.4)	82 (21.6)	36 (18.1)

* Patients attended 5 of 7 study visits, inclusive of visits 1 and 7. † Efficacy population, n = 1282. ‡ Multiple responses possible. ETN: etanercept; csDMARD: conventional synthetic disease-modifying antirheumatic drug; PsA: psoriatic arthritis; DAS28: 28-joint count Disease Activity Score; BSA: body surface area; TJC: tender joint count; SJC: swollen joint count.

was similar in both treatment groups. In a subpopulation of patients with peripheral arthritis only, demographics, baseline disease activity related to the joints, and use of systemic therapies prior to study start were similar (data not shown).

In the ETN monotherapy group, 317 patients (83.4%) had received MTX as previous systemic therapy for PsA, compared to 191 patients (96.0%) in the combination therapy group (Table 1). About ≤ 50% had received other systemic therapies at any time prior to study start.

Efficacy outcomes. At 52 weeks, data for all 3 treatment targets of DAS28 < 3.2, BSA ≤ 3%, and SF-12 > 45 were available for 402 patients: 251 patients receiving monotherapy and 151 receiving combination therapy. Over 52 weeks, 98 (24.4%) of the 402 patients achieved all 3 treatment targets simultaneously (Figure 1A). Achievement of this composite measure was similar regardless of treatment group: 24.3% and 24.5% of patients in the monotherapy and combination therapy groups, respectively (Figure 1B and Figure 1C). A significantly greater proportion of patients met the target of SF-12 > 45 in the monotherapy group [n = 108 (43.0%)] than in the combination therapy group [n = 48 (31.8%), p < 0.05]. Similarly, a greater proportion of patients in the monotherapy group met the target of DAS28 LDA [n = 182 (72.5%)] than in the combination therapy group [n = 94 (62.3%), p < 0.05]. Conversely, BSA ≤ 3% was achieved by a significantly greater proportion of patients in the combination therapy group [n = 114 (75.5%)] than the monotherapy group [n = 142 (56.6%), p < 0.001]. In the overall population with data for all 3 disease domains (n = 402), the percentage of patients reaching the treatment target was not considerably different when the more stringent goal of DAS28 remission (DAS28 < 2.6) was used in place of DAS28 LDA [85 (21.1%) vs 98 (24.4%) patients, respectively].

Of 579 patients, 495 had data available for the analysis of mMDA; 323 received ETN monotherapy and 172 received

