Methods: In the phase 3, randomized, placebo (PBO) and active-controlled SELECT-COMPARE trial, pts on stable background MTX received UPA 15 mg once daily, PBO, or ADA 40 mg every other week. Pts not achieving 20% improvements in tender/swollen joint counts (Weeks 14-22) or LDA (CDAI ≤ 10 at Week 26) were rescued from UPA to ADA or PBO/ADA to UPA; all non-rescued PBO pts were switched to UPA at Week 26. This post hoc analysis evaluated clinical REM (CDAI ≤ 2.8 ; SDAI ≤ 3.3), LDA (CDAI ≤ 10 ; SDAI ≤ 11), and DAS28(CRP) $< 2.6/\leq 3.2$ at first occurrence before Week 72 or prior to treatment switch; additionally, these measures were evaluated at 3, 6, and 12 months after the first occurrence for the total number of pts randomized to UPA (n=651) or ADA (n=327). Sustainability of response was evaluated by Kaplan-Meier only for those pts who achieved REM/LDA and was defined as time to the earliest date of losing response at two consecutive visits, discontinuation of study drug, or losing response at the time of rescue. The predictive ability of time to clinical REM/LDA was assessed using Harrell's concordance (c)-index (for reference, an index ~ 0.5 , indicates no ability to predict; an index of 1 or -1 would be a perfect prediction). The date of the last follow up was 6 July, 2018, when all pts had reached the Week 72 visit.

Results: Through Week 72, a significantly higher proportion of pts receiving UPA + MTX vs ADA + MTX achieved CDAI REM (41% vs 31%, p=.0035) as well as CDAI LDA (70% vs 59%, p=.0007). 26%/22% of pts randomized to UPA + MTX and 16%/14% of pts randomized to ADA + MTX achieved sustained CDAI REM at 6/12 months after the first occurrence. Additionally, 49%/46% of pts randomized to UPA + MTX and 36%/34% of pts randomized to ADA + MTX achieved sustained CDAI LDA at 6/12 months after the first occurrence (Figure 1). Time to initial clinical REM/LDA did not appear to be associated with sustained disease control. The c-indices (95% CI) for CDAI REM in the UPA + MTX and ADA + MTX groups were 0.528 (0.48, 0.58) and 0.510 (0.43, 0.59) and that of LDA were 0.601 (0.56, 0.64) and 0.555 (0.50, 0.61), respectively. Through last follow-up visit, 51% of UPA + MTX pts and 45% of ADA + MTX pts remained in CDAI REM while 65% of UPA + MTX pts and 58% of ADA + MTX pts remained in CDAI LDA, respectively (Figure 2). Similar results were observed across other disease activity measures (SDAI REM/LDA and DAS28(CRP) $< 2.6/\leq 3.2$).

Conclusion: A significantly greater proportion of pts with RA and prior inadequate response to MTX receiving UPA + MTX vs ADA + MTX achieved clinical REM or LDA across disease activity measures. REM and LDA were sustained through Week 72 in both treatment arms, with numerically higher proportions retaining response among UPA-treated pts.

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Figure 1. Proportion of patients sustaining CDAI remission or low disease activity at 3, 6, and 12 months after the first occurrence of response among the total randomized population

UPA, upadacitinib; ADA, adalimumab; MTX, methotrexate; QD, once daily; EOW, every other week; CDAI, Clinical Disease Activity Index; n, total number of patients randomized to UPA or ADA.
Data for patients who maintained response through the cut-off (6 July 2018, when all patients had reached Week 72 visit) were assessed. Non-responder imputation was used for missing data.

Figure 2. Kaplan-Meier analysis of time to loss of CDAI remission or low disease activity after the first occurrence of response

UPA, upadacitinib; ADA, adalimumab; MTX, methotrexate; QD, once daily; EOW, every other week; CDAI, Clinical Disease Activity Index; n, number of patients who had achieved CDAI remission or low disease activity.
Results are for patients who had achieved CDAI remission or low disease activity. UPA 15 mg QD + MTX: CDAI ≤ 2.8 n = 267; CDAI ≤ 10 n = 496. ADA 40 mg EOW + MTX: CDAI ≤ 2.8 n = 102; CDAI ≤ 10 n = 193.
Data for patients who maintained response through the cut-off (6 July 2018, when all patients had reached Week 72 visit) were assessed. Non-responder imputation was used for missing data. Week 0 indicates the first occurrence of response.

