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ORIGINAL RESEARCH

Real-World Treatment Persistence with Biologic Disease-Modifying Antirheumatic Drugs Among German Patients with Psoriatic Arthritis—A Retrospective Database Study

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ABSTRACT

Introduction: To investigate drug survival for biologic disease-modifying antirheumatic drugs (bDMARDs) in a real-world cohort of German adult biologic-naïve patients with psoriatic arthritis (PsA).

Methods: Claims data for patients with a diagnosis of PsA, a bDMARD claims record (index date) between 1 January 2014 and 31 December 2017, and no bDMARD prescription for 365 days before the index date were retrospectively analyzed. The primary outcomes were the overall and individual bDMARD persistence rates over 12 months. Nonpersistence was defined as a treatment gap exceeding the days of supply plus 60 days or switching to a bDMARD other than the index therapy. Sensitivity analysis was performed, wherein the treatment gap was found to vary depending on the bDMARD regimen. Kaplan–Meier curves were plotted to determine persistence; the log-rank test was used to evaluate differences in the persistence rate. Factors associated with treatment discontinuation were evaluated using Cox regression analysis.

Results: Among 10,954 patients with a PsA diagnosis, 348 were eligible. The overall bDMARD persistence rate was 57.5%; individual bDMARD persistence rates were 81.3% for ustekinumab, 66.7% for infliximab, and 60.0% for golimumab. The mean (SD) overall persistence with bDMARDs was 289 (103) days; the mean persistence was 334 (72) days for ustekinumab, 309 (82) days for golimumab, and 305 (92) days for infliximab. The main reasons for nonpersistence were switching to another bDMARD (15.8%) and treatment discontinuation (26.7%). Male gender was significantly associated with a lower risk of treatment discontinuation (hazard ratio 0.54, 95% confidence interval 0.39–0.77; $P < 0.001$). The sensitivity analysis yielded similar results.

Conclusion: The one-year persistence rate for bDMARDs in German PsA patients is modest, although the persistence rate depends on the bDMARD considered.

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Keywords: Biologic disease-modifying antirheumatic drugs; Germany; Persistence; Psoriatic arthritis

Key Summary Points

Persistence with biologic disease-modifying antirheumatic drugs is moderate in German patients with psoriatic arthritis.

The persistence rate depends on the biologic disease-modifying antirheumatic drug considered.

Male gender is associated with a lower risk of treatment discontinuation.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.13636769.

INTRODUCTION

Psoriatic arthritis (PsA) is a common chronic inflammatory rheumatic disease characterized by pain, stiffness, swollen joints, joint erosion, and bone formation, as well as psoriasis as a concomitant condition [1, 2]. The age-standardized prevalence of PsA in Germany from 2009 to 2012 was reported to be 1.8–2.1 per 100,000 in men and 2.1–2.5 per 100,000 in women, resulting in an estimated 200,000 patients with PsA living in Germany in 2018 [3]. PsA negatively impacts health-related quality of life (HRQoL) due to fatigue, impairment of daily functions and ability to work, and diminished social participation [4, 5]. PsA has also been associated with a high economic burden. Jacob et al. [6] analyzed German claims data and reported average healthcare costs in treated prevalent patients with PsA to be €5557 within a year of diagnosis and €5761 in the second year. A similar claims data analysis by Sondermann et al. [7] revealed that the average cost of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) was €322 per patient per year, and the average cost of biologic DMARDs (bDMARDs) was €15,304 per patient per year.

Treatment options for PsA include traditional symptomatic therapies such as nonsteroidal anti-inflammatory drugs and glucocorticoids; DMARDs such as methotrexate, leflunomide, and cyclosporine; bDMARDs such as tumor necrosis factor inhibitors (TNFis) and interleukin-12/23 or interleukin-17 inhibitors; or targeted synthetic DMARDs (tsDMARDs) such as phosphodiesterase-4 or Janus kinase inhibitors [8–10]. For patients with active PsA refractory to conventional drugs or those with a poor prognosis, treatment with tsDMARDs or bDMARDs is recommended [10]. In Germany, most patients with PsA were treated systemically (53.7%); most of those patients were treated with DMARDs (72.1%), while 20.9% were treated with a combination of DMARDs and biologics [7]. Currently, nine bDMARDs (etanercept, infliximab, adalimumab, certolizumab pegol, golimumab, ustekinumab, secukinumab, abatacept, and ixekizumab) and two tsDMARDs (apremilast and tofacitinib) are approved in Germany for the treatment of patients with PsA. Apremilast has been available since 2015, while abatacept, ixekizumab, and tofacitinib have been available since 2018.