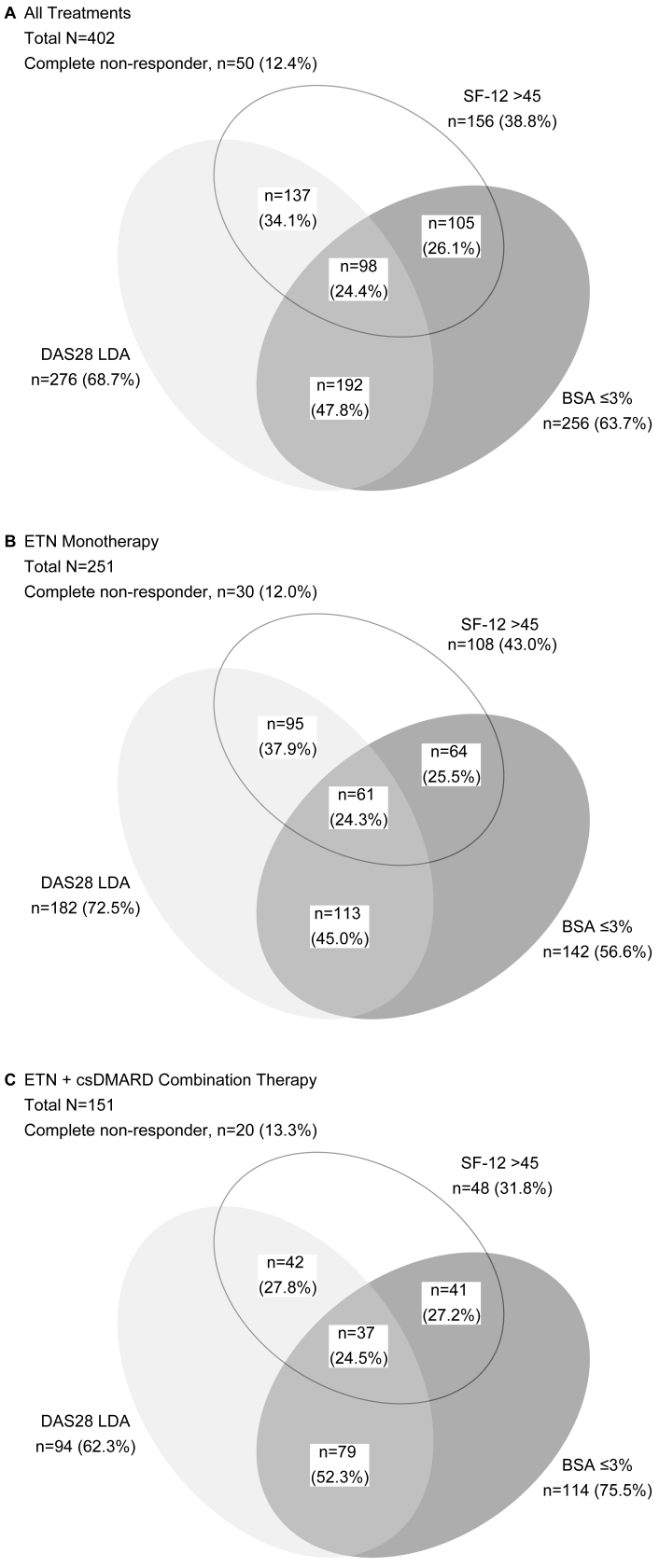

Figure 1. Venn diagram of patients who achieved or maintained at Week 52 the composite endpoints of DAS28 LDA (DAS28 < 3.2), BSA ≤ 3, and SF-12 > 45 for (A) all treatments, (B) ETN monotherapy, and (C) ETN plus csDMARD combination therapy. BSA: body surface area; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DAS28 LDA: 28-joint count Disease Activity Score low disease activity; ETN: etanercept; SF-12: Medical Outcomes Study Short Form-12 health survey physical component summary.

ETN plus csDMARD therapy. Similar proportions of patients attained mMDA in the monotherapy [n = 122 (37.8%)] and combination therapy groups [n = 60 (34.9%)].

Over 52 weeks, the overall improvements in BSA (Figure 2A), DAS28 (Figure 2B), and SF-12 (Figure 2C) were similar regardless of treatment group. No considerable difference in improvement in BSA, DAS28, or SF-12 was noted between patients with PsA overall versus patients with peripheral arthritis only (Supplementary Figure 1, available with the online version of this article). High rates (about 50%) of DAS28 remission were observed in all patients by Week 52, and remission rates were similar between ETN monotherapy and combination therapy groups at all timepoints (Supplementary Figure 2A, available with the online version of this article). No considerable difference in remission rates was noted between the full study population and the patients with exclusively peripheral arthritis (Supplementary Figure 2B).

Treatment persistence. Persistence data were available for 895 patients: 574 who received ETN monotherapy and 321 who received combination therapy. The percentage of patients persisting with treatment for the duration of the study was slightly higher in the monotherapy vs combination therapy group [n = 420 (73.2%) vs n = 216 (67.3%)]; the difference was not statistically significant. Across both groups, the most common reasons for stopping treatment were inadequate response or adverse events (AE; Table 2). A greater percentage of patients discontinued because of inadequate response in the combination therapy group (17.1% vs 11.7%, $p < 0.05$). In the combination therapy group, 25% of patients had stopped treatment at 260 days (95% CI 181–347) and in the monotherapy group, 25% of patients had stopped treatment at 360 days (95% CI 254–387; Figure 3).

