STATISTICAL ANALYSIS PLAN

Study Title:	An Open-label Study to Assess the Long-term Safety and Efficacy of Tirabrutinib in Subjects with Relapsed/Refractory B-cell Malignancies
Name of Test Drug:	Tirabrutinib (GS-4059)
Study Number:	GS-US-401-1787
Protocol Version (Date):	Amendment 5 (29 October 2019)
Analysis Type:	Final Analysis
Analysis Plan Version:	Version 3.0
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Analysis Plan Authors:	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ALP	alkaline phosphatase
BLQ	below the limit of quantitation
BMI	body mass index
CI	confidence interval
CLL	chronic lymphocytic leukemia
CR	complete response
CRF	case report form
CSR	clinical study report
CTCAE	Common Toxicity Criteria for Adverse Events
DMC	data monitoring committee
DOR	duration of response
ECG	Electrocardiogram
ECOG	Eastern Corporation Oncology Group
ET	early termination
FAS	Full Analysis Set
Gilead	Gilead Sciences
HLT	high-level term
LTT	lower-level term
LOQ	limit of quantitation
MedDRA	Medical Dictionary for Regulatory Activities
NE	not evaluable
NHL	non-Hodgkin’s lymphoma
NLP	Natural Language Processing
ORR	overall response rate
OS	overall survival
PD	progressive disease
PK	pharmacokinetic
PR	partial response
PFS	progression-free survival
PT	preferred term
Q1, Q3	first quartile, third quartile
SAP	statistical analysis plan
SD	stable disease
SPD	sum of the products of the greatest perpendicular diameters
StD	standard deviation

SAE	serious adverse event(s)
SAP	statistical analysis plan
SOC	system organ class
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
ULN	upper limit of normal
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) in the clinical study report (CSR) for study GS-US-401-1787. This SAP is based on the study protocol amendment 5 dated 29 October 2019 and the electronic case report form (eCRF). The SAP will be finalized before database finalization. Any changes made after the finalization of the SAP will be documented in the CSR.

1.1. Study Objectives

The primary objective of this study is as follows:

- To determine the long-term safety and tolerability of tirabrutinib in subjects in a prior tirabrutinib study ONO-4059POE001 (parent study) and whose disease had not progressed on the parent study.

The secondary objective of this study is as follows:

- To determine the long term efficacy of tirabrutinib

1.2. Study Design

The analysis of this rollover study GS-US-401-1787 will integrate the data from the parent study. Thus, the study design of the parent study is also described in Section 1.2.1, followed by the rollover study design in Section 1.2.2.

1.2.1. Study ONO-4059POE001 (Parent Study)

This is an open-label Phase 1 multi-center study with a non-randomized, adaptive dose-escalating design, to investigate the safety and tolerability of tirabrutinib administered as monotherapy to subjects with relapsed/refractory NHL and CLL. Subjects with no therapy of higher priority available and for whom treatment with a BTK inhibitor is deemed appropriate will be eligible.

Tirabrutinib was administered orally at the assigned dose levels for up to 6 cycles of treatment. Each treatment cycle consists of 28 days of continuous dosing. Continuation of treatment beyond 6 cycles is possible for subjects deriving clinical benefit from the treatment. Intra-patient dose escalation or dose de-escalation after completion of the initial 6 month treatment period is allowed to provide patients with an opportunity to maximize upon their already established clinical response. Patients may receive continuous treatment until disease progression as assessed by the investigator or until experiencing an intolerable AE leading to discontinuation of drug.

CT with contrast or MRI assessment at screening served as the baseline of efficacy evaluation. The response was assessed every 3 months during the first year of treatment and then every 6 months thereafter using the appropriate response criteria for CLL and NHL.

Study ONO-4059POE001 has completed and all subjects are now off study or have rolled over to study GS-US-401-1787. The full CSR of study ONO-4059POE001 has been completed. Adverse events and laboratory abnormalities were graded using the Common Terminology for Adverse Events (CTCAE), Version 4.0, adverse events preferred terms were coded using MedDRA 18.1, and concomitant medications were coded using WHODRUG Q2-2015.

1.2.2. Study US-US-401-1787 (Rollover Study)

This study is an open-label rollover study for subjects who have tolerated and achieved stable disease or responded to tirabrutinib treatment while enrolled in the parent study ONO-4059POE001.

Subjects who meet eligibility criteria will continue to receive tirabrutinib. Each cycle will consist of 28 days of therapy. If there is no evidence of disease progression by clinical assessment or by CT (or MRI), a subject may continue receiving tirabrutinib until disease progression (clinical or radiographic) for a maximum duration of 5 years from the start of this rollover study GS-US-401-1787. After discontinuation of treatment, subjects will be followed for safety for 30 days.

CT with contrast or MRI will be obtained to document disease, in accordance with the NHL and CLL response assessment guidelines. If not performed in the previous 90 days prior to Cycle 1 Day 1 on study GS-US-401-1787, CT scan with contrast or MRI will be performed between C1D1 and C1D28, and at approximately week 12 and then every 24 weeks. Bone marrow examination (core biopsy and/or aspirate as per local standard of care) will be performed for follow-up only (for both NHL and CLL subjects) if previously positive and/or to confirm CR, if physical examination and CT-scans demonstrate a CR.

1.3. Sample Size and Power

The number of subjects enrolled will be determined by the number of subjects who complete a prior tirabrutinib study who are still alive without disease progression, wish to continue therapy with tirabrutinib, and meet the study entry criteria.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

No formal interim analysis is planned.

This study does not have a data monitoring committee (DMC). Therefore, no analyses will be conducted for the DMC.

2.2. Final Analysis

After all subjects have completed/discontinued the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized, the final analysis of the data will be performed.

2.3. Follow-Up Analysis

No follow-up analysis is planned.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

Analysis results will be presented using descriptive statistics. For categorical variables, the number, percentage, and 95% confidence intervals (CIs) on the percentage of subjects in each category will be presented; for continuous variables, the number of subjects (n), mean, standard deviation (StD), 95% CIs on the mean, median, first quartile (Q1), third quartile (Q3), minimum, and maximum will be presented.

By-subject listings will be presented for all subjects in the All Enrolled Analysis Set and sorted by subject ID number, visit date, and time (if applicable). Data collected on log forms, such as adverse events (AEs), will be presented in chronological order within subject. Age, sex at birth, race, and ethnicity for each subject will be presented in the listings, as space permits.

3.1. Analysis Sets

Analysis sets define the subjects to be included in an analysis. Analysis sets and their definitions are provided in this section. The analysis set will be identified and included as a subtitle of each table, figure, and listing.

For each analysis set, the number and percentage of subjects will be summarized.

A listing of reasons for exclusion from analysis sets will be provided by subject.

3.1.1. All Enrolled Analysis Set

The All Enrolled Analysis Set consists of all subjects who were enrolled in the GS-US-401-1787 study. This analysis set will be used for the listings.

3.1.2. Full Analysis Set

The Full Analysis Set consists of all enrolled subjects who took at least 1 dose of study drug in the GS-US-401-1787 study. This analysis set will be used for the efficacy endpoints.

3.1.3. Safety Analysis Set

The Safety Analysis Set includes all subjects who took at least 1 dose of study drug in the GS-US-401-1787 study. This is the primary analysis set for safety analyses.

3.1.4. Pharmacokinetic Analysis Set

The Pharmacokinetic Analysis Set consists of all subjects who enrolled in the GS-US-401-1787 study and have at least 1 evaluable PK sample.

3.2. Subject Grouping

For analyses based on the All Enrolled Analysis Set and Full Analysis Set, subjects will be grouped according to the treatment to which they were initially assigned at the entry of GS-US-401-1787. For analyses based on the Safety Analysis Set, subjects will be grouped according to the actual treatment with the longest exposure duration in parent and rollover study.

For the PK Analysis Set, subjects will be grouped according to the actual treatment they received prior to the PK sampling time.

All analyses will be performed for CLL and NHL subjects separately, unless otherwise specified.

The applicable dose levels of tirabrutinib are:

Dose Levels for CLL	Dose Levels for NHL
20mg QD	20mg QD
40mg QD	40mg QD
80mg QD	80mg QD
160mg QD	160mg QD
320 mg QD	320 mg QD
400 mg QD	400 mg QD
500 mg QD	480 mg QD
600 mg QD	600 mg QD
300mg BID	240mg BID

Summary of efficacy will be presented by integrating the parent study data and rollover study data, using only subjects who rolled over to GS-US-401-1787.

Summary of safety will be presented using only subjects who rolled over to GS-US-401-1787:

- All safety summaries will be provided combining data from both parent study (ONO-4059POE001) and rollover study (GS-US-401-1787).
- Selected safety summaries will also be provided only using data from rollover study GS-US-401-1787.

