Digestive Diseases and Sciences (2024) 69:1785–1792
https://doi.org/10.1007/s10620-024-08394-w

ORIGINAL ARTICLE

Effect of Tofacitinib on One-Year Colectomy Risk in Anti-TNF Refractory Ulcerative Colitis: A Prospective Multicenter Italian Study

Anna Maria Carvalhas Gabrielli[1] · Francesca Ferretti[1] · Camilla Maria Monico[1] · Enrico Tombetti[2,3] · Giovanni Maconi[1,3] · Samanta Romeo[4] · Nicole Piazza O Sed[5] · Flavio Caprioli[5,6] · Anna Maria Mazzola[7] · Saverio Alicante[4] · Roberto Bertè[4] · Elisabetta Lolli[8] · Maria Lia Scribano[9] · Elisabetta Buscarini[4] · Chiara Ricci[7,10] · Stefania Carmagnola[1] · Sandro Ardizzone[1] · Rosanna Cannatelli[1]

Received: 31 January 2024 / Accepted: 16 March 2024 / Published online: 26 March 2024

Abstract

Background Tofacitinib is an oral Janus kinase inhibitor recently approved to induce and maintain remission in ulcerative colitis (UC).

Aims Considering the number of anti-TNF non-responders, this study aims to assess the effectiveness and safety of tofacitinib in a cohort of multi-failure patients with moderate-to-severe UC at 52 weeks.

Methods From January 2021 to March 2023, we performed a prospective multicenter study observing adult patients with moderate-to-severe UC starting tofacitinib after an anti-TNF failure for a 52-week-long period. Effectiveness and safety were assessed in terms of colectomy rate, clinical remission and response, endoscopic remission, steroid-free clinical remission, and rate of adverse events.

Results We included 58 patients with UC with an age of 42 ± 14.4 years, 59% males, 96.6% left-sided or pancolitis, who were failure to a single (65.5%) or more than one anti-TNF (34.5%). Only 6 (10.3%) patients underwent colectomy. Colectomy was clinically associated with the necessity and the number of extra cycles of tofacitinib 10 mg bid at W8 ($p = 0.023$) and W24 ($p = 0.004$), and with a higher partial Mayo score at W8 ($p = 0.025$). At W52, clinical remission, clinical response, and steroid-free clinical remission were 53.4%, 43.1%, and 48.3%, respectively. Of 22 performed colonoscopies at W52, 11 (50%) showed endoscopic remission. Adverse events occurred in 14 (24.1%) patients, but only 2 (3.4%) led to tofacitinib discontinuation.

Conclusions In a real-life setting of patients with anti-TNF refractory UC, tofacitinib has proved to be effective in preventing colectomy and inducing clinical and endoscopic remission at 52 weeks with a good safety profile.

Keywords JAK-inhibitor · Inflammatory bowel disease · Biologic therapy · Surgery

✉ Anna Maria Carvalhas Gabrielli
amcgabrielli@gmail.com

[1] Gastroenterology Unit, ASST Fatebenefratelli-Sacco, L. Sacco Hospital, Via Giovanni Battista Grassi, 74, 20157 Milan, MI, Italy

[2] Internal Medicine and Rheumatology Unit, ASST Fatebenefratelli-Sacco, Milan, Italy

[3] Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy

[4] Gastroenterology and Digestive Endoscopy Dept, ASST Ospedale Maggiore Di Crema, Crema, Italy

[5] Gastroenterology and Endoscopy Unit, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico Di Milano, Milan, Italy

[6] Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

[7] Department of Clinical and Sperimental Sciences, University of Brescia, Brescia, Italy

[8] Gastroenterology Department, Policlinico Tor Vergata, Rome, Italy

[9] Villa Stuart Multi-Speciality Clinic, Rome, Italy

[10] Gastroenterology Unit, Spedali Civili Di Brescia, Brescia, Italy

Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterized by colonic inflammation [1]. The clinical course may be difficult to predict, ranging from a quiescent disease to a chronic refractory condition, leading to surgery or life-threatening complications such as cancer [2]. The primary goal of treatment is to induce and maintain remission of the disease. In the last decade, different therapeutic options including multiple biologic agents and small molecules have been added to the more traditional anti-inflammatory and immunosuppressive agents [3, 4].