Safety. The rate of AE was similar for the ETN monotherapy and combination therapy groups: 99/380 (26.1%) versus 71/199 (35.7%) patients, respectively (Table 3). AE potentially related to treatment occurred in 58 patients (15.3%) in the monotherapy group and 48 (24.1%) patients in the combination therapy group. Serious AE were reported in 17 (4.5%) and 15 (7.5%) patients, respectively. The AE profile in the exclusively peripheral arthritis population was comparable to the full analysis population (data not shown).

DISCUSSION

In this prospective observational study, patients with active PsA treated with ETN responded well in all 3 disease domains of musculoskeletal disease, skin disease, and QoL. However, only about one-fourth of patients achieved the treatment targets in all 3 domains simultaneously. No additional effect on clinical efficacy with concomitant csDMARD therapy was observed in this real-world, clinical practice setting, and this was also confirmed in the subgroup of patients with peripheral disease only. AE were comparable in both monotherapy and combination therapy groups. Concomitant use of csDMARD (primarily MTX) did not demonstrate any positive effect on drug adherence and treatment duration. Overall, persistence with treatment for the study duration was similar in both groups; a greater proportion of patients in the combination therapy group discontinued because of inadequate response. In both groups, the most common reasons for treatment discontinuation were inadequate response and AE.

ETN plus csDMARD treatment was not advantageous to ETN monotherapy. This finding is in agreement with results of a comparative effectiveness study of biologic monotherapy versus combination therapy in patients with PsA enrolled in the US-based COnsortium of Rheumatology Researchers Of North America (Corrona) registry[13], wherein patients experienced similar time to Clinical Disease Activity Index (CDAI) remission regardless of the treatment regimen. Although CDAI is a useful measure of disease activity, it focuses mainly on the rheumatic aspects of the disease. Optimal treatment of PsA requires the improvement of both skin and joint symptoms, as well as the attainment of acceptable QoL. Thus, our current study provides further support that concomitant csDMARD therapy may not be superior to ETN monotherapy, in any aspect of the disease. Interestingly, when csDMARD were added to ETN, the proportion of patients with improved BSA increased, but fewer patients experienced improvement in QoL. To optimize the outcome in patients with PsA, it is necessary to take into account not only objective measures of disease activity in the skin and joints but also patient QoL. As shown, an increase in drug treatment may optimize objective measures of disease activity, but it can impair QoL.

The proportion of patients with combined substantial improvement in skin symptoms, joint manifestations, and QoL observed in this real-world observational study was similar to that previously reported in a posthoc analysis of the Psoriasis Randomized Etanercept STudy in Subjects with Psoriatic Arthritis (PRESTA)[9], a randomized trial of ETN treatment in patients with psoriasis and comorbid PsA. The analysis found that 25.8–30.6% of patients in PRESTA achieved all 3 outcomes of Psoriasis Area and Severity Index (PASI) improvement > 75%, American College of Rheumatology (ACR) 50% improvement, and EQ-5D VAS > 82 at Week 24[9]. Although the use of different disease activity measures makes it difficult to directly compare our findings with those of the PRESTA trial, our study confirms that the benefits of ETN on all 3 disease domains are measurable in the real-world setting and not just in clinical trial settings.

Though treat-to-target or the accomplishment of minimal disease activity is not yet an established treatment goal for PsA, the principle is gaining impetus[14,15,16,17]. Several composite disease activity measures have been proposed[18,19,20]. A comparison of different disease activity indices applied in the real-world setting revealed that the classification of patients into disease activity levels differed and remission rates were index-specific[21]. Because there is