3.3. Strata and Covariates

This study does not use a stratified randomization schedule in enrolling subjects. No covariates will be included in efficacy and safety analyses.

3.4. Examination of Subject Subgroups

Due to the limited sample size at each dose level, no subgroup analysis will be performed.

3.5. Multiple Comparisons

Adjustments for multiplicity will not be made, because no formal statistical testing will be performed in this study.

3.6. Missing Data and Outliers

3.6.1. Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified. Exceptions are presented in this document.

For missing last dosing date of study drug, imputation rules are described in Section 4.2, for death in Section 6.2.4, for new anticancer therapy in Section 6.2.2, for AE onset is described in Section 7.1.5.2.

3.6.2. Outliers

Unless otherwise specified, outliers will not be excluded from the analysis in general.

3.7. Data Handling Conventions and Transformations

In general, age (in years) on the date of the first dose of study drug in the parent study will be used for analyses and presentation in listings. If only birth year is collected on the CRF, "01 July" will be used for the unknown birth day and month for the purpose of age calculation. If only birth year and month are collected, "01" will be used for the unknown birth day.

Non-PK Data that are continuous in nature but are less than the lower limit of quantitation (LOQ) or above the upper LOQ will be imputed as follows:

- A value that is 1 unit less than the LOQ will be used for calculation of descriptive statistics if the datum is reported in the form of "< x" (where x is considered the LOQ). For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will be used for calculation of summary statistics. An exception to this rule is any value reported as < 1 or <0.1, etc. For values reported as < 1 or < 0.1, a value of 0.9 or 0.09, respectively, will be used for calculation of summary statistics.
- A value that is 1 unit above the LOQ will be used for calculation of descriptive statistics if the datum is reported in the form of "> x" (where x is considered the LOQ). Values with decimal points will follow the same logic as above.
- The LOQ will be used for calculation of descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the LOQ).

If methods based on the assumption that the data are normally distributed are not adequate, analyses may be performed on transformed data or nonparametric analysis methods may be used, as appropriate.

Natural logarithm transformation will be used for plasma/blood concentrations and analysis of PK parameters. Plasma concentration values that are below the limit of quantitation (BLQ) will be presented as "BLQ" in the concentration data listing. Values that are BLQ will be treated as 0 at predose time points, and one-half the value of the LOQ at postbaseline time points, where LOQ is corrected for the dilution factor (ie, reported LOQ/dilution factor) for determination of summary and order statistics.

The following conventions will be used for the presentation of summary and order statistics:

- If at least 1 subject has a concentration value of BLQ for the time point, the minimum value will be displayed as "BLQ."
- If more than 25% of the subjects have a concentration data value of BLQ for a given time point, the minimum and Q1 values will be displayed as "BLQ."
- If more than 50% of the subjects have a concentration data value of BLQ for a given time point, the minimum, Q1, and median values will be displayed as "BLQ."
- If more than 75% of the subjects have a concentration data value of BLQ for a given time point, the minimum, Q1, median, and Q3 values will be displayed as "BLQ."
- If all subjects have concentration data values of BLQ for a given time point, all order statistics (minimum, Q1, median, Q3, and maximum) will be displayed as "BLQ."

3.8. Analysis Visit

3.8.1. Definition of Study Day

Study day will be calculated from the first dosing date of study drug in parent study ONO-4059POE001 and derived as follows:

- For postdose study days: Assessment Date – First Dosing Date + 1
- For days prior to the first dose: Assessment Date – First Dosing Date

Therefore, study day 1 is the day of first dose of study drug administration in the parent study.

3.8.2. Analysis Visit Windows

Baseline is defined as the last nonmissing value on or prior to first dosing date of study drug, unless specified differently.

For postbaseline, nominal visit as recorded on the CRF will be used when data are summarized by visit, if any. Any data relating to unscheduled visits will not be assigned to a particular visit or time point. However, the following exceptions will be made:

- An unscheduled visit prior to the first dosing of study drug may be included in the calculation of the baseline value, if applicable.
- Unscheduled visits after the first dose of study drug will be included in order to determine the maximum post-baseline toxicity grade.

3.8.3. Selection of Data in the Event of Multiple Records at Baseline

For baseline, the last nonmissing value on or prior to first dosing date of study drug will be selected, unless specified differently. If there are multiple records with the same time or no time recorded on the same day, the baseline value will be the average of the measurements for continuous data, or the measurement with the lowest severity (eg, normal will be selected over abnormal for safety electrocardiogram [ECG] findings) for categorical data.

3.9. Changes From Protocol-Specified General Considerations

In protocol, the Full Analysis Set is defined as all subjects who enrolled and treated in the parent study, and will be used for the safety and efficacy endpoints analysis. Given the study objective is to determine the long-term safety and efficacy in subjects who were in the parent study and whose disease had not progressed on the parent study (a.k.a. the rollover patient), analysis only include these rollover patient is better aligned with the study objective. Thus, in this SAP, the efficacy and safety analysis will only include subjects who enrolled in the GS-US-401-1787 study as specified in Section 3.1 and Section 3.2.

4. SUBJECT DISPOSITION

4.1. Subject Enrollment and Disposition

A summary of subject enrollment will be provided by disease type (CLL, NHL) and dose level for each country, investigator, and overall as specified in Section 3.2 using All Enrolled Analysis Set. The summary will present the number and percentage of subjects enrolled. For each column, the denominator for the percentage calculation will be the total number of subjects analyzed for that column.

This summary will present the number of subjects screened, the number of subjects who met all eligibility criteria but were not enrolled with reasons subjects not enrolled, the number of subjects enrolled, and the number of subjects in each of the categories listed below:

- Enrolled in Study GS-US-401-1787
- Treated in Study GS-US-401-1787
- Completed study drug per protocol specified duration
- Discontinued study drug in GS-US-401-1787 with reason
- Discontinued Study GS-US-401-1787 with reasons

For the status of study drug and study completion and reasons for discontinuation, the number and percentage of subjects in each category will be provided. The denominator for the percentage calculation will be the total number of subjects in the All Enrolled Analysis Set corresponding to that column. In addition, a flowchart will be provided to depict the disposition.

A by-subject listing will be provided by subject identification (ID) number in ascending order to support the above summary table.

4.2. Extent of Study Drug Exposure and Adherence

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug and the level of adherence relative to the study drug regimen specified in the protocol.

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dosing date minus first dosing date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks and cycles using up to 1 decimal place (eg, 4.5 weeks). If the last study drug dosing date is missing, the following imputation rule will be applied:

- If the study drug is permanently withdrawn, the latest date among the study drug end date, clinical visit date, laboratory sample collection date, and vital signs assessment date will be used.

The total duration of exposure to study drug and the total number of cycles a subject was exposed to study drug, and number and percentage of subjects who have dose reduction or interruptions will be summarized using descriptive statistics. The number (ie, cumulative counts) and percentage of subjects exposed to study drug will be summarized by cycle, where each cycle consists of 28 days of therapy. Summaries will be provided by dose level for the Safety Analysis Set.

No formal statistical testing is planned.

4.2.2. Adherence to Study Drug

ONO-4059POE001 collected number of doses dispensed but didn't collect dose strength of the drug kit. GS-US-401-1787 collected number of tablets/capsules dispensed but subjects may receive different strength of tablets/capsules throughout the study. Due to the inconsistent way of drug dispensation data collection in the two studies, it's not feasible to track total number of doses or total amount drug administered. Thus, drug adherence analysis will not be performed.

A by-subject listing of study drug administration and drug accountability will be provided by subject ID number (in ascending order), and visit (in chronological order).

A by-subject listing of study drug administration for subjects with dose modifications at any time will also be provided.

4.3. Protocol Deviations

Subjects who did not meet the eligibility criteria for study entry, but enrolled in the study will be summarized regardless of whether they were exempted by the sponsor or not. The summary will present the number and percentage of subjects who did not meet at least 1 eligibility criterion and the number of subjects who did not meet specific criteria by disease and dose level based on the All Enrolled Analysis Set. A by-subject listing will be provided for those subjects who did not meet at least 1 eligibility (inclusion or exclusion) criterion. The listing will present the eligibility criterion (or criteria if more than 1 deviation) that subjects did not meet and related comments, if collected.

Protocol deviations occurring after subjects entered the study are documented during routine monitoring. The number and percentage of subjects with important protocol deviations by deviation reason (eg, nonadherence to study drug, violation of select inclusion/exclusion criteria) will be summarized by disease type and dose level for the All Enrolled Analysis Set. A by-subject listing will be provided for those subjects with important protocol deviation and will be sorted by subject ID number (in ascending order), and visit (in chronological order).

