Rheumatol Ther (2023) 10:1519–1533
https://doi.org/10.1007/s40744-023-00594-6

ORIGINAL RESEARCH

A Real-World Effectiveness Study Using a Mobile Application to Evaluate Early Outcomes with Upadacitinib in Rheumatoid Arthritis

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Received: June 21, 2023 / Accepted: August 18, 2023 / Published online: September 20, 2023

ABSTRACT

Introduction: The impact of upadacitinib on rheumatoid arthritis (RA) symptoms was evaluated during the first 12 weeks of treatment via patient-reported outcomes (PROs) using a mobile health application (app).

Methods: Participating rheumatologists from the CorEvitas RA Registry (prospective, observational cohort) recruited patients with RA initiating upadacitinib treatment. A modified version of the ArthritisPower® app was used to collect PROs, including the Routine Assessment of Patient Index Data 3 (RAPID3), duration of morning joint stiffness, and the Patient-Reported Outcomes Measurement Information System (PROMIS)-Fatigue 7a Short Form at baseline and weeks 1–4, 8, and 12. RAPID3 responses over time were assessed using Kaplan–Meier estimation to determine the proportion of patients achieving disease activity improvement and minimal clinically important difference (MCID). Results were analyzed for all patients initiating upadacitinib and a subsample of TNF inhibitor (TNFi)-experienced patients with moderate to severe disease at baseline.

Results: A total of 103 patients with RA initiating upadacitinib (62.1% TNFi-experienced) were included. At week 12, 53 patients (51.4%) completed the study and provided PRO data via the app. Among all patients, improvements in RAPID3, pain, morning stiffness, and fatigue were observed at week 1 and were maintained or further improved through week 12. At week 12, 37.5% of patients achieved RAPID3 low disease activity. Starting at week 1, improvements in RAPID3 disease activity category (19.4% of patients) and achievement of MCID (16.3%) were reported, with nearly 50% of patients achieving these outcomes by week 4 (RAPID3 category: 48.8%; MCID: 49.2%) and 60% by week 12 (RAPID3 category: 59.6%; MCID: 59.8%). TNFi-experienced patients generally reported similar outcomes. Patient-reported

Prior Publication: These data were originally presented at the American College of Rheumatology (ACR) Convergence 2022 Annual Congress (Philadelphia, PA, USA; November 10–14, 2022) [1].

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40744-023-00594-6.

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medication convenience and compliance were generally high.
Conclusions: In this real-world cohort of patients with RA, treatment with upadacitinib was associated with early and significant improvement in RAPID3, pain, morning stiffness, and fatigue regardless of prior TNFi experience. Clinically meaningful improvement in RAPID3 patient-reported disease activity was observed as early as week 1, with continued improvement reported through week 12.

Keywords: CorEvitas; Janus kinase (JAK) inhibitor; Digital health; Observational; Patient-reported outcomes; Prospective; Real-world effectiveness; Routine Assessment of Patient Index Data 3 (RAPID3); Rheumatoid arthritis; Upadacitinib

Key Summary Points

Why carry out this study?

Little is known about the impact of upadacitinib in patients with rheumatoid arthritis (RA) during the initial weeks of therapy in real-world clinical practice.

Our objective was to evaluate patient-reported outcomes (PROs) in patients with RA during the first 12 weeks of treatment with upadacitinib using a mobile health application.

What was learned from the study?

In this prospective, observational cohort of patients with RA, treatment with upadacitinib was associated with early, significant improvement in disease activity and other PROs, including the Routine Assessment of Patient Index Data 3 (RAPID3), pain, morning stiffness, and fatigue, regardless of prior tumor necrosis factor inhibitor (TNFi) experience.

Improvement in RAPID3 patient-reported disease activity was observed as early as week 1 of upadacitinib treatment, with nearly 50% of patients reporting improvement by 4 weeks and 60% by 12 weeks.

This study successfully utilized a novel mobile application to gather patient-derived data for assessing early treatment response in clinical practice; future studies should consider providing additional patient support to maintain digital adherence over time.

INTRODUCTION

Advanced therapies for the treatment of rheumatoid arthritis (RA) have helped to slow disease progression, decrease the signs and symptoms of the disease, and improve the patient's quality of life [2–4]. Despite improved outcomes compared to traditional therapies, 30–40% of patients on tumor necrosis factor inhibitors (TNFi) do not respond to therapy and fail to achieve a long-term clinical response [5, 6]. In recent years, Janus kinase (JAK) inhibitors have been introduced as an alternative therapy to traditional biologics [7, 8]. Upadacitinib, an oral JAK inhibitor, was originally approved to treat patients with moderate-to-severe RA who had prior inadequate response or intolerance to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), and was later modified by the FDA in December 2021, to include patients with moderate-to-severe RA and an inadequate response or intolerance to TNFi [9]. The safety and efficacy of upadacitinib, an oral JAK inhibitor, to treat patients with moderate-to-severe RA who are naïve to or have prior experience with biologic therapy has been established across six phase 3 clinical trials from the SELECT program [10–15]. Furthermore, in the SELECT trials, response to upadacitinib treatment in the first 1–2 weeks was observed across several different efficacy endpoints, including patient-reported outcomes (PROs) [10, 12, 15]. However, there are limited data on the impact of upadacitinib in RA from the patient's perspective in real-world clinical practice, particularly during the initial weeks of therapy. Patient-derived data can help clinicians better understand the patient's

experience [16], which can lead to more tailored care to meet their individual needs.

