excluding NMSC, NMSC and treatment-emergent adverse events (TEAEs) leading to death, according to FIL dose (200 vs 100 mg) and age (<65 vs ≥65 years); no statistical testing was performed, so all differences are numerical. MACE and VTE were adjudicated by an independent committee; the cutoff for adjudication was April 3, 2022.

Results: Overall, 3691 patients were treated with FIL for a total of 12,541 PYEs. Median (max) PYE was 3.8 (8.3) years for FIL200 and 3.3 (7.8) years for FIL100. Baseline characteristics are shown in the **Table 1**. A greater proportion of those aged ≥65 years vs <65 years had a CV medical history in both the FIL200 (75.7% vs 36.1%) and FIL100 (71.8% vs 40.9%) groups. Overall EAIRs (95% confidence interval [CI]) were 0.40 (0.3, 0.5) for MACE, 0.19 (0.1, 0.3) for VTEs, 0.69 (0.6, 0.9) for malignancy excluding NMSC, 0.29 (0.2, 0.4) for NMSC and 0.65 (0.5, 0.8) for TEAEs leading to death. EAIRs of MACE and VTE were higher in patients aged ≥65 vs <65 years but were generally similar for FIL200 and FIL100 within each age group (**Figure 1**). EAIRs of malignancies, NMSC and TEAEs leading to death were also higher in the ≥65- vs <65-year group. Within the ≥65-year group, EAIRs (95% CI) of these events were numerically higher in the FIL200 vs FIL100 group: 2.0 (1.3, 2.9) vs 0.99 (0.5, 1.9) for malignancies, 1.38 (0.8, 2.2) vs 0.44 (0.1, 1.1) for NMSC, and 1.59 (1.0, 2.5) vs 1.20 (0.6, 2.2) for TEAEs leading to death, respectively.

Conclusion: Rates of MACE and VTE in FIL-treated patients were low and similar for FIL200 and FIL100. There was a higher proportion of patients aged ≥65 years vs <65 years with a CV medical history. In patients aged ≥65 years, EAIRs of malignancies, NMSC and TEAEs leading to death were higher with FIL200 vs FIL100, although CIs overlapped.

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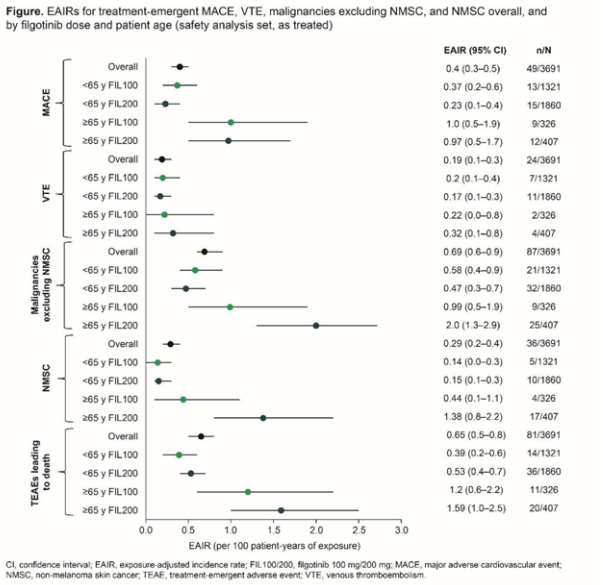
Table 1. Baseline characteristics

	FIL200		FIL100	
	<65 y (n=1860)	≥65 y (n=407)	<65 y (n=1321)	≥65 y (n=326)
Age, y, mean (SD)	48.8 (10.7)	70.0 (4.4)	49.0 (10.5)	70.2 (4.5)
Female, n (%)	1506 (81.0)	322 (79.1)	1075 (81.4)	244 (74.8)
BMI, kg/m^2, mean (SD)	27.5 (6.3)	28.1 (5.9)	27.7 (6.4)	27.2 (5.1)
Creatinine clearance, mL/min, mean (SD)	122 (37.4)	84 (23.4)	122 (38.1)	83 (22.5)
CRP, mg/L, mean (SD)	19.0 (24.3)	18.4 (25.2)	18.9 (25.9)	17.2 (24.7)
Current smoker, n (%)*	207 (14.4)	37 (10.9)	165 (15.3)	28 (9.7)
CV family history, n (%)†	43 (3.0)	10 (2.9)	47 (4.3)	12 (4.2)
Any CV medical history, n (%)	672 (36.1)	308 (75.7)	540 (40.9)	234 (71.8)
Current alcohol use, n (%)*	296 (20.6)	78 (22.9)	213 (19.7)	54 (18.7)

*FIL200 <65 y: n=1436, ≥65 y: n=340; FIL100 <65 y: n=1081, ≥65 y: n=289.†FIL200 <65 y: n=1434, ≥65 y: n=339; FIL100 <65 y: n=1081, ≥65 y: n=289.BMI, body mass index; CRP, C-reactive protein; CV, cardiovascular; FIL100/200, filgotinib 100 mg/200 mg; SD, standard deviation.



CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL100/200, filgotinib 100 mg/200 mg; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

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POS0825

CANCER RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH JANUS KINASE INHIBITORS: A NATIONWIDE DANISH REGISTER-BASED COHORT STUDY

Keywords: Targeted synthetic drugs, Malignancy, Real-world evidence

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Background: Concerns regarding the risk of cancer with janus kinase inhibitor (JAKi) use in patients with rheumatoid arthritis (RA) escalated after the release of results from Pfizer's clinical trial, *ORAL Surveillance*.[1] The trial showed increased risks of major adverse cardiovascular events and cancer in tofacitinib compared with tumour necrosis factor inhibitor recipients. Precautionary considerations on JAKi use in high-risk subsets of patients with RA have since been issued by the European Medicines Agency.

Objectives: We aimed to investigate the risk of first primary cancer in patients with RA treated JAKi (tofacitinib and baricitinib) compared with those who received biologic disease-modifying anti-rheumatic drugs (bDMARDs) in a real-world setting.
Methods: We performed an observational cohort study using the nationwide registers in Denmark. Patients with RA aged 18+ years, without a previous cancer diagnosis, and who initiated treatment with JAKi or bDMARDs from 1 January 2017 to 31 December 2020 were identified in the Danish Rheumatology Quality Register (DANBIO) and followed for any cancer (except non-melanoma skin cancer). We applied inverse probability of treatment weighting (IPTW) to account for covariate differences between treatment groups. IPTW-generated weights were used with cause-specific Cox (CSC) models to calculate hazard ratios (HRs) for cancer incidence in JAKi-treated compared with bDMARD-treated patients with RA. Multiple subgroup and sensitivity analyses were performed.
Results: We identified 875 and 4247 RA patients treated with JAKi and bDMARDs, respectively. The JAKi group contributed with 1315 person years (PYRS) and 19 cancers, while the bDMARD group contributed with 8597 PYRS and 111 cancers. The corresponding crude incidence rates per 1000 PYRS for cancer were 14.4 (JAKi) and 12.9 (bDMARD). Comparing the two groups using weighted CSC models, a HR of 1.41 (95%CI 0.76 to 2.37, 95% confidence intervals) was seen for JAKi- versus bDMARD-treated patients with RA.
Conclusion: JAKi treatment in real-world patients with RA was not associated with a statistically significant increased risk of first primary cancer compared with those who received bDMARDs. However, risk estimates were elevated in many analyses, and an excess risk of cancer with JAKi treatment cannot be ruled out. More studies investigating JAKi and cancer risk in patients with RA are highly warranted.
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Table 1. Number of patients, person years (PYRS), cancers, crude incidence rates (IR), and hazard ratios (HRs) for cancer by type of analysis, by choice of statistical model, and by groups of JAKi- and bDMARD-treated patients with rheumatoid arthritis

	N patients	N PYRS	N Cancers (except NMSC)	Crude IR (per 1000 years)	HR (95%CI)
JAKi vs bDMARD (all patients)					
JAKi group	875	1315	19	14.4	
bDMARD group	4247	8597	111	12.9	
IPTW + CSC [a]					1.41 (0.76 to 2.37)
CSC model 1 [b]					1.17 (0.72 to 1.91)
CSC model 2 [c]					1.37 (0.81 to 2.32)
Age 50+					
JAKi group [d]	653	-	≥15	18.3	
bDMARD group	3099	6274	103	16.4	
IPTW + CSC					1.37 (0.75 to 2.30)
CSC model 1					1.19 (0.72 to 1.97)
CSC model 2					1.40 (0.81 to 2.42)
Age 65+					
JAKi group	268	401	11	27.4	
bDMARD group	1364	2711	65	24.0	
IPTW + CSC					1.34 (0.55 to 2.81)
CSC model 1					1.20 (0.62 to 2.29)
CSC model 2					1.25 (0.61 to 2.56)

NotesJAKi: janus kinase inhibitors, bDMARDs: biological disease-modifying anti-rheumatic drugs, N: number of, 95%CI: 95% confidence intervals, NMSC: non-melanoma skin cancer, IPTW: inverse probability of treatment, CSC: cause-specific Cox proportional hazard regression with death as the competing risk.a: IPTW weights combined with CSC.b: CSC model 1 unweighted with age as underlying timescale and adjustment for sex.c: CSC model 2 as CSC model 1 but with adjustment for all covariates (not shown in this abstract) with no missing information. d: PYRS and N cancers not shown according to Danish data legislation on indirect anonymisation.