4.4. Assessment of COVID-19 Impact

This study was ongoing during the novel coronavirus (2019 nCOV [COVID-19]) pandemic, and the COVID-19 pandemic has caused a disruption in the regular visit schedules for this study. Some subjects were unable to attend onsite visits due to shelter in place guidelines, site closures,

or other reasons. This section provides how to handle special situations due to COVID-19 in the analysis.

Adverse events (AEs) due to COVID-19 will be included in AE analyses if applicable. A by-subject listing of Adverse Events due to COVID-19 may be provided. The COVID-19 Standardized MedDRA Queries (SMQ) with Broad Scope in Appendix 1 will be implemented.

4.4.1. Study Drug or Study Discontinuation Due to COVID-19

A by-subject listing of reasons for premature study drug or study discontinuation due to COVID-19 will be created.

4.4.2. Protocol Deviations Due to COVID-19

A by-subject listing will be provided for subjects with important protocol deviation related to COVID-19. A separate listing will be provided for subjects with non-important protocol deviation related to COVID-19.

4.4.3. Missed and Virtual Visits Due to COVID-19

A by-subject listing of subjects with missed or virtual visits due to COVID-19 will be provided by subject ID number in ascending order .

Information regarding virtual or missed visits due to COVID-19 was collected as free text in the CRF comment fields. The determination of missing or virtual visits due to COVID-19 was done using Natural Language Processing (NLP) to search the CRF comment fields. A detailed explanation of the algorithm is given in Appendix 2.

5. BASELINE CHARACTERISTICS

5.1. Demographics

Subject demographic variables (ie, age, sex, race, and ethnicity) were collected in the parent study, and will be summarized by disease type and dose level using descriptive statistics for age, and using number and percentage of subjects for sex, race, and ethnicity. The summary of demographic data will be provided for the FAS.

A by-subject demographic listing, including the informed consent date, will be provided and sorted by subject ID number in ascending order.

5.2. Other Baseline Characteristics

Other baseline characteristics include body weight (in kg), height (in cm), body mass index (BMI; in kg/m^2), and ECOG Performance Status. These baseline characteristics were collected in the parent study, and will be summarized by disease type and dose level using descriptive statistics for continuous variables and using number and percentage of subjects for categorical variables. The summary of baseline characteristics will be provided for the FAS. No formal statistical testing is planned.

A by-subject listing of other baseline characteristics will be provided and sorted by subject ID number in ascending order.

5.3. Medical History

Medical history will be based on data collected in the parent study, and ongoing AE from the parent study collected as general medical history in the rollover study.

Medical history data in the rollover study will not be coded. All medical history data including parent and rollover study will be listed only.

5.4. Disease History

The disease history was collected in the parent study. A summary of disease-specific medical history will be provided for the Full Analysis Set.

Time since initial diagnosis (years) will be calculated as (first dosing date of study drug – date of initial diagnosis + 1) / 365.25. Time since initial diagnosis will be summarized using descriptive statistics for a continuous variable.

Disease stage at screening will be summarized using number and percentage of subjects. History of the disease staging or prognostic characterization including FLIPI (follicular lymphoma international prognostic index), IPI (international prognostic index), or MIPI (Mantle cell lymphoma International prognostic index) for NHL subjects and Binet/Rai staging for CLL subjects, will be summarized.

NHL disease subtypes (Diffuse Large B Cell Lymphoma [DLBCL], Mantle Cell Lymphoma [MCL], Follicular Lymphoma [FL], Small Lymphocytic Lymphoma [SLL], Waldenstrom's macroglobulinemia [WM], and Other) as well as DLBCL subtypes will be summarized.

The DLBCL category may be further broken down to

- DLBCL (ABC)
- DLBCL (GCB)
- DLBCL (other non-specified)

For CLL subjects, disease will be classified according to results for CLL prognostic markers as:

- 11q deletion (yes/no)
- 17p deletion (yes/no)
- TP53 mutation (yes/no)
- IgVh mutation (yes/no)

For both NHL and CLL, disease will also be classified based on response to last treatment as:

- Refractory
- Relapsed

A listing of disease-specific history will be provided.

5.5. Prior Treatments

Prior treatments including prior systemic therapy, radio therapies, transplants and surgeries are collected in the parent study. The number of prior treatments a subject used in each of these categories will be summarized by disease type and dose level using the FAS.

A listing will be provided for each category of the prior treatments.

6. EFFICACY ANALYSES

6.1. Definition of Efficacy Endpoint

Subjects' efficacy data will be integrated with the parent study as specified in Section 3.2. The efficacy analysis will be based on FAS defined in Section 3.1.2.

The efficacy endpoints are:

- Overall response rate (ORR): defined as the proportion of subjects who achieve partial response (PR) or complete response (CR) in either the parent or roll-over study
- Progression free survival (PFS): defined as the interval from date of the first dose of tirabrutinib on the parent study to the earlier of the first documentation of definitive disease progression as assessed by the investigator, or death from any cause
- Duration of response (DOR): defined as the interval from first documentation of CR or PR to the earlier of the first documentation of definitive disease progression as assessed by the investigator, or death from any cause in subjects who achieve a response.
- Overall Survival (OS): defined as the interval from date of the first dose of tirabrutinib on the parent study until death from any cause

The response or definitive disease progression for ORR, PFS, and DOR are based on the Modified IWCLL Criteria {Hallek 2008} for CLL subjects and standardized response criteria for malignant lymphoma for NHL subjects {Cheson 2007, Owen 2013}.

6.2. Analysis Methods for Efficacy Endpoints

6.2.1. Overall Response Rate

Best overall response (BOR) is defined as the best response recorded after first dose and prior to the time of initiation of anti-cancer therapy other than the study treatment. BOR could be assessed as CR, PR, Stable Disease (SD), or Progressive Disease (PD). In addition, a response category of Not Evaluable (NE) is provided for situation in which there is inadequate information to otherwise categorize response status.

Based on the investigator assessments, the following will be performed for the FAS by disease type and dose level:

- BOR will be summarized using the number and the percentage of subjects in each category.
- ORR will be presented with corresponding 2-sided 95% exact confidence intervals (CIs) based on Clopper-Pearson method. Subjects who do not have sufficient baseline or on-study tumor assessments to characterize response will be counted as non-responders and included in the denominator in calculate of response rates.

A by-subject listing of response will be provided by subject ID and by visit in ascending order. A by-subject listing of bone marrow results for those with CR will be provided by subject ID and by visit in ascending order.

6.2.2. Progression-Free Survival

The date of definitive progression will be the time point at which progression is first identified by relevant radiographic, imaging, or clinical data. Subjects without progression or death will be censored at the last adequate post-baseline tumor assessment time. If subjects received the anti-cancer therapy or have ≥ 2 consecutive missing post-baseline tumor assessments immediately before documented progression or death, they will be censored at the last adequate post-baseline tumor assessment time before starting anti-cancer therapy or before ≥ 2 consecutive missing assessments, whichever is earlier. If subjects don't have an adequate baseline tumor assessment or any adequate post-baseline tumor assessments, they will be censored on the date of Study Day 1 unless they died before or on the 2nd scheduled post-baseline tumor assessment without receiving anti-cancer therapy.

PFS in months = (date of event/censoring – date of first dose + 1) / 30.4375.

When imaging examinations for one visit are conducted on various dates, the following rules apply for the calculation of the assessment date:

- The response date will be the last date associated with that particular imaging time point.
- The progression date will be the first date associated with that particular imaging time point.

When the date of initiation of anticancer therapy other than the study treatment is incomplete or missing, the following algorithm will be followed:

- If the day is missing but the month and year are available, then the imputed day will be the first day of the month.
- If day and month are missing but year is available, then the imputed day and month will be 01Jan or the last day of the month for the last adequate disease assessment if they have the same year, whichever is later.

In case that PFS event is a death with incomplete date, the imputation algorithm is as specified in section 6.2.4.

The analysis of PFS will be performed using the Kaplan-Meier method for FAS. Medians, Q1, Q3, the proportion of subjects who are progression-free at 6, 12, 18, 24, 30, 36, 42, 48, and 60 months from Study Day 1 will be provided along with corresponding 95% CIs. Kaplan-Meier curves will be provided.

The follow-up time for PFS, defined as the interval from the first dosing date of study drug to the loss to PFS follow-up, will be summarized by treatment groups using statistics such as median,

Q1, Q3 with corresponding 95% CIs estimated with the reverse K-M method. The reverse K-M model switches the event/censoring indicators of subjects in the original PFS analysis with Kaplan-Meier method. It considers subjects lost to PFS follow-up as achieving the full follow-up, and the full follow-up time of those subjects who had disease progression or died could not be observed as it is "censored" by the event.

A listing will be provided for the information of subject PFS, date of progression or censor, and reason.

A listing will be provided for the information of post-treatment anticancer therapy.