Current assessment of a patient's disease activity and treatment experience in real-world clinical practice is typically limited to periodic office visits that occur every 3 or 6 months. Alternative data sources, such as remotely captured patient-reported data via mobile or web-based applications, can provide important interim data to supplement these periodic clinical assessments to better track disease status and treatment response. In addition, these remotely captured PROs can augment traditional measures collected in clinical trials and observational studies [17–19], while decreasing the burden placed on patients to complete in-person assessments [18]. These alternative data sources have been increasingly utilized and their merit recognized within the medical community [18, 20]. The objective of this study was to evaluate the impact of upadacitinib on PROs in patients with RA during the first 12 weeks of treatment using a mobile health application.

METHODS

Patients and Study Design

The CorEvitas (formerly known as Corrona) RA Registry is an independent, prospective, national, observational cohort established in 2001 in which treatment and outcome data for patients with RA are collected and analyzed. The registry currently (as of December 31, 2022) includes 218 private and academic active clinical sites with over 947 physicians throughout 42 states in the U.S. For this study, participating rheumatologists from the CorEvitas RA Registry recruited patients across 17 sites between July 2020 and October 2021 who were initiating upadacitinib 15 mg once-daily treatment. The decision to treat a patient with upadacitinib preceded the rheumatologist's decision to recruit/enroll patients into this study. To be eligible for enrollment, patients had to be willing and able to complete online weekly surveys on a personal computer or mobile device using a modified version of the ArthritisPower® application (refer to Supplemental Fig. 1 for representative screenshots from the application). ArthritisPower, an IRB-approved Patient-Powered Research Network, was created in 2014 by CreakyJoints in partnership with the University of Alabama Birmingham and with support from the Patient-Centered Outcomes Research Institute (PCORI). ArthritisPower protects participant data using industry standards of computer encryption and data security as described in the ArthritisPower informed consent form. Application registration was completed during the in-clinic visit using a custom URL provided by the research staff. After initial enrollment, patients utilized the application independently and PRO data were not automatically provided to the treating rheumatologist/CorEvitas clinical site staff unless the patient chose to share this information. Throughout the course of the study, patients received reminders via e-mail and/or application notifications to confirm treatment status and complete required PRO assessments according to the protocol schedule. Application support was provided by case managers, and they also contacted patients who failed to complete their weekly assessments. At enrollment, patients received a gift card for their involvement in the study. Given the negative impact of the COVID-19 global pandemic on patient in-office visits [21], which could impact study recruitment, at 6 months following study initiation, additional modest, recurring incentives were provided to patients at critical weeks following data collection (i.e., gift cards at weeks 1–4, 8, and 12) to improve response rate and retention for the duration of the 12-week observation period. Additional efforts to increase patient engagement included enhanced site communications and additional trainings, more frequent reminders, and a direct phone line for questions. All efforts to increase patient engagement were approved by the Institutional Review Boards (IRBs). Patients who did not initiate upadacitinib treatment within 12 weeks of in-clinic registration were exited from the study. Patients who discontinued treatment with upadacitinib prior to week 12 continued to receive regularly scheduled assessments through the application.

The CorEvitas RA Registry is conducted in accordance with the Declaration of Helsinki 1964 and its later amendments. All participating investigators were required to obtain full board approval for conducting research involving human subjects. Sponsor-level and site-level approval for this sub-study was obtained from the New England Independent Review Board (NEIRB; no. 20201379). All patients provided written informed consent and authorization prior to participating in the study.

Outcomes

For this study, the ArthritisPower application was used to collect PROs through week 12 following initiation of upadacitinib treatment. Baseline was defined as the application response closest to the first dose of upadacitinib, which varied per patient and occurred from enrollment up to 4 days after the first dose was received. PROs were assessed at weeks 1, 2, 3, 4, 8, and 12 and included Routine Assessment of Patient Index Data 3 (RAPID3; pooled index of three patient-reported American College of Rheumatology RA core data set measures, including physical function, pain, and patient global assessment of disease status, which were each scored 0–10, for a total of 30) [22], pain score (11-point visual analogue scale [VAS] derived from RAPID3, range 0–10), duration of morning joint stiffness (hours), and the Patient-Reported Outcomes Measurement Information System (PROMIS)-Fatigue 7a Short Form (total score 29.4–83.2; a score ≤ 55 is considered within normal limits for the general population) [23, 24]. The proportion of patients achieving RAPID3 low disease activity (LDA, defined as RAPID3 ≤ 6; includes patients achieving RAPID3 remission) [25] was assessed at weeks 1, 2, 3, 4, 8, and 12. In addition, RAPID3 responses were assessed as the proportion of patients achieving disease activity improvement (defined as a reduction of at least one RAPID3 disease activity category, such as moderate disease activity to low disease activity) or the proportion of patients achieving a minimal clinically important difference (MCID; defined as a decrease in RAPID3 ≥ 3.8 from baseline) [26] at weeks 1, 2, 4, 8, and 12. The Treatment Satisfaction Questionnaire for Medication (TSQM-9; range: 0–100 for effectiveness, convenience, and overall satisfaction subscales, with higher scores indicating greater satisfaction) [27] and the five-item Compliance Questionnaire for Rheumatology (CQR5; range, 0–20, with a higher score indicating greater adherence) [28] were assessed at weeks 8 and 12.

