ORIGINAL ARTICLE

Biological therapy in psoriatic arthritis patients with and without previous biologic experience

Terapia biológica em pacientes com artrite psoriásica com e sem experiência prévia no uso de medicamentos biológicos

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RESUMO:

Objetivo: avaliar os efeitos da terapia biológica sobre a atividade da doença, funcionalidade, qualidade de vida, persistência no tratamento e segurança em pacientes com artrite psoriásica sem experiência e com experiência prévia em terapia biológica. **Métodos:** um estudo observacional prospectivo de um ano foi realizado. Os desfechos avaliados foram a persistência no tratamento, atividade da doença, funcionalidade, qualidade de vida e segurança. Um modelo de regressão linear múltipla foi utilizado para avaliar os fatores preditores de resposta clínica. **Resultados:** foram incluídos 205 pacientes, dos quais 155 não tinham e 50 tinham experiência prévia com medicamentos biológicos. As taxas de persistência no tratamento foram maiores para pacientes sem experiência prévia em comparação aos experientes em seis meses de acompanhamento, mas não em 12 meses. As taxas de persistência no tratamento foram 71,5% em pacientes sem experiência prévia e 70% em pacientes com experiência prévia em 12 meses. Todos os desfechos clínicos avaliados melhoraram em ambos os grupos de pacientes. Aos 12 meses, 63% dos pacientes sem experiência prévia e 52% dos pacientes com experiência prévia apresentaram melhora na qualidade de vida. Além disso, 48% dos pacientes sem experiência prévia e 42% dos pacientes com experiência prévia apresentaram melhora na funcionalidade. A doença axial melhorou em 67% dos pacientes sem experiência prévia e em 56% dos pacientes com experiência prévia. Um bom controle da doença articular periférica foi observado em 49% dos pacientes sem experiência prévia e em 44% dos pacientes com experiência prévia. Os principais fatores preditores de pior resposta clínica foram sexo feminino, uso de etanercepte ou infliximabe, bem como pior funcionalidade e qualidade de vida no início do estudo. **Conclusão:** a saúde dos pacientes melhorou após o início do tratamento com os medicamentos biológicos. Em geral, pacientes com experiência prévia com medicamentos biológicos apresentaram mais reações adversas e menor efetividade.

Palavras-Chave: Artrite psoriásica, Inibidores do fator de necrose tumoral, Qualidade de vida, Efetividade, Segurança.

ABSTRACT

Objective: this study evaluated the biological therapy effects on disease activity, functionality, quality of life, drug survival, and safety of patients with psoriatic arthritis naïve and experienced in biological therapy. **Methods:** a one-year prospective observational study was performed. The outcomes assessed were drug survival, disease activity, functionality, quality of life, and safety. Multiple linear regression was used to assess predictive factors for clinical response. **Results:** a total of 205 patients were included, 155 of whom were biologic naïve and 50 biologic experienced. Drug survival rate was greater for naïve patients than experienced patients at 6 months, but not at 12 months. Drug survival rates were 71.5% for naïve patients and 70.0% for experienced patients at 12 months. All clinical parameters improved for both biologic naïve and experienced patients. At 12 months, 63% of naïve patients and 52% of experienced patients had an improvement in their quality of life. Besides, 48% of naïve patients and 42% of experienced patients had an improvement in functionality. The axial disease improved in 67% of naïve individuals and 56% of experienced patients. Good control of peripheral disease was achieved by 49% of naïve patients and 44% of experienced patients. Female sex, use of etanercept or infliximab, and lower functionality or quality of life at baseline were the main predictors of poor clinical response. **Conclusion:** Patients' health improved after starting biological therapy. In general, biologic experienced patients had more adverse reactions and lesser effectiveness.

Keywords: Psoriatic arthritis, Tumor necrosis factor inhibitors, Quality of life, effectiveness, Safety.

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INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease of the skin and musculoskeletal system caused by an immune-mediated response. PsA patients' quality of life decreases due to the psychosocial burden, physical function impairment, and comorbidities[1]. In this sense, the effectiveness and safety of biological therapy are critical for improving patient health[2].

Biologic drugs are therapeutic proteins that inhibit or modulate pro-inflammatory immune cells and cytokines that have significantly improved the effectiveness of the treatment of PsA, delaying disease progression and articular damage. The first widely used biologics have been those targeting tumor necrosis factor-alpha (TNF), which include adalimumab, certolizumab, etanercept, golimumab, and infliximab[3-4].

