Non-Interventional Study Protocol
A3921390

Retrospective non-interventional multicenter patient chart data study on tofacitinib real-world experience in ulcerative colitis in Finland (FinTofUC)

Statistical Analysis Plan
(SAP)

Version: 1.0

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1 AMENDMENTS FROM PREVIOUS VERSION(S)

NA

2 INTRODUCTION

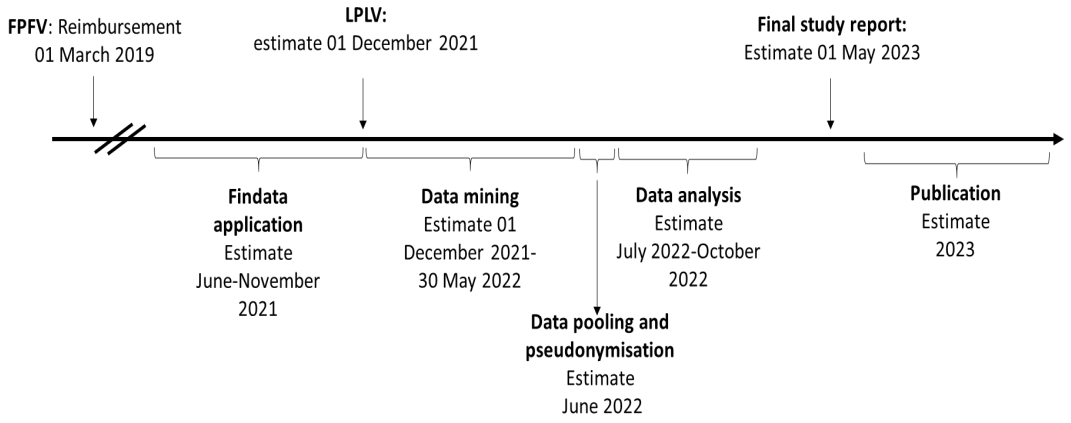
2.1 STUDY DESIGN

The target population for this study is adult ulcerative colitis patients who were prescribed tofacitinib. Estimated number of patients in this study is 100-150, with the aim of covering all ulcerative colitis patients in Finland treated with tofacitinib. The main inclusion criteria are a diagnosis of ulcerative colitis (ICD-10: K51) between January 2010 and December 2021 and treatment with tofacitinib. The main exclusion criteria are age under 18 years, use of tofacitinib before national reimbursement decision on 01 March 2019 and history of panproctocolectomy, ileal pouch-anal anastomosis (IPAA) or ileostomy.

The data collected has been generated as part of standard clinical care, treatment, and follow-up of ulcerative colitis patients. In accordance with the Finnish Act on Secondary Use of Health and Social Data 552/2019 (in Finnish: Laki sosiaali- ja terveystietojen toissijaisesta käytöstä), health registry data can be processed in scientific studies without patient consent. The purpose of this act is to establish conditions for the effective and secure processing of, and access to, personal health and social data for certain secondary purposes, such as research and statistics, innovation and development, knowledge management, teaching and authority planning. Thus, the Secondary Act creates a clear legal basis for the use of such registered data for research and innovation related to, for example, the health and well-being of citizens, the prevention of disease and the development of new treatment methods. This relatively new legislation is also a welcome unification of the fragmented Finnish national rules regarding the use of healthcare and social welfare data. In addition, it takes into consideration current data protection requirements.

The data will be collected by data miners in all hospital districts across Finland and entered into an electronic data mining tool (eDMT) which will be designed for the study in collaboration with Finnish clinicians. The data will be used to investigate and describe the patient population, treatment strategies and disease development.

Figure 1. Study Timeline



FPFV= First patient first visit, LPLV= Last patient last visit.

Please note that dates are subject to change depending on how long permit process with Findata takes.

Study population

The study is a descriptive single cohort study. Patients must meet all of the following inclusion criteria to be eligible for inclusion in the study:

1. *Xeljanz (tofacitinib) usage for ulcerative colitis.*
2. *Diagnosis of ulcerative colitis (ICD-10: K51.0, K51.1, K51.2, K51.3, K51.5, K51.8, K51.9) between January 2010 and December 2021 (incident or prevalent).*

Patients will be excluded if:

1. *Age <18 years at the start of tofacitinib use.*
2. *Use of tofacitinib before reimbursement (01 Mar 2019).*
3. *< 8 weeks of treatment with tofacitinib at the start of data mining.*
4. *History of panproctocolectomy, IPAA or ileostomy.*

The primary variable is the first recording (date) with tofacitinib for the treatment of ulcerative colitis (ICD-10: K51). Additional variables to be collected according to the list in Table 1.

