CELLTRION, Inc
CT-P13 4.3

An Observational, Prospective Cohort Study to Evaluate the Safety and Efficacy of Remsima™ in Patients with Crohn's Disease (CD) or Ulcerative Colitis (UC)

19th June 2020

Statistical Analysis Plan

Final version 6.0

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Approved by: _____ Date: ___/___/___

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

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List of Abbreviations

Abbreviation	Definition
ADA	Anti-Drug Antibody
AE	Adverse Event
BMI	Body Mass Index
CD	Crohn's Disease
CDAI	Crohn's Disease Activity Index
CTCAE	Common Terminology Criteria for Adverse Events
eCRF	Electronic Case Report Form
EOS	End of Study
ESI	Events of Special Interest
EU	European Union
[redacted]	[redacted]
HBV	Hepatitis B Virus
HLT	High-Level Terms
HLGT	High-Level Group Terms
HIV	Human Immunodeficiency Virus
HSTCL	Hepatosplenic T-Cell Lymphoma
IBD	Inflammatory Bowel Disease
ICH	International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IGRA	Interferon-gamma Release Assay
MedDRA	Medical Dictionary for Regulatory Activities
IRR	Infusion Related Reaction
MELAS	Mitochondrial Encephalomyopathy, Lactic acidosis, and Stroke-like Episodes
PT	Preferred Term
PCDAI	Pediatric Crohn's Disease Activity Index
PUCAI	Pediatric Ulcerative Colitis Activity Index
PY	Patient Years
SAP	Statistical Analysis Plan
SAE	Serious Adverse Event
SMQ	Standardized MedDRA Queries
TB	Tuberculosis
TEAE	Treatment-Emergent Adverse Event
TESAE	Treatment-Emergent Serious Adverse Event
UC	Ulcerative Colitis
WHO	World Health Organization

1 Study Administration Structure

- Study conduct, project manager, data management, clinical monitoring
  - Celltrion Inc, Incheon, South Korea
  - [redacted]
  - [redacted]
- Routine blood analysis, urinalysis, urine pregnancy test.
  - Local laboratory
- Bioanalytical laboratory (Immunogenicity, IGRA analyses)
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
- Preparation of Statistical Analysis Plan (SAP), statistical analysis
  - Celltrion Inc, Incheon, South Korea
- Medical writing
  - Celltrion Inc, Incheon, South Korea
  - [redacted]

1.1 Data Quality Assurance

CELLTRION will work to ensure that the data collected, analyzed, and reported for this study are of the highest quality possible. This will be accomplished in part by having thorough edit checks written, programmed, and updated as needed to guarantee high quality data.

All analyses will be conducted using [redacted].

2 Introduction

This Statistical Analysis Plan (SAP) defines the statistical methods and data presentations to be used by the CELLTRION Clinical Statistics team in the analysis and presentation of data for annual analysis of CELLTRION study number CT-P13 4.3, entitled an observational, prospective cohort study to evaluate the safety and efficacy of Remsima™ in patients with Crohn's disease (CD), or Ulcerative Colitis (UC).

This SAP is based on the following documents:

- Study protocol Version 3.0 (Korea Specific) – 27 May 2015
- Study protocol Version 4.0 (Korea Specific) – 03 August 2016
- Case Report Form Version 3.0 (Korea) – 17 July 2015
- Case Report Form Version 4.0 (Korea) – 01 September 2016
- Study protocol Version 2.1 (EU Specific) – 03 June 2015

- Mock Screen Layout Final Version 4.1 (EU) – 23 November 2015

This SAP covers following analyses in aforementioned documents:

- Incidence of Treatment-emergent Adverse events (TEAEs)
- Incidence of TEAEs in the categories of Event of special interest
- Incidence of Treatment-emergent Serious Adverse events (TESAEs)
- Incidence of TEAEs leading to permanent discontinuation of study drug
- Deaths
- Results of interferon-gamma release assay (IGRA)
- Results of chest X-ray
- Immunogenicity
- Proportion of patients with Clinical Response, Clinical Remission, Sustained Clinical Response, Sustained Clinical Remission and Loss of Response in each indications
- Descriptive statistics of CDAI scores
- Descriptive statistics of PCDAI scores
- Descriptive statistics of the Number of Draining Fistulas
- Descriptive statistics of Mayo scores
- Descriptive statistics of PUCAI scores
- Health-Economics Evaluation

3 Objectives

The primary objective of this study is to assess the safety of Remsima™ by evaluation of Events of Special Interest (ESI) in inflammatory bowel disease (IBD) patients, who have active Crohn's Disease (CD), fistulizing Crohn's Disease (CD), or Ulcerative Colitis (UC) for up to 5 years for each patient.

The secondary objectives of this study are to evaluate additional safety and efficacy of Remsima™ in IBD patients, who have active CD, fistulizing CD or UC.

4 Study Design

4.1 Overall Study Design

This study is a longitudinal, observational, prospective cohort, phase IV study to assess the safety and efficacy of Remsima™ in patients with active CD, fistulizing CD or UC up to 5 years from the initiation of treatment for each patient. Patients treated with Remsima™ will be considered as Remsima™. Patients either with or without the experience of Remicade® can participate in this study. If a patient has been treated with Remicade® prior to enrollment, their analysis group will be classified as "Switched to Remsima™", and otherwise, "Remsima™". The study will be conducted according to the Declaration of Helsinki and the International

Council for Harmonisation of technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) – Good Clinical Practice. Informed consent from all patients and/or legal guardian according to the regulatory and legal requirements will be obtained prior to enrollment. Patients will undergo safety and efficacy assessments in accordance with routine medical practice. The decision to treat with Remsima™ will be independent of the decision to enroll the patient in this registry.

Patients will be included in this registry who are receiving treatment with 5mg/kg of Remsima™ by IV infusion at weeks 0, 2 and 6, and every 8 weeks thereafter in accordance with the product label. Dose and treatment schedule are recommended to comply with the approved posology in each regulatory authority or investigator's clinical decision. A dose visit window of ± 3 days is recommended up to and including Dose 3; a visit window of ± 14 days at maximum is recommended after Dose 3 including the End-of-Study (EOS) Visit. Practicing physician will choose an assessment timepoint among the visits about every 6 months or 1 year. If a patient has been treated with infliximab prior to enrollment, their dosing schedule will be continued appropriately. Participating patients will be followed for a period of up to 5 years after the first dose of Remsima™. The EOS visit only needs to be completed if the patient withdraws prior to study completion. An EOS visit will be made 8 weeks after the last dose is received. If the patient has completed the full 5-year study period, a separate EOS visit is not required. In this case, last visit will be considered the EOS visit. For those patients who initially respond to 5 mg/kg Remsima™ but who subsequently loose response, dose escalation is permitted in accordance with the local guidelines of the institution in which the patient is receiving treatment. Pre-treatment with antihistamines, hydrocortisone and/or paracetamol are permitted and infusion rate could be slowed down in order to decrease the risk of infusion-related reactions especially, if infusion-related reactions have occurred previously.