Despite the significant improvements achieved by treating PsA patients with new immunomodulatory therapies in the biologic treatment era, there is still a need for improvement[5-6]. At 6 months of treatment, around 45% of the patients did not achieve adequate disease control and 20% discontinued the biological therapy[7-8]. At 12 months, approximately 45% of the patients discontinued the biological therapy[8-9]. In this regard, the choice of new treatment after a failure of first biological therapy is a role point to achieve the effectiveness of the treatment[10]. Furthermore, biological therapy has a high cost for the Health Systems, accounting for more than 90% of total psoriatic arthritis expenses[8].

In 2015, TNF inhibitors were the first line of biologic therapy for PsA, and since 2020 both TNF inhibitors and interleukin inhibitors (IL 17 or IL 12/23 inhibitor) can be chosen as the first line of treatment. After an inadequate response with biologic therapy, a second biologic or a target-specific synthetic can be used. The second biologic can be either TNF or interleukin inhibitor[10].

Notwithstanding advances in the treatment of psoriatic arthritis observed over years, few studies have been performed to evaluate separately naive and experienced patients to biological therapy. Overall, these studies evaluated clinical response to a single biologic drug or the discontinuation and switch of biological therapy. When compared to biologic-naive patients, biologic-experienced patients took less time to discontinuation of therapy and were more likely to discontinue or switch[11]. A recent network meta-analysis identified that the most effective biological therapy can vary between biologic-naïve and biologic-experienced individuals[12]. The stratified evaluation is important to help understand the pattern of clinical response for these different groups of patients, which can contribute to the management of treatment and optimize its results[11-12].

This study aimed to assess the effectiveness, functionality, quality of life, and safety of biological therapy with TNF inhibitors in PsA patients who had or had not previously used biologic drugs.

METHODS

Type of study, patients' characteristics, and data collection

A prospective observational study was conducted from January 2012 to July 2019 at a single center in Belo Horizonte city, Brazil, which assists about 320 PsA patients.

The eligibility criteria were being 18 years of age or older, having a diagnosis of PsA by the Classification Criteria for Psoriatic Arthritis (CASPAR)[13], and using adalimumab, etanercept, or infliximab. Certolizumab and golimumab were not evaluated because the first was not approved by the SUS for PsA, and the last was only incorporated in 2017. Patients were assessed at starting biological therapy, and after six and 12 months. The analyses were carried out for two groups of patients: those who had never used biologic drugs before, called naive patients, and those who had used, called experienced patients.

A standardized research form was created and tested previously. Sociodemographic data, as well as clinical variables, were collected. Age, sex, schooling, marital status, self-declared race, disease duration, current and previous PsA drug use, comorbidities, adverse reactions, disease activity, functionality, and quality of life were predictors variables. The interviews were conducted face-to-face with patients, and all researchers

were trained in a Rheumatology Specialized Center where PsA patients could be followed up on.

Outcomes

The outcomes assessed were drug survival, effectiveness through disease activity, functionality, quality of life, and safety.

Drug survival was defined as biological therapy continuation over time. The absence of medication dispensation after 90 days from the last date of dispensation was considered therapy discontinuation (lack of drug survival). This period refers to the time to renewal biological therapy by SUS[14].

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Clinical Disease Activity Index (CDAI) were used to assess disease activity. Functionality was assessed using the Health Questionnaire Assessment Disability Index (HAQ-DI), and quality of life was assessed using the European Quality of Life Five Dimensions Questionnaire (EQ-5D), both of which had been validated for use in Brazil[15-16]. BASDAI < 4 and CDAI ≤ 10 were used to define good clinical response (GCR). In addition, a BASDAI reduction of 2 points, or 50%, was assessed[16-17]. A minimal clinically important difference (MCID) was defined as a ≥ 0.05 improvement in EQ-5D quality of life and a ≥ 0.35 reduction in HAQ-DI functionality[18-19].

Finally, patients reported the occurrence of adverse reactions.

Statistical analysis

The sample size was calculated using a ≥ 0.35 improvement on the HAQ-DI[18]. Thus, a difference of 0.35 between 12 months of follow-up and baseline (difference=0.35), a standard deviation of 0.60, a significance level of 5% (alpha=0.05), and a test power of 80% (beta=0.80) were used, resulting in a minimum sample of 47 patients per group, in a total of 94 patients.

The frequencies' distribution, means, and standard deviation (SD) were used in a descriptive analysis. For continuous variables, an independent T-test was used for two independent groups and a paired T-test for two paired variables. For categorical variables, Pearson's Chi-square was used. Drug survival was assessed by log-rank test and Kaplan-Meier graph.

Multiple imputations were used to fill the missing data using a predictive mean matching method, considering the monotonic pattern observed in the missing data[20]. As a result, an intention-to-treat analysis was carried out, and all patients included in the study were examined.

