Received: 1 August 2022 | Revised: 7 December 2022 | Accepted: 21 December 2022

DOI: 10.1002/hsr2.1034

ORIGINAL RESEARCH

Health Science Reports Open Access WILEY

# Impact of access to treatment on patient-reported outcomes among rheumatoid arthritis patients with tDMARDs and bDMARDS in two Latin-American countries: A prospective observational study

Juan M. Reyes[1] | Magda V. Gutierrez-Ardila[2] | Hugo Madariaga[3] | William Otero[4] | Renato Guzman[5] | Jorge Izquierdo[6] | David J. Del Castillo[6] | Mauricio Abello[7] | Patricia Velez[8] | Dario Ponce de Leon[9] | Tatjana Lukic[10] | Luisa F. Amador[1] | Natalia Castaño[1]

[1]Pfizer, Bogota, Colombia

[2]Pfizer, Santiago, Chile

[3]Centro Médico CEEN, Arequipa, Peru

[4]Centro Servimed, Bucaramanga, Colombia

[5]Centro IDEARG, Bogotá, Colombia

[6]Clínica del Occidente, Cali, Colombia

[7]Centro Integral de Reumatología Circaribe, Barranquilla, Colombia

[8]Centro Médico CIREEM, Bogota, Colombia

[9]Pfizer, Lima, Peru

[10]Pfizer Inc, New York, USA

**Correspondence**

Juan Reyes, Pfizer S.A.S, Av. Suba #95-66, Bogotá 111211, Colombia.
Email: JuanManuel.Reyes@pfizer.com

**Funding information**

Pfizer SAS

## Abstract

**Background and Aims:** A noninterventional prospective study was performed in Colombia and Peru. The aim was to describe the impact of access to treatment on Patient-reported outcomes (PRO) in patients with Rheumatoid arthritis (RA) after failure to conventional disease-modifying antirheumatic drugs (DMARDs) in real-life conditions.

**Methods:** The impact of access to treatment was measured by access barriers, time to supply (TtS) and interruption evaluating their effect in changes of PROs between baseline and 6-month follow-up between February 2017 and November 2019. The association of access to care with disease activity, functional status, health-related quality of life was assessed using bivariate and multivariable analysis. Results are expressed in least mean difference; TtS in mean number of days for delivery of treatment at baseline. Variability measures were standard deviation and standard error.

**Results:** One hundred seventy patients were recruited, 70 treated with tofacitinib and 100 with biological DMARDs. Thirty-nine patients reported access barriers. The mean of TtS was 23 ± 38.83 days. The difference from baseline to 6-month visit in PROs were affected by access barriers and interruptions. There was not statistically significant difference in the of PRO's score among visits in patients that reported delay of supply of more than 23 days compared to patients with less days of delay.

**Conclusion:** This study suggested the access to treatment can affect the response to the treatment at 6 months of follow-up. There seems to be no effect in the PROs for delay of TtS during the studied period.

KEYWORDS
bDMARDs (biologic), disease activity, healthcare access, Latin American, rheumatoid arthritis, tofacitinib

## 1 | INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune, chronic, systemic disorder that affects approximately 1% of the world's population.[1] It is characterized by synovial membrane swelling that causes joint swelling, stiffness, and pain, which subsequently leads to the progressive erosion and destruction of cartilage and bone tissue in the affected joints. Between 17.85% and 40.9% of patients with RA may experience extra-articular manifestations that may involve skin, eye, respiratory, oral, cardiovascular, neurological, hematological, and/or vascular function.[2–5] Patients with RA are also likely to experience depression, sexual dysfunction, and social relationship disruption.[6]

Biological disease modifying antirheumatic drugs (bDMARDs) and tofacitinib have demonstrated consistent efficacy in reducing the signs and symptoms of RA and have shown improvements in patient-reported outcomes (PROs) with manageable safety profiles.[7–13] In Latin America, rheumatologists have clinical experience in treating RA patients with bDMARDs[14] or tofacitinib.[15] In contrast to bDMARDs, tofacitinib is orally administered and has been used as a monotherapy more frequently than bDMARDs.[16] Both treatments have been recommended for the treatment of RA in the clinical guidelines of the Colombia and Peru.[17,18]

However, access to treatments in those countries is limited. The health care systems of the different Latin American countries change, and depending on if the government provides treatments then the coverages can vary from 60% to 100% of the population, and not all bDMARDs are available.[14] These varying degrees of coverage have negative effects on patient welfare and on disease activity.[19] A noninterventional study was conducted in Colombia and Peru to describe the baseline changes at 6 months in the outcomes associated to physical activity, disease activity, quality of life, and safety in patients with RA treated with tofacitinib or bDMARDs after the failure of conventional DMARDs in real-life conditions register in Clinical trial. According to the analysis, access barriers and other related variables were significant associated to the baseline clinical outcomes changes observed for both treatments.[20]

