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ORIGINAL RESEARCH ARTICLE

Drug utilization and medication adherence for the treatment of psoriatic arthritis: an Italian study

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ABSTRACT

Introduction: This study aims to evaluate the persistence, treatment adherence and drug cost associated with biologic and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) in the management of psoriatic arthritis (PsA) in Italy, with a focus on biosimilar drugs.

Methods: This was a retrospective observational study involving eight hospital pharmacies, between January 2017 and December 2020, on naïve patients with at least one b/tsDMARD dispensation indicated for PsA. Patients were followed up for 12 months and persistence and adherence were evaluated by proportion of days covered (PDC). The originator and biosimilar for adalimumab and etanercept were compared. Furthermore, the real annual cost per patient based on adherence to therapy was calculated.

Results: Patients initiating b/tsDMARDs for PsA had a mean persistence of 263 days and 48.6% remained persistent for 1 year. Adherent patients (PDC ≥ 0.8) were 47.6% for the overall population. Similar persistence and adherence were observed between patients treated with the adalimumab originator and its biosimilar, while patients treated with the etanercept originator showed lower persistence and adherence compared to those treated with its biosimilar (mean persistence: 222 vs. 267 days, patient persistent at 1 year: 29.4% vs. 51.5%, mean PDC: 0.53 vs. 0.70, adherent patients: 23.5% vs. 51.5%). The average annual drug cost ranged from €8,724 (etanercept) to €14,783 (ustekinumab), with an annual saving of more than €2,500 by using biosimilars.

Conclusion: Poor adherence to medications contributes to suboptimal clinical outcomes. The comparison between biosimilar and originator offers further evidence in support of the biosimilar to optimizing resources in healthcare.

Keywords: Adherence, bDMARDs, Biosimilar, Persistence, Psoriatic arthritis

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Introduction

Psoriatic arthritis (PsA) is a complex and debilitating chronic inflammatory systemic disease that combines articular and periarticular manifestations with extra-musculoskeletal manifestations (1). PsA has an incidence that ranges approximately from 3.6 to 7.2 per 100,000 person years and a prevalence of

approximately 1 to 2 per 1000 in the general population (2-4). Although PsA has a low prevalence in the general population, it is often associated with psoriasis; the estimates of the prevalence of PsA among patients with psoriasis range from 14 to 41 per 100 (5-7).

PsA symptoms, as well as comorbidities, can have a profound impact on patients' quality of life and may even shorten their life expectancy. An early diagnosis, a thorough assessment of the disease and a suitable treatment are the pillars to guarantee the best outcome for patients with PsA (8).

Over the past two decades, treatment options for PsA have expanded considerably with the introduction of several new biologic and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs). Not only tumor necrosis factor inhibitors (TNFis; adalimumab, certolizumab, etanercept, golimumab and infliximab) but also interleukin (IL)-17A inhibitors (ixekizumab and secukinumab), IL-12/23 inhibitors (ustekinumab), IL-23 inhibitors (guselkumab, risankizumab, and tildrakizumab), Janus kinase inhibitors (JAKis; tofacitinib and upadacitinib), cytotoxic T-lymphocyte–associated protein 4 blockade (abatacept), phosphodiesterase 4 inhibitors (apremilast) and, most recently, a IL-17A/IL-17F inhibitor (bimekizumab) are now recommended for PsA when conventional synthetic DMARDs (csDMARDs) fail to control disease or are not tolerated (9-11)

The World Health Organization (WHO) considers adherence to treatment as taking medication according to the prescribed dosage and with persistence over time (12). Therapeutic adherence is a key component of the management of chronic diseases and is of fundamental importance for the success of the therapeutic regimen through improvement of patient's health outcomes and reduction of healthcare costs (13) Conversely, poor medication adherence can significantly increase the risk of treatment failure, worsen patient health outcomes and generate additional financial burden (14). In the treatment of PsA, adherence is crucial and continuous monitoring of the drug's use, in terms of implementation and persistence to therapy, can help healthcare professionals and patients to achieve greater awareness and improve the benefits and outcomes.

