CELLTRION Inc.
CT-P13 3.7

A Randomized, Placebo Controlled, Double-Blind, Phase 3 Study to Evaluate the Efficacy and Safety of the Subcutaneous Injection of CT-P13 (CT-P13 SC) as Maintenance Therapy in Patients with Moderately to Severely Active Ulcerative Colitis

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Statistical Analysis Plan

Final Version 1.0

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Upon review of this document, including table, listing and figure shells, the undersigned approves the final statistical analysis plan. The analysis methods and data presentation are acceptable, and the table, listing and figure production can begin.

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List of Abbreviations

Abbreviation	Definition
ADA	Anti-Drug Antibody
ADE	Adverse Device Effect
ADR	Adverse Drug Reaction
AE	Adverse Event
ANCOVA	Analysis of Covariance
ATC	Anatomical Therapeutic Chemical
BLQ	Below the Lower Limit of Quantification
BMI	Body Mass Index
CI	Confidence Interval
C_{max}	Observed Maximum Serum Concentration
CRP	C-Reactive Protein
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
C_{trough}	Trough Concentration
CT-P13	Infliximab (CELLTRION, Inc.)
CV%	Percent Coefficient of Variation
DRM	Data Review Meeting
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EOS	End-of-Study
ESR	Erythrocyte Sedimentation Rate
FC	Fecal Calprotectin
FDA	United States Food and Drug Administration
HBcAb	Hepatitis B Core Antibody
HBsAb	Hepatitis B Surface Antibody
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HLGT	High Level Group Term
HLT	High Level Term
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IGRA	Interferon Gamma Release Assay
IRR	Infusion-Related Reaction
ISR	Injection Site Reaction
ITT	Intent-to-treat
IWRS	Interactive Web Response System
JAK	Janus kinase
LLN	Lower Limit of Normal
LLT	Lowest Level Term
LLoQ	Lower Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
N/A	Not Applicable
Nab	Neutralizing Antibody
NCA	Non-compartmental Analysis
NRR	Not Reported Result

NYHA	New York Heart Association
PD	Pharmacodynamic
PFS	Pre-filled Syringe
PK	Pharmacokinetic
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
[redacted]	[redacted]
SC	Subcutaneous
SD	Standard Deviation
SE	Standard Error
SI	System International
SIBDQ	Short Inflammatory Bowel Disease Questionnaire
SIR	Systemic Injection Reaction
SOC	System Organ Class
SUSAR	Suspected Unexpected Serious Adverse Reaction
TB	Tuberculosis
TEAE	Treatment-Emergent Adverse Event
TESAE	Treatment-Emergent Serious Adverse Event
TLF	Table, Listing and Figure
UC	Ulcerative Colitis
ULN	Upper Limit of Normal
VAS	Visual Analogue Scale
WHO	World Health Organization

1. ADMINISTRATIVE STRUCTURE

This study is being conducted under the sponsorship of CELLTRION, Inc (hereinafter referred to as "CELLTRION"). The clinical monitoring, medical writing and bioanalytical lab analysis are being performed under contract with [redacted], in collaboration with CELLTRION. Endoscopic image analysis is being performed under contract with [redacted], in collaboration with CELLTRION. Pharmacokinetics analysis is being performed under contract with [redacted], in collaboration with CELLTRION. The data management and statistical analysis are being performed by CELLTRION.

2. INTRODUCTION

This statistical analysis plan (SAP) defines the statistical methods and data presentations to be used by CELLTRION Clinical Statistics team in the analysis and presentation of data for CELLTRION study number CT-P13 3.7, entitled as "A Randomized, Placebo-Controlled, Double-Blind, Phase 3 Study to Evaluate the Efficacy and Safety of the Subcutaneous Injection of CT-P13 (CT-P13 SC) as Maintenance Therapy in Patients with Moderately to Severely Active Ulcerative Colitis".

The following clinical study reports (CSR) will be generated during the entire study period:

- A report of all data for each patient up to Week 54. The following data will be included.

	Ongoing at Week 54	**Withdrawal on or before Week 54**
Scheduled Visit (excluding EOS)	Up to Week 54	All available data
EOS	Not Applicable	All available data up to the latest date of all patients' Week 54 visit date.
Unscheduled Visit	On or before Week 54 visit date for each patient*	
Non-visit based data (e.g. adverse events and medications)	All available data having a start date/or imputed start date on or before the Week 54 visit date for each patient*.	

* For patients who are ongoing and skip the Week 54 visit, the latest of the Week 54 visit date for other patients will be used instead of the Week 54 visit date for each patient.
Note: Exceptionally, the endoscopic and/or histologic data that is performed between Week 54 and Week 56 study drug administration date could be included in the analysis as a result at Week 54 based on determination during the blinded DRM.

- A report of all data for each patient after completion of all visits

This SAP covers all specified analysis and is based on the following documents:

- Study Protocol Version 5.0 – 4th August 2020
- Study Protocol Version 5.0 Country specific A.0 – 7th August 2020
- Study Protocol Version 5.0 Country specific B.0 – 7th August 2020
- Study Protocol Version 5.0 Country specific C.0 – 7th August 2020
- Unique Case Report Form (CRF) Version 2.2 – 21st August 2020

Table, Listing and Figure (TLF) mock shells will be presented as an addendum to this document.

3. STUDY OBJECTIVES

Primary, secondary and exploratory objectives are described as below.

3.1. Primary Objective

The primary objective of this study is to demonstrate superiority of CT-P13 subcutaneous (SC) over Placebo SC based on clinical remission at Week 54.

3.2. Secondary Objective

The secondary objective of this study is to evaluate additional efficacy, PK, PD, and overall safety including immunogenicity.

3.3. Exploratory Objective

The exploratory objective of this study is to evaluate additional efficacy.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a randomized, placebo controlled, double-blind, multicenter, parallel-group, Phase 3 study to evaluate the efficacy, PK, PD, and safety of the SC injection of CT-P13 (CT-P13 SC) as maintenance therapy in patients with moderately to severely active Ulcerative colitis (UC) who have had an inadequate response to conventional therapy. Approximately 615 patients with moderately to severely active UC will be enrolled in the open-label Induction Phase. All enrolled patients will receive induction doses of CT-P13 5 mg/kg via IV infusion at Weeks 0, 2, and 6. After the patients receive 3 full doses of CT-P13 via IV infusion, those patients classified as a clinical responder at Week 10 based on modified

Mayo score without physician global assessment (PGA) subscore, and also have no safety concerns at the investigator's discretion will be randomly assigned before Week 10 treatment in a 2:1 ratio into either CT-P13 SC or Placebo SC treatment groups. Patients classified as non-responders at Week 10 will not continue the study drug treatment. A clinical responder at Week 10 is defined as a patient with a decrease in modified Mayo score from baseline of at least 2 points and at least 30%, with an accompanying decrease in the rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1 point.

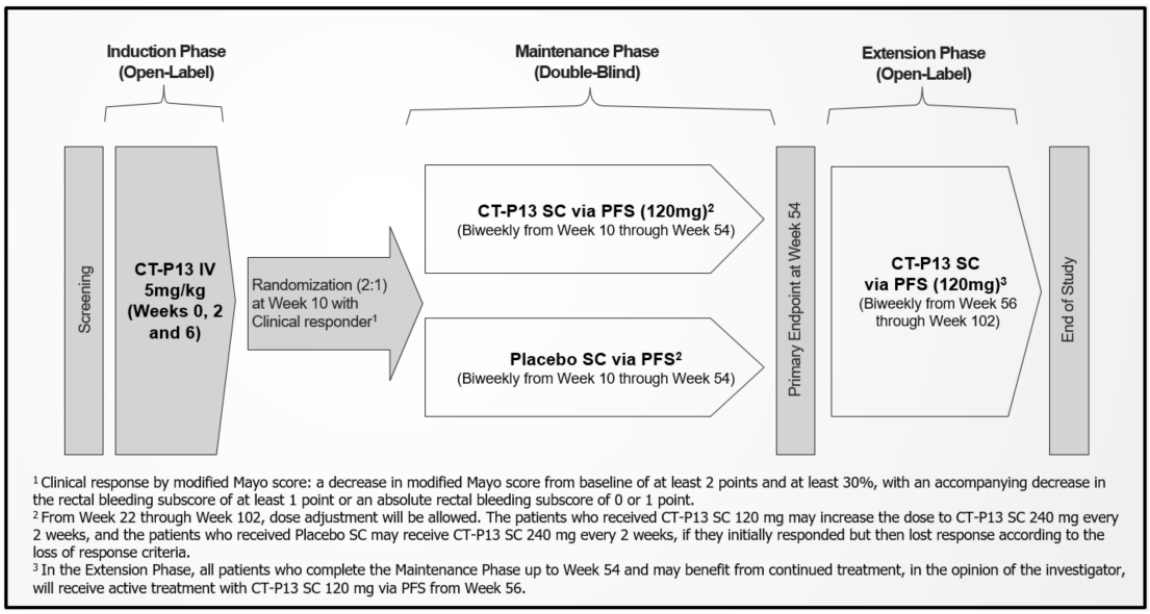
It is estimated that at least 417 patients (278 in CT-P13 SC group and 139 in Placebo SC group) will enter the double-blind Maintenance Phase. The Maintenance Phase treatment will continue up to Week 54 and the subsequent open-label Extension Phase treatment will continue up to Week 102. In the open-label Extension Phase, all patients will receive CT-P13 SC.

The duration of the study will be up to 112 weeks, which includes Screening (up to 6 weeks) and Treatment Period (up to the last dosing visit of study drug at Week 102) followed by End-of-Study (EOS) visit (after 4 weeks off-dose period).

The study will be unblinded to the predefined unblinded teams of CELLTRION and [redacted] for reporting purposes after completion of the Week 54 assessments in all patients. However, the treatment assignment for the Maintenance Phase will remain blinded to the investigators, patients, and other teams of CELLTRION and [redacted] until the completion of the study.

The overview of study design is presented in Figure 1.

Figure 1. Study Design Overview



Abbreviations: IV, intravenous; PFS, pre-filled syringe; SC, subcutaneous

This study will comprise 3 study periods including Screening, Treatment Period (Induction Phase, Maintenance Phase, and Extension Phase), and EOS visit.

Screening: Screening will take place between Days –42 and 0 (up to 6 weeks) prior to the first CT-P13 IV infusion during the Induction Phase.

Treatment Period:

- Open-label Induction Phase (dosing at Weeks 0, 2, and 6)
- Double-blind Maintenance Phase (dosing from Week 10 through Week 54)
- Open-label Extension Phase (dosing from Week 56 through Week 102)

In the open-label Induction Phase, the patients who meet all of the inclusion criteria and none of the exclusion criteria will be enrolled on Day 0 (Week 0). All enrolled patients will receive a 2-hour CT-P13 IV infusion (5 mg/kg) during onsite visits at Weeks 0, 2, and 6 as induction treatments. At Week 8, only endoscopy and biopsy for histologic assessment will be performed for the evaluation of Mayo score and endoscopic-histologic mucosal improvement at Week 10. The endoscopy result at Week 8 will be used for randomization at Week 10. Patients who are classified as a clinical responder at Week 10 based on modified Mayo score after receiving 3 full doses of CT-P13 via IV infusion and for whom there are no safety concerns based on the investigator's discretion will be randomly assigned to receive either CT-P13 SC or Placebo SC, before treatment on Day 70

(Week 10). A clinical responder at Week 10 is defined as a patient with a decrease in modified Mayo score from baseline of at least 2 points and at least 30%, with an accompanying decrease in the rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1 point.

The randomization of treatment assignment will be stratified by the following:

- Previous exposure to biologic agent and/or Janus kinase (JAK) inhibitors (used or not used)
- Use of treatment with oral corticosteroids at Week 0 (used or not used)
- Clinical remission at Week 10 (remitter or non-remitter by modified Mayo score)

The double-blind Maintenance Phase will consist of further doses of CT-P13 SC or Placebo SC with the last dose administered no later than Week 54.

- Treatment group 1, CT-P13 SC: from Week 10, CT-P13 SC 120 mg will be administered every 2 weeks via Pre-filled syringe (PFS) through Week 54.
- Treatment group 2, Placebo SC: from Week 10, Placebo SC (matching volume to CT-P13 SC 120 mg) will be administered every 2 weeks via PFS through Week 54.

In the open-label Extension Phase, all patients who complete the Maintenance Phase up to Week 54 and may benefit from continued treatment in the opinion of the investigator, will receive active treatment with CT-P13 SC 120 mg via PFS from Week 56. The patients who received the adjusted dose of CT-P13 SC 240 mg in the Maintenance Phase will continue receiving the same doses of CT-P13 SC for the study treatment in the Extension Phase. The Extension Phase will continue up to Week 102.

From Week 22 through Week 102, dose adjustment will be allowed as follows:

- The patients who received CT-P13 SC 120 mg may increase the dose to CT-P13 SC 240 mg (double injection [2 shots] of CT-P13 SC 120 mg) every 2 weeks, if patients initially responded but then lost response according to the loss of response criteria.
- The patients who received Placebo SC may receive CT-P13 SC 240 mg (double injection [2 shots] of CT-P13 SC 120 mg) every 2 weeks, if patients initially responded but then lost response according to the loss of response criteria.

Loss of response is defined as follows: an increase in modified Mayo score ≥ 2 points and ≥ 30% from the Week 10 modified Mayo score with actual value of ≥ 5 points, and endoscopic subscore of ≥ 2 points.

On the day of initiation of dose adjustment, blood samples for PK and immunogenicity analysis will be collected before study drug administration. The patients whose dose was adjusted to CT-P13 SC 240 mg prior to Week 54 will be considered as non-remitter or non-responder at Week 54 in the analysis of the primary endpoint and key secondary endpoints.

Patients may also be premedicated 30 to 60 minutes prior to the start of infusion of CT-P13 IV and any premedications such as, but not limited to, antihistamine (at equivalent dose of 2 to 4 mg of chlorpheniramine), hydrocortisone, paracetamol, and/or nonsedating antihistamine (at equivalent dose of 10 mg of cetirizine) can be given at the investigator's discretion. The patients who receive CT-P13 SC or Placebo SC may also be treated with premedications at the investigator's discretion.

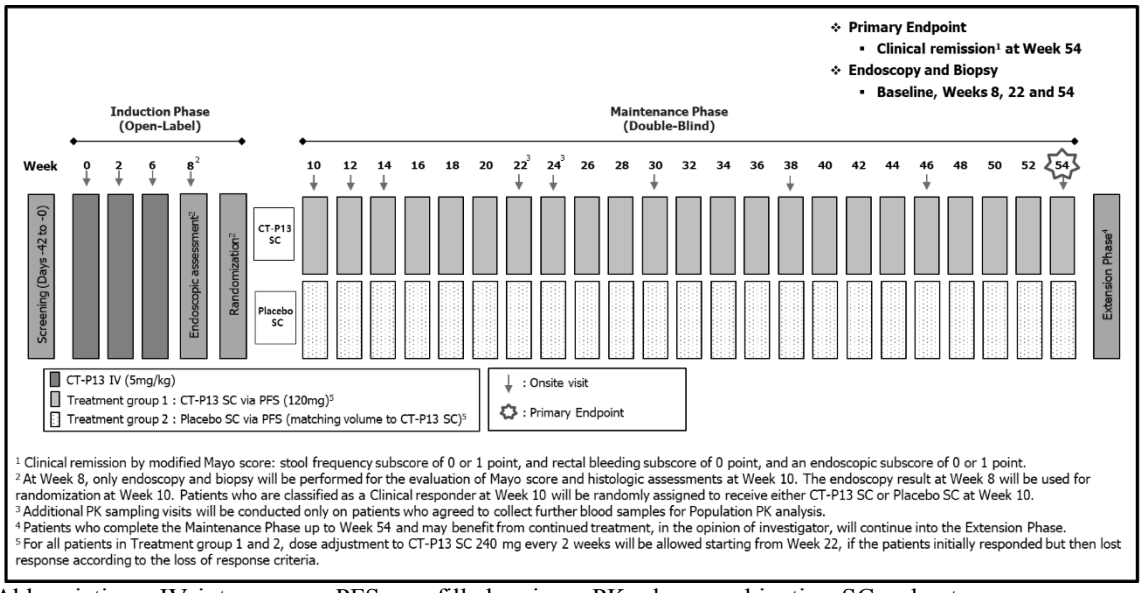
Patients will comply with all appropriate visits and assessments. Patients will return to the study center at predefined time intervals for clinical assessments and blood sampling. At each visit, patients will be questioned about adverse events (AEs) and concomitant medications and will be monitored for the clinical signs and symptoms of tuberculosis (TB) and/or cardiovascular disease. The efficacy, PK, PD, and safety assessments will be performed at the time points specified in the schedule of events (Appendix 1-1 and Appendix 1-2).