Table 1. Variables Collected in This Study

Data source for all variables is the eDMT based on patient charts.

Variable	***Role***	***Operational definition***
Tofacitinib start date	*Index* *Inclusion criteria 1* *Exclusion criteria 2*	*First day on tofacitinib administration*
Date of birth	*Exclusion criteria 1* *Primary objective 7.2.1.a*	*Age will be defined as of index date*
History of bowel surgery	*Exclusion criteria 4*	*Panproctocolectomy, IPAA or ileostomy*
Gender	*Primary objective 7.2.1.a* CCI [redacted]	*Male/female*
Smoking status	*Primary objective 7.2.1.a* CCI [redacted]	*Current/ex-smoker/non-smoker/unknown*
BMI	*Primary objective 7.2.1.a* CCI [redacted]	*Derived from weight and height*
Weight	*Primary objective 7.2.1.a*	*kg*
Height	*Primary objective 7.2.1.a*	*cm*
Treating hospital	*Primary objective 7.2.1.a* CCI [redacted]	*name of treating hospital*
Mayo score	*Primary objective 7.2.1.c* *Secondary objectives 7.3.1.b, 7.3.1.c, 7.3.1.d, 7.3.1.e, 7.3.1.f, 7.3.1.i, 7.3.1.j, 7.3.1.k, 7.3.1.l, 7.3.1.o, 7.3.1.p.* CCI [redacted]	*Sum of "endoscopic findings", "stool frequency", Doctors assessment of disease severity" and "rectal bleeding"*
First UC diagnose	*Primary objective 7.2.1.b* *Inclusion criteria 2* CCI [redacted]	*Date*
Extent of colonic involvement	*Primary objective 7.2.1.b* CCI [redacted]	*Montreal classification: E1, E2 or E3*
Endoscopic findings	*Primary objective 7.2.1.c and 7.2.1.e.* *Secondary objective 7.3.1.m* CCI [redacted]	*0-3 (mayo score component)*

Variable	***Role***	***Operational definition***
Histological activity	*Primary objective 7.2.1.e* *Secondary objective 7.3.1.n* CCI	*Active disease (2) / inactive disease (1) /normal histology (0) / not determined*
Clinician's assessment of disease severity	*Primary objective 7.2.1.c* CCI	*0-3 (mayo score component)*
Stool frequency	*Primary objective 7.2.1.c* *Secondary objectives 7.3.1.r*	*0-3 (mayo score component)*
Rectal bleeding	*Primary objective 7.2.1.c* *Secondary objective 7.3.1.s*	*0-3 (mayo score component)*
Fecal calprotectin	*Primary objective 7.2.1.d,* *Secondary objectives 7.3.1.g and 7.3.1.h.* CCI	*mg/kg*
Plasma CRP	*Primary objective 7.2.1.d* *Secondary objective 7.3.1.t* CCI	*mg/L*
Blood hemoglobin	*Primary objective 7.2.1.d,* *Secondary objective 7.3.1.u* CCI	*g/L*
Blood leukocytes	*Primary objective 7.2.1.d* *Secondary objective 7.3.1.v* CCI	*cells/L*
Blood thrombocytes	*Primary objective 7.2.1.d* *Secondary objective 7.3.1.w* CCI	*cells/L*
Blood lymphocytes	*Primary objective 7.2.1.d* *Secondary objective 7.3.1.x* CCI	*cells/L*
Blood neutrophiles	*Primary objective 7.2.1.d* *Secondary objective 7.3.1.y* CCI	*cells/L*
Plasma albumin	*Primary objective 7.2.1.d* *Secondary objective 7.3.1.z* CCI	*g/L*
Tofacitinib dose	*Secondary objectives 7.3.1.a, 7.3.1.aa and 7.3.1.bb*	*mg*times/per day or "not on treatment"*
Colectomies	*Secondary objective 7.3.1.cc* CCI	*Date*
Type of healthcare contact	*Secondary objective 7.3.1.cc* CCI	*outpatient visit, remote contact, emergency visit or hospitalization*

