for: AbbVie, Consultant of: AbbVie, Asahi Kasei, Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Toshihisa Kojima Speakers bureau: AbbVie, Pfizer, Eisai, Grant/research support from: AbbVie, Sung-Hwan Park: None declared, Kichul Shin: None declared, Han Joo Baek: None declared, Yun Jong Lee Grant/research support from: research fund, In Ah Choi Speakers bureau: Abbvie, Eisai, Grant/research support from: Abbvie, Eisai, Jinhyun Kim: None declared, Ping-Ning Hsu: None declared, Chang-Fu Kuo: None declared, Chun-Ming Huang Paid instructor for: AbbVie, Pfizer, Meng-Yu Weng Consultant of: AbbVie, Wan-Yu Sung: None declared, Wen-Chan Tsai: None declared, Tien-Tsai Cheng Paid instructor for: AbbVie, Grant/research support from: AbbVie, Takehiro Taninaga Shareholder of: Eisai Co., Ltd., Employee of: Eisai Co., Ltd., Masahiko Mori Shareholder of: Eisai Co., Ltd., Employee of: Eisai Co., Ltd., Hideaki Miyagishi Employee of: Eisai Co., Ltd., Yasunori Sato: None declared, Tsutomu Takeuchi Speakers bureau: Astellas, Abbvie, Daiichi Sankyo, Ayumi, Eisai, GlaxoSmithKline, Mitsubishi Tanabe, Chugai, Novartis, Eli Lilly, Pfizer, Bristol Myers Squibb, Janssen, UCB, Taisho Toyama, Sanofi-Aventis, Nipponkayaku, Taiho, Gilead, Boehringer Ingelheim, Grant/research support from: Asahikasei, Astellas, Abbvie, Daiichi Sankyo, Ayumi, Eisai, Takeda, Mitsubishi Tanabe, Chugai, Eli Lilly, UCB, Sanofi-Aventis, Nipponkayaku, Boehringer Ingelheim
DOI: 10.1136/annrheumdis-2021-eular.762

AB0254

NEUROPSYCHIATRIC ADVERSE DRUG REACTIONS ASSOCIATED WITH LOW DOSE METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Neuropsychiatric adverse drug reactions (NPADRs) are well known with high dose methotrexate treatment. However, NPADRs have also been observed with low dose methotrexate (DMTX) treatment in real world rheumatology data.

Objectives: To evaluate the association between LDMTX and NPADRs, the impact of these NPADRs on further treatment and on health related quality of life (HRQoL) in patients with rheumatoid arthritis (RA) using real world data.

Methods: The nature and frequency of NPADRs associated with LDMTX in the Dutch DREAM-RA registry were described. We assessed the causality of each NPADR with the Naranjo Probability Scale (NPS), the impact of NPADRs on further LDMTX treatment and the impact on patient reported HRQoL. NPADRs were structured using terminology of the Medical Dictionary for Regulatory Activities.

Results: A total of 71 NPADRs (frequency 6.8%) associated with LDMTX were captured in the DREAM-RA registry. NPADRs were registered for 62 (5.9%) out of 1048 patients with 10.9 NPADRs per 1000 patient years (Table 1). The most frequently reported NPADRs were headache, dizziness and depression. The causality was considered probable for 67 NPADRs (94.4%) and definite for 1 NPADR (1.4%). The NPADRs led to LDMTX withdrawal in 34 cases (47.9%) and LDMTX was not restarted in 16 cases (47.1%). Median mental HRQoL was significantly decreased around the occurrence of the NPADR and remained significantly lower after the event. Median physical HRQoL was not significantly affected.