In moderate-to-severe forms of UC, conventional therapies are often insufficient to maintain remission of disease or may have to be discontinued due to adverse events (AEs); thus, in this setting, therapeutic choice should be made considering the different emerging alternatives, all of which demonstrated high rates of efficacy and good safety profiles in clinical trials. However, it must be considered that in real-life approximately 20% of patients are primary non-responders to a first-line biologic agent, and 50% present secondary loss of response during follow-up [5], and that surgery is still the only curative option for UC, with a 5 and 10-year cumulative risk of surgery of 10%–15% [6].

Among the most recently approved agents, the oral, small-molecule JAK (Janus kinase) inhibitor Tofacitinib demonstrated its effectiveness as induction and maintenance therapy in moderate-to-severely active UC, with an acceptable safety profile and rapid onset of action, emerging as a valuable alternative therapeutic option with promising results [7]. However, as the selection criteria in clinical trials are very restrictive, more real-world studies (RWS) are necessary to confirm these preliminary data.

The main purpose of our study was to prospectively evaluate the effectiveness of tofacitinib in preventing colectomy at one year in patients with moderate-to-severe UC refractory to anti-tumor necrosis factor (TNF) agents. The secondary endpoints were to evaluate rates of clinical response and the onset of any AE during treatment.

Methods

Design of Study

This was a prospective multicenter observational study and it was approved by the Valpadana Ethical Committee on August 8th, 2022. Finally, it involved six different referral IBD units in Italy.

Patients

We enrolled adult patients with moderate-to-severe UC refractory to anti-TNF agents, referred to IBD centers to start tofacitinib for active disease. All patients were followed for at least 52 weeks.

Enrollment and data collection was performed from January 1st, 2021, to April 30th, 2023.

We consecutively included adult patients (age ≥ 18) with confirmed diagnosis of moderate-to-severe UC, defined by a total Mayo score (tMS) ≥ 6 and/or endoscopic Mayo score (eMS) ≥ 2 and/or partial Mayo score (pMS) ≥ 5. All patients had to be failure (inadequate response or loss of response) to previous anti-TNF agents, with negative microbial tests on stool specimens. Patients could be refractory also to other biologics, such as vedolizumab (VDZ) or ustekinumab. Exclusion criteria were: ongoing pregnancy or lactation, previous tofacitinib exposure, recent or ongoing infectious disease, and any absolute contraindication to Tofacitinib. Patients with acute severe UC were excluded.

Before starting Tofacitinib, all patients were screened for HBV, HCV, HIV and tuberculosis. In case of any positivity, adequate treatment or prophylaxis treatment were introduced before starting tofacitinib.

Clinical, Laboratory and Endoscopic Data

Baseline patient demographic and clinical characteristics were collected, including age, age at diagnosis, gender, smoking habit, family history of IBD, UC extent according to Montréal classification [8], disease duration, pMS [9], history of medical treatment and baseline eMS [9], if available. Biochemical data included white blood count (WBC), hemoglobin (Hb), platelets (PLTs), C reactive protein (CRP), fecal calprotectin (FC) and immunological Cytomegalovirus (CMV) profile if performed.

All patients received tofacitinib at the standard induction dose [7] of 10 mg twice daily (bid) for 8 weeks, followed by the standard maintenance dose (5 mg bid), or by the continuation of the induction dosage of 10 mg bid for a maximum of 16 weeks at physician discretion.

No standardized tapering was set in patients receiving steroids and/or immunosuppressants at inclusion and treatments were continued at the investigator's discretion.

Follow-up clinical data were collected at week 8 (W8), week 24 (W24) and week 52 (W52). They included disease activity (pMS), steroid intake, biochemical data, UC-related hospitalization, surgery, tofacitinib discontinuation and time between tofacitinib introduction and discontinuation, any AE, concomitant maintenance therapy

(5-aminosalicylates, immunosuppressants), and the number of induction cycles with 10 mg bid of tofacitinib.

At W52, besides clinical data, endoscopic evaluation (eMS) and FC were collected. Endoscopic evaluation was performed by different IBD expert endoscopists.

Aims and Outcomes

The primary aim of this study was to evaluate the effectiveness of tofacitinib preventing colectomy in patients with moderate-to-severe UC refractory to anti-TNF agents in terms of colectomy rate, survival without colectomy, and survival without tofacitinib discontinuation.