4.2 Sample Size

This study aims to recruit at least 500 patients taking Remsima™ including patients switched to Remsima™ in participating study centers, as part of amalgamated registry data of 3100 patients. The sample size of 3100 achieves 80% power with 5% one-sided significance level to detect the difference of incidence rates of Tuberculosis (TB) between patients treated with Remsima™ and patients treated with Remicade®, as small as 0.247%. The incidence rate of TB in patients group with Remicade® is estimated as 0.223% from TREAT [Lichtenstein *et al*, 2012] and BSRBR [Dixon *et al*, 2010] studies and the calculation of power is based on the post-marketing surveillance sample size calculation procedure of [redacted]. In terms of relative risk in a registry setting, the ratio of the probability of developing TB with Remsima™ versus Remicade® is 2.108. This provides sufficient statistical power to discern any statistical difference in reported TB rates. At least 50 percentage of target number of patients will be enrolled in European regions; recruitment in selected Eastern European and Western European countries will continue for 5 years after respective launches.

5 General Statistical Considerations

Continuous data will be summarized using descriptive statistics: n, mean, standard deviation (SD), median, minimum and maximum, unless otherwise indicated. Minimum and maximum will be presented to the same number of decimal places as the raw data, mean and median will be presented to one more decimal place than the raw data, and SD will be presented to two more decimal places than the raw data. In summary tables, all available decimal places will be used although rounded value is listed.

Categorical data will be summarized using counts and percentages. Percentages will be rounded to one decimal place and will be suppressed when the count is zero. A row denoted "Missing" will be included in count tabulations where necessary to account for missing values. The denominator for all percentages will be the number of patients within the indication subgroup and analysis group for the analysis set of interest, unless otherwise indicated.

Data will be displayed in all listings sorted by indication, analysis group, and followed by patient number and the number of dose, if applicable. In cases where more ordering is required, other variables will be included in the sorting order as applicable.

5.1 Analysis Sets

Two analysis sets and four subsets will be analyzed: Safety Analysis Set, Efficacy Analysis Set, Safety – ADA Positive Subset, Safety – ADA Negative Subset, Efficacy – ADA Positive Subset and Efficacy – ADA Negative Subset. A table will be produced by showing the numbers and percentages of patients in each analysis set and subset by indication and analysis group.

5.1.1 Safety Analysis Set

The Safety Analysis Set will consist of all patients who receive at least one dose of the study treatment during any dosing period. A patient will be considered to have received study medication if the patient is recorded as having study drug administered or if a date of infusion is recorded on the study drug infusion eCRF page.

5.1.2 Efficacy Analysis Set

The Efficacy Analysis Set will consist of all patients who receive at least one dose of the study treatment during any dosing period and had at least one efficacy result (CDAI score, PCDAI score, number of draining fistulas, Total/Partial Mayo score, PUCAI score) corresponding to indication used for analysis after treatment. A patient will be considered to have received study medication if the patient is recorded as having the study drug administered or if a date of infusion is recorded on the study drug infusion eCRF page.

5.1.3 ADA Positive Subsets

The Safety – ADA Positive Subset and Efficacy – ADA Positive Subset will consist of all patients who have at least one "Positive" result from immunogenicity tests (anti-drug antibody [ADA]) (excluding the result on or before the date of first infusion of study drug) in Safety and Efficacy Analysis Set, respectively.

5.1.4 ADA Negative Subsets

The Safety – ADA Negative Subset and Efficacy – ADA Negative Subset will consist of all patients who have all "Negative" results including "NRR" from immunogenicity tests (ADA) (excluding the result on or before the date of first infusion of study drug) in Safety and Efficacy Analysis Set, respectively.

5.2 Analysis Group

The analysis group will be determined based on treatments that patients have received before enrollment. Definition of analysis groups are like below.

- Remsima:
  Patients who were not treated with Remicade® before enrollment.
- Switched to Remsima:
  Patients who were treated with Remicade® before enrollment.

All tables and listings will be generated by all analysis group.

5.3 Indication

All analyses will be conducted by indication consisting of moderate to severe active CD, pediatric severe active CD, fistulizing active CD, moderate to severe active UC and pediatric severe active UC. Patients with active CD or UC aged 6 to 17 will be considered as pediatric patients. The moderate to severe active CD, UC and fistulizing active CD will include adult patients only. Only the indications allowed for this registry will be included for the all analysis sets.

5.4 Baseline

A baseline value will be defined as a last non-missing value on or before the date of first infusion of study drug.

6 Patient Disposition

The total number of screened patients will be tabulated. Among the patients in Safety Analysis Set, the number and percentage of patients completed or discontinued the study will also be displayed by indication and analysis group.

The number and percentage of patients who discontinued the study will also be displayed by primary reason for discontinuation using the following categories and orderings:

- withdrawal of consent or refusal to continue treatment or procedures/observations
- development of signs of disease progression
- loss of efficacy
- any AEs that would compromise the safety of the patient if the patient continues to participate in the study
- a significant or major protocol violation
- lost to follow-up

- death of the patient
- other: study close
- other: except for study close

Especially, patients who discontinued the study because they did not meet the inclusion/exclusion criteria according to the Korean version eCRF, will be counted in "a significant or major protocol violation" category.

The time on study drug prior to discontinuation will be calculated as (Date of last visit [For Korea, Date of permanent discontinuation] – Date of Visit 1 + 1) and summarized separately for patients who initiate study treatment and discontinue study treatment prematurely.

Summary will be repeated for Efficacy Analysis Set.

It will be listed by patients whether the patient failed screening or not. The dates of Visit 1 and Last visit and, if applicable, the reason for discontinuation will also be listed by patient in addition to whether the patient initiated treatment, and completed the study.