The introduction of the biosimilars for adalimumab and etanercept, which promise overlap in terms of efficacy and safety compared to the originators with significantly lower costs, has changed the landscape of bDMARDs (15). In this regard, being able to provide real-world data comparing originators and biosimilars through drug utilization studies could help understand the real impact of biosimilars and, consequently, increase their use in clinical practice.

The aim of this study was to evaluate the persistence, treatment adherence and drug cost associated with b/tsDMARDs in the management of PsA in Italy by conducting a retrospective observational study with a focus on biosimilar drugs.

Methods

A retrospective observational cohort study involving eight hospital pharmacies distributed in five regions of Italy (Piemonte, Lombardia, Lazio, Abruzzo and Puglia) was conducted. This study evaluated the use of b/tsDMARDs for the treatment of PsA. Since patients obtain these medications from the hospital pharmacy based on a specialist's prescription, the data from hospital pharmacies can be used to study therapeutic continuity. For this study, treatment plans were used to identify patients and the PsA indication, while administrative databases were used to collect information on drug dispensations from hospital pharmacies. Only drugs administered subcutaneously and orally were considered, since patients are assumed to be adherent to drugs administered intravenously. Data collection ranged from January 2017 to December 2020 and information on patients' demographics, therapeutic indication, drug dispensed, quantity, dosage and date of dispensation was collected. The study followed the approval by the pertinent ethical committees and competent authorities, in accordance with all the regulations in force and regulatory requirements.

All patients with at least one b/tsDMARD dispensation with indication for PsA between 1 January 2018 and 31 December 2019 were included and the date of the first drug dispensation during this period constituted the index date. The study was performed on naïve patients, who were defined as patients without any b/tsDMARDs in the year preceding the index date. Only patients at least 18 years of age on the index date were considered.

Patients were followed up for 12 months from the index date (follow-up period) for outcome evaluation and patients with only one prescription during the follow-up were excluded from the analysis. This follow-up period was selected based on the duration commonly used in similar published studies. The duration of the medication supplied was determined based on the quantity of pills, syringes and packages and by considering the prescribed dosage recorded in the therapeutic plan and, if not available, the standard posology. Furthermore, a 60-day permissible gap between two successive drug dispensations was considered to define the discontinuation of therapy, that is, therapy was considered discontinued if no refill of the index drug within 60 days was collected after the previous days' supply was exhausted (16).

Persistence was defined as the number of days of continuous therapy from index date until one of the following events: therapy discontinuation, switch to a different treatment or end of the follow-up, whichever occurred first. Stockpiling of drugs 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).

To evaluate adherence to the treatment, proportion of days covered (PDC) was calculated as the number of days in which a patient had access to the medication (number of days covered by prescriptions) divided by the number of days of the follow-up period regardless of discontinuation, that is, 365 days. To identify patients who were adherent to their medication, those with PDC ≥ 80% were classified as adherent, as conventionally reported (17).

Furthermore, an additional analysis was conducted to evaluate the comparison between the originator and the biosimilar drugs for adalimumab and etanercept. In this analysis, new patients in treatment with the originator and biosimilar

drug were followed from the index date until therapy discontinuation, switch to a different treatment, also including the respective originator or biosimilar, or end of the follow-up. The aim of this analysis was to compare the persistence and adherence data of patients treated with adalimumab and etanercept, comparing patients treated with the originator vs. patients treated with the biosimilar. The same methodologies and statistical analyses utilized for the main analysis were used for this analysis.

Finally, a cost analysis considering only the cost of the drug was carried out accounting the ex-factory costs of the drugs updated in November 2023 and calculating the real annual cost per patient based on the actual adherence to therapy. The mean annual cost was calculated considering only patients who were persistent at 1 year and adhered to the treatment (PDC≥0.8).