Variable	*Role*	*Operational definition*
Prior IBD treatments ○ *corticosteroids* ○ *5-aminosalicylic acid (5-ASA)* ○ *azathioprine* ○ *6-mercaptopurine* ○ *methotrexate* ○ *cyclosporine* ○ *ustekinumab* ○ *vedolizumab* ○ *adalimumab* ○ *infliximab* ○ *golimumab*	*Secondary objective 7.3.2* CCI [redacted]	*Yes/no (For each treatment)*
Concomitant medications ○ *corticosteroids* ○ *5-ASA*	*Secondary objective 7.3.1.q,* CCI [redacted]	*product & dose*
Extraintestinal manifestations: arthralgia, arthritis, sacroiliitis, pyoderma gangrenosum, erythema nodosum, primary sclerosing cholangitis, uveitis, ankylosing spondylitis, aphthous stomatitis, psoriasis	CCI [redacted]	*Yes/no per pre-specified list*
Prior diagnoses	CCI [redacted]	*Yes/no per pre-specified list*
Death date or lost to follow up	*Used to define end of follow up*	*Date*

Further operational definitions from the collected data include:

Active disease:

- *An endoscopic Mayo sub-score of ≥2 or fecal-calprotectin (f-calpro) >250mg/kg.*

Clinical response:

- *A full Mayo score decrease of ≥3 points and a decrease of ≥30% from baseline, with a decrease of ≥1 point on the rectal bleeding sub score or an absolute rectal bleeding score of ≤1.*

- *A partial Mayo score (ie, Mayo score without endoscopic assessment) decrease of ≥2 points and reduction of at least 25% in partial Mayo (pMayo) score from baseline with an accompanying decrease in rectal bleeding sub score of ≥1 point or absolute rectal bleeding sub score of ≤1.*

Clinical remission:

- *A full Mayo score of ≤2 points with no individual sub score exceeding 1 point, with rectal bleeding sub-score of 0.*

- *A pMayo score <2 points with rectal bleeding sub-score of 0.*

Data source

This study relies on a secondary use of existing and available data in patient registers and patient charts in Finland. The data will be gathered from hospital patient information systems. All data in this study is collected from these patient information systems and made available in aggregated form for data-analysis.

2.2 STUDY OBJECTIVES

Primary objective - To Characterize the UC Patient Group Treated with Tofacitinib.

a. *Patient demographics at tofacitinib treatment initiation: age, gender, weight, height, smoking status, body mass index (BMI), treating hospital.*

b. *Disease characteristics: age at diagnosis, duration of disease, and extent of colonic involvement according to the Montreal classification: E1 (ulcerative proctitis), E2 (left sided, distal colitis), E3 (pancolitis).*

c. *Disease severity as assessed by Mayo score and f-calpro at the initiation of tofacitinib use.*

d. *Laboratory results for biochemical inflammatory markers plasma C-reactive protein (P-CRP), blood thrombocytes (B-thromb), plasma albumin (P-alb), blood leukocytes (B-leuk), blood lymphocytes (B-ly), blood neutrophiles (B-neutr), blood hemoglobin (B-hb) and f-calpro at the start of tofacitinib treatment (baseline data).*

e. *Endoscopic findings including histology at the start of tofacitinib treatment (baseline data).*

Secondary objective 1 - To Assess the Real-world Effectiveness of Tofacitinib.

a. *Proportion of patients who are taking tofacitinib at week 8, 16, 24 and 52.*

b. *To assess rates of clinical remission defined by a full or partial Mayo score at week 8, 16, 24 and 52.*

c. *To assess rates of clinical response defined by a full or partial Mayo score at week 8, 16, 24 and 52.*

   - *note, objectives b and c were formulated as "rates" in the protocol, whereas the goal is to report "proportion of patients" as in majority of the other effectiveness objectives*

d. *Proportion of patients in steroid-free clinical remission at weeks 8, 16, 24, and 52 as defined by full or partial Mayo who did not require any corticosteroid treatment during the period ≥4 weeks prior to the visit (for all patients and for those treated with corticosteroids at baseline).*

e. ~~*Proportion of patients reaching clinical response as defined by full or partial Mayo score at week 8, 16, 24 and 52.*~~

