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Original article

Retention and response rates in 14 261 PsA patients starting TNF inhibitor treatment—results from 12 countries in EuroSpA

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Abstract

Objective. To investigate TNF inhibitor (TNFi) retention and response rates in European biologic-naïve patients with PsA.

Methods. Prospectively collected data on PsA patients in routine care from 12 European registries were pooled. Heterogeneity in baseline characteristics between registries were explored (analysis of variance and pairwise comparison). Retention rates (Kaplan–Meier), clinical remission [28-joint count DAS (DAS28) <2.6; 28 joint Disease Activity index for Psoriatic Arthritis $\leqslant 4$] and ACR criteria for 20% improvement (ACR20)/ACR50/ACR70 were calculated, including LUNDEX adjustment.

Results. Overall, 14 261 patients with PsA initiated a first TNFi. Considerable heterogeneity of baseline characteristics between registries was observed. The median 12-month retention rate (95% CI) was 77% (76, 78%), ranging from 68 to 90% across registries. Overall, DAS28/28 joint Disease Activity index for Psoriatic Arthritis remission rates at 6 months were 56%/27% (LUNDEX: 45%/22%). Six-month ACR20/50/70 responses were 53%/38%/22%, respectively. In patients initiating a first TNFi after 2009 with registered fulfilment of CIASsification for Psoriatic ARthritis (CASPAR) criteria ($n = 1980$) or registered one or more swollen joint at baseline ($n = 5803$), the retention rates and response rates were similar to those found overall.

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CLINICAL SCIENCE

Conclusion. Approximately half of >14 000 patients with PsA who initiated first TNFi treatment in routine care were in DAS28 remission after 6 months, and three-quarters were still on the drug after 1 year. Considerable heterogeneity in baseline characteristics and outcomes across registries was observed. The feasibility of creating a large European database of PsA patients treated in routine care was demonstrated, offering unique opportunities for research with real-world data.

Key words: psoriatic arthritis, spondyloarthritis, TNFi, effectiveness, drug survival, response, epidemiology, register, DAS28, DAPSA28

Rheumatology key messages

- A large European database of >14 000 PsA patients treated in routine care has been created.
- Almost half of PsA patients starting first TNFi were in DAS28 remission at 6 months.
- Three-quarters of PsA patients were still on the first TNFi drug after 1 year.

Introduction

In patients with PsA, TNF-α inhibitor (TNFi) agents are frequently prescribed. Randomized controlled trials (RCTs) show that TNFi in general are well tolerated, reduce radiographic progression, improve symptoms and ameliorate a broad range of PsA disease manifestations [1]. However, some patients treated with a first-line TNFi fail to respond, lose treatment response or develop side effects requiring a treatment switch to another TNFi or a non-TNF biologic [2, 3].

In RCTs, the efficacy of TNFi is investigated in populations with strict inclusion and exclusion criteria. In contrast, patients treated in routine care constitute a heterogeneous population with a broad spectrum of various comorbidities and concomitant medications. Thus, only ~20–30% of patients receiving TNFi in routine care would have been eligible to be enrolled in the RCTs that led to approval of the agents that patients were taking [4–7]. This difference between the RCTs and real-world patients is increasingly acknowledged and emphasizes the need for real-world observational studies as a valuable supplement to RCTs [8–11].

To date, real world evidence of TNFi treatments in PsA has only been reported from single countries [12]. Increased knowledge of TNFi exposure, treatment adherence and response rates of TNFi across countries would improve our understanding of the effectiveness of TNFi treatment in PsA patients.

A research network of 15 European registries, the EuroSpA collaboration, has recently been created to strengthen research on patients with SpA in the real-world setting based on data from European registries. Twelve registries contributed data to this first study, where we aimed to investigate retention and response rates among TNFi-naïve PsA patients initiating TNFi treatment. This was investigated in the individual registries and in a pooled dataset, as well as in subgroups of patients registered as ClASsification for Psoriatic ARthritis (CASPAR) criteria and patients with one or more swollen joint at baseline. The heterogeneity of patient characteristics at treatment start between registries was also investigated.

Methods

The EuroSpA research collaboration network

This study included secondary use of data on patients registered with a diagnosis of PsA in one of the following 12 registries: ARTIS (Sweden), DANBIO (Denmark), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey) and RRBR (Romania). The registries had started data collection between 1999 and 2013.

Data sources

The current study is based on secondary use of data already collected in the different registries. Study variables and statistical analyses were pre-defined in a study protocol and a statistical analysis plan. Datasets including only variables relevant for the statistical analyses were uploaded. The EuroSpA datasets were anonymized at the registry level and data were uploaded through secure Virtual Private Network pipelines to a common EuroSpA server, enabling analyses not only by registry but also on pooled data.

