Impact of a non-medical switch from tocilizumab to upadacitinib in a cohort of patients with rheumatoid arthritis in routine clinical practice

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The COVID-19 pandemic caused significant disruption in medicine supply lines. From 1 October 2021 in New Zealand, publicly funded access to the only available IL-6 receptor inhibitor, tocilizumab (administered intravenously in New Zealand), was widened to treat moderate-to-severe cases of COVID-19.[1] In order to preserve the remaining tocilizumab stock for patients at highest risk, prescribers were asked to transition their patients with rheumatoid arthritis (RA) from tocilizumab to upadacitinib from 1 October 2021.[2] Prescribers were given just 2 weeks' notice to begin making the switch.

Upadacitinib is a selective and reversible inhibitor of Janus kinase (JAK) 1. In New Zealand, upadacitinib is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA).[3] Approval was based on the results from a comprehensive clinical trial programme assessing efficacy and safety across a range of patient types and treatment strategies in patients with RA, including patients with inadequate response or intolerance to prior biologic disease-modifying antirheumatic drugs (bDMARDs).[4–9] However, the effectiveness and safety of a direct non-medical switch (NMS) to upadacitinib, defined as a switch for reasons unrelated to patient health, has not been investigated in these bDMARD-experienced patients.

This study therefore represents a unique opportunity to address a significant data gap where no data currently exist—to investigate the impact of a non-medical switch from tocilizumab to upadacitinib on outcomes in a cohort of patients with RA in routine clinical practice.

Methods

This was a non-interventional, observational, single-centre cohort study with a retrospective phase and a prospective phase.

1) Retrospective phase

The medical records of adults with RA receiving tocilizumab prior to 1 October 2021 who have attended the Rheumatology Clinic at Waikato Hospital, Hamilton, New Zealand were reviewed for the data extraction period, defined as 6 months after the initiation of upadacitinib. For a patient's records to be considered for inclusion in the study, the initiation of upadacitinib must have occurred after 1 October 2021. The date of initiation of upadacitinib was recorded as the index date. Upadacitinib was prescribed in accordance with the approved New Zealand Datasheet and in line with expectations of the government agency responsible for managing access in this situation.

2) Prospective phase

Six months from the index date, a small number of questionnaires related to secondary outcomes were provided to patients and the treating physician.

Health and Disability Ethics Committee approval was obtained (2022 EXP 11553). This study was a low-risk observational study.

The primary outcome was treatment persistence, defined as the proportion of patients continuing therapy with upadacitinib at 6 months. Key secondary outcomes assessed at 6 months included: reasons and time to permanent discontinuation of upadacitinib for any reason, change in Physician Global Assessment of disease activity (PhGA) on 100mm visual analogue scale (VAS), maintenance of Remission/Low Disease Activity at 6 months after switch from tocilizumab in the physician's opinion, change in disease control (notably better/no change/notably worse) in the physician's opinion, Patient Global Assessment of disease activity (PtGA) on 10cm (100mm) visual analogue scale (VAS; scores range from 0 to 10, higher scores represent a higher

level of disease activity) and patient treatment satisfaction using the abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9).[10–11] The TSQM-9 provides a validated score for three subscales: effectiveness, convenience and global satisfaction. Scores range from 0 to 100, with 0 representing complete dissatisfaction and 100 maximum satisfaction.

The primary outcome was estimated as a proportion with corresponding two-sided 95% confidence interval (CI) using the Clopper–Pearson exact method. Data description and analyses used IBM SPSS version 29.

Results

Baseline demographics of the 43 patients receiving tocilizumab for RA are detailed in Table 1. The median age of those receiving tocilizumab was 56 years, with a range of 43 to 89 years. Mean (SD) disease duration was 15 (12) with a range of 1 to 68 years. As anticipated, patients had long-standing disease recalcitrant to multiple previous treatments.

The decision to switch to upadacitinib was made for 26 patients. Twenty proceeded with the medication change and six elected not to (Figure 1). Reasons given were concern about adverse effects, wondering whether they would be all right without treatment, resentment at the treatment change being forced upon them and feeling they needed more time to consider their options. Five of the six elected to start upadacitinib at a later date and are excluded from further discussion here. Upadacitinib was therefore used following 1 bDMARD in 1 patient, 2 bDMARDs in 4 patients, 3 bDMARDs in 10 patients and 4 bDMARDs in 5 patients.

The number of patients who continued treatment with upadacitinib after 6 months was 17/20, a proportion (95% CI) of 85% (62 to 97). (Primary outcome: Figure 1).