Statistical analysis

The baseline characteristics were assessed using descriptive statistics. Continuous variables were summarized using means and standard deviations (SDs) or medians and interquartile ranges (IQRs), while categorical variables were presented using absolute and relative frequencies. Mean persistence in days, proportion of patients who were persistent at 1 year, mean PDC and proportion of patients adhering to treatment (PDC≥0.8) were also calculated. The time to discontinuation (persistence) was modeled using Cox proportional hazards regression models and the adherence to treatment (PDC ≥ 0.80) using logistic regression model. The covariates used in those models included age, gender and treatment. Adjusted odds ratio (OR) and 95% confidence intervals (CIs) were reported for the logistic regression model while adjusted hazard ratio (HR) and 95% CI were reported for the Cox regression model. All the analyses were performed using SAS® software, version 9.4.

Results

A total of 685 patients initiated treatment with b/tsDMARDs during 2018-2019. In particular, 25.7% patients were treated with adalimumab, 19.7% with etanercept, 19.3% with apremilast, 17.2% with secukinumab (Tab. 1). Six patients who initiated treatment with ixekizumab, 5 with infliximab and 1 with abatacept were excluded from the analysis due to the insufficient number of patients, while in the period considered no patient started the treatment with other b/tsDMARDs not previously mentioned.

Overall, 62.3% patients were female, and the median age of the population was 55 years. Demographic characteristics were quite similar among the groups, with a slightly higher proportion of females and younger patients observed in the certolizumab group (Tab. 1).

The mean persistence period was 263 days and approximately half of the population (48.6%) remained persistent at 1 year (Tab. 2). Time to discontinuation was similar between groups and ranged from 255 days (secukinumab) to 271 days (golimumab). Patients who were persistent at 1 year ranged from 42.9% (ustekinumab) to 58.6% (golimumab). Overall, the mean PDC was 0.68 and adherent patients (PDC ≥ 0.8) were 326 (47.6%) (Tab. 2). The prescribed dose was missing on 13.9% of the data.

The results of the Cox proportional hazard regression analysis, assessing the factors associated with the time to discontinuation, and of the logistic regression analysis revealing the factors associated with adherence to treatment are reported in Table 3. Male patients were significantly associated with a longer time to discontinuation compared to females (HR 0.76, p = 0.020), while patients treated with apremilast were more likely to be adherent in comparison with patients treated with secukinumab (OR 1.98, p = 0.009).

The results of the additional analysis performed on adalimumab and etanercept aimed at studying the differences

TABLE 1 - Baseline patient characteristics stratified by treatment

	Adalimumab n = 176 (25.7%)	Apremilast n = 132 (19.3%)	Certolizumab n = 60 (8.8%)	Etanercept n = 135 (19.7%)	Golimumab n = 29 (4.2%)	Secukinumab n = 118 (17.2%)	Ustekinumab n = 35 (5.1%)	Overall n = 685
Sex, n (%)								
Female	108 (61.4)	81 (61.4)	52 (86.7)	77 (57.0)	15 (51.7)	70 (59.3)	24 (68.6)	427 (62.3)
Male	68 (38.6)	51 (38.6)	8 (13.3)	58 (43.0)	14 (48.3)	48 (40.7)	11 (31.4)	258 (37.7)
Age (in years), median (IQR)	52 (44.5,59)	59 (49.5,65)	48 (35.5,60)	56 (46,63)	54 (49,59)	55 (47,61)	56 (50,62)	55 (46,62)
Age distribution, n (%)								
≤40 years	23 (13.1)	8 (6.1)	25 (41.7)	17 (12.6)	3 (10.3)	16 (13.6)	2 (5.7)	94 (13.7)
>40 and ≤50 years	52 (29.6)	27 (20.5)	6 (10.0)	28 (20.7)	5 (17.2)	23 (19.5)	7 (20.0)	148 (21.6)
>50 and ≤60 years	65 (36.9)	44 (33.3)	17 (28.3)	43 (31.9)	16 (55.2)	47 (39.8)	17 (48.6)	249 (36.4)
>60 and ≤70 years	26 (14.8)	34 (25.8)	9 (15.0)	34 (25.2)	4 (13.8)	20 (17.0)	7 (20.0)	134 (19.6)
>70 years	10 (5.7)	19 (14.4)	3 (5.0)	13 (9.6)	1 (3.5)	12 (10.2)	2 (5.7)	60 (8.8)

IQR = interquartile range.