6.2.3. Duration of Response

DOR will be evaluated using investigator assessments based on subset of FAS subjects who achieve a CR or PR and maintain the response. DOR will be summarized using Kaplan-Meier methods (median, Q1, Q3, and corresponding 95% CI). The same censoring rules as for PFS will be applied to DOR.

DOR in months = (date of event/censoring – date of first response [CR or PR] + 1) / 30.4375.

A by-subject listing of DOR will be provided by subject ID number in ascending order.

6.2.4. Overall Survival

Subjects who are lost to follow-up or survived until the end of study will be censored at the last date that they were known to be alive.

Every attempt will be made to ensure that complete death dates are recorded. In those rare instances where complete death dates are not recorded, the following algorithm will be used:

- If day is missing but the month and year are available, then the imputed date will be the 1st day of the month or the last known alive date + 1, whichever is later.
- If day and month are missing but year is available, then the imputed date and month will be 01Jan or the last known alive date + 1, whichever is later.

If the last known alive date is not complete, the following algorithm will be used:

- If day is missing but the month and year are available, then the imputed date will be the 1st day of the month.

- If day and month are missing but year is available, then the imputed date and month will be 01Jan

The analysis of OS will be performed using the Kaplan-Meier method for FAS. Medians, Q1, Q3, the proportion of subjects who are alive at 6, 12, 18, 24, 30, 36, 42, 48, and 60 months from Study Day 1 will be provided along with corresponding 95% CIs. Kaplan-Meier curves will be provided. A listing will be provided for the information of subject OS, date of death or censor, and reason.

The follow-up time for OS, defined as the interval from the first dosing date of study drug to the loss to follow-up, will be summarized by treatment groups using statistics such as median, Q1, Q3 with corresponding 95% CIs estimated with the reverse Kaplan-Meier (K-M) method. The reverse K-M model switches the event/censoring indicators of subjects in the original OS analysis with Kaplan-Meier method. It considers subjects lost to follow-up as achieving the full follow-up, and the full follow-up time of those subjects who died could not be observed as it is "censored" by death.

7. SAFETY ANALYSES

As specified in Section 3.2, subjects' safety data of GS-US-401-1787 will be integrated with the parent study for all safety analysis. Some selected safety summaries will also be provided only using data from rollover study GS-US-401-1787.

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

Clinical and laboratory adverse events (AEs) for the rollover study GS-US-401-1787 will be coded using the current version of MedDRA. The coding of clinical and laboratory adverse events for the completed parent study ONO-4059POE001 will be upversioned to the current version of MedDRA, and integrated with GS-US-401-1787 for analysis. System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lower-level term (LLT) will be provided in the AE dataset.

7.1.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1, 2, 3, 4, or 5 according to CTCAE Version 4.03 in 401-1787, and CTCAE Version 4.0 in ONO-4059POE001. The severity grade of events for which the investigator did not record severity will be categorized as "missing" for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" on the AE case report form (CRF) to the question of "Related to Study Treatment." Relatedness will always default to the investigator's choice, not that of the medical monitor. Events for which the investigator did not record relationship to study drug will be considered related to study drug for summary purposes. However, by-subject data listings will show the relationship as missing.

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured as SAEs if AEs met the definitions of SAE that were specified in the study protocol. Serious adverse events captured and stored in the clinical database will be reconciled with the SAE database from the Gilead Pharmacovigilance and Epidemiology Department before data finalization.

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as one or both of the following:

- Any AEs with an onset date on or after the study drug start date of parent study and no later than 30 days after permanent discontinuation of study drug
- Any AEs leading to premature discontinuation of study drug.

7.1.5.2. Incomplete Dates

In case when the AE onset date is incomplete and needs to be imputed, the following algorithm will be followed:

- If the day is missing but the month and year are available, then the imputed day will be the first day of the month or the first dosing date if they have the same month and year, whichever is later.
- If the day and month are missing but year is available, then the imputed day and month will be 01Jan or the first dosing date if they have the same year, whichever is later.

An AE with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dosing date of study drug, will be considered to be treatment emergent. In addition, an AE with the onset date missing and incomplete stop date with the same or later month and year (or year alone if month is not recorded) as the first dosing date of study drug will be considered treatment emergent.

7.1.6. Summaries of Adverse Events and Deaths

Treatment-emergent AEs will be summarized based on the Safety Analysis Set.

7.1.6.1. Summaries of AE Incidence by Severity

The number and percentage of subjects who experienced at least 1 TEAE will be provided and summarized by SOC, PT, and dose level. For other AEs described below, summaries will be provided by SOC, PT, maximum severity and dose level:

- TEAEs
- TEAEs of Grade 3 or higher
- TE Treatment-related TEAEs
- TE Treatment-related TEAEs of Grade 3 or higher

- TE SAEs
- TE treatment-related SAEs
- TEAEs leading to dose modification of study drug
- TEAEs leading to temporary interruption of study drug
- TEAEs leading to discontinuation of study drug
- TEAEs leading to discontinuation of study
- TEAEs leading to death

A brief, high-level summary of AEs described above will be provided by dose level and by the number and percentage of subjects who experienced the above AEs. In addition, all death will also be included in this high-level summary.

In addition, TEAE by PT only will also be summarized.

In addition to the above summary tables, the following AE tables will also be provided using different grouping rule or data scope:

Data Scope	Grouping Rule	AE Summaries
Integrate data from both ONO-4059POE001 and GS-US-401-1787	• Combine all subjects regardless of disease type or dose level	Brief high-level summary of AE TEAE, TEAEs of Grade 3 or higher, SAE, TEAE leading to death by SOC, PT, and Severity
Only data from GS-US-401-1787	• Separate table by NHL and CLL • Combine all subjects regardless of disease type or dose level	Brief high-level summary of AE TEAE, TEAEs of Grade 3 or higher, SAE, TEAE leading to death by SOC, PT, and Severity

Multiple events will be counted only once per subject in each summary. Adverse events will be summarized and listed first in alphabetic order of SOC, and then by PT in descending order of total frequency within each SOC. For summaries by severity grade, the most severe grade will be used for those AEs that occurred more than once in an individual subject during the study.

In addition, data listings will be provided for the following:

- All AEs
- All AEs of Grade 3 or higher
- SAEs

- AEs leading to death
- Deaths
- AEs leading to discontinuation of study drug
- AEs leading to dose modifications or temporary interruption of study drug
- AEs leading to discontinuation of study

7.1.7. Treatment-Emergent Adverse Events of Interest

The treatment-emergent AEs of interest (AEI) include:

AEI	Grouped Terms
Hemorrhage/Bleeding	MST-CT Bleeding/Haemorrhage (Appendix 3)
Infections	SOC: Infections and infestations
Hypersensitivity	MST-CT Hypersensitivity (Appendix 4)
Cytopenia	MST: Anemia-related events, leukopenias, neutropenia, thrombocytopenias (Appendix 5)
Cardiac Arrhythmias	MST-CT Cardiac arrhythmia and bradycardia_narrow (Appendix 6)
Diarrhoea	PT: Diarrhoea
Rash	MST-CT Rash - specific to ONC (Appendix 7)

The following summaries will be provided for AEIs by SOC, PT, and maximum severity:

- TEAE
- TEAEs leading to dose modifications or temporary interruption of study drug
- TEAEs leading to discontinuation of study drug

A data listing of AEIs will be provided by alphabetic ascending order of AEI name, then by subject ID.

7.2. Laboratory Evaluations

Laboratory data collected during the study will be analyzed and summarized using both quantitative and qualitative methods. Summaries of laboratory parameters listed in Appendix 8 will be provided for the Safety Analysis Set and will include data collected up to the last dose of study drug plus 30 days for subjects who have permanently discontinued study drug. The analysis will be based on values reported in conventional units. When values are below the LOQ, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics as specified in Section 3.7.

A by-subject listing for laboratory test results will be provided by subject ID number and time point in chronological order for hematology, serum chemistry, and urinalysis separately. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher on the CTCAE severity grade will be flagged in the data listings, as appropriate.

No formal statistical testing is planned.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics of selected laboratory results will be provided by treatment group as follows:

- Baseline values
- Postbaseline maximum
- Postbaseline minimum
- Change from baseline to postbaseline maximum
- Change from baseline to postbaseline minimun

A baseline laboratory value will be defined as the last measurement obtained on or prior to the date/time of first dose of study drug in parent study. Change from baseline to a postbaseline visit will be defined as the visit value minus the baseline value. Laboratory test results collected at unscheduled visits will be included for the baseline and postbaseline maximum and minimum value selection. The mean, median, Q1, Q3, minimum, and maximum values will be displayed to the reported number of digits; StD values will be displayed to the reported number of digits plus 1.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3.

7.2.2. Graded Laboratory Values

CTCAE Version 4.03 will be used for assigning toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (ie, increased, decreased) will be presented separately.