7 Demographics and Baseline Characteristics

7.1 Demographics

The following demographic measures will be tabulated for the Safety Analysis Set by indication and analysis group; age (years); sex (male, female); race (white, black, asian, other); weight (kg), height (cm) as recorded at Screening visit, Body Mass Index (BMI) (kg/m^2); region (European, Non-European).

Patient's age will be automatically calculated in the eCRF system based on the date of informed consent signed and the date of birth. The BMI will be calculated as (weight (kg)/[height (m)]^2) using results of Screening visit.

Percentages will be calculated using the number of patients in the Safety Analysis Set by indication and analysis group as the denominator. Descriptive statistics of height and BMI will not include the patients whose height is not collected according to Korea eCRF version 4.0.

A listing of demographics for each patient will also be provided.

7.2 Smoking Status

At Screening and EOS visit, smoking status will be collected. Smoking status of patients enrolled based on Korea eCRF version 4.0 is not collected. The following measures will be tabulated for Safety Analysis Set by status; smoking status (Current Smoking, Never Smoking, Former Smoking); average cigarettes per day; duration of smoking (years). The duration of smoking will be collected in eCRF for only Korean patients and this will be derived for European patients as follows:

- Current smoking: (Date of collection - Date when started smoking+1)/365.25
- Former smoking: (Date when stopped smoking - Date when started smoking+1)/365.25

If an incomplete smoking start or end date is recorded for European patients, this will be imputed using the latest possible date for calculating duration of smoking (years). For instance, if the day is missing (i.e. XXMAR2010) the date will be the last day of the month (i.e. 31MAR2010). If the day and month are missing (i.e. XXXXX2010) the date will be set to the 31st December (i.e. 31DEC2010). If the imputed date is later than the collection date or date when stopped smoking, this will be imputed using the collection date or date when stopped smoking respectively. If the whole date is missing, the date will not be imputed and duration of smoking will not be calculated.

Percentages will be calculated using the number of patients in the Safety Analysis Set by indication and analysis group.

A listing of smoking status for each patient will also be provided.

7.3 IBD Surgeries

Patients' IBD related surgeries during the study will be collected in eCRF only for European patients. All IBD related surgeries data will be summarized by indication, analysis group, system organ class and preferred term details of surgery displaying the number and percentage of patients. At each level of summarization, a patient is counted once if they reported one or more findings. IBD related surgeries will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 22.1 or the higher version. Percentages will be calculated using the number of patients in the Safety Analysis Set for each indication and analysis group as the denominator. Surgical details will also be listed by analysis group and indication.

7.4 IBD History

IBD history is captured at Screening visit. The descriptive statistics of time since initial IBD diagnosis will be tabulated by indication for the Safety Analysis Set.

Time since initial IBD diagnosis (duration of IBD) is defined as the duration in years from the date of initial IBD diagnosis to the date of screening, and will be calculated as [date of screening visit – date of diagnosis + 1)/365.25]. In the IBD history eCRF page, patients can check all of their diagnosed IBD diseases (Active CD, Fistulizing active CD and UC). If an incomplete date is recorded for a patient, this will be imputed using the latest possible date. For instance, if the day is missing (i.e. XXMAR2010) the date will be the last day of the month (i.e. 31MAR2010). If the day and month are missing (i.e. XXXXX2010) the date will be set to the 31st December (i.e. 31DEC2010). If the whole date is missing, the date will not be imputed and time since IBD diagnosis will not be calculated. If the imputed date is later than the screening date, this will be imputed using the date of screening.

IBD history will also be listed for the Safety Analysis Set by analysis group and indication. Time since IBD diagnosis will be presented to two decimal places.

7.5 Medical History

Medical history is captured at the Screening visit and will be coded using the MedDRA version 22.1 or the higher version. Medical history will be summarized by indication, analysis group, system organ class and preferred term for the Safety Analysis Set. The following measures will be listed for the Safety Analysis Set by analysis group and indication; condition and diagnosis;

system organ class and preferred term; start and stop date of medical history; ongoing ("Yes", "No"); interpretation (If Clinically Significant, Specify). Interpretations are collected only for Korean patients. In Korea eCRF, only year and month are collected for start dates of medical history. Stop dates of medical history are not collected in the Korea eCRF.

7.6 Hepatitis A, B and C, and human immunodeficiency virus testing

At Screening, viral serology tests will be performed at the investigator's medical judgement based on results of previously performed test or patient's status in EU and Korea eCRF. Hepatitis A test is only performed in Korea eCRF and viral serology tests are not conducted after revision to Korea eCRF version 4.0. Viral serology test results will be listed by analysis group and indication for the Safety analysis set.

8 Treatments and Medications

8.1 Biologic Therapy

Biologic therapy details will be coded using the World Health Organization (WHO) Drug Dictionary (WHO Drug Global B3 Version September 1, 2019 or the later). For the summary of biologic therapy, incomplete dates will be imputed as described in Section 8.2.

Prior biologics will be tabulated by drug class and preferred term for the Safety Analysis Set by indication and analysis group. Prior biologics will be defined as the biologics that actual or imputed start date is earlier than date of the first infusion of study drug.

Duration of the prior biologics with preferred term of "INFLIXIMAB" will be summarized using descriptive statistics in a separate table. The duration will be calculated by each patient as follows;

- Patient having continuous prior infliximab: (the first infusion date after study enrollment – the earliest start date of the prior infliximab +1)
- Patient not having continuous prior infliximab: (the earlier date of [the latest end date of the prior infliximab or the first infusion date after study enrollment] – the earliest start date of the prior infliximab + 1)

The following measures will be listed for the Safety Analysis Set by analysis group and indication; drug class, preferred term and drug name; start and end date of biologic therapy; duration of previous exposure to infliximab; single dose; frequency; unit; route; discontinuation reason.

8.2 Prior and Concomitant Medication

Prior and concomitant medications will be coded using the WHO Drug Dictionary (WHO Drug Global B3 Version September 1, 2019 or the later). For the purpose of inclusion in prior or concomitant medication listings, incomplete medication start and end dates will be imputed as follows:

If the end 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 end date is after the date of death, the end date will be imputed as the date of death. If the start date is incomplete the following rules will be applied. If the end date is incomplete, imputed end date will be used instead of reported end date.

- Missing day: Assume the day is the 1st of the month. If the partial date and the date of first infusion of study drug (defined as the earliest date recorded on the study drug infusion eCRF page) lie within the same month and year, set to the date of first infusion of study drug, if not after the end date for the medication, otherwise set to end date of the medication.