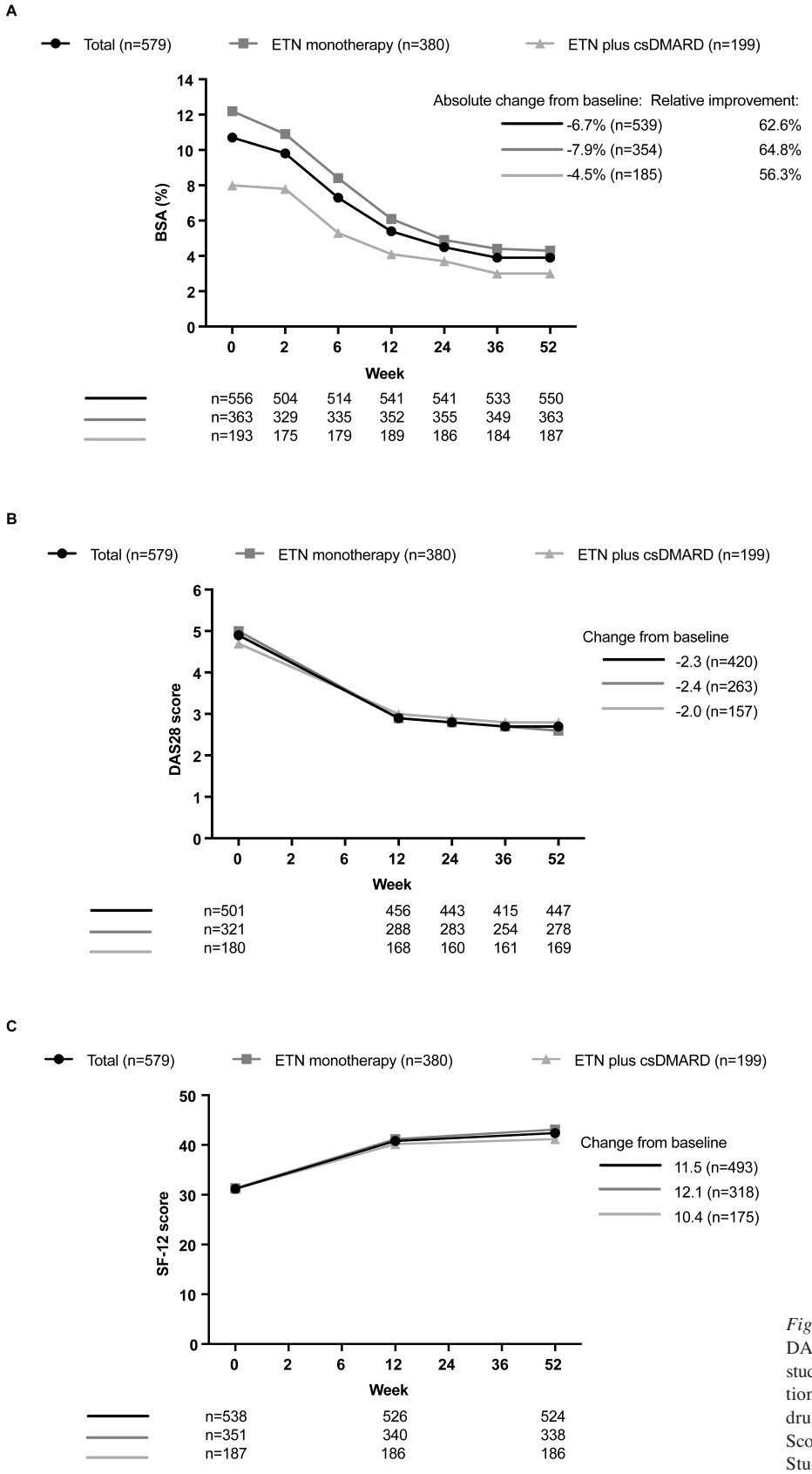

Figure 2. Improvement in (A) affected BSA, (B) DAS28 score, and (C) SF-12 over the course of the study. BSA: body surface area; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DAS28: 28-joint count Disease Activity Score; ETN: etanercept; SF-12: Medical Outcomes Study Short Form-12 health survey physical component summary.

Table 2. Reasons for nonpersistence. Values are n (%).