   - *note, objectives c and e were unintentional duplicates left in the protocol development*

f. *Time to response as assessed by a decrease as defined by full or partial Mayo score.*

g. *Proportion of responders defined by a f-calpro reduction of ≥50%, ≥75% or ≥90% at week 8, 16, 24 and 52 compared to baseline.*

h. *Proportion of patients reaching f-calpro below 250 mg/kg at week 8, 16, 24 and 52 of those that had f-calprotectin above 250 mg/kg at baseline and change from baseline in f-calpro at week 8, 16, 24 and 52.*

i. *Proportion of patients in sustained remission (pMayo and full Mayo score) from week 8 to week 16, 24 and 52.*

j. *Proportion of patients in sustained remission (pMayo and full Mayo score) from week 16 to week 24 and 52.*

k. *Proportion of patients in sustained steroid free remission (pMayo and full Mayo score) at week 16 to 24 and 52 (for all patients and for those treated with corticosteroids at baseline).*

l. *Change in partial and full Mayo score at weeks 8/16/24/52.*

m. *Proportion of patients in sustained endoscopic remission (sub score = 0), mucosal healing (sub score 0-1) or endoscopic response (sub score reduction from baseline of ≥1) from week 8 to week 16, 24 and 52.*

n. *Proportion of patients in physician assessed histological remission determined as inactive disease, or normal histology, and change from baseline in histology assessment (0= normal histology, 1= inactive disease and 2 = active disease) at week 8/16/24/52.*

o. *Proportion of patients in sustained steroid free remission (pMayo and full Mayo score) (for all patients and for those treated with corticosteroids at baseline) and endoscopic remission (sub score = 0), mucosal healing (sub score 0-1) or endoscopic response (sub score reduction from baseline of ≥1) from week 8 to week 16, 24 and 52.*

p. *Comparison of response and remission (pMayo and full Mayo score) based on the extent of colonic involvement.*

~~q. *Proportion of patients with corticosteroid tapering at weeks 8/16/24/52 and their tapering rates and doses.*~~

- *note after further discussions, the data required for objective q might not be present in the available medical records and/or prescriptions*

r. *Proportion of patients with improvement in stool frequency sub score of 1 or more points and change from baseline in stool frequency sub score at week 8, 16, 24 and 52.*

s. *Proportion of patients with improvement in rectal bleeding sub score of 1 or more points and change from baseline in rectal bleeding sub score at week 8, 16, 24 and 52.*

t. *Proportion of patients reaching normal P-CRP levels (below 4mg/L) and change from baseline in P-CRP levels at week 8/16/24/52.*

u. *Proportion of patients reaching normal B-hb levels (men: 134–167 g/L, women: 117–155 g/L) and change from baseline in B-hb levels at week 8/16/24/52.*

v. *Proportion of patients reaching normal B-leuk levels (3.4-8.2 x 10^9/L) and change from baseline in B-leuk levels at week 8/16/24/52.*

w. *Proportion of patients reaching normal B-Thromb (150–360 x 10^9/L) and change from baseline in B-Thromb levels at week 8/16/24/52.*

x. *Proportion of patients reaching normal B-ly (1.3-3.6 x 10^9/L) and change from baseline in B-ly levels at week 8/16/24/52.*

y. *Proportion of patients reaching normal B-neutr (1.5-6.7 x 10^9/L) and change from baseline in B-neutr levels at week 8/16/24/52.*

z. *Proportion of patients reaching normal P-alb (18-39 years: 36-48 g/L, 40-69 years: 36-45 g/L, 70 years and over: 34-45 g/L) and change from baseline in P-alb levels at week 8/16/24/52.*

aa. *Proportion of patients with extended tofacitinib induction dose (additional 8 weeks with 10mg).*

bb. *Real-world dosing of tofacitinib, e.g., usage of a higher dose (10 mg) as maintenance therapy.*

cc. *Survival without drug discontinuation, colectomy or UC-related hospitalization (using time to event analysis).*

Secondary objective 2 - To Assess Treatment Lines Prior to Tofacitinib Treatment.

a. *Number and type of previous UC treatments.*

CCI [redacted]

CCI [redacted]

[redacted]

CCI [redacted]

CCI [redacted]

3 HYPOTHESES AND DECISION RULES

There is no a priori hypotheses to be tested. All analyses are descriptive in nature, and there is no comparison between groups.