- Missing day and month: Assume January 1st. If the partial date and the date of first infusion of study drug lie within the same year, set to the date of first infusion of study drug, if not after the end date for the medication, otherwise set to end date of the medication.

- Missing day, month and year: Assume the date of first infusion of study drug, if not after the end date for the medication, otherwise set to the end date for the medication.

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

- Example 1:
  Medication start: UNJUN2011
  Medication end: 20OCT2011
  Date of first infusion of study drug: 16OCT2011
  Medication start imputed: 01JUN2011

- Example 2:
  Medication start: UNOCT2011
  Medication end: 20OCT2011
  Date of first infusion of study drug: 16OCT2011
  Medication start imputed: 16OCT2011

- Example 3:
  Medication start: UNOCT2011
  Medication end: 20OCT2011
  Date of first infusion of study drug: 24OCT2011
  Medication start imputed: 20OCT2011

Medications will be classed as either prior or concomitant. A prior medication is defined as a medication where actual or imputed start and end dates are before the date of the first infusion of study drug. A concomitant medication is defined as one where the actual or imputed end date is either on or after the date of first infusion of study drug, continuing or missing. Actual

or imputed start date of a concomitant medication can be before or after date of the first infusion of study drug.

Prior and concomitant medications will be listed separately for the Safety Analysis Set. The following measures will be listed for the Safety Analysis Set by analysis group and indication; drug class; preferred term; drug name; start and end date of prior or concomitant medication; reason for medication/indication; single dose; frequency; unit; route.

8.3 Exposure of Study Drug

A frequency table for the maximum dose received (mg/kg) and dose duration (months), and the descriptive statistics of dose duration will be presented by indication and analysis group for patients in the Safety Analysis Set. For the summary of maximum dose received (mg/kg), the latest available weight will be used if the weight is missing at the visit of interest. If the weight of the first visit is missing, screening weight will be imputation to the first visit. The study drug exposure for each patient will be listed by analysis group and indication. The following measures will be listed for the Safety Analysis Set by analysis group and indication; Visit; Remsima Administered; Reason Not Administered; Date of Infusion; Start Time/ Stop Time; Dose Administered (mg); Dose Administered (mg/kg); Dose Change Reason.

9 Safety Analysis

All safety analyses will be performed using the Safety Analysis Set unless otherwise indicated.

9.1 Adverse Events

An adverse event (AE) is defined as any untoward medical occurrence, including a clinically significant laboratory finding, symptom, or disease in a patient enrolled into this study regardless of its causal relationship to study drug.

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

The MedDRA version 22.1 or the higher version will be used to code all AEs. AEs will be graded for severity according to the Common Terminology Criteria for Adverse Events (CTCAE) V4.0.

Listings for AEs will include the following information from the eCRF: indication; system organ class, preferred term and reported term; start and stop date; whether the event is a TEAE; frequency (continuous, intermittent); outcome (recovered, recovering, recovered with sequelae, not recovered, fatal, unknown); any treatment required (no, yes with specified treatment); intensity (CTCAE Grade 1: mild, Grade 2: moderate, Grade 3: severe, Grade 4: life-threatening and Grade 5: death); action taken with study drug (dose increased, dose decreased, dose not changed, permanently discontinued, stopped temporarily, dose interruption, unknown); relationship to study drug (unrelated, possible, probable, definite); whether the event was serious (yes, no); and ESI to which the AE corresponds; batch number. Listings will be

generated by analysis group and indication for the Safety Analysis Set. Patients in the Safety – ADA Positive Subset and Safety – ADA Negative Subset will be flagged in the listing.

Events will be considered to be related if relationship is possible, probable or definite. Events with no relationship recorded will be summarized separately under a missing category.

For the purpose of inclusion in TEAE tables, an incomplete AE start date and end date will be imputed.

Incomplete AE end dates will be handled as follows:

- Missing day (e.g. XXFEB2017): Assume the last day of the month (e.g. 28FEB2017)
- Missing day and month (e.g. XXXXX2017): Assume December 31st (e.g. 31DEC2017)
- Missing day, month and year (e.g. XXXXXXXXX): Leave it as missing.

Incomplete AE start dates will be handled as follows:

- If the day of an Adverse Event is missing (e.g. XXFEB2017), the month and the year of the partial date will be compared to the date of the first infusion of study drug.
    - If 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 infusion of study drug, or (ii) the actual or imputed end date of the AE. If the actual or imputed end date of the AE is missing, AE start date will be imputed as the date of the first infusion of study drug.
    - If the month and the year are not equal, the AE start date will be imputed as the first day of the month (e.g. 01FEB2017).
- If the day and the month are missing (e.g. XXXXX2017), the year of the partial date will be compared to the date of the first infusion of 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 infusion of study drug, or (ii) the actual or imputed end date of the AE. If the actual or imputed end date of the AE is missing, AE start date will be imputed as the date of the first infusion of study drug.
    - If the year is not equal, start date will be imputed as the 1st of January of the partial date year (e.g. 01JAN2017).
- 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 infusion of study drug, or (ii) the actual or imputed end date of the AE.

9.1.1 Incidence of Treatment-emergent Adverse Events

TEAEs will be summarized by indication, analysis group, relationship, intensity, system organ class and preferred term, 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 will also be displayed. Separately, TEAEs that were reported in at least 3% of patients at preferred term in any analysis group will

be summarized by indication, analysis group, relationship, intensity, system organ class and preferred term for the safety population. All the summarization of TEAEs for the patients in Safety – ADA Positive Subset and Safety – ADA Negative Subset will be provided additionally.

9.1.2 Deaths

A listing will be provided showing any deaths during the course of the trial in the Safety Analysis Set by analysis group and indication including following variables: system organ class, preferred and reported term; date of first dose; whether the event is a TEAE; date of death; days from first dose until death; date of last visit; days on study and relationship to study drug.

9.1.3 Serious Adverse Events

A serious adverse event (SAE) is defined as any event that: results in death, is immediately life threatening (includes events which put patients at risk of death at the time of the event but not events which may have caused patient death if more severe), requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is an important medical event based on appropriate medical judgment, or is a congenital anomaly/birth defect.

Treatment-Emergent Serious Adverse Events (TESAEs) will be summarized by indication, analysis group, relationship, intensity, system organ class and preferred term displaying the number and percentage of patients with at least one TESAE using only the worst intensity recorded at each level of summarization. The total number of events and number of patients with at least one TESAE will also be displayed.

