Conclusion: It is speculated that the downstream biological cascade for TOF, BAR and TCZ treatment might be shared, as IL-6 signaling is mediated by JAK1/JAK2/TYK2 activation. However, the influence of these treatments over the transcriptome in the peripheral blood seems to be disparate. Enrichment analysis using GO terms also indicated that different biological processes were involved in the effect of each treatment. Our findings will support a rationale for switching each other if one of these treatments resulted in lack of efficacy. An increased risk of herpes zoster by a treatment with JAK inhibitors has been well recognized. It makes sense because IFN signaling is also mediated by JAK/STAT pathway. On the other hand, we have experienced a case with exacerbation of skin ulcer during TCZ treatment despite the activity of RA was absolutely under control. It is accounted for by the suppression of genes involved in wound healing after TCZ treatment.

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THU0209

UPTAKE OF JANUS KINASE INHIBITORS FOR MANAGEMENT OF RHEUMATOID ARTHRITIS IN AUSTRALIA

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Background: JAK inhibitors (JAKi) are oral tsDMARDs with a different mode of action (MOA) to both oral cs- and parenteral bDMARDs. In Australia the cost of b/tsDMARDs for treatment of RA is subsidized if the patient has documented high levels of clinical/laboratory disease activity and has not responded to a pre-specified combination of csDMARDs, including MTX. Once eligible for subsidy the clinician can prescribe the b/tsDMARD deemed most clinically appropriate.

Objectives: To determine the patterns of use and reasons for initiation and discontinuation of JAKi in real-world rheumatology practice in Australia.

Methods: Deidentified clinical data were sourced from the OPAL dataset, which is collected in a custom-built electronic medical record at the time of the consultation¹ by 94 rheumatologists in Australia, representing one third of Australian clinical rheumatologists. Data from patients >18 years with a diagnosis of RA who commenced a b/tsDMARD between Jan-2007 and Sept-2019 were included in the analysis. Tableau[®] was used to display data on medication initiation and cessation dates, and reasons for starting and stopping b/tsDMARDs, which is recorded at the time of the decision.

Results: At Sept 2019, there were 45,317 patients with RA in the data set, with 27% prescribed b/tsDMARDs. Of patients currently on treatment at Sept 2019, 53% were receiving a TNFi and 21% a JAKi, with the remainder receiving tocilizumab, abatacept or rituximab. Of patients who commenced their current treatment after JAKi's became available in Sept 2015, 46% were treated with a TNFi, and 32% were treated with a JAKi. Tofacitinib (TOF) has been the most prescribed b/tsDMARD since Sept 2015 with 22% of all initiations; however, since baricitinib (BARI) became available in Sept 2018, it has taken over as the preferred JAKi with 24% of new initiations compared to 14% for TOF. From Sept 2018-Sept 2019 etanercept and adalimumab were the most commonly prescribed agents in first line, followed by TOF then BARI; however, BARI was the most prescribed agent in lines 2-6+ (figure 1). The main clinician-listed reason for choice of TOF was MOA in 54%, efficacy compared with alternatives in 30%, mode of administration in 7%, efficacy as monotherapy in 7%, and safety in 1%. BARI was chosen for MOA in 35%, efficacy compared with alternatives in 38%, mode of administration in 12%, efficacy as monotherapy in 12%, and safety in 1%. The main reasons for stopping TOF were lack of efficacy (34%), better alternative (25%) and adverse reaction (13%); those for BARI were lack of efficacy (35%) and adverse reaction (25%) which is consistent with the rates observed in the first 12-months of clinical experience with TOF, and better alternative (12%). Patient non-adherence was listed in 1% and 2% of cessations for TOF and BARI, respectively. 45% of patients discontinuing a JAKi in first line switched to a TNFi in second line, and 40% switched to another JAKi, citing lack of efficacy, adverse reaction, and better alternative as the reason for switching.

Figure 1. Rank of new initiations by line of therapy (Sept 2018-Sept 2019)

Conclusion: There has been significant and sustained uptake of JAKi for the management of RA in Australia. MOA and perceived efficacy rate much higher than mode of administration for clinicians when selecting a JAKi. Clinical outcomes and persistence following JAKi cycling requires further investigation.

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THU0210

EARLY DISCONTINUATION OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS CO-TREATED WITH RIFAMPIN FOR LATENT TUBERCULOSIS: RESULTS FROM THE REAL-WORLD DATA

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Background: Rheumatoid arthritis (RA) patients need to undergo screening and receive treatment for latent tuberculosis infection (LTBI) before starting tofacitinib, which is primarily metabolized by cytochrome P450 (CYP) 3A4. Among chemoprophylactic agents, rifampin is known to be a potent CYP3A4 inducer; therefore, it is expected to decrease the efficacy of tofacitinib. However, tofacitinib and rifampin have been co-administered practically because of the short duration of chemoprophylaxis.

Objectives: The aim of this study was to determine the efficacy of tofacitinib on co-administration with rifampin.

Methods: Biologic-naïve RA patients treated with tofacitinib were selected, and electronic medical reports were reviewed retrospectively. All patients underwent screening for LTBI before starting tofacitinib, and patients with positive results were treated to prevent progression to active tuberculosis. To evaluate the efficacy of tofacitinib with or without rifampin, the discontinuation rates of tofacitinib were examined during the first 6 months. Kaplan-Meier analysis was used to construct cumulative discontinuation curves, and comparisons were performed using the log-rank test.