Persistence with bDMARDs and tsDMARDs, i.e., the time interval from initiation to discontinuation of treatment [11], varies with the treatment under investigation and with the type of health center and the country considered [12–14]. In Germany, the persistence rate for patients with PsA who were prescribed biologics was reported to be 57.9% after 1 year [13] and 33.2% after 5 years [15]. However, these persistence rates are for prescriptions of biologics as a class, not for individual biologics. Studies from other countries have reported that persistence rates of biologics that are used to treat PsA vary depending on the drug prescribed at the index date [12, 14], but corresponding data for Germany are still awaited, despite their

importance for clinical and health economic decision-making. To address this knowledge gap, we evaluated the real-world bMARD persistence rate of patients with PsA using data from a large German claims database.

METHODS

Data Source

Deidentified patient data were obtained from the Institute for Applied Health Research Berlin (InGef) research database. The authors had the permission to use this private dataset. This database comprises comprehensive longitudinal patient-level electronic records of health insurance claim information such as inpatient and outpatient treatments, prescription drugs, and other health-related claims data for about 4 million members of the German statutory health insurance (SHI) system, who were structured to represent the German population in terms of age and gender according to the Federal Office of Statistics (DESTATIS) [16]. The representativeness of the database compared to the general German population in terms of morbidity, mortality, and drug usage has been externally validated [17]. In Germany, around 90% and 10% of the population are covered by statutory health insurance and private insurance, respectively. The InGef database has been extensively utilized for health services research [18, 19]. Ethics approval was not required, as this study used anonymized German claims data.

Study Population

This retrospective cohort study spanned from 1 January 2013 to 31 December 2018. Patients who were classified with PsA according to the International Classification of Diseases German Modification, 10th Revision (ICD-10-GM) code L40.5 in combination with M07.0/07.1/07.2/07.3 (Table S1 in the "Supplementary Information") in the inpatient setting (primary or secondary diagnosis) or outpatient setting (verified diagnosis) and who had a claims record of biologic treatment licensed for PsA as per Anatomical Therapeutic Chemical (ATC) classification codes (Table S2 in the "Supplementary Information") between 1 January 2014 and 31 December 2017 were included. The index date was defined as the first observed prescription (i.e., the dispense date) of the bDMARD. A diagnosis of PsA and a biologic claim in the same quarter (the "index quarter"), age $\geq$ 18 years old in the index quarter, biologic-naïve status at the index date, and the presence of at least 365 days of continuous enrollment prior to and after the index date were essential for inclusion in the study. Biologic-naïve patients were defined as those who had no prescription record for any PsA-licensed biologic at any strength during the first 12 months of their observation period ("washout"). Patients with Crohn's disease (ICD-10 K50), ulcerative colitis (ICD-10 K51), ankylosing spondylitis (ICD-10 M45), or rheumatoid arthritis (ICD-10 M05-M07) were excluded, as were patients with two different bDMARD index prescriptions on the same day (Fig. 1).

Covariates

Age, gender, insurance status, degree of polypharmacy, use of corticosteroids, diagnosis of psoriasis in the same quarter as the index event, and the Charlson Comorbidity Index (CCI) [20] were the baseline covariates of interest. Polypharmacy and corticosteroid prescriptions were assessed based on ATC codes for specific comedications used in the 12-month pre-index period (Table S3 in the "Supplementary Information"). Psoriasis was diagnosed using the ICD-10-GM codes L40.0–L40.4, L40.8, and L40.9. The CCI included 19 comorbidities as given in Table S4 of the "Supplementary Information" (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, mild liver disease, diabetes without chronic complication, diabetes with chronic complication, hemiplegia or paraplegia, renal disease, tumors without metastasis, lymphoma, leukemia, moderate or severe liver disease,