Multiple linear regression with a 95% confidence interval was used to assess predictive factors for clinical response by CDAI, BASDAI, HAQ-DI, and EQ-5D at 12 months. As independent variables, sex, age, schooling, marital status, ethnicity, disease duration, comorbidity, disease activity, functionality, quality of life, biologic drug use, non-steroidal anti-inflammatory drug use, conventional synthetic drug use, and glucocorticoid use were considered. A 5% significance level was used in these analyses.

Stata version 16.1 was used to perform the statistical analyses.

Ethical disclosure

The Research Ethics Committee of the Federal University of Minas Gerais approved this study under Opinion Nº 0069.0.203.000-11. This study was performed in line with the principles of the Declaration of Helsinki.

RESULTS

Baseline characteristics

A total of 205 PsA patients were included, of whom 155 had not previously used biological therapy, referred to as biologic naive patients. The other 50 patients had previously used biologics, referred to as biologic experienced patients. At six months, 36 patients (17.6%) lost to follow-up, and at 12 months, 78 patients (38.0%) lost to follow-up. At 12 months, 55 naive patients (35.5%) and 23 experienced patients (46.0%) had dropped out of the study (Figure 1). Lack of effectiveness

(23.1%) and adverse reactions (14.1%) were the main reasons for the loss of follow-up.

The mean time between the first (baseline) and second (6-month) evaluations was 203.79 days (SD=44.46). The mean time between the second (6-month) and third (12-month) evaluations was 196.67 days (SD=48.80). Finally, the mean time between the first (baseline) and third (12-month) evaluations was 400.47 days (SD=59.21).

The mean age was 51.04 years (SD=11.52), and the disease lasted 5.83 years (SD=7.30). Most patients were white (52.0%), married (58.1%), and had until high school (66.5%; Table 1). Of the 205 patients, 113 (55.1%) used adalimumab, 68 (33.8%) etanercept, and 24 (11.7%) infliximab. In addition, 92 (44.9%) patients used concurrently csDMARD, 56 (27.3%) corticosteroids, and 49 (23.9%) NSAIDs. The mean of CDAI, BASDAI, HAQ, and EQ-5D scores at baseline were 22.83 (SD=16.94), 5.26 (SD=2.46), 1.22 (SD=0.70), and 0.65 (SD=0.18), respectively. The difference between naive and experienced patients was in the duration of disease, which was longer for experienced patients. Furthermore, adalimumab was the most used drug by naive patients, while infliximab was the least used (Table 1).

Drug survival

At 6 months, the drug survival was greater in naive patients (91.4%) than in experienced patients (80.0%) (p=0.027). However, this difference did not maintain at 12 months (p=0.817), with drug survival rates of 71.5% for naive patients and 70.0% for experienced patients (Figure 2).

Effectiveness, functionality, and quality of life

For both naive and experienced patients, all clinical measures of disease activity, functionality, and quality of life improved significantly at 6 and 12 months compared to baseline (p<0.05) (Table 2)

At 12 months, it was observed that 63% of naive patients and 52% of experienced patients achieved a minimal clinically important difference (MCID) by EQ-5D. Furthermore, 48% of naive patients and 42% of experienced patients achieved a minimal clinically important difference (MCID) by HAQ-DI. In addition, 59% of naive patients and 38% of experienced patients had a BASDAI reduction of 2 points or 50%, and 67% of naive patients and 56% of experienced patients had a BASDAI < 4 points. Finally, 49% of naive patients and 44% of experienced patients achieved remission or low disease activity by CDAI (Figure 3).

Predictors of clinical response

For naive patients at 12 months, female sex, comorbidity, etanercept use, and worse functionality were predictors of poorer CDAI response. Being female, using corticosteroids, using etanercept or infliximab, having poor functionality, and having a low quality of life were predictors of a poorer BASDAI response. Being female and using etanercept were predictors of poorer functionality by HAQ-DI, whereas having a better quality of life, being married, and having a higher education were associated with better functionality. Finally, worse functionality was a predictor of poorer quality of life.

For experienced patients at 12 months, worse quality of life and etanercept or infliximab use were the predictors of poorer CDAI, BASDAI, and HAQ-DI response. Finally, worse functionality and infliximab use were the predictors of poorer quality of life by EQ-5D (Table 3).

Safety

Alopecia, headache, flu, injection site reaction, sinusitis, and infections were the most common adverse reactions reported by patients. Adverse reactions were most common in biologic-experienced patients. There were no reported cases of tuberculosis (Table 4).

DISCUSSION

This study evaluated multiple outcomes in PsA patients naive and experienced in biolo-

gic therapy. The loss of follow-up was 17.6% at 6 months and 38.0% at 12 months of follow-up. This result was similar to the medication non-persistence in Brazil[21].

