# AFTER JAK INHIBITOR FAILURE, “SWITCHING” OR “CYCLING”?

Muñoz Martínez, Pablo Francisco, Mas Sánchez L, Grau García E, Torrat Noves AM, Ramos Castro D, Riesco Barcena C, Huaylla Quispe AV, Leal Rodríguez S, Cánovas Olmos I, Charia H, González Puig L, Ivorra Cortés J, Martínez Cordellat I, Nájera Herranz C, Negueroles Albuixech R, Oller Rodríguez J, Ortiz-Sanjuán F, Tovar Sugrañes E, Vicens Bernabéu E, Román Ivorra JA.

Rheumatology Department, Hospital Universitari i Politècnic La Fe. Valencia,Spain

## BACKGROUND

The appearance of JAK inhibitors (JAKi) in the last few years has proved a great clinical application in rheumatic pathology and it has become an innovative and widely-used therapeutic line. In fact, JAKi has been recently included in the management algorithms of psoriatic arthritis, axial spondyloarthritis or rheumatoid arthritis. Nevertheless, the evidence of therapeutic alternatives in real life after the failure of a JAK inhibitor is limited: another JAKi or the change in therapeutic target.

## PURPOSE

The purpose of the study is to analyze the treatment alternatives after JAKi failure in real life conditions and in multiple diseases.

## METHODS

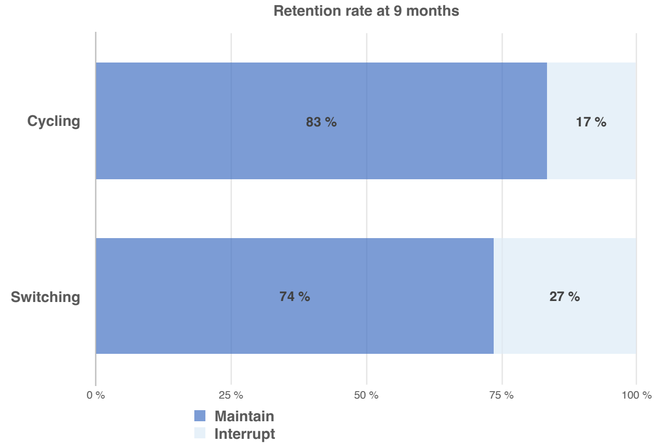
Retrospective longitudinal observational study of patients that started JAKi treatment and was discontinued from 2013 to 2022. Demographic and clinical variables were collected from the electronic medical record. “Switching” and “cycling” were analyzed depending on the prescribed medicine after the JAKi, classifying them in the following targets: anti-TNF, anti-IL6, anti-CTLA4, anti-IL12/23, anti-IL17, anti-IL23, another JAKi or other situations like anti-CD20. We studied the retention rate at 9 months after the start of the new treatment.

## CONCLUSIONS

After a JAKi failure, “switching” is the most recurrent alternative in our series, used most frequently in patients with side events or primary failure. “Cycling” was the most common alternative used with patients who stopped receiving treatment due to secondary failure and in patients with a major proportion of failure to bDMARD. The retention rate after 9 months was 83,33% for “cycling” and 73,50% for “switching” groups.

## RESULTS

In our series, the most prescribed JAKi was Tofactinib (n=119), followed by Baricitinib (n=76), Upadacitinib (n=66) and Filgotinib (n=4). The most recurrent indications for JAKi treatment were rheumatoid arthritis (n=71) and psoriatic arthritis (n=12). Out of 265 JAKi prescriptions, 95 failures to JAKi treatment were included in this study. The JAKi with higher failure rate was tofacitinib (n=61) followed by baricitinib (n=22) and upadacitinib (n=12). We do not have data from filgotinib due to its recent incorporation to the Spanish national market. The main cause of end of treatment was adverse reaction (34.74%), followed by secondary failure (28.42%). After all the JAKi failures, “switching” to other familieslike anti-TNF or anti-IL6 wasthe main therapeutical choice (n=57), followed by “cycling” to another JAKi (n=25). 8 patients did not start a new treatment after JAKI failure. The retention rate at 9 moths after the treatment showed that the 83,33% of the “cycling” to another JAKi and the 73,5% of the “switching” to another therapeutic target maintained the treatment (see image). The retention rate was not studied in 17 patients because the treatment period was less than 9 months.