Statistical Analysis

For this study, all patients with RA initiating upadacitinib treatment with baseline information were analyzed. In addition, a subsample of TNFi-experienced patients with moderate-to-severe disease at baseline (defined as RAPID3 $>$ 6) was also analyzed. Baseline demographics and patient-reported characteristics are presented as frequency of patients (with proportions) for categorical variables and means (with standard deviation [SD]) for continuous measures. PROs are summarized as mean change from baseline (with 95% confidence intervals [CI]) for continuous outcomes (i.e., RAPID3 [including pain], fatigue, and duration of morning stiffness) and as the proportion of patients achieving a response (95% CI) for binary outcomes (i.e., RAPID3 LDA) among patients with data available at the respective follow-up timepoint. The TSQM-9 is summarized as mean (SD) and CQR5 is summarized as the proportion of patients classified as high adherers. For continuous outcomes, differences between baseline and follow-up values were assessed using paired *t* tests, with a P value < 0.05 considered statistically significant. RAPID3 disease activity improvement and MCID were estimated using the Kaplan–Meier method and are shown as the proportion of patients achieving response (95% CI). Patients were censored at the time of their last follow-up encounter if (1) they withdrew from the study without achieving improvement in disease activity category or MCID, or (2) they completed the 12-week study without achieving improvement. No imputations were made for missing data. As a sensitivity analysis to assess potential confounding, RAPID3 was modeled as

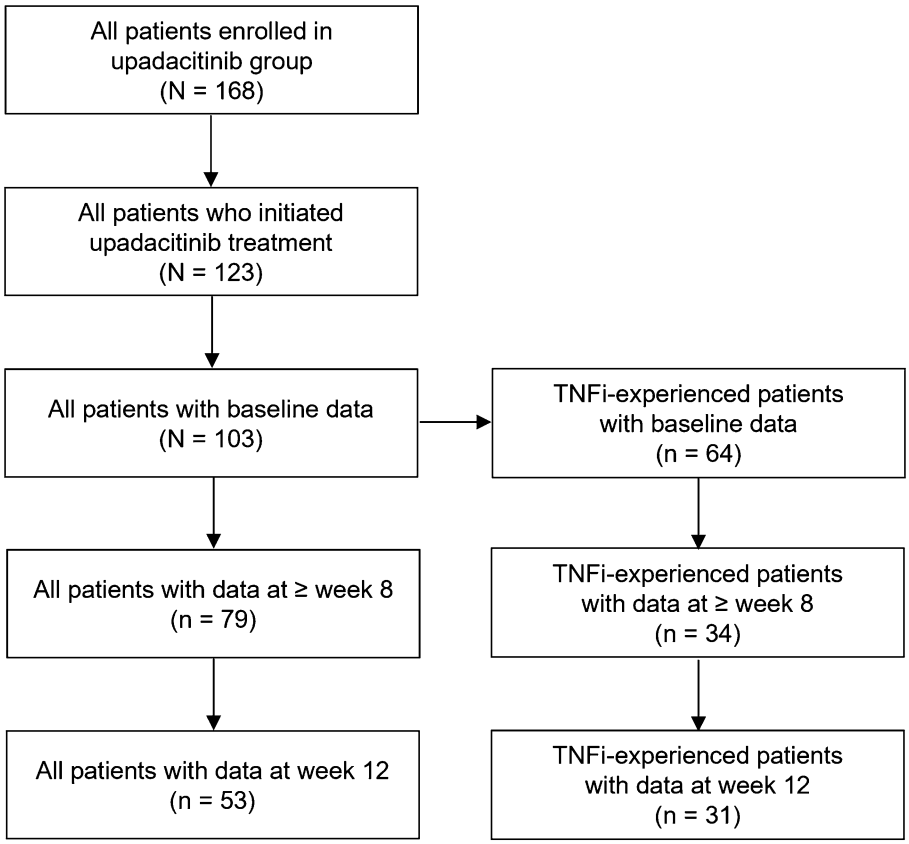


Fig. 1 Patient disposition. *TNFi* tumor necrosis factor inhibitor

the continuous dependent outcome of a linear mixed fixed-and-random-effects model, specifying a random intercept and adjusting for age, gender, and race, with estimates of mean change in RAPID3 over 12 weeks.

RESULTS

Study Population

In total, 168 patients with RA were enrolled in this study from July 2020 to February 2022 and 123 patients subsequently initiated upadacitinib treatment. Of these patients, 103 initiated upadacitinib treatment, had baseline data, and were included in this analysis (Fig. 1). Of the total patient population, 62.1% of patients (n = 64) had prior experience with a TNFi and were initiating upadacitinib in moderate or high disease activity. At week 12, 53 patients (51.4%) completed the study and provided PRO data via the mobile application. Patients initiating upadacitinib treatment were on average 59.9 years old, most were female (81.6%), and they had a mean (SD) RAPID3 score of 14.9 (5.2) (Table 1). Baseline demographics and patient-reported characteristics were largely similar between the full study sample and the subsample of TNFi-experienced patients.

Patient-Reported Outcomes over Time

Among all patients initiating upadacitinib treatment, significant improvements in mean change from baseline in RAPID3 were observed starting at week 1, with responses maintained or further improved through week 12 (Fig. 2A). Similar improvements were observed over time for the mean change from baseline in pain score (Fig. 2B), as well as an increase in the proportion of patients that achieved RAPID3 LDA (Fig. 2C).

Table 1 Baseline demographics and patient-reported characteristics in patients with RA initiating upadacitinib treatment