Patients

We included patients with a diagnosis of PsA, aged ⩾18 years at initial diagnosis, treated with their first TNFi after diagnosis, registered with a start and, if relevant, a stop date of TNFi treatment. Analyses were conducted separately for patients initiating their first TNFi since registry start and in a cohort of patients initiating first TNFi after 1 January 2009. By 2009 all relevant TNFi were on the market and the 2009 cohort was expected to better reflect patients that start treatment as of today. In the 2009 cohort, the following subcohorts were also studied: patients known to be fulfilling CASPAR criteria [13] and patients with one or more swollen joints (swollen joint count ⩾1) at baseline. All cohorts were followed for 24 months.

Clinical variables

Baseline data included age, sex, BMI, previous and current treatment with conventional synthetic DMARDs

(csDMARDs), disease duration, smoking status and TNFi agent. Disease activity was assessed by DAS28 and the newly developed modified Disease Activity index for Psoriatic Arthritis (DAPSA28) [DAPSA28 = (28TJC × 1.6) + (28SJC × 1.6) + patient's global assessment (0–10 visual analogue scales) + patient's pain assessment (0–10 visual analogue scales) + CRP (mg/dl)] [14] at 6, 12 and 24 month follow-up. Outcomes based on 28 joints were chosen, because 66–68 joints were only available in a subgroup of patients. In addition to the components required for calculation of the composite scores, fatigue scores on visual analogue scales were also obtained. In general, patients were registered with a clinical diagnosis of PsA according to the treating rheumatologist, and therefore information on, for example, fulfilment of CASPAR criteria was not widely available.

Treatment

Treatment with a TNFi was based on registered treatment start (and stop) dates as recorded in each registry. Patients would only be included in the analysis if they had been followed in the registry since start of TNFi treatment (defined as baseline).

Retention rates

Time on drug was defined as the number of days that individual patients continued treatment. The drug was assumed to have been discontinued if a new TNFi was recorded in the registry and the discontinuation date was defined as the date of next TNFi start. If the same drug was re-started within 3 months of the recorded treatment stop date, with no other TNFi recorded in between, the treatment periods were considered as one period. Retention rates were calculated as the percentage of patients still on TNFi at specified time points. Observations were censored by the date of data extraction, date of death or end of registry follow-up, whichever came first. Drug withdrawal was assessed in prespecified categories: lack of efficacy and adverse events. Lack of efficacy was defined in the individual registries and transferred as one variable to the dataset. Patients who withdrew due to remission and other reasons (e.g. planning for pregnancy) were censored.

Treatment response

Clinical response was evaluated as achievement of clinical remission, defined as either DAS28 remission (DAS28 <2.6) or modified DAPSA28 remission (DAPSA28 score $\leqslant 4$), or achievement of an ACR20/50/70 response.

Study outcomes

The primary outcome was the overall 12-month TNFi drug retention rate. Secondary outcomes were the overall 6- and 24-month retention rates. Percentages of PsA patients in remission (DAS28) or (DAPSA28) and ACR20/50/70 responses at 6, 12 and 24 months were also secondary outcomes. Additional secondary outcomes were retention rates at 6, 12 and 24 months in the individual registries. Response rates in individual registries were exploratory outcomes (at 6, 12 and 24 months).

All data from individual databases of the participating registries that were sent to the coordinating centre to build a common database were anonymized according to legal, compliance and regulatory requirements. The participating registries obtained necessary approvals from the local national Data Protection agencies and Research Ethics Boards prior to data transfer. This study was designed and is reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines and with the ethical principles laid down in the Declaration of Helsinki.

Statistical analysis

Statistical analyses were performed using R version 3.4.3 software. All calculations were based on observed data, and no imputation of missing data was performed. The number of patients with available data at baseline and follow-up are shown in Table 1 and supplementary Tables 1–3, available at *Rheumatology* online. Descriptive statistics (median, interquartile range for categorical variables and/or percentage with 95% CI for categorical variables) were applied for patient characteristics and outcomes.

To assess heterogeneity between individual registries, differences between the baseline values were tested with analysis of variance. For those variables that analysis of variance showed to have significant heterogeneity, pairwise comparison was performed with the two-tailed Student's *t*-test (for normally distributed continuous data), Mann–Whitney test (for non-normally distributed continuous data) and the χ^2 test (for categorical variables).

Kaplan–Meier estimation was used to investigate TNFi retention rates (in the entire study population and stratified per registry), including 95% CI. Standardized (age and gender) drug retention rates were calculated by use of the World Health Organization European standard population [15].

Response rates (crude and LUNDEX adjusted [16]) were calculated for DAS28 remission, DAPSA28 remission and ACR20/50/70 responses. LUNDEX-adjusted response rates were calculated as the fraction of patients adhering to therapy multiplied by the fraction of patients fulfilling the selected response criterion at a given time [16].