7.2.2.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to and including the date of last dose of study drug plus 30 days for subjects who permanently discontinued study drug. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered treatment emergent. Local labs will be graded based on the central lab normal ranges with in-house macro. In the event that both central and local lab results are collected in the clinical database, the worst toxicity grade will be used for the summary of lab toxicities. All central and local laboratory values will be listed.

7.2.2.2. Treatment-Emergent Marked Laboratory Abnormalities

Treatment-emergent marked laboratory abnormalities are defined as values that increase from baseline by at least 3 toxicity grades at any postbaseline time point, up to and including the date of the last dose of study drug plus 30. If the relevant baseline laboratory value is missing, any Grade 3 or 4 values observed within the timeframe specified above will be considered treatment-emergent marked abnormalities.

7.2.2.3. Summaries of Laboratory Abnormalities

The following summaries (number and percentage of subjects) for treatment-emergent laboratory abnormalities will be provided by lab test and treatment group; subjects will be categorized according to the most severe postbaseline abnormality grade for a given lab test:

- Graded laboratory abnormalities
- Grade 3 or 4 laboratory abnormalities
- Marked laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of subjects with nonmissing postbaseline values up to 30 days after last dosing date.

In addition to the summary above, the Graded laboratory abnormalities and Grade 3 or 4 laboratory abnormalities will also be summarized using only the data from GS-US-401-1787.

A by-subject listing of treatment-emergent Grade 3 or 4 laboratory abnormalities and marked laboratory abnormalities will be provided by subject ID number and visit in chronological order. This listing will include all test results that were collected throughout the study for the lab test of interest, with all applicable severity grades or abnormal flags displayed.

7.2.3. Liver-related Laboratory Evaluations

Liver-related abnormalities after initial study drug dosing will be examined and summarized using the number and percentage of subjects who were reported to have the following laboratory test values for postbaseline measurements:

- Aspartate aminotransferase (AST): (a) > 3 times of the upper limit of reference range (ULN); (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- Alanine aminotransferase (ALT): (a) > 3 x ULN; (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- AST or ALT: (a) > 3 x ULN; (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- Total bilirubin: > 2 x ULN
- Alkaline phosphatase (ALP) > 1.5 x ULN
- AST or ALT > 3 x ULN and total bilirubin: (a) > 1.5 x ULN; (b) > 2 x ULN

The summary will include data from all postbaseline visits up to 30 days after the last dose of study drug. For individual laboratory tests, subjects will be counted once based on the most severe postbaseline values. For both the composite endpoint of AST or ALT and total bilirubin, subjects will be counted once when the criteria are met at the same postbaseline visit date. The denominator is the number of subjects in the Safety Analysis Set who have nonmissing postbaseline values of all relevant tests at the same postbaseline visit date. A listing of subjects who met at least 1 of the above criteria will be provided.

7.2.4. Shifts Relative to the Baseline Value

Shift tables will be presented by showing change in severity grade from baseline to the worst postbaseline grade.

7.3. Body Weight and Vital Signs

Descriptive statistics will be provided by treatment group for body weight, BMI, and vital signs as follows:

- Baseline value
- Postbaseline maximum
- Postbaseline minimum
- Change and percent change from baseline to postbaseline maximum
- Change and percent change from baseline to postbaseline minimum

A baseline value will be defined as the last available value collected on or prior to the date/time of first dose of study drug in the parent study. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value. Body weight and vital signs measured at unscheduled visits will be included for the baseline value selection, and postbaseline maximum and minimum value selection.

A by-subject listing of vital signs will be provided by subject ID number and time point in chronological order. Body weight and BMI will be included in the vital signs listing, if space permits. If not, they will be provided separately.

7.4. Prior and Concomitant Medications

Medications collected in the GS-US-401-1787 study will be coded using the current version of the World Health Organization (WHO) Drug dictionary. The coding of Medications collected in the parent study ONO-4059POE001 will be upversioned to the current version of WHODrug, and integrated with GS-US-401-1787 for analysis.

7.4.1. Prior Medications

Prior medications are defined as any medication taken before a subject took the first study drug of parent study.

Prior medications will be summarized by Anatomical Therapeutic Chemical (ATC) drug class Level 2 and preferred name using the number and percentage of subjects for each treatment group and overall. A subject reporting the same medication more than once will be counted only once when calculating the number and percentage of subjects who received that medication. The summary will be ordered alphabetically by ATC medical class and then by preferred term in order of descending overall frequency within each ATC medical class. For drugs with the same frequency, sorting will be done alphabetically.

For the purposes of analysis, any medication with a start date prior to the first dosing date of study drug will be included in the prior medication summary regardless of when the stop date is. If a partial start date is entered the medication will be considered prior unless the month and year (if day is missing) or year (if day and month are missing) of the start date are after the first dosing date. Medications with a completely missing start date will be included in the prior medication summary, unless otherwise specified.

Summaries will be based on the Safety Analysis Set. No formal statistical testing is planned.

7.4.2. Concomitant Medications

Concomitant medications are defined as medications taken while a subject took study drug. Use of concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) drug class Level 2 and preferred name using the number and percentage of subjects for each treatment group. A subject reporting the same medication more than once will be counted only once when calculating the number and percentage of subjects who received that medication. The summary will be ordered alphabetically by ATC medical class and then by preferred term in descending overall frequency within each ATC medical class. For drugs with the same frequency, sorting will be done alphabetically.

For the purposes of analysis, any medication with a start date prior to or on the first dosing date of study drug and continued to take after the first dosing date, or started after the first dosing date but prior to or on the last dosing date of study drug will be considered concomitant medications. Medications started and stopped on the same day as the first dosing date or the last dosing date of study drug will also be considered concomitant. Medications with a stop date prior to the date of first dosing date of study drug or a start date after the last dosing date of study drug will be excluded from the concomitant medication summary. If a partial stop date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the date of first study drug administration will be excluded from the concomitant medication summary. If a partial start date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date will be excluded from the concomitant medication summary. Medications with completely missing start and stop dates will be included in the concomitant medication summary, unless otherwise specified. Summaries will be based on the Safety Analysis Set. No formal statistical testing is planned.

All prior and concomitant medications (other than per-protocol study drugs) will be provided in a by-subject listing sorted by subject ID number and administration date in chronological order.

7.5. Electrocardiogram Results

Electrocardiogram (ECG) analysis results are intended to identify meaningful changes in the QT interval. If potential abnormalities of interest are identified, further analyses may be conducted.

A shift table of the investigators' assessment of ECG results at each visit compared with baseline values will be presented by treatment group using the following categories: normal; abnormal, not clinically significant; abnormal, clinically significant; or missing. The number and percentage of subjects in each cross-classification group of the shift table will be presented. Subjects with a missing value at baseline or postbaseline will not be included in the denominator for percentage calculation. No formal statistical testing is planned.

A by-subject listing for ECG assessment results will be provided by subject ID number and time point in chronological order.

7.6. Other Safety Measures

No additional safety measures are specified in the protocol.

7.7. Changes From Protocol-Specified Safety Analyses

There are no deviations from the protocol-specified safety analyses.

8. PHARMACOKINETIC ANALYSES

8.1. Pharmacokinetics (PK) Sample Collection

Plasma samples for PK will be collected to measure concentrations of tirabrutinib at pre-dose of GS-US-401-1787 Cycles 2 and 3 only.

8.2. Statistical Analysis Methods

8.2.1. Tirabrutinib Plasma Concentration

PK concentration data from GS-US-401-1787 will be summarized. PK analysis set will be grouped as specified in Section 3.2.

Tirabrutinib plasma concentration data will be summarized using descriptive statistics for subjects in the PK Analysis Set by time point and visit. Subjects in different dose levels will be presented separately. The sample size for each time point will be based on the number of subjects with nonmissing concentration data at that time point. The number of subjects with concentration BLQ will be presented for each time point. For summary statistics, BLQ values will be treated as 0 at predose and one-half of the lower limit of quantitation (LLOQ) for postdose time points.

The following table will be provided by disease type and dose level:

- Individual subject concentration data and summary statistics

Tirabrutinib plasma concentration data and PK sampling details will be listed for all subjects in the PK Analysis Set.

8.3. Changes From Protocol-Specified PK Analyses

There are no deviations from the protocol-specified pharmacokinetic analyses.

9. REFERENCES

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Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Dohner H, et al. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) updating the National Cancer Institute-Working Group (NCI-WG) 1996 guidelines. Blood 2008;111 (12):5446-56.

Owen RG, Kyle RA, Stone MJ, Rawstron AC, Leblond V, Merlini G, et al. Response assessment in Waldenstrom macroglobulinaemia: update from the VIth International Workshop. Br J Haematol 2013;160 (2):171-6.

10. SOFTWARE

SAS® Software Version 9.4. SAS Institute Inc., Cary, NC, USA.