TABLE 2 - Persistence and adherence levels to treatment

	Adalimumab	Apremilast	Certolizumab	Etanercept	Golimumab	Secukinumab	Ustekinumab	Overall
	n = 176 (25.7%)	n = 132 (19.3%)	n = 60 (8.8%)	n = 135 (19.7%)	n = 29 (4.2%)	n = 118 (17.2%)	n = 35 (5.1%)	n = 685
Persistence (in days), mean (SD)	267 (115.0)	264 (122.9)	268 (103.8)	258 (118.5)	271 (122.0)	255 (119.0)	264 (111.5)	263 (116.7)
Patients persistent at 1 year, n (%)								
No	86 (48.9)	62 (47.0)	33 (55.0)	74 (54.8)	12 (41.4)	65 (55.1)	20 (57.1)	352 (51.4)
Yes	90 (51.1)	70 (53.0)	27 (45.0)	61 (45.2)	17 (58.6)	53 (44.9)	15 (42.9)	333 (48.6)
PDC, mean (SD)	0.69 (0.31)	0.70 (0.33)	0.73 (0.27)	0.67 (0.31)	0.69 (0.31)	0.62 (0.30)	0.74 (0.29)	0.68 (0.31)
Adherent patients (PDC ≥ 0.8), n (%)								
No	90 (51.1)	59 (44.7)	32 (53.3)	74 (54.8)	15 (51.7)	72 (61.0)	17 (48.6)	359 (52.4)
Yes	86 (48.9)	73 (55.3)	28 (46.7)	61 (45.2)	14 (48.3)	46 (39.0)	18 (51.4)	326 (47.6)

PDC = proportion of days covered; SD = standard deviation.

TABLE 3 - Time to discontinuation and adherence to treatment (PDC ≥ 0.80) modeling

	Time to discontinuation		Adherence to treatment (PDC ≥ 0.8)	
	Hazard ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Male vs. female	0.76 (0.61-0.96)	**0.020**	1.12 (0.81-1.54)	0.486
Age distribution (reference: >70 years)				
≤40 years	0.87 (0.56-1.35)	0.527	1.39 (0.70-2.75)	0.344
41 to ≤50 years	0.82 (0.55-1.24)	0.347	1.61 (0.86-2.99)	0.135
51 to ≤60 years	0.74 (0.51-1.09)	0.123	1.66 (0.92-2.98)	0.092
61 to ≤70 years	0.92 (0.61-1.38)	0.678	1.55 (0.83-2.90)	0.173
Treatment (reference: secukinumab)				
adalimumab	0.84 (0.61-1.17)	0.301	1.47 (0.91-2.37)	0.113
apremilast	0.81 (0.57-1.15)	0.239	1.98 (1.19-3.29)	**0.009**
certolizumab	0.87 (0.56-1.34)	0.526	1.44 (0.75-2.77)	0.268
etanercept	0.98 (0.70-1.36)	0.889	1.29 (0.78-2.14)	0.321
golimumab	0.74 (0.40-1.37)	0.335	1.39 (0.61-3.16)	0.430
ustekinumab	0.97 (0.59-1.60)	0.898	1.62 (0.76-3.48)	0.213

CI = confidence interval; PDC = proportion of days covered.
p-Values <0.05 were considered statistically significant and are presented in bold.

between patients taking biosimilar and originator drugs, are shown in Table 4.