Results

Patient characteristics

Data on 14 261 patients with PsA initiating a first TNFi were uploaded and pooled. For PsA patients initiating the first TNFi after 2009 ($n = 10\,542$), a subcohort of patients who were registered as fulfilling the CASPAR criteria ($n = 1980$) and a subcohort of patients registered with one or more swollen joint at baseline ($n = 5803$) were identified (Fig. 1).

A total of 34% of all patients were prescribed etanercept, 31% adalimumab, 22% infliximab, 11% golimumab and 4% certolizumab (Table 1). Sixty percent of patients received concomitant csDMARDs. Median (interquartile

Table 1 Baseline characteristics of all PsA patients and of PsA subcohorts

	All patients		Patients fulfilling CASPAR criteria[a]		Patients with ⩾1 swollen joints[b]	
	No. of patients with available data	Median (IQR) or percentage	No. of patients with available data	Median (IQR) or percentage	No. of patients with available data	Median (IQR) or percentage
Age, years	14 261	49 (40–57)	1980	49 (40–58)	5803	50 (41–59)
Male	14 261	49	1980	52	5803	48
BMI, kg/m^2	5218	27 (24–31)	1468	27 (24–30)	2311	27 (24–31)
Concomitant csDMARD	14 144	60	1925	59	5803	66
Prior csDMARD	11 959	81	1855	76	5156	85
Time since diagnosis, years	10 058	4 (1–9)	1947	3 (1–8)	4398	4 (1–9)
Current smoking	12 868	16	1813	15	5255	15
Infliximab	3069	22	245	12	1048	18
Etanercept	4788	34	492	25	1782	31
Adalimumab	4364	31	703	36	1828	32
Certolizumab	524	4	96	5	279	5
Golimumab	1516	11	444	22	866	15
DAS28	9450	4.3 (3.4–5.1)	1198	4.4 (3.5–5.3)	5130	4.5 (3.8–5.2)
DAPSA28	8717	26.7 (17.6–39.2)	1136	28.4 (18.4–42.2)	4701	29.9 (21.5–41.2)
CRP, mg/l	11 138	7 (3–17)	1462	8 (3–17)	5542	7(3–18)
SJC (0–28)	10 777	3 (1–6)	1463	3 (1–7)	5803	4 (2–7)
TJC (0–28)	10 764	5 (2–9)	1462	5 (2–10)	5781	6 (3–10)
SJC (0–66)	3815	4 (1–7)	982	4 (2–8)	2416	5 (3–8)
TJC (0–68)	4655	8 (4–14)	999	7 (3–14)	3022	9 (5–15)
Pain score (VAS 0–100 mm)	10 033	62 (42–75)	1275	68 (48–80)	4926	64 (45–78)
Fatigue score (VAS 0–100 mm)	5228	64 (40–80)	311	70 (49–82)	2973	65 (43–80)

Data are as observed, median [interquartile range (IQR)] or percentage. [a]CASPAR: ClASsification for Psoriatic ARthritis criteria initiating treatment after 2009. [b]Initiating treatment after 2009. csDMARD: conventional synthetic DMARD; TNFi: TNF inhibitor; SJC: swollen joint count; TJC: tender joint count; VAS: visual analogue scale; DAS28: DAS 28 joint-count; DAPSA28: Disease Activity index for Psoriatic Arthritis 28 joint-count.

range) disease duration was 4 (1–9) years and DAS28 was 4.3 (3.4–5.1).

Baseline variables for the individual 12 registries are shown in Table 2. Analysis of variance showed statistically significant differences between the registries for all baseline variables ($P < 0.001$). Subsequent pairwise comparison of registries showed statistically significant differences for most baseline variables (data not shown).

Drug retention rates at 6, 12 and 24 months

Overall, the 12-month retention rate was 77% (95% CI: 76, 78%). Corresponding retention rates for patients fulfilling CASPAR criteria and patients with one or more swollen joints were 78% (77, 80%) and 76% (74, 77%), respectively (Table 3). Retention rates at 6 and 24 months are shown in Table 3. The overall retention rates of the individual registries at 12 months ranged from 68 to 90% (Table 4 and Fig. 2). At 6 and 24 months, retention rates in individual registries were 80–98% and 59–89%, respectively.