Lack of effectiveness and adverse reactions were the main reasons for the loss to follow-up, described by other studies[22-24]. According to other studies, experienced patients had a lower likelihood of achieving clinical effectiveness and higher discontinuation rates than naive patients[11,24-26]. In addition, longer disease duration was observed in TNFi experienced patients, which is associated with a greater risk of disease progression, shorter medication persistence, and increased likelihood of discontinuation and switch[11-27].

Although adverse reactions contributed to the discontinuation of follow-up, the use of TNFi can be considered safe and adverse reactions are manageable[28].

Drug survival rate was greater in naive patients at 6 months, but not at 12 months. Harrold and collaborators observed that biologic-naïve patients had greater drug survival compared with biologic-experienced patients in the United States[29]. Oelke and collaborators observed a drug survival rate of 56.4% in biological therapy in the United State at 12 months, lower than observed in Brazil (70.0-71.5%)[9].

At 6 and 12 months, all clinical measures of disease activity, functionality, and quality of life improved significantly in both naive and experienced patients. In this sense, a recent meta-analysis demonstrated the efficacy and tolerability of biologic drugs for PsA[30]. Overall, TNFi therapy improves the signs and symptoms of articular and cutaneous involvement, as well as patient functionality and quality of life[28,30-31]. Oliveira Junior et al. (2020) reported clinical improvement in the quality of life, regardless of the biological therapeutic regimen in patients with rheumatic diseases. Most of the participants showed significant clinical improvement in the quality of life at 6 and 12-month to follow-up[32].

Few comparative observational studies have been conducted between naive and experienced patients in biologic therapy. Mease et al. (2019) discovered that experienced patients took less time to discontinue or switch biological therapy than naive patients[11].

According to Oliveira Junior and collaborators (2020), functional disability (HAQ-DI), lower quality of life, and having comorbidities at baseline were predictive of EQ-5D response at 12 months follow-up[32]. Poor baseline functionality predicted poor CDAI response. According to other studies, better functionality is associated with lower pain levels and structural damage, as well as higher work productivity, all of which contribute to a good clinical response by CDAI[33-34]. Furthermore, psoriatic arthritis and its associated comorbidities, such as fibromyalgia and depression, also presented a significant impact on patients' quality of life[34]. Overall, female sex, lower marker levels, and poor clinical status at baseline have been identified as predictors of poor disease control over time[26,36].

According to Costa et al. (2017), no specific biological agent was more effective than others for experienced patients[22]. The decision to switch to a different drug should be based primarily on the drug's safety profile, comorbidities, previous therapy, costs, and patient preferences, such as drug administration route and frequency[37]. According to Merola et al. (2017), switching between TNFi can be effective for many patients, but biologic drugs with different action mechanisms may be superior alternatives that should be prioritized[38].

Another important approach to optimizing biological therapy is to reduce the time it takes to get the drug in SUS and to improve the home storage of these drugs. According to recent studies, the median time from medical prescription to the patient receiving the biologic drug in Brazil is two months, and more than 80% of patients do not store these drugs adequately. As a result, multidisciplinary and individualized care, including pharmaceutical care, can help to improve these outcomes, resulting in better pharmacotherapy for PsA patients[14,39].

In terms of costs, TNFi drugs have shown significant price reductions in recent years in Brazil, which has improved its cost-effectiveness ratio. As a result, regardless of the treatment regimen, they continue to be important therapeutic options[8,40-41].

These results have implications for psoriatic arthritis treatment. First, patients with prior biological experience had poorer outcomes, indicating the importance of regular monitoring for patients

with an inadequate response[11,24-26]. Furthermore, the choice of the new drug should consider the response to the first biological agent used, as it may be necessary in some cases to use a drug with a different mechanism of action[12,38]. In this regard, clinical outcomes and disease control can be improved, which can contribute to a better patients' quality of life[34]. In addition, this study provides contextualized information to the Brazilian health services. Therefore, all the measures discussed thus far have the potential to contribute to clinical practice and improve health outcomes[8,14,39-41].

Finally, the findings corroborate the current clinical protocol and therapeutic guideline for psoriatic arthritis in the Unified Health System (2021) and the Brazilian Society of Rheumatology 2020 guidelines for psoriatic arthritis, which recommend the use of any biological drug available or tofacitinib as options after failure with first line of biological drugs[42-43].

This research has both strengths and limitations. As a strength, this is the first study conducted in a Brazilian real-life setting that evaluates multiple outcomes for naive and experienced PsA patients separately. It was also carried out in a real-world setting, which increases the external validity of the results. As a limitation, skin involvement was not evaluated because the Brazilian Clinical Guideline for PsA only began to consider this manifestation after its update in 2018. Furthermore, the convenience method used to select patients is a limitation because only individuals who attended the health center were eligible to participate in the study. As a result, the findings should be interpreted and generalized with caution, and more severe cases of PsA may have been left out.