Although there are studies assessing PROs and the safety of RA treatment, particularly with bDMARDs, data related to current access to treatments, especially to tofacitinib, are scarce in Latin American countries. Additionally, there are no data on the association between PROs and the access barriers patients face; and thus, researchers are unable to capture the differences in treatment outcomes with tofacitinib or bDMARDs. Therefore, using the data of the cohort study previously mentioned the present study aimed to describe the impact of access to treatment (access barriers, time to supply [TtS], and interruption) on PROs in patients with RA treated with tofacitinib or bDMARDs after failure with conventional DMARDs, in clinical practice in Colombia and Peru.

## 2 | MATERIAL AND METHODS

### 2.1 | Setting and population

The impact of access to treatment was determined by describing the changes between baseline and 6-month follow-up in PROs. The prospective observational study was conducted on the index date when the treatment was prescribed. One hundred seventy patients with established RA who were treated with tofacitinib or bDMARDs as a second line of therapy after failure of conventional DMARDs were recruited in the study. The selection of the treatment, its modification and any use of concomitant medications assessed at follow-up were within current practice guidelines and were decided upon by their rheumatologist under routine clinical practice. The patients were recruited from two Latin American countries, Colombia (10 sites) and Peru (3 sites), between February 2017 and November 2019. Clinical trial number NCT03073109.

The inclusion criteria used to collect unanimously the information in 13 centers were patients with 18 years or older; had received a diagnosis of moderate to severe RA more than 6 months before enrollment in the trial, considered as established RA; activity of the disease defined as Disease Activity Score (28-joint count, based on erythrocyte sedimentation rate [DAS28-ESR]); failure to conventional DMARDs which was defined as inadequate response to conventional DMARDs at least 12 weeks before study entry based on disease activity, and no experience with bDMARDs.

The patients' baseline data were collected after prescription of the treatments, and these data corresponded to the patient's demographic and clinical characteristics for the study of RA status and comorbidities. The follow-up of patients was performed by interviewing patients at months 0 and 6 (±1 month) to measure the PROs. The flow diagram of the study is presented in the Figure 1.

### 2.2 | Outcome measures

The access to treatment was evaluated as follows: TtS; interruption of supply; and access barriers. Access barriers were defined as any constraints caused by administrative issues with the health care insurance or supplier reported by the patient during the follow-up visit. The TtS was measured only for the first prescription dosage delivery from the Health Maintenance Organization (HMO) or supplier to the patient, and it was expressed as the number of days required for the delivery of treatment from the time of prescription. It was dichotomized using as cut-off based on the mean of days observed in the cohort. An interruption occurred if the patient lost 1 day or more during the treatment.