Variables	ETN Monotherapy, n = 574	ETN plus csDMARD, n = 321	p
Nonpersistent	154 (26.8)	105 (32.7)	0.06
Reason for nonpersistence			
Inadequate response	67 (11.7)	55 (17.1)	0.02
Adverse event	77 (13.4)	36 (11.2)	0.90
Other	19 (3.3)	18 (5.6)	0.10
Patient decision	7 (1.2)	7 (2.2)	
Good response/no disease activity	2 (0.3)	7 (2.2)	
Other	9 (1.6)	5 (1.6)	
Default*	8 (1.4)	7 (2.2)	

Multiple reasons are possible. * Patient answered "No" in ≥ 1 visit but did not provide a reason for nonpersistence. ETN: etanercept; csDMARD: conventional synthetic disease-modifying antirheumatic drug.

yet no consensus on the best measures to use to assess overall disease activity in PsA, we attempted to combine 3 easily applied measures of disease activity to assess the effect of ETN treatment in routine care. PASI75 is the benchmark for efficacy in clinical trials of psoriasis[22]; however, skin symptoms in the clinic are more often assessed using simpler measures, such as the percent BSA, which is why we selected it for our study. Similarly, the DAS28 for assessment of joint activity is more feasible for regular clinical use[23] than more complex measures such as the ACR criteria. The SF-12 has also been used to assess QoL in patients with PsA in tertiary care settings and has been suggested as a useful tool for assessing QoL in patients with psoriasis[24,25].

DAS28 remission is a commonly assessed goal in clinical trials of arthritis but in reality, patients in routine care may not meet the criteria for remission[26,27]. The inclusion of DAS28 LDA may thus be a more realistic goal for many patients. We therefore believe that our findings are clinically relevant and representative of patient outcomes in clinical

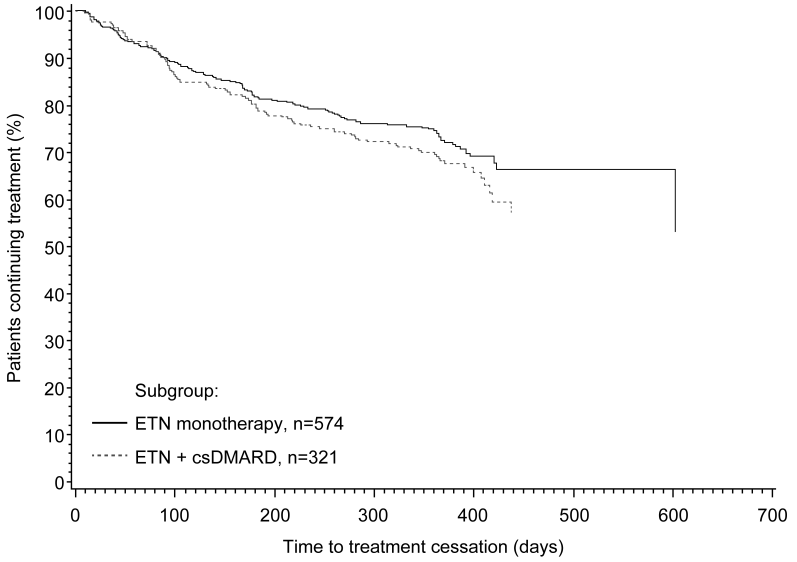

Figure 3. Time to treatment cessation. csDMARD: conventional synthetic disease-modifying antirheumatic drug; ETN: etanercept.

Table 3. Adverse events. Values are n (%).

