ORIGINAL RESEARCH

Clinical Outcomes in Patients with Rheumatoid Arthritis After Switching Between Interleukin-6-Receptor Inhibitors and Janus Kinase Inhibitors: Findings from an Observational Study

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31 **SUPPLEMENTARY MATERIAL**

32 **Table S1: Demographic characteristics of IL-6Ri vs JAKi initiators, including those**

33 **who discontinued and switched prior to the follow-up (sensitivity analysis)**

Covariates	IL-6Ri Initiators N = 122	JAKi Initiators N = 144	Standardized Difference[a]
Age (years), mean (SD), N	56.2 (11.3), 122	58.9 (12.6), 143	0.232
RA duration (years), mean (SD), N	14.9 (10.4), 121	15.2 (10.3), 144	0.021
Female, n (%), N	102 (84), 122	119 (83), 143	0.010
White, n (%), N	109 (89), 122	110 (76), 144	0.349
Private insurance, n (%), N	93 (76), 122	101 (70), 144	0.138
Working status, n (%)	N = 118	N = 142	
Full time	44 (37)	49 (35)	
Part time	10 (8)	6 (4)	0.294
Retired	22 (19)	42 (30)	
Other	42 (36)	45 (32)	
Smoking status, n (%)	N = 122	N = 144	
Never	58 (48)	76 (53)	0.277
Previous	28 (23)	42 (29)	
Current	36 (30)	26 (18)	
Alcohol use: Yes, n (%), N	46 (40), 116	56 (41), 136	0.031
BMI (kg/m^2), mean (SD), N	29.9 (7.6), 122	30.3 (7.2), 144	0.060
Seropositivity, n (%)	N = 115	N = 135	
CCP+ and/or RF+	62 (54)	79 (59)	0.121
CCP- and RF-[b]	14 (12)	12 (9)	
CCP and RF missing	39 (34)	44 (33)	
History of comorbidities, n (%)	N = 122	N = 144	
CVD[c]	21 (17)	18 (13)	0.133
Malignancy[d]	3 (2)	8 (6)	0.158
Serious infection[e]	13 (11)	13 (9)	0.055

[a]Presented as absolute values.
[b]If a patient was CCP- and RF information was missing, or vice-versa, they were included in this group.
[c]History of CVD includes myocardial infarction, stroke, acute coronary syndrome, coronary artery disease, congestive heart failure, revascularization procedure including percutaneous coronary intervention, coronary artery bypass grafting or coronary artery stents, ventricular arrhythmia, cardiac arrest, unstable angina, peripheral arterial disease, other CVDs, pulmonary embolism, carotid artery disease, deep vein thrombosis, and transient ischemic attack.
[d]History of malignancy includes lymphoma, lung cancer, breast cancer, non-melanoma skin cancer, and other cancer.
[e]Serious infections include infections that led to hospitalization or intravenous antibiotics: joint/bursa, cellulitis, sinusitis, diverticulitis, sepsis, pneumonia, bronchitis, gastroenteritis, meningitis, urinary tract infection, upper respiratory tract infection, or infection of other specified sites.
BMI, body mass index; CCP, anti-cyclic citrullinated peptide; CVD, cardiovascular disease; IL-6Ri, interleukin-6 receptor inhibitor; JAKi, Janus kinase inhibitor; n/N, number of patients; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation.

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Table S2: Clinical characteristics of IL-6Ri vs JAKi initiators, including those who discontinued and switched prior to the follow-up (sensitivity analysis)