The secondary aim was to evaluate clinical remission, steroid-free (SF) clinical remission, and clinical response to tofacitinib. Clinical remission was defined as a pMS < 3, and clinical response as a reduction in the pMS from baseline of at least 3 points. Endoscopic remission was defined as eMS ≤ 1, and endoscopic response as a reduction in the eMS of ≥ 1 point. Failure was defined as the interruption of tofacitinib before the end of follow-up due to colectomy, serious AEs, or non-response as in the absence of the objective response criteria mentioned above, despite the continuation of tofacitinib.

Finally, we evaluated the safety of the drug. AEs were classified as severe when they led to hospitalization, disability or persistent damage and death.

Statistical Analysis

Statistical analysis was performed with SPSS software (version 28.0.1.0, IBM Corporation, Armonk, New York, United States).

Qualitative variables were expressed as numbers and percentages (%). Quantitative variables, considered to have a normal distribution, were expressed as mean ± standard deviation (SD), while median and interquartile range (IQR), were used for the remaining variables. All patients included were evaluated and analyzed on an intention-to-treat basis in the present study. Associations between qualitative variables and the primary and secondary outcomes were analyzed by Chi-square statistic, or Fisher's test, as appropriate. Kaplan Meier curves were plotted to analyze survival outcomes.

Risk factors associated with the occurrence of the primary and secondary outcomes were investigated with logistic regression. Multivariate analysis was not performed because of the low number of cases (colectomies).

All the analysis were two-tailed, and p-values < 0.05 were considered statistically significant.

Results

Baseline Patients' Characteristics

From January 2021 to April 2023, 58 patients with UC (34 male, 59%) were included in the study.

The median age was 42 ± 14.4 years with a median disease duration of 10 years (IQR 4–15). According to Montreal classification [8], 29 (50%) patients had pancolitis (E3), 27 (46.6%) left-sided colitis (E2) and only 2 (3.4%) had proctitis (E1). Baseline characteristics are reported in Table 1.

All patients had a moderate-to-severe disease in terms of clinical and/or endoscopic activity of disease. Of all patients, 51 (91%) had a tMS above 6 and 56 of 56 (100%) had an eMS ≥ 2.

Medical history is reported in Table 1. All patients previously received anti-TNF agents and 19 (32.8%) failed two different anti-TNF molecules whereas 1 patient failed three different anti-TNF molecules. Thirty-three patients (56.9%) were failure to three or more therapeutic lines; 9 patients had previous history of combined therapy (anti-TNF agent plus an immunomodulator); 41 patients (70.7%) experienced also VDZ and 3 (5.2%) ustekinumab.

Colectomy Risk and Survival Curves

Among 58 patients, 6 (10.3%) underwent colectomy. All patients underwent colectomy because of non-response to treatment.

All colectomies were performed before W24 and specifically between week 10 and 22. Survival without colectomy at W24 (as W52) was 89.2 (95% CI 81.0–97.4). Kaplan–Meier is shown in Fig. 1.

Overall, 22 patients (37.9%) discontinued tofacitinib after a mean treatment duration of 42 weeks. Among them 14 patients discontinued the JAK inhibitor because of non-response (63.6%), 2 (9.1%) because of AEs and 6 (27.3%) for colectomy. Survival without treatment discontinuation was 79.3 (95%CI 68.9–89.7) at W24 and 65.5 (95% CI 53.3–77.6) at W52. Kaplan–Meier is shown in Fig. 2.

Clinical Remission and Response

Clinical remission was reached by 25 patients (43.1%) at W8, using all patients as denominator, by 28 (48.3%) at W24, and by 31 patients (53.4%) at W52.

Clinical response was achieved by 22 patients (37.9%) at W8, by 31 patients (53.4%) at W24 and by 25 patients (43.1%) at W52. Results are reported in Fig. 3.

