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DISEASE ACTIVITY AND PATIENTS-REPORTED OUTCOMES AFTER SWITCHING BETWEEN IL-6 RECEPTOR INHIBITORS AND JAK INHIBITORS: AN ANALYSIS FROM THE CORRONA REGISTRY

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Background: Rheumatoid arthritis (RA) patients who fail therapy may be switched to any of the five classes of biological disease-modifying antirheumatic drugs (DMARDs) and targeted synthetic DMARDs, to meet treatment goals. Physicians may hesitate to switch between Janus Kinase inhibitors (JAKi) and interleukin-6 receptor inhibitors (IL-6Ri) since they both impact IL-6 signalling and due to limited data on switching between the two classes.

Objectives: This retrospective, observational study based on the real-world Corrona RA registry aimed to describe the response in RA patients switching between IL-6Ri and JAKi.

Methods: Adult RA patients who initiated either IL-6Ri or JAKi after November 2012 and had a six-month post-initiation follow-up visit were eligible. Patients in 'Cohort A' initiated an IL-6Ri following discontinuation of a JAKi and those in 'Cohort B' initiated a JAKi following discontinuation of an IL-6Ri. Disease activity measures and patient-reported outcomes (PROs) were evaluated at baseline and at six-month follow-up. Within each group, change from baseline was assessed for Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire (HAQ), pain, fatigue, tender joint count (TJC), swollen joint count (SJC), physician global assessment (MDGA), patient global assessment (PtGA) and morning stiffness duration. Proportion of patients achieving CDAI low disease activity (LDA), CDAI remission and minimal clinically important difference (MCID) for HAQ, pain, fatigue, MDGA, PtGA were assessed. Adjusted linear and logistic regression models were performed for between-group comparisons (Cohort A vs Cohort B) excluding initiators who switched therapy prior to six-month visit.

Results: Cohorts A and B included 122 and 144 initiators, respectively. Patients who switched to IL-6Ri (vs JAKi) were younger (mean [SD] age, 56.2 [11.3] vs 58.9 [12.6] years), had higher baseline CDAI (23.2 [12.9] vs 20.2 [12.8]), had higher prior use of ≥2 csDMARDs (75% vs 65%), and were less likely to initiate therapy as monotherapy (44% vs 50%).

In Cohort A, significant changes from baseline were observed for all continuous outcomes except HAQ and fatigue. In Cohort B, a significant improvement was observed only for patient-reported pain (Table 1).

Table 1. Unadjusted Within-Group Change from Baseline to Six Months, Mean (95% CI), n

Outcomes	Cohort A, N = 122	Cohort B, N = 144
CDAI	-4.7 (-7.6, -1.9), 109	-2.4 (-5.2, 0.4), 116
HAQ	-0.0 (-0.1, 0.1), 105	-0.1 (-0.1, 0.0), 118
Patient-reported pain	-8.2 (-13.4, -3.0), 109	-5.9 (-11.5, -0.2), 120
Patient-reported fatigue	-4.4 (-9.0, 0.2), 109	-1.7 (-6.6, 3.3), 117
TJC	-1.6 (-3.0, -0.1), 112	-1.2 (-2.6, 0.3), 117
SJC	-1.5 (-2.5, -0.4), 112	-0.4 (-1.3, 0.6), 117
MDGA	-10.9 (-15.6, -6.3), 112	-4.3 (-8.7, 0.2), 117
PtGA	-6.0 (-11.2, -0.8), 109	-4.8 (-10.5, 0.8), 120
Morning stiffness duration ^a	-1.3 (-2.2, -0.5), 109	-0.1 (-1.1, 0.8), 118

^aAmong those reporting morning stiffness at baseline.

In the adjusted between-group comparison (data not shown) of change from baseline, there were no significant differences in clinical outcomes between Cohorts A and B.

In both cohorts, patients achieved CDAI LDA, CDAI remission, and MCIDs across other PROs (Figure 1). In the adjusted between-group comparison (data not shown), the results were similar with the exception of achievement of CDAI LDA among patients with moderate to high disease activity at baseline.

^bCDAI LDA: >2.8 to ≤10 units; CDAI remission: ≤2.8 units; MCID for PROs were assessed, MCID for HAQ: ≥0.3 units; MCID for VAS of pain, fatigue, MDGA, and PtGA: ≥10 units. ^cAmong those in moderate or high disease activity at baseline. ^dAmong those in low, moderate, or high disease activity at baseline.

Figure 1. Rates of CDAI LDA, CDAI Remission, and MCID for PROs^a at Six Months

Conclusion: In general, in both cohorts a substantial proportion of patients achieved CDAI LDA and MCID across PROs. Despite some overlap of JAKi and IL-6Ri therapies' on the IL-6 pathway, there are some distinct mechanisms of action which may result in meaningful improvements for a subset of patients.

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