In the 3 patients who discontinued, primary non-response was the reason; all were transitioned back to tocilizumab with resumption of supply. Mean time to discontinuation was 92 days with a range of 31 to 139 days.

The PhGA at 6 months following a switch from tocilizumab to upadacitinib was felt to be improved in 4 of 20 cases. Maintenance of Remission/Low Disease Activity at 6 months after switch from tocilizumab, in the physician's opinion, was reported in 17/20 cases (85%; Figure 2). Only in the 3/20 cases (15%) where lack of efficacy was reported was loss of Remission/Low Disease Activity noted. For change in disease control (notably better/no change/notably worse), in the physician's opinion, corresponding patient numbers were 4/13/3 (20%/65%/15%).

Patient treatment satisfaction data was available for 15 of the 17 participants remaining on upadacitinib: mean (SD) TSQM-9 scores were 82.7 (17) for effectiveness, 89.5 (14.3) for convenience and 75.3 (24.8) for global satisfaction. The median PtGA at 6 months was 2 with a range of 1 to 5. One adverse event (sinus infection) was reported among the 20 participants.

Discussion

Upadacitinib treatment persistence was high following a switch from tocilizumab in this cohort of RA patients in routine clinical practice. Disease control following the switch was maintained in the majority of patients. Satisfaction with upadacitinib treatment was excellent and felt to be effective and convenient.

Not all those patients receiving tocilizumab at Waikato Hospital were transitioned to upadacitinib. There are likely to be several reasons for this. Firstly, some switch decisions were made by the physician before the availability of upadacitinib was announced. In six cases, the patient prescribed upadacitinib had reservations and elected not to start treatment. Since many of the consultations took place by telephone during the prevailing COVID-19 restrictions and the need to contact many patients urgently, it is likely there was less opportunity to discuss and explore these reservations than during a standard face-to-face consultation.

There were some limitations to our study. Waikato DHB experienced a cyberattack in May 2021 which hampered access to records and the ability to record formal disease activity measures prior to the loss of supply of tocilizumab. Assessment of disease activity was based on subjective outcomes that may be influenced by self-presentational and recall biases.

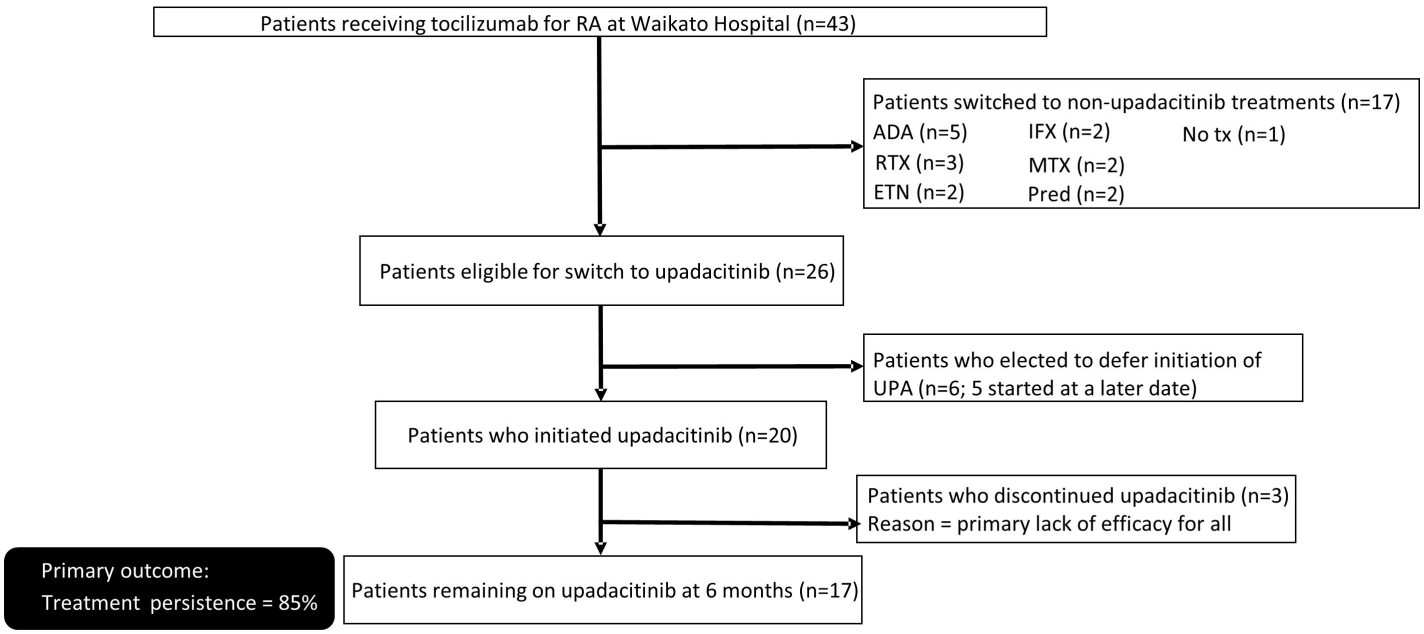
Our study showed that a non-medical switch from tocilizumab to upadacitinib is effective in a cohort of patients with RA in routine clinical practice.