Table 1 Population baseline characteristics

		Patients on tofacitinib ($n=58$)
Demographic and clinical data		
	Age, mean ± sd, years	42 ± 14.4
	Male, *n* (%)	34 (59%)
	Age at diagnosis, mean ± sd, years	32 ± 13.5
	Duration of disease, median (range), years	10 (4–15)
	Extent of disease, *n* (%)	
	Proctitis (E1)	2 (3.4%)
	Left-sided colitis (E2)	27 (46.6%)
	Extended colitis/pancolitis (E3)	29 (50%)
Medical history		
	Appendicectomy, *n* (%)	2 (3.4%)
	Ongoing smoking	3 (5.2%)
	Previous smoking	15 (25.9%)
	Family history of IBD	4 (6.9%)
	Frequent NSAIDs consumption	0 (0%)
Disease activity scores		
Total MS*	0	0 (0%)
	3–5	5 (8.9%)
	6–10	44 (78.6%)
	> 10	7 (12.5%)
Partial MS	< 2	2 (3.4%)
	2–4	13 (22.4%)
	5–7	35 (60.3%)
	> 7	8 (13.8%)
Endoscopic MS*	0	0 (0%)
	1	0 (0%)
	2	13 (23.2%)
	3	43 (76.8%)
Laboratory data		
	C-reactive protein, mg/dL, median	0.3 (0.12–0.93)
	Fecal calprotectin, mcg/g**	
	< 250, *n* (%)	4 (12.9%)
	≥ 250, *n* (%)	27 (87.1%)
	Hemoglobin—g/dL, media ± sd	13.3 ± 1.7
	VZV IgG positive, *n* (%)	31 (77.5%)
History of treatment, *n* (%)		
	Ongoing oral steroids	31 (53.4%)
	Ongoing oral aminosalicylates	43 (74.1%)
	Previous steroid therapy	55 (94.8%)
	Previous aminosalicylates	56 (96.6%)
	Previous ISS	37 (63.8%)
	Previous anti-TNF	58 (100%)
	Previous single anti-TNF	38 (65.5%)
	Previous double anti-TNF	19 (32.8%)
	Previous triple anti-TNF	1 (1.7%)
	Previous ISS + anti-TNF	9 (15.5%)
	Previous vedolizumab	41 (70.7%)
	Previous ustekinumab	3 (5.2%)
	Previous ozanimod	1 (1.7%)

Table 1 (continued)

	Patients on tofacitinib ($n=58$)
Number of previous treatment lines	
1	7 (12.1%)
2	18 (31%)
3	18 (31%)
4	11 (19%)
5	4 (6.9%)

n number, NSAIDs non-steroidal anti-inflammatory drugs, *MS* mayo score, *VZV IgG* immunoglobulins G for Varicella-Zoster virus, *ISS* immunosuppressants, *TNF* tumor necrosis factor, *IBD* inflammatory bowel disease

*Data were available for 56 patients

**Data were available for 31 patients

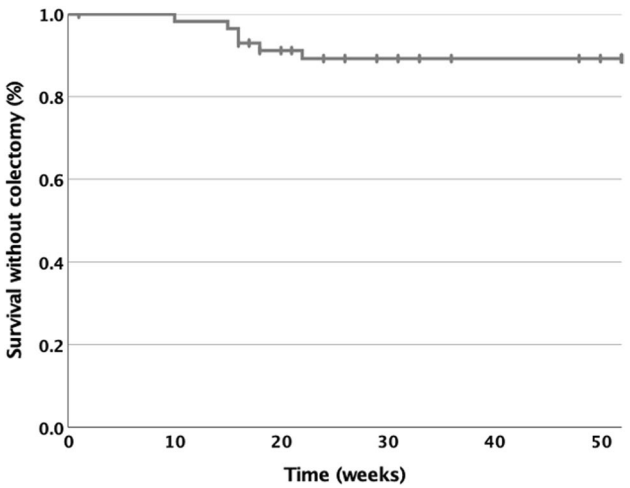

Fig. 1 Survival without colectomy in a 52-week-long follow up among 58 patients with highly refractory moderate-to-severe UC, treated with tofacitinib

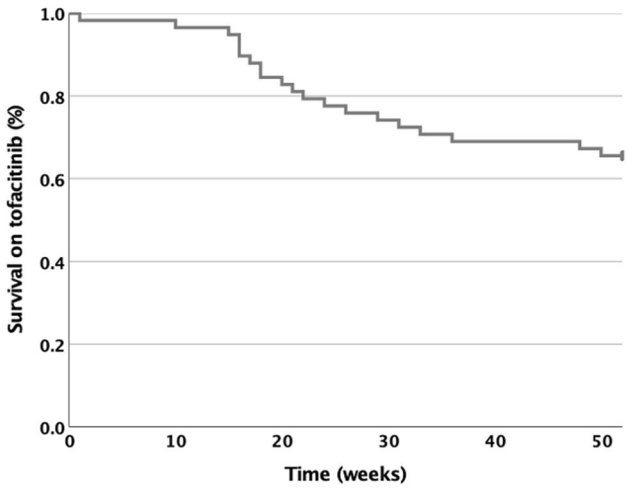

Fig. 2 Survival without treatment interruption in a 52-week-long follow up among 58 patients with highly refractory moderate-to-severe UC, treated with tofacitinib

Considering concomitant steroid therapy at baseline in 31 patients (53.4%), 24 patients (41.3%) were in SF clinical remission at W8, 27 patients (46.6%) at W24, and 28 patients (48.3%) at W52.

