Real-World Outcomes of Tofacitinib for Ulcerative Colitis at 52 and 78 Weeks

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Introduction

- Tofacitinib (tofa) is an oral Janus kinase inhibitor for the treatment of ulcerative colitis (UC).
- What is known about the long-term clinical effectiveness of tofacitinib stems largely from clinical trials.
- Real-world cohort studies have assessed primarily short-term clinical outcomes.[1-8]

Objective

- We sought to assess clinical, endoscopic, and safety outcomes through 78 weeks of tofacitinib therapy for UC.

Methods

- **Design:** Retrospective cohort study
- **Population:** Adults initiating tofa therapy between 5/1/18-4/1/21 at a large, US academic medical center.
- **Primary outcome:** Steroid-free clinical remission (SFCR; i.e. simple clinical colitis activity index ≤2 or per provider global assessment and no use of oral/IV corticosteroids for ≥30 days) at 12, 52, and 78 (+/-4) weeks.
- **Secondary outcomes (during all available follow-up):**
  - Endoscopic response (decrease in Mayo endoscopic subscore by ≥1 pt)
  - Endoscopic remission (Mayo endoscopic subscore 0) at >8 weeks
  - Biochemical response (improvement in elevated C-reactive protein [CRP] or fecal calprotectin [FC] by ≥25% from baseline)
  - Biochemical remission (normalized CRP or FC) at >8 weeks
  - Dose de-escalation
  - Improvement in arthralgia
  - Colectomy
  - Hospitalization
  - Adverse events (AEs)
  - Treatment discontinuation during follow-up
- **Analysis:** Continuous data were reported as medians with interquartile range (IQR, i.e. quartile 1 - quartile 3) due to lack of normality and categorical data were reported as proportions.

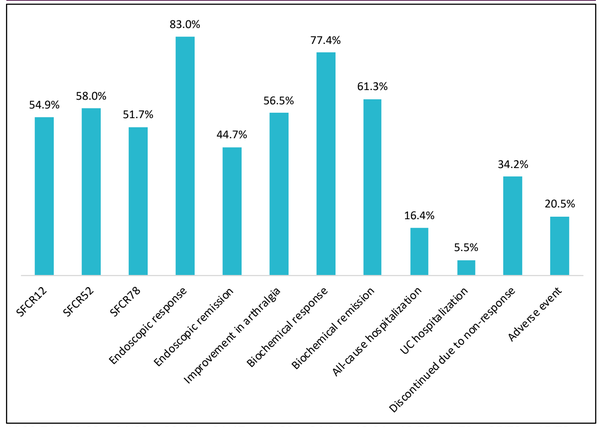
Results

Table 1. Baseline characteristics

Characteristic	Value (N=73)
Demographics	
Female	44 (60%)
Age, y, median (IQR)	41.2 (28.1-54.0)
UC duration, y, median (IQR)	9.5 (4.4-15.5)
Race	
Caucasian	67 (92%)
Black	0 (0%)
Asian	4 (5%)
Other/Unknown	2 (3%)
Hispanic ethnicity	0 (0%)
Prior and current medications	
≥2 prior anti-TNFs	40 (55%)
Prior ustekinumab	8 (11%)
Prior vedolizumab	54 (74%)
Prior 5-ASA	71 (97%)
Current 5-ASA	12 (16%)
Prior immunomodulator	54 (74%)
Current immunomodulator	6 (8%)
Current Prednisone/methylprednisolone	33 (45%)
Current Budesonide	7 (10%)
Current oral contraceptive	6 (8%)
Comorbid conditions	
Hypertension	19 (26%)
Hyperlipidemia	13 (18%)
Diabetes	7 (10%)
Coronary artery disease	5 (7%)
History of cerebrovascular accident	1 (1%)
BMI, median (IQR)	25.6 (21.6-28.9)
Arthralgia at time of initiation	27 (37%)
Disease severity	
UC hospitalization within 12 months	19 (26%)
Serum albumin, g/dL, median (IQR)	4.1 (3.8-4.3)
CRP, mg/L, median (IQR)	5.1 (1.7-16.7)
Fecal calprotectin > 120 ug/g	27 (90%)
SCCAI, median (IQR)	5 (3, 8)
Daily bowel movement frequency, median (IQR)	6 (3.5-10)
Endoscopic extent >E1 (i.e. >proctitis)	62 (85%)
Endoscopic severity	
None	6 (8%)
Mild	9 (12%)
Moderate	38 (52%)
Severe	20 (27%)
Substance use	
Smoking	
Never	59 (81%)
Current	2 (3%)
Former	12 (16%)
Current cannabis use	11 (15%)
Current opioid use	7 (10%)