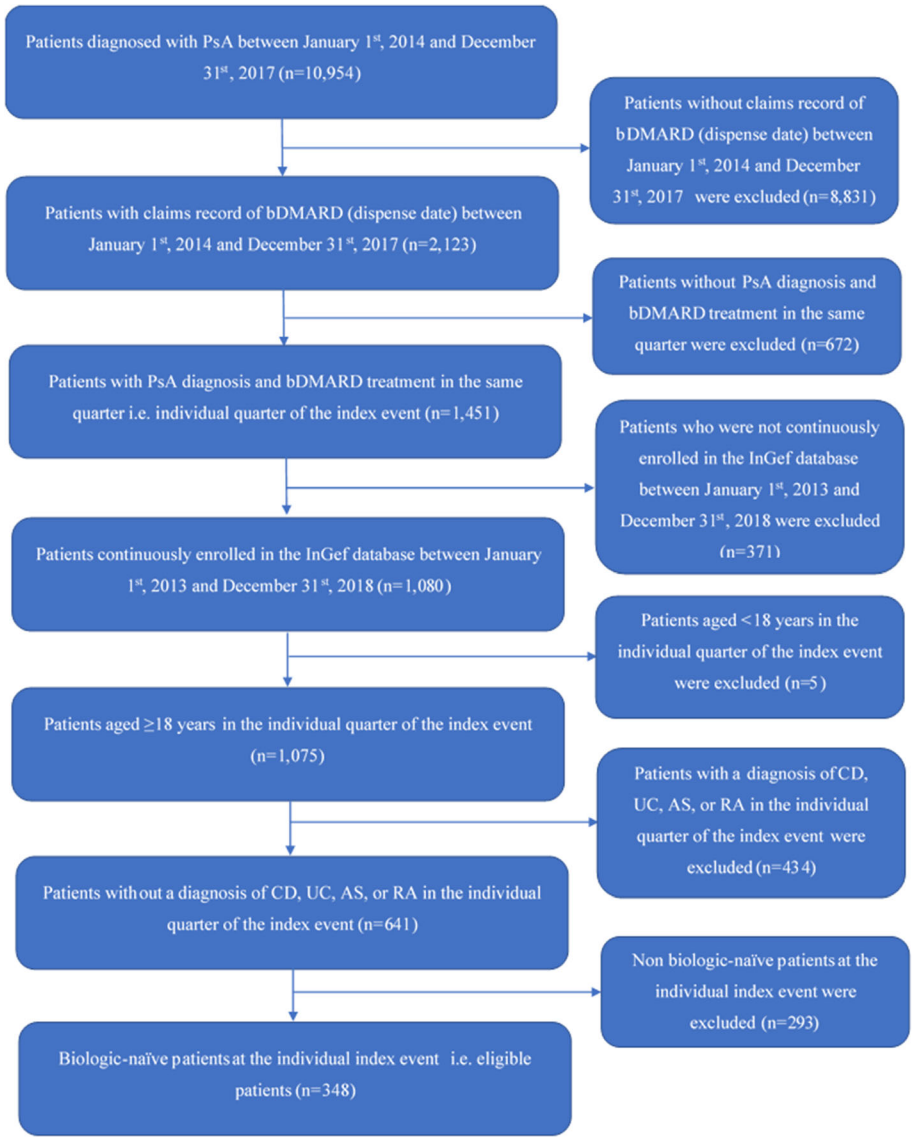

Fig. 1 Dataset for analysis. *AS* ankylosing spondylitis, *bDMARD* biologic disease-modifying antirheumatic drug, *CD* Crohn's disease, *PsA* psoriatic arthritis, *RA* rheumatoid arthritis, *UC* ulcerative colitis

metastatic solid tumors, and AIDS/HIV), and a weight of between 1 and 6 was assigned to each comorbidity. A higher CCI indicates greater morbidity of the patient.

Outcomes

The primary outcome was the persistence rate with biologics over 12 months in the post-index period. Kaplan–Meier curves were used to assess the overall bDMARD persistence as well as the persistence with each individual bDMARD. The persistence period was defined as the time from treatment initiation (index date) until discontinuation of the index biologic or the treatment was switched to another biologic during follow-up, whichever came first. Nonpersistence occurred if (1) a gap exceeding 60 days (grace period) after the end of supply of the index bDMARD was found or (2) the patient switched from the index bDMARD to one or more non-index treatments. This definition of drug

survival was consistent with that employed in other studies of persistence [21–23]. Days of supply were calculated based on the daily defined doses (DDD) as reported by the World Health Organization for each bDMARD (Table S2 in the "Supplementary Information") [24]. Some biologics require an initiation phase with shorter treatment intervals, so the recommended dosing during the initiation phase can differ from the DDD. Stockpiling of biologic compounds was not allowed in the calculation of days of supply (renewal of a prescription during the days of supply of the first prescription set the days of supply of the first prescription to zero).

For example, an adalimumab prescription administered every two weeks would be renewed within 14 days. If it was not renewed, the gap began on day 15 and accounted for 60 days of no medical supply. In this case, the patient was still considered persistent if the prescription was renewed 74 days after the initial prescription (14 + 60 = 74), but they were considered to have discontinued after 74 days without a refill. If a patient with adalimumab as the index treatment received another biologic prescription of, for example, etanercept after 15 days, the patient was considered a switcher. If the etanercept prescription was filled on day 75 after the index prescription, the patient was considered to have discontinued.

