Rheumatology International (2019) 39:525–531
https://doi.org/10.1007/s00296-018-4194-y

Rheumatology
INTERNATIONAL

PHARMACOVIGILANCE

Persistence with biological drugs in patients treated in rheumatology practices in Germany

Louis Jacob[1] · Thomas Chevalier[2] · Karel Kostev[3]

Received: 5 September 2018 / Accepted: 2 November 2018 / Published online: 24 November 2018

Abstract

The goal of this study was to investigate the persistence with biological drugs in patients treated in rheumatology practices in Germany. This study included patients diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PA), or ankylosing spondylitis (AS) who received a first prescription of biological drugs between 2008 and 2016 (index date) in 21 rheumatology practices in Germany ($n = 4925$; Disease Analyzer database). The main outcome measure was the rate of persistence within 5 years of the index date. Kaplan–Meier analyses were performed to study treatment persistence as a function of diagnosis, gender and age. A Cox proportional hazards regression model was used to estimate the relationship between non-persistence and diagnosis, gender, age, and comorbidities. After 5 years of follow-up, the rate of persistence was 31.8% in patients with RA, 35.2% in those with AS, and 33.2% in those with PA (log-rank p value = 0.028). Furthermore, 33.8% of men and 31.9% of women were persistent (log-rank p value = 0.035). The rate of persistence was 20.8%, 27.9%, 33.0%, 36.6%, 35.2%, and 32.0% in people aged ≤ 30, 31–40, 41–50, 51–60, 61–70, and > 70 years, respectively (log-rank p value = 0.002). The risk of discontinuation was lower in participants diagnosed with AS than in those diagnosed with RA [hazard ratio (HR) = 0.87; 95% confidence interval (CI) 0.79–0.96]. In addition, patients aged ≤ 30 years were more likely to discontinue their biological therapy than those aged > 70 years (HR = 1.29; 95% CI 1.10–1.52). Persistence with biological drugs was low after 5 years of follow-up in rheumatology practices.

Keywords Persistence · Biological drugs · Rheumatology practices · Germany · Retrospective study

Introduction

Rheumatoid arthritis (RA), psoriatic arthritis (PA), and ankylosing spondylitis (AS) are inflammatory diseases affecting a significant proportion of the global population [1–3]. These three inflammatory conditions pose a significant burden on healthcare systems worldwide [4–6]. In Germany, RA, PA, and AS are found in approximately 1.0%, 0.3%, and 0.9% of individuals, respectively [7–9]. These inflammatory disorders are associated with an increased risk of morbidity and mortality in Germany [10–13], underlining the need for an improvement in the management and treatment of these conditions in this country.

The prescription of biological drugs to patients with inflammatory diseases has increased in recent decades. Biological drugs are used when therapeutic goals are not reached with first-line therapies [e.g., non-steroidal anti-inflammatory drugs (NSAIDs) or conventional synthetic disease-modifying antirheumatic drugs (csDMARDs)], or when unfavorable prognostic factors, such as high disease activity or early erosions, are present [14–16]. The most frequent targets of biological drugs are cytokines, B cells, and co-stimulation molecules [15, 17–19]. Major advantages associated with the use of these treatments are established long-term efficacy, high selectivity for target molecules, and maximum compliance [20]. However, biological drugs are often prescribed on a long-term basis,

✉ Karel Kostev
kare.kostev@iqvia.com; kostev@de.imshealth.com

Louis Jacob
louis.jacob.contacts@gmail.com

Thomas Chevalier
thom2389@gmail.com

[1] Faculty of Medicine, University of Versailles Saint-Quentin-en-Yvelines, 78180 Montigny-le-Bretonneux, France

[2] Hospital Saint-Antoine, Paris, France

[3] Epidemiology, IQVIA, Commercial GmbH & Co OHG, Unterschweinstiege 2-14, 60549 Frankfurt am Main, Germany

and persistence is thus of particular importance. In recent years, several authors have investigated the rate of persistence with biological drugs in patients with RA, PA, or AS [21–34]. Although these studies have shed some light on the rate of persistence with biological drugs, and although several of them were conducted in Germany [23–25, 31], there is—to the best of our knowledge—a lack of recent data from this country. Furthermore, since most of these analyses focused solely on one inflammatory disease (e.g., RA) and several of them only on one family of drugs [e.g., Tumor Necrosis Factor (TNF) inhibitors], it is difficult to draw conclusions regarding the overall persistence with biological drugs prescribed by rheumatologists.