Parameter	All patients (N = 103)	TNFi-experienced patients (n = 64)
Age (years), *n*, mean (SD)	103, 59.9 (11.6)	64, 59.8 (11.9)
Sex[a] *n*/*N* (%)		
Female	84/103 (81.6)	52/64 (81.3)
Male	19/103 (18.4)	12/64 (18.7)
Race[a,b] *n*/*N* (%)		
American Indian or Alaska Native	0	0
Asian	–	–
Black or African American	5/103 (4.9)	–
Native Hawaiian or Other Pacific Islander	0	0
Multiple race	–	–
Refused to answer	–	–
White	90/103 (87.4)	59/64 (92.2)
Hispanic ethnicity[a] *n*/*N* (%)		
Yes	6/102 (5.9)	–
No	96/102 (94.1)	–
Unknown	0	0
Work status, *n*/*N* (%)		
Full time	34/99 (34.3)	18/62 (29.0)
Part time	7/99 (7.1)	5/62 (8.1)
Retired	30/99 (30.3)	16/62 (25.8)
Other[c]	28/99 (28.3)	23/62 (37.1)
Insurance, *n*/*N* (%)		
Private	71/101 (70.3)	40/63 (63.5)
Medicare	25/101 (24.8)	19/63 (30.2)
Medicaid	3/101 (3.0)	3/63 (4.8)
None	2/101 (2.0)	1/63 (1.6)
RAPID3 (0–30), *n*, mean (SD)	103, 14.9 (5.2)	64, 15.8 (4.4)
Pain (VAS 0–10), *n*, mean (SD)	103, 6.1 (2.3)	64, 6.5 (2.1)
Morning stiffness duration (hours),[d] *n*, mean (SD)	99, 2.6 (3.3)	62, 2.8 (3.8)
PROMIS-Fatigue 7a SF (29.4–83.2), *n*, mean (SD)	102, 56.8 (10.3)	63, 57.4 (9.2)
CQR5 (0–20), *n*, mean (SD)	101, 16.4 (2.1)	63, 16.3 (2.1)

Table 1 continued

Parameter	All patients (N = 103)	TNFi-experienced patients (n = 64)
CQR5-defined high adherence,[e] n/N (%)	92/103 (89.3)	57/64 (89.1)

CQR5 5-item Compliance Questionnaire for Rheumatology, *PROMIS-Fatigue 7a SF* Patient-Reported Outcomes Measurement Information System-Fatigue 7a Short Form, *RA* rheumatoid arthritis, *RAPID3* Routine Assessment of Patient Index Data 3, *TNFi* tumor necrosis factor inhibitor, *VAS* visual analogue scale

[a]At enrollment, patients self-reported sex, race, and Hispanic ethnicity

[b]Cells with $n < 5$, denoted "–", are not displayed to avoid the potential of identifying individual patients

[c]Includes "self-employed," "looking for work," and "disabled"

[d]Calculated among patients reporting morning stiffness at baseline

[e]Each patient was classified as either a "high" or "low" adherer using their CQR5 scores according to the following standard: defining $D0 = -27.611 + (4.407^{*}Q1) + (0.939^{*}Q2) + (6.101^{*}Q3) + (2.366^{*}Q4) + (2.531^{*}Q5)$ and $D1 = -33.304 + (2.801^{*}Q1) + (5.008^{*}Q2) + (6.471^{*}Q3) + (1.215^{*}Q4) + (3.252^{*}Q5)$, where $Q1 - Q5$ are items on the questionnaire, patients having $D0 > D1$ were classified as likely low adherers, and patients having $D1 > D0$ were classified as likely high adherers

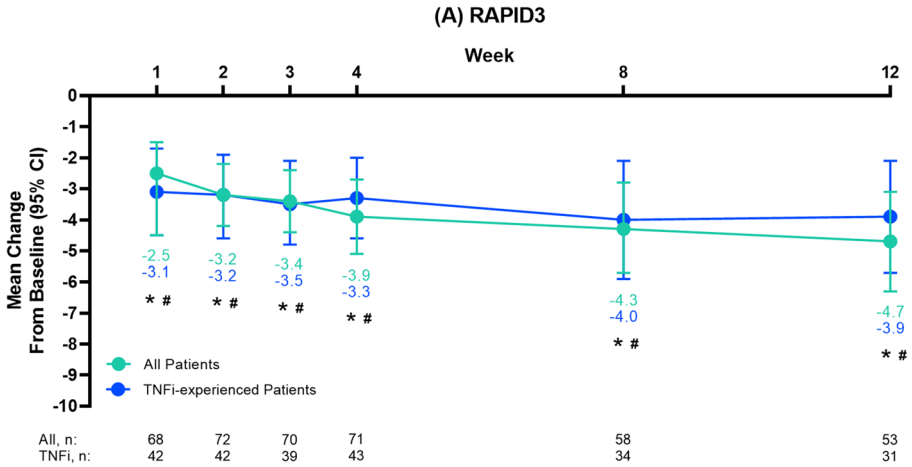
Mean change from baseline in patient-reported morning stiffness (Fig. 3A) and fatigue (Fig. 3B) also showed significant improvement through week 8 for morning stiffness and through week 12 for fatigue among all patients initiating upadacitinib treatment. Starting at week 1, significant improvements in RAPID3 disease activity (Fig. 4A) and achievement of RAPID3 MCID (Fig. 4B) were reported in the full study sample, with nearly 50% of patients achieving these outcomes by week 4 and 60% by week 12. TNFi-experienced patients generally reported similar outcomes to those observed in the full study sample. A sensitivity analysis was performed using patients with data available at any follow-up encounter. Estimates in the improvement in RAPID3 on average over the 12-week study were comparable to those of the overall study population.

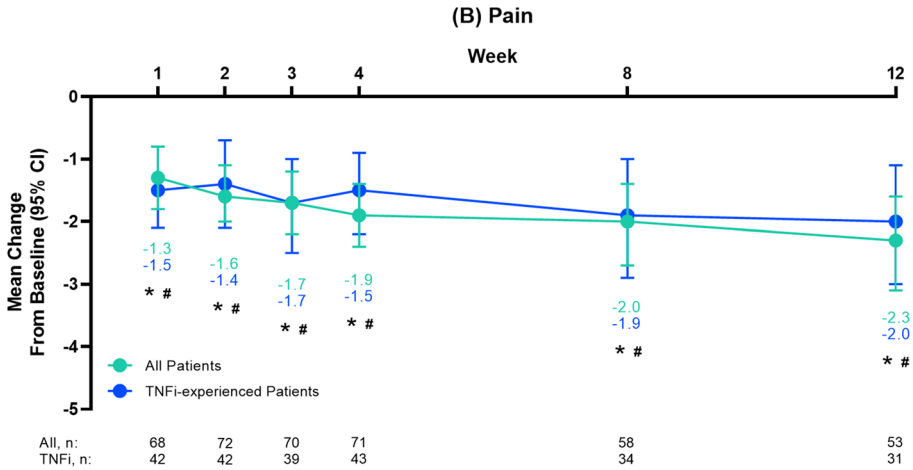
Satisfaction and Compliance with Upadacitinib Treatment