Of 58 patients, 22 (37.9%) needed at least one extra cycle of 10 mg bid tofacitinib: 11 patients needed one extra cycle, 10 patients two extra cycles and one patient needed three extra cycles.

Endoscopic Remission and Response

At W52, 22 patients out of 36 underwent colonoscopy. Endoscopic remission was observed in 11 patients (50%), but endoscopic response was observed in 18 patients (81.8%).

Safety

AEs occurred in 14 patients (24.1%). The severity and type of adverse events are summarized in Table 2.

Only 3 patients (5.2%) had serious AEs, one leading to hospitalization (acute renal failure) and two leading to tofacitinib discontinuation (chest pain and Herpes Zoster infection). Most frequent AEs were infections (6.9%), leukopenia (5.2%) and hypercholesterolemia (5.2%). No thromboembolic or cardiovascular events, nor neoplasia or death occurred. No reactivation of tuberculosis was observed during the follow-up.

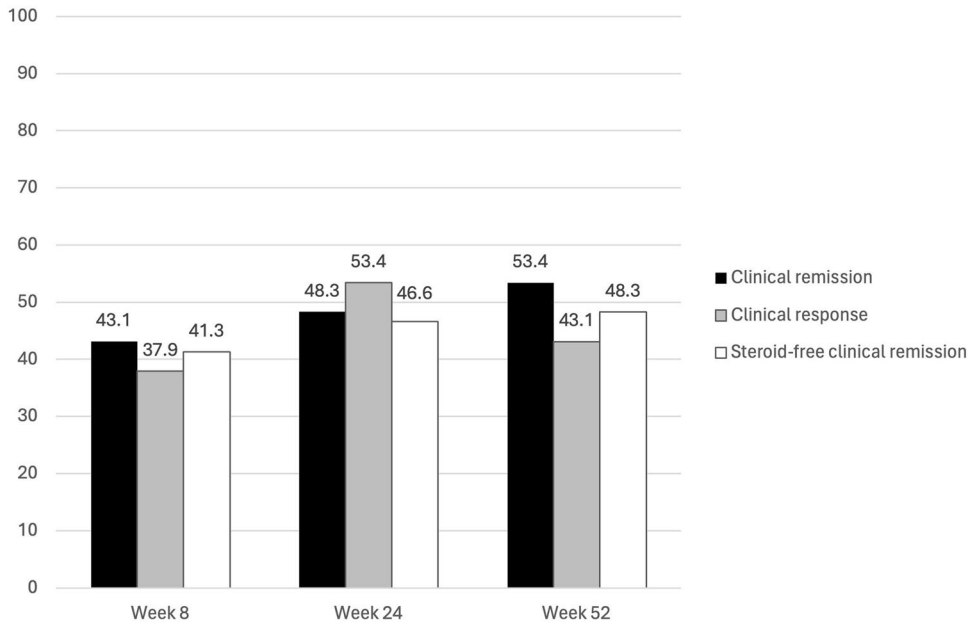

Fig. 3 Efficacy outcomes (clinical remission, clinical response and steroid-free clinical remission) at different timepoints (W8 = week 8; W24 = week 24; W52 = week 52)

Table 2 Adverse events under tofacitinib treatment

	Tofacitinib $n = 58$
Adverse event, *n* (%)	14 (24.1%)
Leukopenia, *n* (%)	3 (5.2%)
Hypercholesterolemia, *n* (%)	3 (5.2%)
Acute renal failure	1 (1.7%)
Infective adverse event, *n* (%)	4 (6.9%)
Urinary tract infection	1 (1.7%)
Campylobacter gastroenteritis	1 (1.7%)
C. Difficile gastroenteritis	1 (1.7%)
Herpes Zoster	1 (1.7%)
Serious infection, *n* (%)	1 (1.7.%)
Any serious adverse event, *n* (%)	3 (5.2%)
MACE, *n* (%)	0 (0%)
Thromboembolism, *n* (%)	0 (0%)
Neoplasia, *n* (%)	0 (0%)
Death, *n* (%)	0 (0%)

n number, *MACE* major adverse cardiovascular events

Logistic Regression

In the univariate analysis, colectomy was clinically associated with the necessity of extra cycles of tofacitinib 10 mg bid particularly at W8 ($p = 0.023$) and before W24 ($p = 0.004$), and with a higher pMS at W8 ($p = 0.025$). In addition, also a higher number of cycles of tofacitinib 10 mg bid ($p = 0.007$) was correlated to the risk of colectomy. Other variables such as sex, smoking, family history, the number of previous therapeutic lines, the pMS, eMS, and tMS at enrollment were not associated with colectomy (Supplementary Table 1).