Table 1. Baseline characteristics of DREAM-RA patients using methotrexate with at least one neuropsychiatric adverse drug reaction

Characteristics N=62	N (%)
Female sex	40 (64.5%)
Age in years, mean (± SD), range	59.8 (± 13.1), 25 – 82
Rheumatoid factor	Positive 43 (69.4%) Negative 13 (21.0%) Unknown 6 (9.7%)
Anti-CCP, n (%)	Positive 34 (54.8%) Negative 19 (30.7%) Unknown 9 (14.5%)
Methotrexate dosage in mg/week, mean (± SD)	18.7 (± 5.9)
Specific methotrexate dosage	< 15 mg / week 5 (7.0%) 15 mg/week 28 (39.4%) 20 mg/week 11 (15.5%) 25 mg/week 14 (19.7%) 30 mg/week 5 (7.0%) Unknown 8 (11.3%)
Concomitant medication at moment of NPADR	Folic acid 68 (95.8%) Prednisolone 20 (28.2%)

Anti-CCP: anti cyclic citrullinated peptides, NPADR: neuropsychiatric adverse drug reaction, SD: Standard Deviation

Conclusion: The association between NPADRs and LDMTX in RA patients was recognised by HCPs and frequently led to LDMTX withdrawal and a decrease in mental HRQoL. Many NPADRs scored 'probable' using the NPS. Knowledge on the nature, frequency and impact of these NPADRs will enhance attention towards potential NPADRs during LDMTX therapy allowing better risk assessment and communication to patients.

Disclosure of Interests: Jette van Lint: None declared, Tom Bakker: None declared, Peter ten Klooster: None declared, Harald Vonkeman Consultant of: BMS, Celgene, Celltrion, Galapagos, Gilead, Janssen-Cilag, Lilly, Novartis, Pfizer, Sanofi-Genzyme, Grant/research support from: Abbvie, Naomi Jessurun: None declared

DOI: 10.1136/annrheumdis-2021-eular.882

AB0255

BASELINE CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH UPADACITINIB IN GERMAN REAL-WORLD PRACTICE: RESULTS FROM THE POST-MARKETING OBSERVATIONAL UPwARds STUDY

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Background: The efficacy and safety of upadacitinib (UPA), a selective Janus kinase inhibitor, has been evaluated in the SELECT rheumatoid arthritis (RA) clinical program,¹⁻⁶ but its real-world effectiveness remains to be investigated. The UPwArds study will assess the association of C-reactive protein (CRP) level with remission and other efficacy outcomes in patients with RA treated with UPA in German real-world practice.

Objectives: To describe the baseline characteristics of patients enrolled in the UPwArds study.

Methods: The prospective, open-label, multicenter, non-interventional, post-marketing UPwArds study included adult patients with moderate-to-severe RA (swollen joint count [SJC28] ≥3 and inadequate response or intolerance to ≥1 disease-modifying antirheumatic drug [DMARD]). Patients were treated with UPA 15 mg once daily, as monotherapy or in combination with methotrexate (MTX; 50:50 mono:combo enrollment planned), according to the German label. Variables assessed included medical history (disease duration, previous RA therapy, and vaccination status), CRP level, and disease activity (disease activity score [DAS28(CRP)], tender joint count [TJC28], and SJC28). There was no recruitment restriction regarding CRP level. This descriptive interim analysis reports patient baseline characteristics after enrollment was complete. All data were analyzed as observed, with no imputation of missing data.

Results: 533 patients (UPA monotherapy: 257 [48%]; UPA plus MTX: 276 [52%]) were included. Mean patient age was 58 years; mean disease duration was 9 years (Table 1). Despite having active RA, almost half the population (44%; n=237) did not have elevated CRP at the start of UPA treatment. Mean DAS28(CRP) was 4.6; mean TJC28 and SJC28 were 7.7 and 5.6, respectively. Overall, 39% of patients had not been treated with any biologic (b) DMARD or targeted synthetic (ts) DMARD before enrollment; 25% and 36% had previously been treated with 1 or ≥2 bDMARDs or tsDMARDs, respectively (Figure 1). 8.7% of patients had previously received a herpes zoster vaccination (8.1% Shingrix; 0.6% Zostavax).

Conclusion: In German clinical practice, the population of patients with RA in the UPwArds study was predominantly treatment-refractory. Half of these patients had no elevated CRP despite active disease; future analyses will assess the impact of CRP on efficacy outcomes.