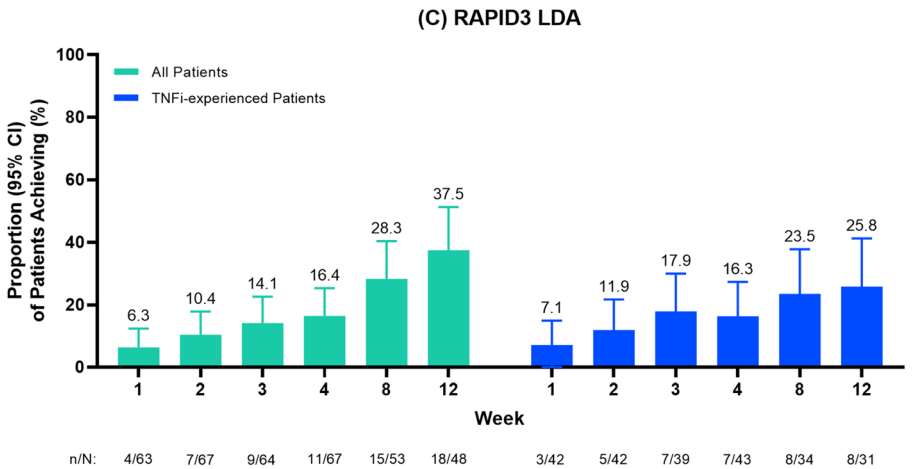
Treatment satisfaction at weeks 8 and 12 (mean [SD]), as measured using the TSQM-9, in all patients initiating upadacitinib treatment was 64.5 (18.3) and 66.8 (18.7) for the effectiveness subscale, 83.7 (14.6) and 83.6 (13.8) for the convenience subscale, and 65.8 (19.9) and 68.5 (20.3) for overall satisfaction, respectively. Compliance to upadacitinib treatment (proportion of patients classified as high adherers), as measured using CQR5, was 90% at week 8 and 96% at week 12 for the full study sample.

DISCUSSION

In this study, a mobile health application was successfully used to gather PRO data from a real-world cohort of patients with RA during the first 12 weeks of upadacitinib treatment. Patients treated with upadacitinib showed significant improvements across several PRO outcomes, including reductions in pain, morning stiffness, and fatigue, as well as reductions in RAPID3 disease activity and achievement of RAPID3 MCID. Improvements in these outcomes were observed starting at week 1 and were maintained or further improved through week 12 of the study. Starting at week 1, a significant proportion of patients reported improvement in RAPID3 disease activity category, with nearly 60% of patients reporting at least one level of improvement by week 12 across both patient populations. Similar results were observed for RAPID3 MCID, with ~ 60% of all patients and ~ 62% of TNFi-experienced patients achieving this outcome by week 12. Combined, these data demonstrate that patients with RA initiating upadacitinib therapy reported rapid and significant improvement in PRO measures


(A) RAPID3
Week
1 2 3 4 8 12
0 -1 -2 -3 -4 -5 -6 -7 -8 -9 -10
Mean Change From Baseline (95% CI)
-2.5 -3.1 * #
-3.2 -3.2 * #
-3.4 -3.5 * #
-3.9 -3.3 * #
-4.3 -4.0 * #
-4.7 -3.9 * #
All Patients
TNFi-experienced Patients
All, n: 68 72 70 71 58 53
TNFi, n: 42 42 39 43 34 31


(B) Pain
Week
1 2 3 4 8 12
0 -1 -2 -3 -4 -5
Mean Change From Baseline (95% CI)
-1.3 -1.5 * #
-1.6 -1.4 * #
-1.7 -1.7 * #
-1.9 -1.5 * #
-2.0 -1.9 * #
-2.3 -2.0 * #
All Patients
TNFi-experienced Patients
All, n: 68 72 70 71 58 53
TNFi, n: 42 42 39 43 34 31


(C) RAPID3 LDA
100 80 60 40 20 0
Proportion (95% CI) of Patients Achieving (%)
All Patients
TNFi-experienced Patients
6.3
10.4
14.1
16.4
28.3
37.5
7.1
11.9
17.9
16.3
23.5
25.8
1 2 3 4 8 12 1 2 3 4 8 12
Week
n/N: 4/63 7/67 9/64 11/67 15/53 18/48 3/42 5/42 7/39 7/43 8/34 8/31

◀**Fig. 2** RAPID3 in all patients and TNFi-experienced patients treated with upadacitinib over time. **A** Mean change from baseline in RAPID3 (0–30). **B** Mean change from baseline in pain (VAS 0–10). **C** Proportion of patients achieving RAPID3 LDA (defined as RAPID3 ≤ 6) among patients with moderate-to-high disease (RAPID3 > 6) at baseline. For all figures, patients with data available at each respective timepoint are shown. $^{*}P < 0.05$ for all patients, and $^{\#}P < 0.05$ for TNFi-experienced patients, indicates a statistically significant difference between baseline and follow-up values based on paired *t* test for continuous outcomes. *CI* confidence interval, *LDA* low disease activity, *RAPID3* Routine Assessment of Patient Index Data 3, *TNFi* tumor necrosis factor inhibitor, *VAS* visual analogue scale

of treatment effectiveness during the first 12 weeks of treatment. These PRO measurements contribute to our understanding of the impact of upadacitinib during the initial weeks of treatment in real-world clinical practice from the patient's perspective. Findings from this real-world cohort of patients with RA align with observations from the RA SELECT clinical trial program, where significant improvements across various efficacy endpoints, as well as PROs, were observed starting at 1 week following upadacitinib treatment [10, 12, 15].

