

Background

- In 2021, The Food and Drug Administration added a black box warning to Janus Kinase (JAK) inhibitors due to the increased risk of serious heart-related events
- Tumor necrosis factor α inhibitors (TNFi) do not carry this black box warning
- Previous black box warning additions have altered prescribing patterns and patient behavior; however, it is unknown if the addition to the JAK inhibitors has impacted patterns of behaviors

Objective

- To identify and examine if any changes occurred in prescribing patterns or patient behavior (adherence or persistence) in rheumatoid arthritis (RA) patients with the addition of the black box warning associated with JAK inhibitors

Methods

- This is a retrospective cohort study of RA patients receiving a JAK inhibitor or TNFi
- Patients were included if they received at least 3 fills for a JAK inhibitor or TNFi between 4/1/2021 and 8/31/2022 and maintained coverage until 9/30/2022
- Three periods were assessed:
 - pre-black box warning (4/1/2021 - 8/31/2021)
 - washout (9/1/2021-12/1/2021)
 - post-black box warning (12/2/2021-8/31/2022)
- Propensity score (PS) matching was conducted utilizing the patient's demographic profile, including age, gender, socioeconomic status (SES), location, and comorbid conditions
- Adherence was measured using proportion of days covered (POC) and was evaluated overall and during each period
- Discontinuation was determined if the last fill occurred greater than 30 days from the end of the study; rates were calculated for each period
- P-values <0.05 were significant

Results

Unmatched cohort

- 815 patients were included in the unmatched analysis, with 215 (26.4%) receiving JAK inhibitors
 - Differences in age and gender were found between JAK inhibitor and TNFi patients (Table 1)
 - No differences in SES or comorbidity were found
 - Patients prescribed JAK inhibitors had higher median PDC (5.6%; p=0.022) during the study compared to TNFi patients and higher median PDC (7.1%; p=0.014) during the post-black box warning period
 - No difference in discontinuation rates were found overall and stratified by study period
- Matched cohort**
- 408 patients were evaluated with 50% receiving JAK inhibitors
 - No differences in demographics or comorbidities were found
 - Adherence metrics were similar between matched cohorts
 - There were no significant differences in median PDC (1.8%; p=0.235) or discontinuation rates (28.9% vs 27.9%), in JAK inhibitor and TNFi groups, respectively, p = 0.529

Table 1: Demographics

Variable	Overall N=815	JAK N=215	TNFi N=600	P-value
Male gender, n (%)	385 (227) (26.4%)	96 (167) (73.6%)	149 (24.8)	0.02*
Age, mean (SD)	53.0 (10.9)	54.8 (8.9)	52.4 (11.4)	0.002*
Months covered, mean (SD)	42.3 (6.4)	43.0 (7.9)	42.1 (6.5)	0.28*
SES, n (%)				0.275*
Very Low	77 (9.4)	20 (9.3)	57 (9.5)	
Low	223 (27.4)	50 (23.3)	173 (28.8)	
Medium	239 (29.3)	66 (30.7)	173 (28.8)	
High	146 (17.9)	36 (16.7)	110 (18.3)	
Very High	47 (5.8)	13 (6.0)	34 (5.7)	
Unknown	83 (10.2)	30 (14.0)	53 (8.8)	
Charlson Comorbidity Index, mean (SD)	1.9 (1.5)	2.0 (1.5)	1.9 (1.5)	0.204*

Table 2: Adherence Outcomes

Outcome	Differences in JAK vs TNFi	P-value	
POC (Overall), mean difference (95% CI)	-0.46 (-7.6%)	0.072*	
POC (Overall), median difference	5.6%	0.022*	
POC (Pre-BBOX), mean difference (95% CI)	-4.74% (-3.4%)	0.398*	
POC (Pre-BBOX), median difference	2%	0.768*	
POC (Washout), mean difference (95% CI)	-3.9% (-5.9%)	0.348*	
POC (Washout), median difference	1%	0.234*	
POC (Post-BBOX), mean difference (95% CI)	1.37% (0.6%)	0.016*	
POC (Post-BBOX), median difference	7.1%	0.014*	
Discontinued Medication, n (%)	63 (29.3)	35 (26.0)	0.397*
Discontinuation Period, n (%)			0.984*
None	152 (70.7)	444 (74.0)	
Pre-BBOX	4 (1.9)	17 (2.8)	
Washout	25 (11.8)	48 (8.0)	
Post-BBOX	34 (15.8)	91 (15.2)	

