Results: Overall, 1218 eligible TC (from 1028 patients) were initiated during the study period (273 in BARI, 154 other tsDMARD, 473 in TNFi and 318 in OMA). Drug maintenance was significantly shorter for TNFi compared to BARI, even after adjustment for potential confounders (Hazard ratio (HR) for drug discontinuation 1.85 (95% CI [1.40 – 2.43]); $p < 0.001$). Drug maintenance was also numerically shorter for the OMA group compared to BARI, but the difference was not significant (HR 1.18 (95% CI [0.87 – 1.60]); $p = 0.28$). These differences were larger when analysing only bDMARD-naïve patients (Figure 1a).

All TC taken together, the rates of LDA and remission did not differ significantly between the 3 groups at 12 months. LDA ranged from 63% to 67% (BARI vs OMA $p = 0.87$; BARI vs TNFi $p = 0.81$) and remission from 19% to 23% (BARI vs OMA $p = 0.30$; BARI vs TNFi $p = 0.77$; Figure 1b).

Conclusion: BARI demonstrated a significantly higher overall drug maintenance than TNFi, and a similar drug maintenance to OMA, both in a bDMARD-naïve population and in the overall population. The adjusted 12-month response rates did not differ between BARI, TNFi and OMA groups. These results suggest that prescription of BARI after csDMARD has at least similar outcomes as alternative bDMARDs.

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Disclosure of Interests: Benoit GILBERT: None declared, Delphine Courvoisier: None declared, Denis Mongin: None declared, Kim Lauper Consultant of: Gilead Galapagos, Grant/research support from: AbbVie, Clementine Perrier Shareholder of: Eli Lilly, Employee of: Eli Lilly, Rudiger Muller Consultant of: AbbVie, Novartis, Grant/research support from: GEBRO Pharma, Axel Finckh Speakers bureau: AbbVie, BMS, Pfizer, Eli-Lilly, Consultant of: AbbVie, BMS, Pfizer, Eli-Lilly, Grant/research support from: BMS, Pfizer, Eli-Lilly

DOI: 10.1136/annrheumdis-2021-eular.1781

POS0669 HYOGLYCAEMIA FOLLOWING JAK INHIBITOR TREATMENT IN DIABETES MELLITUS PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Janus kinase (JAK) inhibitors are effective small molecular drugs for rheumatoid arthritis (RA) and other immune mediated inflammatory diseases (IMIDs). JAK inhibitors exert their immunosuppressive effects by suppressing the action of JAK, an intracellular tyrosine. Although infections are the most reported side effects, potential glucose lowering effects in patients with diabetes mellitus (DM) have been described in literature and have also been reported as suspected adverse drug reactions (ADRs) to the National Pharmacovigilance Centre Lareb in the Netherlands (1).

Objectives: To assess and describe suspected adverse effects of JAK inhibitors on glucose levels in diabetic patients with rheumatic diseases and other IMIDs, as reported in daily practice.

Methods: We describe ADR reports of tofacitinib and baricitinib in the European pharmacovigilance Eudravigilance (EV) database from initiation to 12 January 2021. All ADRs in EV are coded according to the Medical Dictionary for Regulatory Activities (MedDRA). We included all reports indicating hypoglycaemia in patients with reported DM type 1 and 2 or with antidiabetic drugs as concomitant medication. This could include oral antidiabetics as well as insulins.

Results: On 12 January 2021 the EV database included 32 ADR reports, concerning 32 diabetic patients, indicating hypoglycaemia associated with the use of JAK inhibitors (15 tofacitinib, 17 baricitinib), out of 32,484 ADR reports in total concerning tofacitinib or baricitinib (Table 1). Most patients (25 patients, 78%) used the JAK inhibitor for rheumatoid arthritis. The suspected ADR with MedDRA Preferred Term 'Hypoglycaemia' was reported for 16 patients and MedDRA Preferred Term 'Decreased blood glucose' was reported for 15 patients. In one case, increased insulin sensitivity was described as suspected ADR of baricitinib. In this case, the insulin dose had to be reduced to prevent hypoglycaemia. Of note, the insulin dose had to be increased after temporary discontinuation of baricitinib and was reduced again after baricitinib was restarted. Additionally, in six cases improvements of glycaemic control were described after discontinuation or dose reduction of the JAK inhibitor or antidiabetic drug. Improvements were also described after unknown action or unchanged treatment with JAK inhibitor in eight cases.

Conclusion: JAK inhibitors may induce hypoglycaemia by increasing insulin sensitivity, and consequently may reduce the need for antidiabetic medication (2-3). Healthcare professionals should be alert for these potential ADRs when starting a JAK inhibitor in patients with DM as comorbidity. More research is needed to support our findings and elucidate the underlying pharmacological mechanisms of this potentially beneficial effect of JAK inhibitors.

