effects, and tended to have more comorbidities at MTX initiation than those who persisted on therapy.

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Clinical Disease Characteristics and Outcomes by Pattern of MTX Use				
	Discontinued/Restarted (N=34)	Discontinued (N=174)	Persisted (N=577)	P-value
CDAI change over 2-year follow-up				
Change from baseline in CDAI, mean $\pm$ SD	3.1 $\pm$ 15.6	7.4 $\pm$ 14.9	10.4 $\pm$ 13.6	<0.01
Achieved LDA, ^a n (%)	10 (29.4)	58 (33.3)	213 (36.9)	0.50
Achieved MCID, ^b n (%)	14 (41.2)	86 (49.4)	332 (57.5)	0.04
Outcomes at end of MTX use or 2-year follow-up				
CDAI, mean $\pm$ SD	15.6 $\pm$ 14.4	10.1 $\pm$ 9.3	8.8 $\pm$ 9.5	0.001
mHAQ, mean $\pm$ SD	0.5 $\pm$ 0.7	0.4 $\pm$ 0.5	0.2 $\pm$ 0.4	<0.001
Physician Global Assessment, mean $\pm$ SD	22.0 $\pm$ 20.6	18.1 $\pm$ 16.4	14.4 $\pm$ 15.4	<0.01
Patient Global Assessment, mean $\pm$ SD	39.4 $\pm$ 32.5	31.3 $\pm$ 26.7	25.2 $\pm$ 25.0	<0.01
Pain, mean $\pm$ SD	39.1 $\pm$ 32.5	33.9 $\pm$ 27.3	27.2 $\pm$ 26.2	<0.01
Fatigue, mean $\pm$ SD	44.0 $\pm$ 35.0	32.5 $\pm$ 29.5	27.2 $\pm$ 26.8	0.06
Morning stiffness, n (%)	23 (67.7)	127 (74.3)	359 (63.5)	0.03
Morning stiffness duration (h), mean $\pm$ SD	1.5 $\pm$ 4.0	1.3 $\pm$ 3.2	0.7 $\pm$ 1.9	<0.001

CDAI, Clinical Disease Activity Index; CPP, cyclic citrullinated peptide; LDA, low disease activity; MCID, minimum clinically important difference; mHAQ, modified Health Assessment Questionnaire; SD, standard deviation.

^aAchievement of LDA (CDAI $\leq$ 10) in those patients who initiated therapy in moderate (10<CDAI $\leq$ 22) or high disease activity (CDAI $\geq$ 22).

^bCDAI change $\geq$ 1 for those in LDA (CDAI $\leq$ 10) at baseline, CDAI change $\geq$ 6 for those in moderate disease activity (10<CDAI $\leq$ 22) at baseline, and CDAI change $\geq$ 12 for those in high disease activity (CDAI $\geq$ 22) at baseline.

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FRI0153

OPHTHALMOLOGICAL ADVERSE EVENTS UNDER JAK INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: CASE ANALYSIS OF THE EUROPEAN PHARMACOVIGILANCE DATABASE

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Background: Ophthalmological manifestations in rheumatoid arthritis (RA) include dry syndrome, scleritis, episcleritis, uveitis and peripheral ulcerative keratitis (PUK). Recently, a new class of synthetic molecules has been developed, called JAK inhibitors (JAKinhib). We observed one case of PUK occurring two months after the introduction of baricitinib treatment with corneal perforation with secondary improvement after discontinuation of JAKinhib.

Objectives: The aim of this study is to describe and characterize the ophthalmological side effects of JAK inhibitors (JAK inhib) in patients with rheumatoid arthritis (RA) from European pharmacovigilance (PV) data.

Methods: The ophthalmological manifestations that appeared under JAK inhib were extracted from the European PV database (May 2018), EUDRAVIGILANCE following a request addressed to the National Drug Safety Agency carried out according to the following MedDRA classification "SOC eye disorders and BARICITINIB" and "SOC eye disorders and TOFACITINIB".

Results: A total of 41 patients with ophthalmic adverse events (AEs) on JAK inhib were reported. Among patients, 12 were treated with BARICITINIB and 29 with TOFACITINIB. Of these AEs, 51% were reported by the medical profession, 39% by patients and 10% by paramedical teams. The database analysis revealed 4 scleritis, 3 uveitis, 1 PUK and 1 corneal ulceration. The average time to onset of AEs was 13.2 months. The infectious causes had been eliminated.