CONCLUSION

All clinical outcomes of disease activity, functionality, and quality of life improved six and 12 months after the start of treatment, even in patients who had previously used the biologic drug. The treatment was well-tolerated and had know adverse reactions, which were most common in biologic-experienced patients. In general, biologic experienced patients had more adverse reactions and lesser clinical effectiveness. Therefore, biological therapy can be considered effective and safe for psoriatic arthritis patients.

TABLES AND FIGURES

Table 1

Baseline sociodemographic and clinical characteristics for biologic naïve and experienced patients.

Variables	Biologic Naïve (155)	Biologic Experienced (50)	Total (205)	p-value
Sex n (%)				0.680
Female	91 (58.7)	31 (62.0)	122 (59.5)	
Male	64 (41.3)	19 (38.0)	83 (40.5)	
Age *mean (SD)*	*51.22 (12.06)*	*50.51 (9.77)*	*51.04 (11.52)*	0.705
Duration of disease *mean (SD)*	*5.11 (6.76)*	*8.05 (8.46)*	*5.83 (7.30)*	0.013
Race n (%)				0.894
White	81 (52.3)	25 (51.0)	106 (52.0)	
Brown	52 (33.6)	18 (36.7)	70 (34.3)	
Other	22 (14.2)	6 (12.2)	28 (13.7)	
Marital status n (%)				0.591
Single	37 (24.2)	15 (30.0)	52 (25.6)	
Married	92 (60.1)	26 (52.0)	118 (58.1)	
Other	24 (15.7)	9 (18.0)	33 (16.3)	
Education level n (%)				
Elementary school	44 (28.8)	13 (26.0)	57 (28.1)	0.739
High school	60 (39.2)	18 (36.0)	78 (38.4)	
Undergraduate	49 (32.0)	19 (38.0)	68 (33.5)	

(Continuação)

Table 1

(continuação)

Variables	Biologic Naïve (155)	Biologic Experienced (50)	Total (205)	p-value
Comorbidity n (%)	115 (74.2)	38 (76.0)	153 (74.6)	0.799
Concomitant csDMARD n (%)	64 (41.3)	28 (56.0)	92 (44.9)	0.069
Concomitant NSAID n (%)	37 (23.9)	12 (24.0)	49 (23.9)	0.985
Concomitant corticoid n (%)	41 (26.4)	15 (30.0)	56 (27.3)	0.624
Biologic drug in use n (%)				
Adalimumab	91 (58.7)	22 (44.0)	113 (55.1)	0.007
Etanercept	52 (33.6)	16 (32.0)	68 (33.2)	
Infliximab	12 (7.7)	12 (24.0)	24 (11.7)	
CDAI *mean (SD)*	*22.90 (16.63)*	*22.57 (18.04)*	*22.83 (16.94)*	*0.909*
BASDAI *mean (SD)*	*5.36 (2.50)*	*4.93 (2.47)*	*5.26 (2.49)*	*0.286*
HAQ-DI *mean (SD)*	*1.22 (0.72)*	*1.22 (0.63)*	*1.22 (0.70)*	*0.987*
EQ-5D utility *mean (SD)*	*0.65 (0.18)*	*0.66 (0.19)*	*0.65 (0.18)*	0.749
EQ-5D *VAS mean (SD)*	*62.40 (20.66)*	*64.20 (21.01)*	*62.81 (20.71)*	0.589

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CDAI: Clinical Disease Activity Index; csDMARD: conventional synthetic disease-modifying antirheumatic drug; EQ-5D: EuroQol-5 Dimensions; HAQ: Health Assessment Questionnaire; n: number of patients; SD: standard deviation; NSAIDs: Nonsteroidal anti-inflammatory drugs; VAS: visual analogic scale.

Statistical tests: chi-square (categorical variables); independent T-test (continuous variables).

p-value: 0.05 (significance level of 5%)

Table 2

Effectiveness, functionality, and quality of life between biologic naïve and experienced PsA patients in use of biological therapy at baseline, six and 12 months.