Disclosure of Interests:

Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Arthur Kavanaugh Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB – grant/research support, Maya H Buch Grant/research support from: Pfizer, Roche, and UCB, Consultant of: Pfizer; AbbVie; Eli Lilly; Gilead Sciences, Inc.; Merck-Serono; Sandoz; and

Sanofi, Bernard Combe Grant/research support from: Novartis, Pfizer, Roche-Chugai, Consultant of: AbbVie; Gilead Sciences, Inc.; Janssen; Eli Lilly and Company; Pfizer; Roche-Chugai; Sanofi, Speakers bureau: Bristol-Myers Squibb; Gilead Sciences, Inc.; Eli Lilly and Company; Merck Sharp & Dohme; Pfizer; Roche-Chugai; UCB, Louis Besette Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB Pharma, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sanofi, In-Ho Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Yanna Song Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Roy Fleischmann Grant/research support from: AbbVie, Akros, Amgen, AstraZeneca, Bristol-Myers Squibb, Boehringer, Ingelhel Centrexion, Eli Lilly, EMD Serono, Genentech, Gilead, Janssen, Merck, Nektar, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Samsung, Sandoz, Sanofi Genzyme, Selecta, Taiho, UCB, Consultant of: AbbVie, ACEA, Amgen, Bristol-Myers Squibb, Eli Lilly, Gilead, GlaxoSmithKline, Novartis, Pfizer, Sanofi Genzyme, UCB

DOI: 10.1136/annrheumdis-2020-eular.1230

FRI0132 EFFICACY AND SAFETY OF SWITCHING JAKINIBS IN RHEUMATOID ARTHRITIS

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Background: Different Jakinibs (JAKi) have shown efficacy in rheumatoid arthritis (RA) but in an important proportion of patients, insufficient response leads to therapy withdrawal. The different JAKi show variable selectivity for the four Jak isoforms (Jak1,2,3 y Tyk2) but there are no clinical trials analyzing the response to a JAKi after the suspension of another JAKi and therefore, observational data may be useful in this regard.

Objectives: To describe efficacy and safety of the second JAKi in patients with suspension of the first due to failure or side effects.

Methods: Spanish observational multicentric study. Data were retrospectively obtained from medical records of 28 patients with RA sequentially treated with baricitinib or tofacitinib in any order.

Results: We identified 28 patients with RA treated with baricitinib and tofacitinib. Patient's characteristics are summarized in Table 1. Half of the patients received tofacitinib first, and the other half baricitinib as the first JAKi. Mean survival for the first JAKi was 7,6 $\pm$ 6,1 months. The reason for withdrawal was inefficacy in 17 cases (61%) and adverse effects in 11 (39%). Mean follow-up after starting on the second JAKi was 9,6 $\pm$ 5,6 [3-19] months. Disease activity data along follow-up are depicted in Table 2. Survival on the second JAKi was 82% at 3, 76% at 6, and 62% at 12 months when 13 of the 21 patients maintained the therapy. In all 8 patients who discontinued the second JAKi, the reason was inefficacy. The treatment suspension rate was similar among patients discontinuing the first JAKi for inefficacy (n=5, 29,4%) or for adverse effects (n=3; 27,3%).

Table1. Baseline Characteristics.

	N 28
Clinical characteristics	
Female	24 (86%)
Age*	61,2 $\pm$ 13,2
ACPA (+)	19 (67,9%)
Erosions	13 (46,4%)
Extra-articular manifestations	8 (28,6%)
TJC*	10,8 $\pm$ 5,4
SJC *	7,4 $\pm$ 4,6
DAS28-CPR*	5,4 $\pm$ 0,91
High disease activity	71,5%
Moderate disease activity	23,8%
Low disease activity	4,7%
Previous treatment	
bDMARD	24 (86%)
Nº of previous bDMARDs *	3,9 $\pm$ 2,2
ITNF	75%
No-ITNF	67,9%

(*) Mean $\pm$ SD

Tabla 2. Treatment results during the follow-up period.

