Real-world treatment patterns, patient-reported outcomes, and effectiveness of flexible-dosing etanercept in patients with plaque psoriasis in Greece

Dimitris Rigopoulos,[1] Aikaterini Patsatsi,[2] Christina Antoniou,[1] Dimitrios Sotiriadis,[3] Angeliki Roussaki-Schulze,[4] Nadia Boubouchairopoulou,[5] Ioannis Skiadas,[5] Vasillios Tsekouras,[6] Ana Cristina Hernandez Daly[5]

[1]University of Athens Medical School, Athens, Greece; [2]Papageorgiou General Hospital, Thessaloniki, Greece; [3]Aristotle University of Thessaloniki, Thessaloniki, Greece; [4]University of Thessaly and University Hospital of Larissa, Larissa, Greece; [5]Pfizer Hellas, Athens, Greece; [6]Pfizer Hellas, Cyprus Branch, Nicosia, Cyprus

Abstract

Etanercept is approved for continuous or intermittent use and flexible dosing in plaque psoriasis (PsO). The objectives of this study were to investigate real-world treatment patterns with etanercept in Greek adults with moderate-to-severe PsO. This non-interventional multicenter study included a retrospective-to-prospective (RP) cohort, previously treated with etanercept for ≥24 months and followed for an additional 6 months, and a biologic-naïve, prospective-only (PO) cohort, followed for 6 months after treatment initiation. Parameters assessed included Psoriasis Area and Severity Index (PASI), percentage of body surface area (BSA) affected, Dermatology Life Quality Index (DLQI), and adverse events (AEs). This study enrolled 123 patients (RP, n = 56; PO, n = 67), who mostly adhered to continuous treatment (RP, 68%; PO, 95%). The two cohorts had similar mean baseline-to-endpoint decreases in PASI (-9.5 *vs* -10.1) and BSA (-11.9 *vs* -12.3). The PO-CTP population had a mean DLQI baseline-to-endpoint score decrease of -5.8, which was statistically significant and clinically meaningful. Treatment-emergent AE rates were 58.9% (RP) *versus* 26.9% (PO). These real-world data suggest a similar effectiveness of continuous and intermittent etanercept treatment in Greek patients with PsO.

Introduction

Long-term management of moderate-to-severe plaque psoriasis (PsO) usually requires phototherapy and/or systemic treatments, which can include biologics.[1] Flexible treatment regimens are of interest, as environmental factors (*e.g.*, positive effects of sunlight and exacerbations in winter and times of stress) can affect PsO.[2]

In July 2009, etanercept (ETN) became the only biologic approved for PsO with an indication for both continuous and intermittent use,[3] and it can be used in both pediatric[4] and adult[5] patients. ETN also has a flexible-dosing option, with dosage adjusted according to patients' preferences. Patients are routinely prescribed 25 mg twice weekly (BIW), 50 mg once weekly (QW), or 50 mg BIW for the first 12 weeks of treatment, followed by 25 mg BIW or 50 mg QW thereafter. When treatment is interrupted and later re-started, dosing is resumed at 25 mg BIW or 50 mg QW.[3] Intermittent ETN dosing has been shown to be effective and well tolerated in patients with PsO.[6] In clinical trials, intermittent use of ETN was not associated with loss of efficacy upon re-starting treatment[5,7-10] and did not adversely affect improvements in patient-reported outcomes (PROs).[11,12] Both continuous and intermittent ETN therapy are well-tolerated long-term[13] and result in improvements of secondary disease manifestations, such as joint pain and nail psoriasis.[14] Real-world studies have also demonstrated the effectiveness and safety of intermittent treatment with ETN in patients with PsO.[15-20]

A 2010 epidemiological study of PsO in Greece found significantly lower rates of disease exacerbation during the summer, when sun exposure could alleviate the symptoms,[21] that Greek patients with PsO could take advantage of flexible ETN treatment (i.e., discontinue treatment in the summer). However, data from Greece on the impact of flexible ETN dosing on PsO are very limited. Such data would be of interest to both patients and physicians.

This study was designed to investigate real-world ETN treatment patterns among adult patients with PsO in Greece.