Therefore, the goal of this study was to investigate persistence with biological drugs in patients treated in rheumatology practices in Germany.

Methods

Database

The present retrospective study was based on the nationwide Disease Analyzer database (IQVIA). This database contains demographic, clinical, and pharmaceutical variables anonymously obtained by IQVIA from a nationwide sample of general and specialist practices [35]. The quality of these data is assessed on a regular basis, and it has been shown that the Disease Analyzer database is representative of German practices [35]. The sampling method for the Disease Analyzer database is based on summary statistics from all physicians in Germany, which are published every year by the German Medical Association. IQVIA uses these statistics to determine the panel design according to the specialist group, German federal state, community size category, and age of physician. Finally, several studies focusing on rheumatic diseases have already been conducted using this database [36–38].

Study population

The current study sample included patients who received a first prescription of biological drugs between 2008 and 2016 in 21 rheumatology practices in Germany (index date). These patients were diagnosed with RA [International Classification of Diseases, 10th revision (ICD-10): M05, M06], PA (L40.5), or AS (M45). Since no case of arthritis psoriatica (ICD-10: M07) was found, this ICD-10 code was not used for the identification of patients with PA. Participants were retrospectively followed for up to 5 years.

Study outcome

The main outcome measure was the rate of persistence within 5 years of the index date. Discontinuation was defined as a gap of at least 90 days without biological therapy, except for rituximab (270 days) [39]. The expected duration for each prescription was calculated on the basis of the package size, number of packages, and drug strength specified in the prescription. A longitudinal medication supply dataset was thereby established for each individual patient, and non-persistence with antidepressants was calculated based on these criteria. In cases where a new therapy was initiated within the 90-day window, patients were considered as persistent.

This study included 13 different biological drugs: abatacept (ATC: L04AA24), adalimumab (L04AB04), anakinra (L04AC03), certolizumab pegol (L04AB05), etanercept (L04AB01), golimumab (L04AB06), infliximab (L04AB02), ixekizumab (L04AC13), rituximab (L01XC02), secukinumab (L04AC10), tocilizumab (L04AC07), ustekinumab (L04AC05), and sarilumab (L04AC14). Other variables were diagnosis (RA, PA, or AS), gender, age, and index year. These demographic and clinical variables were available for all patients included in this study. We further selected chronic conditions that may have impacted persistence with biological drugs, although these conditions were not commonly specified by rheumatologists. These disorders were diabetes (ICD-10: E10-14), hypertension (I10), obesity (E66), and depression (F32, F33). Finally, prescriptions of systemic corticosteroids within 6 months prior to the index date were included [Anatomical Therapeutic Chemical (ATC) Classification System: H02].

Statistical analyses

Kaplan–Meier analyses were performed to study treatment persistence as a function of diagnosis, gender, and age. Individuals were censored at the time of loss to follow-up or treatment discontinuation, whichever occurred first. A Cox proportional hazards regression model was further used to estimate the relationship between non-persistence and diagnosis, gender, age, and comorbidities. It was not possible to stratify any of the previous analyses by the type of drug (e.g., abatacept). A p value < 0.05 was considered statistically significant. All analyses were carried out using SAS 9.4 (SAS Institute, Cary, USA).

Table 1 Basic characteristics of study patients

Variable	Number (*N*) and proportion (%)
N	4925
Women	3048 (61.9)
Men	1877 (38.1)
Age (Mean, SD)	52.2 (14.6)
Age ≤ 30	454 (9.2)
Age 31–40	605 (12.3)
Age 41–50	1048 (21.3)
Age 51–60	1393 (28.3)
Age 61–70	865 (17.6)
Age > 70	560 (11.4)
Diagnoses (ICD-10 Codes)	
Rheumatoid arthritis (M05, M06)	3358 (68.2)
Ankylosing spondylitis (M45)	1024 (20.8)
Psoriatic arthritis (L40.5)	543 (11.0)
Index year: 2008	411 (8.4)
Index year: 2009	581 (11.8)
Index year: 2010	483 (9.8)
Index year: 2011	468 (9.5)
Index year: 2012	487 (9.9)
Index year: 2013	650 (13.2)
Index year: 2014	638 (13.0)
Index year: 2015	577 (11.7)
Index year: 2016	630 (12.8)
Documented co-diagnoses (ICD-10 codes)	
Diabetes (E10-14)	442 (9.0)
Hypertension (I10)	961 (19.5)
Obesity (E66)	316 (6.4)
Depression (F32, F33)	328 (6.7)
Prescription of a systemic corticosteroid within 6 months prior to the index date (ATC: H02)	2082 (42.3)