Table 1. Suspected adverse drug reaction reports indicating hypoglycaemia in diabetic patients using tofacitinib or baricitinib in the Eudravigilance database

	Tofacitinib N (%)	Baricitinib N (%)
No. of reports	15 (100)	17 (100)
Mean age years (range)	65 (56 - 78)	62.2 (48 - 78)
Female gender	13 (87)	13 (76)
Indication for JAK inhibitor		
Rheumatoid arthritis	11 (73)	14 (82)
Unknown	3 (20)	3 (18)
Arthritis	1 (7)	
Reported adverse drug reaction		
Hypoglycaemia	6 (40)	11 (65) ^a
Decreased blood glucose	9 (60)	6 (35) ^a
Time to onset after start JAK inhibitor ^b		
Within 1 month	6 (40)	3 (18)
2-6months	2 (13)	2 (12)
More than 6 months	1 (7)	
Improvement after action:		
Drug withdrawal	3 (20) ^c	1 (6) ^d
Dose adjustments		1 (6) ^e
Other	1 (7) ^f	

a. In one case of baricitinib hypoglycaemia as well as decreased blood glucose were reported as adverse drug reactions.

b. Time to onset was unknown in 6 reports of tofacitinib and 12 reports of baricitinib

c. Tofacitinib withdrawal: 1, sitagliptin withdrawal: 1, tofacitinib and insulin withdrawal: 1

d. Baricitinib withdrawal: 1

e. Baricitinib: after insulin dose adjustments: 1

f. After tofacitinib withdrawal and insulin dose adjustments

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Disclosure of Interests: Jette van Lint: None declared, Florence van Hunsel: None declared, Sander Tas Consultant of: Gebro, GSK, AbbVie, Galvani, Arthrogen, Galapagos, Grant/research support from: Pfizer, GSK, Celgene, BMS, Sanofi, AstraZeneca, Michael Nurmohamed Speakers bureau: speaker's fees from AbbVie, Bristol-Myers Squibb, Eli Lilly, Roche, and Sanofi, Consultant of: consulting fees from AbbVie, Celgene, Celltrion, Eli Lilly, Janssen, and Sanofi, Grant/research support from: research funding from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, MSD, Mundipharma, Novartis, Pfizer, Roche, and Sanofi, Harald Vonkeman Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Celltrion, Galapagos, Gilead, GSK, Janssen-Cilag, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Genzyme, all outside the submitted work., Renske Hebing: None declared, Frank Hoentjen Speakers bureau: served on advisory boards or as speaker for Abbvie, Janssen-Cilag, MSD, Takeda, Celltrion, Teva, Sandoz and Dr Falk, Consultant of: Celgene, Janssen-Cilag, Grant/

research support from: Dr Falk, Janssen-Cilag, Abbvie, Takeda, Martijn van Doorn Grant/research support from: reports personal fees from Leopharma, grants and personal fees from Novartis, personal fees from Abbvie, personal fees from BMS, personal fees from Celgene, personal fees from Lilly, personal fees from MSD, personal fees from Pfizer, personal fees from Sanofi-Genzyme, personal fees from Janssen Cilag, outside the submitted work., Bart van den Bemt: None declared, Eugène van Puijenbroek: None declared, Naomi Jessurun: None declared

DOI: 10.1136/annrheumdis-2021-eular.1851

POS0670 ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3 (RAPID3) IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH LONG-TERM UPADACITINIB THERAPY

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Background: Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of 3 patient-reported measures: patient global assessment, pain, and physical function. RAPID3 was shown to correlate with other composite measures of disease activity¹ and is recommended by the American College of Rheumatology for use in clinical practice.²

Objectives: To evaluate the impact of upadacitinib (UPA) versus comparators on RAPID3 over 60 weeks, as well as the correlation of RAPID3 scores with other disease measures in the UPA phase 3 SELECT clinical program.

Methods: This post hoc analysis included placebo-controlled (SELECT-NEXT, -BEYOND, and

-COMPARE) and active comparator-controlled (SELECT-EARLY, -MONOTHERAPY, and

-COMPARE) trials. Patients received UPA as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs). Mean change from baseline in RAPID3 and the proportion of patients reporting RAPID3 remission (≤ 3), low (LDA, >3 to ≤ 6), moderate (MDA, >6 to ≤ 12), and high disease activity (HDA, >12) were assessed. Correlations between absolute scores for RAPID3 and Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), and 28-joint Disease Activity Score with C-reactive protein (DAS28[CRP]) were assessed using Spearman correlation coefficients. All data are as observed.