3.1 STATISTICAL HYPOTHESES

There is no a priori hypotheses to be tested. All analyses are descriptive in nature, and there is no comparison between groups.

3.2 STATISTICAL DECISION RULES

The alpha level will be 0.05, 2-sided. No adjustments for multiple comparisons will be made.

CCI [redacted]

4 ANALYSIS SETS/POPULATIONS

4.1 FULL ANALYSIS SET

Full analysis set includes all patients fulfilling inclusion criteria, and not excluded due to exclusion criteria.

1. Xeljanz® (tofacitinib) usage for ulcerative colitis.
2. Diagnosis of ulcerative colitis (ICD-10: K51.0, K51.1, K51.2, K51.3, K51.5, K51.8, K51.9) between January 2010 and December 2021 (incident or prevalent).

Patients will be excluded if:

1. Age <18 years at the start of tofacitinib use.
2. Use of tofacitinib before reimbursement (01 Mar 2019).
3. < 8 weeks of treatment with tofacitinib at the start of data mining.
4. History of panproctocolectomy, IPAA or ileostomy.

4.2 SAFETY ANALYSIS SET

NA

4.3 OTHER ANALYSIS SET

NA

4.4 SUBGROUPS

CCI [redacted]

5 ENDPOINTS AND COVARIATES

5.1 EFFICACY/EFFECTIVENESS ENDPOINT(S)

- Proportion of patients who are taking tofacitinib at week 8, 16, 24 and 52
- Rate of clinical remission
- Rate of clinical response
- Proportion of patients in steroid-free clinical remission
- Proportion of patients reaching clinical response
- Time to response
- Proportion of responders defined by a f-calpro reduction of ≥50%, ≥75% or ≥90%
- Proportion of patients reaching f-calpro below 250 mg/kg of those that had f-calprotectin above 250 mg/kg at baseline
    - change from baseline in f-calpro
- Proportion of patients in sustained remission (pMayo and full Mayo score) from week 8 to week 16, 24 and 52
- Proportion of patients in sustained remission (pMayo and full Mayo score) from week 16 to week 24 and 52
- Proportion of patients in sustained steroid free remission (pMayo and full Mayo score) at week 16 to 24 and 52 (for all patients and for those treated with corticosteroids at baseline).
- Change in partial and full Mayo score
- Proportion of patients in sustained endoscopic remission (sub score = 0), mucosal healing (sub score 0-1) or endoscopic response (sub score reduction from baseline of ≥1) from week 8 to week 16, 24 and 52
- Proportion of patients in physician assessed histological remission determined as inactive disease
    - change from baseline in histology assessment

- Proportion of patients in sustained steroid free remission (pMayo and full Mayo score) (for all patients and for those treated with corticosteroids at baseline) and endoscopic remission (sub score = 0), mucosal healing (sub score 0-1) or endoscopic response (sub score reduction from baseline of ≥1) from week 8 to week 16, 24 and 52
- Proportion of patients with corticosteroid tapering
    - tapering rates and doses
- Proportion of patients with improvement in stool frequency sub score of 1 or more points
    - change from baseline in stool frequency sub score
- Proportion of patients with improvement in rectal bleeding sub score of 1 or more points
    - change from baseline in rectal bleeding sub score
- Proportion of patients reaching normal P-CRP/ B-hb/ B-leuk/ B-Thromb/ B-ly/ B-neutr/ P-alb levels
    - and change from baseline levels
- Proportion of patients reaching normal B-hb levels
    - change from baseline in B-hb levels
- Proportion of patients with extended tofacitinib induction dose (additional 8 weeks with 10mg).
- Real-world dosing of tofacitinib
- Survival without drug discontinuation, colectomy or UC-related hospitalization

5.2 SAFETY ENDPOINTS

NA

5.3 OTHER ENDPOINTS

NA

5.4 COVARIATES

See table 1 for variables to be collected with their operational definitions.

6 HANDLING OF MISSING VALUES

No imputation for missing values will be performed. Proportion of missing values will be reported where appropriate.