ICD-10 International Classification of Diseases, 10th revision, *ATC* anatomical therapeutic chemical

Results

Patient characteristics are shown in Table 1. A total of 4925 patients followed in rheumatology practices were included in the present study. Of these, 61.9% were women, and the mean patient age was 52.2 years (SD = 14.6 years). The most frequent diagnosis was RA (68.2%). After 1 year of follow-up, 68.2% of patients with RA, 72.1% of those with AS, and 71.4% of those with PA were persistent with their treatment (log-rank *p* value < 0.001; Fig. 1). After 5 years of follow-up, the rate of persistence was 31.8% in patients with RA, 35.2% in those with AS, and 33.2% in those with PA (log-rank *p* value = 0.028). Furthermore, 33.8% of men and 31.9% of women were persistent (log-rank *p* value = 0.035; Fig. 2). The rate of persistence was 20.8%, 27.9%, 33.0%, 36.6%, 35.2%, and 32.0% in people aged ≤ 30, 31–40, 41–50, 51–60, 61–70 and > 70 years, respectively (log-rank *p* value = 0.002; Fig. 3). In the rheumatology practice with the lowest proportion of patients with a persistence duration of at least 5 years, 15% of patients were persistent, and in the practice with the highest proportion, 53% were persistent.

Table 2 shows the results of the Cox proportional hazard regression model. The risk of discontinuation was lower in participants diagnosed with AS than in those diagnosed with RA [hazard ratio (HR) = 0.87; 95% confidence interval (CI) 0.79–0.96]. In addition, patients aged ≤ 30 years were more likely to discontinue their biological therapy than those aged > 70 years (HR = 1.29; 95% CI 1.10–1.52).

Discussion

The present study found that persistence with biological drugs was between 32% and 34% after 5 years of treatment in rheumatology practices. Moreover, the risk of non-persistence was significantly lower in participants with AS than in those with RA. Finally, young patients were more likely to discontinue biological drug therapy than older patients.

One major finding of this study is that persistence with biological drugs was relatively low. With respect to RA, Fisher and colleagues observed in 2923 patients that median persistence was 3.7 years for infliximab, 3.3 years for adalimumab, and 3.8 years for etanercept [22]. Later, Mahlich and Sruamsiri showed that persistence with biological drugs was higher than 85% after 1 year of treatment in 16214 patients with RA from Japan [27]. Interestingly, persistence was higher in the elderly and lower in people with a high comorbidity score. Finally, in 2018, Lee and colleagues reported that 1-year persistence with biological drugs was between 53 and 56% in a cohort of 4114 individuals with RA [33]. The fact that we obtained higher persistence rates after 1 year of follow-up in our retrospective study is likely explained by the fact that the gap used for the definition of discontinuation was longer in our study (90 days) than in the Lee study (45 days) as well as the fact that these analyses were conducted in different countries (Germany and South Korea).

In 2009, Saad et al. showed that approximately 82%, 70%, and 59% of the population in a study involving 566 participants with PA remained on the first anti-TNF drug after 1, 2, and 3 years of treatment, respectively [21]. More recently, in 2016, Palmer and colleagues observed in 990 PA patients receiving anti-TNFα drugs that mean persistence was approximately 17 months in those receiving first-line therapy [28]. Two years later, Fagerli et al. estimated that approximately 47% of 625 participants diagnosed with PA remained on their initial anti-TNFα therapy after 5 years of