Sensitivity Analysis

In the sensitivity analysis, the determination of discontinuation was altered by defining a treatment gap based on the particular regimen of the maintenance dosage of each bDMARD. Consequently, the treatment gap varied and was assessed individually for each bDMARD after taking the respective product information for the bDMARD (Table S5 in the "Supplementary Information") into account. For example, an adalimumab prescription administered every two weeks had an individual gap of 14 days based on the recommended dose. In this case, the patient was considered persistent if the prescription was renewed 28 days after the initial prescription (14 + 14 = 28), and was considered to have discontinued after 28 days without a refill. If a patient with adalimumab as the index treatment received another biologic prescription of, for instance, etanercept after 15 days, the patient was considered a switcher. If the etanercept prescription was filled on day 29 after the index prescription, the patient was considered to have discontinued.

Statistical Analysis

Means and standard deviations were calculated for continuous variables, and counts and percentages were calculated for categorical variables. Kaplan–Meier curves were plotted to show the overall persistence with bDMARDs and the persistence with each bDMARD. The log-rank test was used to test for statistically significant differences ($P < 0.05$) between the persistence curves. Cox regression analysis was performed to examine the association between variables such as age, gender, CCI, degree of polypharmacy, insurance status, use of corticosteroids, and presence or absence of a psoriasis diagnosis in the same quarter as the index event. The parameter estimate, standard error, Z value, $\Pr > Z$, hazard ratio (HR), and 95% confidence interval (CI) were determined for each variable included in the Cox regression. $P < 0.05$ was considered statistically significant. All analyses were undertaken using R software version 3.5.0.

RESULTS

Population Characteristics

Among the 10,954 patients diagnosed with PsA, 348 were eligible for the study (Fig. 1). The final sample included 105 patients on adalimumab, 29 on certolizumab pegol, 100 on etanercept, 20 on golimumab, 9 on infliximab, 53 on secukinumab, and 32 on ustekinumab. Table 1 shows the baseline characteristics. The mean (SD) age of the patients was 50.4 (12.4) years, and the majority of the patients (80.2%) were $\leq$ 60 years old. Most of the patients were full members (73.3%) as compared to family-

insured (6%) or pensioners (20.7%). The mean (SD) CCI score of the patients was 0.99 (1.24), and the majority of the patients had a CCI score ≤ 2 (89.1%). Most of the patients were prescribed 1–2 medications (68.7%), and the mean (SD) number of medications among the patients was 1.7 (1.03). Baseline characteristics were balanced across the different compounds (Table S6 in the "Supplementary Information").

Persistence

Table 2 shows the persistence rates. The 12-month overall bDMARD persistence rate was 57.5%, with a mean (SD) persistence of 289 (103) days. Figure 2 displays the overall Kaplan–Meier drug survival curve. Major reasons for nonpersistence were treatment discontinuation (26.7%) and switching to another therapy (15.8%). Patients most often switched to secukinumab (3.2%) or adalimumab or certolizumab pegol (both 2.9%). Among the bDMARDs, ustekinumab (81.3%), infliximab (66.7%), and golimumab (60.0%) had high persistence rates (Table 2 and Fig. 3). Mean (SD) persistence (measured in days on treatment) was 334 (72) for ustekinumab, 309 (82) for golimumab, and 305 (92) days for infliximab. The ustekinumab group showed a significantly longer duration of persistence than the other bDMARD groups except for golimumab and infliximab ($P < 0.05$ for all). Nonpersistence was highest in patients on etanercept (49.0%) and lowest in patients on ustekinumab (18.8%). Most patients discontinued their treatment rather than switching to another biologic. Patients on secukinumab were most likely to discontinue treatment (41.5%), while those on ustekinumab were least likely to discontinue treatment (15.6%). Patients on certolizumab pegol switched therapy the most (24.1%) (Table 2).

In the sensitivity analysis, the 12-month overall bDMARD persistence rate was 57.8%, with a mean (SD) persistence of 285 (110) days; among the individual bDMARDs, ustekinumab (87.5%), infliximab (66.7%), and golimumab (65.0%) had high persistence rates (Table S7 and Fig. S1 in the "Supplementary Information"). A high mean (SD) persistence (in days on treatment) was observed for ustekinumab: 344 (59); golimumab: 321 (72); and infliximab: 316 (79). The ustekinumab group showed significantly greater persistence than the other bDMARD groups except for golimumab and infliximab ($P < 0.001$ for all). Patients on secukinumab were most likely to discontinue treatment (39.6%), while those on golimumab, infliximab, and ustekinumab were least likely to discontinue treatment (< 5 patients).

Factors Affecting Risk of Treatment Discontinuation

The results of the Cox regression analysis are presented in Table 3. Male gender was significantly associated with a lower risk of treatment discontinuation (HR 0.54, 95% CI 0.39–0.77; $P < 0.001$). Although patients with a higher degree of polypharmacy or an insurance status of 'full member' or 'pensioner' had a higher risk of treatment discontinuation, these risk increases were not statistically significant (Table 3). Male gender was significantly associated with a lower risk of treatment discontinuation in the sensitivity analysis too (HR 0.51, 95% CI 0.36–0.73; $P < 0.001$) (Table S8 in the "Supplementary Information").