Materials and methods

This study was performed in accordance with the Declaration of Helsinki and was approved by the Institutional Review Boards at each study site: Hospital of Venereal and Skin Disease "Andreas Syggros" 5, Ionos Dragoumi str, Athens PC

Correspondence: Aikaterini Patsatsi, Papageorgiou General Hospital, Ring Road, N. Efkarpia, 56403 Thessaloniki, Greece.
Tel.: + 302310991583. E-mail: apatsats@auth.gr

Key words: Etanercept, Greece, psoriasis, real-world evidence.

Acknowledgments: The authors would like to thank all study investigators and patients who participated in this study. The authors would also like to thank Maria Angelina Dilleen of Pfizer (United Kingdom) for statistical support and for substantial contributions to manuscript development. Medical writing support was provided by Lorna Forse, PhD, of Engage Scientific Solutions, and was funded by Pfizer.

Contributions: All authors made substantial contributions to the conception/design of the work or the acquisition, analysis, or interpretation of data, revised the manuscript critically for important intellectual content, and approved the final version. All authors agree to be accountable for all aspects of the work in this manuscript.

Conflicts of interest/competing interests: Christina Antoniou has no conflicts to declare. Aikaterini Patsatsi has received consulting fees/honoraria from Leo, AbbVie, Janssen, Novartis, Lilly, UCB, and Genesis Pharma; has participated in speakers' bureau/advisory boards for Leo Pharma, UCB, Janssen, and Genesis Pharma. Dimitris Rigopoulos has received grants from Leo Pharma, AbbVie, Janssen, Novartis, and Sanofi; has received consulting fees/honoraria from Leo Pharma, AbbVie, Janssen, Novartis, Sanofi, Galderma, and Genesis Pharma; has participated in speakers' bureau/advisory boards for Leo Pharma, AbbVie, Janssen, Novartis, Sanofi, Galderma, and Genesis Pharma; and has conducted clinical trials for Lilly, Genesis Pharma, and AbbVie. Angeliki Roussaki-Schulze has conducted clinical trials for Lilly, Genesis Pharma, and AbbVie. Dimitrios Sotiriadis has conducted clinical trials for IQVIA RDS Eastern Holdings GmbH, PAREXEL International GmbH, Abbott Laboratories, AbbVie, Janssen Cilag, Merck Sharp & Dohme, Novartis, Johnson & Johnson, Leo Pharma, and Qualitis Clinical Research & Medical Consulting. Nadia Boubouchairopoulou, Ioannis Skiadas, and Vasillios Tsekouras are employees of Pfizer and may own company stock. Ana Cristina Hernandez Daly was an employee of Pfizer at the time the study was conducted and may own company stock.

Funding: This study was funded by Pfizer.

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 anonymized participant data. See https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.

Ethics approval: This study was performed in accordance with the Declaration of Helsinki and was approved by the Institutional Review Boards at each study site: Hospital of Venereal and Skin Disease "Andreas Syggros" 5, Ionos Dragoumi str, Athens PC 16121 (reference number 968); Thessaloniki Hospital of Venereal and Skin Disease, 124 Delfon str, Thessaloniki, PC 54643 (202d con/411 [5d con135o sub]); University General Hospital "Attiko", 1 Rimini str, Haidari PC 12462 (14d con); General Hospital of Athens "Evaggelismos" 45-47 Ypsilantou str, PC 10676 Athens (23769); University General Hospital of Larisa Mezourlo, PC 41110 Larisa (18997); 401 General Military Hospital of Athens 138, Mesogeion Avenue and Katechaki, PC 11525, Athens (3). Informed consent was obtained prior to any study-related procedures.

Consent to participate: Patients in this study were enrolled after providing informed consent.

Received for publication: 14 May 2021.
Accepted for publication: 11 January 2022.

Dermatology Reports 2022; 14:9265
doi:10.4081/dr.2022.9265

16121 (reference number 968); Thessaloniki Hospital of Venereal and Skin Disease, 124 Delfon str, Thessaloniki, PC 54643 (202[d] con/411 [5[d] con135[o] sub]); University General Hospital "Attiko", 1 Rimini str, Haidari PC 12462 (14[d] con); General Hospital of Athens "Evaggelismos" 45-47 Ypsilantou str, PC 10676 Athens (23769); University General Hospital of Larisa Mezourlo, PC 41110 Larisa (18997); 401 General Military Hospital of Athens 138, Mesogeion Avenue and Katechaki, PC 11525, Athens (3). Informed consent was obtained prior to any study-related procedures.