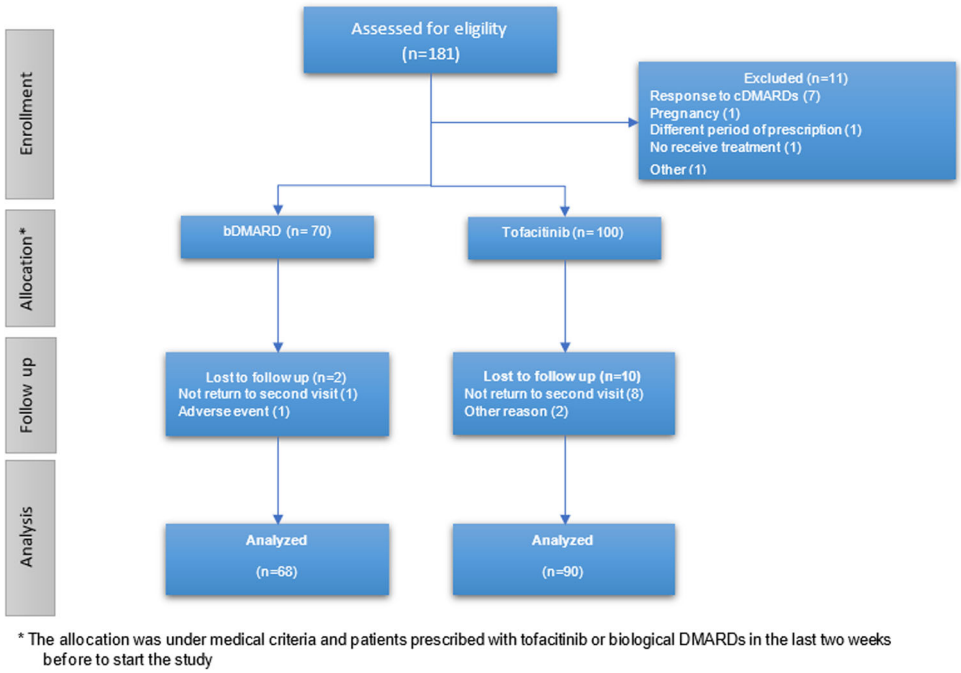


**FIGURE 1** Diagram flow of patients in the study

Functional status was evaluated using the Health Assessment Questionnaire—Disability Index (HAQ-DI), which was adapted since eight of the questions were included in the Routine Assessment of Patients Index Data 3 (RAPID3). Quality of life was evaluated using the HAQ 3-level (EQ-5D-3L); disease activity was evaluated using the RAPID3; and disease activity score was evaluated using the 28 (DAS28-ESR) tender and swollen joint counts. All questionnaires were validated in the Spanish language.

## 2.3 | Statistical analysis

Data were summarized by descriptive statistics. Univariate analyses were performed on the patients' demographic and clinical characteristics regarding RA status and comorbidities in both groups (access barriers and without access barriers). For continuous variable, *t* test was used when it has a normal distribution or Wilcoxon Rank-Sum test for nonparametric distribution. In categorical variables, $X^2$ test and Kruskal–Wallis test depending on the number of categories. The statistical software package R (version 4.0.5) was used to conduct the statistical analysis.

The clinical outcomes were analyzed by estimating the difference in means using least square means between periods and patients that reported access barriers, interruption, or TtS higher than the mean. Therefore, a bivariate and multivariable analysis was performed to identify the association between potential confounding variables.

In the difference between visits in each PROs, linear regression was conducted for the multivariable analysis. The adjusted full model was composed of all potential confounding variables such as demographic and clinical characteristics, concomitant treatment, treated with tofacitinib or bDMARD, among others (e.g., age, gender, country of origin, previous treatments, neutrophils, insurance, and baseline clinical data such as DAS28-ESR). The reduced model was developed from the results of multivariable analysis selecting the variables with $p$ value less than 0.05, it was considered as statistically significant. For comparison between PRO's score in the baseline and 6-month visit for each studied groups were used paired *t*-test for unadjusted analysis and mixed effects regression analysis for adjusted results.

The changes in the clinical outcomes during the period of follow-up were expressed as the least mean difference, and variability measures were standard deviation (SD) and standard error (SE). Multiple imputation was used to manage the missing data from the different variables using multiple imputation methods Multivariate Imputation by Chained Equations (MICE) with five imputations using the predictive mean matching based all the variables available to conduct the prediction (outcomes and treatment were not used as predictors). It was run with the package MICE in R software (version 4.0.5).

## 2.4 | Ethics statement

The protocol was approved by the Independent Ethics Committee at each center. All the patients provided written informed consent.

# 3 | RESULTS

One hundred seventy patients were recruited and treated with tofacitinib (100 patients) and bDMARDS ($n = 70$ patients). Twelve patients were withdrawn from the study, principally due to loss to

follow-up ($n = 9$ patients). The mean of duration of the treatment was 5.21 ± 2.27 months. For tofacitinib group was 4.82 ± SD 2.53 months and bDMARDs group 5.83 ± SD 1.61 months.

The mean age was 53.53 ± SD 13.77 years old and 6.31 ± SD 7.02 years since RA diagnosis. Among the patients, methotrexate (58.82%), leflunomide (19.41%), or chloroquine (11.76%) were the most frequent conventional DMARDs used previously. Corticosteroids were used previously by 82.94% of the patients. The main access mechanisms for treatments were private health insurance ($n = 91$) and public health insurance ($n = 53$); there was no information available for 12 patients. Private health insurance was more frequently used in both countries.

Among the imputed variables, highest percentage of missing values were 21%. The outcome variables do not report missing data at baseline (See the reported the variables with missing data in Supporting Informaton Material).

## 3.1 | Access barriers

Thirty-nine patients reported access barriers during follow-up; these barriers were most frequently reported by Colombian patients. The barriers were observed with almost all health insurance, but particularly with private insurance. The patients with access barriers reported longer length of time since initial diagnosis (Table 1).

The difference from baseline to 6-month visit in RAPID3, adapted HAQ-DI, DAS28-ESR, and EQ-5D-3L were affected by access barriers (Table 2). When PROs were evaluated by group of patients with access barriers or without access barriers, the first group reported slight reduction in disease activity than second group in RAPID3 and DAS28-ESR scores ($p < 0.001$ and $p = 0.011$, respectively). The covariables included in the multivariable analysis are reported in Supporting Information Material.

A similar proportion of patients by type of disease activity (high, moderate, low, and remission) was reported between groups with or without access barriers at baseline. At the 6-month follow-up, 69% of the patients without access barriers achieved remission or low activity, while only 29% of the patients who experienced access barriers achieved remission or low activity (Figure 2).