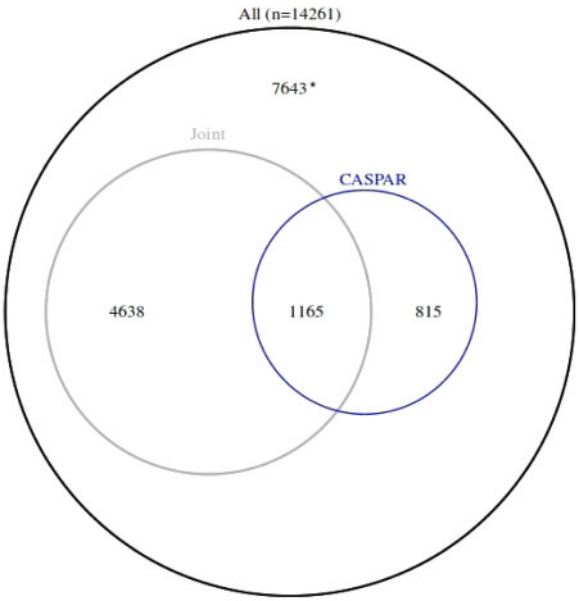
Standardized retention rates (age and gender) for the individual registries at 6, 12 and 24 months showed results similar to the non-standardized retention rates (Table 4).

Remission and response rates at 6, 12 and 24 months

Overall, crude DAS28 remission rates at 6, 12 and 24 months were 56, 61 and 65%, respectively. For DAPSA28 remission they were 27, 30 and 33%, respectively, whereas ACR20/50/70 response rates were 53%/38%/22% at 6 months, 55%/42%/26% at 12 months and 59%/46%/30% at 24 months. Corresponding LUNDEX-adjusted rates at 6, 12 and 24 months were 45, 40 and 31%, respectively, for DAS28 remission, and 22, 20 and 16% for DAPSA28 remission. ACR 20/50/70 response rates were 43%/31%/18% at 6 months, 36%/28%/17% at 12 months and 28%/22%/14% at 24 months, respectively (Table 4).

The subcohorts of patients fulfilling CASPAR criteria and patients with one or more swollen joint at baseline had similar DAS28 remission and DAPSA28 remission

Fig. 1 Venn diagram of all PsA patients



Number of patients starting treatment after 2009 and registered as fulfilling CASPAR criteria and as having one or more swollen joints at baseline are shown. CASPAR: ClASsification for Psoriatic ARthritis criteria.

rates at all time points compared with the group of all patients, both crude and LUNDEX adjusted. Numerical differences in ACR20 crude response rates were found. Thus, the ACR20 responses at 6, 12 and 24 months for patients fulfilling CASPAR criteria were 58%/60%/62%, and for patients with one or more swollen joint were 71%/75%/77%, respectively (Table 4).

Reasons for withdrawal of TNFi treatment

The reason for drug withdrawal for all patients during the 24-month follow-up was lack of efficacy in 63% ($n = 2457$) and adverse events in 37% ($n = 1427$) of patients. For the patients who withdrew during 24 months of follow-up ($n = 3884$), the median (interquartile range) time to withdrawal was 7 months (7–13).

Among patients fulfilling the CASPAR criteria and patients with one or more swollen joint, the patterns of withdrawal and median time to withdrawal were comparable to the cohort of all patients (supplementary Table 4, available at *Rheumatology* online).

Discussion

This first study from the EuroSpA research collaboration network, including >14 000 European patients with PsA treated in routine care, demonstrated that 77% of patients initiating their first TNFi were still on this treatment 12 months later, both in the entire population and in subgroups of patients fulfilling CASPAR criteria or with one or more swollen joint. Further, 56% of patients were in DAS28 remission at 6 months. The large number of patients allowed us to analyse data on subcohorts. For the first time, heterogeneity in the characteristics of PsA patients initiating TNFi treatment across Europe was demonstrated. Not unexpectedly, the clinical characteristics of the patients with PsA initiating TNFi treatment varied across the European countries. Differences included, but were not limited to, disease characteristics (e.g. disease duration, use of concomitant csDMARD) and lifestyle factors (BMI, smoking habits), as well as demographics. Patients selected to receive their first TNFi varied across the countries; for instance, the median pre-treatment disease activity in individual countries varied from 3.7 to 5.8 for DAS28 and from 19.1 to 49.8 for DAPSA28. Moreover, the percentage of patients treated with prior csDMARD varied from 36 to 100%. The heterogeneity in baseline characteristics, reflecting differences in prescription patterns and drug availability across Europe, provides opportunities and challenges. The combination of registries enabled us to compare prescription patterns across countries, which is generally not possible. On the other hand, differences in access to treatment and in prescription patterns imply that the results achieved by pooling of data across countries should be interpreted with caution [17]. Future studies should investigate the impact of such differences on retention and response rates.

Overall, three-quarters patients were still receiving treatment 12 months after start, and this was regardless of whether patients fulfilled CASPAR criteria or had swollen joints at baseline. The retention rates of individual registries, however, varied widely, ranging from 68 to 90%.