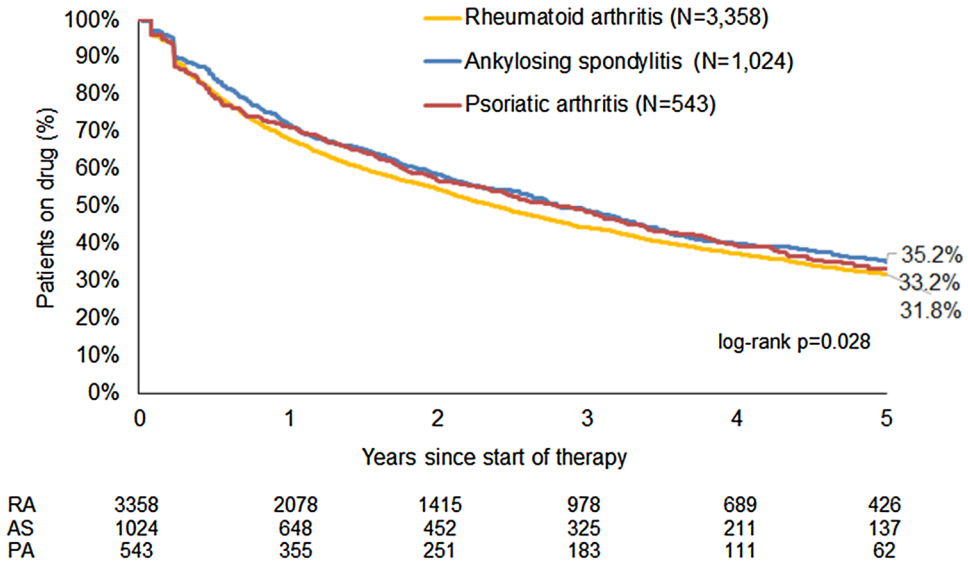

Fig. 1 Kaplan–Meier curves for persistence with biological drugs by diagnosis after 5 years of follow-up in rheumatology practices in Germany

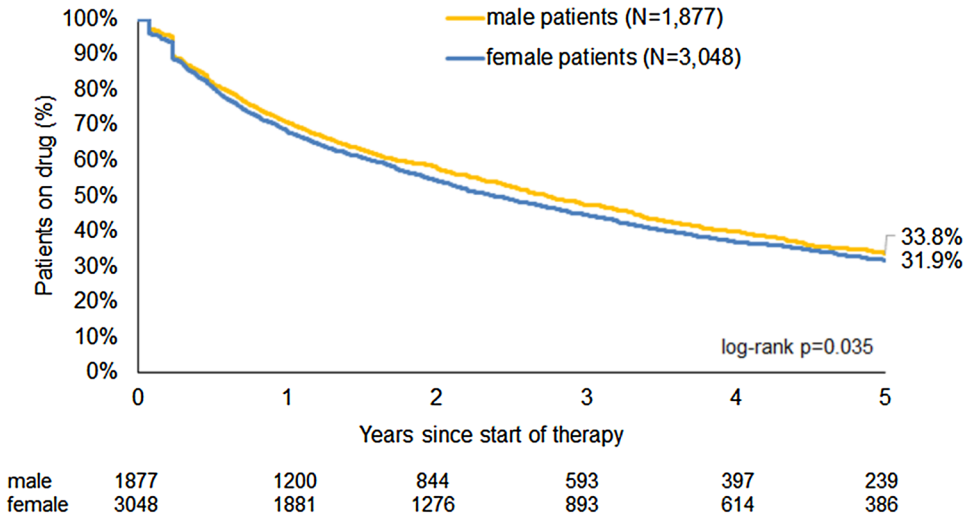

Fig. 2 Kaplan–Meier curves for persistence with biological drugs by gender after 5 years of follow-up in rheumatology practices in Germany

treatment [32]. Five-year persistence was positively associated with male gender, prescription of etanercept or adalimumab (as opposed to infliximab), and absence of comorbidity at baseline. Since the definition of persistence was similar in this UK study and the present study conducted in Germany, it is very likely that there are some important differences between these two countries in terms of persistence with biological drugs in patients with PA.

