Methods: Patients with RA initiating treatment with BARI 2 or 4 mg (cohort A) or any b/tsDMARD (cohort B) for the first time were included. The primary outcome is time to discontinuation (TTD) for any cause (excluding sustained response) at 2 years; TTD at 6 months has been published [1]. Discontinuation (Kaplan-Meier analyses and rates) and effectiveness (Clinical Disease Activity Index [CDAI] low disease activity [LDA] and remission rates) of treatment to 2 years, based on prior b/tsDMARD status (experienced/naïve) and age (<65/≥65 years) were analysed post-hoc and descriptively for cohort A and subgroups of cohort B.

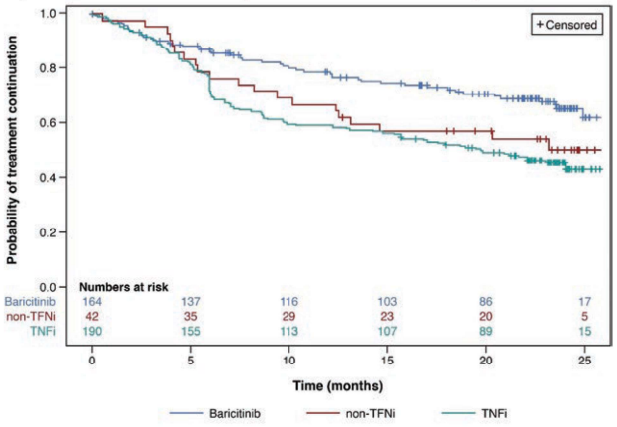
Results: Key baseline characteristics of 1008 RA patients and effectiveness at 2 years for the subgroups in this analysis are shown in the Table 1. Numerically more BARI-treated patients were receiving monotherapy (Table 1). By 2 years, 31.1%, 54.7% and 47.6% of b/tsDMARD-naïve patients aged <65 years receiving BARI, tumour necrosis factor inhibitors (TNFi) and non-TNFi, respectively, had discontinued treatment; corresponding discontinuation rates for b/tsDMARD-naïve patients aged ≥65 years were 28.4%, 65.6% and 44.0%, b/tsDMARD experienced patients aged <65 years were 47.9%, 59.0% and 65.5% and b/tsDMARD experienced patients aged ≥65 years were 42.0%, 78.3% and 66.7%. An example of TTD is presented in the Figure 1. Consistent CDAI LDA and remission rates were observed with BARI regardless of age and prior treatment (Table 1).

Conclusion: Two-year discontinuation rates and effectiveness with BARI in a real-world setting were consistent irrespective of previous treatment or patient age.

REFERENCE:

[1] Alten et al. Rheumatol Ther. 2022;13:1–21

Figure. Time to discontinuation over 2 years in b/tsDMARD-naïve patients aged <65 years



Patients with sustained clinical response were not included in this analysis

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POS0849

LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB OR ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: 5-YEAR DATA FROM THE SELECT-COMPARE STUDY

Keywords: Safety, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Upadacitinib (UPA) is an oral reversible Janus kinase inhibitor. In patients (pts) with RA, UPA 15 mg once daily (QD) demonstrated better clinical responses at 12 weeks (wks) vs adalimumab (ADA) 40 mg every other week (EOW) in the phase 3 SELECT-COMPARE study; these were maintained through 3 years (yrs) in the ongoing long-term extension (LTE), along with an acceptable safety profile.[1,2]

Objectives: To assess the safety and efficacy of UPA vs ADA through 5 yrs in the SELECT-COMPARE LTE.

Methods: Pts receiving background methotrexate were randomized 2:2:1 to UPA 15 mg QD, placebo (PBO), or ADA 40 mg EOW. Rescue (PBO to UPA, UPA to ADA, or ADA to UPA) was mandated for lack of response (<20% improvement in tender or swollen joint counts at wks 14, 18, or 22), or failure to achieve Clinical Disease Activity Index (CDAI) low disease activity (LDA) at wk 26. All remaining PBO pts switched to UPA at wk 26. Pts who completed the 48-wk double-blind period could continue to receive open-label UPA or ADA in the LTE for up to 10 yrs total. Rates of treatment-emergent adverse events (TEAEs) and AEs of special interest were calculated per 100 pt-yrs through 5 yrs for all pts receiving UPA or ADA. Efficacy assessments at 5 yrs were performed by original randomized group for CDAI LDA (≤10) and remission (≤2.8), and disease activity score for 28-joints C-reactive protein (DAS28[CRP]) ≤3.2 and <2.6. Radiographic progression (change from baseline in modified total Sharp score [mTSS]) and proportion of pts with no radiographic progression (change from baseline in mTSS ≤0) were assessed at 192 wks (latest available timepoint; data collected at wks 96/192/520 only) by treatment sequence. No formal statistical comparisons were performed.

