Real World Single Center Use and Effectiveness of Jak Inhibitors in Patients with Rheumatoid Arthritis

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Background

Currently, the intracellular targeting with Jak inhibitors (JAKi) represents an important therapeutic advance in patients with rheumatoid arthritis (RA). Its enormous physiological importance lies in the fact that more than 60 cytokines and hormones use the JAKSTAT3 pathway for their intracellular signalling. Long-term data from clinical trials have been published but the use and efficacy of these treatments in clinical practice is still scarce

Objective

To evaluate the effectiveness and use patterns of JAKi in patients with RA in "real world" conditions.

Methods

Data from an observational prospective cohort RA-Paz including patients with RA initiating treatment with a JAKi from a single centre between 2018 and 2022 were analysed. RA was defined in clinical practice according to the prescribing rheumatologist, based on ACR/EULAR 2010 rheumatoid arthritis classification criteria. Demographic and clinical characteristics were obtained from electronic clinical records. Clinical activity was measured at baseline and after 6 months of JAKi starting using the following parameters: disease activity score-28 (DAS28), tender joint count (TJC), swollen joint count (SJC), patient global assessment (PtGA), physician global assessment (PhGA), morning stiffness (MS) and visual analogue scale of pain (VAS). We used parametric test (test t) for DAS28 and non-parametric test (Wilcoxon test) for the rest of the parameters. The limit of statistical significance was established at $p < 0.05$.

Results

Of the 568 RA patients treated with biological or target specific DMARDs (b/ts-DMARDs), 105 treated with JAKi were included. Patients characteristics are summarized in Table 1. Mean age at start of treatment was 57 years. JAKi prescription patterns were: tofacitinib (TOFA) in 32.4%, baricitinib (BARI) in 39%, upadacitinib (UPA) in 22,9% and filgotinib (FILGO) in 5,7% of patients (see Table1). Most of patients were previously with a b/ts DMARD (78%) and only 25% were on monotherapy. There was a significant decrease in several disease activity parameters (see Table 2). Remission by DAS28 was achieved in 35% of patients and 54% achieved low disease activity according to a DAS28 less than 3.2. We found no differences for DAS28 between the 4 jak inhibitors (p=0.066).
Only 28 (26%) out of 105 patients had to discontinue the treatment. The reasons to discontinue were: primary inefficacy (16), adverse events (7) and infections (5). There were no thrombotic events due to treatment.

Table 1. Demographic and clinical characteristics of RA patients under JAKi

	TOTAL n=105	TOFA n=34	BARI n=41	UPA n=24	FILGO n=6
Demographic characteristics					
Age (mean±sd)	57,8 ±11,3	57,2 ±11.7	57,1 ± 11,3	59 ± 12,2	61,3 ±4,3
Sex (female)	91 (86%)	31 (91%)	34 (82%)	21 (87%)	5 (83%)
BMI (Median, IQR)	24,8 (21,7-29,2)	26,1 (22,8 - 29,2)	24,7 (20,6-29,2)	24,4 (21,6-30,9)	26,3 (21,2-27,9)
Comorbidities					
Diabetes	15 (14%)	5 (14%)	5 (12%)	5 (21%)	0 (0%)
Arterial Hypertension	27 (25%)	8 (23%)	11 (26,8)	7 (29%)	1 (16%)
Active smoker	22 (21%)	7 (20%)	10 (24%)	4 (17%)	1 (17%)
Isquemic cardiopathy	4 (3,8%)	0 (0%)	3 (7%)	1 (4.2%)	0 (0%)
Previous TE	2 (2%)	1 (2.9%)	0 (0%)	1 (4.2%)	0 (0%)
Dyslipidemia	51 (48%)	14 (41%)	23 (56)	11 (46%)	3 (50%)
Treatment					
Monotherapy	26 (25%)	3 (9%)	11 (27%)	9 (37%)	3 (50%)
b/ts DMARD näive	23 (22%)	8 (23%)	9 (22%)	5 (21%)	1(18%)
Prior b/tsDMARD use:					
1 prior b/tsDMARD	29 (28%)	9 (26%)	12 295%)	6 (25%)	2 (33%)
2 prior b/tsDMARD	25 (24%)	9 (26%)	10 (24%)	4 (17%)	2 33%)
3 prior b/tsDMARD	11 (10%)	3 (9%)	4 (10%)	3 (13%)	1 (17%)
≥4 prior b/tsDMARD	17 (16%)	7(21%)	6 (15%)	4 (17%)	0 (0%)
Previous JAKi use	8 (7%)	1 (3%)	1 (2.4%)	5 (21%)	1 (17%)

Table 2. Comparison of clinical parameters

	Baseline	6 months	P
ESR-DAS28 (mean±sd)	4,5 ± 1,2	3,2 ± 1,3	<0.001[1]
TJC (median, p_{25}-p_{75})	8 (4 -12,5)	2 (0- 6)	<0.001[2]
SJC (median, p_{25}-p_{75})	6 (3 - 9)	2 (0 - 4,8)	<0.001[2]
PtGA (median, p_{25}-p_{75})	53 (31 – 70)	30 (15 - 53,8)	<0.001[2]
PhGA (median, p_{25}-p_{75})	50 (40 – 70)	20 (10 - 40)	<0.001[2]
VAS (median, p_{25}-p_{75})	50 (24,8 -70)	30 (15 -50)	<0.001[2]
HAQ (median, p_{25}-p_{75})	9 (3 - 13)	9 (3 -12	=0.326[2]

[1] Pruebas paramétricas; [2] Pruebas no paramétricas
Disease activity score-28 (DAS28), tender joint count (TJC), swollen joint count (SJC), patient global assessment (PtGA), physician global assessment (PhGA), and visual analogue scale of pain (VAS)

Conclusions:

Jak inhibitors are an effective and safe option for the treatment of RA in the real-world clinical practice. They produce a significant decrease in pain as observed in the decrease in VAS and TJC.