All SAEs will be listed by analysis group and indication including the serious criteria.

9.1.4 Incidence of TEAEs Leading to Permanent Discontinuation of Study Drug

TEAEs which lead to permanent discontinuation of the study drug will be summarized by indication, analysis group, relationship, intensity, system organ class and preferred term displaying the number and percentage of patients. All AEs leading to permanent discontinuation of study drug will be listed by analysis group and indication.

9.1.5 Incidence of TEAEs of Special Interest

In order to assess the safety of Remsima™, the following TEAEs of special interest will be evaluated:

- Hepatitis B virus (HBV) reactivation
- Congestive heart failure
- Opportunistic infections (excluding tuberculosis)
- Serious infections including sepsis (excluding opportunistic infections and tuberculosis)
- Tuberculosis
- Serum sickness (delayed hypersensitivity reactions)
- Haematologic reactions
- Systemic lupus erythematosus/lupus like syndrome

- Demyelinating disorders
- Lymphoma (not HSTCL)
- Hepatobiliary events
- Hepatosplenic T cell lymphoma (HSTCL)
- Intestinal or perianal abscess (in Crohn's disease)
- Serious infusion reactions during a re-induction regimen following disease flare
- Sarcoidosis/sarcoid-like reactions
- Pediatric malignancy
- Leukaemia
- Malignancy (excluding lymphoma)
- Colon carcinoma/dysplasia (in Ulcerative colitis)
- Skin cancer
- Pregnancy exposure
- Bowel stenosis, stricture, obstruction (in Crohn's disease)
- Infusion related reaction/hypersensitivity/anaphylactic reaction

AEs will be determined as ESI using the detailed algorithm in Appendix 1 and Appendix 2. TEAEs of special interest will be summarized by indication, analysis group, relationship, intensity, system organ class and preferred term displaying the number and percentage of patients with at least one TEAE of special interest using only the worst intensity recorded at each level of summarization. The summary table will include the total number of events, the number and percentage of patients with at least one TEAE of special interest, and the number of patients per 100 patient-years (PY). The number of patients with TEAE of special interest per 100PY is calculated as 100 X (the number of patients with TEAE of special interest) / (the sum of treatment duration [years] for each patients). Treatment duration (years) is calculated as [Date of Last visit (For Korea, Date of permanent discontinuation) – Date of first infusion of study drug + 1]/365.25.

Signs and symptoms of Infusion Related Reaction (IRR) will be presented in separate listing by analysis group and indication including categories of sign and symptom, intensity and blood pressure (systolic blood pressure, diastolic blood pressure).

9.2 Tuberculosis Assessment

Interferon-gamma Release Assay (IGRA) assessment will be conducted at the scheduled visit prior to infusion of study drug in EU and Korea eCRF and changed to optional after revision to Korea eCRF version 4.0. IGRA results will be classified as "Positive", "Negative" or "Indeterminate". 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. If there is a discrepancy in eCRF data recorded as [redacted] result, data from [redacted], and result from local laboratory, then the following rule will be applied.

- If there is at least one "Positive" result, IGRA at the visit of interest will be "Positive".
- Otherwise, results from [redacted] will be used. In case that IGRA from [redacted] is missing,

result from local laboratory will be used.

The number and percentage of patients who did not assess IGRA on screening, defined as missing IGRA at baseline (as defined in Section 5.4) will be displayed by indication and analysis group for the Safety Analysis Set. The number and percentage of patients with IGRA negative at baseline and developed positive results after first infusion of study drug, defined as IGRA conversion will also be displayed.

TEAEs of patients with IGRA conversion will be summarized by indication, analysis group, relationship, intensity, system organ class and preferred term displaying the number and percentage of patients with at least one TEAE using only the worst intensity recorded at each level of summarization. TEAEs with no relationship recorded will be summarized separately under a missing category. The total number of events and number of patients with at least one TEAE will also be displayed.

Listing for IGRA assessment will be provided by analysis group, indication and visit for the Safety Analysis Set. In addition, flag for whether IGRA results were converted or not for each visit will be presented in the listing for IGRA assessments.

In addition, chest X-ray will be assessed and results will be classified as either “Normal”, “Abnormal, Not Clinically Significant” or “Abnormal, Clinically Significant”. Assessment of chest X-ray is optional in EU eCRF, and changed to optional after revision to Korea eCRF version 4.0. Listing for chest X-ray assessment will be provided by analysis group, indication and visit for the Safety Analysis Set.

TB clinical monitoring will be assessed in EU and Korea eCRF and changed to optional after revision to Korea eCRF version 4.0. Listing for TB clinical monitoring results will be provided by analysis group, indication and visit for the Safety Analysis Set.

9.3 Pregnancy Test

Pregnancy tests will be conducted and listed only for female patients of childbearing potential who have not been surgically sterilized. Pregnancy tests consist of serum and urine pregnancy tests and will be carried out in accordance with the investigator’s medical judgement. If available, a serum pregnancy test results will be performed at Screening and EOS. Urine pregnancy tests will be performed at the scheduled visit prior to infusion of study drug. Pregnancy test is not conducted after revision to Korea eCRF version 4.0. All pregnancy test results will be listed for each patient tested by analysis group, indication and visit.

9.4 Immunogenicity Testing

The immunogenicity (ADA) assessments will be performed at the scheduled visit prior to infusion of study drug. The ADA test is optional in EU eCRF and not conducted after revision to Korea eCRF version 4.0. The ADA test will involve a screening and specificity/confirmatory assay to confirm positive results. The test outcome for the screening assay will be: {‘Potential Positive’, ‘Negative’, or ‘NRR: No Result Reported’}. Samples that are ‘Potential Positive’ in

the screening assay will be spiked with excess study drug to determine if patients are a true positive. The test outcome for the specificity/confirmatory assay will be: {'Reactive', 'Negative', 'N/A', or 'NRR'}. 'Reactive' indicates a true positive test outcome and will be labeled as 'Positive' in outputs, 'Negative' is considered negative, 'N/A' indicates the assay was either negative or NRR at the screening phase of the process, and 'NRR' indicates the assay was NRR at the specificity/confirmatory phase of the process. Patients with a 'Negative' test outcome for either the screening or specificity/confirmatory assay will be considered negative for the overall ADA assessment.