Patient eligibility and study design

This was a non-interventional, multicenter cohort study of ETN-treated patients with moderate-to-severe PsO in Greece, conducted in a real-world setting of eight major outpatient dermatology clinics. The study included a retrospective portion, intended to capture long-term treatment utilization data, and a prospective portion, designed to collect information on quality of life (QoL) and patient-reported outcomes unlikely to be captured in pre-existing patient files (Figure 1).

To participate in the study, adult patients (aged ≥18 years) were eligible for ETN treatment and willing and able to inject ETN. Key exclusion criteria were pregnancy, breastfeeding, and treatment with an experimental drug or another biologic agent while receiving ETN. Patients were prescribed ETN at the discretion of their healthcare provider (HCP) according to the approved ETN summary of product characteristics (SmPC) and as per usual clinical practice. Any decision to prescribe ETN was made independently of this study and prior to patient enrollment. Patients were enrolled after providing informed consent.

Patients could be included in the retrospective-to-prospective (RP) or the prospective-only (PO) cohort. Patients were eligible for inclusion in the RP cohort if they were being treated with ETN at the time of study initiation, had been treated with ETN for ≥24 months (continuously or intermittently), and had medical records available on file. Patients were eligible for inclusion in the PO cohort if they were biologic-naïve, and if the decision to initiate treatment with ETN had already been taken. Treatment in the PO cohort was initiated at study baseline. Patients in both cohorts were followed prospectively for 6 months after study baseline (Figure 1).

Within each cohort, patients were further categorized into those receiving continuous (CTP) or intermittent treatment pattern (ITP), depending on the duration of ETN discontinuation during the study period (CTP, 15-29 days; ITP, ≥30 days). Discontinuation due to an adverse event (AE) for ≥30 days in duration was considered temporary.

Study objectives

The primary objective was to describe real-life treatment patterns for adult patients with PsO in Greece receiving continuous or intermittent ETN treatment in a flexible-dosing environment, where HCPs can discontinue a patient's treatment based on their symptoms. Secondary objectives were to capture baseline demographic and disease-related characteristics of Greek patients, to assess clinical parameters (Psoriasis Area Severity Index [PASI] and body surface area [BSA]), and to investigate the impact of short-term ETN treatment (6 months) on patients' QoL using the Dermatology Life Quality Index (DLQI) questionnaire.

Data collection

Patient data were collected from July 16th 2009, following the addition of the intermittent treatment option in the ETN SmPC, to December 2015. Retrospective data were collected at ETN initiation, at every dosing change, or at least every 6 months for ≥2 years, meaning that the timing of visits varied between patients in the retrospective part of this study (Figure 1). The desirable minimum number of retrospective visits was four. Demographic data were collected at study baseline (Visit n for the RP cohort/Visit 1 for the PO cohort). Prospective data were collected at three pre-specified time points: week 0 (Visit n for the RP cohort/Visit 1 for the PO cohort), week 12, and week 24.

Statistical methodology

The full analysis set (FAS) consisted of patients in the RP cohort who had been treated with ETN for ≥24 months before study baseline, had data available for ≥4 retrospective visits, and had ≥1 prospective visit post-baseline, as well as patients in the PO cohort who had been treated with ≥1 dose of ETN and had data available for ≥1 study visit post-baseline. The safety analysis set consisted of all patients who had been treated with ≥1 dose of ETN during the study, regardless of cohort. Owing to the different time periods over which data were available for collection, no direct comparisons could be made between the RP and PO cohorts, with the exception of initial disease characteristics. Within each cohort and population, parameters assessed included clinical measures (PASI and BSA), PROs (DLQI), and safety (AEs), provided sufficient data were available to allow for meaningful assessments. Descriptive statistics were summarized for all outcomes. *P*-values for differences between demographic and baseline clinical characteristics were calculated using a *t*-test for continuous variables and chi-squared test for categorical variables. Changes from the start of treatment in PASI, BSA, and DLQI to pre-specified study visits were assessed using the paired *t*-test. Missing baseline values were imputed using values prior to the baseline visit within 4 weeks for the RP cohort. There was no adjustment for multiple hypothesis testing. Missing values for any other visits were not imputed. For the DLQI, a sample size of 30 patients was calculated as sufficient, assuming 90% power and 20% dropout rate, to detect a statistically significant difference (assuming a meaningful clinical difference in overall DLQI score of 5 points from initial visit to study end).