	Baseline (n 28)	3 m (n 28)	6 m (n 25)	12 m (n 21)
TJC	10,8±5,4	3,8±3,3	4,23±2,5	1,9±1,5
SJC	7,2±4,6	1,8±1,7	1,7±2	0,7±1
CPR mg/dL	1±0,6	0,54±0,48	0,64±0,9	0,33±0,24
DAS28CPR	5,4±0,91	3,29±0,97	3,15±1,2	2,15±0,6
Prednisone mg	7,2±4,2	6,8±3,5	5,3±2,5	3,1±2,1

Conclusion: Our data show that therapy with a second JAKi is a safe and efficacious option after discontinuation of the first JAKi due to either inefficacy or side effects. The response rate to the second JAKi is similar in patients with inefficacy or side effects which suggests that failure to the first does not reduce the chance of response to the second.

Acknowledgments: M. Retuerto was recipient of a training grant from Sociedad Española de Reumatología (SER).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6284

FRI0133

RELATIONSHIP BETWEEN MELATONIN SERUM LEVELS AND THE EFFICACY OF SELECTIVE SEROTONIN REUPTAKE INHIBITOR PAROXETINE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Numerous clinical and epidemiological studies have established that there is a close relationship between inflammation, chronic pain and psycho-emotional disorders in rheumatoid arthritis [1, 2]. The common pathogenetic mechanism is manifested in the defect of melatonin mediation and cytokine stimulation [3]. Therefore, features of the use of selective serotonin reuptake inhibitors is relevant.

Objectives: To study the relationship between serum melatonin level and the efficacy of selective serotonin reuptake inhibitor paroxetine in patients with RA.

Methods: A total of 127 RA patients and 71 healthy volunteers were examined. The following information was collected for each patient: medical history data, physical examination results, serum melatonin levels. RA patients were randomly categorized into two treatment groups – 63 and 64 patients. The basic treatment for patients of both groups included nonsteroidal anti-inflammatory drugs, glucocorticoids (equivalent to 10 mg of prednisolone), and disease-modifying antirheumatic drugs (methotrexate, leflunomide or sulfasalazine). To evaluate the effectiveness of treatment, patients of both groups were further divided into three subgroups depending on the serum melatonin level (low level corresponds to 25 percentile, medium - 25-75, high - 75 percentile). First group received paroxetine 20mg once a day for 12 weeks in addition to the basic treatment. Effectiveness of the treatment was evaluated according to the ACR/EULAR criteria.

Results: The mean baseline plasma melatonin levels in RA patients were significantly higher than in the healthy volunteers (26.1±32.7 vs 13.6±4.6 pg/mL at 8 am and 11.5±15.5 vs 3.6±4.6 pg/mL at 20 pm (p<0.001), respectively). A good response to basic treatment was observed in groups with medium and high serum melatonin levels, who received paroxetine (p<0.05). However, patients who did not receive paroxetine gave best response to treatment in group with low serum melatonin levels (p<0.05).

Conclusion: Obtained data suggest that the high level of serum melatonin is one of the predictors of resistance for basic RA treatment. The proposed scheme of treatment with addition of paroxetine demonstrated high efficacy concerning the main manifestations of the disease in RA patients with high melatonin serum level. This study demonstrates the possible influence of serotonergic interactions on the melatonergic system and their contribution to the pathogenesis of RA.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5483

FRI0134

EFFECT OF JAK INHIBITORS ON PAIN AND QUALITY OF LIFE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Pain control is considered a treatment priority from most patients with Rheumatoid Arthritis (RA). Despite the treat to target approach, residual pain is commonly reported by patients with RA. Treatment with JAK inhibitors (JAKi) has been associated to a rapid control of pain.

Objectives: To investigate the effect of JAKi on pain and quality of life in a mono-centric real-life clinical setting.