The number and percentage of patients for the overall ADA assessment will be tabulated by indication, analysis group and timepoint (every one year) during the study. Timepoint will be calculated from the date of first infusion and visit window is "± 6 weeks". Additionally, the number and percentage of patients who achieved at least one positive ADA result and all negative ADA results respectively after first infusion of study drug will be displayed by indication and analysis group for the Safety Analysis Set. In summary of patients who achieved at least one positive ADA result after first infusion of study drug, results on subcategory for "Baseline Positive" and "Newly Positive" will be presented together. "Baseline Positive" is defined as patients who have ADA Positive result at Baseline and "Newly Positive" is defined as patients who have ADA Negative or NRR or missing result at Baseline. Listing for ADA assessments will be provided by analysis group, indication and visit for the Safety Analysis Set.

10 Efficacy Analysis

Efficacy analysis will be conducted at Day 0 and every 6 months (± 6 weeks) by applying different criteria for each indication. The different criteria will be defined in Section 10.1, 10.2, 10.3, 10.4 and 10.5 in details. Clinical response, clinical remission, sustained clinical response, sustained clinical remission and loss of response will be used for efficacy endpoints. Analyses will be based on Efficacy Analysis Set, Efficacy – ADA Positive Subset and Efficacy – ADA Negative Subset by indication and analysis group. In summary of clinical remission and sustained clinical remission, results on subgroup whether a patient was clinical remission on Day 0 will be presented together. The percentages will be calculated using the number of patients with non-missing efficacy results at each timepoint as denominator. In case of sustained clinical response/remission summary, the denominators of proportions are the numbers of patients with all non-missing efficacy results from 6 months (inclusive) to the visit of interest (inclusive) at each timepoint. Only patients with baseline value are applicable for denominators of clinical response/sustained clinical response summary. For the summaries by every 6 months, the results at visit which is nearest to each timepoint and within window of ± 6 weeks will be used regardless of the visit order. The timepoint will be based on the date of first infusion of study drug. If the nearest visits are two, best response of two results will be used. Only the efficacy results corresponding patients' indication will be included in tables and listings.

10.1 Efficacy Analysis for Moderate to Severe Active Crohn's Disease

The descriptive statistics of CDAI scores and a proportion of patients with following efficacy endpoints, by every 6 months (± 6 weeks), will be summarized.

- Clinical Response (CDAI-70): decrease from baseline (if applicable, as defined in Section 5.4) in a CDAI score≥70 points.
- Clinical Response (CDAI-100): decrease from baseline in a CDAI score≥100 points.
- Clinical Remission: a CDAI score<150 points.
- Sustained Clinical Response: achieving clinical response at every 6 months visits from 6 months (inclusive) to the visit of interest (inclusive).
- Sustained Clinical Remission: achieving clinical remission at every 6 months visits from 6 months (inclusive) to the visit of interest (inclusive).
- Loss of Response: not achieving clinical remission in the visit of interest, patients who achieved clinical remission in the latest efficacy visit (excluding Day 0).

Patients' CDAI scores at each visit will be listed by analysis group.

10.2 Efficacy Analysis for Pediatric Severe Active Crohn's Disease

The descriptive statistics of PCDAI scores and a proportion of patients achieving following efficacy endpoints, by every 6 months (± 6 weeks), will be summarized.

- Clinical Response: a PCDAI score≤30 points and decrease from baseline≥15 points.
- Clinical Remission: a PCDAI score≤10 points.

In addition, a proportion of patients achieving sustained clinical response, sustained clinical remission and loss of response (as defined in Section 10.1 using PCDAI score), by every 6 months (± 6 weeks), will be presented separately.

Patients' PCDAI scores at each visit will be listed by analysis group.

10.3 Efficacy Analysis for Fistulizing Active Crohn's Disease

The descriptive statistics of the number of draining fistulas and a proportion of patients achieving following efficacy endpoints, by every 6 months (± 6 weeks), will be summarized.

- Clinical Response: decrease from baseline in the number of draining fistulas (over a period of ≥4 weeks)≥50%.
- Clinical Remission: absence of draining fistulas.

In addition, a proportion of patients achieving sustained clinical response, sustained clinical remission and loss of response (as defined in Section 10.1 using the Number of Draining Fistulas), by every 6 months (± 6 weeks), will be presented separately.

The numbers of patients' draining fistulas at each visit will be listed by analysis group.

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10.4 Efficacy Analysis for Moderate to Severe Active Ulcerative Colitis

Total and partial mayo scores are used for efficacy assessment in patients with moderate to severe active UC. Total mayo score is the sum of scores from 4 categories (stool frequency, rectal bleeding, findings on endoscopy, and physicians' global assessment). Partial mayo score is the sum of scores from 3 categories except findings on endoscopy.

The descriptive statistics of total and partial mayo scores and a proportion of patients achieving following efficacy endpoints, by every 6 months (± 6 weeks), will be summarized.

- Clinical Response (Total Mayo score): decrease from baseline in total mayo score at least 3 points and at least 30%, 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.
- Clinical Response (Partial Mayo score): decrease from baseline in partial mayo score 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.
- Clinical Remission (Total Mayo score): a total Mayo score≤2 points, with no individual subscore exceeding 1 point.
- Clinical Remission (Partial Mayo score): a partial Mayo score<2 points, with no individual subscore exceeding 1 point.

In addition, a proportion of patients achieving sustained clinical response, sustained clinical remission and loss of response (as defined in Section 10.1 using Total and Partial Mayo score), by every 6 months (± 6 weeks), will be presented separately.

Patients' Total and Partial Mayo scores at each visit will be listed by analysis group.

10.5 Efficacy Analysis for Pediatric Severe Active Ulcerative Colitis

The descriptive statistics of PUCAI scores and a proportion of patients achieving following efficacy endpoints, by every 6 months (± 6 weeks), will be summarized.

- Clinical Response: decrease from baseline in a PUCAI score≥20 points.
- Clinical Remission: a PUCAI score<10 points.

In addition, a proportion of patients achieving sustained clinical response, sustained clinical remission and loss of response (as defined in Section 10.1 using PUCAI score), by every 6 months (± 6 weeks), will be presented separately.

Patients' PUCAI scores at each visit will be listed by analysis group.

11 Health-Economics Analysis

For cost-effectiveness, the following information will be collected throughout the study in eCRF only for European patients.