Variable	Clinical Disease Activity Index (CDAI)									
Group	Baseline		6 months				12 months			
	mean	SD	mean	SD	Δ	p-value*	mean	SD	Δ	p-value**
Biologic naïve	22.90	16.63	13.26	12.67	-9.64	< 0.001	13.19	12.81	-9.71	< 0.001
Biologic experienced	22.59	18.04	15.11	14.02	-7.48	0.001	14.87	11.34	-7.72	< 0.001
Variable	Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)									
Group	Baseline		6 months				12 months			
	mean	SD	mean	SD	Δ	p-value*	mean	SD	Δ	p-value**
Biologic naïve	5.36	2.50	3.59	2.43	-1.77	< 0.001	3.13	2.12	-2.23	< 0.001
Biologic experienced	4.93	2.47	3.83	2.44	-1.10	< 0.001	3.74	2.09	-1.19	< 0.001
Variable	Funcionality (HAQ)									
Group	Baseline		6 months				12 months			
	mean	SD	mean	SD	Δ	p-value*	mean	SD	Δ	p-value**
Biologic naïve	1.22	0.72	0.87	0.67	-0.35	< 0.001	0.83	0.61	-0.39	< 0.001
Biologic experienced	1.22	0.63	0.92	0.59	-0.30	< 0.001	0.91	0.54	-0.31	< 0.001
Variable	Quality of Life (EQ-5D)									
Group	Baseline		6 months				12 months			
	mean	SD	mean	SD	Δ	p-value*	mean	SD	Δ	p-value**
Biologic naïve	0.65	0.18	0.74	0.18	0.09	< 0.001	0.75	0.16	0.10	< 0.001
Biologic experienced	0.66	0.19	0.73	0.18	0.07	0.008	0.75	0.17	0.09	0.002

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CDAI: Clinical Disease Activity Index; EQ-5D: EuroQol-5 Dimensions; HAQ: Health Assessment Questionnaire; SD: standard deviation;

p-value * = six months versus baseline; p-value ** = 12 months versus baseline.

Statistical test: paired T-test. p-value: 0.05 (significance level of 5%)

Table 3

Predictors of effectiveness, functionality, and quality of life for biologic naïve and experienced patients at 12 months. Only multiple models were presented.

Biologic naïve				Biologic experienced			
CDAI response							
Predictors	β (coefficient)	CI 95%	p-value	Predictors	β (coefficient)	CI 95%	p-value
HAQ	5.91	3.32 : 8.51	<0.001	EQ-5D	-23.68	-36.89 : -10.46	0.001
Sex (female)	5.01	1.27 : 8.76	0.009				
Comorbidity (No)	4.70	0.53 : 8.86	0.027				
Biologic drug				Biological drug			
Etanercept	4.36	0.49 : 8.22	0.027	Etanercept	9.63	3.88 : 15.38	0.002
Infliximab	3.18	-3.66 : 10.01	0.443	Infliximab	16.29	9.98 : 22.60	< 0.001
BASDAI response							
Predictors	β (coefficient)	CI 95%	p-value	Predictors	β (coefficient)	CI 95%	p-value
HAQ	0.72	0.16 : 1.29	0.012				
EQ-5D	-3.37	-5.60 : -1.15	0.003	EQ-5D	-6.09	-8.36 : -3.82	< 0.001
Sex (female)	0.58	0.00 : 1.15	0.049				
Corticoid (yes)	0.73	0.10 : 1.37	0.024				
Biologic drug				Biologic drug			
Etanercept	0.78	0.18 : 1.38	0.011	Etanercept	1.38	0.40 : 2.37	0.007
Infliximab	1.10	0.06 : 2.15	0.039	Infliximab	2.78	1.70 : 3.87	< 0.001
HAQ response							
Predictors	β (coefficient)	CI 95%	p-value	Predictors	β (coefficient)	CI 95%	p-value
EQ-5D	-1.41	-1.85 : -0.96	<0.001	EQ-5D	-1.92	-2.48 : -1.37	< 0.001
Sex (female)	0.27	0.10 : 0.43	0.002				
Marital status (single)	0.22	0.03 : 0.41	0.021				
Education							
Elementary	0.38	0.17 : 0.58	<0.001				
High School	0.23	0.04 : 0.42	0.018				
Biologic drug				Biologic drug			
Etanercept	0.38	0.21 : 0.55	<0.001	Etanercept	0.30	0.06 : 0.54	0.017
Infliximab	0.24	-0.06 : 0.54	0.114	Infliximab	0.58	0.32 : 0.85	<0.001
EQ-5D response							
Predictors	β (coefficient)	CI 95%	p-value	Predictors	β (coefficient)	CI 95%	p-value
HAQ	-0.08	-1.85 : -0.96	<0.001	HAQ	-0.12	-0.18 : -0.06	<0.001
Biological drug				Biologic drug			
Etanercept	-0.04	-0.09 : 0.01	0.085	Etanercept	-0.08	-0.16 : 0.01	0.085
Infliximab	-0.08	-0.17 : 0.00	0.057	Infliximab	-0.19	-0.29 : -0.10	<0.001

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CDAI: Clinical Disease Activity Index; CI: confidence interval; EQ-5D: EuroQol-5 Dimensions; HAQ: Health Assessment Questionnaire;

Statistical test: simple and multiple linear regression. p-value: 0.20 (simple) and 0.05 (multiple).

