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).

REFERENCES:

- [1] van Vollenhoven RF, et al. "Tofacitinib or adalimumab versus placebo in rheumatoid arthritis." *NEJM* 367.6 (2012): 508-519.
- [2] Fleischmann R, et al. "Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy)." *The Lancet* 390.10093 (2017): 457-468.

Acknowledgement: The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of this publication.

Disclosure of Interests: Christopher Edwards Grant/research support from: Abbvie, BMS, Biogen, Celgene, Fresenius, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Consultant for: Abbvie, BMS, Biogen, Celgene, Fresenius, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Speakers bureau: Abbvie, BMS, Biogen, Celgene, Fresenius, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Ruta Sawant Shareholder of: AbbVie, Employee of: AbbVie, Ella Du Employee of: Analysis Group, Inc., which has received consultancy fees from AbbVie to conduct this study, Jordan Cammarota Employee of: Analysis Group, Inc., which has received consultancy fees from AbbVie to conduct this study, Patrick Tang Employee of: Analysis Group, Inc., which has received consultancy fees from AbbVie to conduct this study, Vishvas Garg Shareholder of: AbbVie, Employee of: AbbVie, Alan Friedman Shareholder of: AbbVie, Employee of: AbbVie, Keith Betts Employee of: Analysis Group, Inc., which has received consultancy fees from AbbVie to conduct this study

DOI: 10.1136/annrheumdis-2019-eular.7189

THU0169

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

adverse effects (1 deranged LFTs, 3 infection, 1 rash, 1 headache, 2 flares of IBD, 1 dizziness, 1 malignancy). Despite the refractory nature of their RA, 14 patients responded sufficiently to remain on Tofacitinib for an average of 24.5 months to date. 1 Patient who failed 3 bDMARDs achieved remission (DAS28 1.82) with 4 confirmed as having moderate disease activity (Mean DAS 3.58, SD 0.42). Of the 39 patients to receive Baricitinib, three had primary non-response, whilst the others remain on therapy. Response is to be determined in 16, 4 have achieved remission (Mean DAS 2.2, SD 0.32) and 14 MDA (Mean DAS 4.04, SD 0.44). 5 patients received both JAKis sequentially, switching from Tofacitinib to Baricitinib, 2 due to adverse events (both flares of IBD) and 3 due to non-response. Of these 5, 1 patient to date has shown a good response at 3 months, 2 have shown no response, with results pending for others. **Conclusion:** Our experience of patients treated with JAKi for RA indicates improvement in disease activity. Benefit was observed in a severely refractory subgroup that had previously failed multiple biologic therapies.

REFERENCES:

- Genovese, M.C. et al. Response to baricitinib based on prior biologic use in patients with refractory rheumatoid arthritis. *Rheumatology (Oxford)*. 2018, 57(5), pp.900-908.
- Genovese, M.C. et al. Baricitinib in Patients with Refractory Rheumatoid Arthritis. *N Engl J Med*. 2016, 374(13), pp.1243-52.

Disclosure of Interests: John Fitton: None declared, Andrew Melville: None declared, Shouvik Dass: None declared, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead, Samsung, Sandoz and Lilly, Jacqueline Nam: None declared, Maya Buch Grant/research support from: Pfizer LTD, UCB, Consultant for: AbbVie, Eli Lilly, EMD Serono, Pfizer Ltd., Sanofi
DOI: 10.1136/annrheumdis-2019-eular.7246

THU0170

A MULTICENTER STUDY ASSESSING THE EFFICACY AND SAFETY OF REPOSITORY CORTICOTROPIN INJECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: INTERIM DATA FROM THE OPEN-LABEL TREATMENT PERIOD

Roy Fleischmann¹, Dan Furst², Jingyu Liu³, Julie Zhu³, Erin Connolly-Strong³, Richard Brasington⁴. ¹University of Texas Southwestern Medical Center, Dallas, Texas, United States of America; ²David Geffen School of Medicine at UCLA, Los Angeles, California, United States of America; ³Mallinckrodt ARD, LLC, Bedminster Township, New Jersey, United States of America; ⁴Washington University School of Medicine, St. Louis, Missouri, United States of America

Background: Rheumatoid arthritis (RA) is an autoimmune disorder associated with chronic inflammation and is treated with disease-modifying anti-rheumatic drugs (DMARDs) for active disease. Both American College of Rheumatology (ACR) and EULAR recommend that short-term administration of corticosteroids (CSs) may be beneficial for its anti-inflammatory effects. Repository corticotropin injection (RCI) is a complex mixture containing purified porcine pituitary adrenocorticotrophic hormone (ACTH)-analogue and an agonist for all 5 melanocortin receptors (MCRs). Activation of MCRs by ACTH has been shown to have direct and indirect anti-inflammatory and immunomodulatory effects. RCI is approved in the United States as adjunctive therapy for short-term administration in RA.

Objectives: To present interim data after 100% enrollment from the initial 12-week open-label phase of a multicenter, 2-part study evaluating the efficacy, safety, and appropriate duration of RCI therapy in patients with persistently active RA despite receiving 1 or 2 DMARDs and/or CSs.

Methods: In the open-label period (Part 1, Weeks 0–12), all enrolled patients received RCI 1 mL (80 U SC) twice weekly for 12 weeks. Patients who achieved low disease activity (LDA; DAS28-ESR score <3.2) at Week 12 continued in the double-blind, randomized maintenance phase of the trial (Part 2) for an additional 12 weeks. The primary endpoint was the proportion of patients who achieved LDA at Week 12. Secondary endpoints included assessment of the safety and tolerability of RCI. Disease activity was also assessed by the proportion of patients who achieved ACR 20%, 50%, and 70% (ACR20, 50, 70) responses and patient reported outcomes at Week 12. Bone turnover markers were assessed as an exploratory endpoint.