## 3.2 | Interruption

Thirteen patients reported any interruptions during the follow up which six patients were treated with bDMARDs and seven with tofacitinib. Interruption of treatment impacted the improvement of PROs, mainly the associated with disease activity, in which DAS28-ESR was the only statistically significant (Table 2). The impact was higher in the comparison between visits, the differences for all PROs were not changed significantly in patients with interruptions, contrary tendency occurs in patients without interruptions (see details in Supporting Information Material).

**TABLE 1** Clinical and demographic characteristics by access barriers

| | With access barriers | Without access barriers | *p* Value |
|---|---|---|---|
| Number of subjects | 39 | 119 | |
| Age—Mean (SD) | 56 (17) | 52.1 (13) | 0.190 |
| Female—% (no. of patients) | 82% (32) | 91% (108) | 0.230 |
| Country—% (no. of patients) | | | |
| Peru | 7.7% (3) | 66% (78) | <0.001 |
| Colombia | 92% (36) | 34% (41) | |
| Urban area—% (No. of patients) | 92% (36) | 99% (108) | 0.076 |
| Health insurance % (no. of patients) | | | |
| Complementary | 0% (0) | 2.5% (3) | 0.024 |
| Patient | 23% (9) | 1.7% (2) | |
| Private | 46% (18) | 61% (73) | |
| Public | 31% (12) | 34% (41) | |
| Time to supply (days)—Mean (SD) | 46 (64) | 8 (30) | 0.057 |
| Disease year—Mean (SD) | 9.1 (8.7) | 5.4 (6.2) | 0.018 |
| Time previous treatment (months) | 23 (22) | 29 (33) | 0.210 |
| Advanced therapy | | | 0.024 |
| Tofacitinib | 74% (29) | 52% (62) | |
| bDMARDs | 26% (10) | 48% (57) | |
| Concomitant therapy—% (No. of patients) | | | |
| Leflunomide | 28% (11) | 20% (24) | 0.050 |
| Methotrexate | 87% (34) | 48% (57) | <0.001 |
| Aminoquinolines | 38% (15) | 6.7% (8) | <0.001 |
| Corticosteroids | 87% (34) | 87% (103) | 1.000 |
| Clinical characteristics | | | |
| Lymphocytes/mm$^3$—mean (SD) | 3.200 (1.100) | 2.200 (1.100) | 0.080 |
| Neutrophils/mm$^3$—mean (SD) | 5.000 (2.00) | 4.400 (2.300) | 0.250 |
| Swollen joins—mean (SD) | 7.2 (5.4) | 8.1 (6.3) | 0.430 |
| Tender joints—mean (SD) | 8.9 (6) | 11 (5.9) | 0.0780 |
| Medical condition—% (no. of patients) | 13% (5) | 2.5% (3) | 0.030 |
| DAS28-ESR—mean (SD) | 5.2 (8.) | 5.6 (3.5) | 0.230 |

**TABLE 1** (Continued)

| | With access barriers | Without access barriers | *p* Value |
|---|---|---|---|
| Previous treatment—% (no. of patients) | | | |
| Deflazacort | 13% (5) | 22% (26) | 0.320 |
| Leflunomide | 18% (7) | 13% (16) | 0.670 |
| Methotrexate | 69% (27) | 25% (30) | <0.001 |
| Prednisolone | 44% (17) | 45% (53) | 1.000 |
| Folic acid | 0% (0) | 1% (1) | 1.000 |
| Chloroquine | 13% (5) | 4.2% (5) | 0.120 |
| Hydroxychloroquine | 10% (4) | 1(1) | 0.017 |
| Sulfasalazine | 2.6% (1) | 1% (1) | 0.990 |
| Methylprednisolone | 2.6% (1) | 1% (1) | 0.990 |

**TABLE 2** PROs at difference changes in patients groups adjusted for multivariable analysis

| | Mean | SE | *p* Value |
|---|---|---|---|
| Access barriers | | | |
| RAPID3 | −1.59 | 0.454 | <0.001 |
| Adapted HAQ-DI | −0.345 | 0.12 | 0.006 |
| EQ-5D-3L | 0.091 | 0.07 | 0.202 |
| DAS28-ESR | −0.721 | 0.278 | 0.011 |
| Interruption | | | |
| RAPID3 | −1.22 | 0.665 | 0.069 |
| Adapted HAQ-DI | −0.232 | 0.177 | 0.191 |
| EQ-5D-3L | 0.161 | 0.1 | 0.110 |
| DAS28- ESR | −1.03 | 0.377 | 0.007 |
| Time to supply more than 23 days | | | |
| *RAPID3* | −1.03 | 0.543 | 0.061 |
| Adapted HAQ-DI | −0.11 | 0.11 | 0.304 |
| EQ-5D-3L | 0.083 | 0.0627 | 0.186 |
| DAS28-ESR | −0.051 | 0.233 | 0.827 |

Abbreviations: DAS28-ESR, Disease Activity Score (28-joint count, based on erythrocyte sedimentation rate); EQ-5D-3L, quality of life was evaluated using the Health Assessment Questionnaire 3-level; HAQ-DI, Health Assessment Questionnaire—Disability Index; PROs, patient reported outcomes; RAPID3, Routine Assessment of Patient Index Data 3; SE, standard error.