The CT-P13 SC or Placebo SC via PFS will be injected by the investigator or designee at Weeks 10 and 12, or until the patient (or caregiver, if needed) is properly trained and confident to administer the study drug at home, or until the investigator considers patient self-injection (or injection by caregiver, if needed) is appropriate. After proper training in PFS injection technique, patients (or caregiver, if needed) may self-inject with CT-P13 SC or Placebo SC via PFS at home or the study center at the scheduled administration week if their investigator determines that it is appropriate. CT-P13 SC or Placebo SC via PFS can be administered by another person, such as a family member or friend who is trained properly by the investigator or designee.

End-of-Study visit: The EOS visit will occur 4 weeks after the last dose of study drug is received. For patients who early discontinue the study drug before administration of CT-P13 SC or Placebo SC at Week 10, the EOS visit will occur 8 weeks after the last dose of CT-P13 IV is received.

The study design for each treatment phase is illustrated in Figure 2 and Figure 3.

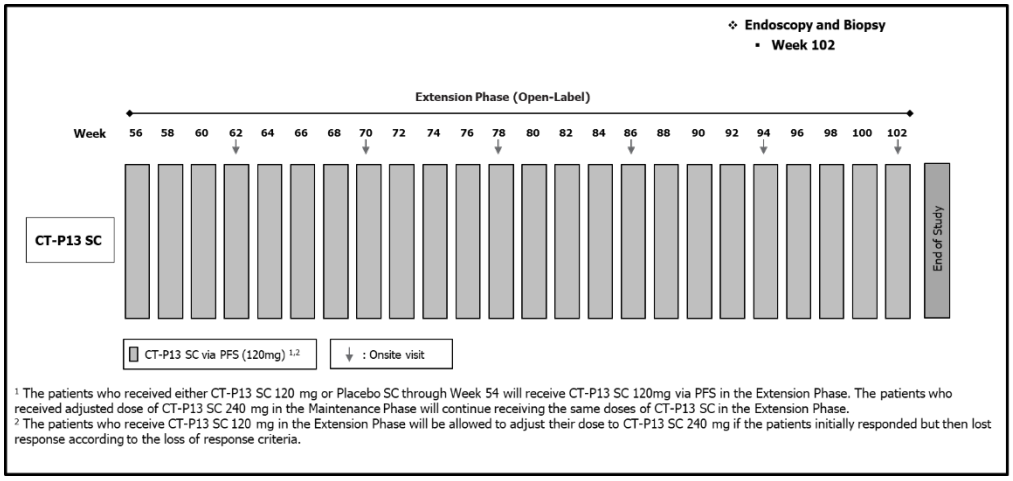
Figure 1. Study Design for Induction and Maintenance Phase



[1] Clinical remission by modified Mayo score: stool frequency subscore of 0 or 1 point, and rectal bleeding subscore of 0 point, and an endoscopic subscore of 0 or 1 point.
[2] At Week 8, only endoscopy and biopsy will be performed for the evaluation of Mayo score and histologic assessments at Week 10. The endoscopy result at Week 8 will be used for randomization at Week 10. Patients who are classified as a Clinical responder at Week 10 will be randomly assigned to receive either CT-P13 SC or Placebo SC at Week 10.
[3] Additional PK sampling visits will be conducted only on patients who agreed to collect further blood samples for Population PK analysis.
[4] Patients who complete the Maintenance Phase up to Week 54 and may benefit from continued treatment, in the opinion of investigator, will continue into the Extension Phase.
[5] For all patients in Treatment group 1 and 2, dose adjustment to CT-P13 SC 240 mg every 2 weeks will be allowed starting from Week 22, if the patients initially responded but then lost response according to the loss of response criteria.

Abbreviations: IV, intravenous; PFS, pre-filled syringe; PK, pharmacokinetics; SC, subcutaneous

Figure 3. Study Design for Extension Phase



[1] The patients who received either CT-P13 SC 120 mg or Placebo SC through Week 54 will receive CT-P13 SC 120mg via PFS in the Extension Phase. The patients who received adjusted dose of CT-P13 SC 240 mg in the Maintenance Phase will continue receiving the same doses of CT-P13 SC in the Extension Phase.
[2] The patients who receive CT-P13 SC 120 mg in the Extension Phase will be allowed to adjust their dose to CT-P13 SC 240 mg if the patients initially responded but then lost response according to the loss of response criteria.

Abbreviations: PFS, pre-filled syringe; SC, subcutaneous

5. GENERAL STATISTICAL CONSIDERATIONS

Continuous data will be summarized by using descriptive statistics: the number of observations (n), mean, standard deviation (SD), median, minimum and maximum unless otherwise specified. The descriptive statistics will be calculated using raw data before rounding although rounded values are listed. The following rules will be followed with regard to the number of decimal places:

- Minimum and maximum will be displayed without rounding from values in the source listing.

- Mean, median, geometric mean and percent coefficient of variation (CV%) will be rounded to one more decimal place than the maximum decimal place of values in the source listing. If the minimum value from the data is zero, then the geometric mean will not be calculated.

- SD and Standard Error (SE) will be rounded to one more decimal place than mean.

Categorical data will be summarized in a frequency table showing the numbers and percentages of patients. Percentages will be rounded to one decimal place and will be suppressed when the count is zero. The denominator for all percentages will be the number of patients within the treatment group for the population of interest, unless otherwise specified.

Point estimate and confidence interval (CI) obtained from statistical procedures will be presented using the same number of decimal places as mean for continuous data or percentage for categorical data. P-value obtained from statistical procedures will be displayed to four decimal places if the value is greater than 0.0001, otherwise <.0001.

In addition, data collected at unscheduled and EOS visits will also not be summarized in visit-based tables, unless otherwise specified. But all data will be displayed in listings. Unless otherwise specified, listings will be sorted by the treatment group, patient number, and visit, if applicable. In cases where more ordering is required, other variables will be included in the sort order as applicable.

For the purpose of summarization, any numeric values recorded below the lower limit or above the upper limit of quantification will be set to the respective limit for all related summaries. In listings, original results containing inequality sign will be displayed, unless otherwise specified.

5.1. Software

All analyses will be conducted using [redacted] PK parameters will be calculated by noncompartmental methods using the appropriate validated software such as [redacted]

5.2. Sample Size

The sample size of 417 patients (278 in CT-P13 SC group and 139 in Placebo SC group) was estimated to provide 80% statistical power to detect a statistically significant effectiveness of CT-P13 SC in comparison with Placebo SC based on the clinical remission at Week 54 assuming a treatment difference of 15% and Placebo rate of 45% at the 1-sided significance level of 2.5%.

Considering a 32% non-responder rate of clinical response at Week 10 before randomization, a total of approximately 615 patients provides at least 90% statistical power for clinical response at Week 54, one of the key secondary endpoints, under the assumption of a treatment difference of 20% and placebo rate of 50% at the 1-sided significance level of 2.5%. Key secondary endpoints other than clinical response at Week 54 are not applicable for power calculation due to lack of relevant references.

5.3. Randomization, Stratification, and Blinding

An Interactive Web Response System (IWRS) will be used for the randomization. Biostatistician will generate the randomization schedule for the IWRS, which will link sequential patient randomization numbers to treatment codes. Patients classified as a clinical responder by modified Mayo score at Week 10 after receiving 3 full doses of CT-P13 via IV infusion and have no safety concern based on the investigator's discretion will be randomized in a 2:1 ratio to receive either CT-P13 SC or Placebo SC, before starting treatment Day 70 (Week 10). The randomization will be stratified by previous exposure to biologic agent and/or JAK inhibitors (used or not used), use of treatment with oral corticosteroids at Week 0 (used or not used) and clinical remission at Week 10 (remitter or non-remitter by modified Mayo score). Permuted block design will be used to randomize patients to treatment groups, where within each block the same pre-specified ratio of patients will be allocated to the treatment groups. The block size will not be revealed.

As this study has a double-blind Maintenance Phase, the treatment assignment for the Maintenance Phase will be blinded to the investigators, patients and predefined CELLTRION and [redacted] blinded teams until the final CSR is generated.

Under normal circumstances, the blind should not be broken. The blind should be broken only if specific emergency treatment would be dictated by knowing the study drug assignment is required for medical management. In such cases, the investigator may, in an emergency, determine the identity of the study drug by using the applicable procedure in the IWRS (found in the study manual).

The date, time, and reason for the unblinding must be documented in the appropriate field of the eCRF and source documents. The medical monitor must be informed as soon as possible. All calls resulting in an unblinding event will be recorded and reported by the IWRS to the medical monitor and CELLTRION. Any patients for whom the blind is broken may continue in the study and receive the study drug at the investigator's discretion. Suspected unexpected serious adverse reactions (SUSAR), which are subject to expedited reporting, should be unblinded before submission to the regulatory authorities if required.

The overall randomization code will be broken only for reporting purposes. This will occur after the database is locked for the data of all patients collected up to Week 54. The unblinded team will be predefined prior to performing the analyses. The study drug assignment for the Maintenance Phase will remain blinded to the investigators, patients, and predefined CELLTRION and [redacted] blinded teams until the final CSR is generated.

5.4. Population of Analysis

The following patient analysis populations are defined: Intent-to-Treat (ITT), All-randomized, Per-protocol (PP), Pharmacokinetic (PK), Pharmacodynamics (PD) and Safety.

Determinations on the population will be made at the blinded Data Review Meeting (DRM) held in accordance with International Council for Harmonisation Technical Requirements for Registration of Pharmaceuticals for Human Use harmonised tripartite guideline E9.

Analysis of the Safety and PP Populations will be performed according to the actual treatment group. The populations except for Safety and PP Populations will be analyzed according to the treatment group they will be randomized to at Week 10. The actual treatment group will be assigned according to their treatment actually administered during Double-blind Maintenance Phase even if there is a discrepancy between the treatment actually administered and the randomized treatment group. If there is a patient with such a discrepancy, the patient receiving at least one dose of CT-P13 SC prior to initiation of dose adjustment during Double-blind Maintenance Phase will be treated as CT-P13 SC treatment group. All other patients will be treated as Placebo SC treatment group.

For randomized patients, data before randomization at Week 10 will be displayed under the treatment group based on randomized or actual administered study drug. If a patient discontinues the study before the randomization at Week 10, the patient will be listed under treatment group of "Not Applicable" and will not be included in summary tables.

The number of patients in each analysis population will be tabulated by the treatment group. A listing will also be produced displaying data on ITT Population.

5.4.1. Intent-to-Treat Population

The ITT Population is defined as all enrolled patients. A patient will be considered to have enrolled if it is recorded as 'Yes' to 'Is the patient eligible to be enrolled in this study?' on the 'Screening Pass/Fail' page of the eCRF. Some of listings will be generated on the ITT Population to include patients who discontinued the study prior to randomization at Week 10.

5.4.2. All-randomized Population

The All-randomized Population is defined as all randomly assigned patients at Week 10, regardless of whether or not any study drug dosing was completed. This will therefore include all patients who have been allocated randomization ID at Week 10 based on 'Randomization' page of eCRF. The All-randomized Population will be used for analysis of primary and key secondary endpoints.

5.4.3. Per-protocol Population

The PP Population is defined as all randomly assigned patients who receive at least one full dose of study drug at Week 10 or thereafter prior to Week 54 and who have at least

one efficacy evaluation result after Week 10 treatment and who do not have any major protocol deviation that is relevant to efficacy analysis. The PP Population will be used to provide supportive results of primary and key secondary endpoints.

A patient will be considered as receiving full dose if the total dose administered (mg) of the patient is equal to prescribed dose (mg) based on 'Study Drug Administration for SC' page of eCRF.

A patient will be considered as having an efficacy evaluation result if the patient has a non-missing result from at least one of the following assessments:

- Mayo Score
- Short Inflammatory Bowel Disease Questionnaire (SIBDQ)
- Mayo Endoscopic subscore and Robarts Histopathology Index (RHI) score

5.4.4. Pharmacokinetic Population

The PK Population is defined as all randomly assigned patients who receive at least one full dose of study drug at Week 10 or thereafter and who have at least one PK concentration result after Week 10 treatment.

5.4.5. Pharmacodynamic Population

The PD Population is defined as all randomly assigned patients who receive at least one full dose of study drug at Week 10 or thereafter and who have at least one PD result (Fecal calprotectin [FC] or C-reactive protein [CRP]) after Week 10 treatment.

5.4.6. Safety Population

The Safety Population is defined as all randomly assigned patients who receive at least one (partial or full) dose of study drug at Week 10 or thereafter. A patient will be considered to have received a study drug if the patient is recorded as study drug administered or if a date of administration is recorded on the 'Study Drug Administration for SC' page of the eCRF.

5.5. Definition of Baseline

The baseline value will be considered to be the last non-missing value before the first administration, unless otherwise specified. Post-baseline values will be considered to be all values collected after the first administration.

5.6. Protocol Deviations

Protocol deviation will be categorized as "major" or "minor". Category of protocol deviation will be identified during the blinded DRM. A major protocol deviation is one that may affect the interpretation of efficacy results or the patient's rights, safety or welfare.

Major protocol deviations and population to be excluded are defined as follow (but not limited to):

- Mis-randomizations (PK and PP Population): Patients who received the other treatment (prior to initiation of dose adjustment) than that to which they are assigned will be defined as mis-randomized.

- Significant GCP non-compliance (All populations): CELLTRION will identify the sites which have been closed or patients who have been affected due to suspected scientific misconduct and/or serious GCP non-compliance.

- Non-compliance of inclusion or exclusion criteria which affect the efficacy results (PP Population): CELLTRION will identify via review of data sourced from the site monitoring database.

- Randomization without clinical response at Week 10 (PP Population): Patients who are classified as non-responder at Week 10 after applying the data handling rules defined in Section 5.7.2 regardless of eCRF data, among the patients randomized at Week 10.

- Prohibit Therapy during Treatment Period (PP Population): Patients who have received them which affect the efficacy results, among the prohibit medications or treatments described in Section 5.9 of the protocol. The list of prohibit medications or treatments will be determined during the blinded DRM.

The major protocol deviations will be summarized for the All-randomized Population by treatment group. A listing of major protocol deviations for each patient will also be provided by treatment group for the ITT Population.

5.7. Data Handling Rules

5.7.1. Dose Adjustment

For patients with dose adjustment, data of the patients will be included in the summary as following Table 1, unless otherwise specified.

Table 1. Data Analysis Scope by Endpoints

Endpoint	CT-P13 SC group *	Placebo SC group *
Efficacy, PK and PD	Only data collected before initiation of dose adjustment	
Safety and Immunogenicity (Including Treatment and Medication)	All data collected regardless of dose adjustment	Only data collected before initiation of dose adjustment

*The randomized or actual treatment group will be determined by the analysis population.

Data collected before initiation of dose adjustment will be identified using the following Table 2:

Table 2. Rule of Data Collected before initiation of dose adjustment

		Time collected	Time not collected
Visit based data (including EOS, Unscheduled)	Assessments to be performed at Pre-dose	Assessment date/time <= Initiation of dose adjustment date/time *	Assessment date <= Initiation of dose adjustment date *
	Assessments to be performed at Post-dose **	Assessment date/time < Initiation of dose adjustment date/time *	Assessment date < Initiation of dose adjustment date *
Non-visit based data (e.g. adverse events and medications)		Event start date/time (or imputed start date/time) < Initiation of dose adjustment date/time *	Event start date (or imputed start date) <= Initiation of dose adjustment date *

* Date (or Date/time) of initiation of dose adjustment will be taken as the earliest date (or date/time) of CT-P13 SC administration satisfying the following two conditions:
- Recorded as '240 mg' to 'Total Dose Administered' on the 'Study Drug Administration for SC' page of the eCRF
- Recorded as 'Yes' to 'Does a patient adjust the dose at this visit? or Did a patient adjust the dose at least once?' on the 'Visit Date' page of the eCRF.