Results: Among 81 patients who started tofacitinib, 21 (25.9%) were LTBI-positive and 18 (22.2%) were administered rifampin concomitantly with tofacitinib. The median follow-up time was 6 months in both patients who received rifampin (interquartile range [IQR] 2.21, 6.00) and those who did not receive rifampin (IQR 5.97, 6.00) ($p = 0.083$). There were no significant differences between patients who received rifampin and those who did not receive rifampin in all baseline characteristics, except the swollen joint count (3.00 [1.75, 5.25] vs. 5.00 [4.00, 7.00]; $p = 0.025$), at the time of starting tofacitinib. In patients who received rifampin at the time of starting tofacitinib, the mean duration of co-administration was 47.00 ± 23.54 days (median 56; IQR 28.75, 59.00). During follow-up, 14 of the 81 patients (17.3%) discontinued tofacitinib. As shown in the Figures 1 and 2, the discontinuation rate of tofacitinib within the first 6 months was significantly higher among patients who received rifampin for LTBI than among those who did not receive rifampin (lack of efficacy: 24.7% vs. 5.1%, $p = 0.008$; all causes: 38.9% vs. 11.2%, $p = 0.002$). Seven patients discontinued tofacitinib because of

uncontrolled RA activity, and rifampin had been administered concomitantly in four of these seven patients. Of the four patients, three stopped taking tofacitinib in the middle of LTBI treatment, and the DAS28-ESR scores of these patients were higher at discontinuation than at baseline.

Conclusion: Discontinuation rates were higher in RA patients who started tofacitinib during chemoprophylaxis involving rifampin than in those who did not receive rifampin. Physicians should be aware that the efficacy of tofacitinib could be decreased by the chemoprophylactic regimen for tuberculosis.

Figure 1. Discontinuation rates of tofacitinib owing to lack of efficacy within 6 months

Figure 2. Discontinuation rates of tofacitinib owing to all causes within 6 months

Disclosure of Interests: None declared

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THU0211

RADIOGRAPHIC OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING UPADACITINIB AS MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE: RESULTS AT 2 YEARS FROM THE SELECT-COMPARE AND SELECT-EARLY STUDIES

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Background: For patients with rheumatoid arthritis (RA), long-term prevention of structural joint damage is a key treatment goal.¹ In the SELECT-EARLY and SELECT-COMPARE trials, upadacitinib (UPA), an oral JAK inhibitor, inhibited the progression of structural joint damage at 6 months and 1 year when used either as monotherapy or in combination with methotrexate (MTX) in patients (pts) with active RA.²

Objectives: To describe the radiographic progression up to 2 years (96 wks) among pts with RA receiving UPA either as monotherapy or in combination with MTX.

Methods: Both the SELECT-EARLY and SELECT-COMPARE phase 3, randomized controlled trials enrolled pts at high risk for progressive structural damage with baseline (BL) erosive joint damage and/or seropositivity.^{3,4} In SELECT-EARLY, MTX-naïve pts (N=945) were randomized to UPA 15 mg or 30 mg once

daily (QD) or MTX monotherapy. In SELECT-COMPARE, pts with an inadequate response to MTX (N=1629) were randomized to UPA 15 mg, placebo (PBO), or adalimumab (ADA) 40 mg every other wk, with all pts continuing background MTX; at wk 26, all pts receiving PBO were switched to UPA 15 mg, regardless of response. In both trials, mean changes from BL in modified Total Sharp Score (mTSS), joint space narrowing, and joint erosion as well as the proportion of pts with no radiographic progression (change in mTSS ≤ 0) were evaluated based on X-rays taken at wks 24/26, 48, and 96 for those patients in whom wk 96 X-rays were available. Data are reported as observed (AO).

Results: BL demographics have been reported previously.^{3,4} In the SELECT-EARLY study, at wk 96 UPA monotherapy (15 mg and 30 mg doses) significantly inhibited radiographic progression compared with MTX as measured by mean change in mTSS and by the proportion of patients with no radiographic progression (Figures 1 and 2). When patients who were rescued (MTX added to UPA or UPA added to MTX) were removed from the analysis, changes in mTSS from baseline remained similar. By the same measures, in SELECT-COMPARE, the degree of inhibition of structural progression observed was comparable between UPA and ADA. Following the switch of all PBO patients to UPA, the rate of progression slowed and was comparable to that observed in pts receiving UPA from BL. Among pts from both studies that had no radiographic progression at wk 24/26, >90% remained without radiographic progression at wk 48 and 96.

Conclusion: UPA was effective in inhibiting the progression of structural joint damage through 2 years both in MTX-naïve patients receiving UPA monotherapy and MTX-inadequate responder patients receiving UPA in combination with MTX.

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Figure 1. Mean Change in mTSS from Baseline in SELECT-COMPARE (A) and SELECT-EARLY (B)

Figure 2. Proportion of Patients with No Radiographic Progression in SELECT-COMPARE (A) and SELECT-EARLY (B)

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