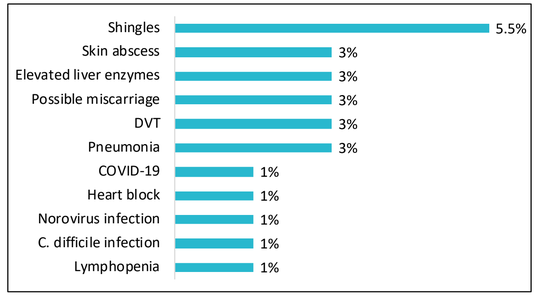
Albumin, C-reactive protein, fecal calprotectin, SCCAI, and bowel movements were the most recent values available within 3 months prior to drug initiation. The most recent endoscopic data preceding tofacitinib initiation was used: median 19.1 weeks (IQR 6.1-46.1 weeks) prior to tofacitinib initiation. Abbreviations: IQR = interquartile range, TNF= tumor necrosis factor, ASA = aminosalicylic acid, CRP = C-reactive protein, SCCAI = simple clinical colitis activity index

Figure 1. Clinical and endoscopic outcomes



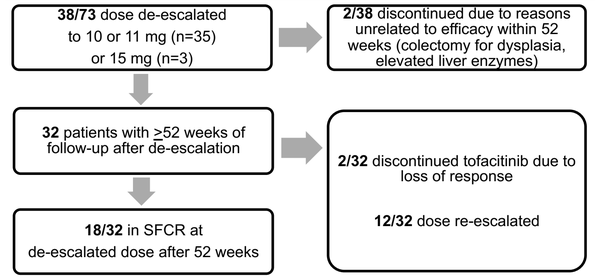
Number after SFCR reflects number of weeks. All other outcomes have no time restriction (all available follow-up). Patients who discontinued therapy due to non-response at earlier endpoints were included in the denominators for later endpoints (i.e. they were considered treatment failures). Denominators vary due to availability of outcome data. Abbreviations: SFCR = steroid-free clinical remission

Figure 2. Adverse events during follow-up.



There were 19 adverse events reported among 15 patients (all individual events are included in figure). Abbreviations: DVT = deep venous thrombosis

Figure 3. Dose de-escalation outcomes.



Dose de-escalation occurred after a median of 36.9 weeks (IQR 20.6-62.3 weeks) from tofacitinib initiation. Doses listed reflect total daily dosing.

Subgroup analysis

- Among patients with prior anti-TNF and vedolizumab failure, proportions of patients achieving SFCR 12, 52, and 78 with tofacitinib were 26/50 (52.0%), 26/49 (53.1%), and 21/44 (47.7%), respectively.

Conclusions

- In a real-world refractory UC population, tofa was effective in achieving SFCR for the majority (52%) of patients through 78 weeks.
- Remission was maintained for at least 52 weeks for the majority (56%) of patients who underwent dose de-escalation.
- Adverse events are similar to those previously reported.[9]
- There is a need for head-to-head clinical trials and real-world comparative effectiveness studies to help health care providers and patients make appropriate treatment decisions.

Limitations

- Retrospective design, potential omissions/errors in clinical documentation, variable follow-up time, limited ability to detect adverse events at outside institutions.
- Endoscopic data was available only for a subset of patients.
- Due to the limited sample size, larger real-world studies are needed to corroborate our findings.

Abbreviations

UC = ulcerative colitis, SRCR = steroid-free clinical remission, CRP = C-reactive protein, FC = fecal calprotectin, AE = adverse event, IQR = interquartile range

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Disclosures of interest

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