Ocular adverse events under JAK inhibitors

	BARICITINIB n=12	TOFACITINIB n=29	Mean Delay (in days)
Ophthalmological events	AEs	AEs	
Scleritis**, n (%)	2 (17)	2 (7)	344
Corneal ulceration**, n (%)	0	1 (3)	90
PUK**, n (%)	1 (8)	0	57
Uveitis**, n (%)	0	3 (10)	838
Blurry vision*, n (%)	3 (25)	8 (28)	9
Red eyes*, n (%)	3 (25)	1 (3)	33
Dry eyes*, n (%)	2 (17)	3 (10)	NA
Photophobia*, n (%)	0	1 (3)	NA
Decreased visual acuity*, n (%)	1 (8)	1 (3)	124
Retinal detachment**, n (%)	0	1 (3)	480
Retinal haemorrhage**, n (%)	0	2 (7)	541
Cataract**, n (%)	2 (17)	5 (17)	413
Glaucoma**, n (%)	0	4 (14)	489
Age related macular degeneration**, n (%)	0	1 (3)	NA

*Adverse event reported by the patient **Adverse event reported by the medical profession
PUK: Peripheral Ulcerative Keratitis NA: Not Available

Conclusion: Ophthalmological manifestations under JAKinhib seem to be rare but not exceptional, the rheumatologist must be aware of them in order to discuss the imputability of the treatment. A discontinuation of it seems justified pending an ophthalmological opinion.

Disclosure of Interests: None declared

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FRI0154

SAFETY AND EFFICACY OF FILGOTINIB IN PATIENTS AGED 65 YEARS AND OLDER: RESULTS FROM A PHASE 3 STUDY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDS (BDMARD-IR)

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Background: Filgotinib (FIL), an oral selective Janus kinase 1 (JAK1) inhibitor, demonstrated efficacy and safety vs placebo (PBO) in bDMARD-IR patients with active RA in a global phase 3 study (FINCH2, ClinicalTrials.gov NCT02873936).¹

Objectives: We performed a prespecified subgroup analysis of the safety and efficacy of FIL in patients aged $\geq$ 65 years vs <65 years in FINCH2 to understand FIL effects in older patients.

Methods: 449 patients were randomized 1:1:1 to FIL 200 mg, FIL 100 mg, or PBO on a background of csDMARDs for 24 weeks. The primary efficacy endpoint was ACR20 response at week 12.

Results: Of 448 patients who received $\geq$ 1 dose of study drugs, 113 (25.2%) were $\geq$ 65 years of age; baseline disease characteristics were similar for both age groups. Safety and efficacy parameters by age group are in Tables 1 and 2. The most common treatment-emergent adverse events (TEAEs, by System Organ Class) category was infections and infestations; nasopharyngitis, upper respiratory tract infections, and bronchitis were the most common infections and infestations in the FIL arms in both age groups. There were no cases of opportunistic infection, active tuberculosis, malignancy, gastrointestinal perforation, or death. Efficacy outcomes were similar for both groups.

Conclusion: Overall, older age was not associated with higher incidence of safety events (serious infections, herpes zoster, MACE occurred in the group <65 yrs) and efficacy was similar in older and younger bDMARD-IR patients with active RA.

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[1] MC Genovese, et al. ACR, 2018. Abstract L06.

Table 1. TEAEs and Key Safety Outcomes Week 0-24 by Age Group, n (%)

Regimen	<65 yrs (n=335)			≥65 yrs (n=113)		
	FIL 200 (n=112)	FIL 100 (n=117)	PBO (n=106)	FIL 200 (n=35)	FIL 100 (n=36)	PBO (n=42)
TEAE	72 (64.3)	81 (69.2%)	70 (66.0%)	30 (85.7%)	16 (44.4%)	30 (71.4%)
Serious AE	4 (3.6)	7 (6.0%)	4 (3.8%)	2 (5.7%)	1 (2.8%)	1 (2.4%)
TEAE leading to study drug discontinuation	4 (3.6)	6 (5.1%)	1 (0.9%)	1 (2.9%)	0	2 (4.8%)
Infection	39 (34.8)	47 (40.2%)	27 (25.5%)	14 (40.0%)	5 (13.9%)	11 (26.2%)
Herpes Zoster (uncomplicated)	2 (1.8)	2 (1.7)	0	0	0	0
Serious infection	1 (0.9)	3 (2.6)	2 (1.9)	0	0	0
MACE	0	1 (0.9)	1 (0.9)	0	0	0
Retinal vein occlusion	1 (0.9)	0	0	0	0	0

Table 2. Week 24 Key Efficacy Measures by Age Group

Regimen	<65 yrs (n=335)			≥65 yrs (n=113)		
	FIL 200 (n=112)	FIL 100 (n=117)	PBO (n=106)	FIL 200 (n=35)	FIL 100 (n=36)	PBO (n=42)
ACR20 n (%) ¹	78 (70)‡	60 (51)†	33 (31)	24 (69)*	24 (67)*	18 (43)
DAS28(CRP) <2.6 n (%) ¹	33 (30)‡	26 (22)*	11 (10)	12 (34)	14 (39)*	7 (17)
HAQ-DI mean CFB (SD)	-0.75 (0.66)‡	-0.60 (0.66)*	-0.40 (0.58)	-0.74 (0.48)*	-0.59 (0.67)	-0.48 (0.65)
SF-36 PCS mean CFB (SD)	9.4 (8.6)‡	9.2 (8.7)†	6.2 (8.2)	9.4 (6.7)*	8.5 (7.8)	7.5 (7.4)
FACIT-Fatigue mean (SD)	11.2 (11.6)†	9.6 (11.1)	7.2 (10.1)	12.9 (12.2)*	10.3 (8.3)	6.4 (10.7)

*p<0.05, †p<0.01, ‡p<0.001 CFB, change from BL. ¹Nonresponder imputation.