Satisfaction with upadacitinib treatment, as assessed by the TSQM-9, was highest for the convenience subscale (8- and 12-week scores were > 80 out of 100), which is likely attributed to upadacitinib being an oral therapy versus many advanced therapies that require injection or infusion. TSQM-9 satisfaction was moderate for both the effectiveness and overall satisfaction subscales (both 8- and 12-week scores were ~ 65–70 out of 100). In a recent cross-sectional study, patients with RA who were prescribed a variety of medications (methotrexate was the most prevalent at 59.3% of patients), reported lower TSQM-9 scores for the convenience, effectiveness, and overall satisfaction subscales compared to those observed in this study [29]. In addition, a web-based survey of patients with RA receiving stable biologic disease-modifying antirheumatic drug (bDMARD) treatment also reported slightly lower TSQM-9 scores for the convenience and effectiveness subscales, but a similar global (overall) satisfaction score, to that observed in this study [30]. Compliance with upadacitinib treatment in the all-patient population, as measured using the CQR5, was high, with at least 90% of patients classified as having high adherence at both 8 and 12 weeks. In a recent study, approximately 83% of patients with RA treated with tofacitinib were identified as adherers [31].

It is challenging to evaluate early and consistent real-world response to treatment in patients with RA via the traditional approach of periodic office visits and disease assessments every few months, especially because RA is a dynamic disease that can improve, worsen, and flare frequently. The use of digital technology, such as the ArthritisPower mobile health application, offers a novel and practical approach to remotely collect patient-derived data in between office visits [32–34]. These real-time data could help clinicians better understand the patient's experience, more quickly identify patients who are unresponsive to treatment, and better tailor individual patient care. In addition, the use of these technologies could help patients communicate better with their provider and/or become more engaged with their care. Indeed, in a recent qualitative study of an electronic PRO web-based application, patients with RA reported that app use encouraged them to continuously monitor their health, and provided an overview of their disease progression, which ultimately helped them to provide their health care providers with better and more comprehensive insights [35]. As remote treatment monitoring was recently made reimbursable for rheumatologists, we are likely to see an increase in the use of novel digital technologies in clinical practice.

Limitations of this study should be noted. First, patients consenting to use the mobile health application for this study may not be representative of patients with RA at large or patients with RA starting upadacitinib treatment, as they may be more health conscious or younger in age. Second, this study focused on PROs, which are subjective, and the relationship to the patient's disease activity or outcomes using objective measures, such as tender or