** Including electrocardiograms

All data will be displayed in listings along with a flag indicating data after initiation of dose adjustment.

5.7.2. Calculation of the Mayo score

The Mayo score is composed of the patient's Mayo score diary entries (stool frequency and rectal bleeding) and assessments performed by the site investigator including PGA and flexible proctosigmoidoscopy.

To determine eligibility, the Mayo score diary will be completed within 3 days immediately prior to the first administration of the study drug (Week 0), and the Mayo score will be calculated at Day 0. With the exception of Screening, the Mayo score diary will be collected by patients for 7 days immediately prior to the Mayo score assessment and the most recent 3 days (not necessarily consecutive days) within the 7 days will be used to calculate the Mayo score.

Patient is given the Mayo score diary at each scheduled visit and is asked to complete the Mayo score diary for 7 consecutive days prior to the next scheduled visit. In order to secure diary compliance, information on the date of next visit schedule is provided with the Mayo score diary. In case of change in the visit schedule, patient can complete the diary for more than 7 days using spare pages within the diary. However, site staff should only enter the most recent 3 days of Mayo score diary to the eCRF. If any of the most recent 3 days in the diary overlap with the dates of colonoscopy procedure, site staff should replace the overlapped dates with the other recent diary dates in case there are replaceable dates.

However, to minimize missing data, even if the date of some Mayo diaries collected in eCRF as above is out of the diary instruction, the Mayo score diaries will be considered valid for the Mayo score calculation if the following conditions are met:

- Screening: Mayo score diaries are recorded within 14 days prior to the first study drug administration date (Week 0).

- Other scheduled visits: Mayo score diaries are recorded after the date of study drug administration of the previous visit.

- Mayo score diary dates do not overlap with either the day of bowel preparation (the day before colonoscopy procedure) or the day of colonoscopy procedure.

Subscores for stool frequency and rectal bleeding will be calculated only if all 3 days of diaries entered in the eCRF are valid. Otherwise, the subscores will be considered missing.

5.7.3. Week 54 Endoscopic and Histologic Data

When the endoscopic and/or histologic assessment are not performed at Week 54, another endoscopic and/or histologic data that are performed between Week 50 and Week 54 study drug administration date will be used as the data for Week 54 in the relevant summary. The endoscopic and/or histologic data that is performed between Week 54 and Week 56 study drug administration date could be included in the analysis as a result at Week 54 based on determination during the blinded DRM. In a listing, a flag will be added to the data used instead of the missed Week 54 endoscopic and/or histologic data.

6. PATIENT DISPOSITION

The total number of patients who were screened and screening failure will be displayed along with the primary reason for screening failure based on the 'Screening Pass/Fail' page of the eCRF.

The reasons for screening failure will be displayed using the following categories and ordering:

- Inclusion/Exclusion Criteria Not Met
- Subject Withdrew Consent
- Other

A listing of patients reported as screening failures will be provided.

The number of patients who were enrolled, treated in each phase, randomized, discontinued in each phase and completed the study will also be displayed on the All-randomized Population along with percentage, if applicable.

Patient disposition will be defined as follows:

- A patient will be considered to have enrolled if it is recorded as 'Yes' to 'Is the patient eligible to be enrolled in this study?' on the 'Screening Pass/Fail' page of the eCRF.

- A patient will be considered to have been treated in the Induction Phase if it is recorded as at least one 'Yes' to 'Was study drug administered?' on the 'Study Drug Administration for IV' page of the eCRF at Week 0, Week 2 and/or Week 6.
- A patient will be considered to be randomized if the patient was allocated a randomization ID at Week 10 based on the 'Randomization' page of the eCRF.
- A patient will be considered to have been treated in the Maintenance Phase if it is recorded as at least one 'Yes' to 'Was study drug administered?' on the 'Study Drug Administration for SC' page of the eCRF from Week 10 to Week 54.
- A patient will be considered to have been treated in the Extension Phase if it is recorded as at least one 'Yes' to 'Was study drug administered?' on the 'Study Drug Administration for SC' page of the eCRF on or after Week 56.
- A patient will be considered to have completed the study if it is recorded that they completed ('Yes' box checked) on the 'Study Treatment Termination' page of the eCRF. Conversely, a patient is considered to have discontinued the study if it is recorded in the 'Study Treatment Termination' page of the eCRF that they did not complete ('No' box checked). If the patient who is considered to have discontinued the study has received a study drug administration on or after Week 56, the patient will be considered to have discontinued in the Extension Phase. Else if the patient who is considered to have discontinued the study has been randomized at Week 10 and has not received the study drug on or after Week 56, the patient will be considered to have discontinued in the Maintenance Phase, otherwise, in the Induction Phase.

The total number of patients who discontinued the study in the Induction Phase will be presented by primary reason. The number and percentage of patients who discontinued the study in the Maintenance Phase and Extension Phase will also be displayed by primary reason for discontinuation and treatment group. The reasons for discontinuation will be displayed using the following categories and ordering:

- Progressive Disease
- Non-responder at Week 10
- Adverse Event
- Protocol Deviation
- Lost to Follow-up
- Death
- Physician Decision
- Withdrawal by Subject
- Pregnancy
- Study Terminated by Sponsor
- Other

In addition, the time on study drug prior to discontinuation will also be summarized using descriptive statistics by treatment group, if applicable, for those patients who have

discontinued study treatment prematurely in the Induction Phase, Maintenance Phase or Extension Phase, respectively. The treatment duration in days will be calculated as (Date of last administration - date of first administration + 1).

The date of first administration will be taken as the earliest date recorded on the 'Study Drug Administration for IV' page of the eCRF. The date of last administration will be taken as recorded on the 'Study Treatment Termination' page of the eCRF.

The patient disposition data collected for the ITT Population will be listed by treatment group.

7. DEMOGRAPHICS, BASELINE, AND BACKGROUND CHARACTERISTICS

7.1. Demographics and Stratification Details

The following demographic measures will be summarized for the All-randomized Population by treatment group: Age (years); Gender (male, female); Female fertility status (Pre-Menarche, Surgically Sterilized, Post-Menopausal, Potentially Able to bear Children, Other); Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Not allowed by investigator country regulations, Other); Ethnicity (Hispanic or Latino, Non-Hispanic or non-Latino, Unknown); Height (cm), Weight (kg) and Body Mass Index (BMI) (kg/m^2) as recorded at the screening.

The following stratification details will also be summarized for the All-randomized Population by treatment group: Previous exposure to biologic agent and/or JAK inhibitors (used or not used); Use of treatment with oral corticosteroids at Week 0 (used or not used); Clinical remission at Week 10 (remitter or non-remitter by modified Mayo score). If there is a difference for data entered between IWRS and eCRF, the stratification factors will be summarized using the final data collected on the eCRF.

Demographics will be listed for the ITT Population by treatment group. Stratification details will be listed for the All-randomized Population by treatment group.

7.2. Hepatitis B and C and Human Immunodeficiency Virus 1 and 2

The following assessments will be performed at each scheduled visit:

- Hepatitis B Surface Antigen (HBsAg)
- Hepatitis B Surface Antibody (HBsAb)
- Hepatitis B Core Antibody (HBcAb)
- Hepatitis B virus (HBV)- DNA
- Hepatitis C Antibody
- Hepatitis C virus (HCV)- RNA
- Human Immunodeficiency Virus (HIV) 1&2

Viral serology results will be summarized at Baseline by treatment group and parameter for the All-randomized Population. A listing will be produced by treatment group for the ITT Population. All collected results will be listed.

7.3. Medical History

Medical history is captured at Screening and will be coded using Medical Dictionary for Regulatory Activities (MedDRA Version 22.1 or higher). Medical history will be summarized by treatment group, system organ class (SOC) and preferred term (PT) for the All-randomized Population. The total number of medical history and the number and percentage of patients with at least one medical history will also be presented in the table by treatment group. Medical history will also be listed for the ITT Population by treatment group.

7.4. Ulcerative Colitis Disease History

Active Ulcerative Colitis (UC) history is captured at the Screening. The time since active UC diagnosis will be tabulated for the All-randomized Population by treatment group. Time (years) since active UC diagnosis will be calculated as [(date of first administration – date of diagnosis)/365.25]. If an incomplete active UC diagnosis date is recorded for a patient this will be imputed using the latest possible date. That is, if the day is missing (i.e. XXMAR2022) the date will be the last day of the month (i.e. 31MAR2022). If the day and month are missing (i.e. XXXXX2022), the date will be set to the 31st December (i.e. 31DEC2022). If the imputed date is later than date of first administration, then it will be imputed using the date of first administration. If the whole date is missing, the date will not be imputed and time since active UC diagnosis will not be calculated. Active UC history will also be listed by treatment group for the ITT Population.

7.5. Stool Microbiology

Stool microbiology [enteric pathogens, ova and parasites (concentrate and trichrome), and *clostridium difficile* toxin test] will be performed at Screening and at any point in the study when a patient becomes symptomatic, including worsening or return of disease activity, at the investigator's discretion. Analysis will be performed at the central laboratory. All collected results will be listed by treatment group for the ITT Population.

7.6. Inclusion and Exclusion Criteria

Details of Inclusion and Exclusion criteria can be found in Sections 4.2 and 4.3 of the protocol. Inclusion and Exclusion criteria for each patient including date of informed consent will be presented for the ITT Population by treatment group.

The listing will indicate which protocol the patient was recruited under and hence which criteria applied.

8. TREATMENTS AND MEDICATIONS

For patients with dose adjustment, all data collected regardless of dose adjustment for CT-P13 SC group and data collected before initiation of dose adjustment for Placebo SC group will be included in the summary, unless otherwise specified. All data will be displayed in listing along with a flag indicating data after dose adjustment.

8.1. Prior and Concomitant Medications

All prior and concomitant medications for the treatment of UC, latent TB, and/or hepatitis C (if applicable) from the diagnosis of disease until the EOS visit, will be collected on the eCRF. All medications for other purposes, from within 30 days prior to the first study drug administration (Day 0) or from when the ICF is signed, whichever is earlier, will be collected on the eCRF until the EOS visit. All concomitant medications will also be recorded when any Adverse Drug Reaction (ADR) is ongoing at the EOS visit. All medications will be coded according to the World Health Organization drug dictionary (WHODrug Dictionary Global B3 version September, 2019 or later version).

Medications will be classed as either prior or concomitant. For the purpose of inclusion in prior or concomitant medication tables, incomplete medication start and stop dates will be imputed as follows:

If the stop date is incomplete the following rules will be applied:

- Missing day: Assume the last day of the month.
- Missing day and month: Assume December 31st.
- Missing day, month and year: Leave it as Missing.

In the case of the death of a patient, and the imputed stop date is after the date of death, the stop date will be imputed as the date of death. In addition, if a medication, checked as 'Yes' to 'If stop date is unknown, was this drug stopped before the first administration of study drug (Day 0)?' on the 'Prior & Concomitant Medications' page of the eCRF, has imputed stop date on or after the date of the first study drug administration, the stop date will be set to one day before the date of the first study drug administration.

If the start date is incomplete the following rules will be applied. If the stop date is incomplete, imputed stop date will be used instead of actual stop date:

- Missing day: Assume the first day of the month.
  However, if the partial date and the date of the first study drug administration lie within the same month and year and the date of the first study drug administration is not after the stop date of the medication, set to the date of the first study drug administration. Otherwise, set to stop date of the medication.

- Missing day and month: Assume January 1st.
  However, if the partial date and the date of the first study drug administration lie within the same year and the date of first administration is not after the stop date of the

medication, set to the date of the first study drug administration. Otherwise, set to stop date of the medication.

- Missing day, month and year: Assume date of the first study drug administration, if not after the stop date for the medication. Otherwise, set to stop date for the medication.

For the missing day imputation, the following examples should be used for reference:

- Example 1:
  Medication start: UNJUN2022
  Medication stop: 20OCT2022
  Date of the first study drug administration: 16OCT2022
  Medication start imputed: 01JUN2022
- Example 2:
  Medication start: UNOCT2022
  Medication stop: 20OCT2022
  Date of the first study drug administration: 16OCT2022
  Medication start imputed: 16OCT2022
- Example 3:
  Medication start: UNOCT2022
  Medication stop: 20OCT2022
  Date of the first study drug administration: 24OCT2022
  Medication start imputed: 20OCT2022

A prior medication is defined as following, and all other medications will be defined as concomitant medication.

- A medication having actual/imputed stop date of medication before date of the first study drug administration, or

- A medication checked as yes to "If stop date is unknown, was this drug stopped before the first administration of study drug (Day 0)?" on eCRF.

The prior and concomitant medications will be summarized by treatment group, drug class (using Anatomical Therapeutic Chemical [ATC] level 2), and PT along with the total number of prior/concomitant medications and the number and percentage of patients with at least one prior/concomitant medication for the Safety Population, respectively. When ATC level 2 for drug class is not available, level 1 will be used instead. The summaries will be repeated in separate tables for concomitant medications in Maintenance Phase. A concomitant medication in Maintenance Phase is defined as follows:

1) Patients treated in the Maintenance Phase and not treated in the Extension Phase: a concomitant medication with actual/imputed stop date on or after the Week 10 study drug administration date or marked as ongoing or missing

2) Patients treated in both the Maintenance and the Extension Phase: a concomitant medication with actual/imputed stop date on or after the Week 10 study drug

administration date or marked as ongoing or missing, and actual/imputed start date before the first study drug administration date in the Extension Phase

All prior and concomitant medications will be listed separately along with the Maintenance Phase flag by treatment group for the ITT Population.

8.2. Exposure to Study Drug

The number and percentage of patients with dose administered at each scheduled visit will be summarized by treatment group for the Safety Population. For patients who are not administered with the study drug, the number and percentage of patients with each reason why the dose was not administered (AE, Other) will be displayed by scheduled visit. For patients who were administered the study drug, a table will be provided displaying descriptive statistics of the prescribed dose and actual dose administered by treatment group at each scheduled dose.

Prescribed and actual administered dose per weight (mg/kg) for IV infusion and prescribed and actual administered dose (mg) for SC injection will be summarized. The dose per weight (mg/kg) for IV infusion will be calculated using the Prescribed Dose (mg) and Total Dose Administered (mg) based on the 'Study Drug Administration for IV' page of eCRF and Weight (kg) on the 'Vital Signs' page of eCRF.

In addition, the total number of doses received and total administered dose (mg) of each patient during the Induction Phase, Maintenance Phase and Extension Phase will be summarized using descriptive statistics by treatment group for the Safety Population.

The number and percentage of patients who received adjusted dose during the Maintenance Phase and Extension Phase on or after Week 22 will be additionally summarized in a table by treatment group and scheduled visit for the Safety Population. The number and percentage of patients who received at least one adjusted dose during each phase will also be included in this summary. A patient will be considered to receive adjusted dose if the actual administered dose that the patient received on or after the date of initiation of dose adjustment is more than CT-P13 SC 120 mg.

A listing will be provided by treatment group for the ITT Population showing the details of study drug administration. This listing will include data collected on the "Kit Number Dispensation" page of eCRF, "Study Drug Administration for IV" page of eCRF and "Study Drug Administration for SC" page of eCRF.

9. EFFICACY ANALYSIS

Efficacy will be assessed by the Mayo score, RHI score and Short Inflammatory Bowel Disease Questionnaire (SIBDQ). For Efficacy analysis related to Mayo and RHI score, Data handling rule defined in Section 5.7.2 and 5.7.3 will be applied.

For the efficacy endpoints related remission or response, the following patients will be considered as non-remitter or non-responder:

- Patients who do not meet the clinical remission or response criteria
- Patients with missing or incomplete data for the evaluation of each endpoint at their scheduled visit of interest
- Patients with dose adjustment to CT-P13 SC 240mg prior to their scheduled visit of interest

In addition, Efficacy analyses based on endoscopic and/or histologic assessment will be conducted using the endoscopic subscore of Mayo score and RHI score that are determined at central level.

For patients with dose adjustment, only data collected before initiation of dose adjustment for both treatment groups will be included in the summary, unless otherwise specified. All data will be displayed in listing along with a flag indicating data after initiation of dose adjustment.