7 STATISTICAL METHODOLOGY AND STATISTICAL ANALYSES

7.1 STATISTICAL METHODS

General:

Means, medians, and standard deviations, and 25% and 75% quartiles will be provided for continuous variables when performing descriptive analysis of continuous data. Numbers and percentages will be provided for dichotomous and polychotomous variables when performing descriptive analysis of categorical data.

Serial measures collected will be handled by "carry forward imputation", i.e. the latest value will be assumed unchanged until otherwise proven. Thus for each timepoint, the latest available measure will be used. Patients will be censored from the study post the last available contact/data entry. Missing values will not be imputed.

An unadjusted Kaplan Meier curve will be drawn to illustrate time-to-event and to estimate medians for time-to-event outcomes.

CCI [redacted]

All data analysis will be executed using R, a language and environment for statistical computing and graphics, version 4.0.3 or later in Rstudio environment.

7.2 STATISTICAL ANALYSES

Primary objectives a-e:

Describe the patient population at the baseline (initiation of tofacitinib), using the data collected. For each continuous variables (age, BMI, age at diagnosis, duration of disease, laboratory measures), provide the mean, median, sd, 25%Q and 75%Q values. For categorical variables (sex, smoking status, extent of colonic involvement, disease severity, endoscopic findings), report the number of patients, and proportion. Report proportion of missing values if present.

Secondary objective - Assess the Real-world Effectiveness of Tofacitinib

Secondary objective a:
For each patient, define the "on treatment" as Yes/No based on the latest available dose (at each timepoint 8, 16, 24 and 52 weeks). Patients marked with "not on treatment" prior to timepoint will be regarded as discontinued.
Report the proportion of patients on treatment, not censored at each timepoint.

Secondary objectives b, c, d, e, g, n:
For each patient, define the fulfilment of the remission/response criteria as Yes/No based on the latest available data (at each timepoint 8, 16, 24 and 52 weeks).
Report the proportion of patients on fulfilling the response/remission criteria, not censored at each timepoint.

Secondary objective f:
Define the time of response for each patient as first ever data-entry that fulfils response criteria. Fit competing-risk time-to-event model to the data, with time-to-event defined as time from index until response (event) or discontinuation (competing event), or end of data collection (censoring event).
Assess the cumulative incidence as function of time for both types of events. Illustrate the Aalen-Johansen state probabilities of multistate model.

Secondary objective h:
Select only patients with baseline f-calprotectin above 250 mg/kg at baseline. For each subsequent f-calprotectin measure, define below 250 mg/kg as Yes/No variable. Additionally, estimate the absolute delta change per baseline value.
For each timepoint (week 8, 16, 24 and 52), report the proportion of patients on fulfilling the <250mg/kg criteria, and summary statistics (mean, median, sd, 25%Q and 75%Q) of delta change, among patients not censored at each timepoint.

Secondary objectives i, j, k, m, o:
Select only patients that were on remission/steroid free remission at the timepoints. For each patient, define the fulfilment of the remission/response criteria as Yes/No based on the latest available data (at each timepoint 16, 24 and 52 weeks). Report the proportion of patients on fulfilling the remission criteria, not censored at each timepoint.

Secondary objective l:
For each available Mayo score (full or partial), estimate the absolute delta change from baseline value. For each timepoint (week 8, 16, 24 and 52), report the summary statistics (mean, median, sd, 25%Q and 75%Q) of delta change, among patients not censored at each timepoint.

Secondary objective p:
Perform analyses described in secondary objective b and c, stratified by the extent of colonic involvement

Secondary objective q:
For each patient, define the corticosteroid tapering as Yes/No based on the latest available data (at each timepoint 8, 16, 24 and 52 weeks). Additionally, define the tapering rates and doses based on latest available data.
For each timepoint (week 8, 16, 24 and 52), report the proportion of patients that had corticosteroid tapered, among patients not censored at each timepoint. Additionally,

report summary statistics (mean, median, sd, 25%Q and 75%Q) of tapering rates and doses among patients that had corticosteroids tapered.

Secondary objectives r and s:
For each patient, define the fulfilment of the improvement criteria as Yes/No based on the latest available data (at each timepoint 8, 16, 24 and 52 weeks). Additionally, estimate the absolute delta change per baseline value
Report the proportion of patients on fulfilling the response/remission criteria, report the summary statistics (mean, median, sd, 25%Q and 75%Q) of delta change, among patients not censored at each timepoint.