Demographic characteristics were comparable between groups. A slightly higher percentage of females were found in the originator adalimumab group compared to the biosimilar group. Similar persistence and adherence findings were observed between patients treated with the adalimumab originator and its biosimilar, while patients treated with the etanercept originator showed lower persistence and adherence compared to those treated with etanercept biosimilar (mean persistence: 222 vs. 267 days, adherent patients: 23.5% vs. 51.5%) (Tab. 4). After adjusting for age and gender, patients initiating adalimumab biosimilar had similar time to discontinuation and similar adherence compared to those initiating the adalimumab originator (Tab. 5). Conversely, patients initiating the etanercept biosimilar had longer time to discontinuation and higher adherence compared to those initiating the etanercept originator. Furthermore, male patients were more likely to have had longer time to discontinuation than female patients (Tab. 5).

TABLE 4 - Additional analysis on biosimilars and originators of adalimumab and etanercept

	Adalimumab		Etanercept	
	Biosimilar	**Originator**	**Biosimilar**	**Originator**
	n = 83 (48.0%)	**n = 90 (52.0%)**	**n = 101 (74.8%)**	**n = 34 (25.2%)**
Sex, n (%)				
Female	47 (56.6)	59 (65.6)	57 (56.4)	20 (58.8)
Male	36 (43.4)	31 (34.4)	44 (43.6)	14 (41.2)
Age (in years), median (IQR)	54 (44,60)	52 (45,57)	55 (46,62)	59.5 (48,64)
Age distribution, n (%)				
≤40 years	10 (12.1)	12 (13.3)	12 (11.9)	5 (14.7)
>40 and ≤50 years	24 (28.9)	27 (30.0)	24 (23.8)	4 (11.8)
>50 and ≤60 years	31 (37.4)	34 (37.8)	32 (31.7)	11 (32.4)
>60 and ≤70 years	13 (15.7)	13 (14.4)	26 (25.7)	8 (23.5)
>70 years	5 (6.0)	4 (4.4)	7 (6.9)	6 (17.7)
Persistence (in days), mean (SD)	255 (123.6)	264 (113.2)	267 (117.4)	222 (119.6)
Patients persistent at 1 year, n (%)				
No	41 (49.4)	46 (51.1)	49 (48.5)	24 (70.6)
Yes	42 (50.6)	44 (48.9)	52 (51.5)	10 (29.4)
PDC, mean (SD)	0.65 (0.33)	0.69 (0.30)	0.70 (0.32)	0.53 (0.29)
Adherent patients (PDC ≥ 0.8), n (%)				
No	47 (56.6)	46 (51.1)	49 (48.5)	26 (76.5)
Yes	36 (43.4)	44 (48.9)	52 (51.5)	8 (23.5)

IQR = interquartile range; PDC = proportion of days covered; SD = standard deviation.

TABLE 5 - Time to discontinuation and adherence to treatment (PDC ≥ 0.80) modeling for additional analysis

	Time to discontinuation		Adherence to treatment (PDC ≥ 0.8)	
	Hazard ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Adalimumab				
Male vs, female	1.13 (0.72-1.78)	0.598	0.68 (0.35-1.31)	0.252
Age distribution (reference: >70 years)				
≤40 years	1.27 (0.33-4.82)	0.726	1.49 (0.30-7.35)	0.622
41 to ≤50 years	2.43 (0.74-7.99)	0.144	0.46 (0.11-1.95)	0.291
51 to ≤60 years	1.82 (0.56-5.95)	0.321	0.71 (0.17-2.91)	0.632
61 to ≤70 years	2.16 (0.62-7.53)	0.227	0.64 (0.14-2.97)	0.569
Biosimilar vs. originator	1.00 (0.65-1.53)	0.991	0.82 (0.44-1.52)	0.533
Etanercept				
Male vs. female	0.59 (0.36-0.96)	**0.034**	1.92 (0.92-4.00)	0.082
Age distribution (reference: >70 years)				
≤40 years	0.96 (0.38-2.40)	0.922	0.91 (0.19-4.30)	0.905
41 to ≤50 years	0.83 (0.34-2.04)	0.680	1.40 (0.34-5.82)	0.640
51 to ≤60 years	0.84 (0.37-1.91)	0.671	0.96 (0.25-3.72)	0.957
61 to ≤70 years	0.81 (0.35-1.90)	0.632	1.11 (0.28-4.37)	0.883
Biosimilar vs. originator	0.59 (0.36-0.98)	**0.043**	3.35 (1.35-8.33)	**0.009**

CI = confidence interval; PDC = proportion of days covered.
p-Values <0.05 were considered statistically significant and are presented in bold.