Previous studies have investigated retention rates for PsA patients initiating the first TNFi. In an observational study of 764 Danish PsA patients [18], drug retention

Table 2 Baseline characteristics of all PsA patients, stratified by registry

Country	ARTIS Sweden	ATTRA Czech Republic	BIOBADASER Spain	Biorx.si Slovenia	DANBIO Denmark	ICEBIO Iceland	NOR-DMARD Norway	Reuma.pt Portugal	RRBR Romania	ROB-FIN Finland	SCQM Switzerland	TURKBIO Turkey
All patients (*n*)	5721	796	592	374	2412	338	915	759	104	592	1333	325
Patients fulfilling CASPAR criteria (*n*)[a]	NA	NA	NA	335	225	46	50	444	92	NA	757	31
Patients with ⩾1 swollen joint (*n*)[b]	2298	567	206	303	803	154	336	390	101	179	368	98
Age, years	49 (40–58)	49 (39–56)	49 (40–57)	49 (42–57)	48 (39–56)	50 (39–59)	48 (39–57)	48 (39–56)	54 (46–61)	50 (41–56)	49 (40–57)	42 (33–52)
Male (%)	49	53	51	53	46	40	51	52	44	54	50	35
BMI, kg/m^2	NA	28 (25–32)	27 (24–31)	27 (24–29)	27 (24–31)	30 (26–33)	27 (25–30)	27 (24–30)	29 (25–33)	28 (25–31)	26 (24–30)	29 (25–31)
Concomitant csDMARD (%)	55	78	70	73	63	47	68	39	97	79	55	47
Prior csDMARD (%)	79	98	NA	97	100	100	81	36	100	NA	68	100
Time since diagnosis, years	3 (1–9)[c]	6 (3–12)	4 (2–9)	6 (2–12)	3 (1–8)	5 (1–10)	4 (1–11)	4 (1–9)	3 (1–6)	7(3–13)	2 (1–7)	3 (1–8)
Current smoking (%)	13	13	17	13	27	21	25	17	7	15	11	23
Infliximab (%)	25	14	18	10	26	59	12	12	10	25	12	18
Etanercept (%)	41	23	34	20	24	22	36	39	19	35	30	25
Adalimumab (%)	27	47	29	48	37	7	15	26	45	32	39	41
Certolizumab (%)	0	5	7	4	7	0	21	1	0	2	2	6
Golimumab (%)	8	11	12	18	7	12	16	21	26	6	17	10
DAS28	4.2 (3.5–5)	5.3 (4.7–5.9)	3.7 (3–4.4)	5 (4.2–5.6)	4.3 (3.4–5.2)	4.4 (3.9–5)	3.7 (2.8–4.5)	4.4 (3.6–5.2)	5.8 (5.1–6.5)	3.9 (3.3–4.7)	3.7 (2.9–4.6)	4.3 (3.5–5)
DAPSA28	26.6 (18.3–38)	40.6 (28.8–51.6)	NA	38 (26.9–52)	26.8 (17.6–39.7)	29 (22.1–37.6)	19.1 (12.7–29.4)	28 (18.7–41.4)	49.8 (39.6–60.9)	21.9 (15.7–33.2)	20.9 (13–30.6)	26.8 (19.1–34.4)
CRP, mg/l	7 (3–16)	15 (7–29)	2 (1–8)	8 (3–19)	7 (2–15)	7 (3–13)	5 (3–14)	10 (4–23)	23 (14–46)	8(3–18)	8 (3–11)	10 (3–18)
SJC (0–28)	3 (1–6)	7 (4–10)	2 (0–4)	6 (4–10)	2 (0–5)	4 (2–6)	1 (0–4)	3 (1–6)	6 (4–9)	3 (1–6)	2 (0–4)	2 (0–4)
TJC (0–28)	5 (2–9)	9 (5–14)	3 (1–6)	8 (4–12)	5 (2–11)	5 (2–8)	3 (1–7)	5 (2–10)	12 (7–16)	3 (1–6)	3 (1–7)	4 (2–8)
SJC (0–66)	3 (1–6)	NA	NA	NA	3 (0–6)	8 (6–10)	NA	4 (1–8)	8 (7–14)	NA	3 (1–7)	1 (0–4)
TJC (0–68)	6 (3–11)	13 (8–21)	NA	NA	9 (4–17)	9 (7–16)	NA	7 (3–15)	18 (11–24)	NA	5 (2–12)	6 (4–9)
Pain score (VAS 0–100 mm)	62 (45–75)	70 (45–80)	NA	70 (50–80)	62 (42–76)	68 (51–79)	49 (30–65)	62 (49–80)	80 (80–90)	60 (38–74)	60 (30–70)	75 (59–80)
Fatigue score (VAS 0–100 mm)	61 (36–77)	65 (49–80)	NA	NA	69 (49–82)	72 (52–83)	52 (30–75)	NA	NA	NA	50 (30–70)	70 (50–75)

Data are as observed, median (interquartile range) or percentage. [a]CASPAR: ClASsification for Psoriatic ARthritis criteria initiating treatment after 2009. [b]Initiating treatment after 2009. [c]Time since inclusion in ARTIS. csDMARD: conventional synthetic DMARD; TNFi: TNF inhibitor; SJC: swollen joint count; TJC: tender joint count; VAS: visual analogue scale; DAS28: DAS 28 joint-count; DAPSA28: Disease Activity index for Psoriatic Arthritis 28 joint-count; NA: not available.