Regarding clinical remission at W52, negative predictive features were the necessity of steroids at W8 ($p = 0.009$), and the need of extra cycles of tofacitinib 10 mg bid at W24 ($p = 0.045$). Also, an increasing number of extra cycles of tofacitinib 10 mg bid shows a positive correlation with clinical remission at W52, even if not statistically significant ($p = 0.064$). Moreover, clinical remission at W24 was associated to clinical remission at W52 ($p = 0.024$).

Finally, the need ($p = 0.014$) and the number ($p = 0.004$) of extra cycles of tofacitinib 10 mg bid were the only factors associated to treatment failure.

Discussion

Even if phase II/III data demonstrated the efficacy of Tofacitinib in achieving mucosal healing and clinical response [7], the bias due to patient selection makes other studies mandatory to confirm these preliminary data. In fact, the inclusion of a large portion of naïve patients, as well as the exclusion of VDZ-experienced patients, does not reflect the real-life setting, where Tofacitinib is often a second- or third-line therapeutic option.

Thus, the aim of our multicenter Italian study was to prospectively evaluate a specific subset of patients with moderate-to-severe UC who already failed at least one anti-TNF agent.

Our population was demographically comparable to the cohort in OCTAVE trials [7], including mostly men with a mean age of 42 years, with a 10-year-long disease duration,

and mostly with a left-sided colitis or pancolitis. However, patients in our cohort were refractory to at least a single (65.5%) or multiple (34.5%) anti-TNF agent. Approximately 70% were refractory also to VDZ. Furthermore, our study population had a severe disease as most patients had a PMS above 5 and a eMS equal to 3. This is a frequent and challenging real-life scenario that IBD specialists must deal with, as well as the difficult choice among multiple therapeutic options, including surgery.

In our cohort, since the introduction of tofacitinib, the rate of colectomy at W52 was 10%. Although first studies showed higher colectomy rates reaching 18% in Lair-Mehiri et al. [10] and 24% in Weisshof et al. [11], a recent meta-analysis by Taxonera [12], reported similar results, with a colectomy rate of 9% (95% CI, 6.4%–11.6%; range, 3.7%–26.3%). In another recent study, the colectomy rate at W52 was 8%, and it was higher in the group of acute severe colitis [13]. In our study, a higher risk of colectomy was associated with a poor clinical response at W8, and with the need and number of extra cycles of tofacitinib at induction dose (10 mg bid). In a recent RWS, a high PMS at W8 was correlated with treatment discontinuation at the multivariate regression [14]. In the *post-hoc* analysis of OCTAVE clinical trial, colectomy was a rare event; however, all patients who underwent colectomy were anti-TNF failure, and most of them had a disease duration ≥ 6 years, MES of 3, total Mayo score ≥ 6 before colectomy and higher dose of tofacitinib [15]. Both the colectomy event and the need of extra cycles at induction dose mainly occurred in the first 24 weeks. This time point seems to be critical in the management of severe and multi-refractory disease, confirmed also by the fact that clinical remission at W24 was a positive predictor of long-term response at W52. A recent retrospective multicenter RWS confirmed that clinical remission obtained at W16 in two-thirds of patients was maintained at W52 [16]. On the contrary, the necessity of steroids at W8 and the need for extra-cycle at induction dose of tofacitinib (and their number) within W24 were negatively correlated to clinical remission at W52.