Figure 1: Therapy persistence differences between JAK and TNFi

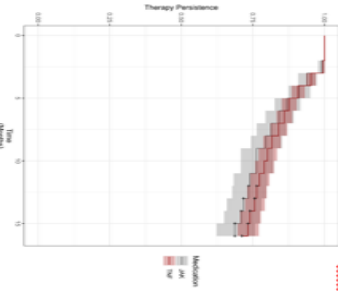


Table 3: Demographics (Matched)

Variable	Overall N=408	JAK N=204	TNFi N=204	P-value
Male gender, n (%)	71 (71.4)	35 (72.2)	36 (71.6)	1*
Age, mean (SD)	55.2 (10.1)	54.5 (9.0)	55.9 (11.2)	0.17*
Months covered, mean (SD)	42.3 (6.5)	43.0 (8.0)	41.7 (9.0)	0.126*
SES, n (%)				0.522*
Very Low	46 (11.3)	19 (9.3)	27 (13.2)	
Low	109 (26.7)	49 (24.0)	60 (29.4)	
Medium	144 (35.3)	62 (30.4)	82 (39.5)	
High	65 (16.3)	36 (17.6)	29 (14.2)	
Very High	25 (6.1)	13 (6.4)	12 (5.9)	
Unknown	49 (12.0)	25 (12.3)	24 (11.8)	
Charlson Comorbidity Index, mean (SD)	2.1 (1.5)	1.9 (1.3)	2.2 (1.7)	0.08*

Table 4: Adherence outcomes (Matched)

Outcome	Differences in JAK vs TNFi	P-value	
POC (Overall), mean difference (95% CI)	-1.5%	0.485*	
POC (Overall), median difference	-3.1%	0.235*	
POC (Pre-BBOX), mean difference (95% CI)	-2.4%	0.91*	
POC (Pre-BBOX), median difference	-6.5% (-3.7%)</td <td>0.883*</td>	0.883*	
POC (Washout), mean difference (95% CI)	3.4%	0.789*	
POC (Washout), median difference	1.1%	0.802*	
POC (Post-BBOX), mean difference (95% CI)	2.1%	0.19*	
POC (Post-BBOX), median difference	-1.6% (-10.0%)	0.196*	
Discontinued Medication, n (%)	59 (28.9)	57 (27.9)	0.913*
Discontinuation Period, n (%)			0.529*
None	145 (71.1)	147 (72.1)	
Pre-BBOX	4 (2.0)	7 (3.4)	
Washout	22 (10.8)	15 (7.4)	
Post-BBOX	33 (16.2)	35 (17.2)	

Figure 2: Therapy persistence differences between JAK and TNFi

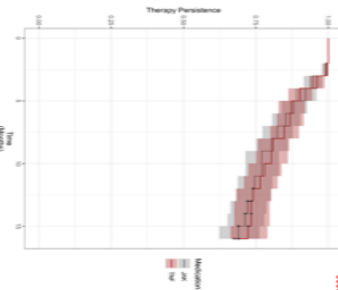


Figure 3: Propensity score distribution pre- and post-matching

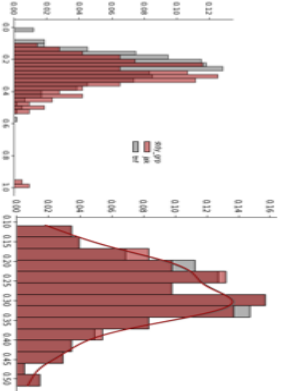
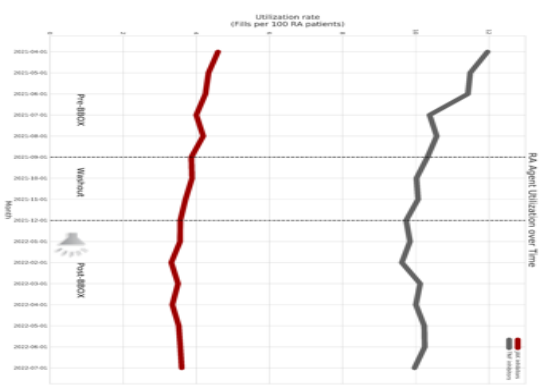


Figure 4: Medication utilization rates during study period



Conclusions

- Adherence and persistence to JAK inhibitors were not significantly impacted by the addition of the black box warning