Table 3 Retention and response rates in PsA patients

	All patients		Patients fulfilling CASPAR criteria		Patients with ⩾1 swollen joints	
	Retention rates					
6 months, % (95% CI)	86 (86, 87%)		88 (87, 90%)		85 (84, 86%)	
12 months, % (95% CI)	77 (76, 78%)		78 (77, 80%)		76 (74, 77%)	
24 months, % (95% CI)	68 (67, 69%)		69 (67, 71%)		67 (65, 68%)	
	Response rates[a]					
	Crude[b]	LUNDEX adjusted[c]	Crude[b]	LUNDEX adjusted[c]	Crude[b]	LUNDEX adjusted[c]
DAS28 remission at 6 months (%)	56	45	59	49	55	43
DAS28 remission at 12 months (%)	61	40	65	43	63	38
DAS28 remission at 24 months (%)	65	31	68	32	69	29
DAPSA28 remission at 6 months (%)	27	22	30	25	27	21
DAPSA28 remission at 12 months (%)	30	20	33	22	32	20
DAPSA28 remission at 24 months (%)	33	16	34	16	34	14
ACR20/50/70 at 6 months (%)	53/38/22	43/31/18	58/43/23	48/36/19	71/52/30	56/41/23
ACR20/50/70 at 12 months (%)	55/42/26	36/28/17	60/46/28	40/31/19	75/58/36	46/36/22
ACR20/50/70 at 24 months (%)	59/46/30	28/22/14	62/46/31	29/21/14	77/61/40	33/26/17

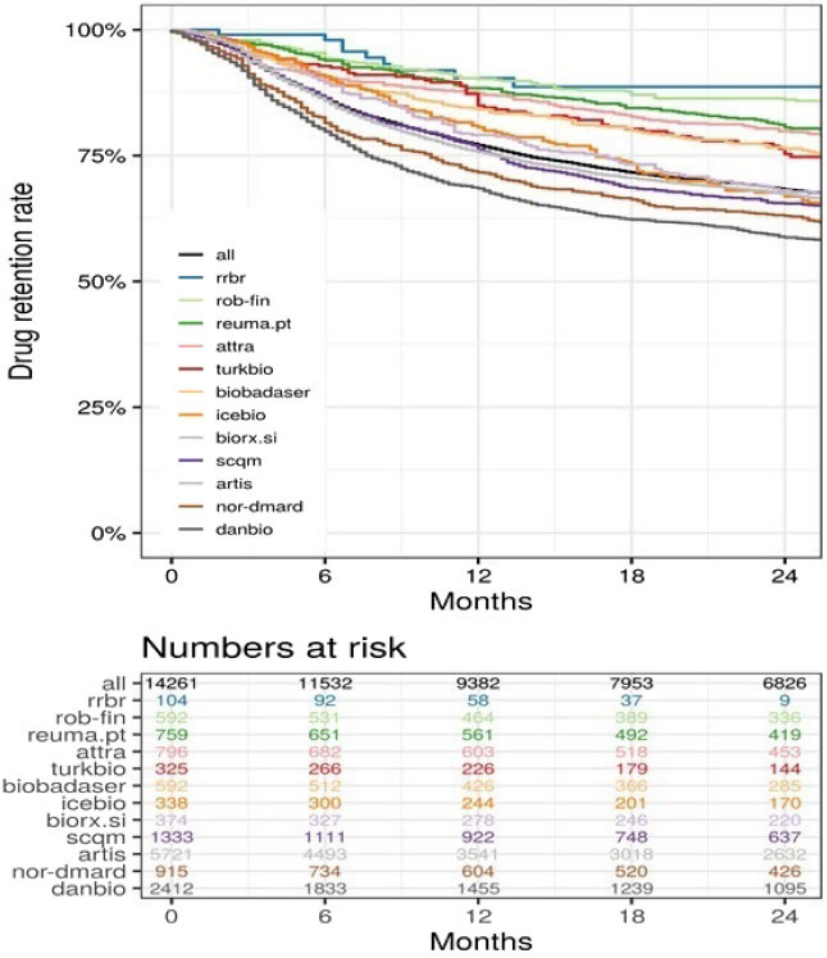
Data are as observed, median (interquartile range) or percentage. [a]Details on numbers of patients are found in supplementary Tables 1–3, available at *Rheumatology* online. [b]Crude value: the fraction responding of those still on drug at 6, 12 and 24 months, respectively. [c]LUNDEX adjusted: crude value adjusted for drug retention. DAS28: DAS 28 joint count; DAPSA28: Disease Activity index for Psoriatic Arthritis 28 joint-count; CASPAR: ClASsification for Psoriatic ARthritis criteria.