Our results confirm a high rate of long-term response to tofacitinib. In fact, clinical remission rates at W8 and at W52 were 43.1% and 53.4%, respectively, and SF clinical remission was achieved by 41.3% and by 48.3% at W8 and W52, respectively. These results are higher than in other RWS, such as 34% in a small French cohort [10] after 48 weeks and 27% at W52 in a retrospective American RWS [11]. However, more recent studies [17, 18] reported percentages with a SF remission rate of 55.4% and 58% at W52. The efficacy of tofacitinib is also supported by the higher rates of endoscopic remission (50%) at W52 observed in our population compared to Lair-Mehiri et al. [10] (7.9%) and Weisshof et al. [11] (13.2%). As already observed in the prospective Dutch study [18], these differences could be ascribable to smaller population cohorts, including mostly VDZ-experienced patients with UC [18], and to different induction regimens with a 5 mg bid dose in the American study [11].

Besides its efficacy, in our study Tofacitinib showed a good tolerability and safety profile with a discontinuation rate of 38%, similar to previous real-life data [19]. The AEs rate was 24.1%, including only 3 severe AEs: of them, just two led to drug discontinuation (Herpes Zoster infection and chest pain). From RWS and a systematic review regarding patients with IBD or other immune-mediated diseases, it is appreciated that Tofacitinib has a good safety profile, besides the increased risk of Herpes Zoster [20–22]. In our cohort, all other adverse events had a mild entity (infections 6.9%, hypercholesterolemia 5.2%, leukopenia 5.2%). No major thrombotic events or deaths occurred in the observation period. Considering the 52 week-long follow-up and the accordance with other recent RWS [10, 14, 23, 24] these results can be reassuring when choosing Tofacitinib in patients with UC.

To our knowledge, this is one of the first prospective multicenter real-life cohort studies enquiring the long-term efficacy of tofacitinib in terms of colectomy rate. It involved some of the most important referral IBD units in Italy, including a cohort of patients who were all previously exposed to one or more anti-TNF agent. Our study demonstrates how patients, despite multiple refractoriness, have a good and sustained clinical and endoscopic response to this new small molecule administered orally. Moreover, to limit subjective evaluation, we used standard and worldwide validate clinical and endoscopic scores.

Due to the prospective nature and design of the study, our population was limited and multi-failure, therefore data concerning the use of tofacitinib as a first line approach in moderate-to-severe UC was not available. Besides, it could be argued that endoscopy was not available for all patients. Nevertheless, this may reflect the real-life assessment where follow-up endoscopies are not always performed. Even so, endoscopic remission was achieved in half of patients, similarly to results obtained in a recent retrospective multicenter Italian study [25].

In this study we demonstrated that patients who failed anti-TNF agents have a low rate of colectomy since starting tofacitinib, with a good rate of clinical remission and response. Better outcomes are associated with response at W24, whereas the necessity of extra cycles of tofacitinib 10 mg bid seems to be associated to colectomy or treatment failure.

In conclusion, our multicentric prospective study demonstrates that tofacitinib is effective in a real-world scenario with a high percentage of multi-refractory patients, and that it is a valid alternative therapeutic option to avoid colectomy after anti-TNF failure.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10620-024-08394-w.

Acknowledgments No funds have been sourced for this manuscript.

Author's contribution All authors have contributed to and agreed on the content of the manuscript. In particular, AMCG, RC, FF, SR, and SA planned the study; AMCG, RC, and FF drafted the article, collected and interpreted data. All other authors were involved in data collection and critical revision of the article for important intellectual content. All authors approved the final version of the manuscript including the authorship list.

Data availability Data are available upon reasonable request.

Declarations

Conflict of interest None declared.