DISCUSSION

The overall 12-month persistence rates observed in the current study (primary analysis: 57.5%; sensitivity analysis: 57.8%) were moderate but were similar to the results of claims data-based studies from Germany (58.7% and 71.4%) [13, 15], Brazil (66.4%) [14], and the US (43.4% and 44.5%) [12, 25] covering various time periods, as well as that in a systematic review by Murage et al. (61%) [26]. Although the current study did not evaluate persistence beyond 12 months, previous research has shown that persistence rates decrease with time. Walsh et al. reported a decrease in persistence rate from 44.5% after 12 months [25] to 19.7% after 24 months [27] of follow-up. A change in persistence rate after an even longer period of time was reported by Jacob et al. [15] (from 71.4%

Table 1 Baseline characteristics

Parameter	Total (n = 348)	Men (n = 184)	Women (n = 164)
Age in years, mean (SD)	50.4 (12.4)	50.5 (11.7)	50.4 (13.2)
Age groups, n (%)			
≤ 60	279 (80.2)	149 (81.0)	130 (79.3)
61–70	49 (14.1)	25 (13.6)	24 (14.6)
> 70	20 (5.8)	10 (5.4)	10 (6.1)
Insurance status, n (%)			
Full member	255 (73.3)	149 (81.0)	106 (64.6)
Family-insured	21 (6.0)	< 5 (–)	20 (12.2)
Pensioner	72 (20.7)	34 (18.5)	38 (23.2)
CCI score, mean (SD)	0.99 (1.24)	–	–
CCI score, n (%)			
≤ 2	310 (89.1)	162 (88.0)	148 (90.2)
3–5	36 (10.3)	22 (12.0)	14 (8.5)
> 5	< 5 (–)	0	< 5 (–)
Degree of polypharmacy, mean (SD)	1.7 (1.03)	–	–
Degree of polypharmacy, n (%)			
0	46 (13.2)	24 (13.0)	22 (13.4)
1–2	239 (68.7)	132 (71.7)	107 (65.2)
3–5	63 (18.1)	28 (15.2)	35 (21.3)
Corticosteroid prescriptions/patient, mean (SD)	1.3 (1.9)		
Corticosteroid prescribed, n (%)			
No	184 (52.9)	103 (56.0)	81 (49.4)
Yes	164 (47.1)	81 (44.0)	83 (50.6)
Psoriasis diagnosis in the same quarter as the index event, n (%)			
No	62 (17.8)	26 (14.1)	36 (22.0)
Yes	286 (82.2)	158 (85.9)	128 (78.0)

Patient counts below 5 are reported as < 5 due to data protection regulations
CCI Charlson Comorbidity Index, *SD* standard deviation

after 12 months to 33.2% after 60 months of follow-up). The variation in persistence rate among these studies can be attributed to the different regions considered, clinical practices applied, databases employed, and inclusion criteria used. In the primary and sensitivity analyses of the current study, ustekinumab (81.3% and 87.5%), infliximab (66.7% for both),

Table 2 Persistence rates for biologic compounds at 12 months

Persistence	Total (*n* = 348)	ADA (*n* = 105)	CER (*n* = 29)	ETA (*n* = 100)	GOL (*n* = 20)	INF (*n* = 9)	SEC (*n* = 53)	UST (*n* = 32)
Persistence, mean no. of days (SD)	289 (103)	285 (107)*	273 (120)*	276 (110)**	309 (82)	305 (92)	291 (92)*	334 (72)
Did not persist, *n* (%)	148 (42.5)	44 (41.9)	14 (48.3)	49 (49.0)	8 (40.0)	< 5 (–)	24 (45.3)	6 (18.8)
Discontinued, *n* (%)	93 (26.7)	22 (21.0)	7 (24.1)	30 (30.0)	5 (25.0)	< 5 (–)	22 (41.5)	5 (15.6)
Switched, *n* (%)	55 (15.8)	22 (21.0)	7 (24.1)	19 (19.0)	< 5 (–)	< 5 (–)	< 5 (–)	< 5 (–)
bDMARD after first switch, *n* (%)								
ABA	< 5 (–)	0	< 5 (–)	0	0	0	0	0
ADA	10 (2.9)	0	< 5 (–)	5 (5.0)	< 5 (–)	0	0	< 5 (–)
CER	10 (2.9)	< 5 (–)	0	< 5 (–)	0	< 5 (–)	< 5 (–)	0
ETA	8 (2.3)	7 (6.7)	< 5 (–)	0	0	0	0	0
GOL	< 5 (–)	< 5 (–)	0	0	0	0	0	0
INF	< 5 (–)	< 5 (–)	0	< 5 (–)	0	0	0	0
IXE	< 5 (–)	0	0	< 5 (–)	< 5 (–)	0	< 5 (–)	0
SEC	11 (3.2)	< 5 (–)	< 5 (–)	6 (6.0)	0	0	0	0
UST	7 (2.0)	< 5 (–)	< 5 (–)	< 5 (–)	< 5 (–)	0	0	0
Persisted, *n* (%)	200 (57.5)	61 (58.1)	15 (51.7)	51 (51.0)	12 (60.0)	6 (66.7)	29 (54.7)	26 (81.3)