11. SAP REVISION

Revision Date (DD MMM YYYY)	Section	Summary of Revision	Reason for Revision
10 Apr 2020, version 2.0	1.2.2	Update the 401-1787 study design to maximum duration of 5 years treatment, per the protocol amendment 5 dated 29 October 2019	Align with protocol amendment 5 dated 29 October 2019
10 Apr 2020, version 2.0	2.1, 3.1.2, 6	Administrative changes	Language clarification
10 Apr 2020, version 2.0	6.2.2	Added PFS follow-up time analysis	To add additional analysis per new Gilead oncology standard
10 Apr 2020, version 2.0	6.2.2	Revised the data imputation rule for incomplete date of anti-cancer therapy	Update per Gilead oncology standard
10 Apr 2020, version 2.0	6.2.4	Added OS follow-up time analysis	To add additional analysis per new Gilead oncology standard
10 February 2021, version 3.0	4.4	Added the section to provide how to handle special situations due to COVID-19 in the analysis	To assess the COVID-19 impact

12. APPENDICES

Appendix 1. COVID-19 SMQ with Broad Scope

Note: The list presented below is based on MedDRA Version 23.1. The actual list will be up-versioned to the MedDRA version used at the time of database finalization.

MedDRA Preferred Term	PT Code
Asymptomatic COVID-19	10084459
Coronavirus infection	10051905
Coronavirus test positive	10070255
COVID-19	10084268
COVID-19 immunisation	10084457
COVID-19 pneumonia	10084380
COVID-19 prophylaxis	10084458
COVID-19 treatment	10084460
Exposure to SARS-CoV-2	10084456
Multisystem inflammatory syndrome in children	10084767
Occupational exposure to SARS-CoV-2	10084394
SARS-CoV-2 antibody test positive	10084491
SARS-CoV-2 carrier	10084461
SARS-CoV-2 sepsis	10084639
SARS-CoV-2 test false negative	10084480
SARS-CoV-2 test positive	10084271
SARS-CoV-2 viraemia	10084640
Suspected COVID-19	10084451
Antiviral prophylaxis	10049087
Antiviral treatment	10068724
Coronavirus test	10084353
Coronavirus test negative	10084269
Exposure to communicable disease	10049711
Pneumonia viral	10035737
SARS-CoV-2 antibody test	10084501
SARS-CoV-2 antibody test negative	10084509
SARS-CoV-2 test	10084354
SARS-CoV-2 test false positive	10084602
SARS-CoV-2 test negative	10084273

Appendix 2. Determining Missing and Virtual Visits Due to COVID-19

This appendix describes the clinical trial site collection of COVID-19 data pertaining to missed/virtual visits and the data processing algorithm used to determine which visits were missing and which visits were virtual.

Data collection

A COVID-19 supplement to the eCRF Completion Guidelines (CCG) was provided by data management to instruct clinical trial sites with respect to data entry expectations pertaining to scenarios related to the COVID-19 pandemic. If a visit was missed, sites should enter "Visit missed due to COVID-19." If an in-person visit was conducted virtually, sites should enter "Virtual visit due to COVID-19."

Determination of Missed and Virtual visits

NLP was used to search the CRF comment fields to identify instances of "COVID-19" (or synonyms, see the table below) and "Virtual" (or synonyms, see the table below). The search terms are maintained in a global lookup table and can be modified to tune the NLP model. For any comments with COVID-19 search terms, assign "Missed visit" or "Virtual visit as follows:

i. If COVID-19 terms are identified through NLP and the visit date is missing, then result is "Missed Visit"
ii. If COVID-19 and Virtual terms are identified through NLP for a visit, then result is "Virtual Visit". When there are multiple records for the same subject and the same visit, NLP will be based on multiple records to ensure 1 unique category per subject per visit
iii. Otherwise result is missing

Examples of Search Terms for "COVID-19" and "Virtual" Used to Identify Missed and Virtual Visits

Search Terms for "COVID-19"	Search Terms for "Virtual"
COVID19	VIRTUAL
CORONA	TELEMED
CORONAVIRUS	TELEHEALTH
PANDEMIC	TELEPHONE
OUTBREAK	REMOTE
CRISIS	TELEMEDICINE
LOCKDOWN	TELECONSULTATION
QUARANTINE	TELEPHONICALLY
SHELTER	PHONE
	HOME VISIT
	ZOOM
	SKYPE

Appendix 3. Bleeding/Haemorrhage Medical Search Term

Note: The list presented below is based on MedDRA Version 22.0. The actual list will be up-versioned to the MedDRA version used at the time of database finalization.

MedDRA Preferred Term	PT Code
Abdominal wall haematoma	10067383
Haemorrhagic adrenal infarction	10079902
Eye haematoma	10079891
Spontaneous hyphaema	10080110
Anal fissure haemorrhage	10079765
Paranasal sinus haemorrhage	10080108
Peripheral artery aneurysm rupture	10079908
Aortic annulus rupture	10079586
Peripheral artery haematoma	10081077
Subgaleal haemorrhage	10080900
Von Willebrand's factor antibody	10080829
Nephritis haemorrhagic	10029132
Renal cyst haemorrhage	10059846
Renal haematoma	10038459
Renal haemorrhage	10038460
Ureteric haemorrhage	10065743
Extraischaemic cerebral haematoma	10080347
Gastrointestinal vascular malformation haemorrhagic	10080561
Abdominal wall haemorrhage	10067788
Abnormal clotting factor	10049862
Abnormal withdrawal bleeding	10069195
Acquired dysfibrinogenaemia	10051122
Acquired haemophilia	10053745
Acquired haemophilia with anti FVIII, XI, or XIII	10056496
Acquired protein S deficiency	10068370
Acquired Von Willebrand's disease	10069495
Activated partial thromboplastin time abnormal	10000631
Activated partial thromboplastin time prolonged	10000636
Activated partial thromboplastin time ratio abnormal	10075284
Activated partial thromboplastin time ratio fluctuation	10075286
Activated partial thromboplastin time ratio increased	10075287
Acute haemorrhagic leukoencephalitis	10058994
Acute haemorrhagic ulcerative colitis	10075634
Administration site bruise	10075094
Administration site haematoma	10075100
Administration site haemorrhage	10075101
Adrenal haematoma	10059194
Adrenal haemorrhage	10001361
Anal haemorrhage	10049555
Anal ulcer haemorrhage	10063896
Anastomotic haemorrhage	10056346
Anastomotic ulcer haemorrhage	10002244
Aneurysm ruptured	10048380
Angina bullosa haemorrhagica	10064223
Anorectal varices haemorrhage	10068925
Anti factor IX antibody positive	10058748
Anti factor V antibody positive	10058745
Anti factor VII antibody positive	10058746
Anti factor VIII antibody positive	10049013
Anti factor X activity abnormal	10077670
Anti factor X activity increased	10077671
Anti factor X antibody positive	10058747
Anti factor XI antibody positive	10058749
Anti factor XII antibody positive	10058750
Antithrombin III increased	10051115
Aortic aneurysm rupture	10002886
Aortic dissection rupture	10068119
Aortic intramural haematoma	10067975

MedDRA Preferred Term	PT Code
Aortic perforation	10075729
Aortic rupture	10060874
Aponeurosis contusion	10075330
Application site bruise	10050114
Application site haematoma	10068317
Application site haemorrhage	10072694
Application site purpura	10050182
Arterial haemorrhage	10060964
Arterial intramural haematoma	10074971
Arterial ligation	10003165
Arterial perforation	10075732
Arterial rupture	10003173
Arteriovenous fistula site haematoma	10055150
Arteriovenous fistula site haemorrhage	10055123
Arteriovenous graft site haematoma	10055152
Arteriovenous graft site haemorrhage	10055126
Atrial rupture	10048761
Auricular haematoma	10003797
Basal ganglia haematoma	10077031
Basal ganglia haemorrhage	10067057
Basilar artery perforation	10075736
Benign familial haematuria	10060876
Bladder tamponade	10062656
Bleeding time abnormal	10049227
Bleeding time prolonged	10005140
Bleeding varicose vein	10005144
Blood blister	10005372
Blood fibrinogen abnormal	10005518
Blood fibrinogen decreased	10005520
Blood thrombin abnormal	10005818
Blood thrombin decreased	10005820
Blood thromboplastin abnormal	10005824
Blood thromboplastin decreased	10005826
Blood urine	10005863
Blood urine present	10018870