9.1. Primary Efficacy Analysis

The primary endpoint for the study is as follows:

- Clinical remission at Week 54, defined as the following modified Mayo score:

  (1) Stool frequency subscore of 0 or 1 point, and

  (2) Rectal bleeding subscore of 0 point, and

  (3) Endoscopic subscore of 0 or 1 point

The primary endpoint will be tested at the 2-sided significance level of 5% on the All-randomized Population using the p-value from Cochran-Mantel-Haenszel (CMH) test stratified by Previous exposure to biologic agent and/or JAK inhibitors (used or not used), Use of treatment with oral corticosteroids at Week 0 (used or not used) and Clinical remission at Week 10 (remitter or non-remitter by modified MAYO score). If the p-value is ≤ 0.05, the statistical significance of the primary endpoint will be concluded. If the primary endpoint is significant, the fixed sequence procedure will be used for key secondary endpoints in order to preserve the Type I error. For the supportive analysis, the primary endpoint will be performed on the PP Population.

The primary endpoint will be summarized using frequency table along with the p-value from stratified CMH test. Difference in proportion between two treatment groups estimated using CMH weights and corresponding 95% stratified Newcombe CI with CMH weights will also be provided.

In addition, for the descriptive comparison of the treatment effect between patients with and without dose adjustment to CT-P13 SC 240mg prior to Week 54 within CT-P13 SC treatment group, the primary endpoint will be summarized by patients with/without dose adjustment in CT-P13 SC treatment group using frequency table without the statistical test.

In this analysis, remitter will be determined as per remission criteria regardless of dose adjustment.

9.1.1. Sensitivity Analysis

A sensitivity analysis will be performed on the primary efficacy endpoint, utilizing Fisher's exact test and a logistic regression model.

Fisher's exact test will be performed on the All-randomized Population. The difference of proportions between two treatment groups and corresponding 95% exact CI (Chan and Zhang 1999) will be presented along with p-value obtained from the Fisher's exact test.

A logistic regression model with treatment as a fixed effect and Previous exposure to biologic agent and/or JAK inhibitors (used or not used), Use of treatment with oral corticosteroids at Week 0 (used or not used) and Clinical remission at Week 10 (remitter or non-remitter by modified Mayo score) as covariates will also be performed on the All-randomized Population. Difference in proportion and its 95% CI estimated using Delta method will be presented along with p-value for treatment obtained from the logistic regression model.

In addition, to assess robustness of primary efficacy findings with respect to missing data, tipping point analysis will be conducted on the All-randomized population. The following patients will be considered as having missing result.

- Patients with missing or incomplete data for the evaluation of each endpoint at Week 54, even after applying the data handling rule defined in Section 5.7 (if applicable)

- Patients with dose adjustment to CT-P13 SC 240 mg prior to Week 54

Stratified CMH test, the same method for the primary endpoint analysis, will be performed by gradually increasing the number of remitters for each group starting with the scenario where all patients with missing result are non-remitters up to the scenario where all patients with missing result are remitters. All p-values calculated from the stratified CMH test for the difference between two proportions (CT-P13 SC and Placebo SC) will be displayed as a shift table. The results from tipping point analysis will also be presented using 2-dimensional plot.

In order to evaluate the impact of the war in Ukraine, a sensitivity analysis will be performed on the primary endpoint by excluding war-affected patients in Ukraine and excluding all patients in Ukraine, respectively. The analysis will be performed using the same method as primary endpoint on the All-randomized Population. War-affected patients in Ukraine will be defined as patients who meet the following two conditions:

- Site location: Study site located in Ukraine
- Randomization date: Randomization date within 44 weeks (308 days) before Russian invasion of Ukraine on 24 February 2022

9.1.2. Subgroup Analysis

For the primary endpoint, subgroup analyses will be performed using the same method for the primary endpoint on the All-randomized Population. For each specific subgroup, if there are not enough patients (i.e., <5% All-randomized population), the corresponding analyses will not be performed. The following are the pre-defined subgroups:

- Gender (Male, Female)
- Age (<35 years, ≥35 years)
- Race (White, Black or African American, American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, Not Allowed by Investigator Country Regulations, Other)

9.2. Key Secondary Efficacy Analysis

The following efficacy parameters are determined as the key secondary efficacy endpoints, and the fixed sequence procedure will be used for key secondary endpoints in order to preserve the Type I error in the following order in case the statistical significance of the primary efficacy endpoint is declared:

- Clinical response at Week 54, defined as a decrease in modified Mayo score from baseline of at least 2 points and at least 30%, with an accompanying decrease in the rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1 point

- Endoscopic-histologic mucosal improvement at Week 54, defined as an absolute endoscopic subscore of 0 or 1 point from modified Mayo score and an absolute Robarts Histopathology Index (RHI) score of 3 points or less with an accompanying laminal propria neutrophils and neutrophils in epithelium subscore of 0 point

- Corticosteroid-free remission at Week 54, defined as being in clinical remission by modified Mayo score in addition to not requiring any treatment with corticosteroid for at least 8 weeks at Week 54, among the patients who used oral corticosteroids at Baseline. The corticosteroid is defined as follows:

  1) ATC level 2 = “CORTICOSTEROIDS FOR SYSTEMIC USE” or Preferred Term = “BUDESONIDE”, and

  2) Indication not including “Premedication”, and

  3) Route:

  3-1) Route for Baseline: including oral only

  3-2) Route for Week 54: all route excluding topical administration (RESPIRATORY[INHALATION])

For the comparison between treatment groups, the key secondary endpoints will be tested at the 2-sided significance level of 5% on the All-randomized Population using the p-value from the CMH test stratified by Previous exposure to biologic agent and/or JAK inhibitors (used or not used), Use of treatment with oral corticosteroids at Week 0 (used or not used) and Clinical remission at Week 10 (remitter or non-remitter by modified Mayo score). The first key secondary endpoint will be tested only if the primary endpoint is statistically significant, and the next key secondary endpoint will be tested only if the previous key secondary endpoint is statistically significant. For the supportive analysis, the key secondary endpoints analysis will be performed on the PP Population.

The key secondary endpoints will be summarized using frequency table along with the p-value from stratified CMH test. Difference in proportion between two treatment groups estimated using CMH weights and corresponding 95% stratified Newcombe CI with CMH weights will also be provided.

In order to evaluate the impact of the war in Ukraine, a sensitivity analysis will be performed on the primary endpoint by excluding war-affected patients in Ukraine and excluding all patients in Ukraine, respectively. The analysis will be performed using the same method as primary endpoint on the All-randomized Population.

For the subgroup analyses, the key secondary endpoints will be performed on the All-randomized Population using the same method as key secondary endpoints and pre-defined subgroups as the primary endpoint (Section 9.1.2).

For the descriptive comparison of the treatment effect between patients with and without dose adjustment to CT-P13 SC 240 mg prior to Week 54 within CT-P13 SC treatment group, the key secondary endpoints will be summarized by patients with/without dose adjustment in CT-P13 SC treatment group using frequency table without the statistical test. In this analysis, remitter or responder will be determined as per remission or response criteria regardless of dose adjustment.

9.3. Other Secondary Efficacy Analysis

The following secondary efficacy endpoints will be assessed at each scheduled visit:

- Clinical remission assessed at Weeks other than Week 54, defined as the following modified Mayo score:

  (1) Stool frequency subscore of 0 or 1 point, and

  (2) Rectal bleeding subscore of 0 point, and

  (3) Endoscopic subscore of 0 or 1 point

- Maintenance of clinical remission at Week 54, defined as being in clinical remission by modified Mayo score, among the patients in clinical remission by modified Mayo score at Week 10

- Sustained remission at both Week 22 and Week 54, defined as a stool frequency subscore of 0 or 1, and rectal bleeding subscore of 0

- Clinical response assessed at Weeks other than Week 54, defined as a decrease in modified Mayo score from baseline of at least 2 points and at least 30%, with an accompanying decrease in rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1 point

- Endoscopic-histologic mucosal improvement assessed at Weeks other than Week 54, defined as an absolute endoscopic subscore of 0 or 1 point from modified Mayo score and an absolute RHI score of 3 points or less with an accompanying laminal propria neutrophils and neutrophils in epithelium subscore of 0 point

- The scores and change from baseline in Short Inflammatory Bowel Disease Questionnaire (SIBDQ)

The secondary efficacy endpoints listed in this section will be analyzed at each scheduled visit by treatment group on the All-randomized population. Confidence interval and p-value will be presented for comparison between treatment groups in a descriptive manner with no adjustments for multiple testing.

Binary endpoints will be summarized using frequency table, and difference of proportions between two treatment groups estimated using CMH weights and corresponding 95% stratified Newcombe CI with CMH weights will be presented along with p-value from stratified CMH test. The same stratified analysis used for the primary endpoint will be applied.

Continuous endpoints will be summarized using descriptive statistics and analyzed using Analysis of Covariance (ANCOVA) presenting a point estimate, p-value and 95% CI for the treatment difference. Covariates for ANCOVA will include stratification factors used for the primary analysis.

The point estimate, 95% CI and p-value for the difference between treatment groups will be presented only for results after Week 10 randomization.

9.4. Exploratory Efficacy Analysis

The following exploratory efficacy endpoints will be assessed at each scheduled visit:

- Clinical remission, with normalization of stool frequency at Week 54, defined as the following modified Mayo score:

  (1) Stool frequency subscore of 0 point, and

  (2) Rectal bleeding subscore of 0 point, and

  (3) Endoscopic subscore of 0 or 1 point

- Total clinical remission, defined as a total Mayo score (stool frequency, rectal bleeding, endoscopic, and PGA subscores) of 2 points or lower with no individual subscore exceeding 1 point

- Total clinical response, defined as a decrease in total Mayo score from baseline of at least 3 points and at least 30%, with an accompanying decrease in rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1 point

- Partial clinical remission, defined as a partial Mayo score (stool frequency, rectal bleeding, and PGA subscores) of 1 point or lower

- Partial clinical response, defined as a decrease in partial Mayo score from baseline of at least 2 points, with an accompanying decrease in the subscore for rectal bleeding of at least 1 point, or an absolute subscore for rectal bleeding of 0 or 1 point

The exploratory endpoints listed in this section will be analyzed on the All-randomized Population. Confidence interval and p-value will be presented for comparison between treatment groups in a descriptive manner with no adjustments for multiple testing. The same statistical method as the secondary efficacy endpoints will be used only for results after Week 10 randomization.

9.5. Mayo Score Assessment

Clinical response and remission will be assessed by the Mayo score. The Mayo score will be calculated at scheduled visits. The Mayo score is composed of the patient's Mayo score diary entries and assessments performed by the site investigator including PGA and flexible proctosigmoidoscopy. The components of Mayo scoring system are as following:

Table 1. Mayo Scoring System

No.	Items	Score
1	**Stool frequency**[1]	
	Normal no. of stools for this patient	0
	1 to 2 stools more than normal	1
	3 to 4 stools more than normal	2
	5 or more stools more than normal	3
2	**Rectal bleeding**[2]	
	No blood seen	0
	Streaks of blood with stool less than half the time	1
	Obvious blood (more than just streaks) or streaks of blood with stool most of the time	2
	Blood alone passes	3
3	**Findings of flexible proctosigmoidoscopy**[3]	
	Normal or inactive disease	0

	Mild disease (erythema, decreased vascular pattern)	1
	Moderate disease (marked erythema, absent vascular pattern, friability, erosions)	2
	Severe disease (spontaneous bleeding, ulceration)	3
4	**Physician's global assessment**[4]	
	Normal	0
	Mild disease	1
	Moderate disease	2
	Severe disease	3

Total Mayo score ranges from 0 to 12, with higher scores indicating more severe disease.
Modified Mayo score ranges from 0 to 9, excluding PGA, with higher scores indicating more severe disease.

1. Each patient serves as his or her own control to establish the degree of abnormality of the stool frequency.
2. The daily bleeding score represents the most severe bleeding of the day. Rectal bleeding subscore of the Mayo Score is modified in accordance with FDA guidance so that a value of 2 is consisted of obvious blood (more than just streaks) and streaks of blood with stool most of the time.
3. Endoscopic subscore of the Mayo Score is modified in accordance with FDA guidance so that a value of 1 does not include friability.
4. The physician's global assessment acknowledged the 3 other criteria; the patient's recollection of abdominal discomfort and general sense of well-being, and other observations, such as physical findings and the patient's performance status.

Source: Schroeder et al. 1987

The total Mayo score is summed up of the stool frequency, rectal bleeding, endoscopic and PGA subscores. The modified Mayo score is summed up of the 3 components of the total Mayo score excluding PGA subscore, and the partial Mayo score is summed up of the 3 components of the total Mayo score excluding endoscopic subscore.
The stool frequency and rectal bleeding subscores will be calculated using the average of the daily scores over the 3 days.

Flexible proctosigmoidoscopy will be assessed according to endoscopic subscore criteria of the Mayo score. Flexible proctosigmoidoscopy will be performed in all patients at Screening and at each scheduled visit. At Screening, full colonoscopy will be performed, instead of flexible proctosigmoidoscopy, for the patients who had an increased risk of colorectal cancer according to the exclusion criteria 8 or who require full colonoscopy at the investigator's discretion for the reasons including suspected extensive colitis or pancolitis. For the patients who had been performed full colonoscopy at Screening, full colonoscopy will be performed at Week 54. Full colonoscopy may also be performed based on the investigator's discretion at other time points after Screening. If full colonoscopy has been performed, it can replace flexible proctosigmoidoscopy. Flexible proctosigmoidoscopy (or full colonoscopy) for endoscopic subscore assessment will be performed within 14 days prior to the Mayo score assessment. Flexible proctosigmoidoscopy (or full colonoscopy) can be performed whenever needed based on investigator's discretion including determination of loss of response. Endoscopic subscore of the Mayo score by flexible proctosigmoidoscopy (or full colonoscopy) will be evaluated at the central level by an independent reviewer blinded to treatment allocation to confirm eligibility, determine loss of response and for reporting purposes. The local endoscopic

subscore will be considered during evaluation of the endoscopic subscore at the central level.

Descriptive statistics for actual and change from baseline of modified, partial and total Mayo scores at each scheduled visit will be summarized by treatment group for All-randomized population. All Mayo score assessment information including the endoscopic subscore (at the central and local level) will be listed by treatment group for the All-randomized Population.

9.6. Endoscopic-histologic mucosal improvement

Endoscopic-histologic mucosal improvement will be assessed by endoscopic subscore of the Mayo score (as defined in Section 9.5) and histologic assessment by the Robarts Histopathology Index (RHI). The histologic assessment by RHI score evaluates the degree of histologic inflammation using a categorical system containing 4 microscopic features of UC. The components and features of RHI are as following:

Table 2. Robarts Histopathology Index

Component	Features	Score
Chronic inflammatory infiltrate	No increase	0
	Mild but unequivocal increase	1
	Moderate increase	2
	Marked increase	3
Lamina propria neutrophils	None	0
	Mild but unequivocal increase	1
	Moderate increase	2
	Marked increase	3
Neutrophils in epithelium	None	0
	<5% crypts involved	1
	<50% crypts involved	2
	>50% crypts involved	3
Erosion or ulceration	No erosion, ulceration or granulation tissue	0
	Recovering epithelium + adjacent inflammation	1
	Probable erosion-focally stripped	1
	Unequivocal erosion	2
	Ulcer or granulation tissue	3

Robarts histopathology index = 1×chronic inflammatory infiltrate level + 2×lamina propria neutrophils + 3×neutrophils in epithelium + 5×erosion or ulceration

Source: Mosli et al. 2017

Histologic assessment will be evaluated at the central level by an independent reviewer blinded to treatment allocation for reporting purposes. Biopsy for histologic assessment

will be performed on all patients at Screening and at scheduled visits. Biopsy will be performed within 14 days prior to the histologic assessment.

Descriptive statistics for actual and change from baseline of endoscopic subscore (at the central level) and RHI score at each scheduled visit will be summarized by treatment group for All-randomized population. All histologic assessment information will be listed by treatment group for the All-randomized Population.

9.7. Short Inflammatory Bowel Disease Questionnaire

The SIBDQ is a quality-of-life questionnaire for patients with inflammatory bowel disease. It has 10 questions measuring physical (systemic and bowel), social and emotional status. Scores for this questionnaire range from 1 (poorest quality of life) to 7 (best quality of life). The total score will be the sum of the scores obtained for physical, social and emotional status for physical, social and emotional status for each patient and visit. The SIBDQ will be assessed at each scheduled visit.