Patient counts below 5 are reported as < 5 due to data protection regulations

ABA abatacept, *ADA* adalimumab, *CER* certolizumab pegol, *ETA* etanercept, *GOL* golimumab, *INF* infliximab, *IXE* ixekizumab, *SD* standard deviation, *SEC* secukinumab, *UST* ustekinumab

*$P < 0.05$ and **$P < 0.01$ compared with ustekinumab using the log-rank test

and golimumab (60.0% and 65.0%) had high persistence rates. Walsh et al. also reported that 50.6% of patients persisted with ustekinumab after 12 months [25] and 27.2% persisted after 24 months [27] of follow-up. High persistence rates with ustekinumab have been consistently observed in patients with psoriasis regardless of the study design or operationalization of persistence [22, 28–31]. Data from big European registries such PSOLAR, DERMBIO, and BABDIR [32–35] as well as a recent meta-analysis support this conclusion [36]. The high persistence rate for ustekinumab may be attributed to its low immunogenicity, high efficacy, convenient administration, and favorable risk profile [37].

Consistent with previous research, in the current study, only male gender was observed to be significantly associated with a lower risk of treatment discontinuation in both the primary and sensitivity analyses. Da Silva et al. [14] evaluated a historical cohort of Brazilian patients with PsA who were treated with TNFi and reported that female gender was associated with medication nonpersistence (HR 2.65, 95% CI 1.4–5.0; $P = 0.003$). Similar results were reported by Stober et al. [38] in a single-center retrospective cohort study of patients with PsA initiating TNFi therapy (HR 2.57, 95% CI 1.3–5.2; $P = 0.01$). Previous research has also reported other factors such as age ≤ 30 years (HR 1.29, 95% CI 1.1–1.5; $P = 0.002$) [15] and

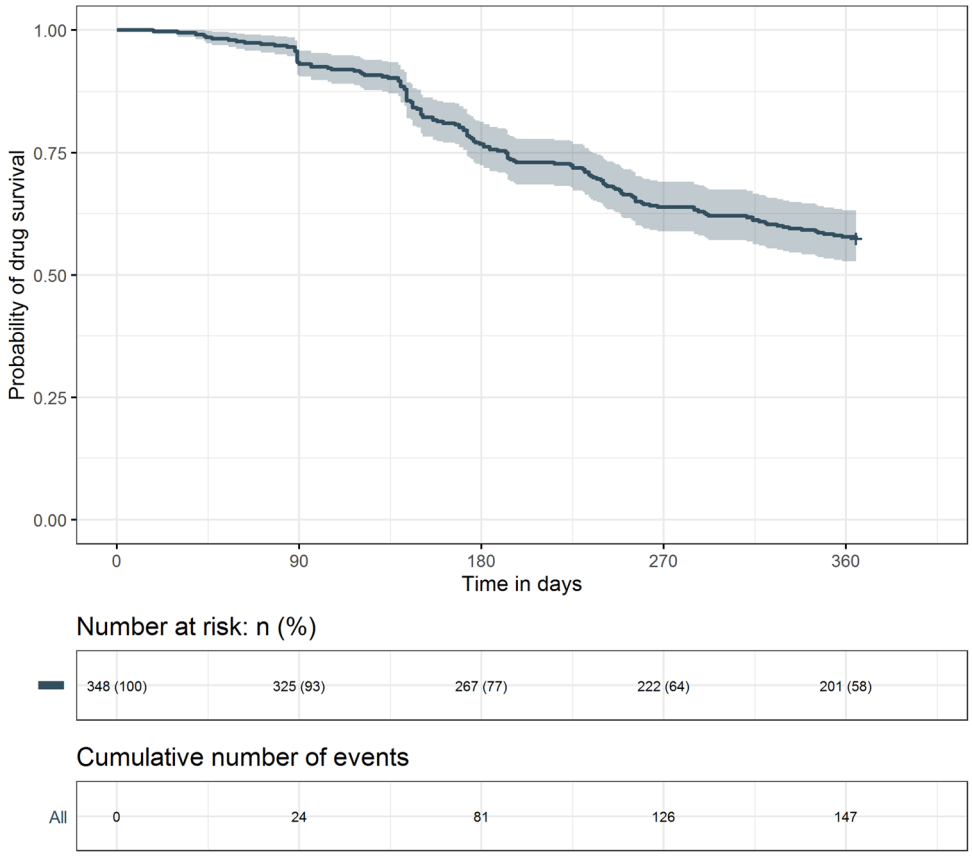

Fig. 2 Kaplan–Meier drug survival curve at 12 months for all biologics combined

any baseline metabolic syndrome-related comorbidity (HR 2.65, 95% CI 1.2–5.7; $P = 0.01$) to be associated with a lack of persistence with bDMARDs in patients with PsA [38].