MedDRA Preferred Term	PT Code
Bloody discharge	10057687
Bloody peritoneal effluent	10067442
Bone contusion	10066251
Bone marrow haemorrhage	10073581
Brain contusion	10052346
Brain stem haematoma	10073230
Brain stem haemorrhage	10006145
Brain stem microhaemorrhage	10071205
Breast haematoma	10064753
Breast haemorrhage	10006254
Broad ligament haematoma	10006375
Bronchial haemorrhage	10065739
Bronchial varices haemorrhage	10079163
Bursal haematoma	10077818
Capillary fragility abnormal	10007192
Capillary fragility increased	10007194
Capillary permeability increased	10007200
Cardiac contusion	10073356
Carotid aneurysm rupture	10051328
Carotid artery perforation	10075728
Catheter site bruise	10063587
Catheter site haematoma	10055662
Catheter site haemorrhage	10051099
Central nervous system haemorrhage	10072043
Cephalhaematoma	10008014
Cerebellar haematoma	10061038
Cerebellar haemorrhage	10008030
Cerebellar microhaemorrhage	10071206
Cerebral aneurysm perforation	10075394
Cerebral aneurysm ruptured syphilitic	10008076
Cerebral arteriovenous malformation haemorrhagic	10008086
Cerebral artery perforation	10075734
Cerebral haematoma	10053942
Cerebral haemorrhage	10008111

MedDRA Preferred Term	PT Code
Cerebral haemorrhage foetal	10050157
Cerebral haemorrhage neonatal	10008112
Cerebral microhaemorrhage	10067277
Cervix haematoma uterine	10050020
Cervix haemorrhage uterine	10050022
Chest wall haematoma	10076597
Choroidal haematoma	10068642
Choroidal haemorrhage	10008786
Chronic gastrointestinal bleeding	10050399
Chronic pigmented purpura	10072726
Ciliary body haemorrhage	10057417
Circulating anticoagulant	10053627
Clot retraction abnormal	10009669
Clot retraction time prolonged	10009675
Coagulation disorder neonatal	10009732
Coagulation factor decreased	10009736
Coagulation factor deficiency	10067787
Coagulation factor IX level abnormal	10061770
Coagulation factor IX level decreased	10009746
Coagulation factor mutation	10065442
Coagulation factor V level abnormal	10061771
Coagulation factor V level decreased	10009754
Coagulation factor VII level abnormal	10061772
Coagulation factor VII level decreased	10009761
Coagulation factor VIII level abnormal	10061773
Coagulation factor VIII level decreased	10009768
Coagulation factor X level abnormal	10061774
Coagulation factor X level decreased	10009775
Coagulation factor XI level abnormal	10061775
Coagulation factor XI level decreased	10009779
Coagulation factor XII level abnormal	10061776
Coagulation factor XII level decreased	10009783
Coagulation factor XIII level abnormal	10061777
Coagulation factor XIII level decreased	10009787
Coagulation time abnormal	10009791
Coagulation time prolonged	10009799
Coagulopathy	10009802
Coital bleeding	10065019
Colonic haematoma	10009996
Congenital coagulopathy	10063563
Congenital dysfibrinogenaemia	10051123
Conjunctival haemorrhage	10010719
Contusion	10050584
Corneal bleeding	10051558
Cullen's sign	10059029
Cystitis haemorrhagic	10011793
Deep dissecting haematoma	10074718
Diarrhoea haemorrhagic	10012741
Dilutional coagulopathy	10060906
Disseminated intravascular coagulation	10013442
Diverticulitis intestinal haemorrhagic	10013541
Diverticulum intestinal haemorrhagic	10013560
Duodenal ulcer haemorrhage	10013839
Duodenitis haemorrhagic	10013865
Dysfunctional uterine bleeding	10013908
Ear haemorrhage	10014009
Ecchymosis	10014080
Encephalitis haemorrhagic	10014589
Endometriosis	10014778
Enterocolitis haemorrhagic	10014896
Epidural haemorrhage	10073681
Epistaxis	10015090
Ethanol gelation test positive	10062650
Exsanguination	10015719
Extra-axial haemorrhage	10078254
Extradural haematoma	10015769
Extravasation blood	10015867
Eye contusion	10073354
Eye haemorrhage	10015926
Eyelid bleeding	10053196

MedDRA Preferred Term	PT Code
Eyelid contusion	10075018
Eyelid haematoma	10064976
Factor I deficiency	10016075
Factor II deficiency	10016076
Factor III deficiency	10052473
Factor IX deficiency	10016077
Factor V deficiency	10048930
Factor VII deficiency	10016079
Factor VIII deficiency	10016080
Factor X deficiency	10052474
Factor Xa activity abnormal	10078667
Factor Xa activity decreased	10078676
Factor XI deficiency	10016082
Factor XII deficiency	10051806
Factor XIII deficiency	10016083
Femoral artery perforation	10075739
Femoral vein perforation	10075745
Fibrin abnormal	10016575
Fibrin D dimer decreased	10016579
Fibrin D dimer increased	10016581
Fibrin decreased	10016584
Fibrin degradation products	10016585
Fibrin degradation products increased	10016588
Fibrinolysis abnormal	10016604
Fibrinolysis increased	10016607
Foetal-maternal haemorrhage	10016871
Fothergill sign positive	10081749
Gardner-Diamond syndrome	10078888
Gastric haemorrhage	10017788
Gastric occult blood positive	10067855
Gastric ulcer haemorrhage	10017826
Gastric ulcer haemorrhage, obstructive	10017829
Gastric varices haemorrhage	10057572
Gastritis alcoholic haemorrhagic	10017857
Gastritis haemorrhagic	10017866

MedDRA Preferred Term	PT Code
Gastroduodenal haemorrhage	10053768
Gastrointestinal angiectasia	10078142
Gastrointestinal haemorrhage	10017955
Gastrointestinal organ contusion	10078655
Gastrointestinal polyp haemorrhage	10074437
Gastrointestinal ulcer haemorrhage	10056743
Genital contusion	10073355
Genital haemorrhage	10061178
Gingival bleeding	10018276
Graft haemorrhage	10063577
Grey Turner's sign	10075426
Haemarthrosis	10018829
Haematemesis	10018830
Haematochezia	10018836
Haematocoele	10018833
Haematoma	10018852
Haematoma evacuation	10060733
Haematoma infection	10051564
Haematosalpinx	10050468
Haematospermia	10018866
Haematotympanum	10063013
Haematuria	10018867
Haematuria traumatic	10018871
Haemobilia	10058947
Haemophilia	10061992
Haemophilia A with anti factor VIII	10056492
Haemophilia A without inhibitors	10056493
Haemophilia B with anti factor IX	10056494
Haemophilia B without inhibitors	10056495
Haemophilic arthropathy	10065057
Haemophilic pseudotumour	10073770
Haemoptysis	10018964
Haemorrhage	10055798
Haemorrhage coronary artery	10055803
Haemorrhage foetal	10061191

MedDRA Preferred Term	PT Code
Haemorrhage in pregnancy	10018981
Haemorrhage intracranial	10018985
Haemorrhage neonatal	10061993
Haemorrhage subcutaneous	10018999
Haemorrhage subepidermal	10019001
Haemorrhage urinary tract	10055847
Blood loss anaemia	10082297
Haemorrhagic arteriovenous malformation	10064595
Haemorrhagic ascites	10059766
Haemorrhagic breast cyst	10077443
Haemorrhagic cerebral infarction	10019005
Haemorrhagic cyst	10059189
Haemorrhagic diathesis	10062713
Haemorrhagic disease of newborn	10019008
Haemorrhagic disorder	10019009
Haemorrhagic erosive gastritis	10067786
Haemorrhagic hepatic cyst	10067796
Haemorrhagic infarction	10019013
Haemorrhagic necrotic pancreatitis	10076058
Haemorrhagic ovarian cyst	10060781
Haemorrhagic pneumonia	10077933
Haemorrhagic stroke	10019016
Haemorrhagic thyroid cyst	10072256
Haemorrhagic transformation stroke	10055677
Haemorrhagic tumour necrosis	10054096
Haemorrhagic urticaria	10059499
Haemorrhagic varicella syndrome	10078873
Haemorrhagic vasculitis	10071252
Haemorrhoidal haemorrhage	10054787
Haemostasis	10067439
Haemothorax	10019027
Henoch-Schonlein purpura	10019617
Hepatic haemangioma rupture	10054885
Hepatic haematoma	10019676
Hepatic haemorrhage	10019677
Hereditary haemorrhagic telangiectasia	10019883
Hermansky-Pudlak syndrome	10071775
Hyperfibrinolysis	10074737
Hyphaema	10020923
Hypocoagulable state	10020973
Hypofibrinogenaemia	10051125
Hypoprothrombinaemia	10021085
Hypothrombinaemia	10058517
Hypothromboplastinaemia	10058518
Iliac artery perforation	10075731
Iliac artery rupture	10072789
Iliac vein perforation	10075744
Immune thrombocytopenic purpura	10074667
Implant site bruising	10063850
Implant site haematoma	10063780
Implant site haemorrhage	10053995
Incision site haematoma	10059241
Incision site haemorrhage	10051100
Increased tendency to bruise	10021688
Induced abortion haemorrhage	10052844
Inferior vena cava perforation	10075742
Infusion site bruising	10059203
Infusion site haematoma	10065463
Infusion site haemorrhage	10065464
Injection site bruising	10022052
Injection site haematoma	10022066
Injection site haemorrhage	10022067
Instillation site bruise	10073630
Instillation site haematoma	10073609
Instillation site haemorrhage	10073610
Internal haemorrhage	10075192
International normalised ratio abnormal	10022592
International normalised ratio increased	10022595
Intestinal haematoma	10069829
Intestinal haemorrhage	10059175