| Total of “switching” and “cycling” n=82 | JAKi n=25 | Anti-TNF n=16 | Anti-IL6 n=15 | Anti-CTLA4 n=7 | Anti-IL12/23 n=1 | Anti-IL17 n=2 | Anti-IL23 n=3 | Others n=13 | Lost follow-up n=5 |
|---|---|---|---|---|---|---|---|---|---|
| **Age when JAKi starts-years (sd)** | 51,56 (12,21) | 52,81 (16,19) | 55,07 (10,31) | 62,57 (12,93) | 69 (NA) | 50,5 (7,78) | 56,33 (4,16) | 47,69 (16,6) | 63,6 (16,46) |
| **Female – n(%)** | 24 (96) | 11 (68,75) | 12 (80) | 6 (85,71) | 1 (100) | 1 (50) | 1 (33,33) | 9 (69,23) | 5 (100) |
| **Diagnosis - n (%)** | | | | | | | | | |
| **Rheumatoid Arthritis** | 21 (84) | 12 (75) | 14 (93,33) | 6 (86) | 0 (0) | 0 (0) | 0 (0) | 8(62) | 3 (60) |
| **Axial Spondyloarthritis** | 0 (0) | 2 (12,5) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (40) |
| **Psoriatic arthritis** | 2 (8) | 1(6,25) | 0(0) | 1 (14) | 1(100) | 2(100) | 3(100) | 2(15) | 0(0) |
| **Juvenile Idiopathic Arthritis** | 1 (4) | 1(6,25) | 1(6,67) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (23) | 0 (0) |
| **Others** | 1 (4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| **Previous bDMARD - n (%)** | | | | | | | | | |
| **Failure to 1** | 3 (12,5) | 4 (30,8) | 5 (36) | 2(33) | 1 (100) | 0 (0) | 0 (0) | 1 (7,7) | 1 (20) |
| **Failure to 2** | 4 (16) | 1 (7,7) | 5 (38) | 2(33) | 0 (0) | 0 (0) | 1 (33) | 0 (0) | 0 (0) |
| **Failure to 3** | 9 (37,5) | 5 (33,33) | 3 (21) | 1 (17) | 0 (0) | 2 (100) | 2 (67) | 10 (77) | 2 (40) |
| **Original JAKi - n (%)** | | | | | | | | | |
| **Tofacitinib** | 17 (68) | 12 (75) | 8 (53) | 6 (85,71) | 1 (100) | 2 (100) | 1 (33,33) | 6 (46,15) | 2 (40) |
| **Baricitinib** | 7 (28) | 1 (6,25) | 7 (47) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 6 (46,15) | 1 (20) |
| **Upadacitinib** | 1 (4) | 3 (18,75) | 0 (0) | 1 (14,29) | 0 (0) | 0 (0) | 2 (66,67) | 1 (7,69) | 2 (40) |
| **Cause of failure - n (%)** | | | | | | | | | |
| **Primary** | 3(12) | 7 (43,75) | 4 (26,67) | 1 (14,29) | 0 (0) | 0 (0) | 1 (33,33) | 3 (23,07) | 0 (0) |
| **Secondary** | 14 (56) | 2 (11,76) | 3 (20) | 1 (14,29) | 0 (0) | 1 (50) | 1 (33,33) | 5 (38,46) | 0 (0) |
| **Side effects** | 6 (24) | 5 (32,73) | 6 (40) | 4 (57,13) | 1 (100) | 1 (50) | 1 (33,33) | 4 (30,77) | 3 (60) |
| **Others** | 2 (8) | 2 (11,76) | 2 (13,33) | 1 (14,29) | 0 (0) | 0 (0) | 0 (0) | 1 (7,7) | 2 (40) |