### 3.3 | TtS

The mean of TtS was 23 ± 38.83 days. Forty-eight patients presented TtS for more than 23 days after prescriptions, 26 patients with bDMARDs and 22 patients with tofacitinib. After multivariable analysis, there was numerical difference without being statistically significant in the of PRO's score among visits in patients that reported delay of supply of more than 23 days compared to patients with less days of delay. This reduction is mainly observed in RAPID3 and adapted HAQ-DI (Table 2). The comparison of PRO´s score between baseline visit and 6-month visit is presented in detail in Supporting Information Material.

The type of treatment (tofacitinib or bDMARDs) was not associated to difference from baseline to month 6 in the analysis in both groups of patients of access barriers, interruption and TtS. However, treatment was a covariable included in the multivariable analysis when the scores were compared between visits. Other relevant variables were country, previous use of leflunomide, previous use of methotrexate, DAS28-ESR baseline, neutrophils, corticosteroids, diagnosis year, type of health insurance, and among others (see details in Supporting Information Material).

## 4 | DISCUSSION

The purpose of this study was to describe the impact of access to treatment on PROs in patients with RA treated with tofacitinib or bDMARDs; Access barriers negatively affected the PROs measured at the 6-month follow-up; interruption affected mainly DAS28-ESR; and TtS has not was statistically difference between groups in all PROs. This result suggested that access to treatment are relevant factors to consider in different real-world conditions situations assessing health-related effects of treatments, such as in clinical practice and research using noninterventional studies.

In Peru, tofacitinib and bDMARDs are included in the national health benefits plan of Healthcare Social Security (ESSALUD) for the treatment of moderate to severe RA in patients who failed a methotrexate-based therapy; in contrast, in Colombia, tofacitinib was not included in the national health benefits plan at the moment of this study; however, it was reimbursed by the government. Although the health care systems in Colombia and Peru are heterogeneous (i.e., characteristics of the health care system, regulation, financing, and reimbursement decisions), the results show the presence of access barriers for 32% of the patients, regardless of health insurance. In Latin American countries, affiliation or contribution does not guarantee effective access to treatments, which can be restricted by economic barriers, such as copayments,[21] constraints on health service provision, delays in scheduling medical appointments, and long distances and difficulties of travel,[22] among other factors. In Colombia a previous reported difficulties in access to medications associated with authorizations by the insurer in patients with bDMARD or tofacitinib.[23]

Few studies have evaluated the access barriers among RA patients specifically related to the use of biologics. The Health Outcomes Patient Environment (HOPE) study conducted in Greece reported a higher proportion of access barriers among RA patients treated with biologics (49%) during 12 months of follow-up, which was mainly related to the prescribing process, the long distances patients had to travel to receive treatment, and the nonavailability of

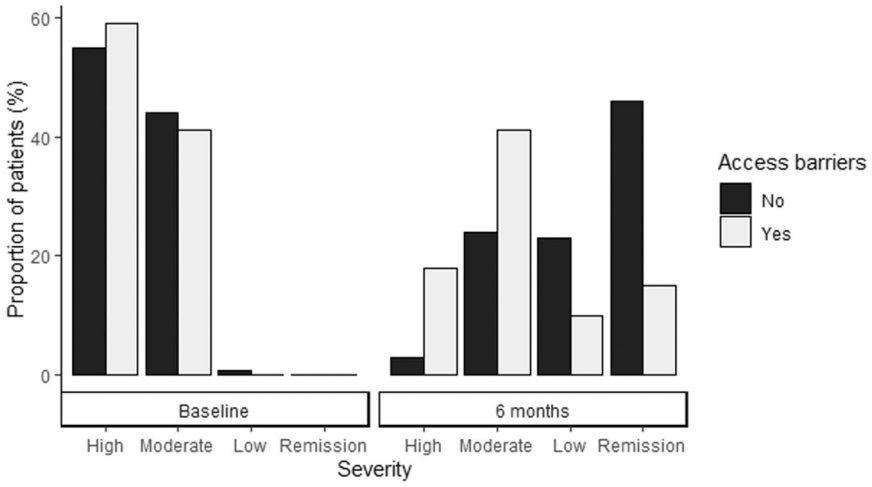


**FIGURE 2** DAS28-ESR results categorized by severity of the diseases at baseline and 6 month visit for access barriers. DAS28-ESR, disease activity score was evaluated using the 28.