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Disclosure of Interests: Rasmus Westermann: None declared, René Lindholm Cordtz: None declared, Kirsten Duch: None declared, Lene Mellemkjær Shareholder of: Have an immediate family member who owns stocks in Novo Nordisk., Employee of: Have an immediate family member who is employed at Novo Nordisk., Merete Lund Hetland Speakers bureau: Pfizer, Medac, Sandoz. No personal income. Paid to my institution., Grant/research support from: AbbVie, Biogen, BMS, Celtrion, Eli Lilly Denmark A/S, Janssen Biologics B.V, Lundbeck Fonden, MSD, Novartis, Pfizer, Roche, Samsung Biopis, Sandoz: No personal income. Paid to my institution. MLH has chaired the steering committee of the Danish Rheumatology Quality Registry (DANBIO, DRQ), which receives public funding from the hospital owners and funding from pharmaceutical companies. MLH co-chairs EuroSpA, which generates real-world evidence of treatment of psoriatic arthritis and axial spondylorthritis based on secondary data and is partly funded by Novartis., Andrea Michelle Burden: None declared, Ole Hejlesen: None declared, Martin Bøgsted: None declared, Lene Dreyer Grant/research support from: BMS: Reports of safety. Grant to our institution. Member of the Steering comity of the national DANBIO database for 6 years, which receives public funding from the hospital owners and funding from pharmaceutical companies.
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POS0826

SAFETY PROFILE OF UPADACITINIB UP TO 6.5 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Safety

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Background: Upadacitinib (UPA) is an oral JAK inhibitor that has demonstrated safety and efficacy in patients (pts) with moderate-to-severe active RA in the phase 3 SELECT clinical program.[1–6]
Objectives: To describe the long-term integrated safety profile of UPA relative to active comparators in pts with RA from the SELECT clinical program through the cutoff date of 15 August 2022.
Methods: Pooled safety data were analyzed from 6 randomized controlled trials evaluating UPA in RA.[1–6] Treatment-emergent adverse events (TEAEs) and AEs of special interest were summarized for the following groups: pooled UPA 15 mg once daily (QD; UPA15, 6 trials), MTX (1 trial), and adalimumab (ADA) 40 mg every other week (EOW; 1 trial). TEAEs were defined as AEs with an onset after the first dose and ≤ 30 days (UPA and MTX) or ≤ 70 days (ADA) after the last dose of study drug and reported as exposure-adjusted event rates (EAERs) per 100 patient-years (PY; E/100 PY). The standardized mortality ratio (SMR) was estimated for the general population using World Health Organization country-age-gender specific mortality rates through 2016.
Results: 3209 pts received ≥ 1 dose of UPA15 with 10 782.7 PY of exposure. EAERs of AEs, serious AEs (SAEs), and AEs leading to discontinuation on UPA15 were comparable to MTX and ADA (**Table 1**). COVID-19 pneumonia was the most common SAE with UPA15 (0.7 E/100 PY). Rates of serious infections were similar between UPA15 and ADA but higher compared with MTX (**Figure 1**). Herpes zoster (HZ) rates were higher with UPA15 vs MTX and ADA. Most HZ cases with UPA15 were non-serious (95%) and affected a single dermatome (75%) or unilateral multiple dermatomes (16%); 8% of cases were reported as disseminated and none involved the central nervous system. Creatine phosphokinase elevations were transient and more common with UPA15 than MTX or ADA. Anemia and neutropenia rates were similar between UPA15 and ADA. Most hepatic disorders were mild or moderate transaminase elevations. Treatment discontinuation due to these lab events was rare (≤ 0.1 E/100 PY). Similar rates of adjudicated MACE, adjudicated VTE, and malignancy (excluding non-melanoma skin cancer [NMSC]) were observed across treatment groups. The rate of NMSC was numerically higher with UPA15 vs ADA; no cases occurred with MTX. SMR analysis indicated that the mortality rate among pts with RA treated with UPA15 was not higher than what would be expected among the general population (SMR [95% CI]: 0.67 [0.52, 0.86] including COVID-19 deaths; 0.41 [0.29, 0.56] excluding COVID-19 deaths).
Conclusion: The integrated safety profile of UPA in pts with RA remained consistent with previous findings,[7] with no new safety risks identified up to 6.5 years of exposure. Similar rates of AEs of special interest were observed for UPA15 and ADA, except for higher rates of HZ, CPK elevations, and NMSC with UPA.