Covariates	IL-6Ri Initiators N = 122	JAKi Initiators N = 144	Standardized Difference[a]
CDAI (0 – 76), mean (SD), N	23.2 (12.9), 111	20.2 (12.8), 119	0.235
CDAI category, n (%)	N = 111	N = 119	
Remission (CDAI ≤ 2.8)	1 (1)	5 (4)	
Low (2.8 < CDAI ≤ 10)	14 (13)	28 (24)	0.379
Moderate (10 < CDAI ≤ 22)	45 (41)	37 (31)	
High (CDAI > 22)	51 (46)	49 (41)	
TJC (0–28), mean (SD), N	8.0 (6.9), 112	7.3 (6.9), 120	0.097
SJC (0–28), mean (SD), N	5.7 (5.4), 112	4.5 (5.0), 120	0.224
MDGA (VAS 0–100), mean (SD), N	40.3 (23.2), 112	31.4 (20.6), 119	0.410
PtGA (VAS 0–100), mean (SD), N	53.7 (24.2), 111	52.6 (26.7), 120	0.045
HAQ (0 – 3), mean (SD), N	1.1 (0.6), 107	1.2 (0.7), 120	0.140
Patient reported pain (VAS 0–100), mean (SD), N	56.8 (25.3), 111	54.3 (27.2), 120	0.094
Patient reported fatigue (VAS 0–100), mean (SD), N	57.7 (26.4), 111	53.8 (29.1), 117	0.140
Morning stiffness, n (%), N	101 (91), 111	110 (92), 120	0.024
Morning stiffness duration (h)[b], mean (SD), N	2.5 (4.7), 111	2.4 (4.0), 120	0.021
Prior use of csDMARDs, n (%)	N = 122	N = 144	
0	5 (4)	8 (6)	0.219
1	26 (21)	43 (30)	
2+	91 (75)	93 (65)	
Prior use of TNFi, n (%)	N = 122	N = 144	
0	11 (9)	17 (12)	0.102
1	30 (25)	37 (26)	
2+	81 (66)	90 (63)	
Prior use of non-TNFi, n (%)	N = 122	N = 144	
0	47 (39)	0 (0)	1.307
1	52 (43)	58 (40)	
2+	23 (19)	86 (60)	
Prednisone dose, n (%)	N = 122	N = 144	
No use	85 (70)	93 (65)	
Current use, missing dose	1 (1)	4 (3)	0.216
Current use, dose <10 mg daily	22 (18)	34 (24)	
Current use, dose ≥10 mg daily	14 (11)	13 (9)	
Concomitant therapy, n (%)	N = 122	N = 144	
Monotherapy	54 (44)	72 (50)	0.238
Combination with MTX	30 (25)	42 (29)	
Combination with other csDMARDs	38 (31)	30 (21)	
Line of therapy, n (%)	N = 122	N = 144	
2nd line	8 (6)	10 (7)	0.033
3rd line	15 (12)	19 (13)	
4th+ line	99 (81)	115 (80)	

[a]Presented as absolute values.
[b]Only calculated for patients reporting morning stiffness.
CDAI, Clinical Disease Activity Index; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; HAQ, Health Assessment Questionnaire; IL-6Ri, interleukin-6 receptor inhibitor; JAKi, Janus kinase inhibitor; MDGA, Physician Global Assessment; MTX, methotrexate; n/N, number of patients;

Covariates	IL-6Ri Initiators N = 122	JAKi Initiators N = 144	Standardized Difference[a]

PtGA, Patient Global Assessment; SD, standard deviation; SJC, swollen joint count; TJC, tender joint count; TNFi, tumor necrosis factor inhibitors; VAS, visual analog scale.

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Table S3: Therapy patterns for IL-6Ri and JAKi initiators (including those who discontinued and switched prior to the follow-up) between initiation and the six-month follow-up visit (sensitivity analysis)

Therapy Status at Six Months	IL-6Ri Initiators	JAKi Initiators
All initiations, N	122	144
Remain on therapy, N_R (% of N)	71 (58%)	97 (67%)
Discontinue therapy, N_D (% of N)	51 (42%)	47 (33%)

IL-6Ri, interleukin-6 receptor inhibitors; JAKi, Janus kinase inhibitors; N, number of patients.

Table S4: Continuous clinical outcomes for IL-6Ri and JAKi initiators (including those who discontinued and switched prior to the follow-up): Change from baseline to 6 months post-initiation (sensitivity analysis)

Continuous Outcomes	IL-6Ri Initiators (N = 122)	JAKi Initiators (N = 144)	IL-6Ri vs JAKi Initiators[b]			
	Unadjusted Change, Mean (95% CI)[a], n		Unadjusted β (95% CI)	p-value	Adjusted β (95% CI)[c]	p-value
CDAI	-4.1 (-6.3, -1.9), 111	-2.8 (-5.1, -0.5), 116	0.33 (-2.40, 3.05)	0.81	0.66 (-2.01, 3.32)	0.63
HAQ	-0.0 (-0.1, 0.1), 106	-0.1 (-0.2, -0.0), 118	0.06 (-0.04, 0.17)	0.21	0.07 (-0.03, 0.17)	0.17
Patient-reported pain	-6.1 (-10.6, -1.6), 111	-6.1 (-11.4, -0.8), 120	1.27 (-4.80, 7.33)	0.68	1.40 (-4.72, 7.53)	0.65
Patient-reported fatigue	-2.6 (-6.7, 1.5), 111	-2.5 (-7.0, 2.1), 117	1.30 (-4.25, 6.85)	0.64	-2.76 (-9.19, 3.66)	0.40
TJC	-1.3 (-2.4, -0.2), 112	-1.5 (-2.8, -0.3), 117	0.53 (-0.93, 1.98)	0.48	-0.48 (-2.17, 1.21)	0.78
SJC	-1.4 (-2.2, -0.6), 112	-0.5 (-1.3, 0.2), 117	-0.27 (-1.20, 0.65)	0.56	-0.13 (-1.05, 0.79)	0.78
MDGA	-9.7 (-13.6, -5.8), 112	-3.5 (-7.3, 0.3), 117	-2.12 (-7.03, 2.79)	0.40	-2.35 (-7.97, 3.27)	0.41
PtGA	-4.5 (-9.3, 0.3), 111	-4.4 (-9.5, 0.8), 120	0.47 (-5.67, 6.61)	0.88	0.01 (-6.18, 6.20)	1.00
Morning stiffness duration[d]	-1.1 (-1.9, -0.3), 110	-0.1 (-1.0, 0.8), 118	-0.93 (-1.83, -0.03)	0.04	-0.93 (-1.83, -0.03)	0.04