medication at the hospital.[24] In Portugal, rheumatologists reported the longest wait-times for the approval of biologics, from 2 days up to 8 weeks; however, the study did not mention the proportion of patients affected.[25]

Other studies analyzed access or treatment with bDMARDs in different countries. According to a survey conducted in 49 European countries, almost 40% of people have access issues with bDMARDs therapies for RA; financial and administrative restrictions were the main barriers.[26] Another study analyzed patient characteristics associated with a higher probability of initiating a bDMARDs, such as patients older than 70 years, Hispanic ethnicity, household income, being married and residence in a rural environment.[27] Availability, affordability, and acceptability are variables associated with access to medications at the general level. Under availability is affected by the size of the market, by each country's health policies related to low income patients, by the low percentage of the gross domestic product allocated to health care, by pricing and funding, especially in countries with low incomes, and by physicians' and patients' willingness to pursue a treatment despite being familiar with the health care system's barriers, such as administrative and financial constraints.[28]

Based on our findings, patients face significant barriers to accessing effective medications, which constitute major problems in Colombia and Peru because they affect the achievement of clinical outcomes. In a Colombian study of patient complaints gathered in 2013, some of the main issues were delays in the approval of services and constraints on the opportunities for treatment, including access to medicines.[29] Although the study did not characterize the cause of access barriers, lack of access and delay of treatment were factors that impacted the clinical response for both patient groups. Additionally, previous studies of RA patients have shown disparities in access to treatments among European countries[30,31] and a negative relationship between countries' bDMARDs usage and the level of disease activity.[32] Further research may describe alternatives to reduce the gap between the treatments needed by RA patients in the Peruvian and Colombian contexts.

The results of the study need to be analyzed cautiously, specially TtS and interruption, given that sample size was limited, the study did not quantified patients with more than one interruption or more times of delay's supply, duration of the interruption, and time of follow up. In this study those measurement showed reduction a difference between groups without statistically difference, there were only 13 patients with interruption and 48 patients were with TtS more than 23 days after prescriptions of a total of 170 patients. Future research could focus on incorporating or intended to address concerns raised which has the potential to had more relevant the measurement of TtS and interruption.

The inclusion and exclusion criteria were wide to recruit patients more similar to them from clinical practice where tofacitinib and bDMARDs are used. Additionally, the study involved many sites distributed in Colombia and Peru which allowed to count on participants in several regions of the countries. However, the interpretation of results of this study should consider the current situation of use of these treatments and the changes of the health care systems.

This study has some limitations. One of these limitations is the heterogeneity among patients, which is a result of the study design. This study was controlled by multivariable analysis, where different clinical factors were evaluated as influencing the association between access and PROs; however, it was limited to observable covariables. There may be other variables that were not measured and that potentially could affect the association between access barriers and the clinical outcomes; this is a known limitation of observational studies.

In an effort to reduce the barriers identified in the management of RA, Colombia and Peru, as well as other Latin American countries, have established early disease clinics, and at least in Colombia, one study showed that the time to referral from primary to tertiary care among RA patients has improved.[14] With respect to regulation, Colombia institutes laws that mandate epidemiologic surveillance of RA-related prevention, diagnosis, and treatment. The opportunity for treatment, in weeks, from symptom onset until the first treatment with bDMARDs was 26.3 in 2019[33] and 27.0 in 2020[34]; the goal was 20 weeks, which indicates that there are important challenges and improvement opportunities remaining in the provision of services to these patients.

Although this situation may have begun to improve, challenges remain in the availability of therapies, access to treatments, and TtS, which will all have a measurable impact on the well-being of patients with RA.

In conclusion, this study suggested the access to treatment can affect the response to the treatment at 6 months of follow-up. There seems to be no effect in the PROs for delay of TtS during the studied period. Additional studies are required to continue evaluating the impact of these variables in the clinical outcomes.

## AUTHOR CONTRIBUTIONS

All authors have read and approved the final version of the manuscript. Reyes J. M. had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

## ACKNOWLEDGMENT

The authors would like to thank all Research Centers for allowing us to conduct the study Centro Integral de Reumatología del Caribe Circaribe, SERVIMED, Centro de Investigaciones en Reumatología y Especialidades Médicas SAS, Reumalab, Fundación Valle de Lili, Clínica Jockey Salud, Clínica San Judas Tadeo, Clínicos IPS, Centro Medico CEEN, Fundación Instituto de Reumatología Fernando Chalem, Clínica de Occidente, Artmedica and IDEARG and thank all the patients that accepted to participate in the study. This work was funded by Pfizer Inc.