Regarding AS, Govoni et al. discovered that more than 46% of the population were persistent with subcutaneous biological therapies for at least 1 year in a 2014 retrospective study including 108 patients from Germany [23]. In 2016, Machado and colleagues observed that 1-year persistence was around 79% in the anti-TNFα ± DMARD group and 41% in the DMARD group in a study involving 1251 individuals with AS [26]. Finally, in 2018, researchers from the U.S. showed in 426 patients with AS that approximately 41% persisted with the index anti-TNFα drug for at least 12 months, 31% discontinued, 21% switched to another anti-TNFα drug, and 7% discontinued and then restarted [34]. Interestingly, we obtained a higher rate of persistence with biological drugs in patients with AS after 1 year of follow-up (72%). Again, this may be related to the fact that we used a longer interval for the definition of non-persistence (90 days) than the Machado study (30 days) [26]. Moreover, these studies were conducted in different settings [23, 26, 34], and it is possible that treatment and management of AS are not homogeneous across these settings.

Another interesting result of our retrospective study is that younger individuals were at a higher risk of discontinuation than older individuals. This finding is in line with the literature since the Mahlich and Sruamsiri study showed that this risk was lower in RA patients older than 75 years than in those 60 years or younger [27]. They hypothesized that

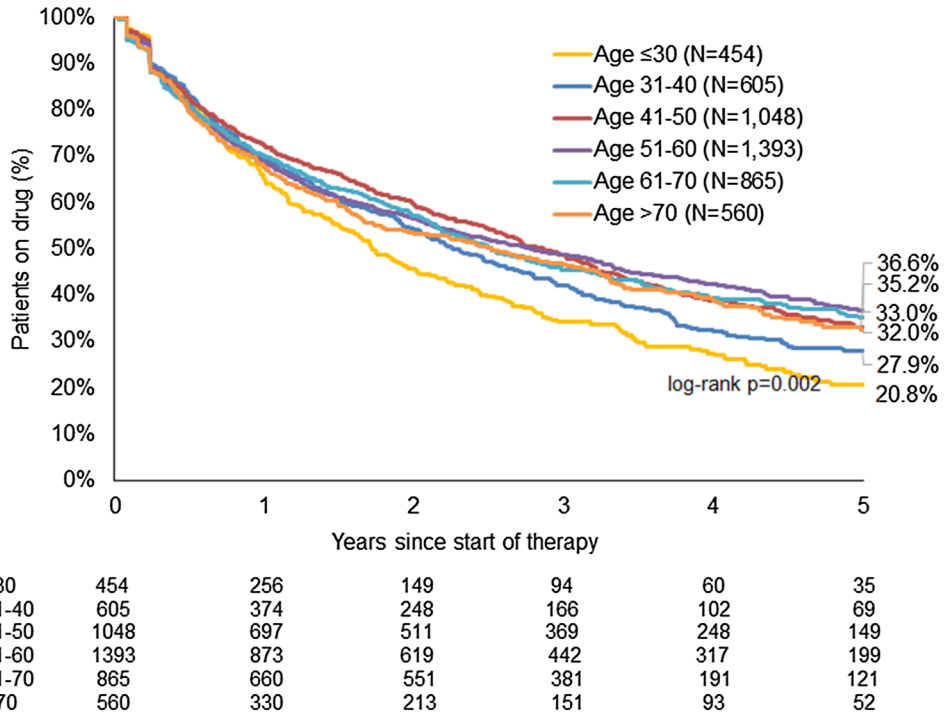

Fig. 3 Kaplan–Meier curves for persistence with biological drugs by age after 5 years of follow-up in rheumatology practices in Germany

Table 2 Association between discontinuation of biological drugs and defined variables in patients treated in rheumatology practices (Cox regression analyses)

Variable	Hazard ratio (95% CI)[a]	*p* value
Rheumatoid arthritis (M05, M06)	Reference	
Ankylosing spondylitis (M45)	0.87 (0.79–0.96)	0.005
Psoriatic arthritis (L40.5)	0.95 (0.85–1.07)	0.449
Women	Reference	
Men	0.96 (0.89–1.03)	0.238
Age ≤ 30	1.29 (1.10–1.52)	0.002
Age 31–40	1.13 (0.97–1.31)	0.112
Age 41–50	0.99 (0.87–1.13)	0.869
Age 51–60	0.96 (0.84–1.08)	0.474
Age 61–70	0.96 (0.84–1.10)	0.543
Age > 70	Reference	
Diabetes	1.04 (0.92–1.18)	0.533
Hypertension	1.04 (0.95–1.14)	0.385
Obesity	0.88 (0.76–1.02)	0.099
Depression	1.05 (0.92–1.20)	0.489
Prescription of a systemic corticosteroid within 6 months prior to the index date	0.95 (0.89–1.03)	0.206