AE	Safety Population, n = 1285	Efficacy Population* Total Efficacy Population, n = 579	ETN Monotherapy, n = 380	ETN plus csDMARD, n = 199
All AE	489 (38.1)	170 (29.4)	99 (26.1)	71 (35.7)
Potentially treatment-related AE	336 (26.1)	106 (18.3)	58 (15.3)	48 (24.1)
SAE	77 (6.0)	32 (5.5)	17 (4.5)	15 (7.5)
Potentially treatment-related SAE	31 (2.4)	11 (1.9)	5 (1.3)	6 (3.0)
AE leading to treatment withdrawal	192 (14.9)	36 (6.2)	26 (6.8)	10 (5.0)

* Patients attended 5 of 7 study visits, inclusive of visits 1 and 7. AE: adverse event; ETN: etanercept; csDMARD: conventional synthetic disease-modifying antirheumatic drug; SAE: serious AE.

practice. Nevertheless, in our study, the proportion of patients achieving the composite endpoint was similar when the more stringent target of DAS28 remission was used.

Discontinuation of biologics in rheumatic diseases can occur for a variety of reasons, including perceptions about the effectiveness and safety of the treatment[28,29]. Persistence rates in real-world studies can be lower than those reported in clinical trials[30]. We found that 73.2% and 67.3% of patients receiving ETN monotherapy or ETN plus csDMARD combination therapy, respectively, were still taking ETN after 52 weeks of treatment. These persistence rates are comparable to those reported by other studies[29,31]. In an analysis of treatment patterns in patients with PsA from a large US claims database, 60.7% of patients treated with ETN were persistent users for ≥ 12 months[32].

Data on the effect of concomitant use of an anti-TNF and a csDMARD on persistence rates in PsA are conflicting. In an Italian cohort, combination therapy was associated with a better persistence rate[31], whereas in the Corrona registry[13], persistence was similar in the combination therapy and monotherapy groups. In our study, persistence rates for ETN did not differ significantly between the patients receiving monotherapy and the patients receiving combination therapy. Another study that evaluated ETN reported that drug withdrawal because of inefficacy or toxicity was not significantly different in patients treated with ETN alone or in combination with MTX[33]. A double-blind, randomized controlled study of patients with PsA is ongoing to compare combination therapy with ETN plus MTX to ETN monotherapy and MTX monotherapy[34]. The results of that clinical trial will be of interest; however, the trial only includes MTX-naive patients.

Persistence results may differ depending on the particular anti-TNF agent and also on the length of followup. An analysis of the NORwegian-DMARD registry found that persistence with infliximab at 3 years was significantly greater in patients receiving concomitant MTX than in patients receiving monotherapy[12]. Conversely, in a large observational study, persistence with adalimumab at 2 years did not differ significantly between monotherapy and concomitant MTX therapy[35]. Regardless of concomitant treatment, there is agreement that common reasons for discontinuation include inadequate response to treatment and AE[31].

The safety profile of ETN as monotherapy or in combination with csDMARD was favorable, especially given the real-world characteristics of the data, rather than the highly selected patient populations participating in clinical trials. The incidence of AE and serious AE was similar to that previously reported in the PRESTA trial that evaluated ETN in the treatment of PsA[36].

Our current study has the inherent limitations of observational, nonrandomized studies, specifically selection or ascertainment bias and the existence of confounding factors. As with any observed case analysis, there is a potential risk of bias because of missing outcome data. Additionally, this analysis used DAS28 as the measurement of arthritis disease activity. The DAS28 only records disease activity in 28 joints, and although this is acceptable in rheumatoid arthritis, it may be considered a limitation in PsA because disease in other joints may be missed. In polyarticular PsA, measuring change using DAS28 is effective; however, values for LDA and remission have not been validated. Nevertheless, our study provides insight into the response to ETN treatment in a real-world setting and provides evidence for the successful use of ETN monotherapy.

We found that about one-fourth of patients with PsA achieved treatment targets in arthritis, skin psoriasis, and QoL simultaneously. Additionally, treatment with ETN plus csDMARD offered no clinical advantage over ETN monotherapy in this real-world clinical population. Persistence with ETN therapy was similar when used as monotherapy or in combination with csDMARD. In addition, the safety profile of each treatment regimen was similar to that observed for ETN in previous clinical trials.

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