The mean annual costs calculated on patients persistent at 1 year and adherent to treatment varied from €8,724 (etanercept) to €14,783 (ustekinumab) and are represented in Table 6. Adalimumab and etanercept biosimilars showed an annual saving of more than €2,500 in comparison to their originators (Tab. 6).

TABLE 6 - Cost analysis

	N	Annual cost (in euro), mean (SD)
Adalimumab	80	11,957 (2,540)
Apremilast	66	10,862 (2,956)
Certolizumab	26	13,560 (1,485)
Etanercept	55	8,724 (1,125)
Golimumab	14	14,097 (1,625)
Secukinumab	40	13,243 (2,479)
Ustekinumab	15	14,783 (1,593)
Additional analysis		
Adalimumab biosimilar	36	10,242 (1,416)
Adalimumab originator	40	12,874 (1,264)
Etanercept biosimilar	50	8,405 (770)
Etanercept originator	7	11,184 (984)

SD = standard deviation.

Discussion

Adherence to treatment has a significant impact on the patient's quality of life and it is associated with morbidity, mortality and healthcare spending. This study found that patients initiating a treatment with b/tsDMARDs for PsA had a mean persistence of 263 days and approximately half of the population (48.6%) remained persistent at 1 year, showing similar persistence between treatments. Similarly, low adherence to treatment was observed: the average PDC was 0.68 and adherent patients (PDC ≥ 0.8) were 47.6% of the overall population, with a greater likelihood of adhering to treatment for patients treated with apremilast, compared to patients treated with secukinumab (OR 1.98, p = 0.009).

A major review on treatment adherence and persistence rates in patients with autoimmune rheumatic diseases showed that both adherence and persistence rates varied widely between studies, ranging between 9.3% and 94% and 23% and 80%, respectively (18). The type of the rheumatic disease, as well as the diversity of the definitions and methods used to assess persistence and adherence contributed to differences in findings.

Although persistence and adherence rates reported in the literature vary widely depending on the study and definition used, our findings were consistent with previously published studies on b/tsDMARD use in PsA, which reported persistence rates ranging from 43.6% to 67% (19-26) and the proportion of highly adherent patients (i.e., PDC ≥ 0.80) from 25% to 63.9% (19,27,28) over 12 months of treatment. As in other chronic conditions, persistence and adherence to treatment are an important part of the therapy and the impact of low adherence can influence the effectiveness of the treatment and lead to suboptimal clinical results (18,29).

The demographic characteristics of the population and the distribution of the use of biologics were in line with those observed in previous studies conducted on PsA patients in Italy (26,30,31). Our study showed that male patients were significantly associated with a longer time to discontinuation compared to female patients (HR 0.76, p = 0.020). The lower persistence of women compared to men is confirmed by the largest study that specifically investigated the effect of sex on treatment persistence in PsA in real-world settings (32). These results therefore suggest that on the one hand there is a need for all operators involved to pay greater attention toward the female gender and on the other hand female PsA patients tended to have more disease activity, worse function and higher disease burden compared to men (33,34).