[a]Multivariate Cox regression, adjusted for diagnosis, gender, age, and comorbidities

the acceptance of disease is higher in the elderly than in young people and that elderly people are followed more frequently by rheumatologists than young people because they are at a great risk for drug interactions and side effects. In addition, we found that AS was associated with a significantly decreased risk of biological drug treatment discontinuation compared to RA. In 2007, Brocq et al. showed in 442 patients with inflammatory joint disease that individuals with AS were more persistent than those with RA [40]. It was hypothesized that escape phenomenon, infections, and absence of therapeutic response are more common in patients with RA than in those with AS [26].

Although these findings are of great interest, this study is subject to several limitations that should be acknowledged at this point. First, there was no information regarding disease severity, even if such severity may play an important role in persistence with biological drugs. Second, we had no access to the data of patients followed in hospitals. Third, information on social status was not available. Fourth, we could not investigate the reasons for discontinuation (e.g., escape phenomenon, side effects, infections, clinical remission, or absence of response). Thus, it is possible that the higher persistence rate observed in patients with AS may not only be due to differences in patient profiles but also to the fact that there are fewer treatment options available to these patients. Finally, since non-rheumatic disorders (e.g., diabetes or depression) were not commonly documented by rheumatologists, this may explain why these comorbidities were not significantly associated with persistence with biological drugs in our study.

Overall, persistence with biological drugs was low in patients treated in rheumatology practices in Germany. Age and type of disorder had a significant impact on the risk of discontinuation. Further studies are needed to gain a better

understanding of the reasons for non-persistence in individuals with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis followed in this setting.

Author contributions LJ and TC contributed to the interpretation of the data, drafted the manuscript and gave the final approval of the version to be published. KK contributed to the conception and the design of the study, revised the manuscript critically for important content, and gave the final approval of the version to be published.

Funding The authors have received no financial support for the research, authorship, and/or publication of this article.

Compliance with ethical standards

Conflict of interest Karel Kostev is an employee of IQVIA. IQVIA (https://www.iqvia.com/) is a commercial research institute providing information, services and technology for the healthcare industry. The other authors declare that they have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval German law allows the use of anonymous electronic medical records for research purposes under certain conditions. According to this legislation, it is not necessary to obtain informed consent from patients or approval from a medical ethics committee for this type of observational study that contains no directly identifiable data. Because patients were only queried as aggregates and no protected health information was available for queries, no IRB approval was required for the use of this database or the completion of this study.