All SIBDQ information will be listed by treatment group for the All-randomized Population.

10. PHARMACOKINETIC ANALYSIS

All PK analysis will be conducted on the PK population unless otherwise specified. For patients with dose adjustment, only data collected before initiation of dose adjustment for both treatment groups will be included in the summary. All data will be displayed in listing along with a flag indicating data after dose adjustment.

10.1. Serum Concentrations

Blood samples for PK analysis will be collected at pre-dose (prior to the beginning of the study drug administration) of Weeks 0, 2, 6, 10, 14, 22, 30, 38, 46, 54, 62, 70, 78, 86, 94, 102, and within 15 minutes after the end of the study drug infusion of Week 6. In case of initiation of dose adjustment other than scheduled visits, additional blood samples will be collected at pre-dose.

In addition, for patients who agreed to collect further blood samples, additional blood samples for further population PK analysis will also be collected at the following time points.

- Any time between 48 and 72 hours after study drug administration of Week 22
- Any time between 120 and 168 hours after study drug administration of Week 22
- Pre-dose of Week 24

Additional blood samples for further population PK analysis and for initiation of dose adjustment other than scheduled visits will not be used to summarize in tables and figures.

In other words, the blood samples collected only at scheduled visits (pre-dose of Weeks 0, 2, 6, 10, 14, 22, 30, 38, 46, 54, 62, 70, 78, 86, 94 and 102, and within 15 minutes after the end of the study drug infusion of Week 6) will be used to summarized in tables and figures. However, all data will be presented in the data listing.

Individual serum concentrations, scheduled visit and actual sampling time will be presented in the data listing by treatment group for the All-randomized Population.

Serum concentrations of Infliximab will be summarized using descriptive statistics (n, mean, SD, CV%, geometric mean, minimum, median, and maximum) by treatment group at each scheduled visit and time point for the PK Population. All concentrations below the lower limit of quantification (BLQ) will be indicated in the data listing.

For summary of serum concentration, BLQ prior to the first administration (Week 0) will be set to zero. All other BLQs after study drug exposure will be set to Lower Limit of Quantification (LLoQ).

Mean serum concentration versus scheduled visit plots for study drugs will also be presented on both linear and semi-logarithmic scales by treatment group for the PK Population.

10.2. Pharmacokinetic Parameters

The serum PK parameters will be calculated by non-compartmental methods using [redacted]

The C_{trough} will be assessed up to Week 100 and C_{max} will be assessed at Week 6.

- C_{trough} trough concentration (concentration before the next dosing of study drug)
- C_{max} observed maximum serum concentration after study drug infusion

To derive PK parameter, all BLQs after the first administration will be set to LLoQ. The results of additional blood samples for further Population PK analysis and for initiation of dose adjustment other than scheduled visits will not be used to calculate the C_{trough}. In other words, the C_{trough} will be calculated only using the blood samples collected at scheduled visits (Pre-dose of Weeks 2, 6, 10, 14, 22, 30, 38, 46, 54, 62, 70, 78, 86, 94 and 102).

The PK parameters will be summarized by treatment group using descriptive statistics (n, mean, median, SD, CV%, geometric mean, minimum, maximum) for the PK Population. All data for PK parameters will be listed by treatment group for the All-randomized Population.

11. PHARMACODYNAMIC ANALYSIS

The CRP and FC will be recorded as numeric PD parameters. Descriptive statistics will be provided for the CRP and FC (actual value and change from baseline) for the PD population by treatment group at each scheduled visit. Descriptive statistics will consist of

n, mean, SD, SE, CV%, geometric mean, minimum, median and maximum. All PD information will be listed by treatment group for the All-randomized population. In addition, a plot will be presented showing the mean (±SE) concentration of the CRP and FC at each scheduled visit for the PD Population by treatment group.

For patients with dose adjustment, only data collected before initiation of dose adjustment for both treatment groups will be included in the summary. All data will be displayed in listing along with a flag data indicating data after initiation of dose adjustment.

12. SAFETY ANALYSIS

All safety analyses will be performed in the Safety Population by treatment group presenting data on AEs, clinical laboratory results (clinical chemistry, hematology and urinalysis [including microscopy]), complement (C3, C4) and total hemolytic complement, vital sign measurements, weight, hypersensitivity monitoring via vital sign measurements (including blood pressure, heart and respiratory rates and body temperature), 12-lead electrocardiograms (ECGs), physical examination findings, signs and symptoms of tuberculosis (TB monitoring, Interferon-γ Release Assay [IGRA] and chest X-ray), monitoring of cardiovascular disease related signs and symptoms, local site pain (using 100 mm Visual Analogue Scale [VAS]), pregnancy tests, NYHA functional classification assessment, anti-ds DNA assessment, and immunogenicity tests.

For patients with dose adjustment, all data collected regardless of dose adjustment for CT-P13 SC group and data collected before initiation of dose adjustment for Placebo SC group will be included in the summary, unless otherwise specified. All safety data will be listed along with a flag indicating data after initiation of dose adjustment for the ITT population unless otherwise specified.

12.1. Adverse Events

An AE is defined as any untoward medical occurrence in a patient enrolled into this study regardless of its causal relationship to study drug.

A treatment-emergent adverse event (TEAE) is defined as any event not present before exposure to study drug or any event already present that worsen in either intensity or frequency after exposure to study drug.

The Medical Dictionary for Regulatory Activities (MedDRA) version 22.1 or the higher version will be used to code all AEs. AEs will be graded for intensity according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0

If the stop date of an AE is partial or missing the following rules will be applied.

- Missing day (e.g. XXJAN2022): Assume the last day of the month. (e.g. 31JAN2022)
- Missing day and month (e.g. XXXXX2022): Assume December 31st. (e.g. 31DEC2022)
- Missing day, month and year (e.g. XXXXXXXXX): Leave it as Missing.

If the start date of an AE is partial or missing the following rules will be applied. If the stop date of the AE is partial, imputed stop date will be used instead of actual stop date.

- If the day of an Adverse Event is missing (e.g. XX JAN2022), the month and year of the partial date will be compared to the date of the first exposure to study drug.
    - If the month and year are equal for both dates, the AE start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, and (ii) the stop date of the AE.
    - If the month and year are not equal, the AE start date will be imputed as the first day of the month (e.g. 01 JAN2022).
- If the day and month is missing (e.g. XXXXX2022), the year of the partial date will be compared to the date of the first exposure to study drug.
    - If the years of both dates are equal, start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, and (ii) the stop date of the AE.
    - If the year is not equal, start date will be imputed as the 1st of January of the partial date year (e.g. 01JAN2022).
- If the AE start date is missing (e.g. XXXXXXXXX), start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, and (ii) the stop date of the AE.

Listings for AEs will include the following information: SOC, PT and Verbatim term; start and stop date; TEAE flag, study phase (Induction Phase, Maintenance Phase, Extension Phase); intensity (CTCAE Grade 1 to 5); frequency (continuous, intermittent, transient); outcome (recovered/resolved, recovering/resolving, recovered/resolved with sequelae, not recovered/not resolved, fatal, unknown); type of sequelae (if result of outcome is Recovered/Resolved with Sequelae); relationship to study drug (unrelated, possible, probable, definite); action taken with study drug (dose not changed, dose increased, dose reduced, drug interrupted, drug withdrawn); any treatment received (no, medication, non-medication treatment: specify, both medication and non-medication treatment: specify the non-medication treatment); whether the event was serious (yes, no); whether the AE is infusion-related reaction/systemic injection reaction (hypersensitivity/anaphylactic reaction) (IRR/SIR), delayed hypersensitivity, localized injection site reaction (ISR), infection, malignancy and adverse device effect (ADE) and Coronavirus Disease 2019 (COVID-19). All AEs will be listed.

In summaries, adverse events will be considered to be related if the relationship is possible, probable, or definite. If relationship or intensity is missing, it will be summarized separately under a missing category.

12.1.1. Incidence of Treatment-Emergent Adverse Events

The TEAEs during the study will be summarized by treatment group and SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE using only the worst intensity recorded at each level of summarization. The total number of events and number of patients with at least one TEAE over all SOCs will

also be displayed. The summaries will be repeated in separate tables for TEAEs occurred in Maintenance Phase and Extension Phase, respectively. TEAEs occurred in Maintenance Phase are defined as follows:

1) Patients not treated in the Extension Phase: TEAEs with actual/ imputed start date on or after date of Week 10 study drug administration

2) Patients treated in the Extension Phase: TEAEs with actual/ imputed start date on or after date of Week 10 study drug administration and before the first study drug administration date in the Extension Phase.

TEAEs occurred in Extension Phase are defined as TEAEs with actual/imputed start date on or after the first study drug administration date in the Extension Phase.

The summary will also be repeated in a separate table for TEAEs classified as COVID-19. TEAEs coded with Preferred Terms of 'COVID-19', 'Asymptomatic COVID-19', 'COVID-19 pneumonia' and 'Coronavirus test positive' will be included. Detailed information on patient infected with COVID-19 will be presented in an additional information listing.

In addition, TEAEs with PT reported for at least 5% of incidence rate which is rounded to one decimal place in any treatment group will be summarized separately. Furthermore, the summary will also be repeated in a separate table for TEAEs occurred in the Maintenance Phase by comparing patients with/without dose adjustment to CT-P13 SC 240 mg during Maintenance Phase in CT-P13 SC treatment group.

12.1.2. Deaths

All patients who have a Serious Adverse Event (SAE) with serious criteria of "Death" will be presented in a listing and the following variables will be included; date of first/last dose, date of last visit, date of death, time to death from first/last dose, days on study, TEAE flag, study phase (Induction Phase, Maintenance Phase, Extension Phase), SOC/ PT/ cause of death, whether an autopsy was performed (yes, no), whether a death certificate was completed (yes, no), relationship to study drug. Time (days) to death from first/last dose will be calculated as (date of death – date of first/last dose + 1). In case of death during the study, days on study will be calculated as (date of death – date of first dose +1). Otherwise, days on study will be calculated as (date of last visit – date of first dose +1).

12.1.3. Serious Adverse Events

An SAE is defined as any event that is immediately life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or results in death. Important medical events that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Treatment-Emergent Serious Adverse Events (TESAEs) will be summarized by treatment group and SOC, PT, relationship and intensity/serious criteria, displaying the number and percentage of patients with at least one TESAE using only the most severe SAE recorded at each level of summarization. The total number of events and number of patients with at least one TESAE over all SOCs will also be displayed. The summary will be repeated in a separate table for TESAEs occurred in Maintenance Phase and Extension Phase, respectively.

The summary will also be repeated in a separate table for TESAEs classified as COVID-19.

All SAEs will be listed including the variables detailed in Section 12.1. Serious criteria and SAE description will be presented in an additional information listing.

12.1.4. Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation

All patients who have a TEAE with an action taken with study drug of "Drug Withdrawn" will be summarized by treatment group and by SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE leading to study drug discontinuation, using only the most severe TEAE recorded at each level of summarization. The total number of events and number of patients with at least one TEAE which led to study drug discontinuation will also be displayed. The summary will be repeated in a separate table for TEAEs leading to study drug discontinuation and occurred in Maintenance Phase and Extension Phase, respectively.

The summary will also be repeated in a separate table for TEAEs leading to study drug discontinuation classified as COVID-19.

All TEAEs leading to study drug discontinuation will be listed including the variables detailed in Section 12.1.

12.1.5. Treatment-Emergent Adverse Events of Special Interest

The AEs of special interest are as following:

- Infusion-related reaction/systemic injection reaction (hypersensitivity/anaphylactic reaction)

  All AEs which are classified as Infusion related reaction/Systemic injection reaction will be captured on eCRF pages, and the AE term will be reported Infusion related reaction/Systemic injection reaction, respectively. Cases that are additionally determined as delayed hypersensitivity will be excluded.

- Delayed hypersensitivity

  Delayed hypersensitivity will be determined on a case-by-case occasion among IRR/SIR reported case on eCRF prior to the database lock.

- Localized injection site reactions

AEs classified as localized ISR in the eCRF will be included.

- Infection

  AEs coded with a System Organ Class of 'Infections and Infestations' will be included.

- Malignancies

  AEs coded with a System Organ Class of 'Neoplasms benign, malignant and unspecified (incl cysts and polyps)' excluding terms which includes 'benign' in High Level Group Term (HLGT), High Level Term (HLT), PT and Lowest Level Term (LLT).

The IRR/SIR and delayed hypersensitivity will be summarized together in one table, and other TEAEs of special interest will be summarized in separate tables. These are displayed by treatment group, SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE using only the most severe TEAE recorded at each level of summarization. The total number of events and number of patients with at least one TEAE of special interest will also be displayed. In addition, tables for signs and symptoms regarding IRR/SIR and delayed hypersensitivity and localized ISR will be provided separately by SOC, PT (as coded by MedDRA version 22.1 or higher version) and intensity. All summaries will be repeated in separate tables for TEAEs of special interest occurred in Maintenance Phase and Extension Phase, respectively.

All TEAEs of special interest will be flagged in listings for AEs. TEAEs classified as IRR/SIR, Delayed hypersensitivity and localized ISR will be presented in separate listings including the variables detailed in Section 12.1. Experienced Signs and symptoms will be presented in additional information listings for IRR/SIR and delayed hypersensitivity and localized ISR, separately.

12.1.6. Adverse Device Effect

An Adverse Device Effect (ADE) is defined as any AE related to the use of an investigational medical device. This includes AEs resulting from insufficient or inadequate instructions for use, the operation, any malfunction of the device or any event that is a result of a use error or intentional abnormal use of the investigational medical device.

All patients who have a TEAE classified as an ADE will be summarized by treatment group and by SOC, PT, relationship and intensity, displaying the number and percentage of patients with at least one TEAE classified as an ADE, using only the most severe TEAE recorded at each level of summarization. The total number of events and number of patients with at least one TEAE which classified as an ADE will also be displayed.

For patients with dose adjustment, all data collected regardless of dose adjustment for both treatment groups will be included in the summary. All ADEs will be flagged in listings for AEs.

12.2. Clinical Laboratory Evaluations

Clinical laboratory (clinical chemistry, hematology and urinalysis [including microscopy]) test samples will be analyzed at the central laboratory at each scheduled visit. Erythrocyte Sedimentation Rate (ESR) samples will be analyzed at the local laboratory using kits supplied. Additional clinical laboratory test samples will be collected if a patient experiences delayed hypersensitivity to determine serum sickness. All summaries will be based on the SI (System International) units provided by the central laboratory. Result of clinical laboratory parameters of the central laboratory and ESR will be tabulated by treatment group at each scheduled visit. All clinical laboratory results will be presented in listings.

Actual value and change from baseline for clinical chemistry, hematology and urinalysis will be summarized using descriptive statistics by treatment group, test parameter and scheduled visit, respectively. For the purpose of summarization, any numeric values recorded below the lower limit or above the upper limit of quantification will be set to the respective limit for all related summaries. In listings, original results containing inequality signs will be displayed.

Shift tables from baseline visit to each scheduled post-baseline visit will be generated for urinalysis results using "Normal" or "Abnormal" classification as appropriate by treatment group.

Some clinical laboratory parameters will be labeled with a CTCAE term, and grading will be applied to post-baseline values for numeric parameters where possible according to CTCAE v 5.0. Grades that require clinical input only will not be assigned to these parameters. Grades which are part numeric and part clinical input will be assigned based on the numeric portion only. If different grades share the same criteria due to exclusion of clinical input, lower grade will be used. The CTCAE terms and ranges for applicable parameters are listed in Appendix 2. The CTCAE grades for this analysis will be Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe) and Grade 4 (Life-threatening). The CTCAE Grade 5 (Death) will not be applied in this analysis since death cannot be determined from a numeric laboratory result. If the post-baseline result for a patient does not satisfy any CTCAE grade, it will be classified as "No Grade".

The number and percentage of patients with a result for each grade will be summarized by laboratory category, treatment group, CTCAE term and scheduled visit.