Table 4

Main adverse reactions reported by PsA patients using TNFi therapy.

Adverse reactions	Biologic naive (155)		Biologic experienced (50)		Total (205)	
	N	%	n	%	N	%
Alopecia	16	10.3%	7	14.0%	23	11.2%
Headache	10	6.4%	7	14.0%	17	8.3%
Flu	7	4.5%	10	20.0%	17	8.3%
Injection site reactions	9	5.8%	7	14.0%	16	7.8%
Sinusitis	7	4.5%	6	12.0%	13	6.3%
Urinary infection	5	3.2%	5	10.0%	10	4.9%
Nausea	3	1.9%	5	10.0%	8	3.9%
Dyslipidemia	6	3.9%	1	2.0%	7	3.4%
Asthenia	4	2.6%	2	4.0%	6	2.9%
Rhinitis	2	1.3%	2	4.0%	4	2.0%
Pruritus	1	0.6%	3	6.0%	4	2.0%
Fungal infection	4	2.5%	0	0.0%	4	2.0%
Swelling	3	1.9%	1	2.0%	4	2.0%
Dizziness	1	0.6%	2	4.0%	3	1.5%
Fever	1	0.6%	2	4.0%	3	1.5%
Diarrhea	1	0.6%	1	2.0%	2	1.0%
Skin rash	0	0.0%	2	4.0%	2	1.0%
Pneumonia	0	0.0%	2	4.0%	2	1.0%
Hypertension	2	1.3%	0	0.0%	2	1.0%
Urticaria	2	1.3%	0	0.0%	2	1.0%
Herpes Zoster	1	0.6%	0	0.0%	1	0.5%
Others	22	22.1%	9	18.0%	31	15.1%

TNFi: tumor necrosis factor inhibitor

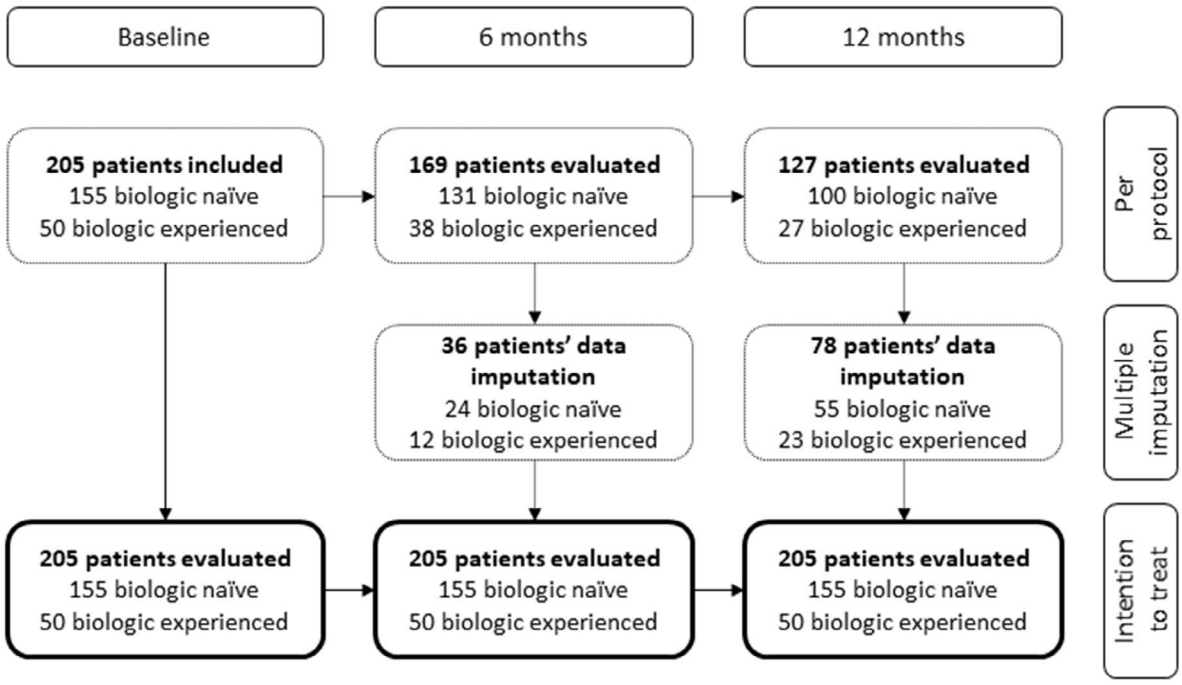

Figure 1: Lost to follow-up of patients in the study at six and 12 months.