Table 1. Baseline data and effectiveness of treatment at 2 years in subgroups based on b/tsDMARD-naïve and -experienced patients aged <65 and ≥65 years[a]

			Age, years[b]	Female[c]	Duration of RA, years[b]	Monotherapy[c]	Baseline CDAI[b]	2-year CDAI remission[d]	2-year CDAI LDA[d]
Naïve <65 years	Cohort A (N=164)	BARI	50.8±9.5	120 (73.2)	5.8±6.4	66 (40.2)	23.0±11.0	20/86 (23.3)	42/86 (48.8)
	Cohort B (N=251)[e]	TNFi (N=192)	49.5±11.0	142 (74.0)	4.9±6.1	48 (25.0)	24.8±13.3	34/130 (26.2)	47/130 (36.2)
		Non-TNFi bDMARD (N=42)	53.1±9.6	32 (76.2)	9.0±8.6	11 (26.2)	20.5±10.5	4/25 (16.0)	10/25 (40.0)
Naïve ≥65 years	Cohort A (N=81)	BARI	73.3±5.7	63 (77.8)	8.9±9.8	49 (60.5)	23.4±11.5	12/37 (32.4)	16/37 (43.2)
	Cohort B (N=93)[e]	TNFi (N=61)	72.7±4.7	37 (60.7)	10.8±11.0	14 (23.0)	24.3±13.1	8/32 (25.0)	16/32 (50.0)
		Non-TNFi bDMARD (N=25)	74.4±5.8	17 (68.0)	8.8±11.5	5 (20.0)	24.8±11.6	4/13 (30.8)	4/13 (30.8)
Experienced <65 years	Cohort A (N=165)	BARI	52.3±9.4	131 (79.4)	11.8±8.5	88 (53.3)	23.9±11.9	21/92 (22.8)	33/92 (35.9)
	Cohort B (N=142)[e]	TNFi (N=61)	48.5±12.4	48 (78.7)	8.6±8.9	29 (47.5)	20.4±11.4	7/37 (18.9)	15/37 (40.5)
		Non-TNFi bDMARD (N=58)	51.6±9.8	51 (87.9)	11.3±10.2	16 (27.6)	21.5±8.9	3/27 (11.1)	14/27 (51.9)
Experienced ≥65 years	Cohort A (N=100)	BARI	72.7±5.6	77 (77.0)	15.1±9.7	55 (55.0)	24.2±11.6	11/51 (21.6)	26/51 (51.0)
	Cohort B (N=77)[e]	TNFi (N=23)	72.7±5.6	14 (60.9)	12.4±12.8	10 (43.5)	24.9±13.0	2/9 (22.2)	3/9 (33.3)
		Non-TNFi bDMARD (N=36)	71.5±4.4	25 (69.4)	16.4±11.9	16 (44.4)	26.4±13.2	2/16 (12.5)	8/16 (50.0)

[a] Effectiveness data were not available for all patients[b] Mean±standard deviation[c] n (%)[d] n/N (%)[e] An additional 65 patients in total received other tsDMARDs (7–23 per group); data for these patients are not shown because of the small numbers

Results: Through 5 yrs, 1417 pts were exposed to UPA (4497 pt-yrs) and 579 to ADA (1472 pt-yrs). UPA was generally well tolerated, with similar rates of TEAEs, serious TEAEs, TEAEs leading to discontinuation of study drug, and COVID-related TEAEs vs ADA (**Figure 1**). Rates of most AEs of special interest with UPA were similar vs ADA, except for numerically higher rates of herpes zoster, creatine phosphokinase elevation, lymphopenia, and hepatic disorder (mainly transaminase elevations) with UPA. In the 651 and 327 pts originally randomized to UPA and ADA, respectively, greater proportions of pts achieved CDAI LDA and remission, and DAS28(CRP) scores ≤3.2 and <2.6, with UPA vs ADA (**Table 1**). Through 192 wks, similar proportions of pts treated with UPA vs ADA had no radiographic progression; mean changes from baseline in mTSS were similar, except for a numerically smaller change with continuous UPA (**Table 1**).

Conclusion: The safety profile of UPA over 5 yrs was consistent with the 3-yr results and the integrated phase 3 safety analysis.[1,2] Consistent with the 3-yr analyses,[2] UPA continued to show numerically better clinical responses than ADA at 5 yrs. Radiographic progression remained similarly low through 192 wks with UPA and ADA.