In addition, the table for the most severe grade in Treatment Period and Maintenance Phase will be generated. For the summary in Treatment Period, all post-baseline results including unscheduled and EOS visits (prior to initiation of dose adjustment for Placebo SC group) will be used. For the summary in Maintenance Phase, following results will be used:

1) Patients treated in the Maintenance Phase and not treated in the Extension Phase: All post-baseline results including unscheduled and EOS visits (prior to initiation of dose adjustment for Placebo SC group) collected after the date of Week 10 study drug administration

2) Patients treated in both the Maintenance and Extension Phase: All post-baseline results including unscheduled visit (prior to initiation of dose adjustment for Placebo SC group) collected after the date of Week 10 study drug administration and on or before the first study drug administration date in the Extension Phase.

Clinical chemistry, hematology and urinalysis data will be presented in separate listings along with interpretation (Normal, Abnormal, High or Low), if applicable, to show if a value was outside the normal range and CTCAE results for applicable parameters.

12.2.1. Incidence of Liver Biochemistry Elevation Potentially Related to Liver Injury

The incidence of abnormalities in AST and ALT levels potentially related to liver injury will be analyzed.

The number and percentages of patients with at least one liver biochemistry elevation which occurred after the first study drug administration in Maintenance Phase using only the worst elevation case at each level of summarization will be summarized.

- Any elevations of AST (>3x-, 5x-, 10x-, and 20xULN)
- Any elevations of ALT(>3x-, 5x-, 10x-, and 20xULN)
- Any elevations of ALT or AST (>3x-, 5x-, 10x-, and 20xULN)

The clinical chemistry listing will include a flag indicating the above elevation potentially related to liver injury.

12.3. Complement (C3, C4) and Total Hemolytic Complement

Complement (C3, C4) and total hemolytic complement will be assessed at Week 0. Additional assessment for complement (C3, C4), total hemolytic complement will be assessed if delayed hypersensitivity occurs to determine serum sickness. All complement tests data will be presented in a listing by treatment group for the ITT Population.

12.4. Vital Signs and Weight

Vital signs (including systolic and diastolic blood pressure, heart rate, respiratory rate and body temperature) and weight will be assessed at each scheduled visit. For hypersensitivity monitoring, vital signs will also be assessed at the following time points of scheduled visit:

- Prior to the beginning of the study drug administration
- Within 15 minutes after the end of study drug administration
- 1 hour (+10 minutes) after the end of the study drug administration

Vital signs data and weight assessed will be summarized using descriptive statistics of actual value and change from baseline by treatment group, parameter at each scheduled visit for the Safety Population. Baseline will be obtained using only data from the “Vital Signs and Weights” page of the eCRF.

The number and percentage of patients who have clinically notable hypersensitivity result will be summarized in a table by treatment group, scheduled visit, time points and parameter for the Safety Population. The criteria for clinically notable results are defined as follows:

Table 3. Hypersensitivity Classification for Vital Signs

Parameter	Low	High
Systolic blood pressure (mmHg)	<= 90	>= 160
Diastolic blood pressure (mmHg)	<= 50	>= 90
Heart rate (beats per minute)	<= 50	>= 100
Respiratory rate (breaths per minute)	<= 12	>= 20
Body temperature (°C)	<= 35.0	>= 38.0

All vital signs data including hypersensitivity monitoring results, weight will be listed for each patient by treatment group, visit, time points and parameter for the ITT Population. High and low flags will also be presented in the listing to show whether a value is outside of the normal range.

12.5. Electrocardiograms

Findings of 12-Lead ECG will be classified as either “Normal”, “Abnormal, not clinically significant”, or “Abnormal, clinically significant”. The number and percentage of patients will be summarized by treatment group and scheduled visit for the Safety Population, in the form of a shift table to detect changes from baseline. All 12-Lead ECG data will be listed for each patient by treatment group and visit for the ITT Population.

12.6. Physical Examination

Physical examinations will be performed on scheduled visit before the beginning of the study drug administration (on the same visit day as the study drug administration). The following body systems will be examined:

- General Appearance
- Head, Ears, Eyes, Nose, Throat
- Neck and Thyroid
- Skin
- Cardiovascular System
- Respiratory System
- Abdominal System
- Neurological System
- Musculoskeletal System
- Lymph Nodes
- Other

Findings of physical examination will be collected as either “Normal”, “Abnormal, not clinically significant” or “Abnormal, clinically significant”. The number and percentage of patients will be summarized in a table by treatment group, scheduled visit and body system for the Safety Population, in the form of a shift table to detect changes from baseline. All physical examination data will be listed for each patient by treatment group, visit and body system for the ITT Population.

12.7. Tuberculosis Assessment

TB will be assessed using IGRA, Chest X-ray and clinically monitored throughout the study.

Results for IGRA will be classified as either “Positive”, “Indeterminate” or “Negative”. If retest is conducted because the IGRA result is indeterminate, the result of the retest will be used for the summary. Both first and retest results will be listed. The baseline value for IGRA will be considered to be the last non-missing value before the first administration during Screening Period. If there are no values during Screening Period, the value at Week 0 will be used for the baseline determination. In Treatment Period and Maintenance Phase, the IGRA results at baseline and in each period will be summarized displaying the number and percentage of patients for the Safety Population. For the summary in Treatment Period and Maintenance Phase, results will be determined using the following methodology, based on data from the same visits included in the summary of the most severe grade of CTCAE (Section 12.2):

- If a patient has at least one result of “Positive” in the Treatment Period/Maintenance Phase, the patient will be considered as “Positive".
- If a patient has no “Positive” results and at least one result of “Indeterminate” in the Treatment Period/Maintenance Phase, the patient will be considered as “Indeterminate”
- If a patient has only “Negative” results in the Treatment Period/Maintenance Phase, the patient will be considered as “Negative”

Results for Chest X-ray will be classified as either “Normal”, “Abnormal, Not Clinically Significant” or “Abnormal, Clinically Significant”. The patients will be monitored throughout the study to confirm the presence of any signs or symptoms indicative of tuberculosis.

Each patient’s IGRA, Chest X-ray and TB clinical monitoring results will be separately listed by treatment group and visit for the ITT Population.

12.8. Local Site Pain

Local site pain measurements using 100 mm Visual Analogue Scale (VAS) will be performed immediately (not exceeding 15 minutes) after the end of the study drug administration at each scheduled visit. Local site pain data (scale standardized) will be summarized using descriptive statistics by treatment group and scheduled visit for the

Safety Population. All local site pain data will be listed by treatment group and visit for the ITT Population.

12.9. Pregnancy Test

Pregnancy tests will be conducted and summarized only for female patients of childbearing potential. Pregnancy tests consist of serum and urine pregnancy tests. Serum pregnancy tests will be performed by a central laboratory at Screening and EOS. Urine pregnancy tests will be performed locally at scheduled visits. Serum pregnancy test results will be classified as "Positive", "Inconclusive" or "Negative". Urine pregnancy test results will be classified as "Positive" or "Negative". If a urine pregnancy test result is "Positive", a confirmatory serum pregnancy test should be performed at the central laboratory. The number and percentage of female patients who have pregnancy test results will be summarized by treatment group, scheduled visit (including Baseline and EOS) and test for the Safety Population. For patients with dose adjustment, all data collected regardless of dose adjustment for both treatment groups will be included in the summary. All pregnancy test results will be listed for each patient tested by treatment group, visit and test for the ITT Population.

12.10. Cardiovascular Disease Assessment

Throughout the study, patients will be monitored for cardiovascular disease related signs and symptoms such as but not limited to shortness of breath, palpitations, chest pain, chest discomfort, and/or fainting.

All cardiovascular disease assessment data will be presented in a listing by treatment group and visit for the ITT Population.

12.11. New York Heart Association Functional Classification

Heart failure will be assessed by New York Heart Association (NYHA) functional criteria at scheduled visits. If a patient had heart failure, corresponding NYHA class will be selected. The criteria for heart failure are defined as follows:

Table 4. New York Heart Association Functional Classification

Class	Symptoms
I (Mild)	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath).
II (Mild)	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath).
III (Moderate)	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea.

IV (Severe)	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

The number and percentage of patients will be summarized by treatment group, scheduled visit and NYHA results for the Safety Population. All NYHA criteria assessment data will be presented in a listing by treatment group and visit for the ITT Population. Patients who have no heart failure will be classed as "No Class".

12.12. Anti-Double-Stranded DNA Test

An anti-ds DNA test will be performed at Screening and EOS. If during the course of the study, a patient develops the signs or symptoms of systemic lupus erythematosus or lupus-like disease, the investigator may obtain unscheduled anti-ds DNA and other tests to aid in the evaluation.

All Anti-DS DNA test results will be listed for each patient by treatment group and visit for the ITT Population.

12.13. Immunogenicity

Serum sample for immunogenicity will be collected before study drug administration at each scheduled visit. Additional serum samples for immunogenicity testing may be collected if a patient experiences any delayed hypersensitivity after study drug administration. On the day of initiation of dose adjustment, serum samples for immunogenicity analysis will be collected before study drug administration. Immunogenicity assessment consists of both anti-drug antibody (ADA) and neutralizing antibody (NAb) assays.

The ADA assay will follow a three-tiered approach consisting of (i) screening assay, (ii) confirmatory assay, and (iii) titration. The test outcome for the screening assay will be "Potential Positive" or "Negative". Samples that are "Potential Positive" in the screening assay will be undergone further testing in the confirmatory assay to determine if samples are a true positive. The test outcome for the confirmatory assay will be: "Reactive", "Negative" or "Not applicable (N/A)". "Reactive" indicates a true positive test outcome and will be labeled as "Positive" in outputs, "Negative" is considered negative and "N/A" indicates the assay was negative at the screening phase of the process. Patients with a "Negative" test outcome for either screening or confirmatory assays will be considered negative for the overall ADA assessment. For further characterization, the antibody level will be assessed by titration in confirmed positive samples.

Samples that are positive in the ADA assay will be analyzed further to conduct a NAb assessment. The test outcome for the screening assay will be: "Positive" or "Negative".

The results of the final ADA and the screening NAb assay will be summarized. The number and percentage of patient will be presented by treatment group and test at each scheduled visit for the Safety Population.

In addition, the number of patients and percentages with positive ADA and NAb conversion in Treatment Period and Maintenance Phase will be summarized for the Safety Population. For the summary in Treatment and Maintenance Phase, data from the same visits included in the summary of the most severe grade of CTCAE (Section 12.2) will be used. The rule of ADA and NAb conversion is following:

- ADA Conversion is defined as patients who reported at least one ADA positive result after Week 0 administration in patients who

  1) Have at least one immunogenicity result (including Not Reported Result [NRR]) after Week 0 administration. And

  2) Have not any ADA positive result before Week 0 administration.

- NAb Conversion is defined as patients who reported at least one Nab positive result after Week 0 administration in patients who

  1) Have at least one immunogenicity result (including NRR) after Week 0 administration. And

  2) Have not any NAb positive result before Week 0 administration.

A listing showing immunogenicity test results for each patient will be provided by treatment group and visit for the ITT Population.

The ADA titer values will be determined as the lowest concentration of the diluted sample that is detected at or above titer cut point and be reported as the reciprocal of that dilution. Descriptive statistics of ADA titer will be displayed by treatment group and scheduled visit for the Safety Population. The results of ADA titer for each visit will also be presented in the listing of immunogenicity results for the ITT Population.

13. Changes in the Planned Analysis

13.1. Changes in the Protocol

- PP population definition

According to Study Protocol, PP population was defined as "*who receive all doses (full) of study drug prior to Week 54 and who have at least 1 efficacy evaluation after Week 10 treatment and who do not have any major protocol deviation that is relevant to efficacy analysis*".

However, due to the safety concerns from global pandemic of COVID-19, numerous dose skip cases have occurred. In addition, it is expected that numerous patients assigned to placebo group will be dropped out prior to Week 54. As a result, these patients will be excluded from PP population although patients comply with the study protocol well throughout the study period. But CELLTRION believes that it is appropriate to include these patients if they follow study protocol well and do not have any major deviation

throughout the study period even though they drop out before Week 54 or do not receive all doses.

To include these patients in PP population, the definition of PP population was changed as "who receive at least one full dose of study drug at Week 10 or thereafter prior to Week 54 and who have at least 1 efficacy evaluation"

- Statistical analysis method for primary and key secondary endpoints

As described in the Study Protocol, the main analysis for the primary and key secondary endpoints was planned to be conducted using fisher's exact test. However, in consideration of IND 140478 Preliminary Comments to Pre-BLA Type B Meeting (13Jun2022), the method was changed to the stratified CMH test that could account for covariates (i.e., the randomization stratification factors). Instead, Fisher's exact test will be performed as a sensitivity analysis.

In accordance with the change of the main analysis method, the significance level of the test was also changed from one-sided 2.5% to two-sided 5%.

- Change of the term of mucosal healing to endoscopic-histologic mucosal improvement

In the Study protocol, mucosal healing defined by combination of endoscopic and histologic assessment was set to key secondary endpoint. However, according to the guidance for industry UC treatment (FDA, 2022), Using *mucosal healing* is not recommended as there is no consensus as to how best to define this concept. Thus, term of mucosal healing was discussed with Regulatory authorities and mucosal healing was changed to endoscopic-histologic mucosal improvement.

14. Reference List

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15. APPENDICES

Appendix 1-1: Schedule of Events for Induction and Maintenance Phase

	Screening	Induction Phase				Maintenance Phase									EOS[1]
Study Week		**0**	**2**	**6**	**8[2]**	**10[3]**	**12[3]**	**14**	**22[4]**	**24[4]**	**30**	**38**	**46**	**54**	
Study Day	**–42 ~ 0**	**0**	**14**	**42**	**56**	**70**	**84**	**98**	**154**	**168**	**210**	**266**	**322**	**378**	
Dosing Window[5]		**N/A**	**± 3 days**			**± 3 days**									
Treatment group 1 [6]		**CT-P13 IV**				**CT-P13 SC**			**CT-P13 SC[7]**						
Treatment group 2 [8]						**Placebo SC**			**Placebo SC[7]**						
Informed consent	X														
Demography	X														
Medical history	X														
Hepatitis B and HBV DNA test[9]	X							(X[10])			(X[10])		(X[10])		(X)
Hepatitis C and HCV RNA test[11]	X							(X[10])			(X[10])		(X[10])		(X)
HIV -1 & -2 test	X														
Stool microbiology[12]	X														
Serum pregnancy test[13]	X														X
Anti-ds DNA test[14]	X														X
Chest X-ray[15]	X														
IGRA[16]	X	X[10]		X[10]				X[10]			X[10]			X[10]	X
Inclusion and exclusion criteria	X	X[10]													
Randomization						X[10]									
Efficacy assessments															
Total & Modified Mayo score assessment[17]	X[18]					X[10]			X[10]					X[10]	X
Partial Mayo score assessment[17]	X[18]		X[10]	X[10]		X[10]		X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	X
Flexible proctosigmoidoscopy (Endoscopic subscore of the Mayo score)[19]	X[20]				X				X[10]					X[10, 20]	X
Histologic assessment (RHI score)[21]	X					X			X					X	X
Biopsy for histologic assessment[22]	X				X				X[10]					X[10]	X
SIBDQ		X[10]	X[10]	X[10]		X[10]		X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	X
Safety and other assessments															
Urine pregnancy test[23]		X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	
Clinical laboratory tests[24]	X	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	X
Physical examinations	X	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	X

	Screening	Induction Phase				Maintenance Phase									EOS[1]
Study Week		**0**	**2**	**6**	**8[2]**	**10[3]**	**12[3]**	**14**	**22[4]**	**24[4]**	**30**	**38**	**46**	**54**	
Study Day	**–42 ~ 0**	**0**	**14**	**42**	**56**	**70**	**84**	**98**	**154**	**168**	**210**	**266**	**322**	**378**	
Dosing Window[5]		**N/A**	**± 3 days**			**± 3 days**									
Vital signs and weight[25]	X	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	X
NYHA class assessment	X	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	X
12-lead ECG[26]	X			X		X		X			X			X	X
Hypersensitivity monitoring[27]		X	X	X		X	X	X	X		X	X	X	X	
Immunogenicity[28]		X[10]				X[10]		X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	X
C3, C4 and total hemolytic complement[29]		X[10]													
PK blood samples[30]		X[10]	X[10]	X[10,30]		X[10]		X[10]	X[10, 30]	X[10, 30]	X[10]	X[10]	X[10]	X[10]	
PD blood samples (CRP)[31]	X	X[10]	X[10]	X[10]		X[10]		X[10]	X[10]		X[10]	X[10]	X[10]	X[10]	X
Fecal calprotectin[32]	X					X[10]			X[10]					X[10]	X
VAS local site pain[33]						X	X	X	X		X	X	X	X	
Prior, concomitant medications[34]	X														
TB clinical monitoring[35]	X														
Cardiovascular disease monitoring[36]	X														
AE monitoring[37]	X														

Abbreviations: AE, adverse event; Anti-ds DNA, anti-double stranded DNA; CRP, C-reactive protein; ECG, electrocardiogram; EOS, End-of-Study; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IGRA, interferon-γ release assay; IV, intravenous; N/A, not applicable; NYHA, New York Heart Association; PD, pharmacodynamic; PK, pharmacokinetic; RHI, Robarts histopathology index; SC, subcutaneous; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; TB, tuberculosis; VAS, Visual Analogue Scale.

