Risk of Tofacitinib-Related Adverse Events in Patients With Ulcerative Colitis: A Nationwide Propensity-Matched Cohort Study

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BACKGROUND

- A recent randomized, open-label, safety end-point trial found an increased risk of major adverse cardiovascular events (MACE) and malignancy in patients with rheumatoid arthritis who received tofacitinib compared to tumor necrosis factor inhibitor (TNFi).
- The risk of adverse events in patients with ulcerative colitis (UC) on tofacitinib from population-based observational studies is limited
- Aim of our study was to evaluate the risk of adverse events in patients with UC on tofacitinib

METHODS

- A retrospective cohort study was conducted using TriNetX, a multi-institutional database of more than 70 million patients from 49 healthcare organizations in the USA.
- We compared the 1-, 2- and 3-year risk of MACE, malignancy, opportunistic infections (OIs) and venous thromboembolism (VTE) between patients with UC on tofacitinib and other biologic agents (control cohort).
- Sub-group analysis was performed based on type of biologic agent which included TNFi, vedolizumab, and ustekinumab.
- Exclusion criteria included patients who were on the biologic agent for less than 3 months or had a prior history of any adverse event. 1:1 propensity-score matching was performed for age, gender, race, ethnicity, other autoimmune diseases, primary thrombophilia and all known risk factors for MACE between all the cohorts.
- Adjusted odds ratios (aOR) with 95% confidence interval (CI) were calculated to express the risk of each adverse event

Outcome	Year	aOR	95% CI
TNFi			
MACE	1	0.87	0.46 – 1.62
	2	0.98	0.56 – 1.69
	3	1.22	0.63 – 2.37
Malignancy	1	0.93	0.50 – 1.76
	2	1.08	0.61 – 1.89
	3	1.61	0.71 – 3.64
OI	1	1.55	1.01 – 2.37
	2	1.32	0.91 – 1.93
	3	1.24	0.79 – 1.94
VTE	1	1.18	0.63 – 2.20
	2	1.06	0.61 – 1.84
	3	1.56	0.78 – 3.13
Vedolizumab			
MACE	1	0.83	0.45 – 1.55
	2	0.97	0.55 – 1.70
	3	0.96	0.51 – 1.82
Malignancy	1	1.17	0.60 – 2.30
	2	1.18	0.66 – 2.10
	3	0.89	0.42 – 1.88
OI	1	1.82	1.15 – 2.87
	2	1.33	0.90 – 1.96
	3	1.42	0.86 – 2.32
VTE	1	1.58	0.76 – 3.28
	2	1.3	0.71 – 2.35
	3	2.1	0.97 – 4.52
Ustekinumab			
MACE	1	1.63	0.73 – 3.62
	2	2.06	0.99 – 4.30
	3	1.78	0.80 – 3.99
Malignancy	1	1.03	0.53 – 1.99
	2	1.32	0.68 – 2.57
	3	0.82	0.38 – 1.74
OI	1	1.91	1.14 – 3.20
	2	2.33	1.36 – 4.01
	3	2.23	1.12 – 4.44
VTE	1	1.97	0.91 – 4.24
	2	1.85	0.85 – 4.02
	3	1.55	0.69 – 3.50

Table 1: Risk of adverse events between patients on tofacitinib compared to TNFi, vedolizumab and ustekinumab *aOR: adjusted odds ratio

RESULTS

- Of a total of 94,321 patients with UC, 1056 patients received tofacitinib (mean age 47 +/- 16, 53% male), 4,285 received an TNFi, 2,402 patients received vedolizumab (VDZ), and 1,335 received ustekinumab.
- There was no difference in the 1-, 2-, and 3-year risk of MACE, malignancy, OIs, and VTE between patients on tofacitinib compared to other biologic agents .
- In sub-group analysis, there was no difference in the 1-, 2- and 3-year risk of MACE, malignancy and VTE between patients on tofacitinib compared individually to TNFi, vedolizumab and ustekinumab (Table 1).
- There is an increased 1-year risk of OIs in patients on tofacitinib compared to TNFi and vedolizumab, and an increased 1-, 2- and 3-year risk of OIs compared to ustekinumab

CONCLUSIONS

- In our propensity-matched cohort study of patients with UC, tofacitinib does not confer a higher risk of MACE, malignancy and VTE compared to other biologic agents.
- Further studies are needed to understand the dose-related effect of tofacitinib on the risk of these adverse events.