Methods: Patients candidate to baricitinib or tofacitinib were evaluated at baseline and after 12 and 24 weeks of treatment. Disease activity was assessed by Disease Activity Score (DAS)28 with C reactive protein (CRP). A reduction of ≥ 50% of pain visual-analogue scale (VAS) 0-100mm was recorded as "very much improved, substantially improved" (1). Pain VAS score ≤ 10mm was considered "no/limited pain" (2). Patients' satisfaction was assessed by the Patient Acceptable Symptom State question (3). Data were expressed as mean (SD) or median (interquartile range) according to the variables' distribution. Mann Whitney test was used and p values <0.05 were considered statistically significant.

Results: Overall 108 patients started a JAK inhibitor (baricitinib n=67, tofacitinib n=41). Eighty-four patients (baricitinib n=51; tofacitinib n=33) were followed-up for at least 3 months and were included in the analysis. Table 1 summarizes demographic and clinical characteristic of the cohort. After 12 and 24 weeks of treatment we detected a significant reduction of DAS28 compared with baseline [from 4.7 (1.5) to 3.2 (1.7) 2.9 (1.5) and 2.7 (1.1), respectively; p<0.001; p<0.00001 and p<0.00001]. At week 4, 27% and 51.8% of patients achieved remission and low disease activity, respectively; the percentages increase to 32.1% and 60.7% at week 12 and 42.2% and 70.3% at week 24. When evaluating the extent of reduction of the single items included in the DAS28 composite index we found that number of tender (TJ) and swollen joints (SJ) decreased from 9 (7.8) to 5 (3.5) to 4 (5) and 1 (3) at week 4, 2 (4) and 1 (3) at week 12, and 2 (4) and 1 (3) at week 24, respectively (p<0.00001 for all); the median reduction of TJ and SJ at week 4, 12 and 24 was 60%, 77% and 88%, and 81%, 86% and 100%, respectively. GH decreased from 70(30) to 40(40) at week 4, 40(30) at week 12 and 37(40) at week 24 (p<0.00001) with a median reduction of 37.5%, 44% and 46%. C reactive protein decreased by 54.5% at week 4, 47% at week 12 and 55% at week 24. VAS pain was significantly reduced at week 4, 12 and 24 [from 70(25) to 40(40),30(40) at the three timepoints, p<0.00001] decreasing by 37.5%, 50% and 54%, respectively. A substantial reduction (≥50%) in VAS pain was reported by 41.3%, 54.4% and 53.9% of patients after 4, 12 and 24 weeks, respectively. Limited/no pain was reported by 21.3%, 24.7% and 36.5% at weeks 4, 12 and 24, respectively. Overall, 81.8% of patients achieved the PASS after a median time of 10 (7-15) days.

Conclusion: JAK inhibitors baricitinib and tofacitinib induce a rapid improvement of disease activity driven both by pain and inflammation control. Even if no/limited pain was described only by one third of the patients, most of them reported a rapid and sustained reduction of pain accounting for the achievement of a satisfactory health condition.

References:

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	Baricitinib (n=51)	Tofacitinib (n=33)	P
F:M	43: 8	26:7	ns
Age, mean (SD)	59±12	60±12	ns
Disease duration, mean (SD)	163±101	170±112	ns
Baseline DAS28(PCR), median (IQR)	4.7 (4-5.6)	4.7 (4.3-5.4)	ns
Concomitant methotrexate, n (%)	27 (52.9)	8 (24.2)	<0.001
Daily prednisone dose, median (IQR)	5 (2.5-9.5)	5 (1.88-9.9)	ns
N° of previous csDMRAs, median (IQR)	3 (1-4)	2.5 (2-3)	ns
N° of previous bDMRAs, median (IQR)	2 (1-4)	1 (0-2.5)	ns

Disclosure of Interests: Francesca Romana Spinelli Grant/research support from: Pfizer, Speakers bureau: Lilly, BMS, Celgene, Cristina Garufi: None declared, Fulvia Ceccarelli: None declared, Silvia Mancuso: None declared, Ilaria Duca: None declared, cristiano alessandri Grant/research support from: Pfizer, Manuela Di Franco: None declared, Roberta Priori: None declared, Valeria Riccieri: None declared, Rossana Scivo: None declared, Guido Valesini: None declared, fabrizio conti Speakers bureau: BMS, Lilly, Abbvie, Pfizer, Sanofi

DOI: 10.1136/annrheumdis-2020-eular.4903