- Days of Hospitalizations Related to Disease
- Medication and Surgery Interventions Related to Disease
- Days off Work in Employed Patients
- Retirement and Return to Work (Working Days Gained)

The number and percentage of patients with above information at each category will be summarized by indication and analysis group at each scheduled visit. The percentages will be calculated using the number of patients who performed evaluation at each visit as denominator. For patients who have duration information, a separate table will be provided displaying descriptive statistics (of number of hospitalization days, number of days off and number of working days gained) by indication and analysis group. Listing for health-economics evaluation will be provided by analysis group, indication and visit for the Safety Analysis Set. .

12 Sensitivity Analysis

For European patients, immunogenicity test is optional and for Korean patients, immunogenicity test is not conducted after revision to Korea eCRF version 4.0.

Sensitivity analysis will be performed assuming ADA positive rates match those in tested patients as below.

Process of missing imputation analysis is as below:

1. Calculate ADA positive rate of tested patients after the first infusion of study drug in Safety Analysis Set by analysis group
2. For patients without ADA subsets, randomly assign ADA subset (positive or negative) by assuming ADA positive rate in the previous step
3. Summarize endpoint rate by actual or imputed ADA subset and analysis group

The 2 and 3 processes will be repeated 1,000 times and average of endpoint rate will be displayed.

Sensitivity analysis (Missing Imputation) for following endpoints will be conducted.

- TEAE - overall indication
- Clinical Response (CDAI-70)/Remission - Moderate to Severe Active CD
- Clinical Response/Remission (Partial Mayo score) - Moderate to Severe Active UC

Timepoints for efficacy endpoints will be determined by internal review.

13 References

[1] Lichtenstein GR, Feagan BG, Cohen RD, et al. Serious infection and mortality in patients with Crohn's disease: more than 5 years of follow-up in the TREAT™ registry. Am J Gastroenterol. 2012;107(9):1409–1422. doi:10.1038/ajg.2012.218

[2] W G Dixon, Drug-specific risk of tuberculosis in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the British Society for Rheumatology Biologics Register (BSRBR), Ann Rheum Dis 2010;69:522-528. 2010.

APPENDIX 1: Capture rule of Event of Special Interest

Hepatitis B virus reactivation	1. Hepatitis B virus infection in medical history (PT term): • Hepatitis B, Hepatitis viral, Hepatitis acute, Hepatitis toxic 2. Diagnosis possibly related to HBV reactivation (PT term): • Hepatitis B, hepatitis, hepatitis toxic, hepatitis acute, hepatotoxicity, hepatomegaly, hepatic steatosis, liver disorder 3. Possible relevant abnormal lab results (PT term): • Alanine aminotransferase increased • Aspartate aminotransferase increased • Gamma-glutamyltransferase increased • Blood alkaline phosphatase increased • Hypertransaminasaemia • Transaminases increased • Hyperbilirubinaemia • Hepatic enzyme increased • Liver function test abnormal • Liver function test increased • Blood bilirubin increased In case of satisfying the 1. Hepatitis B virus infection in medical history and one of 2. Diagnosis possibly related to HBV reactivation (PT term) simultaneously, and also in case when there are at least three elevations among 3. Possible relevant abnormal lab results.
Congestive heart failure	PT: Cardiac failure congestive
Opportunistic infections (excluding tuberculosis)	1. SOC: Infections and infestations, and 2. Reported SAE, and 3. Exclude Tuberculosis, and 4. Systemic and invasive fungal infections (PTs: blastomycosis, Pneumocystis jirovecii pneumonia, mucocutaneous candidiasis, vulvovaginal candidiasis, aspergillus infection, histoplasmosis, coccidioidomycosis, cryptococcosis, herpes simplex, oral herpes, herpes zoster, ophthalmic herpes zoster, herpes zoster oticus and etc.) 5. It would be also determined by medical review, separately.
Serious infections including sepsis (excluding opportunistic infections and tuberculosis)	1. SOC: Infections and infestations, and 2. Reported SAE, and 3. Exclude opportunistic infections and tuberculosis
Tuberculosis	Any PTs with tuberculosis
Serum sickness (delayed hypersensitivity reactions)	1. IRRs captured by capture rule in Appendix 2, and, 2. IRR case which occurs 5 to 14 days after the latest Infliximab infusion. 3. It would be also determined by medical review, separately
Haematological reactions	PTs:

	Anaemia, Anaemia megaloblastic, Eosinophilia, Granulocytopenia, Hypochromic anaemia, Iron deficiency anaemia, Leukocytosis, Leukopenia, Lymphocytosis, Lymphopenia, Macrocytosis, Microcytic anaemia, Monocytosis, Neutropenia, Neutrophilia, Polycythaemia, Thrombocytopenia, Thrombocytosis Haemoglobin decreased, Lymphocyte count increased, Mean cell volume increased, Neutrophil count decreased, Platelet count decreased, Platelet count increased, White blood cell count increased, White blood cell count decreased, Pancytopenia, Red blood cell count decreased
Systemic lupus erythematosus/lupus-like syndrome	PTs: Acute cutaneous lupus erythematosus, Chronic cutaneous lupus erythematosus, Cutaneous lupus erythematosus, Systemic lupus erythematosus, Lupus-like syndrome, Subacute cutaneous lupus erythematosus, Systemic lupus erythematosus disease activity index abnormal, Systemic lupus erythematosus disease activity index decreased, Systemic lupus erythematosus disease activity index increased, Systemic lupus erythematosus rash, Antinuclear antibody increased, Antinuclear antibody positive, Central nervous system lupus, Neuropsychiatric lupus, Pericarditis lupus, Peritonitis lupus, SLE arthritis
Demyelinating disorders	PTs (under SMQ “Demyelination”): Demyelination, Acute disseminated encephalomyelitis, Acute haemorrhagic leukoencephalitis, Chronic inflammatory demyelinating polyradiculoneuropathy, Clinically isolated syndrome, Concentric sclerosis, Demyelinating polyneuropathy, Encephalitis periaxialis diffusa, Encephalomyelitis, Expanded disability status scale score decreased, Expanded disability status scale score increased, Guillain-Barre syndrome, Hypergammaglobulinaemia benign monoclonal, Leukoencephalomyelitis, Leukoencephalopathy, Lewis-Sumner syndrome, MELAS syndrome, Marburg's variant multiple sclerosis, Marchiafava-Bignami disease, Multiple sclerosis, Multiple sclerosis relapse, Multiple sclerosis relapse prophylaxis, Myelitis transverse, Myoclonic epilepsy and ragged-red fibres, Neuromyelitis optica spectrum disorder, ‘Neuropathy, ataxia, retinitis pigmentosa syndrome’, Noninfectious myelitis, Noninfective encephalomyelitis, Optic neuritis, Osmotic demyelination syndrome, Primary progressive multiple sclerosis, Progressive multifocal leukoencephalopathy, Progressive multiple sclerosis, Progressive relapsing multiple sclerosis, Relapsing-remitting multiple sclerosis, Secondary progressive multiple sclerosis, Anti-interferon antibody negative, Anti-interferon antibody positive, Band sensation, Lhermitte's sign, Myokymia, Saccadic eye movement, Trigeminal neuralgia, Uhthoff's phenomenon, Anti-myelin-associated glycoprotein associated polyneuropathy, Anti-myelin-associated glycoprotein antibodies positive, Autoimmune demyelinating disease, Toxic leukoencephalopathy, Tumefactive multiple sclerosis
Lymphoma (excluding HSTCL)	Any PTs with Lymphoma except Hepatosplenic T-cell lymphoma