The persistence rates observed in the current study suggest that usage of bDMARDs could result in better clinical and patient outcomes. However, evidence supporting such an association in the domain of PsA is unavailable. Nevertheless, there are sufficient data in other therapeutic areas to demonstrate the benefits (reduced disease activity and improved HRQoL) that result from persisting with the prescribed medication [39–41].

A recent network meta-analysis reported that bDMARDs were clinically effective and safe to use for the treatment of active PsA [42]. Moreover, continuous treatment with bDMARDs has also been reported to enhance HRQoL [43, 44] and reduce impairment of work productivity [45, 46]. The direct costs of PsA in Europe vary from US $3,693 to US $8,871 per patient-year, with biologics comprising a major proportion of the direct costs [47]. However, the usage and consequent cost of biologics are balanced by the resulting significant improvements in HRQoL and decreased work productivity losses, which result in reduced indirect costs [44, 48]. Evidence from France suggests that increased persistence with bDMARDs may result in fewer healthcare visits and costs, ultimately reducing the clinical and economic burden [49]. Therefore, further research on the impact of treatment persistence on health resource utilization in Germany is needed to quantify its economic benefits.

Limitations

There are a few limitations of the present study. This study is based on anonymized health insurance claims data obtained from the InGef

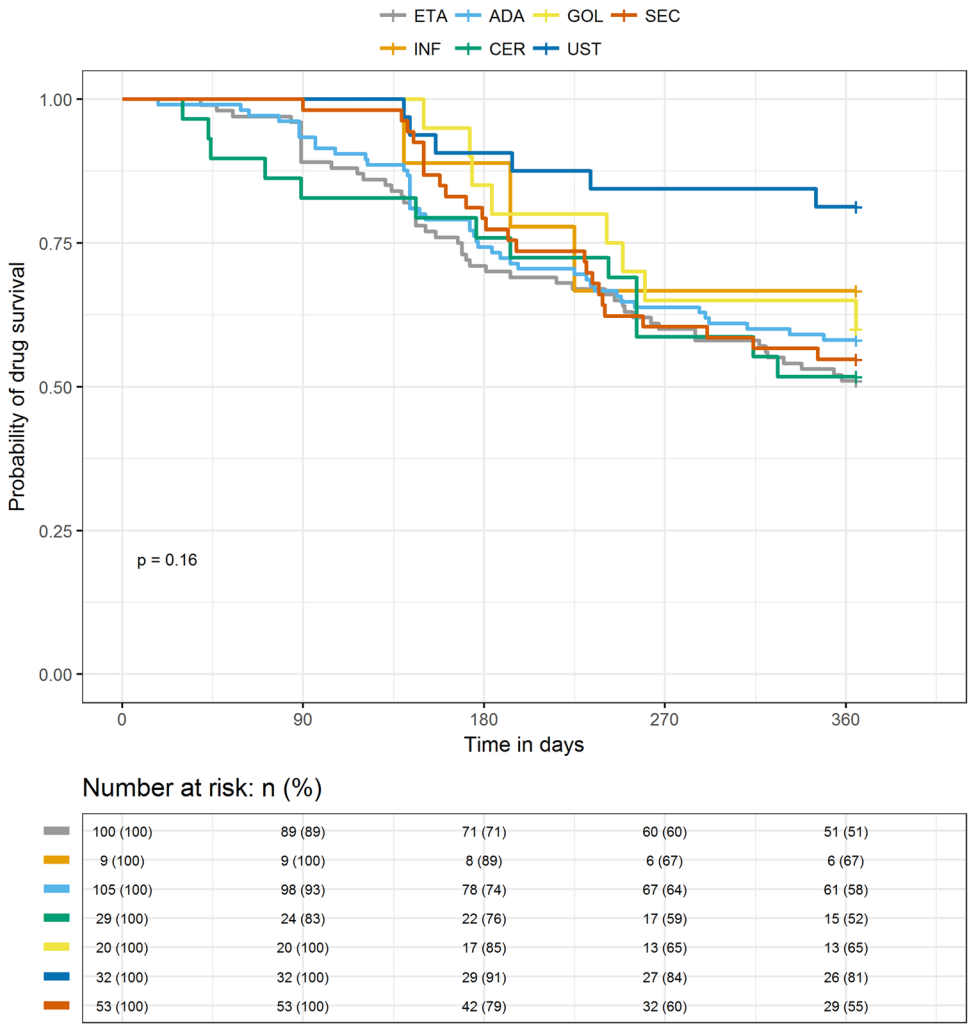

Fig. 3 Kaplan–Meier drug survival curves at 12 months for individual biologics: *ADA* adalimumab, *CER* certolizumab pegol, *ETA* etanercept, *GOL* golimumab, *INF* infliximab, *SEC* secukinumab, *UST* ustekinumab

database. Such data are routinely collected by the SHI for billing, not research, purposes. Hence, appropriate data protection provisions are implemented when using SHI claims data; moreover, single-patient case studies are not possible. As the database solely contains claims data, only recorded services can be reimbursed by the SHI. Consequently, the database does not provide clinical values (e.g., laboratory test data) or services that are not covered by the SHI catalog of benefits. Additionally, the claims data do not include data on disease severity or the quality of life of the patient, personally identifiable information, data on the efficacy and safety of prescribed medications, and data on over-the-counter medications. Therefore, classification criteria such as the Classification Criteria for Psoriatic Arthritis (CASPAR) [50] are unavailable for the entire study population. Due to the nature of health claims data, it is possible that a diagnosis of PsA was reported due to a coding error or misclassification. We included patients who did not receive biologics for 365 days before the index date; however, it is possible that some patients may have been treated with biologics prior to the 365-day washout period. The clinical domains highlighted by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) [51] were not assessed during the