## CONFLICTS OF INTEREST

Reyes J. M., Gutierrez-Ardila M. V., Castano N., Ponce de Leon D., Lukic T., and Amador L. are employees of Pfizer. Del Castillo D. and Izquierdo J. have received speakers fees from several pharmaceutical companies. The remaining authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## ETHICS STATEMENT

The protocol and that informed consent has been obtained from the subjects were approved by the Independent Ethics Committee at each center. The study was conducted in accordance with the Declaration of Helsinki and the local regulation of the participant countries. The patients contributed to the study during the implementation of the protocol responding the different patient-reported outcomes after signing informed consent approved by the Independent Ethics Committee.

## TRANSPARENCY STATEMENT

Reyes JM affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

## ORCID

*Juan M. Reyes* http://orcid.org/0000-0003-0806-7173
*Magda V. Gutierrez-Ardila* http://orcid.org/0000-0001-6455-8685
*Dario Ponce de Leon* http://orcid.org/0000-0003-2250-6849
*Natalia Castaño* http://orcid.org/0000-0001-7383-6800

## REFERENCES

1. Gibofsky A. Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. *Am J Manag Care*. 2012;18(suppl 13):295-302.
2. Myasoedova E, Crowson CS, Kremers HM, Therneau TM, Gabriel SE. Is the incidence of rheumatoid arthritis rising?: results from Olmsted County, Minnesota, 1955-2007. *Arthritis Rheum*. 2010;62(6):1576-1582.
3. Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum*. 2008;58(1):15-25.
4. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American college of Rheumatology/European league against rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62(9):2569-2581.
5. Prete M, Racanelli V, Digiglio L, Vacca A, Dammacco F, Perosa F. Extra-articular manifestations of rheumatoid arthritis: an update. *Autoimmun Rev*. 2011;11(2):123-131.
6. Gettings L. Psychological well-being in rheumatoid arthritis: a review of the literature. *Musculoskeletal Care*. 2010;8(2):99-106.
7. van Vollenhoven RF, Fleischmann R, Cohen S, et al. Tofacitinib or adalimumab versus placebo in rheumatoid arthritis. *N Engl J Med*. 2012;367(6):508-519.
8. Burmester GR, Blanco R, Charles-Schoeman C, et al. Tofacitinib (CP-690,550) in combination with methotrexate in patients with active rheumatoid arthritis with an inadequate response to tumour necrosis factor inhibitors: a randomised phase 3 trial. *Lancet*. 2013;381(9865):451-460.
9. van der Heijde D, Tanaka Y, Fleischmann R, et al. Tofacitinib (CP-690,550) in patients with rheumatoid arthritis receiving methotrexate: twelve-month data from a twenty-four-month phase III randomized radiographic study. *Arthritis Rheum*. 2013;65(3):559-570.
10. Kremer J, Li Z-G, Hall S, et al. Tofacitinib in combination with nonbiologic disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis: a randomized trial. *Ann Intern Med*. 2013;159(4):253-261.
11. Fleischmann R, Kremer J, Cush J, et al. Placebo-Controlled trial of tofacitinib monotherapy in rheumatoid arthritis. *N Engl J Med*. 2012;367(6):495-507. http://www.ncbi.nlm.nih.gov/pubmed/22873530
12. Lee EB, Fleischmann R, Hall S, et al. Tofacitinib versus methotrexate in rheumatoid arthritis. *N Engl J Med*. 2014;370(25):2377-2386.
13. Her M, Kavanaugh A. Patient-reported outcomes in rheumatoid arthritis. *Curr Opin Rheumatol*. 2012;24(3):327-334.
14. Burgos-Vargas R, Catoggio LJ, Galarza-Maldonado C, Ostojich K, Cardiel MH. Current therapies in rheumatoid arthritis: a Latin American perspective. *Reumatología Clínica*. 2013;9(2):106-112.
15. Schneeberger E, Salas A, Medina L, et al. AB0419 Real world use of tofacitinib in rheumatoid arthritis: data from latin america. *BMJ*. 2017;1196:3-1197.
16. Yamaoka K. Expert review of clinical immunology tofacitinib for the treatment of rheumatoid arthritis: an update Tofacitinib for the treatment of rheumatoid arthritis: an update. 2019. doi:10.1080/1744666X.2019.1607298
17. Salinas A, Huaringa-Marcelo J, Alfaro-Lozano J, et al. Guía de práctica clínica para el diagnóstico y manejo inicial de artritis reumatoide en el Seguro Social del Perú (EsSalud). scielo.org.pe