Results: A total of 661, 498, 648, 1629, and 945 patients were included from SELECT-NEXT, -BEYOND, -MONOTHERAPY, -COMPARE, and -EARLY. At baseline, the majority of patients across all studies were in RAPID3 HDA (mean baseline RAPID3 [across all studies], 17.2–19.2) (Table 1 and Figure 1). Improvements from baseline in RAPID3 were observed with UPA 15mg and 30mg through Week 60, with numerically greater improvements observed with UPA compared with active comparators (Table 1). Across studies, mean improvements in RAPID3 exceeded the minimal clinically important difference (MCID) with UPA and adalimumab (ADA) treatment (MCID=3.8³). By Week 60, approximately one-half of UPA-treated patients were in RAPID3 remission or LDA, with only 10–25% remaining in HDA, except for the more refractory population in SELECT-BEYOND, in which ~38% of patients remained in HDA (Figure 1). RAPID3 scores moderately to strongly correlated with CDAI ($\rho=0.69$ – 0.83), SDAI ($\rho=0.69$ – 0.82), and DAS28[CRP] ($\rho=0.58$ – 0.77), across all studies, at Week 60 (all $p<0.001$).

Conclusion: UPA, as monotherapy or in combination with csDMARDs, was associated with improvements in patient-reported disease activity, pain, and physical function, as assessed by RAPID3 over 60 weeks in the phase 3 SELECT clinical program. RAPID3 continues to be an important tool in clinical practice to assess disease activity, as it was shown to correlate to other disease activity measures and allows for rapid scoring.

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Table 1. Change from BL in RAPID3 at Week 60 (as observed)

Phase 3 study	Group	n ^a	Mean (SD) BL score	Mean (SD) change from BL ^b
SELECT-EARLY ^c (MTX-naïve)	MTX	236	18.5 (5.6)	–9.6 (7.5)
	UPA 15 mg QD	269	18.9 (5.6)	–12.0 (7.6)
	UPA 30 mg QD	253	18.2 (5.6)	–13.4 (7.2)
SELECT-NEXT (csDMARD-IR)	UPA 15 mg QD	172	17.7 (5.1)	–11.1 (7.3)
	UPA 30 mg QD	172	17.6 (5.3)	–10.4 (6.8)
SELECT-MONOTHERAPY (MTX-IR)	UPA 15 mg QD	172	17.4 (5.8)	–9.6 (7.4)
	UPA 30 mg QD	180	17.2 (5.9)	–10.6 (7.2)
SELECT-COMPARE ^c (MTX-IR)	UPA 15 mg QD	552	18.5 (5.5)	–10.2 (7.1)
	ADA 40 mg EOW	264	18.7 (5.4)	–8.8 (6.7)
SELECT-BEYOND (bDMARD-IR)	UPA 15 mg QD	133	19.2 (5.1)	–8.6 (6.8)
	UPA 30 mg QD	118	18.5 (5.3)	–9.3 (7.3)

b, biologic; BL, baseline; EOW, every other week; IR, inadequate response; MTX, methotrexate; QD, once daily; SD, standard deviation

^aNumber of patients with RAPID3 values at both BL and Week 60. ^bNegative values indicate improvement from BL. ^cObserved data include patients rescued to UPA and/or ADA; treatment effect may include both the randomized and switch treatments in these patients

Figure Proportion of patients in RAPID3 remission, LDA, MDA, and HDA at BL and Week 60 (as observed)

ADA, adalimumab; bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; DMARD, disease-modifying antirheumatic drug; HDA, high disease activity; IR, inadequate response; LDA, low disease activity; MDA, moderate disease activity; MTX, methotrexate; RAPID3, Routine Assessment of Patient Index Data 3; UPA, upadacitinib

Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Grant Kirkpatrick, MSc, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Disclosure of Interests: Martin Bergman Shareholder of: Johnson & Johnson, Speakers bureau: AbbVie, Celgene, GSK, MSD, Novartis, Pfizer, and Sanofi/Regeneron, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Genentech/Roche, Gilead, Horizon, Janssen, MSD, Novartis, Pfizer, Sandoz, Sanofi/Regeneron, and Scipher, Maya H Buch Consultant of: AbbVie, Eli Lilly, Merck-Serono, Pfizer, Sandoz, and Sanofi, Grant/research support from: Pfizer, Roche, and UCB, Yoshiya Tanaka Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, GSK, Janssen, Mitsubishi Tanabe, Novartis, Pfizer, Sanofi, Takeda, UCB, and YL Biologics, Grant/research support from: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Mitsubishi Tanabe, MSD, Ono, Taisho Toyama, and Takeda, Gustavo Citera Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Genzyme, Pfizer, and Roche, Sami Bahlas: None declared, Ernest Wong Consultant of: AbbVie, Chugai, Eli Lilly, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Chugai, Novartis, and UCB, Yanna Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Namita Tundia Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Jessica Suboticki Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Vibeke Strand Consultant of: AbbVie, Amgen, Arena, AstraZeneca, Bayer, Bristol-Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Gilead, Ichnos, Inmedix, Janssen, Kiniksa, MSD, Myriad Genetics, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Scipher, Setpoint, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.2090