[a]CIs not inclusive of 0 represent statistically significant mean change from baseline within each group.
[b]Baseline value of respective outcome included as covariate along with therapy group. OR are calculated using JAKi initiators as the reference group
[c]Adjusted β from multivariable linear regression models represent the estimated difference in the mean change in the outcome for IL-6Ri initiators compared with JAKi initiators, after adjusting for other covariates; covariates appearing in at least one of the adjusted models: age, race (white), insurance, smoking status, history of cardiovascular disease, history of diabetes, CDAI, TJC, SJC, MDGA, PtGA, patient-reported fatigue, prednisone use, and prior therapy use
[d]Among those reporting morning stiffness at baseline.
CDAI, Clinical Disease Activity Index; CI, confidence interval; HAQ, Health Assessment Questionnaire; IL-6Ri, interleukin-6 receptor inhibitor; JAKi, Janus kinase inhibitor; MDGA, Physician Global Assessment; n/N, number of patients; PtGA, Patient Global Assessment; SJC, swollen joint count; TJC, tender joint count.

Table S5: Categorical clinical outcomes for IL-6Ri and JAKi initiators (including those who discontinued and switched prior to the follow-up): Change from baseline to 6 months post-initiation (sensitivity analysis)

Categorical Outcomes	IL-6Ri Initiators (N = 122)	JAKi Initiators (N = 144)	IL-6Ri vs JAKi Initiators[b]			
	Percent Response (n/N)[a] (95% CI)		Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)[c]	p-value
Achievement of LDA[d]	17.7 (17/96) (10.7, 26.8)	9.3 (8/86) (4.1, 17.5)	2.08 (0.84, 5.14)	0.11	1.98 (0.79, 4.97)	0.15
Achievement of remission[e]	3.6 (4/110) (1.0, 9.0)	7.0 (8/114) (3.1, 13.4)	0.52 (0.15, 1.81)	0.31	0.70 (0.19, 2.52)	0.58
Improvement in HAQ of at least 0.3 units	14.0 (15/107) (8.1, 22.1)	26.7 (32/120) (19.0, 35.5)	0.47 (0.23, 0.96)	0.04	0.21 (0.08, 0.53)	0.00
Improvement of 10+ units of patient-reported pain	26.1 (29/111) (18.2, 35.3)	30.8 (37/120) (22.7, 39.9)	0.72 (0.39, 1.33)	0.31	0.65 (0.35, 1.22)	0.18
Improvement of 10+ units of patient-reported fatigue	21.6 (24/111) (14.4, 30.4)	27.4 (32/117) (19.5, 36.4)	0.67 (0.36, 1.26)	0.21	0.71 (0.37, 1.37)	0.31
Improvement of 10+ units of MDGA	26.8 (30/112) (18.9, 36.0)	31.9 (38/119) (23.7, 41.1)	0.49[f] (0.26, 0.94)	0.03	0.45 (0.22, 0.88)	0.02
Improvement of 10+ units of PtGA	27.9 (31/111) (19.8, 37.2)	28.3 (34/120) (20.5, 37.3)	0.98 (0.52, 1.83)	0.94	1.19 (0.62, 2.31)	0.60

[a]Percent response = (n/N) x 100.
[b]Baseline value of respective outcome included as covariate along with therapy group. OR are calculated using JAKi initiators as the reference group.
[c]Adjusted β from multivariable linear regression models represent the estimated difference in the mean change in the outcome for IL-6Ri initiators compared with JAKi initiators, after adjusting for other covariates; covariates appearing in at least one of the adjusted models: age, race (white), insurance, smoking status, history of cardiovascular disease, history of diabetes, CDAI, TJC, SJC, MDGA, PtGA, patient-reported fatigue, prednisone use, and prior therapy use
[d]Among those in moderate or high disease activity at baseline.
[e]Among those in low, moderate, or high disease activity at baseline.
[f]Unadjusted OR (95% CI) without baseline value: 0.76 (0.43, 1.34)
CDAI, Clinical Disease Activity Index; CI, confidence interval; HAQ, Health Assessment Questionnaire; IL-6Ri, interleukin-6 receptor inhibitor; JAKi, Janus kinase inhibitor; LDA, low disease activity; MDGA, Physician Global Assessment; n/N, number of patients; OR, odds ratio; PtGA, Patient Global Assessment; SJC, swollen joint count; TJC, tender joint count.