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Targeted synthetic drugs , Rheumatoid arthritis, Psoriatic arthritis

Real-world use of JAK inhibitors in rheumatological practice in South London

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Background:

Janus Kinase inhibitors (JAKi) are targeted synthetic disease modifying anti-rheumatic drugs (tsDMARDs) used in the treatment of inflammatory arthritis. Whilst evidence for their efficacy and side-effect profile is supported by data from randomised control studies, real world data is lacking.

Objectives:

The objectives of the study were to evaluate the efficacy and safety of JAKi in real-world clinical rheumatological practice in the South London region.

Methods:

Data was collected from two hospitals; St Georges University Hospitals NHS Trust (SGH; a tertiary centre) and Kingston Hospital NHS Foundation Trust (KH; a district general hospital). All rheumatology patients who were prescribed JAKi between January 2017 and June 2022 were included in the analysis. Baseline patient demographic data included age, gender, rheumatological diagnosis and comorbidities. A retrospective analysis evaluated prescribing practice, drug efficacy (measured using the Disease Activity Score (DAS-28)), adverse events and drug discontinuation rates.

Results:

A total of 288 patients were included in the analysis; 184 from SGH and 104 from KH. The average age was 55.6 (range 20-82), 87% were female. Baricitinib was the most frequently prescribed JAKi (231 patients), followed by tofacitinib, filgotinib and upadacitinib (49, 7 and 1 patients respectively).

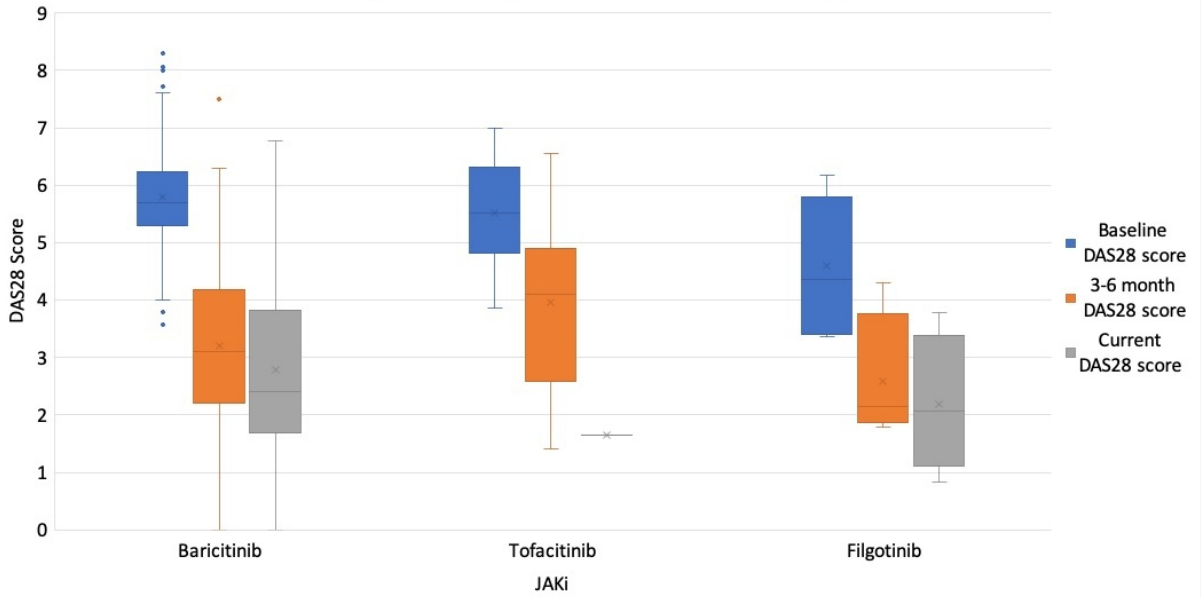
Baricitinib was most prescribed for patients with seropositive rheumatoid arthritis (RA) (62%), seronegative RA (17%) and seronegative inflammatory arthritis (10%). 73% on tofacitinib had a

diagnosis of psoriatic arthritis, 20% had RA. All patients on filgotinib had RA and the one patient on upadacitinib had overlap RA/systemic lupus erythematosus.

In 53% of patients, JAKi was prescribed following biological DMARD (bDMARD) therapy. In these patients; 32%, 13%, 5% and 3% had previously received 1, 2, 3 and 4 bDMARDs respectively.

Median DAS-28 scores improved with all JAKi therapy. This is summarised in figure 1.

Figure 1: Change in DAS-28 with JAKi therapy



The most frequent documented adverse events included bacterial infection (25) hypercholesterolaemia (18), gastrointestinal side effects (18), viral infection (15) and deranged liver function tests (LFTs) (10). These are summarised in table 1.

Adverse events	**Number of events**		
	Baricitinib (n=231)	**Tofacitinib (n=49)**	**Filgotinib (n=7)**
Gastrointestinal side effects	**18**	**0**	**0**
Bacterial infection	**19**	**4**	**2**
Lower respiratory tract	10	1	1
Urinary tract	5	1	0
Genitourinary	1	0	0
Skin	1	1	1
Not specified	2	1	0
Viral/fungal infection	**15**	**1**	**1**
Shingles	6	0	1
COVID-19	4	0	0
Upper respiratory tract	2	0	0
Fungal nail infection	2	0	0

Herpes Simplex Virus	1	0	0
Biochemical abnormalities	**22**	**6**	**0**
Hypercholesterolaemia	14	4	0
Deranged Liver functions tests (LFTs)	8	2	0
Neutropenia	**2**	**0**	**0**
Venous thromboembolism (VTE)	**1**	**1**	**0**
Other side effects	**11**	**1**	**0**

10 patients died whilst on JAKi therapy (8 on baricitinib, 2 on tofacitinib). 5 died from COVID-19, 1 from pancreatic cancer and 4 with unknown cause of death. Excluding deceased patients, 77 discontinued JAKi therapy (56 on baricitinib, 19 on tofacitinib, 2 on filogitinib). Mean duration to discontinuation was 9.3 months (baricitinib), 11.7 months (tofacitinib) and 4.5 months (filgotinib). For all JAKis, drug inefficacy was the most commonly reported reason for discontinuation (40 patients). Other reasons included bacterial infection (8), deranged LFTs (6), perceived high risk for VTE (4), shingles (2) and other side effects (8).

Conclusion:

JAKi are effective across a range of rheumatological diagnoses in a South London real-world analysis, including patients with bDMARD-naïve and bDMARD-refractory disease. JAKi are generally well tolerated and adverse events in this study were in keeping with the current literature.

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