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FRI0155 A COMPARISON OF UPADACITINIB PLUS METHOTREXATE AND UPADACITINIB PLUS OTHER csDMARDs IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN ANALYSIS OF TWO PHASE 3 STUDIES

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has shown efficacy in patients with rheumatoid arthritis (RA) when combined with methotrexate (MTX) or other conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).^{1,2} However, the efficacy of UPA plus MTX has not been directly compared with UPA plus other csDMARDs.

Objectives: To compare the efficacy of UPA in combination with MTX versus UPA in combination with other csDMARDs in patients with an inadequate response (IR) to csDMARDs (SELECT-NEXT¹) or biologic DMARDs (bDMARDs; SELECT-BEYOND²).

Methods: 661 patients in SELECT-NEXT and 498 patients in SELECT-BEYOND received UPA 15 mg or 30 mg once daily (QD) or placebo (PBO) for 12 weeks; all patients received concomitant csDMARD(s). The primary endpoints for both studies were rates of ACR20 response and DAS28(CRP) ≤3.2. Additional endpoints included DAS28(CRP) <2.6, CDAI low disease activity (≤10), and CDAI remission (≤2.8). Patients were grouped according to concomitant csDMARD use (MTX vs non-MTX csDMARDs); patients receiving both MTX and a non-MTX csDMARD were included in the MTX group. p-values were calculated based on a logistic regression model with treatment group and type of background csDMARD as fixed factors, adjusting for demographic and baseline factors. p-values from the interaction between treatment group and background csDMARD were also calculated, to assess the consistency of the effects of study treatments for different background csDMARD type. Non-responder imputation was used for missing data.

Results: In SELECT-NEXT and SELECT-BEYOND, 535 and 410 patients, respectively (80%), were receiving concomitant MTX (mean dose 17 mg/week), and 124 and 82 patients were receiving non-MTX csDMARDs. Demographics and disease characteristics were broadly similar between treatment groups; the majority of patients were female and of white ethnicity, and around half were using oral corticosteroids at baseline. Across all subgroups, the proportion of patients achieving efficacy outcomes was higher with both UPA doses compared with PBO (Table). There were no significant differences between efficacy outcomes with UPA in combination with MTX versus UPA in combination with non-MTX csDMARDs in either patient population. This included ACR20 response as well as low disease activity and remission defined by DAS28(CRP) and CDAI.

Table. Week 12 efficacy outcomes by concomitant treatment

Patients (n)	SELECT-NEXT						p-value ¹
	PBO (n=112)	UPA 15 mg QD (n=117)	UPA 30 mg QD (n=106)	PBO (n=35)	UPA 15 mg QD (n=36)	UPA 30 mg QD (n=42)	
ACR20	27.2	65.1	67.4	27.6	58.8	61.4	0.0001
DAS28(CRP) ≤3.2	16.8	49.1	49.1	20.7	45.1	45.2	0.0001
DAS28(CRP) <2.6	8.9	29.4	29.1	12.2	33.3	34.4	0.0001
CDAI ≤10	18.3	45.4	42.3	24.1	35.3	40.3	0.0001
CDAI ≤2.8	2.6	8.9	13.1	6.9	7.8	6.8	0.0001

Patients (n)	SELECT-BEYOND						p-value ¹
	PBO (n=112)	UPA 15 mg QD (n=117)	UPA 30 mg QD (n=106)	PBO (n=35)	UPA 15 mg QD (n=36)	UPA 30 mg QD (n=42)	
ACR20	27.2	65.1	67.4	27.6	58.8	61.4	0.0001
DAS28(CRP) ≤3.2	16.8	49.1	49.1	20.7	45.1	45.2	0.0001
DAS28(CRP) <2.6	8.9	29.4	29.1	12.2	33.3	34.4	0.0001
CDAI ≤10	18.3	45.4	42.3	24.1	35.3	40.3	0.0001
CDAI ≤2.8	2.6	8.9	13.1	6.9	7.8	6.8	0.0001

¹Based on logistic regression analysis for the comparison of UPA in combination with MTX versus UPA in combination with non-MTX csDMARDs, with treatment group and background csDMARD type as fixed factors and sex and baseline factors as interaction factors.

Conclusion: In this post hoc analysis, the efficacy of UPA in patients with RA appeared comparable whether administered in combination with MTX or non-MTX csDMARDs.