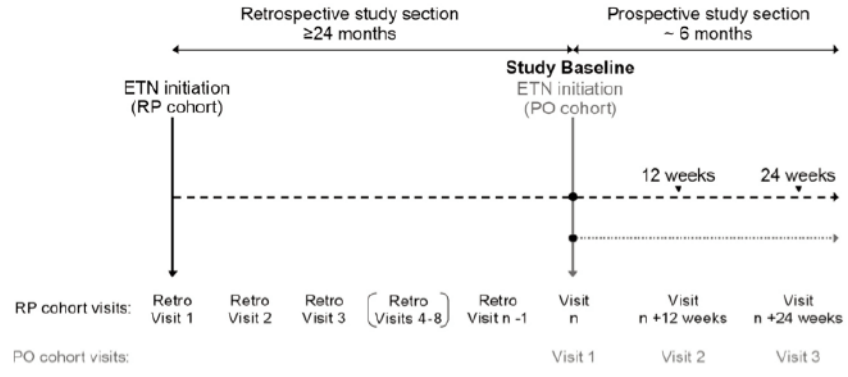

Figure 1. Study design.

Results

Demographics and baseline clinical characteristics

Overall, 123 patients were enrolled (SAS; RP, n=56; PO, n=67; Table 1). Initial PASI, BSA, and DLQI scores were documented at the start of ETN treatment (Retro Visit 1 the RP cohort; Visit 1 for the PO cohort) (Figure 1). Scores were not available for all patients in the RP cohort as these data were collected retrospectively. At the time of ETN initiation, there were no significant between-cohort differences in clinical measures. However, patients in the RP cohort were older (mean ± standard deviation [SD]: 50.8±12.1 years) than those in the PO cohort (45.1±13.9 years; p=0.020). At study baseline, mean ± SD ages were 55.8±12.2 years and 45.1±13.9 years, respectively (p<0.001; Table 1).

Treatment patterns

Of the 123 patients in the SAS, 120 (RP, n=56; PO, n=64) were included in the FAS. Most patients in both the RP (68% [n=38]) and PO (95% [n=61]) cohorts received continuous treatment (CTP population). Only 3 patients in the PO cohort were in the ITP population, limiting the ability to draw conclusions about intermittent *vs* continuous dosing in that cohort. In the RP cohort, most patients (45/56 [80%]) changed their weekly ETN dose at Retro Visit 2: 9 (16%) with a dose increase and 36 (64%) with a dose decrease. Relatively fewer patients changed their dose at Retro Visit 3 (11% and 13% with dose increases and decreases, respectively), and this proportion generally declined further with each subsequent visit. A similar pattern was observed for both the CTP and ITP populations. A five-fold higher proportion of patients in the ITP population had an ETN dose increase compared with the CTP population (78% [n=14] *vs* 16% [n=6], respectively), and time to dose increase was half that of the CTP population (62 *vs* 121 weeks, respectively) (Table 2).

The proportions of patients in the RP cohort who received >50 mg ETN weekly were similar for the CTP and ITP populations at Retro Visit 1 (79% *vs* 89%, respectively). This decreased immediately for the CTP population, with only 5% of patients at Retro Visit 2 and <10% of patients at Retro Visits 3 and 4 receiving that dosage. In the ITP population, the proportion of patients receiving >50 mg/week ETN dropped to 50% at Retro Visit 2 and reached 44% at Retro Visit 4. The number of patients with available data decreased steadily over the remaining retrospective visits (to n=3 at Retro Visit 9), making further proportion assessments unreliable. At the first prospec-

Table 1. Patient and disease characteristics 1) at ETN initiation, 2) at study baseline, or 3) throughout study (SAS).