1. All EOS assessments will be completed after 4 weeks (±3 days) after the last dose of CT-P13 SC or Placebo SC is received, if a patient withdraws prior to Week 102 treatment. For patients who early discontinue the study drug before administration of CT-P13 SC or Placebo SC at Week 10, the EOS visit will be completed after 8 weeks (±3 days) from the last dose of CT-P13 IV is received.
2. At Week 8, only endoscopy and biopsy will be performed for the evaluation of Mayo score and histologic assessments at Week 10. The endoscopy result at Week 8 will be used for randomization at Week 10. Endoscopy and biopsy at Week 8 will be completed within 14 days prior to Mayo score and histologic assessments at Week 10.
3. At Weeks 10 and 12, initial training for self-injection of CT-P13 SC or Placebo SC via PFS will be conducted. If needed, the patient or caregiver will be retrained during the study on how to perform the injection of the study drug.
4. Between Week 22 and Week 24, additional PK sampling visits will be conducted only on patients who agreed to collect further blood samples for Population PK analysis.
5. A dosing window of ±3 days is allowed, including self-injection. The minimal dose interval of 11 days is allowed from Week 10.
6. For Treatment group 1, CT-P13 IV (5 mg/kg) will be administered at Weeks 0, 2, and 6. From Week 10 onwards, CT-P13 SC (120 mg) will be administered during Maintenance Phase. Further doses of study drug with CT-P13 SC will be given every 2 weeks via PFS through Week 54.
7. From Week 22, dose adjustment will be allowed. The patients who received CT-P13 SC 120 mg may increase the dose to CT-P13 SC 240 mg every 2 weeks, if patients initially responded but then lost response according to the loss of response criteria. The patients who received Placebo SC may receive CT-P13 SC 240 mg every 2 weeks, if patients initially responded but then lost response according to the loss of response criteria.

8. For Treatment group 2, CT-P13 IV (5 mg/kg) will be administered at Weeks 0, 2, and 6. From Week 10 onwards, Placebo SC (matching volume to CT-P13 SC 120 mg) will be administered during Maintenance Phase. Further doses of study drug with Placebo SC will be given every 2 weeks via PFS through Week 54.
9. At Screening, HBsAg, HBsAb, and HBcAb must be assessed in all patients (mandatory). If the HBsAg test result is positive, the patient cannot be enrolled. If a patient has results of HBsAg (negative), HBsAb (negative or positive), and HBcAb (positive), a HBV-DNA test will be performed at Screening. If the HBV DNA test result is positive, the patient cannot be enrolled. If the HBV DNA test result is negative and the patient does not have any evidence of liver cirrhosis, the patient can be enrolled. For patients enrolled based on the HBV DNA test, tests for HBsAg, HBsAb, HBV DNA, AST, ALT and total bilirubin will be additionally performed at Weeks 14, 30, 46, 62, 78, 94, and EOS visits. In patients who develop hepatitis B reactivation, study drug should be stopped and the patient must be withdrawn from the study. Hepatitis B analysis will be performed at the central laboratory.
10. Assessed prior to study drug administration.
11. At Screening, hepatitis C antibody and HCV RNA must be assessed in all patients (mandatory). If the HCV RNA test result is positive, the patient cannot be enrolled. If the hepatitis C antibody and HCV RNA test results are both negative, the patient can be enrolled. If the hepatitis C antibody result is positive and HCV RNA test result is negative, the patient can be enrolled as long as the patient does not have liver cirrhosis and achieved a SVR for at least 12 weeks after the completing the hepatitis C infection treatment. For enrolled patients who have a result of hepatitis C antibody (positive), the tests for HCV RNA, AST, ALT, and total bilirubin will be additionally performed at Weeks 14, 30, 46, 62, 78, 94, and EOS visits. In patients who develop hepatitis C activation, study drug should be stopped, and the patient must be withdrawn from the study. Hepatitis C analysis will be performed at the central laboratory.
12. Stool microbiology (enteric pathogens, ova and parasites, and *Clostridium difficile* toxin test) will be performed at Screening and at any point in the study when a patient becomes symptomatic, including worsening or return of disease activity, at the investigator's discretion. Analysis will be performed at the central laboratory.
13. A serum pregnancy test for women of childbearing potential should be conducted at Screening and at the EOS visit. Patients who are of childbearing potential with only negative results from a serum pregnancy test can be enrolled.
14. An anti-ds DNA test will be performed at Screening and at the EOS visit. If during the course of the study, a patient develops the signs or symptoms of systemic lupus erythematosus or lupus-like disease, the investigator may obtain unscheduled anti-ds DNA and other tests to aid in the evaluation. Analysis will be performed at the central laboratory.
15. A chest X-ray (both posterior-anterior and lateral views) is not required at Screening if a chest X-ray result from within the 42 days prior to the first administration of the study drug (Day 0) is available.
16. The IGRA analysis will be performed at the central laboratory.
17. With the exception of Screening, the Mayo score diary will be collected by patients for 7 days immediately prior to the Mayo score assessment and the most recent 3 days (not necessarily consecutive days) within the 7 days will be used to calculate the Mayo score. If the Mayo score assessment is performed at the same date as the flexible proctosigmoidoscopy or full colonoscopy procedure, the 3 days overlapping with endoscopy procedure (i.e., from the day before and up to the next day of the endoscopy procedure) will not be used to calculate the Mayo score.
18. To determine eligibility, the Mayo score diary will be completed within 3 days immediately prior to the first administration of the study drug (Day 0), and the Mayo score will be calculated at Day 0.
19. Full colonoscopy may also be performed based on investigator's discretion. If full colonoscopy has been performed, it can replace flexible proctosigmoidoscopy. Flexible proctosigmoidoscopy (or full colonoscopy) for endoscopic subscore assessment will be performed within 14 days prior to the Mayo score assessment. Flexible proctosigmoidoscopy (or full colonoscopy) can be performed whenever needed based on investigator's discretion including determination of loss of response. Endoscopic subscore by flexible proctosigmoidoscopy (or full colonoscopy) will be evaluated at the central level by an independent reviewer blinded to treatment allocation to confirm eligibility, determine loss of response and for reporting purposes. The local endoscopic subscore will be considered during evaluation of the endoscopic subscore at the central level.
20. The Screening flexible proctosigmoidoscopy (or full colonoscopy) will be performed within 14 days prior to the first administration of the study drug (Day 0). At Screening, full colonoscopy will be performed, instead of flexible proctosigmoidoscopy, for the patients who had an increased risk of colorectal cancer according to the exclusion criteria 8 or who require full colonoscopy at the investigator's discretion for the reasons including suspected extensive colitis or pancolitis. For the patients who had been performed full colonoscopy at Screening, full colonoscopy will be performed at Week 54.
21. Histologic assessment by RHI score will be evaluated at the central level by an independent reviewer blinded to treatment allocation for reporting purposes.
22. Biopsy will be performed within 14 days prior to the histologic assessment.

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23. A urine pregnancy test for women of childbearing potential will be used to confirm that patients are not pregnant before study drug administration on each visit day of scheduled time point or more frequently if required by country-specific legislation. A urine pregnancy test will be performed locally. If a urine pregnancy test result is positive, a confirmatory serum pregnancy test will be performed at the central laboratory.
24. To determine eligibility, retesting will be allowed once during Screening period based on the investigator's discretion. Clinical laboratory (clinical chemistry, hematology, and urinalysis including microscopy) test samples except ESR will be analyzed at the central laboratory. The ESR samples will be analyzed locally using kits supplied. Additional clinical laboratory test samples will be collected if a patient experiences delayed hypersensitivity to determine serum sickness.

Clinical chemistry	Total protein, serum bilirubin (total, direct), ALT, AST, alkaline phosphatase, γ-glutamyltransferase, blood urea nitrogen, creatinine, creatine kinase, creatine kinase-MB, troponin I, albumin, sodium, potassium, calcium, chloride, inorganic phosphorus, glucose, lactate dehydrogenase, total cholesterol, triglyceride, high-density lipoprotein cholesterol, and CRP
Hematology	Red blood cells, ESR, total and differential white blood cell count, absolute neutrophil count, lymphocyte count, platelet count, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and hematocrit
Urinalysis	Bilirubin, blood, glucose, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, and microscopic examination

25. Vital signs (including systolic and diastolic blood pressure, heart and respiratory rates, and body temperature) and weight will be measured after 5 minutes of rest (sitting). In addition, measurement of height will be documented once at Screening.
26. All scheduled 12-lead ECGs must be performed locally after the patient has rested quietly for at least 5 minutes in the supine position. Regardless of the 12-lead ECG result, further cardiological evaluation can be done at the investigator's discretion.
27. Additional vital signs including blood pressure, heart and respiratory rates, and body temperature (prior to the beginning of study drug administration, within 15 minutes after the end of study drug administration, and 1 hour [+10 minutes] after the end of study drug administration) will be monitored for possible hypersensitivity reactions. In addition, hypersensitivity will be monitored by routine continuous clinical monitoring, including patient-reported signs and symptoms. In case of hypersensitivity, emergency equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support including inhalational therapy, oxygen, and artificial ventilation must be available; in addition, any type of ECG can be performed. Delayed hypersensitivity will be monitored, which includes serum sickness-like reactions (myalgia with fever or rash, arthralgia, lymphadenopathy, skin eruption, or edema).
28. Serum samples for immunogenicity testing will be drawn at the same time as the clinical laboratory tests before dosing, where applicable. On the day of initiation of dose adjustment, serum samples for immunogenicity analysis will be collected before study drug administration. Additional serum samples for immunogenicity testing may be collected if a patient experiences any delayed hypersensitivity to determine serum sickness. Analysis will be performed at the central laboratory.
29. Additional serum samples for complement (C3, C4), and total hemolytic complement will be assessed if delayed hypersensitivity occurs to determine serum sickness. Analysis will be performed at the central laboratory.
30. Blood samples for PK analysis will be collected at pre-dose (prior to the beginning of study drug administration) of Weeks 0, 2, 6, 10, 14, 22, 30, 38, 46, 54, 62, 70, 78, 86, 94, 102, and within 15 minutes after the end of the study drug infusion of Week 6. On the day of initiation of dose adjustment, blood samples for PK analysis will be collected at pre-dose. For patients who agreed to collect further blood samples, additional blood samples for further Population PK analysis will be collected at the following time points: any time between 48 hours and 72 hours after study drug administration of Week 22, any time between 120 hours and 168 hours after study drug administration of Week 22, and pre-dose of Week 24.
31. C-reactive protein samples will be drawn at the same time as the clinical laboratory blood samples.
32. Fecal calprotectin analysis will be performed at the central laboratory.
33. All patients will assess local site pain using 100 mm VAS immediately (not exceeding 15 minutes) after the end of administration of study drug.
34. Use of all prior and concomitant medications for the treatment of UC, latent TB, and/or hepatitis C (if applicable) from the diagnosis of disease until the EOS visit, will be recorded in both the source documents and the eCRF. Use of all concomitant medications for other purposes, from within 30 days prior to the first administration of the study drug (Day 0) or from when the ICF is signed, whichever is earlier, will be recorded until the EOS visit. All concomitant medications will also be recorded when any ADR is ongoing at the EOS visit.
35. Throughout the study, patients will be monitored for the clinical signs and symptoms of TB. An additional IGRA or chest X-ray can be performed at the investigator's discretion based on the judgment per the signs and symptoms of TB monitoring. The investigator will confirm the absence of active TB prior to the subsequent dose administration.
36. Throughout the study, patients will be monitored for cardiovascular disease related signs and symptoms such as, but not limited to, shortness of breath, palpitations, chest pain, chest discomfort and/or fainting.

37. Adverse events will be assessed from the date the patient signs the ICF until the last assessment date or EOS visit. Where an ADR (i.e., related to study drug) is ongoing at the EOS visit, the ADR will be followed up until one of the following: resolution or improvement from baseline, relationship reassessed as unrelated, confirmation from the investigator that no further improvement can be expected, end of collection of clinical or safety data, or final database closure. AEs of special interest (i.e., infusion-related reaction/systemic injection reaction, infection, delayed hypersensitivity, localized injection site reaction, and malignancy) should be closely monitored.

Appendix 1-2: Schedule of Events for Extension Phase

	Extension Phase						EOS[1]
Study Week	**62**	**70**	**78**	**86**	**94**	**102**	
Study Day	**434**	**490**	**546**	**602**	**658**	**714**	
Dosing Window[2]	**± 3 days**						
Study Treatment[3]	**CT-P13 SC**						
Hepatitis B and HBV DNA test[4]	(X[5])		(X[5])		(X[5])		(X)
Hepatitis C and HCV RNA test[6]	(X[5])		(X[5])		(X[5])		(X)
Serum pregnancy test[7]							X
Stool microbiology[8]							
Anti-ds DNA test[9]							X[10]
IGRA[11]		X[5]		X[5]		X[5]	X[10]
Efficacy assessments							
Total & Modified Mayo score assessment[12]						X[5]	X[10]
Partial Mayo score assessment[12]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[10]
Flexible proctosigmoidoscopy (Endoscopic subscore of the Mayo score)[13]						X[5]	X[10]
Histologic assessment (RHI score)[14]						X	X[10]
Biopsy for histologic assessment[15]						X[5]	X[10]
SIBDQ		X[5]		X[5]		X[5]	X[10]
Safety and other assessments							
Urine pregnancy test[16]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	
Clinical laboratory tests[17]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
Physical examinations	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
Vital signs and weight[18]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
NYHA class assessment	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
12-lead ECG[19]		X		X		X	X
Hypersensitivity monitoring[20]	X	X	X	X	X	X	
Immunogenicity[21]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X

	Extension Phase						
Study Week	**62**	**70**	**78**	**86**	**94**	**102**	**EOS[1]**
Study Day	**434**	**490**	**546**	**602**	**658**	**714**	
Dosing Window[2]	**± 3 days**						
C3, C4 and total hemolytic complement[22]							
PK blood samples[23]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	
PD blood samples (CRP)[24]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X
Fecal calprotectin[25]		X[5]		X[5]		X[5]	X[10]
VAS local site pain[26]	X	X	X	X	X	X	
Prior, Concomitant medications[27]	X						
TB clinical monitoring[28]	X						
Cardiovascular disease monitoring[29]	X						
AE monitoring[30]	X						

Abbreviations: AE, adverse event; Anti-ds DNA, anti-double stranded DNA; CRP, C-reactive protein; ECG, electrocardiogram; EOS, End-of-Study; HBV, hepatitis B virus; HCV, hepatitis C virus; IGRA, interferon-γ release assay; NYHA, New York heart association; PD, pharmacodynamics; PK, pharmacokinetics; RHI, Robarts histopathology index; SC, subcutaneous; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; TB, tuberculosis; VAS, Visual Analogue Scale.