Table 3 Cox regression

Parameter	Estimate (SE)	*Z*	Pr > *Z*	Hazard ratio (95% CI)
Age group (years)				
≤ 60	− 0.11 (0.43)	− 0.25	0.80	0.90 (0.39–2.08)
61–70	− 0.21 (0.42)	− 0.51	0.61	0.81 (0.36–1.84)
> 70	Reference			
Gender				
Male	− 0.61 (0.18)	− 3.45	< 0.001	0.54 (0.39–0.77)
Female	Reference			
CCI	− 0.12 (0.07)	− 1.60	0.11	0.89 (0.77–1.03)
Degree of polypharmacy				
0	Reference			
1–2	0.21 (0.27)	0.81	0.42	1.24 (0.74–2.09)
3–5	0.40 (0.31)	1.29	0.20	1.50 (0.81–2.77)
Insurance status				
Full member	0.14 (0.34)	0.42	0.67	0.16 (0.59–2.26)
Pensioner	0.14 (0.41)	0.33	0.74	1.15 (0.51–2.57)
Unknown	–	–	–	–
Family-insured	Reference			
Corticosteroid prescription				
No	Reference			
Yes	0.22 (0.17)	1.29	0.20	1.25 (0.89–1.76)
Psoriasis diagnosis in the same quarter as the index event				
No	Reference			
Yes	0.19 (0.22)	0.86	0.39	1.21 (0.78–1.88)

CCI Charlson Comorbidity Index, *CI* confidence interval, *SE* standard error

course of the study and could be assessed only approximately via ICD-10-GM diagnoses, as specific ICD-10-GM diagnosis codes are unavailable and not routinely coded by physicians. Moreover, the German ICD-10-GM catalog is not as specific as the ICD-10 Clinical Modification catalog. Although bDMARD usage was identified using the claims data, we can only presume that the medication was administered, as the data only supports receipt and payment. Moreover, bDMARD prescriptions were assessed only for the outpatient setting. We were unable to determine the cause of treatment discontinuation, which could include adverse events, lack of efficacy, or clinical remission. We also cannot rule out the possibility that different treatment intervals might influence persistence, although this is more likely in the short term. For instance, employing a three-month treatment interval for

ustekinumab and switching patients who do not adequately respond to treatment initiation to second-line treatment after a watch-and-wait period of only three months would lead to an excessive persistence value. As there was only one switcher in the ustekinumab population, we consider the magnitude of this potential bias to be small. Finally, new biologics such as ixekizumab, brodalumab, guselkumab, tildrakizumab, risankizumab, and tofacitinib were excluded from the analysis as data for these agents during the study period were unavailable. Further research can provide insights into these bDMARDs and tsDMARDs as well.

CONCLUSION

One-year persistence rates for biologics prescribed to patients with PsA in a German real-world setting were modest, but they varied depending on the bDMARD considered. This study may aid clinicians and policy makers by showing that optimal persistence can be achieved through careful treatment selection.

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Data Availability. The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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