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[1] Cohen SB, et al. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-218510

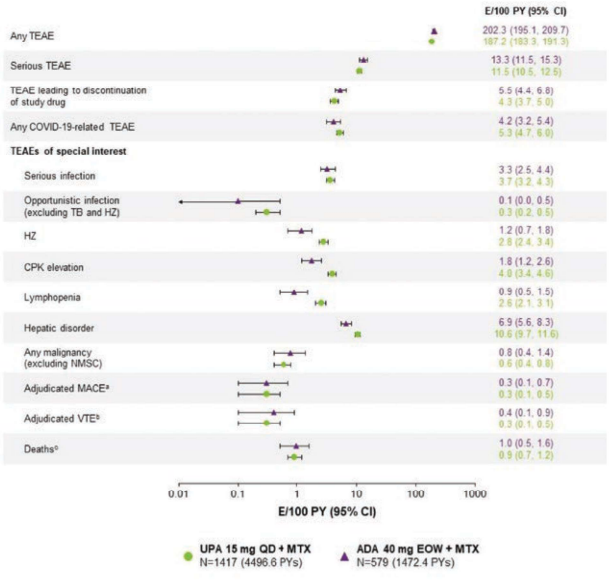
[2] Fleischmann R, et al. *RMD Open* 2022. doi:10.1136/rmdopen-2021-002012

Table 1. Efficacy endpoints

At 5 yrs, by original randomized group (non-responder imputation)	UPA N=651[a,b]		ADA N=327[a,c]		
CDAI ≤10	36.4 (32.7, 40.1)		26.9 (22.1, 31.7)		
CDAI ≤2.8	24.6 (21.3, 27.9)		18.7 (14.4, 22.9)		
DAS28(CRP) ≤3.2	34.7 (31.1, 38.4)		24.8 (20.1, 29.4)		
DAS28(CRP) <2.6	31.8 (28.2, 35.4)		23.2 (18.7, 27.8)		
At 192 wks, by treatment sequence (as observed)	**PBO to UPA N=442**	**UPA N=288**	**UPA to ADA N=150**	**ADA N=109**	**ADA to UPA N=111**
Radiographic progression (change from baseline in mTSS, mean [95% CI])	1.3 (0.8, 1.7)	0.5 (0.2, 0.9)	1.7 (0.7, 2.8)	1.2 (0.5, 1.9)	0.9 (0.2, 1.5)
No radiographic progression (mTSS change from baseline ≤0)	77.1 (73.2, 81.1)	80.9 (76.4, 85.4)	74.0 (67.0, 81.0)	78.0 (70.2, 85.8)	77.5 (69.7, 85.2)

Data are % of pts (95% confidence interval) unless otherwise stated. [a]Pts rescued at or before wk 26 were considered non-responders. [b]252 rescued. [c]159 rescued.

Figure. Exposure-adjusted event rates of TEAEs through 5 yrs



Data for all pts receiving UPA or ADA, including exposure to rescue treatment after switching, with assignment based on drug exposure at the time of event.
[a]Includes cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.
[b]Defined as deep vein thrombosis and pulmonary embolism (fatal and non-fatal).
[c]Includes treatment-emergent deaths (occurring ≤30 days after last dose of UPA or ≤70 days after last dose of ADA) and non-treatment-emergent deaths (occurring >30 days after last dose of UPA or >70 days after last dose of ADA).

CI, confidence interval; CPK, creatine phosphokinase; E, event; HZ, herpes zoster; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, non-melanoma skin cancer; TB, tuberculosis; VTE, venous thromboembolic event.

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POS0850

THE EFFECT OF PERIOPERATIVE JANUS KINASE INHIBITOR WITHDRAWAL ON SURGICAL SITE INFECTION AND FLARE OF RHEUMATOID ARTHRITIS IN ORTHOPEDIC SURGERY: A MULTI-CENTER OBSERVATIONAL STUDY

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Targeted synthetic drugs

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Background: To prevent surgical site infection (SSI), recent guidelines recommend a 3-day preoperative withdrawal of Janus kinase inhibitors (JAKi) in rheumatoid arthritis (RA) patients durling orthopedic surgery [1]. However, there is still insufficient evidence to support this practice. On the other hand, RA flare associated with JAKi withdrawal is also an important outcome, and an appropriate withdrawal period is crucial.

Objectives: We conducted a multicenter observational study to investigate the effect of the perioperative JAKi withdrawal period on SSI and RA flares in orthopedic surgery.

Methods: Patients with RA who visited six tertiary care centers between 2018 and 2021 and underwent JAKi before orthopedic surgery were included. We defined SSI based on the United States Centers for Disease Control criteria and flare as the clinician-assessed newly appearing or worsening joint pain or swelling during JAKi discontinuation.