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Table 1. Baseline characteristics

	UPA	UPA + MTX	Total
Age, years	57.7 (13.2) n=257	58.1 (11.4) n=276	57.9 (12.3) n=533
Disease duration, years	9.4 (8.3) n=253	8.5 (7.7) n=272	9.0 (8.0) n=525
CRP, mg/dL	1.3 (1.9) n=257	1.1 (1.7) n=276	1.2 (1.8) n=533
CRP >ULN, n (%)	137 (53.3) n=257	159 (57.6) n=276	296 (55.5) n=533
TJC28	7.4 (6.0) n=257	7.9 (6.4) n=276	7.7 (6.2) n=533
SJC28	5.5 (3.7) n=257	5.6 (4.1) n=276	5.6 (3.9) n=533
Patient's Global Assessment	6.2 (1.9) n=257	6.3 (1.8) n=276	6.3 (1.8) n=533
Physician's Global Assessment	5.8 (1.5) n=257	5.9 (1.6) n=276	5.9 (1.6) n=533
DAS28(CRP)	4.6 (1.0) n=257	4.6 (1.0) n=276	4.6 (1.0) n=533
DAS28(ESR)	4.8 (1.1) n=224	4.9 (1.2) n=239	4.9 (1.1) n=463
CDAI	24.9 (10.2) n=257	25.7 (10.8) n=276	25.4 (10.5) n=533
SDAI	26.2 (10.5) n=257	26.9 (11.3) n=276	26.6 (10.9) n=533
RAID	5.7 (2.0) n=255	5.7 (2.0) n=275	5.7 (2.0) n=530
Pain (RAID-1)	6.2 (2.2) n=255	6.1 (2.3) n=275	6.2 (2.2) n=530
SF-12 Physical Component Summary	32.6 (8.5) n=245	33.9 (8.6) n=262	33.3 (8.6) n=507
SF-12 Mental Component Summary	42.4 (11.6) n=245	42.6 (11.3) n=262	42.5 (11.5) n=507
HAQ-DI	1.3 (0.7) n=250	1.3 (0.6) n=270	1.3 (0.6) n=520
PHQ-9	8.9 (5.3) n=252	8.6 (5.3) n=272	8.7 (5.3) n=524
Erosions, n (%)	87 (33.9) n=257	95 (34.4) n=276	182 (34.1) n=533

Data are mean (SD), n unless otherwise stated

Figure Number of prior bDMARDs or tsDMARDs for rheumatoid arthritis

bDMARD, biologic DMARD; DMARD, disease-modifying antirheumatic drug; tsDMARD, targeted synthetic DMARD

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

Disclosure of Interests: Torsten Witte Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Chugai, Gilead, Janssen, Lilly, MSD, Mylan, Novartis, Pfizer, Roche, and UCB., Uta Kiltz Consultant of: AbbVie, Biocad, Eli Lilly and Company, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, Amgen, Biogen, Fresenius, GSK, Hexal, Novartis, and Pfizer, Florian Haas Consultant of: AbbVie, Celgene, Novartis, and Pfizer, Grant/research support from: AbbVie, BMS, Celgene, Chugai, MSD, Novartis, Pfizer, Roche, and Sanofi Genzyme, Elke Riechers Consultant of: AbbVie, Chugai, Novartis, and UCB, Grant/research support from: AbbVie, Chugai, Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Ulrich Prothmann Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Chugai, Glaxo Smith Kline, Novartis, Pfizer, Roche, Sanofi, SOBI, and UCB, Daniela Adolf Employee of: Employee of StatConsult and may own stock or options, Carsten Holland Employee of: Employee of AbbVie and may own stock or options, Rouven Hecht Employee of: Employee of AbbVie and may own

stock or options, Alexander Roessler Employee of: Employee of AbbVie and may own stock or options, Kirsten Famulla Employee of: Employee of AbbVie and may own stock or options, Klaus Krueger Grant/research support from: AbbVie, Biogen, BMS, Celltrion, Gilead, Hexal, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Roche, and UCB.