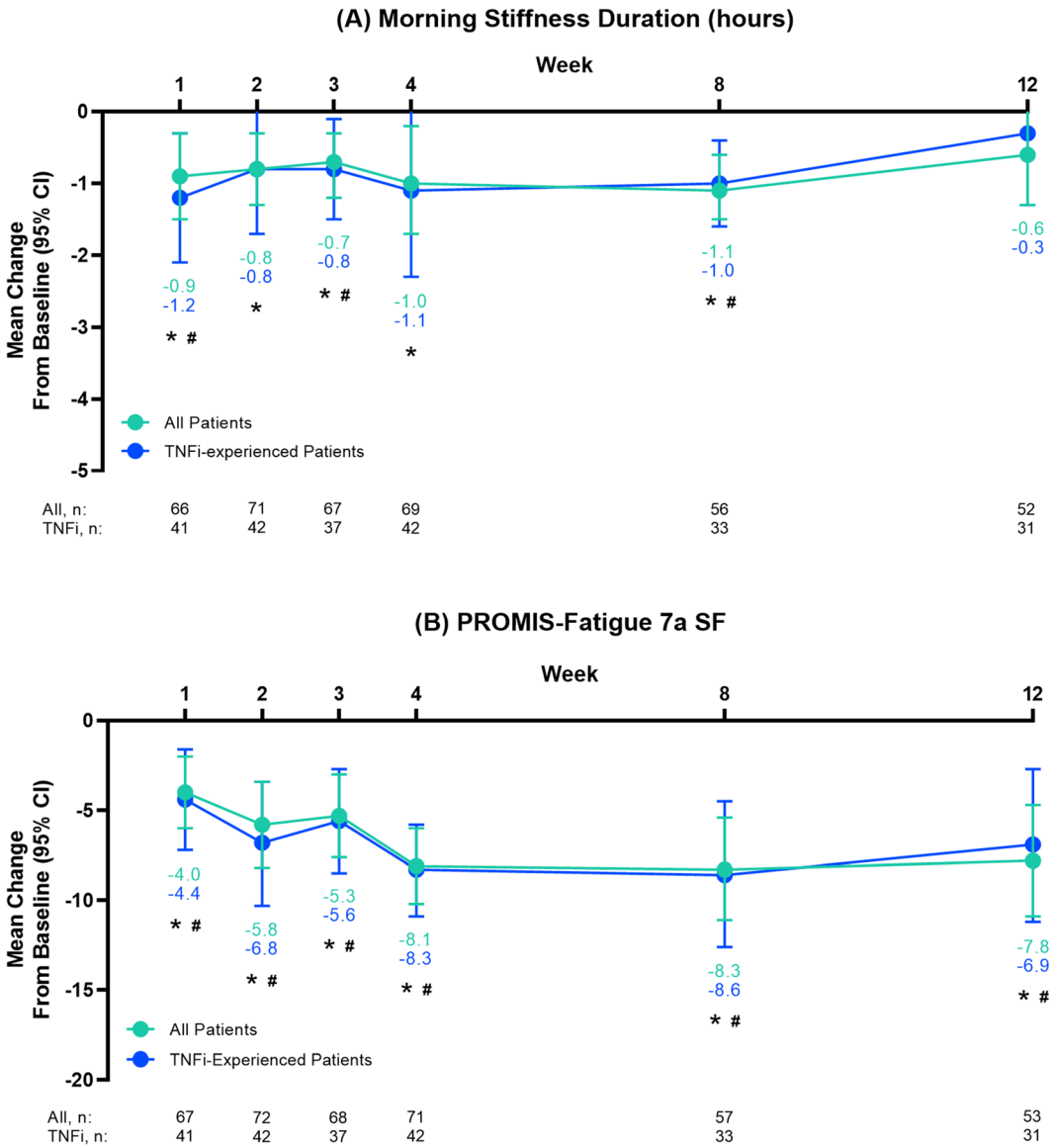


Fig. 3 Morning stiffness and fatigue in all patients and TNFi-experienced patients treated with upadacitinib over time. **A** Mean change from baseline in morning stiffness duration (hours) was calculated among patients reporting morning stiffness at baseline. **B** Mean change from baseline in PROMIS-Fatigue 7a SF (29.4–83.2), where higher scores indicate greater fatigue. For both figures, patients with data available at each respective timepoint are shown. $^{*}P < 0.05$ for all patients, and $^{\#}P < 0.05$ for TNFi-experienced patients, indicates a statistically significant difference between baseline and follow-up values based on paired *t* test for continuous outcomes. *CI* confidence interval, *PROMIS-Fatigue 7a SF* Patient-Reported Outcomes Measurement Information System–Fatigue 7a Short Form, *TNFi* tumor necrosis factor inhibitor

swollen joint counts, is unknown. Third, PRO analyses were restricted to those patients who completed the assessments using the mobile application, which was reduced to nearly 50% of the total patient population by the end of the 12-week study. Previous studies have also reported declining patient engagement over time with mobile application/smartphone-based data collection measures [36–38]. Furthermore, this study was conducted during the