1. All EOS assessments will be completed 4 weeks (±3 days) after the last dose of CT-P13 SC is received.
2. A dosing window of ±3 days is allowed, including self-injection. The minimal dose interval of 11 days is allowed.
3. All patients will receive active treatment with CT-P13 SC 120 mg via PFS from Week 56. The patients who received CT- P13 SC 240 mg in the Maintenance Phase will continue receiving the same doses of CT-P13 SC for the study treatment in the Extension Phase. During the Extension Phase, dose adjustment will be allowed. The patients who received CT-P13 SC 120 mg may increase the dose to CT-P13 SC 240 mg every 2 weeks, if patients initially responded but then lost response according to the loss of response criteria.
4. For patients enrolled based on the HBV DNA test, the tests for HBsAg, HBsAb, HBV DNA, AST, ALT and total bilirubin will be additionally performed at Weeks 14, 30, 46, 62, 78, 94, and EOS visits. In patients who develop hepatitis B reactivation, study drug should be stopped, and the patient must be withdrawn from the study. Hepatitis B analysis will be performed at the central laboratory.
5. Assessed prior to study drug administration.
6. For enrolled patients who have a result of hepatitis C antibody (positive), tests for HCV RNA, AST, ALT and total bilirubin will be additionally performed at Weeks 14, 30, 46, 62, 78, 94 and EOS visits. In patients who develop hepatitis C activation, study drug should be stopped and the patient must be withdrawn from the study. Hepatitis C analysis will be performed at the central laboratory.
7. A serum pregnancy test for women of childbearing potential should be conducted at Screening and at the EOS visit.
8. Stool microbiology (enteric pathogens, ova and parasites, and *Clostridium difficile* toxin test) will be performed at Screening and at any point in the study when a patient becomes symptomatic, including worsening or return of disease activity, at the investigator's discretion. Analysis will be performed at the central laboratory.
9. An anti-ds DNA test will be performed at Screening and at the EOS visit. If during the course of the study, a patient develops the signs or symptoms of systemic lupus erythematosus or lupus-like disease, the investigator may obtain unscheduled anti-ds DNA and other tests to aid in the evaluation. Analysis will be performed at the central laboratory.
10. End-of-Study assessments will only be performed if the assessments were not done at Week 102, or for patients with discontinuation before Week 102.
11. The IGRA analysis will be performed at the central laboratory.

12. With the exception of Screening, the Mayo score diary will be collected by patients for 7 days immediately prior to the Mayo score assessment and the most recent 3 days (not necessarily consecutive days) within the 7 days will be used to calculate the Mayo score. If the Mayo score assessment is performed at the same date as the flexible proctosigmoidoscopy or full colonoscopy procedure, the 3 days overlapping with endoscopy procedure (i.e., from the day before and up to the next day of the endoscopy procedure) will not be used to calculate the Mayo score.
13. Full colonoscopy may also be performed based on investigator's discretion. If full colonoscopy has been performed, it can replace flexible proctosigmoidoscopy. Flexible proctosigmoidoscopy (or full colonoscopy) for endoscopic subscore assessment will be performed within 14 days prior to the Mayo score assessment. Flexible proctosigmoidoscopy (or full colonoscopy) can be performed whenever needed based on investigator's discretion including determination of loss of response. Endoscopic subscore by flexible proctosigmoidoscopy (or full colonoscopy) will be evaluated at the central level by an independent reviewer blinded to treatment allocation to confirm eligibility, determine loss of response and for reporting purposes. The local endoscopic subscore will be considered during evaluation of the endoscopic subscore at the central level.
14. Histologic assessment by RHI score will be evaluated at the central level by an independent reviewer blinded to treatment allocation for reporting purposes.
15. Biopsy will be performed within 14 days prior to the histologic assessment.
16. A urine pregnancy test for women of childbearing potential will be used to confirm that patients are not pregnant before study drug administration on each visit day of scheduled time point or more frequently if required by country-specific legislation. A urine pregnancy test will be performed locally. If a urine pregnancy test result is positive, a confirmatory serum pregnancy test will be performed at the central laboratory.
17. Clinical laboratory (clinical chemistry, hematology, and urinalysis including microscopy) test samples except ESR will be analyzed at the central laboratory. The ESR samples will be analyzed locally using kits supplied. Additional clinical laboratory test samples will be collected if a patient experiences delayed hypersensitivity to determine serum sickness.

Clinical chemistry	Total protein, serum bilirubin (total, direct), ALT, AST, alkaline phosphatase, γ-glutamyltransferase, blood urea nitrogen, creatinine, creatine kinase, creatine kinase-MB, troponin I, albumin, sodium, potassium, calcium, chloride, inorganic phosphorus, glucose, lactate dehydrogenase, total cholesterol, triglyceride, high-density lipoprotein cholesterol, and CRP
Hematology	Red blood cells, ESR, total and differential white blood cell count, absolute neutrophil count, lymphocyte count, platelet count, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and hematocrit
Urinalysis	Bilirubin, blood, glucose, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, and microscopic examination

18. Vital signs (including systolic and diastolic blood pressure, heart and respiratory rates, and body temperature) and weight will be measured after 5 minutes of rest (sitting).
19. All scheduled 12-lead ECGs must be performed locally after the patient has rested quietly for at least 5 minutes in the supine position. Regardless of the 12-lead ECG result, further cardiological evaluation can be done at the investigator's discretion.
20. Additional vital signs including blood pressure, heart and respiratory rates, and body temperature (prior to the beginning of study drug administration, within 15 minutes after the end of study drug administration, and 1 hour [+10 minutes] after the end of study drug administration) will be monitored for possible hypersensitivity reactions. In addition, hypersensitivity will be monitored by routine continuous clinical monitoring, including patient-reported signs and symptoms. In case of hypersensitivity, emergency equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support including inhalational therapy, oxygen, and artificial ventilation must be available; in addition, any type of ECG can be performed. Delayed hypersensitivity will be monitored, which includes serum sickness-like reactions (myalgia with fever or rash, arthralgia, lymphadenopathy, skin eruption, or edema).
21. Serum samples for immunogenicity testing will be drawn at the same time as the clinical laboratory tests before dosing, where applicable. On the day of initiation of dose adjustment, serum samples for immunogenicity analysis will be collected before study drug administration. Additional serum samples for immunogenicity testing may be collected if a patient experiences any delayed hypersensitivity to determine serum sickness, as well. Analysis will be performed at the central laboratory
22. Additional serum samples for complement (C3, C4), total hemolytic complement will be assessed if delayed hypersensitivity occurs to determine serum sickness. Analysis will be performed at the central laboratory.
23. Blood samples for PK analysis will be collected at pre-dose (prior to the beginning of study drug administration) of Weeks 0, 2, 6, 10, 14, 22, 30, 38, 46, 54, 62, 70, 78, 86, 94, 102, and within 15 minutes after the end of the study drug infusion of Week 6. On the day of initiation of dose adjustment, blood samples for PK analysis will be collected at pre-dose.
24. C-reactive protein samples will be drawn at the same time as the clinical laboratory blood samples.
25. Fecal calprotectin analysis will be performed at the central laboratory.
26. All patients will assess local site pain using 100 mm VAS immediately (not exceeding 15 minutes) after the end of administration of study drug.

27. Use of all prior and concomitant medications for the treatment of UC, latent TB, and/or hepatitis C (if applicable) from the diagnosis of disease until the EOS visit, will be recorded in both the source documents and the eCRF. Use of all concomitant medications for other purposes, from within 30 days prior to the first administration of the study drug (Day 0) or from when the ICF is signed, whichever is earlier, will be recorded until the EOS visit. All concomitant medications will also be recorded when any ADR is ongoing at the EOS visit.
28. Throughout the study, patients will be monitored for the clinical signs and symptoms of TB. An additional IGRA or chest X-ray can be performed at the investigator's discretion based on the judgment per the signs and symptoms of TB monitoring. The investigator will confirm the absence of active TB prior to the subsequent dose administration.
29. Throughout the study, patients will be monitored for cardiovascular disease related signs and symptoms such as, but not limited to shortness of breath, palpitations, chest pain, chest discomfort, and/or fainting.
30. Adverse events will be assessed from the date the patient signs the ICF until the last assessment date or EOS visit. Where an ADR (i.e., related to study drug) is ongoing at the EOS visit, the ADR will be followed up until one of the following: resolution or improvement from baseline, relationship reassessed as unrelated, confirmation from the investigator that no further improvement can be expected, end of collection of clinical or safety data, or final database closure. AEs of special interest (i.e., infusion-related reaction/systemic injection reaction, infection, delayed hypersensitivity, localized injection site reaction, and malignancy) should be closely monitored.

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Appendix 2: Table of CTCAE Terms and Grades

CTCAE Term	Laboratory Parameter	Level	Grade 1	Grade 2	Grade 3	Grade 4
Blood bilirubin increased	Serum Bilirubin (Total) *	High	>ULN - 1.5 x ULN if baseline was normal; > 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x ULN if baseline was normal; >1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x ULN if baseline was normal; >3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x ULN if baseline was normal; >10.0 x baseline if baseline was abnormal
Alanine aminotransferase increased	Alanine aminotransferase (ALT) *	High	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Aspartate aminotransferase increased	Aspartate aminotransferase (AST) *	High	>ULN - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 5.0 x ULN if baseline was normal; >3.0 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Alkaline phosphatase increased	Alkaline Phosphatase *	High	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
GGT increased	γ-Glutamyl Transferase *	High	>ULN - 2.5 x ULN if baseline was normal; 2.0 - 2.5 x baseline if baseline was abnormal	>2.5 - 5.0 x ULN if baseline was normal; >2.5 - 5.0 x baseline if baseline was abnormal	>5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	>20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal
Creatinine increased	Creatinine	High	>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN
CPK increased	Creatine Kinase	High	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN
Hypoalbuminemia	Albumin	Low	<LLN - 3 g/dL; <LLN - 30 g/L	<3 - 2 g/dL; <30 - 20 g/L	<2 g/dL; <20 g/L	
Hypernatremia	Sodium	High	>ULN - 150 mmol/L	>150 - 155 mmol/L;	>155 - 160 mmol/L;	>160 mmol/L;
Hyponatremia	Sodium	Low	<LLN - 130 mmol/L	125-129 mmol/L	120-124 mmol/L	<120 mmol/L;
Hyperkalemia	Potassium	High	>ULN - 5.5 mmol/L	>5.5 - 6.0 mmol/L;	>6.0 - 7.0 mmol/L;	>7.0 mmol/L;
Hypokalemia	Potassium	Low	<LLN - 3.0 mmol/L	<LLN - 3.0 mmol/L; #	<3.0 - 2.5 mmol/L;	<2.5 mmol/L;
Hypercalcemia	Calcium	High	Corrected serum calcium of >ULN - 11.5 mg/dL; >ULN - 2.9 mmol/L; @	Corrected serum calcium of >11.5 - 12.5 mg/dL; >2.9 - 3.1 mmol/L; @	Corrected serum calcium of >12.5 - 13.5 mg/dL; >3.1 - 3.4 mmol/L; @	Corrected serum calcium of >13.5 mg/dL; >3.4 mmol/L; @
Hypocalcemia	Calcium	Low	Corrected serum calcium of <LLN - 8.0 mg/dL; <LLN - 2.0 mmol/L; @	Corrected serum calcium of <8.0 - 7.0 mg/dL; <2.0 - 1.75 mmol/L; @	Corrected serum calcium of <7.0 - 6.0 mg/dL; <1.75 - 1.5 mmol/L; @	Corrected serum calcium of <6.0 mg/dL; <1.5 mmol/L; @

CTCAE Term	Laboratory Parameter	Level	Grade 1	Grade 2	Grade 3	Grade 4
Hypoglycemia	Glucose	Low	<LLN - 55 mg/dL; <LLN - 3.0 mmol/L	<55 - 40 mg/dL; <3.0 - 2.2 mmol/L	<40 - 30 mg/dL; <2.2 - 1.7 mmol/L	<30 mg/dL; <1.7 mmol/L;
Blood lactate dehydrogenase increased	Lactate Dehydrogenase	High	>ULN			
Cholesterol high	Total Cholesterol	High	>ULN - 300 mg/dL; >ULN - 7.75 mmol/L	>300 - 400 mg/dL; >7.75 - 10.34 mmol/L	>400 - 500 mg/dL; >10.34 - 12.92 mmol/L	>500 mg/dL; >12.92 mmol/L
Hypertriglyceridemia	Triglyceride	High	150 mg/dL - 300 mg/dL; 1.71 mmol/L - 3.42 mmol/L	>300 mg/dL - 500 mg/dL; >3.42 mmol/L - 5.7 mmol/L	>500 mg/dL - 1000 mg/dL; >5.7 mmol/L - 11.4 mmol/L	>1000 mg/dL; >11.4 mmol/L;
Leukocytosis	Total White Blood Cell Count	High			>100,000/mm3	
White blood cell decreased	Total White Blood Cell Count	Low	<LLN - 3000/mm3; <LLN - 3.0 x 10e9 /L	<3000 - 2000/mm3; <3.0 - 2.0 x 10e9 /L	<2000 - 1000/mm3; <2.0 - 1.0 x 10e9 /L	<1000/mm3; <1.0 x 10e9 /L
Neutrophil count decreased	Absolute Neutrophil Count	Low	<LLN - 1500/mm3; <LLN - 1.5 x 10e9 /L	<1500 - 1000/mm3; <1.5 - 1.0 x 10e9 /L	<1000 - 500/mm3; <1.0 - 0.5 x 10e9 /L	<500/mm3; <0.5 x 10e9 /L
Lymphocyte count decreased	Lymphocyte Count	Low	<LLN - 800/mm3; <LLN - 0.8 x 10e9/L	<800 - 500/mm3; <0.8 - 0.5 x 10e9 /L	<500 - 200/mm3; <0.5 - 0.2 x 10e9 /L	<200/mm3; <0.2 x 10e9 /L
Lymphocyte count increased	Lymphocyte Count	High		>4000/mm3 - 20,000/mm3	>20,000/mm3	
Platelet count decreased	Platelet Count	Low	<LLN - 75,000/mm3; <LLN - 75.0 x 10e9 /L	<75,000 - 50,000/mm3; <75.0 - 50.0 x 10e9 /L	<50,000 - 25,000/mm3; <50.0 - 25.0 x 10e9 /L	<25,000/mm3; <25.0 x 10e9 /L
Anemia	Hemoglobin	Low	<LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	<10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80g/L	<8.0 g/dL; <4.9 mmol/L; <80 g/L	
Hemoglobin increased	Hemoglobin	High	Increase in >0 - 2 g/dL from ULN	Increase in >2 - 4 g/dL from ULN	Increase in >4 g/dL from ULN	
Eosinophilia	Eosinophils	High	>ULN and >Baseline	-	-	-
Glucosuria	Glucose	N/A	Present	-	-	-

Note: LLN = lower limit of normal, ULN = upper limit of normal. The LLN and ULN values will be the lower and upper limits of the normal ranges as provided by the central laboratory. N/A = Not Applicable.

* indicates that baseline results will be considered abnormal only when the baseline result is abnormal and high, otherwise normal.

# indicates that this grade will not be used because this grade shares the same criteria due to exclusion of clinical input.

@ indicates that corrected calcium (mg/dL) = measured total calcium (mg/dL) + 0.8 (4.0 – serum albumin [g/dL]), where 4.0 represents the average albumin level. For SI units as: Corrected calcium (mmol/l) = total Ca (mmol/l) + 0.02 (40 –serum albumin [g/l]). The LLN and ULN values of total calcium will be used.

CELLTRION Inc.
CT-P13 3.7

A Randomized, Placebo Controlled, Double-Blind, Phase 3 Study to Evaluate the Efficacy and Safety of the Subcutaneous Injection of CT-P13 (CT-P13 SC) as Maintenance Therapy in Patients with Moderately to Severely Active Ulcerative Colitis

21st September 2022
Statistical Analysis Plan Addendum

Final Version 1.0

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Upon review of this document, including table, listing and figure shells, the undersigned approves the final statistical analysis plan. The analysis methods and data presentation are acceptable, and the table, listing and figure production can begin.

TABLE OF CONTENTS

1. Statistical Analysis Plan Addendum

The Statistical Analysis Plan (SAP) Addendum describes the change from SAP final version 1.0 dated 14th September 2022.

2. Overview of Changes Required

This SAP addendum describes the change of the definition of Mis-randomization. The purpose of this addendum is to classify patients who have received at least one treatment (prior to initiation of dose adjustment) other than the randomized treatment only prior to Week 54 (the primary and key secondary endpoints assessment visit) as the mis-randomization. This is because the mis-randomization at Week 54 does not affect the results of the primary and key-secondary endpoints which is assessed prior to the study drug administration.

2.1. Protocol Deviations

2.1.1. Change of: Section 5.6

The definition of Mis-randomization will be changed by adding the condition "before Week 54" as follows:
"Mis-randomizations (PK and PP Population): Patients who received the other treatment (prior to initiation of dose adjustment) than that to which they are assigned before Week 54 will be defined as mis-randomized."