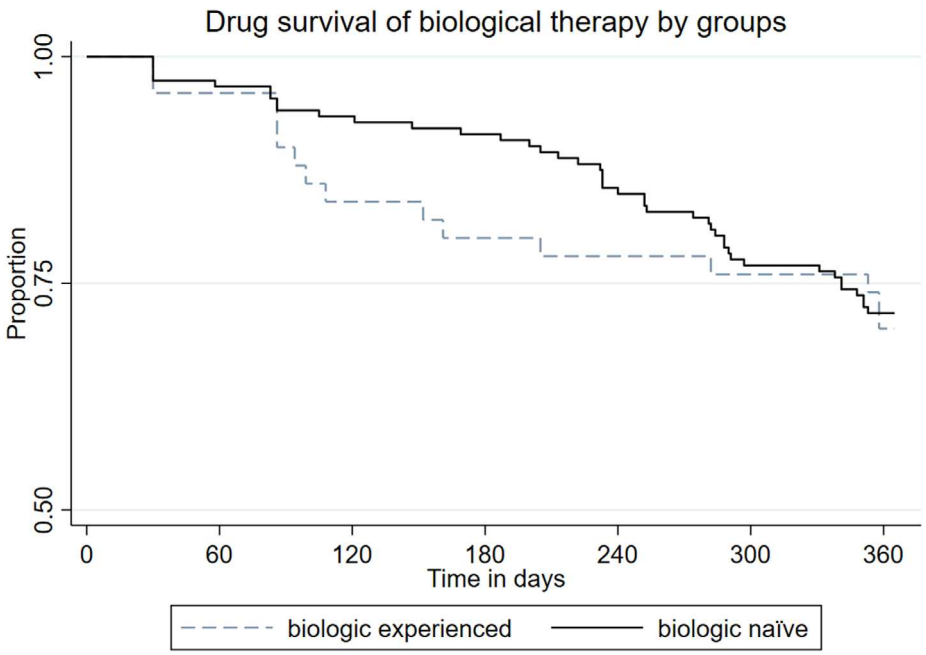

Figure 2: Drug survival with biological therapy by group.

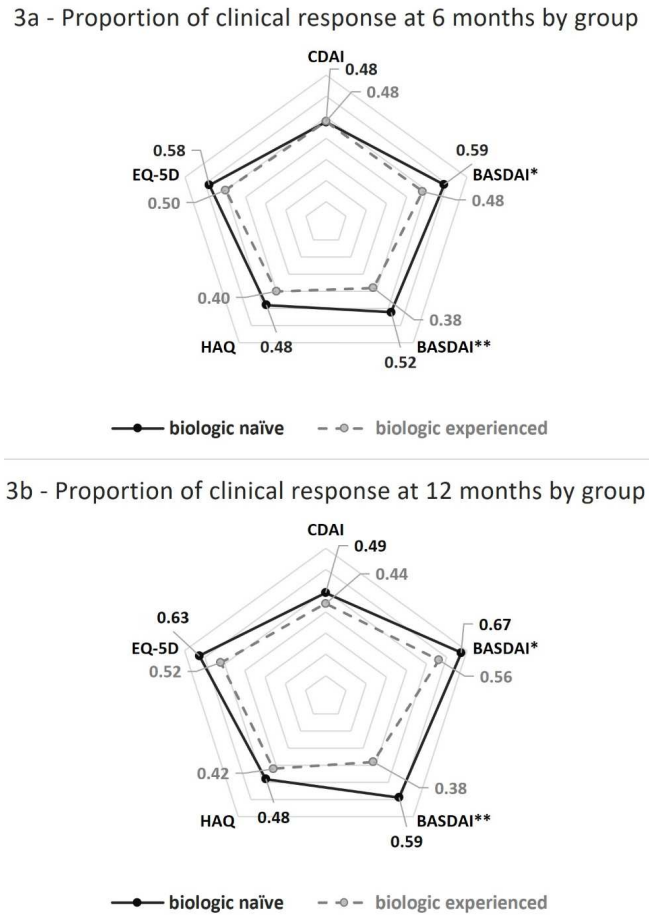

Figure 3: Proportion of clinical response at six (3a) and 12 months (3b) by group.

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Author contributions

Michael Ruberson Ribeiro da Silva and Jéssica Barreto Ribeiro dos Santos were involved in the acquisition, analysis, interpretation of data; and drafting of the work. Adriana Maria Kakehasi, Alessandra Maciel Almeida, Juliana Alvares-Teodoro e Francisco de Assis Acurcio were involved in the conception or design of the work and revising it critically for important intellectual content. All authors approved the final version to be published and agreement to be accountable for all aspects of the work.

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Conflict of interests

The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval

Approval was obtained from the Ethics Committee of the Federal University of Minas Gerais, under Opinion Nº 0069.0.203.000-11. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

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