References

1. Raine T, Bonovas S, Burisch J et al. ECCO guidelines on therapeutics in ulcerative colitis: medical treatment. *J Crohn's Colitis.* 2022;16:2–17.
2. Brostrom O. Prognosis in ulcerative colitis. *Med Clin North Am.* 1990;74:201–218.
3. Cohen BL, Sachar DB. Update on anti-tumor necrosis factor agents and other new drugs for inflammatory bowel disease. *BMJ.* 2017;357:j2505.
4. Ferretti F, Cannatelli R, Monico MC et al. An update on current pharmacotherapeutic options for the treatment of ulcerative colitis. *J Clin Med.* 2022;11:2302.
5. Amiot A, Serrero M, Peyrin-Biroulet L et al. One-year effectiveness and safety of vedolizumab therapy for inflammatory bowel disease: a prospective multicentre cohort study. *Aliment Pharmacol Therapeutics.* 2017;46:310–321.
6. Fumery M, Singh S, Dulai PS et al. Natural history of adult ulcerative colitis in population-based cohorts: a systematic review. *Clin Gastroenterol Hepatol.* 2018;16(343–356):e343.
7. Sandborn WJ, Su C, Sands BE et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 2017;376:1723–1736.
8. Satsangi J, Silverberg MS, Vermeire S et al. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut.* 2006;55:749–753.
9. Walsh AJ, Bryant RV, Travis SP. Current best practice for disease activity assessment in IBD. *Nat Rev Gastroenterol Hepatol.* 2016;13:567–579.
10. Lair-Mehiri L, Stefanescu C, Vaysse T et al. Real-world evidence of tofacitinib effectiveness and safety in patients with refractory ulcerative colitis. *Dig Liver Dis.* 2020;52:268–273.
11. Weisshof R, Aharoni Golan M, Sossenheimer PH et al. Real-world experience with tofacitinib in IBD at a tertiary center. *Dig Dis Sci.* 2019;64:1945–1951.
12. Taxonera C, Olivares D, Alba C. Real-world effectiveness and safety of tofacitinib in patients with ulcerative colitis: systematic review with meta-analysis. *Inflamm Bowel Dis.* 2022;28:32–40.
13. Resal T, Bacsur P, Keresztes C et al. Real-life efficacy of tofacitinib in various situations in ulcerative colitis: a retrospective worldwide multicenter collaborative study. *Inflamm Bowel Dis.* 2023. https://doi.org/10.1093/ibd/izad135.
14. Chaparro M, Acosta D, Rodriguez C et al. Real-world evidence of tofacinitib in ulcerative colitis: short-term and long-term effectiveness and safety. *Am J Gastroenterol.* 2023;118:1237–1247.
15. Rubin DT, Salese L, Cohen M et al. Presence of risk factors associated with colectomy among patients with ulcerative colitis: a post hoc analysis of data from the tofacitinib OCTAVE ulcerative colitis clinical program. *Therapeutic Adv Gastroenterol.* 2023;16:17562848231189122.
16. Molander P, Kosunen M, Eronen H et al. Tofacitinib real-world experience in ulcerative colitis in Finland (FinTofUC): a retrospective non-interventional multicenter patient chart data study. *Scand J Gastroenterol.* 2023. https://doi.org/10.1080/00365521.2023.2298361.
17. Dalal RS, Sharma PP, Bains K et al. Clinical and endoscopic outcomes through 78 weeks of tofacitinib therapy for ulcerative colitis in a US cohort. *Inflamm Bowel Dis.* 2023. https://doi.org/10.1093/ibd/izad242.
18. Straatmijer T, Biemans VBC, Visschedijk M et al. Superior effectiveness of tofacitinib compared to vedolizumab in anti-TNF-experienced ulcerative colitis patients: a nationwide dutch registry study. *Clin Gastroenterol Hepatol.* 2023;21(182–191):e182.
19. Straatmijer T, van Gennep S, Duijvestein M et al. Real-world clinical and endoscopic outcomes after one year tofacitinib treatment in ulcerative colitis. *Eur J Gastroenterol Hepatol.* 2021;33:1288–1297.
20. Sandborn WJ, Panes J, D'Haens GR et al. Safety of tofacitinib for treatment of ulcerative colitis, based on 44 years of data from global clinical trials. *Clin Gastroenterol Hepatol.* 2019;17:1541–1550.
21 Olivera PA, Lasa JS, Bonovas S et al. Safety of Janus kinase inhibitors in patients with inflammatory bowel diseases or other immune-mediated diseases: a systematic review and meta-analysis. *Gastroenterology.* 2020;158:1554-1573 e1512.
22. Curtis JR, Xie F, Yun H et al. Real-world comparative risks of herpes virus infections in tofacitinib and biologic-treated patients with rheumatoid arthritis. *Ann Rheum Dis.* 2016;75:1843–1847.
23. Avni-Biron I, Bar-Gil Shitrit A, Koslowsky B et al. Short-term effectiveness and safety of tofacitinib in ulcerative colitis—real world data from tertiary medical centers in Israel. *Dig Liver Dis.* 2022;54:192–197.
24. Perin RL, Magro DO, Andrade AR et al. Effectiveness and safety of tofacitinib in the management of ulcerative colitis: a Brazilian observational multicentric study. *Crohns Colitis.* 2023;5:otac050.
25. Tursi A, Mocci G, Cingolani L et al. Use of tofacitinib as first or second-line therapy is associated with better outcomes in patients with ulcerative colitis: data from a real-world study. *Expert Opin Pharmacother.* 2023;24:1649–1656.