Identifying Predictors of Response Following Discontinuation of JAKi Therapy in Patients with Rheumatoid Arthritis

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CONCLUSIONS

- **After adjustment, patients with poorer functionality and those receiving abatacept compared to other b/tsDMARDs exhibited less favorable short-term clinical outcomes.**
- **Further investigation is necessary due to the relatively small sample size.**

BACKGROUND

Janus Kinase inhibitors (JAKi) were introduced in Belgium from 2019 onwards and are currently firmly established as therapy for patients suffering from rheumatoid arthritis (RA). Although JAKi are efficient in treating RA, still a considerable number of patients fail therapy, and **it is largely unknown what treatment for RA to start after JAKi cessation**. Previous research from the real-world evidence TARDIS register indicated that interleukine-6 (IL6) inhibitors showed superior clinical response after JAKi cessation compared to other advanced therapies in RA. However, baseline differences in demographic and clinical variables, as well as prior exposure to advanced therapies, were observed among the treatment groups, potentially influencing the findings.

AIM

Therefore, the objective was to identify factors that could predict clinical responses, even after adjustment for confounding factors.

PATIENTS AND METHODS

The Tool for Administrative Reimbursement Drug Information Sharing (TARDIS) is an electronic platform combining the collection of data from all Belgian patients with Rheumatoid Arthritis (RA) on advanced therapies including biologic (b) and targeted synthetic (ts) DMARDs, together with the submission of a request for reimbursement of this medication.

Patients were categorized based on the subsequent therapy they received:

- TNFi
- Abatacept
- IL6 inhibition
- JAKi

Linear and logistic regression models were constructed, with changes in Disease Activity Score 28 (DAS28) between baseline and first follow-up, DAS28 remission (DAS28 < 2.6), and DAS28 low disease activity (LDA, DAS28 ≤ 3.2) as dependent variables.

Following variables were inserted as predictors in the models:

- Age
- Disease duration
- Treatment (b/tsDMARD) naive
- Treatment group
- Baseline values for HAQ, swollen/tender joint count, patient global assessment, ESR, and CRP.

Backward elimination was performed to identify statistically significant predictors. Final models included only variables reaching statistical significance of 0.05.

DAS scores are calculated using DAS28(CRP). If missing, DAS28(ESR) is used. Missing HAQ(0-3) scores were imputed by regression using age and HAQ(0-60) scores.

RESULTS

A total of **193** RA patients with complete baseline and follow-up data were included in the analysis.

Table 1 shows baseline demographic and clinical characteristics.

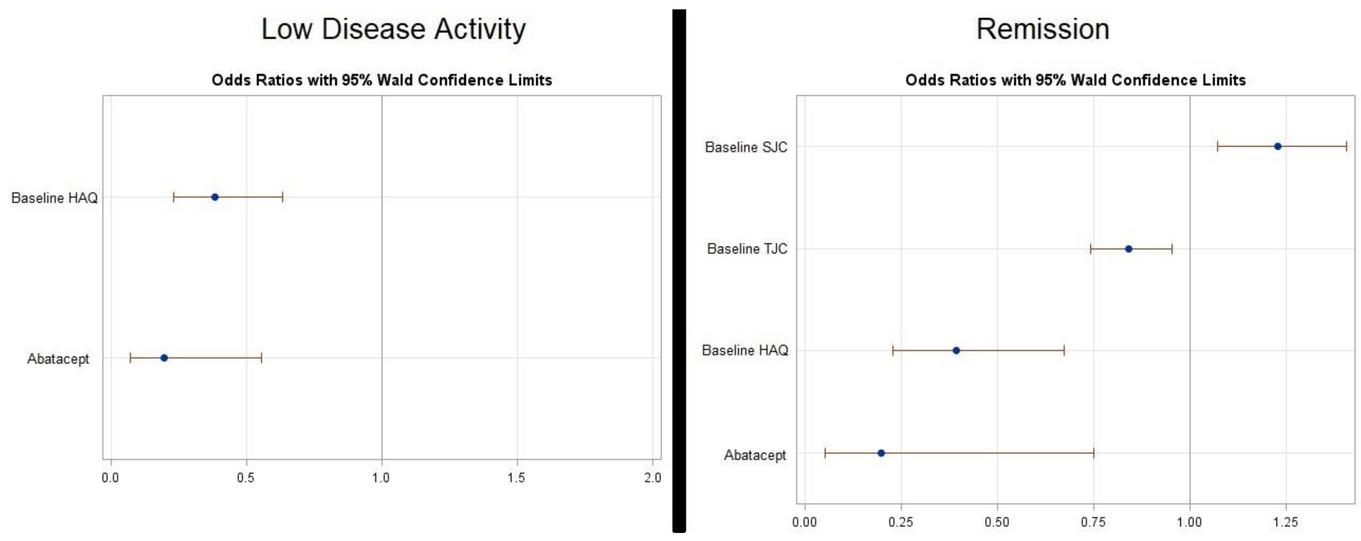
Table 1: Baseline characteristics of TARDIS patients after JAKi cessation

	Total population
Number	193
Age (mean ±SD, years)	57 ±13
Disease duration (mean ±SD, years)	10 ±8
ESR (mean ±SD, mm/hour)	24 ±18
CRP (mean ±SD, mg/L)	11 ±18
SJC28 (mean ±SD)	6 ±5
TJC28 (mean ±SD)	8 ±5
DAS28 (mean ±SD, years)	4.6 ±1.1
HAQ-DI (mean ±SD, 0-3)*	1.3 ±0.7
PGA (mean ±SD, 0-100)	64 ±20
2nd line of therapy after initial JAKi therapy	76/193 (39%)

Legend: Number given are mean ± SD or number, proportion. TNFi = tumour necrosis factor inhibitor, JAKi = Janus Kinase inhibitor, HAQ= health assessment questionnaire, PGA= Patient Global assessment; CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; TJC= tender joint count; SJC= Swollen joint Count; DAS28 = disease activity score based on the 28joints. *Missing HAQ(0-3) scores were imputed by regression using age and HAQ(0-60) scores, the sum of the scores (0-3) on all (20) individual HAQ questions.

TNFi, Abatacept, IL6 inhibition or JAKi therapy was initiated in 33% (63/193), **11% (20/193)**, 18% (34/193) and 39% (76/193) of patients respectively. Remission and LDA were reached in **42**% (81/193) and **63**% (122/193) of patients respectively. Common predictors for achieving remission and LDA were **baseline HAQ and not receiving abatacept (Fig1**). Variables positively associated with a higher DAS28 change were baseline PGA (Relative Risk (RR) 0.02 (0.01, 0.03)), TJC (0.06 (0.01, 0.12), SJC (RR 0.10 (0.03, 0.16)) and CRP (RR 0.02(0.01, 0.03)), while baseline HAQ (RR -0.60 (-0.88, -0.31) and not receiving abatacept (RR -0.70 (-1.25, -0.15)) were negatively correlated with DAS28 change in the adjusted multivariate linear regression model.

Figure 1: Predictors of remission or LDA in final model



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