	RP cohort (SAS) N=56	PO cohort (SAS) N=67	p-value*
At ETN initiation	**Retro visit 1**	**Visit 1**	
Age, years, mean±SD	50.8±12.1	45.1±13.9	*0.020*
Initial PASI score, mean±SD	13.5±9.2 n=30	15.0±10.6	0.502
Initial BSA score, %, mean±SD	14.0±9.5 n=11	15.8±14.4	0.693
Initial DLQI score, mean±SD	10.0±6.8 n=4	9.9±6.7	0.966
At study baseline	**Visit n**	**Visit 1**	
Age, years, mean±SD	55.8±12.2	45.1±13.9	*<0.001*
Men, n (%)	42 (75.0)	44 (65.7)	0.261
BMI, kg/m², mean±SD	28.2±4.1	30.1±6.2	*0.049*
Time since PsO diagnosis, years, mean±SD	16.9±12.1	14.0±11.1	0.176
Previous PsO treatment, n (%)			
Topical steroid	43 (76.8)	60 (89.6)	0.056
Cyclosporine	37 (66.1)	44 (65.7)	0.963
Vitamin D analogs	27 (48.2)	35 (52.2)	0.657
Methotrexate	21 (37.5)	25 (37.3)	0.983
Acitretin	12 (21.4)	9 (13.4)	0.241
Comorbidities, current, n (%)			
Hypertension	18 (32.1)	20 (29.9)	0.784
PsA	17 (30.4)	10 (14.9)	*0.039*
Hyperlipidemia	12 (21.4)	6 (9.0)	0.051
Diabetes mellitus	8 (14.3)	9 (13.4)	0.891
Dislipidemia	1 (1.8)	7 (10.4)	0.052
Latent tuberculosis	3 (5.4)	4 (6.0)	0.884
Throughout study	**All visits**	**All visits**	
Concomitant medication used, n (%)	47 (83.9)	42 (62.7)	
Methotrexate	18 (32.1)	12 (17.9)	0.067
Isoniazid	12 (21.4)	10 (14.9)	0.349
Folic acid	13 (23.2)	8 (11.9)	0.098
Cyclosporine	5 (8.9)	7 (10.4)	0.777
Metformin	6 (10.7)	6 (9.0)	0.743

*p-values were not calculated for characteristics collected at study baseline or throughout the study, as the populations were not comparable (RP – ETN treatment for ≥24 months, PO – biologic-naïve). For the RP cohort, not all clinical/QoL data from time of ETN initiation were available for all patients. Study baseline was Visit n (for the RP cohort) / Visit 1 (for the PO cohort). BMI body mass index, BSA body surface area, DLQI, Dermatology Quality of Life Index, ETN etanercept, PASI Psoriasis Area and Severity Index, PO prospective only, SAS safety analysis set, RP retrospective-to-prospective, SD standard deviation.

tive evaluation (Visit 1), among 56 patients overall with available data, no patients in the CTP population and 11% of patients in the ITP population were receiving >50 mg/week ETN.

In the PO cohort, patients were monitored for a maximum period of 24 weeks, limiting opportunities to change dose or take a treatment holiday. Weekly mean ETN doses were nominally higher for the ITP population, but the low number of patients in this population precludes any meaningful comparisons. No patient in this cohort received a dose of ETN <50 mg/week.

Impact of treatment patterns on ETN effectiveness, QOL, and safety

In the RP cohort, PASI and BSA data were available for 30 and 11 patients, respectively. For the CTP and ITP populations, mean ± standard error of the mean (SE) decreases in PASI from ETN initiation to study end (over ≥30 months) were similar for the CTP and ITP populations (-9.8±2.2 [p<0.001 *versus* initial score] and -8.9±1.8 [p=0.001], respectively). Greater proportions of CTP *versus* ITP patients achieved PASI 50/75/90 by study end (Figure 2A). Mean ± SE changes in BSA scores from ETN initiation to study end for the CTP and ITP populations were similar (-12.0±3.4 *vs* -11.5±8.5). Insufficient BSA data were available for statistical assessment.

In the PO cohort, PASI and BSA data were available for 64 patients, 95% of whom were in the CTP population. The low number of patients in the ITP population (n=3) precluded comparisons with the CTP population. Mean ± SE PASI and BSA scores overall were 15.5±1.3 (n=64) and 16.1±1.8 (n=64) at Visit 1, decreasing to 5.7±1.5 (n=58) and 4.8±1.1 (n=58) by study end (over 24 weeks). For the CTP population, the PASI score significantly decreased at study end (mean ± SE change: -10.0±1.3; p<0.001) *versus* the first visit (mean ± SE score: 15.4±1.3).

Mean ± SE change in BSA score from ETN initiation to study end was -12.5±1.7 and -9.2±8.0 in the CTP and ITP population, respectively (p<0.001 for CTP population) (Figure 2B).

Insufficient DLQI data Retro Visit 1 were available for the RP cohort (n=4) for meaningful statistical or clinical assessments. For the PO cohort, DLQI data were available for 61 and 58 patients at Visit n+12 and study end, respectively, although the ITP population was too small (n=3) for useful analysis. The CTP population had a mean ± SE change in DLQI from ETN initiation to study end of -5.8±1.0, which was both statistically significant (p<0.001) and clinically meaningful.