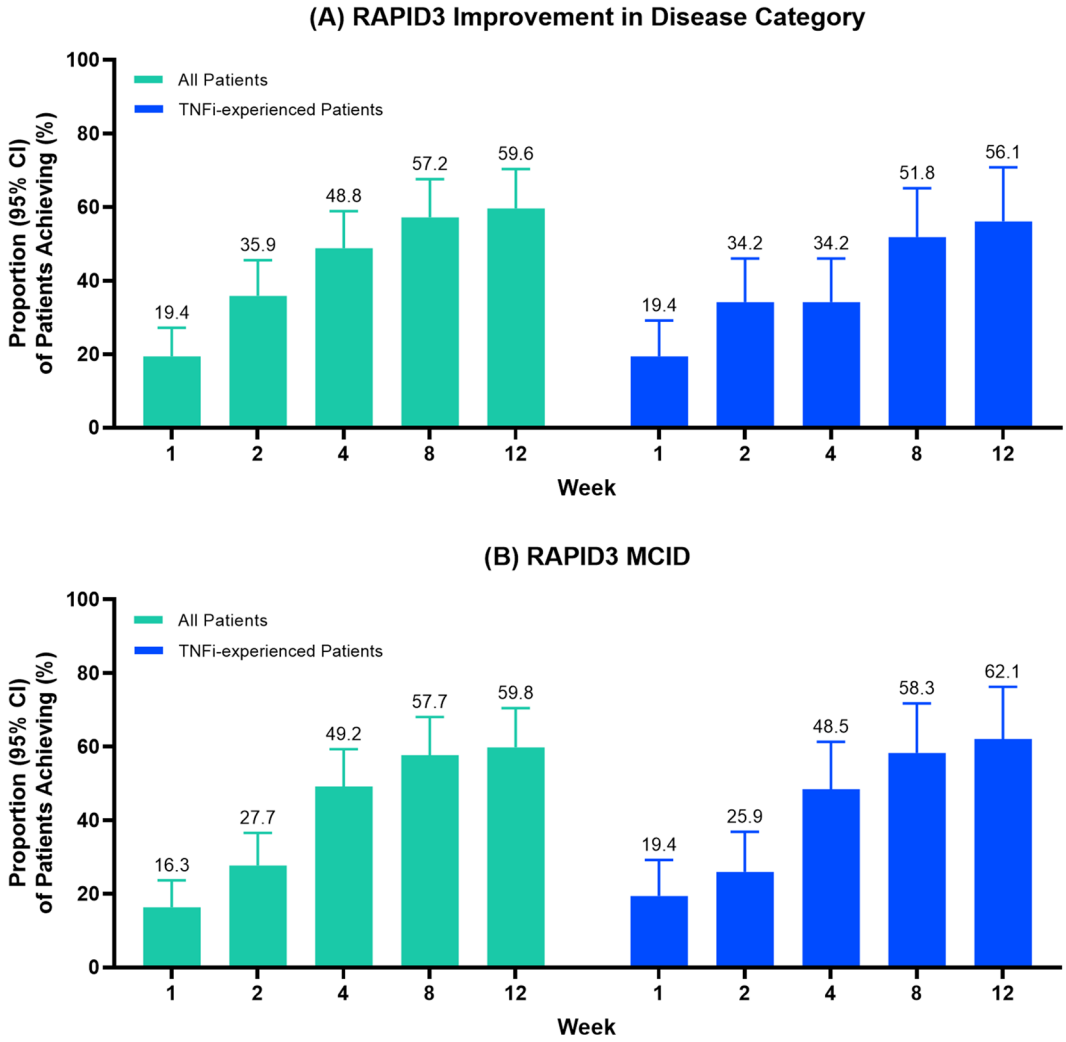


Fig. 4 Kaplan–Meier estimation of RAPID3 responses in all patients and TNFi-experienced patients treated with upadacitinib over time. **A** Proportion of patients achieving RAPID3 improvement in disease category (defined as a reduction of at least one category). **B** Proportion of patients achieving RAPID3 MCID (defined as a decrease in RAPID3 $\geq$ 3.8). For both figures, patients were censored if they withdrew from the study without achieving improvement in disease activity category or MCID, or they completed the 12-week study without achieving improvement. Patients were censored at the time of their last follow-up encounter. *CI* confidence interval, *MCID* minimal clinically important difference, *RAPID3* Routine Assessment of Patient Index Data 3, *TNFi* tumor necrosis factor inhibitor

peak of the COVID-19 global pandemic, which likely contributed to the reduced patient engagement and retention that was observed. Future studies should consider providing additional patient support, such as a "run-in" period where patients are trained to use the application and/or patients are required to complete a certain number of digital tasks in the application prior to receiving compensation and proceeding to the main study. More frequent data collection, so that patients are habituated to opening the application daily, and additional reminders and messaging may also help to maintain digital adherence throughout the course of a study. Fourth, a control group, such as patients starting a different RA treatment, was not included

in this study, making it more difficult to contextualize the improvements observed following upadacitinib treatment. Fifth, due to small sample sizes for the study groups, these findings should be interpreted with caution and will need to be confirmed in future, larger studies.

CONCLUSIONS

In this real-world cohort of patients with RA, treatment with upadacitinib was associated with rapid and significant improvement in RAPID3 disease activity, pain, morning stiffness, and fatigue regardless of prior TNFi experience. Improvement in RAPID3 disease activity was observed as early as week 1, with nearly 50% of patients reporting improvement by 4 weeks and 60% by 12 weeks. This study successfully utilized a novel mobile health application to gather patient-generated data for evaluating treatment response, satisfaction, and compliance. Mobile health technology could provide valuable information to health care providers to better understand the patient's treatment experience, allow for closer monitoring of treatment response, and lead to more individualized and timely intervention to improve management of patients with RA.

ACKNOWLEDGEMENTS

AbbVie and the authors thank the patients, study sites, and investigators who participated in the CorEvitas RA Registry.

Medical Writing/Editorial Assistance Medical writing and editorial support were funded by AbbVie. Medical writing was provided by Monica R.P. Elmore, PhD, of AbbVie. Editorial support was provided by Angela T. Hadsell of AbbVie.

Author Contributions. Leslie R. Harrold, Patrick Zueger, W. Benjamin Nowell, Namita Tundia, and Pankaj A. Patel participated in the design of the study. Leslie R. Harrold, W. Benjamin Nowell, and David Curtis participated in the acquisition of data. Taylor Blachley, Amy Schrader, and Paul R. Lakin participated in the analysis of data. All authors participated in the interpretation of data and contributed to the drafting and critical revision of the manuscript for important intellectual content. All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published. No honoraria or payments were made for authorship. CorEvitas and AbbVie contributed to the study design. The data collection tool and design were provided by Global Healthy Living Foundation. CorEvitas statisticians completed all analyses. All authors had access to relevant data; access to complete registry data was limited to CorEvitas.

Funding. This study was sponsored by CorEvitas, LLC and the analysis was funded by AbbVie. CorEvitas has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Inc., Arena, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Chugai, Eli Lilly and Company, Genentech, Gilead Sciences, Inc., GlaxoSmithKline, Janssen Pharmaceuticals, Inc., Leo Pharma, Novartis, Ortho Dermatologics, Pfizer Inc., Regeneron Pharmaceuticals Inc., Sanofi, Sun Pharmaceutical Industries Ltd., and UCB S.A. AbbVie funded the journal's Rapid Service Fee.

Data Availability. Data are available from CorEvitas, LLC through a commercial subscription agreement and are not publicly available. No additional data are available from the authors.

Declarations

Conflict of Interest. Financial arrangements of the authors with companies whose products may be related to the present manuscript are listed, as declared by the authors. Leslie R. Harrold: Employee and shareholder of CorEvitas, consultant to AbbVie, Bristol Myers Squibb, and Roche, speaker's bureau for Bristol Myers Squibb. Patrick Zueger: Employee of AbbVie and may hold stock or stock options.

W. Benjamin Nowell: Employee of Global Healthy Living Foundation, an independent nonprofit research organization, principal investigator for studies with grant support from AbbVie, Amgen, Janssen, and Scipher Medicine. Taylor Blachley: Former employee of CorEvitas; current employee of Syneos Health. Amy Schrader: Employee of CorEvitas. Paul R. Lakin: Employee of CorEvitas. David Curtis: Employee of Global Healthy Living Foundation, an independent nonprofit research organization. Laura Stradford: Employee of Global Healthy Living Foundation, an independent nonprofit research organization. Shilpa Venkatachalam: Employee of Global Healthy Living Foundation, an independent nonprofit research organization. Namita Tundia: Former employee of AbbVie and may hold stock or stock options; current employee of EMD Serono. Pankaj A. Patel: Employee of AbbVie and may hold stock or stock options.

Ethical Approval. The CorEvitas RA Registry is conducted in accordance with the Declaration of Helsinki 1964 and its later amendments. All participating investigators were required to obtain full board approval for conducting research involving human subjects. Sponsor-level and site-level approval for this sub-study was obtained from the New England Independent Review Board (NEIRB; no. 20201379). All patients provided written informed consent and authorization prior to participating in the study.

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