Secondary objectives t-z:
For each subsequent laboratory measure, define "normal-level" as Yes/No variable. Additionally, estimate the absolute delta change per baseline value. For each timepoint (week 8, 16, 24 and 52), report the proportion of patients on fulfilling the "normal-level" criteria and summary statistics (mean, median, sd, 25%Q and 75%Q) of delta change, among patients not censored at each timepoint.

Secondary objective aa:
Report the proportion of patients that received extended induction

Secondary objective bb:
For each subsequent visit, define the higher (10mg) dosing as Yes/No variable. For each timepoint (week 8, 16, 24 and 52), report the proportion of patients, among patients not censored at each timepoint.

Secondary objective cc:
Create composite endpoint of drug discontinuation, colectomy or UC-hospitalization, with time of the event as earliest of the aforementioned. Analyse time to event using Kaplan-Meier fit, where time to event is defined as time from index until composite endpoint (event) or time of data collection (censoring event).
Plot the Kaplan-Meier fit with the 95% CI and report the median survival if reached.

Secondary objective - Assess Treatment Lines Prior to Tofacitinib Treatment

Secondary objective a:
Summarize and tabulate types of previous UC treatments. Report N and proportion of patients that had corresponding treatment recorded.
Report the summary statistics (mean, median, sd, 25%Q and 75%Q) of number of treatments prior to tofacitinib if feasible.

CCI [redacted]

[redacted]

CCI [redacted]

CCI [redacted]

CCI [redacted]

CCI [redacted]

7.2.1 Safety Analyses

NA

8 TABLE SHELLS

Table 2: Table shell for patient characteristics for primary objective

Variable	categories	mean (sd)	Median (25Q-75Q)	n (%)	missing %
age				-	
sex	male	-	-		
	female	-	-		
weight				-	
height				-	
(BMI)				-	
smoking	current	-	-		
	ex-smoker	-	-		
	non-smoker	-	-		
age at UC diagnosis				-	
duration of UC				-	
Montreal classification	E1	-	-		
	E2	-	-		
	E3	-	-		
Mayo-score				-	
F-calpro				-	
P-CRP				-	
B-thromb				-	
P-alb				-	
B-leuk				-	
B-ly				-	
B-neutr				-	
B-hb				-	
Endoscopic findings	yes	-	-		
	no	-	-		

Table 3: Table shell for outcome objectives

Objective	Outcome	Week 8	Week 16	week 24	week 52
-	N patients	N	N	N	N
P1 - a	Proportion of patients on treatment	n (%)	n (%)	n (%)	n (%)
P1 - b	Proportion of patients with clinical remission (full Mayo)	n (%)	n (%)	n (%)	n (%)
P1 - b	Proportion of patients with clinical remission (partial Mayo)	n (%)	n (%)	n (%)	n (%)
P1 - c	Proportion of patients with clinical response (partial Mayo)	n (%)	n (%)	n (%)	n (%)
P1 - c	Proportion of patients with clinical response (full Mayo)	n (%)	n (%)	n (%)	n (%)
P1 - d	Proportion of patients with steroid free clinical remission	n (%)	n (%)	n (%)	n (%)
P1 - g	Proportion of patients with f-calpro reduction ≥50%	n (%)	n (%)	n (%)	n (%)
P1 - g	Proportion of patients with f-calpro reduction ≥75%	n (%)	n (%)	n (%)	n (%)
P1 - g	Proportion of patients with f-calpro reduction ≥90%	n (%)	n (%)	n (%)	n (%)
P1 - h	Proportion of patients reaching f-calpro below 250 mg/kg, of those that had f-calprotectin above 250 mg/kg at baseline	n (%)	n (%)	n (%)	n (%)
P1 - h	Change in f-calpro, among patients with f-calprotectin above 250 mg/kg at baseline	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)