Treatment-emergent AEs were observed in 58.9% (n=33) and 26.9% (n=18) of patients in the RP and PO cohorts, respectively (Table 3). In the RP cohort, the proportion of patients in the ITP population reporting a treatment-emergent AE was more than double that of the CTP population, and a four-fold higher proportion of patients in the ITP population experienced dose reductions or temporary discontinuations due to AEs compared with the CTP population. General disorders and administration site conditions were experienced by 7.1% and 14.9% of patients in the RP and PO cohorts, respectively.

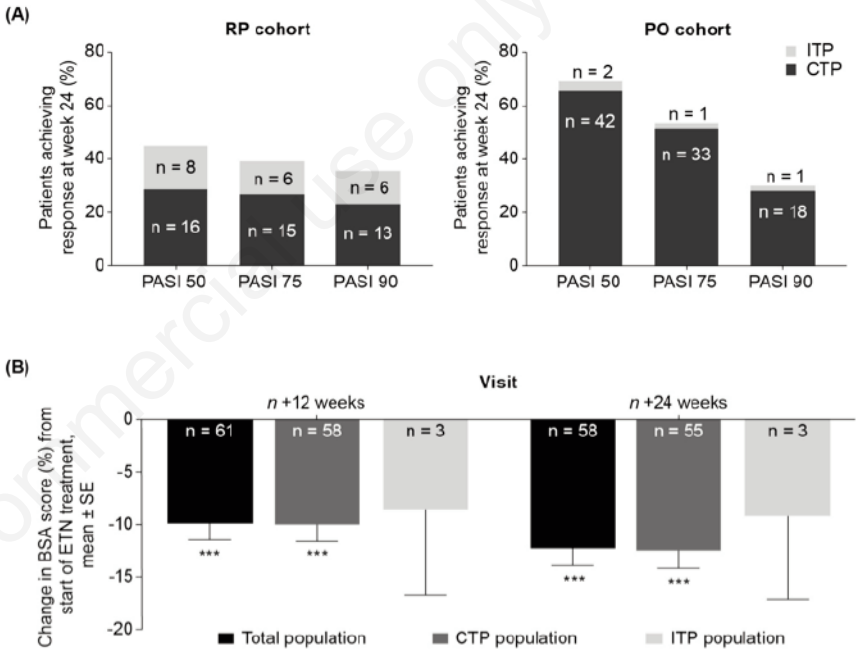

Figure 2. A) Proportions of patients achieving PASI responses at study end and (B) Change in mean BSA (%) scores from the start of ETN treatment for the PO cohort.

Table 2. Treatment patterns.

Parameters	RP cohort (FAS) (N = 56)			PO cohort (FAS) (N = 64)		
	Total population (N=56)	CTP (N=38)	ITP (N=18)	Total population (N=64)	CTP (N=61)	ITP (N=3)
Weekly ETN dose, mg, mean ± SD*	58.5±12.2	55.0±9.0	65.8±15.0	77.8±10.7	77.6±10.6	82.7±15.0
Weekly re-starting ETN dose, mg, mean ± SD*	-	-	75.1±23.1	-	-	66.7±28.9
Patients with ≥1 dose increases, n (%)*	20 (35.7)	6 (15.8)	14 (77.8)	2 (3.1)	1 (1.6)	1 (33.3)
Time to increase in ETN dose, weeks, mean ± SD*	79.7±92.7	121.0±122.8	61.9±75.1	12.0±0.0	12.0±0.0	12.0±0.0
Patients with ≥1 dose decreases, n (%)*	3 (5.4)	2 (5.3)	1 (5.6)	0	-	-
Time to decrease in ETN dose, weeks, mean ± SD*	153.7±26.5	138.5±5.0	184±0.0	-	-	-

*The standard authorized dose for ETN is either 25 mg BIW or 50 mg QW; ETN 50 mg BIW could be used for only 12 weeks but, then, it should be reduced to standard dose; otherwise, the dose is considered increased after 12 weeks. The dose at re-start treatment should be the standard dose; if it is higher, the dose is considered as increased. A similar definition is used for decrease in dose. Data were calculated across the entire study period. BIW twice weekly, CTP continuous treatment pattern, ETN etanercept, FAS full analysis set, ITP intermittent treatment pattern, PO prospective only, QW once weekly, RP retrospective-to-prospective, SD standard deviation.