The biosimilars are expected to provide similar standard care at lower costs, thus facilitating better access to treatment and perhaps earlier treatment during the disease course (35,36). Similar persistence and adherence findings were observed between patients treated with the adalimumab originator and the adalimumab biosimilar, while patients treated with the etanercept originator showed lower persistence and adherence compared to those treated with its biosimilar. This is concordant with two recent studies focused on the initiation of treatment with both adalimumab and etanercept, which demonstrated a longer treatment retention at 1 year in favor of etanercept biosimilar in comparison with etanercept originator, while no differences were found between the adalimumab originator and its biosimilars (37,38). Since the reasons for discontinuation were not collected in our study, a lower persistence rate may be related to the patient's profile or lack of response to treatment, possibly including adverse events, and to a non-medical switch to, for example, the corresponding biosimilar. Switching from the originator adalimumab and etanercept to a currently approved biosimilar has been shown to have no significant impact on safety, immunogenicity or efficacy (39-42). In Italy, the Italian Medicines Agency (AIFA) has stated that biosimilar medicines meet rigorous quality, safety and efficacy standards that are entirely identical to those applied to biological medicines, and considers biosimilars interchangeable with the corresponding original reference products, both for naïve patients and for patients already undergoing treatment (43,44). For biosimilars bDMARDs to be integrated into clinical practice and to maximize cost savings with these drugs, all prescribers and patients must be aware of the consistent efficacy and safety of biosimilars compared to reference biologics.

Finally, our study findings revealed that the average annual drug cost ranged from €8,724 (etanercept) to €14,783 (ustekinumab), with an annual saving of more than €2,500 by using biosimilars compared to their originators. These treatment costs reflect patient adherence to therapy and are in line with previous studies that estimated the cost of biologics in naïve PsA patients in Italy to be €12,606 and in France €10,166 (31,45). In Italy, the average annual healthcare costs

for the management of PsA patients treated with bDMARDs were estimated to range from €12,622 to €14,342 per year, from €9,727 (certolizumab) to €14,994 (ustekinumab) (31,46-48). Although this cost analysis only considers the cost of the drug without evaluating a broader context including all healthcare resource consumption, the cost of the biologic drug DMARD plays a fundamental role in the total cost of treating patients with PsA. Finally, the savings associated with the use of the biosimilar drug highlighted in the present study supports that the availability of biosimilars has the potential to significantly reduce drug spending, thus improving access to biologic therapies (28,49,50).

However, the present study also has some limitations, typical of observational studies performed on retrospective data. A prospective design of the study would have allowed for a more thorough qualitative assessment. Firstly, exposure to treatment is based on the drugs dispensed by pharmacies and, even if the dosage indicated by the doctor was collected, there is no information on the actual use of drugs by patients. Furthermore, patients make regular visits with clinicians and subsequently collect b/tsDMARDs, consequently each interaction with a doctor with subsequent dispensing by the hospital pharmacy could be a motivational boost toward better drug use behavior. Second, details on treatment response, side effects and reasons for nonadherence or gaps in treatment were not available. Therefore, it was not possible to determine whether the discontinuation of treatment was intentional and appropriate, for example, due to adverse effects or loss of efficacy. Third, these data lack patient clinical details and information related to the severity of the disease and symptoms, thus making the study unable to control for confounding variables due to the missing of information. Finally, as with all data analyses, coding errors, misclassification and omissions could affect the results.

Conclusions

From the drug utilization analysis conducted, it emerges that the majority of PsA patients who initiate treatment with b/tsDMARDs in Italy discontinued their treatment before 12 months and were classified as not adherent. These data, therefore, represent a warning for the management of patients suffering from PsA since adherence to medications is deeply connected to clinical benefits. First, patient education is key in improving compliance, but the role in improving patients' adherence and enabling the full benefits of the current therapies played by healthcare professionals such as doctors, pharmacists and nurses is equally important.

The comparison between biosimilars and originators has offered further evidence in support of the biosimilar, leading to an increase in its prescription and use, not only as an economic opportunity but also as an ethical choice in terms of optimizing resources in healthcare. To ensure optimal integration of biosimilars into PsA clinical practice and to realize full cost savings from these drugs, physicians must be aware that communicating to their patients that the efficacy and safety of biosimilars are comparable to those of their originators, is the key to long-term success.

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Conflict of interest: Enrico Pasut declares consultancy for Biogen in 2020. All other authors declare no conflicts of interest.

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