References

1. Silman AJ, Pearson JE (2002) Epidemiology and genetics of rheumatoid arthritis. Arthritis Res 4(Suppl 3):S265–S272. https://doi.org/10.1186/ar578
2. Stolwijk C, van Onna M, Boonen A, van Tubergen A (2016) Global prevalence of spondyloarthritis: a systematic review and meta-regression analysis. Arthritis Care Res 68:1320–1331. https://doi.org/10.1002/acr.22831
3. Scotti L, Franchi M, Marchesoni A, Corrao G (2018) Prevalence and incidence of psoriatic arthritis: a systematic review and meta-analysis. Semin Arthritis Rheum 48:28–34. https://doi.org/10.1016/j.semarthrit.2018.01.003
4. Boonen A, Linden SM van der (2006) The burden of ankylosing spondylitis. J Rheumatol Suppl 78:4–11
5. Lee S, Mendelsohn A, Sarnes E (2010) The burden of psoriatic arthritis. Pharm Ther 35:680–689
6. Cross M, Smith E, Hoy D et al (2014) The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis 73:1316–1322. https://doi.org/10.1136/annrheumdis-2013-204627
7. Braun J, Bollow M, Remlinger G et al (1998) Prevalence of spondylarthropathies in HLA-B27 positive and negative blood donors. Arthritis Rheum 41:58–67
8. Hense S, Luque Ramos A, Callhoff J et al (2016) Prevalence of rheumatoid arthritis in Germany based on health insurance data: regional differences and first results of the PROCLAIR study. Z Rheumatol 75:819–827. https://doi.org/10.1007/s00393-016-0088-0
9. Jacob C, Meier F, Neidhardt K et al (2016) Epidemiology and costs of psoriatic arthritis in Germany—a retrospective claims data analysis. Value Health 19:A566. https://doi.org/10.1016/j.jval.2016.09.1268
10. Reich K, Krüger K, Mössner R, Augustin M (2009) Epidemiology and clinical pattern of psoriatic arthritis in Germany: a prospective interdisciplinary epidemiological study of 1511 patients with plaque-type psoriasis. Br J Dermatol 160:1040–1047. https://doi.org/10.1111/j.1365-2133.2008.09023.x
11. Braun J, Kellner H, Max R, Rihl M, Schmitz-Bortz E, Schulze-Koops H, Zinke S, Fan T, Ding Q, Lyu R (2013) Disease severity, quality of life, and productivity loss among patients with ankylosing spondylitis in Germany. 2013 ACR/ARHP Annual Meeting **(Abstract Number: 1012)**
12. Gerhold K, Richter A, Schneider M et al (2015) Health-related quality of life in patients with long-standing rheumatoid arthritis in the era of biologics: data from the German biologics register RABBIT. Rheumatol Oxf Engl 54:1858–1866. https://doi.org/10.1093/rheumatology/kev194
13. Haase I, Pongratz G, Sander O et al (2018) SAT0698 Mortality of patients with diagnosed rheumatoid arthritis (RA) in germany 2012: analysis of claims data from 60 million people. Ann Rheum Dis 77:1196–1197. https://doi.org/10.1136/annrheumdis-2018-eular.1651
14. Gossec L, Smolen JS, Ramiro S et al (2016) European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis 75:499–510. https://doi.org/10.1136/annrheumdis-2015-208337
15. Smolen JS, Landewé R, Bijlsma J et al (2017) EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 76:960–977. https://doi.org/10.1136/annrheumdis-2016-210715
16. van der Heijde D, Ramiro S, Landewé R et al (2017) 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis 76:978–991. https://doi.org/10.1136/annrheumdis-2016-210770
17. Rosman Z, Shoenfeld Y, Zandman-Goddard G (2013) Biologic therapy for autoimmune diseases: an update. BMC Med 11:88. https://doi.org/10.1186/1741-7015-11-88
18. D'Angelo S, Tramontano G, Gilio M et al (2017) Review of the treatment of psoriatic arthritis with biological agents: choice of drug for initial therapy and switch therapy for non-responders. Open Access Rheumatol Res Rev 9:21–28. https://doi.org/10.2147/OARRR.S56073
19. Ungprasert P, Erwin PJ, Koster MJ (2017) Indirect comparisons of the efficacy of biological agents in patients with active ankylosing spondylitis: a systematic review and meta-analysis. Clin Rheumatol 36:1569–1577. https://doi.org/10.1007/s10067-017-3693-7
20. Mócsai A, Kovács L, Gergely P (2014) What is the future of targeted therapy in rheumatology: biologics or small molecules? BMC Med 12:43. https://doi.org/10.1186/1741-7015-12-43
21. Saad AA, Ashcroft DM, Watson KD et al (2009) Persistence with anti-tumour necrosis factor therapies in patients with psoriatic arthritis: observational study from the British Society of Rheumatology Biologics Register. Arthritis Res Ther 11:R52. https://doi.org/10.1186/ar2670
22. Fisher A, Bassett K, Wright JM et al (2014) Comparative persistence of the TNF antagonists in rheumatoid arthritis—a population-based cohort study. PLoS One 9:e105193. https://doi.org/10.1371/journal.pone.0105193
23. Govoni M, Lyu R, Ding Q, Fan T (2014) Persistence rate with subcutaneous biologic therapies in patients with ankylosing spondylitis (As). Value Health J Int Soc Pharmacoeconomics Outcomes Res 17:A384. https://doi.org/10.1016/j.jval.2014.08.2635