Table 3. Treatment-emergent adverse events (SAS).

	Overall N=123	RP cohort Total N=56	RP cohort CTP N=38	RP cohort ITP N=18	PO cohort Total N=67	PO cohort CTP N=64	PO cohort ITP N=3
TEAEs, n	115	81	35	46	34	26	8
Patients with AEs, n (%)	51 (41.5)	33 (58.9)	16 (42.1)	17 (94.4)	18 (26.9)	16 (25.0)	2 (66.7)
Patients with SAEs, n (%)	3 (2.4)	2 (3.6)	1 (2.6)	1 (5.6)	1 (1.5)	1 (1.6)	0
Patients discontinuing due to AEs, n (%)	8 (6.5)	2 (3.6)	1 (2.6)	1 (5.6)	6 (9.0)	6 (9.4)	0
Patients with dose reductions or temporary discontinuations due to AEs, n (%)	25 (20.3)	21 (37.5)	7 (18.4)	14 (77.8)	4 (6.0)	4 (6.3)	0
Number of patients reporting							
Off-label use (dose that does not correspond to product label)	24 (19.5)	21 (37.5)	7 (18.4)	14 (77.8)	3 (4.5)	2 (3.1)	1 (33.3)
Upper respiratory tract infection	7 (5.7)	6 (10.7)	1 (2.6)	5 (27.8)	1 (1.5)	1 (1.6)	0
Ineffective drug	6 (4.9)	2 (3.6)	1 (2.6)	1 (5.6)	4 (6.0)	4 (6.3)	0
Overdose	4 (3.3)	4 (7.1)	2 (5.3)	2 (11.1)	0	0	0
Respiratory tract infection	3 (2.4)	3 (5.4)	1 (2.6)	2 (11.1)	0	0	0
Gamma-glutamyltransferase increased	3 (2.4)	1 (1.8)	1 (2.6)	0	2 (3.0)	1 (1.6)	1 (33.3)

Medical Dictionary for Regulatory Activities v19.0 coding dictionary applied. AEs adverse events, CTP continuous treatment pattern, ITP intermittent treatment pattern, PO prospective only, RP retrospective-to-prospective, SAEs serious adverse events, SAS safety analysis set, TEAEs treatment-emergent adverse events.

Discussion

This is the first real-world study of ETN treatment patterns in patients with PsO in Greece in patients under continuous or intermittent treatment. No major differences in effectiveness or safety of ETN were noted between the CTP and ITP populations of the RP. Patients in the PO cohort underwent a maximum of three treatment cycles, limiting opportunities to change dose or take a treatment holiday; therefore, very few patients in this cohort received intermittent treatment and it was not possible to draw meaningful conclusions regarding continuous *versus* intermittent dosing in this cohort.

Since 2008, six EU clinical practice-based real-world data (RWD) studies of ETN treatment patterns, which included continuous and intermittent treatment, have been published including three retrospective analyses from Spain.[15-17] Similar to our findings, none of these studies found a difference in effectiveness or safety of continuous *versus* intermittent treatment with ETN, despite differences in trial design and patient selection.[15,16] Similarly, prospective studies from Germany[18] and Spain[20] report-ed no significant differences between effec-tiveness[14,20] or PROs[14] under CTP or ITP, despite study design differences, including different definitions of CTP and ITP.

This general agreement in outcomes from real-world assessments is interesting in the context of less consistent evidence across prospective, interventional clinical trials: some studies comparing continuous and intermittent ETN regimens in patients with PsO found evidence of a greater benefit of continuous treatment,[5,8,12] but others did not.[7,9,11,13]

This study has limitations inherent to its observational and non-randomized design. In addition, data interpretation in the RP cohort is limited by the lack of clinical records during the retrospective period (in particular, DLQI data). Analysis of the PO cohort is limited by the low number (n = 3) of patients who received intermittent treatment in this cohort. Finally, there may have been a site selection bias since all participating sites were public or academic institutions.

Conclusions

Our data suggest that ETN is an effective and safe option for management of PsO in Greece, both as a continuous and intermittent treatment option.