rates were 70 and 57% at 1-year and 2-year follow-up, respectively. The corresponding rates were 79 and 73% in a study of 188 British PsA patients [19], while a study of 439 Norwegian PsA patients showed 57% drug retention at 3-year follow-up [20]. These studies are reports from the registries now within the EuroSpA collaboration. The retention rates in the pooled EuroSpA data set are overall comparable to the drug retention rates in the individual registries. The present study is the first study to investigate retention rates in well-characterized subcohorts of patients with PsA, e.g. patients known to fulfil CASPAR criteria and patients with one or more swollen joint at treatment start. Information on CASPAR criteria and swollen joint count at baseline were not registered in all patients, but it is reassuring that the retention rates in the well-characterized subcohorts were similar to those in the full cohort.

Different prescription patterns, including differences in criteria for receiving TNFi treatment, may contribute to the considerable difference in baseline characteristics and retention rates across countries. The availability of TNFi differs between countries, and in RA, political and health economic factors have been shown to be associated with the prescription of these expensive drugs [21]. In addition, in RA an inverse association between gross domestic product and retention of the TNFi abatacept has been reported, which could reflect an inequity in access to treatment [22]. These findings are likely to also apply to patients with PsA. Despite international recommendations regarding treatment strategies, these may be overruled by national guidelines. Examples of different treatment strategies between countries, which could lead to different retention rates, are different start doses and stepping up strategies [23–25], co-medication with csDMARDs [26–28] and the use of biosimilars, which might lead to earlier TNFi switching in case of lack of effect or side effects [29–31].

DAPSA28 remission has not previously been investigated in registry studies and is of interest, since in contrast to DAS28, it was developed and validated for monitoring patients with PsA [14]. Since most registries only include 28 joint counts, which does not allow calculation of DAPSA, we used the newly developed DAPSA28. The DAPSA28 has been demonstrated to have good validity, and good sensitivity to change [14]. In our study, DAPSA28 remission was consistently achieved in fewer patients than DAS28 remission, and thus clearly represents a stricter remission criterion. We also found that while only 31% of patients achieve DAS28 remission at 24 months, 68% of them remain on therapy. One explanation could be that during the time period of this study

FIG. 2 Kaplan–Meier curves showing drug retention rates for pooled data and per register



The table (bottom) shows the number of patients who were still being treated at the corresponding time points.

there were relatively few alternative treatments available and thus patients were continuing therapy despite limited benefit. The high cost and potential adverse events of TNFi therapy support that therapy should not be continued unless there is a markedly clinical benefit.

In earlier studies different response measures had been applied, which makes comparisons of response rates in these studies difficult. Only few observational studies have investigated remission as the outcome. A Portuguese study reported that DAS28 remission was achieved by 32% of 180 PsA patients at 3 months and 49% at 6 months [32], and in an Irish study, 58% of PsA patients were in DAS28 remission at 12 months [33]. In 75 PsA patients fulfilling CASPAR criteria treated with TNFi in a clinical setting, 21% achieved DAS28 remission at 4 months and the response rate doubled from 4 to 8 months [34]. Improvements in disease activity, e.g. by measuring ACR20 response rates, have been investigated in several studies. In a Finnish study of 127 PsA patients, ACR20 response rates were 76% for infliximab and 79% for etanercept at 3-month follow-up [35]. Another study found that the majority of PsA patients responded to treatment within 3 months, as assessed by improvement of at least 40% in active tender and/or swollen joint count and 50% improvement in the Psoriasis Area and Severity Index score, and that a subgroup of early non-responders had delayed response not apparent until after 1 year [36]. Overall, the response rates from the above studies reflect our findings for crude response rates, but do not yield information about the true fraction of patients actually responding to the first TNFi, since not all patients adhere to therapy. Therefore, by calculating the LUNDEX-adjusted response rates, we add information about the fraction of patients, among those adhering to therapy, who achieve the response criterion after a specific follow-up time. Thus, the LUNDEX-adjusted response rates are corrected for the patients who are no longer on therapy, which is comparable to intention-to-treat analyses in RCT studies.