Table 1: Patient demographics of RA Cohort at Waikato Hospital.

Demographics, n (%)	**n=43 (complete cohort)**	**n=20 (cohort starting UPA)**
Age, median (range)	56 (43 to 89)	55.5 (48 to 89)
Female, n (%)	36 (84)	16 (80)
Ethnicity, n (%)		
NZ European	37 (86)	20 (100)
Māori	4 (9)	
Indian	1 (2)	
Tongan	1 (2)	
Mean disease duration, years (SD)	15 (12)	17.05 (15)
Rheumatoid Factor positive, n (%)	32 (74)	14 (70)
Anti-CCP positive, n (%)	29 (67)	13 (65)
Number of prior csDMARDs (median, range)	4 (3 to 5)	4 (3 to 5)
Prior biologic, n (%)		
Tocilizumab	43 (100)	20 (100)
Adalimumab	25 (58)	14 (70)
Etanercept	24 (56)	16 (80)
Rituximab	9 (21)	7 (35)
Infliximab	3 (7)	0
Golimumab	1 (2)	0
Tocilizumab as 1L/2L/3L/4L biologic	9(21) / 14(33) / 13(30) / 7(16)	0 / 5(25) / 10(50) / 5(25)

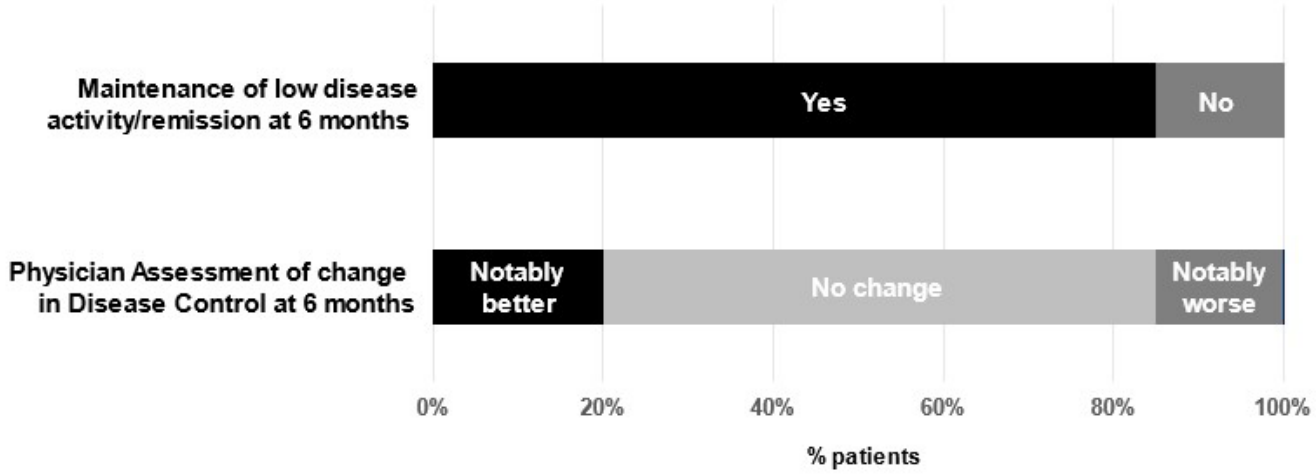
CCP, Cyclic Citrullinated Peptide; csDMARD, Conventional synthetic DMARD; DMARD, Disease Modifying Anti Rheumatic Drug; L, Line; UPA, upadacitinib.

Figure 1: Patient flow and primary outcome.



ADA, adalimumab; ETN, etanercept; IFX, infliximab; Pred, Prednisone; RTX, rituximab; UPA, upadacitinib.

Figure 2: Disease control: physician assessment at 6 months.



COMPETING INTERESTS

AbbVie participated in the study design, interpretation of data, reviewing and approval of the publication. All authors had access to relevant data and participated in the drafting, review and approval of this publication. No honoraria or payments were made for authorship. D White has served as a consultant to AbbVie and has received research funding and speaker fees from AbbVie. D Poppelwell is an employee of AbbVie and owns AbbVie stock.

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