Results: 259 patients had enrolled, 235 had completed and 24 had discontinued the 12-week open-label period of the study; 88.9% were female and mean age was 51 years. RCI treatment resulted in 62.5% of patients achieving LDA at Week 12; results for this interim analysis are presented in the **Table**. Bone turnover markers were stable from baseline

to Week 12, indicating no effect of RCI on bone metabolism. 98 (37.8%) patients reported adverse events (AEs) with 3 (1.2%) patients reporting serious AEs (ie, non-cardiac chest pain, pneumonia, and craniocerebral injury). The most common AEs were urinary tract infection (n=10), headache (n=9), and pharyngitis (n=7).

Abstract THU0170 – Table 1.

Table. Results for Patients Who Completed the Open-label Period (mITT; N=259)

Endpoints	Baseline	Week 4	Week 8	Week 12
LDA (DAS28-ESR <3.2; Primary Endpoint)	-	6.6%	14.3%**	62.5%**
ACR20	-	48.6%**	69.9%**	79.5%**
ACR50	-	12.0%**	35.9%**	62.2%**
ACR70	-	4.6%	8.5%	31.7%**
DAS28-ESR score, mean	6.3	4.9*	4.4*	3.6*
Tender joint count, mean	14.6	7.7*	5.7*	3.9*
Swollen joint count, mean	10.9	5.6*	4.0*	2.8*
Patient global assessment of disease activity (20% improvement)	-	56.0%**	71.8%**	80.3%**
FACIT-F, mean	22.9	17.5*	16.0*	13.9*
HAQ-DI, mean	1.7	1.2*	1.0*	0.8*

FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue Scale; HAQ-DI, Health Assessment Questionnaire – Disability Index; LDA, low disease activity.
 The modified intent to treat (mITT) population includes all subjects who received RCI with any post-treatment efficacy assessments.

*p < 0.001 vs baseline. **p < 0.0001 vs baseline.

Conclusion: In the 12-week open label period of this study, RCI appeared to be generally safe and effective in patients with persistently active RA who were nonresponsive to DMARDs and CSs. This was demonstrated by improvement in multiple measures of disease activity. Further results will be evaluated in Part 2 of the study.

Acknowledgement: Editorial support was provided by MedLogix Communications, LLC, Itasca, Illinois, under the direction of the authors and was funded by Mallinckrodt ARD LLC.

Disclosure of Interests: Roy Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Dan Furst Grant/research support from: AbbVie, Actelion, Amgen, BMS Corbus, NIH, Novartis, Pfizer, Roche/Genentech, Consultant for: AbbVie, Actelion, Amgen, BMS, Cytari, Novartis, Pfizer, Roche/Genentech, Speakers bureau: CMC Connect (McCann Health Company), Jingyu Liu Shareholder of: Mallinckrodt ARC, LLC, Employee of: Mallinckrodt ARC, LLC, Julie Zhu Shareholder of: Mallinckrodt ARC, LLC, Employee of: Mallinckrodt ARC, LLC, Erin Connolly-Strong Shareholder of: Mallinckrodt ARC, LLC, Employee of: Mallinckrodt ARC, LLC, Richard Brasington: None declared
DOI: 10.1136/annrheumdis-2019-eular.6083

THU0171

TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS – THE RESULTS OF RUSSIAN NATIONAL REGISTER OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

Inna Gaydukova¹, V Mazurov¹, Evgeniy Zhilyaev², Iuliia Grabovetskaya³, Irina Marusenko⁴, Elizaveta Vasilenko¹, Diana Abdulganieva⁵, Iliia Smitienko⁶, Anna Misiyuk⁷, Galina Lukina⁸, Larisa Knyazeva⁹, Elena Kalinina¹⁰, Ruzana Samigullina¹¹, Irina Bondareva¹¹, Natalya Yudina¹², N Lapkina¹³, Evgeny Nasonov⁷. ¹North-Western State Medical University n.a. Il Mechnikov, St. Petersburg, Russian Federation; ²European Medical Center, Moscow, Russian Federation; ³Baltic Federal University named after I.Kant, Kaliningrad, Russian Federation; ⁴Petrozavodsk State University, Petrozavodsk, Russian Federation; ⁵Kazan State Medical University, Kazan, Russian Federation; ⁶Medical Center K +31, Moscow, Russian Federation; ⁷VA Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; ⁸Moscow Clinical Scientific Center, Moscow, Russian Federation; ⁹Kursk State Medical University, Kursk, Russian Federation; ¹⁰Volgograd State Medical University, Volgograd, Russian Federation; ¹¹Kemerovo Regional Hospital, Kemerovo, Russian Federation; ¹²Republican Consultative and Diagnostic Clinic, Kyzyl, Russian Federation; ¹³Yaroslavl State Medical University, Yaroslavl, Russian Federation

Background: Tofacitinib (TF) is an oral Janus Kinase inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: To evaluate the one-year effectiveness of tofacitinib as first-line therapy in RA conventional synthetic (cs) DMARDs non-responders.

Methods: Data from 415 patients from Russian national register of patients with RA treated with TF were analyzed. 119 RA patients, who had complete clinical and laboratory data from 4 consecutive visits after baseline with an interval of 3 months between the visits and who used the TF as first-line therapy after failure of cs DMARDs, were included. Treatment with any biologics ever was an exclusion criteria.