This study has strengths and limitations. Generalizability of our results is considered to be high with the inclusion of data from 12 registries across Europe. A limitation is that selection bias based on data availability cannot be ruled

Table 4 Retention rates per registry at 6, 12 and 24 months and response rates at 6 months in PsA patients

Registry	All patients		Patients fulfilling CASPAR criteria		Patients with ⩾1 swollen joints		All patients Standardized retention rates[a] (6/12/24 months), %	All patients	
	Retention rates (6/12/24 months), %	95% CI	Retention rates (6/12/24 months), %	95% CI	Retention rates (6/12/24 months), %	95% CI		Response rates (DAS28 remission), %	
								Crude[b]	LUNDEX adjusted[c]
ARTIS	86/76/67	(85, 87)/(75, 77)/(66, 69)	NA	NA	84/72/64	(82, 86)/(70, 74)/(61, 66)	87/77/69	55	43
BIOBADASER	90/84/76	(87, 92)/(81, 87)/(73, 80)	NA	NA	86/78/69	(81, 91)/(72, 84)/(62, 76)	90/83/76	68	59
Biorx.si	89/79/68	(86, 93)/(75, 83)/(63, 73)	89/77/65	(85, 92)/(73, 82)/(60, 71)	88/77/65	(84, 92)/(72, 82)/(59, 71)	88/78/67	61	53
DANBIO	80/68/59	(78, 81)/(67, 70)/(57, 61)	80/70/61	(75, 86)/(64, 76)/(54, 68)	79/67/58	(76, 82)/(64, 71)/(54, 61)	81/70/61	52	40
ICEBIO	91/81/67	(88, 94)/(76, 85)/(62, 72)	93/76/64	(87, 100)/(64, 89)/(51, 80)	86/74/57	(81, 92)/(67, 81)/(49, 66)	92/83/69	45	40
NOR-DMARD	81/72/63	(79, 84)/(69, 75)/(60, 66)	94/92/85	(88, 100)/(85, 100)/(76, 96)	79/70/63	(74, 83)/(65, 75)/(58, 69)	81/71/62	62	50
Reuma.pt	94/88/81	(92, 96)/(86, 91)/(78, 84)	94/88/79	(92, 97)/(85, 91)/(75, 83)	94/88/80	(92, 97)/(85, 92)/(76, 85)	94/88/81	55	47
ROB-FIN	94/90/86	(92, 96)/(88, 93)/(83, 89)	NA	NA	92/87/80	(89, 96)/(82, 92)/(74, 87)	95/91/87	51	46
RRBR	98/90/89	(95, 100)/(84, 97)/(82, 96)	98/89/87	(95, 100)/(82, 97)/(79, 96)	98/90/88	(95, 100)/(84, 97)/(81, 96)	99/90/89	42	37
SCQM	86/76/65	(85, 88)/(74, 79)/(63, 68)	85/74/65	(83, 88)/(71, 78)/(62, 69)	85/74/65	(81, 89)/(68, 78)/(60, 71)	87/77/66	68	57
TURKBIO	93/85/75	(90, 96)/(81, 89)/(70, 81)	87/80/67	(76, 100)/(67, 96)/(52, 88)	95/92/86	(91, 100)/(86, 98)/(78, 95)	92/83/74	66	54
ATTRA	91/87/80	(89, 93)/(85, 90)/(77, 83)	NA	NA	90/88/79	(88-93)/(85, 90)/(75, 83)	91/88/80	59	51

Data are as observed, median (95% CI). [a]Standardized (age and gender) drug retention rates. [b]Crude value: the fraction responding of those still on drug at 6, 12 and 24 months, respectively. [c]LUNDEX adjusted: crude value adjusted for drug retention. ARTIS (Sweden); BIOBADASER (Spain); Biorx.si (Slovenia); DANBIO (Denmark); ICEBIO (Iceland); NOR-DMARD (Norway); Reuma.pt (Portugal); ROB-FIN (Finland); RRBR (Romania); SCQM (Switzerland); TURKBIO (Turkey). CASPAR: ClASsification for Psoriatic ARthritis criteria; NA: not available.

out. However, data have been collected prospectively and independently of the current research study. Compliant subjects may be more likely to visit their doctor regularly and may therefore have more complete registry data, which could potentially lead to overestimation of drug retention rates. Furthermore, the missing information on, for example, swollen joint count, in some patients, and differences across registries regarding registration of, for example, axial involvement, enthesitis, dactylitis and skin involvement, are also a limitation.

In conclusion, retention, remission and response rates in >14 000 European PsA patients treated with their first TNFiI were reported. Almost half of the patients who started treatment were in DAS28 remission at 6 months, and three-quarters were still on the first TNFi after 1 year. Considerable heterogeneity in baseline characteristics across registries was observed. This study documents the feasibility of creating a large European database of PsA patients treated in routine care. The EuroSpA Network Collaboration offers unique opportunities for providing real-world evidence on the effectiveness of biological drugs in European patients.

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Supplementary data

Supplementary data are available at *Rheumatology* online.

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