[Internet]. 2021. Accessed October 4, 2022. http://www.scielo.org.pe/scielo.php
18. Ministeriode alud y rotección Social. Guía de práctica clínica para la detección temprana, diagnóstico y tratamiento de la Artritis Temprana. 2014;876:196. Accessed October 4, 2022. https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/INEC/IETS/gpc-artritis-idiopatica-pacientes.pdf
19. Putrik P, Ramiro S, Keszei AP, et al. Lower education and living in countries with lower wealth are associated with higher disease activity in rheumatoid arthritis: results from the multinational COMORA study. *Ann Rheum Dis*. 2016;75(3):540-546. doi:10.1136/annrheumdis-2014-206737
20. Madariaga H, Reyes SJ, Gutierrez AM, Ponce LD, Lukic T, Amador L. PMS2 Patient-Reported outcomes in rheumatoid arthritis patients treated with tofacitinib or biological dmards in real life conditions: Colombian and Peru perspective. *Value Health*. 2021;24:S138. https://linkinghub.elsevier.com/retrieve/pii/S1098301521008962
21. Abramo L, Cecchini S, Ullmann H. Enfrentar las desigualdades en salud en América Latina: el rol de la protección social. *Cien Saude Colet*. 2020;25(5):1587-1598.
22. Bonfá E, Gossec L, Isenberg DA, Li Z, Raychaudhuri S. How COVID-19 is changing rheumatology clinical practice. *Nat Rev Rheumatol*. 2021;17(1):11-15.
23. Machado-Alba JE, Machado-Duque ME, Gaviria-Mendoza A, Reyes JM, Gamboa NC. Use of healthcare resources in a cohort of rheumatoid arthritis patients treated with biological disease-modifying antirheumatic drugs or tofacitinib. *Clin Rheumatol*. 2021;40(4):1273-1281.
24. Souliotis K, Papageorgiou M, Politi A, Ioakeimidis D, Sidiropoulos P. Barriers to accessing biologic treatment for rheumatoid arthritis in Greece: the unseen impact of the fiscal crisis—the Health Outcomes Patient Environment (HOPE) study. *Rheumatol Int*. 2014;34:25-33. doi:10.1007/s00296-013-2866-1
25. Laires PA, Mesquita R, Veloso L, Martins AP, Cernadas R, Fonseca JE. Patient's access to healthcare and treatment in rheumatoid arthritis: the views of stakeholders in Portugal. *BMC Musculoskelet Disord*. 2013;14(1):279. doi:10.1186/1471-2474-14-279
26. Putrik P, Ramiro S, Kvien TK, et al. Inequities in access to biologic and synthetic DMARDs across 46 European countries. *Ann Rheum Dis*. 2014;73(1):198-206. doi:10.1136/annrheumdis-2012-202603
27. Yelin E, Tonner C, Kim SC, et al. Sociodemographic, Disease, Health System, and Contextual Factors Affecting the Initiation of Biologic Agents in Rheumatoid Arthritis: a Longitudinal Study. *Arthritis Care Res (Hoboken)*. 2014;66:980-989. doi:10.1002/acr.22244
28. Ugarte-Gil MF, Silvestre AMR, Pons-Estel BA. Access to an optimal treatment. Current situation. *Clin Rheumatol*. 2015;34:59-66. doi:10.1007/s10067-015-3018-7
29. Hernández JMR, Rubiano DPR, Barona JCC. Barreras de acceso administrativo a los servicios de salud en población Colombiana, 2013. *Cien Saude Colet*. 2015;20(6):1947-1958.
30. Inotai A, Tomek D, Niewada M, et al. Identifying patient access barriers for tumor necrosis factor alpha inhibitor treatments in rheumatoid arthritis in five central eastern european countries. *Front Pharmacol*. 2020;11:845.
31. Kaló Z, Vokó Z, Östör A, et al. Patient access to reimbursed biological disease-modifying antirheumatic drugs in the European region. *J Mark Access Health Policy*. 2017;5(1):1345580.
32. Bergstra SA, Branco JC, Vega-Morales D, et al. Inequity in access to bDMARD care and how it influences disease outcomes across countries worldwide: results from the METEOR-registry. *Ann Rheum Dis*. 2018;77:1413-1420.
33. Cuenta de Alto Costo (CAC). Fondo Colombiano de Enfermedades de Alto Costo. Situación de la artritis reumatoide en Colombia 2019. 2020.
34. Cuenta de Alto Costo (CAC). Fondo Colombiano de Enfermedades de Alto Costo. Situación de la artritis reumatoide en Colombia 2020. 2021.

## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Reyes JM, Gutierrez-Ardila MV, Madariaga H, et al. Impact of access to treatment on patient-reported outcomes among rheumatoid arthritis patients with tDMARDs and bDMARDS in two Latin-American countries: a prospective observational study. *Health Sci Rep*. 2023;6:e1034. doi:10.1002/hsr2.1034