Objective	Outcome	Week 8	Week 16	week 24	week 52
P1 - i	Proportion of patients in sustained remission (pMayo) from week 8	-	n (%)	n (%)	n (%)
P1 - i	Proportion of patients in sustained remission (full Mayo score) from week 8	-	n (%)	n (%)	n (%)
P1 - j	Proportion of patients in sustained remission (pMayo) from week 16	-	-	n (%)	n (%)
P1 - j	Proportion of patients in sustained remission (full Mayo score) from week 16	-	-	n (%)	n (%)
P1 - k	Proportion of patients in sustained steroid free remission (pMayo) from week 16	-	-	n (%)	n (%)
P1 - k	Proportion of patients in sustained steroid free remission (full Mayo score) from week 16	-	-	n (%)	n (%)
P1 - l	Change in partial Mayo score	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - l	Change in full Mayo score	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - m	Proportion of patients in sustained endoscopic remission (sub score = 0), mucosal healing (sub score 0-1) or endoscopic response (sub score reduction from baseline of ≥1) from week 8	-	n (%)	n (%)	n (%)

Objective	Outcome	Week 8	Week 16	week 24	week 52
P1 - n	Proportion of patients in physician assessed histological remission determined as inactive disease, or normal histology, and change from baseline in histology assessment (0= normal histology, 1= inactive disease and 2 = active disease)	n (%)	n (%)	n (%)	n (%)
P1 - o	Proportion of patients in sustained steroid free remission (pMayo and full Mayo score) (for all patients and for those treated with corticosteroids at baseline) and endoscopic remission (sub score = 0), mucosal healing (sub score 0-1) or endoscopic response (sub score reduction from baseline of ≥1) from week 8	-	n (%)	n (%)	n (%)
P1 - q	Proportion of patients with corticosteroid tapering	n (%)	n (%)	n (%)	n (%)
P1 - q	Corticosteroid tapering rates	mean ± sd	mean ± sd	mean ± sd	mean ± sd
P1 - q	Corticosteroid tapering doses	mean ± sd	mean ± sd	mean ± sd	mean ± sd
P1 - r	Proportion of patients with improvement in stool frequency sub score of 1 or more points and change from baseline in stool frequency sub score	n (%)	n (%)	n (%)	n (%)

Objective	Outcome	Week 8	Week 16	week 24	week 52
P1 - s	Proportion of patients with improvement in rectal bleeding sub score of 1 or more points	n (%)	n (%)	n (%)	n (%)
P1 - s	change from baseline in rectal bleeding sub score	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - t	Proportion of patients reaching normal P-CRP levels (below 4mg/L)	n (%)	n (%)	n (%)	n (%)
P1 - t	change from baseline in P-CRP levels	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - u	Proportion of patients reaching normal B-hb levels (men: 134–167 g/L, women: 117–155 g/L)	n (%)	n (%)	n (%)	n (%)
P1 - u	change from baseline in B-hb levels	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - v	Proportion of patients reaching normal B-leuk levels (3.4-8.2 x 10^9/L)	n (%)	n (%)	n (%)	n (%)
P1 - v	change from baseline in B-leuk levels	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - w	Proportion of patients reaching normal B-Thromb (150–360 x 109/L)	n (%)	n (%)	n (%)	n (%)
P1 - w	change from baseline in B-Thromb levels	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)

Objective	Outcome	Week 8	Week 16	week 24	week 52
P1 - x	Proportion of patients reaching normal B-ly (1.3-3.6 x 109/L)	n (%)	n (%)	n (%)	n (%)
P1 - x	change from baseline in B-ly levels	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - y	Proportion of patients reaching normal B-neutr (1.5-6.7 x 109/L)	n (%)	n (%)	n (%)	n (%)
P1 - y	change from baseline in B-neutr levels	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - z	Proportion of patients reaching normal P-alb (18-39 years: 36-48 g/L, 40-69 years: 36-45 g/L, 70 years and over: 34-45 g/L)	n (%)	n (%)	n (%)	n (%)
P1 - z	change from baseline in P-alb levels	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)	Δ-from baseline (mean ± sd)
P1 - bb	Proportion of patients with higher dose (10mg) of tofacitinib	n (%)	n (%)	n (%)	n (%)

Table 4: table shell to repost previous treatments

	Value
Number of treatments	mean ± sd
corticosteroids	n (%)
5-ASA	n (%)
Azathioprine	n (%)
6-Merkatopurin	n (%)
Methotrexate	n (%)
Cyclosporine	n (%)
Ustekinumab	n (%)
Vedolizumab	n (%)
Adalimumab	n (%)
Infliximab	n (%)
Golimumab	n (%)

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