Hepatobiliary events	PTs: Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood alkaline phosphatase increased, Cholecystitis acute, Cholecystitis chronic, Gamma-glutamyltransferase increased, Hepatic enzyme increased, Hepatic steatosis, Hepatitis, Hepatitis acute, Hepatitis toxic, Hepatomegaly, Hepatotoxicity, Hyperbilirubinaemia, Hypertransaminasaemia, Liver disorder, Liver function test abnormal, Liver function test increased, Hepatic cyst, Transaminases increased, Autoimmune hepatitis, Cholestasis, Cholelithiasis
Hepatosplenic T-cell lymphoma (HSTCL)	PT: Hepatosplenic T-cell lymphoma
Intestinal or perianal abscess (in CD)	1. CD patients, and, 2. PTs: Anal abscess or Abscess intestinal
Serious infusion reactions during a re-induction regimen following disease flare	1. IRRs captured by capture rule in Appendix 2, and, 2. Reported as SAE, and 3. IRRs which occurred after infliximab-free intervals of more than 16 weeks during a re-induction regimen (Week 0 – Week 6), and 4. It would be also determined by medical review, separately.
Sarcoidosis/sarcoid-like reactions	1. PTs: Heerfordt's syndrome, erythema nodosum, or 2. Any PTs with sarcoidosis, or granuloma
Pediatric malignancy	Patients aged 6 to 17 with Lymphoma (excluding HSTCL), Hepatosplenic T-cell lymphoma (HSTCL), and Malignancies
Leukaemia	Any PTs with Leukaemia
Malignancies (excluding lymphoma)	1. Any terms under the HLTs with malignancy and malignant or PT: Gastric Cancer or Rectal Cancer, and 2. Exclude lymphoma, HSTCL and skin cancer, and 3. It would be also determined by medical review, separately.
Colon carcinoma/dysplasia (in UC)	1. UC patients, and, 2. PTs: Colon Cancer or Colon dysplasia
Skin cancer	1. SOC term: 'Neoplasms benign, malignant and unspecified (incl cysts and polyps)', and 2. It would be also determined by medical review, separately.
Pregnancy exposure	Any PTs with pregnancy except for pregnancy test
Bowel stenosis, stricture, obstruction (in CD)	1. CD patients, and, 2. One of any PTs as below: Bile duct stenosis, Duodenal stenosis, Gastric stenosis, Ileal stenosis, Intestinal obstruction, Intestinal stenosis, Jejunal stenosis, Large intestinal stenosis, Oesophageal stenosis, Prepyloric stenosis, Pyloric stenosis, Rectal stenosis, Small intestinal stenosis, Gastrointestinal stenosis

Infusion related reaction/hypersensitivity/anaphylactic reaction	IRRs captured by capture rule in Appendix 2.

APPENDIX 2: Infusion related reaction/hypersensitivity/anaphylactic reaction AEs

ESI related to infusion related reaction/hypersensitivity/anaphylactic reaction will be identified using the following three algorithms. An AE can be identified as being ESI related to infusion related reaction/hypersensitivity/anaphylactic reaction only if it satisfies any of the three algorithms, and not classed as 'Unrelated' for relationship to study drug.

1. Preferred Term (PT) Selection: Hypersensitivity, Drug hypersensitivity, Anaphylactic shock, Anaphylactic reaction, or Infusion related reaction

2. AE Term selection: The event should be defined by any word in Term 1, as well as one word in the Term 2 - 8 groups.

AE Term 1 (Reported term, mandatory)	Infusion, study drug, drug reaction, hypersensitivity, hipersenstivity, hypersensitiviti, postinfusion
PT Term 2	Pyrexia, body temperature increased, chills
PT Term 3	Pruritus, pruritus allergic, rash pruritic, rash, rash macular, rash maculo-papular, urticaria, eye irritation, burning sensation, erythema, dermatitis allergic, angioedema, lip oedema
PT Term 4	Dyspnoea, non-cardiac chest pain, chest pain, chest discomfort, upper respiratory tract congestion, bronchospasm
PT Term 5	Hypotension, procedural hypotension, hypertension, procedural hypertension, blood pressure increased, supraventricular extrasystoles
PT Term 6	Bradycardia, sinus bradycardia, tachycardia, sinus tachycardia, palpitations, atrial fibrillation
PT Term 7	Vomiting, nausea, oropharyngeal pain, abdominal pain upper, abdominal pain
PT Term 8	Back pain, myalgia, arthralgia, headache, migraine

3. The event should be defined by any PT term listed below for which the AE start date matches an Infliximab infusion date.

    - Pyrexia, body temperature increased, chills, pruritus, pruritus allergic, rash pruritic, rash, rash macular, rash maculo-papular, urticaria, injection site urticaria, eye irritation, burning sensation, erythema, dermatitis allergic, angioedema, lip oedema, dyspnoea, non-cardiac chest pain, chest pain, chest discomfort, upper respiratory tract congestion, bronchospasm, hypotension, procedural hypotension, hypertension, procedural hypertension, blood pressure increased, supraventricular extrasystoles, bradycardia, sinus bradycardia, tachycardia, sinus tachycardia, palpitations, atrial fibrillation, vomiting, nausea, oropharyngeal pain, abdominal pain upper, abdominal pain, myalgia, arthralgia, headache, migraine, dizziness, wheezing, stridor, hypoxia, throat irritation, hypotonia, syncope, incontinence, flushing, lip swelling, swollen tongue, enlarged uvula.