References

1. Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol 2008;58:826-50.
2. Park BS, Youn JI. Factors influencing psoriasis: an analysis based upon the extent of involvement and clinical type. J Dermatol 1998;25:97-102.
3. European Medicines Agency. Enbrel Summary of Product Characteristics 2020 Available from: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000262/WC500027361.pdf. Last accessed: May 22, 2020.
4. Siegfried EC, Eichenfield LF, Paller AS, et al. Intermittent etanercept therapy in pediatric patients with psoriasis. J Am Acad Dermatol 2010;63:769-74.
5. Ortonne JP, Griffiths CEM, Daudén E, et al. Efficacy and safety of continuous versus paused etanercept treatment in patients with moderate-to-severe psoriasis over 54 weeks: the CRYSTEL study. Exp Rev Derm 2008;3:657-65.
6. Cassano N, Loconsole F, Miracapillo A, et al. Treatment of psoriasis with different dosage regimens of etanercept: preliminary results from the Talpharanta Plastic Study Group. Int J Immunopathol Pharmacol 2010;23:797-802.
7. Gordon KB, Gottlieb AB, Leonardi CL, et al. Clinical response in psoriasis patients discontinued from and then reinitiated on etanercept therapy. J Dermatolog Treat 2006;17:9-17.
8. Moore A, Gordon KB, Kang S, et al. A randomized, open-label trial of continuous versus interrupted etanercept therapy in the treatment of psoriasis. J Am Acad Dermatol 2007;56:598-603.
9. Ortonne JP, Taieb A, Ormerod AD, et al. Patients with moderate-to-severe psoriasis recapture clinical response during re-treatment with etanercept. Br J Dermatol 2009;161:1190-5.

10. Griffiths CE, Luger TA, Brault Y, et al. Retreatment in patients with psoriasis achieving response with etanercept after relapse due to treatment interruption: results from the CRYSTEL study. J Eur Acad Dermatol Venereol 2015;29:468-73.
11. Dauden E, Griffiths CE, Ortonne JP, et al. Improvements in patient-reported outcomes in moderate-to-severe psoriasis patients receiving continuous or paused etanercept treatment over 54 weeks: the CRYSTEL study. J Eur Acad Dermatol Venereol 2009;23:1374-82.
12. Gelfand JM, Kimball AB, Mostow EN, et al. Patient-reported outcomes and health-care resource utilization in patients with psoriasis treated with etanercept: continuous versus interrupted treatment. Value Health 2008;11:400-7.
13. Leonardi C, Strober B, Gottlieb AB, et al. Long-term safety and efficacy of etanercept in patients with psoriasis: an open-label study. J Drugs Dermatol 2010;9:928-37.
14. Luger TA, Barker J, Lambert J, et al. Sustained improvement in joint pain and nail symptoms with etanercept therapy in patients with moderate-to-severe psoriasis. J Eur Acad Dermatol Venereol 2009;23:896-904.
15. Ruiz-Villaverde R, Galan-Gutierrez M, Barabash-Neila R, et al. Efficacy and cost of etanercept in long-term psoriasis: Rational use in clinical practice. J Dermatolog Treat 2016;27:37-42.
16. Moreno-Ramirez D, Ojeda-Vila T, Ferrandiz L. Disease control for patients with psoriasis receiving continuous versus interrupted therapy with adalimumab or etanercept: a clinical practice study. Am J Clin Dermatol 2014;15:543-9.
17. Barrera MV, Habicheyn S, Mendiola MV, et al. Etanercept in the treatment and retreatment of psoriasis in daily clinical practice. Eur J Dermatol 2008;18:683-7.
18. Luger T, Schopf RE, Schwanke A, et al. An observational study to evaluate the long-term outcomes of treatment with etanercept in patients with plaque-type psoriasis. J Eur Acad Dermatol Venereol 2016;30:1730-41.
19. Segaert S, Ghislain PD, Boone C. An observational study of the real-life management of psoriasis patients treated with etanercept according to the new reimbursement criteria (in Belgium). J Dermatolog Treat 2016;27:103-9.
20. Puig L, Camacho Martínez FM, Gimeno Carpio E, et al. Efficacy and safety of clinical use of etanercept for the treatment of moderate-to-severe psoriasis in Spain: results of a multicentric prospective study at 12 months follow-up. Dermatology 2012;225:220-30.
21. Rigopoulos D, Gregoriou S, Katrinaki A, et al. Characteristics of psoriasis in Greece: an epidemiological study of a population in a sunny Mediterranean climate. Eur J Dermatol 2010;20:189-95.