DOI: 10.1136/annrheumdis-2021-eular.886

AB0256

BARICITINIB (BARI) VERSUS BIOLOGICS IMPACT ON STEROID TAPERING IN RHEUMATOID ARTHRITIS (RA)

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Background: Biologic and target synthetic disease modifying anti-rheumatic drugs (bDMARDs and tsDMARDs) are recommended to control RA disease activity, pain and steroid use. Following randomized clinical trials (RCTs) and their post-hoc analyses, the Janus Kinase Inhibitor tsDMARDs BARI was superior to reference bDMARD Adalimumab in reducing disease activity, pain and functional disability. In addition, BARI monotherapy also determined more significant pain reduction and functional improvement when compared to Tocilizumab monotherapy (3).

Objectives: to confirm RCT results in a real-life clinical setting, with focus on disease activity, pain, functional disability and steroid tapering, when comparing BARI to bDMARDs for the treatment of active RA.

Methods: RA patients starting BARI or a bDMARD for active RA were retrospectively evaluated from June 2019 to June 2020. Disease activity (DAS28CRP, SDAI, CDAI), pain visual analogic scale (pain_VAS), functional disability (HAQ) assessments and mean prednisone dosage (pred_dose) were collected at baseline (BL), 3 months (3M) and 6 months (6M) after BARI/bDMARD initiation. The changes of the outcome measures were evaluated between BL-3M, 3M-6M and BL-6M, as well as between BARI and bDMARDs groups. Finally, we assessed the variables associated with prednisone tapering in the whole population.

Results: 90 out of 100 RA patients evaluated (baseline: age 57±12 years, disease duration 131±100 months, DAS28PCR 4.8±1.0, pain_VAS 61±23 mm, prednisone dose 5.5±5.3 mg) were eligible for the study; 49 received BARI and 41 bDMARDs (17 abatacept, 12 TNF inhibitors, 11 tocilizumab, 1 rituximab). At BL, the two groups did not differ statistically in terms of age, sex, disease duration, disease activity, pain_VAS, previous bDMARD failure or ts/bDMARD naive, concomitant conventional synthetic DMARDs treatment, pred_dose. Both BARI and bDMARDs determined a significant reduction in activity scales and HAQ when comparing BL-3M and BL-6M, with only pain_VAS and pred_dose showing a significant decrease in the 3M-6M interval. When comparing the two groups, BARI showed a significantly higher reduction of pred_dose (-3.2±5.1 vs -1.7±3.7 mg at BL-3M, and -4.1±5.3 vs -1.9±4.6 mg at BL-6M), which was not significant after adjusting for BL pred_dose. No other difference was seen when the two groups, including the numerically higher reduction of pain_VAS in the BARI group (-29±28 vs -20±27 mm at BL-3M and -35±25 vs -30±28 mm at BL-6M comparison). The analysis of the predictors for steroid tapering (Δmean_pred) in the two intervals, showed that BL DAS28PCR, DAS28PCR BL-3M change and BL pred_dose were associated with BL-3M Δmean_pred, while 3M pain_VAS and 3M pred_dose were associated with 3M-6M Δmean_pred.

Conclusion: Although limited by the small samples and the retrospective nature, our real-life comparison shows similar efficacy of BARI and bDMARDs in terms of disease activity control, functional disability and pain. In addition, the treatment with BARI or bDMARD did not influence the steroid tapering, which was driven mostly by its initial dose, disease activity and pain. Larger real-life multi-center studies are warranted to confirm our results.

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Disclosure of Interests: Laura Cometi: None declared, Cosimo Bruni Speakers bureau: Actelion, Consultant of: Eli Lilly, Grant/research support from: Fondazione Italiana Ricerca sull'Artrite (FIRA), Gruppo Italiano lotta alla Scleroderma (GILS), New Horizon Fellowship, European Scleroderma Trials and Research (EUSTAR) group, Foundation for Research in Rheumatology (FOREUM)., Lorenzo Tofani: None declared, Giulia Tesei: None declared, Francesca Nacci: None declared, Ginevra Fiori: None declared, Francesca Bartoli: None declared, Marco Matucci-Cerinic Speakers bureau: Biogen