THU0168

A MATCHING-ADJUSTED INDIRECT COMPARISON (MAIC) OF UPADACITINIB VERSUS TOFACITINIB IN CSDMARD-IR PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS (RA)

Christopher Edwards¹, Ruta Sawant², Ella Du³, Jordan Cammarota³, Patrick Tang³, Vishvas Garg², Alan Friedman², Keith Betts³. ¹University of Southampton, Southampton, United Kingdom; ²AbbVie Inc., North Chicago, United States of America; ³Analysis Group, Inc., Los Angeles, United States of America

Background: Upadacitinib (UPA), a JAK1 selective inhibitor, is being investigated as monotherapy and combination therapy with DMARDs for the treatment of moderate-to-severe RA. To date, no head-to-head trials have compared the effectiveness of UPA with tofacitinib (TOFA).

Objectives: To compare the efficacy of UPA 15 mg monotherapy and combination therapy with TOFA 5 mg combination therapy using MAICs.

Methods: Two MAICs were conducted. MAIC is an indirect comparison technique that utilizes individual patient data (IPD) for one treatment and aggregate data for the other treatment to provide comparative evidence after balancing differences in patient characteristics. The first MAIC used IPD from the SELECT-MONOTHERAPY trial of UPA monotherapy vs. methotrexate (MTX) and published data from the Oral Standard trial¹ of TOFA+MTX vs. MTX. The second used IPD from the SELECT-COM-PARE trial of UPA+MTX vs. adalimumab (ADA)+MTX and published data from the ORAL Strategy trial² of TOFA+MTX vs. ADA+MTX. UPA monotherapy was not compared to TOFA monotherapy based on feasibility analysis and trial selection criteria. Patients in the UPA trials were re-weighted based on age, gender, race, swollen joint count 66/28, tender joint count 68/28, C-reactive protein (CRP), and patient's global assessment, to match the baseline characteristics in each comparator trial. After matching, ACR20/50/70 and clinical remission (SDAI/CDAI/DAS28-ESR/CRP) were compared for UPA monotherapy vs. TOFA +MTX relative to MTX at month 3 and UPA+MTX vs. TOFA+MTX relative to ADA+MTX at month 3 and 6 using a Wald test.

Figure 1: MAIC results for UPA 15 mg vs. TOFA mg + MTX at Month 3* and UPA 15 mg + MTX vs. TOFA 5 mg + MTX at Month 6

* Clinical remission outcomes not reported for ORAL Standard at Month 3.

Abstract THU0168 – Figure 1

Results: After matching, baseline characteristics were balanced across the trial populations. At month 3, UPA monotherapy patients experienced significantly greater improvement in ACR70 compared to TOFA+MTX with a mean difference in difference (DD) of 9.9% ($p < 0.05$) (Figure 1a) while UPA+MTX was associated with a higher ACR50 compared to TOFA+MTX with a DD of 12.9% ($p < 0.05$). At month 6, UPA+MTX patients experienced significantly larger improvement in SDAI/CDAI/DAS28-ESR clinical remission compared to TOFA+MTX with DDs of 9.1% ($p < 0.05$), 7.5% ($p < 0.05$), and 11.3% ($p < 0.01$), respectively (Figure 1b).

Conclusion: The results from MAICs indicate that treatment with UPA 15 mg when used as monotherapy or in combination with MTX appears to produce improved outcomes at 3/6 months as compared to TOFA 5 mg +MTX (mono: ACR70 and combination: ACR50, SDAI, CDAI and DAS28-ESR remission).

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JANUS KINASE INHIBITORS DEMONSTRATE EFFECTIVENESS IN A REAL-WORLD MULTI-BIOLOGIC DMARD REFRACTORY RHEUMATOID ARTHRITIS POPULATION

John Fitton^{1,2}, Andrew Melville^{1,2}, Shouvik Dass³, Paul Emery^{1,2}, Jacqueline Nam^{1,2}, Maya Buch^{1,2}. ¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Chapel Allerton Hospital, Leeds, United Kingdom; ²NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; ³Leeds Teaching Hospitals NHS Trust, Rheumatology, Leeds, United Kingdom

Background: The Janus Kinase inhibitors (JAKi) Tofacitinib and Baricitinib are licensed for use in Rheumatoid arthritis (RA). Trials in refractory RA (inefficacy and/or toxicity) to date (1, 2) suggest targeting intracellular signalling molecules and interrupting downstream effects of multiple cytokines may confer benefit in the management of patients who have failed multiple targeted therapies.

Objectives: To evaluate safety and efficacy of JAKi in a real-world population, including response in multi-bDMARD refractory RA.

Methods: We evaluated RA patients who had failed at least 2 csDMARD +/- one or more bDMARD, who were commenced on a JAKi. Patients who commenced Tofacitinib on a compassionate use programme in 2014 have been included (with Baricitinib available since February 2018).

Results: Seventy seven RA patients (80% female; mean (SD) age 55.9 (12.52) years) have been treated with one (or more) JAKis; 38 have received Tofacitinib and 39 Baricitinib (5 both). Table 1 details treatment stage and clinical outcomes where available (majority pending assessments). Number of previous bDMARD was higher in the Tofacitinib group (reflecting compassionate access scheme).

Characteristic	Combined JAKi grp (n=77)	Tofacitinib (n=38)	Baricitinib (n=39)
Disease duration, years; mean (SD)	13.8 (5.34)	15.9 (4.52)	11.9 (6.16)
Previous number of targeted therapies (median, range)	4 (0-9)	5 (2-7)	3 (0-9)
Targeted therapy naïve	5	0	5
Baseline DAS28	5.84 (SD 1.07) (n=67)	6.23 (SD 1.08) (n=31)	5.5 (SD 0.95) (n=36)
3m change in DAS28	-1.8 (SD 1.63) (n=29)	-2.07 (SD 1.72) (n=14)	-1.54 (SD 1.6) (n=15)
6m change in DAS28	-1.35 (SD 1.8) (n=13)	-1.05 (SD 2.07) (n=7)	-1.7 (SD 1.52) (n=6)

Of the 38 patients who received Tofacitinib, 24 stopped treatment, 10 due to primary non-response, 2 secondary non-response and 12 due to