24. Neubauer S, Cifaldi M, Mittendorf T et al (2014) Biologic TNF inhibiting agents for treatment of rheumatoid arthritis: persistence and dosing patterns in Germany. Health Econ Rev 4:32. https://doi.org/10.1186/s13561-014-0032-4
25. Lyu R, Govoni M, Ding Q et al (2016) Treatment persistence among patients with rheumatoid disease (RA, AS, PsA) treated with subcutaneous biologics in Germany. Rheumatol Int 36:143–153. https://doi.org/10.1007/s00296-015-3348-4
26. Machado MA de Á, Moura CS de, Ferré F et al (2016) Treatment persistence in patients with rheumatoid arthritis and ankylosing spondylitis. Rev Saude Publica 50:50. https://doi.org/10.1590/S1518-8787.2016050006265
27. Mahlich J, Sruamsiri R (2016) Persistence with biologic agents for the treatment of rheumatoid arthritis in Japan. Patient Prefer Adherence 10:1509–1519. https://doi.org/10.2147/PPA.S110147
28. Palmer JB, Li Y, Herrera V et al (2016) Treatment patterns and costs for anti-TNFα biologic therapy in patients with psoriatic arthritis. BMC Musculoskelet Disord 17:261. https://doi.org/10.1186/s12891-016-1102-z
29. Chastek B, Chen C-I, Proudfoot C et al (2017) Treatment persistence and healthcare costs among patients with rheumatoid arthritis changing biologics in the USA. Adv Ther 34:2422–2435. https://doi.org/10.1007/s12325-017-0617-5
30. Degli Esposti L, Favalli EG, Sangiorgi D et al (2017) Persistence, switch rates, drug consumption and costs of biological treatment of rheumatoid arthritis: an observational study in Italy. Clin Outcomes Res CEOR 9:9–17. https://doi.org/10.2147/CEOR.S108730
31. Wilke T, Mueller S, Lee SC et al (2017) Drug survival of second biological DMARD therapy in patients with rheumatoid arthritis: a retrospective non-interventional cohort analysis. BMC Musculoskelet Disord 18:332. https://doi.org/10.1186/s12891-017-1684-0
32. Fagerli KM, Kearsley-Fleet L, Watson KD et al (2018) Long-term persistence of TNF-inhibitor treatment in patients with psoriatic arthritis. Data from the British Society for Rheumatology Biologics Register. RMD Open 4:e000596. https://doi.org/10.1136/rmdopen-2017-000596
33. Lee M-Y, Shin J-Y, Park S-Y et al (2018) Persistence of biologic disease-modifying antirheumatic drugs in patients with rheumatoid arthritis: an analysis of the South Korean National Health Insurance Database. Semin Arthritis Rheum 47:485–491. https://doi.org/10.1016/j.semarthrit.2017.08.007
34. Walsh JA, Adejoro O, Chastek B, Park Y (2018) Treatment patterns of biologics in US patients with ankylosing spondylitis: descriptive analyses from a claims database. J Comp Eff Res 7:369–380. https://doi.org/10.2217/cer-2017-0076
35. Rathmann W, Bongaerts B, Carius HJ, Kruppert S (2018) Basic characteristics and representativeness of the German Disease Analyzer database. Int J Clin Pharmacol Ther 56(10):459–466. https://doi.org/10.5414/CP203320
36. Gossen N, Jacob L, Kostev K (2016) Second-line therapy with biological drugs in rheumatoid arthritis patients in German rheumatologist practices: a retrospective database analysis. Rheumatol Int 36:1113–1118. https://doi.org/10.1007/s00296-016-3448-9
37. Drosselmeyer J, Jacob L, Rathmann W et al (2017) Depression risk in patients with late-onset rheumatoid arthritis in Germany. Qual Life Res Int J Qual Life Asp Treat Care Rehabil 26:437–443. https://doi.org/10.1007/s11136-016-1387-2
38. Ziegelbauer K, Kostev K, Hübinger M et al (2018) The impact of non-persistence on the direct and indirect costs in patients treated with subcutaneous tumour necrosis factor-alpha inhibitors in Germany. Rheumatol Oxf Engl. https://doi.org/10.1093/rheumatology/key099
39. Oldroyd AGS, Symmons DPM, Sergeant JC et al (2018) Long-term persistence with rituximab in patients with rheumatoid arthritis. Rheumatol Oxf Engl 57:1089–1096. https://doi.org/10.1093/rheumatology/key036
40. Brocq O, Roux CH, Albert C et al (2007) TNFalpha antagonist continuation rates in 442 patients with inflammatory joint disease. Jt Bone Spine Rev Rhum 74:148–154. https://doi.org/10.1016/j.jbspin.2006.06.011