MedDRA Preferred Term	PT Code
Intestinal varices haemorrhage	10078058
Intra-abdominal haematoma	10056457
Intra-abdominal haemorrhage	10061249
Intracerebral haematoma evacuation	10062025
Intracranial haematoma	10059491
Intracranial tumour haemorrhage	10022775
Intraocular haematoma	10071934
Intrapartum haemorrhage	10067703
Intraventricular haemorrhage	10022840
Intraventricular haemorrhage neonatal	10022841
Iris haemorrhage	10057418
Joint microhaemorrhage	10077666
Kidney contusion	10023413
Lacrimal haemorrhage	10069930
Large intestinal haemorrhage	10052534
Large intestinal ulcer haemorrhage	10061262
Laryngeal haematoma	10070885
Laryngeal haemorrhage	10065740
Lip haematoma	10066304
Lip haemorrhage	10049297
Liver contusion	10067266
Lower gastrointestinal haemorrhage	10050953
Lower limb artery perforation	10075730
Lymph node haemorrhage	10074270
Mallory-Weiss syndrome	10026712
Mediastinal haematoma	10049941
Mediastinal haemorrhage	10056343
Medical device site bruise	10075570
Medical device site haematoma	10075577
Medical device site haemorrhage	10075578
Melaena	10027141
Melaena neonatal	10049777
Meningorrhagia	10052593
Menometrorrhagia	10027295
Menorrhagia	10027313

MedDRA Preferred Term	PT Code
Mesenteric haematoma	10071557
Mesenteric haemorrhage	10060717
Metrorrhagia	10027514
Mouth haemorrhage	10028024
Mucocutaneous haemorrhage	10076048
Mucosal haemorrhage	10061298
Muscle contusion	10070757
Muscle haemorrhage	10028309
Myocardial haemorrhage	10048849
Myocardial rupture	10028604
Naevus haemorrhage	10062955
Nail bed bleeding	10048891
Nasal septum haematoma	10075027
Neonatal gastrointestinal haemorrhage	10074159
Nipple exudate bloody	10029418
Occult blood positive	10061880
Ocular retrobulbar haemorrhage	10057571
Oesophageal haemorrhage	10030172
Oesophageal intramural haematoma	10077486
Oesophageal ulcer haemorrhage	10030202
Oesophageal varices haemorrhage	10030210
Oesophagitis haemorrhagic	10030219
Optic disc haemorrhage	10030919
Optic nerve sheath haemorrhage	10030941
Oral contusion	10078170
Oral mucosa haematoma	10074779
Osteorrhagia	10051937
Ovarian haematoma	10033263
Ovarian haemorrhage	10065741
Palpable purpura	10056872
Pancreatic contusion	10078654
Pancreatic haemorrhage	10033625
Pancreatitis haemorrhagic	10033650
Papillary muscle haemorrhage	10059164
Paranasal sinus haematoma	10069702

MedDRA Preferred Term	PT Code
Parathyroid haemorrhage	10059051
Parotid gland haemorrhage	10051166
Pelvic haematoma	10054974
Pelvic haematoma obstetric	10034248
Pelvic haemorrhage	10063678
Penile contusion	10073352
Penile haematoma	10070656
Penile haemorrhage	10034305
Peptic ulcer haemorrhage	10034344
Pericardial haemorrhage	10034476
Perineal haematoma	10034520
Periorbital haematoma	10034544
Periorbital haemorrhage	10071697
Periosteal haematoma	10077341
Peripartum haemorrhage	10072693
Perirenal haematoma	10049450
Peritoneal haematoma	10058095
Peritoneal haemorrhage	10034666
Periventricular haemorrhage neonatal	10076706
Petechiae	10034754
Pharyngeal haematoma	10068121
Pharyngeal haemorrhage	10034827
Pituitary haemorrhage	10049760
Placenta praevia haemorrhage	10035121
Plasminogen activator inhibitor	10059620
Plasminogen activator inhibitor decreased	10059619
Plasminogen decreased	10035493
Plasminogen increased	10035495
Platelet factor 4 decreased	10060220
Polymenorrhagia	10064050
Post abortion haemorrhage	10036246
Post procedural contusion	10073353
Post procedural haematoma	10063188
Post procedural haematuria	10066225
Post procedural haemorrhage	10051077

MedDRA Preferred Term	PT Code
Post transfusion purpura	10072265
Postmenopausal haemorrhage	10055870
Postpartum haemorrhage	10036417
Post-traumatic punctate intraepidermal haemorrhage	10071639
Procedural haemorrhage	10071229
Proctitis haemorrhagic	10036778
Prostatic haemorrhage	10036960
Protein C increased	10060230
Protein S abnormal	10051736
Protein S increased	10051735
Prothrombin level abnormal	10037048
Prothrombin level decreased	10037050
Prothrombin time abnormal	10037057
Prothrombin time prolonged	10037063
Prothrombin time ratio abnormal	10061918
Prothrombin time ratio increased	10037068
Pulmonary alveolar haemorrhage	10037313
Pulmonary contusion	10037370
Pulmonary haematoma	10054991
Pulmonary haemorrhage	10037394
Puncture site haemorrhage	10051101
Purpura	10037549
Purpura fulminans	10037556
Purpura neonatal	10037557
Purpura non-thrombocytopenic	10057739
Purpura senile	10037560
Putamen haemorrhage	10058940
Radiation associated haemorrhage	10072281
Rectal haemorrhage	10038063
Rectal ulcer haemorrhage	10038081
Renal artery perforation	10075737
Respiratory tract haemorrhage	10038727
Respiratory tract haemorrhage neonatal	10038728
Retinal aneurysm rupture	10079121

MedDRA Preferred Term	PT Code
Retinal haemorrhage	10038867
Retinopathy haemorrhagic	10051447
Retroperitoneal haematoma	10058360
Retroperitoneal haemorrhage	10038980
Retroplacental haematoma	10054798
Ruptured cerebral aneurysm	10039330
Russell's viper venom time abnormal	10059759
Scleral haemorrhage	10050508
Scrotal haematocoele	10061517
Scrotal haematoma	10039749
Shock haemorrhagic	10049771
Skin haemorrhage	10064265
Skin neoplasm bleeding	10060712
Skin ulcer haemorrhage	10050377
Small intestinal haemorrhage	10052535
Small intestinal ulcer haemorrhage	10061550
Soft tissue haemorrhage	10051297
Spermatic cord haemorrhage	10065742
Spinal cord haematoma	10076051
Spinal cord haemorrhage	10048992
Spinal epidural haematoma	10050162
Spinal epidural haemorrhage	10049236
Spinal subarachnoid haemorrhage	10073564
Spinal subdural haematoma	10050164
Spinal subdural haemorrhage	10073563
Spleen contusion	10073533
Splenic artery perforation	10075738
Splenic haematoma	10041646
Splenic haemorrhage	10041647
Splenic varices haemorrhage	10068662
Splinter haemorrhages	10041663
Spontaneous haematoma	10065304
Spontaneous haemorrhage	10074557
Stoma site haemorrhage	10074508
Stomatitis haemorrhagic	10042132

MedDRA Preferred Term	PT Code
Subarachnoid haematoma	10076701
Subarachnoid haemorrhage	10042316
Subarachnoid haemorrhage neonatal	10042317
Subchorionic haematoma	10072596
Subchorionic haemorrhage	10071010
Subclavian artery perforation	10075740
Subclavian vein perforation	10075743
Subcutaneous haematoma	10042345
Subdural haematoma	10042361
Subdural haematoma evacuation	10042363
Subdural haemorrhage	10042364
Subdural haemorrhage neonatal	10042365
Subgaleal haematoma	10069510
Subretinal haematoma	10071935
Superior vena cava perforation	10075741
Testicular haemorrhage	10051877
Thalamus haemorrhage	10058939
Third stage postpartum haemorrhage	10043449
Thoracic haemorrhage	10062744
Thrombin time abnormal	10051319
Thrombin time prolonged	10051390
Thrombin-antithrombin III complex abnormal	10053972
Thrombin-antithrombin III complex increased	10053968
Thrombocytopenic purpura	10043561
Thrombotic thrombocytopenic purpura	10043648
Thyroid haemorrhage	10064224
Tongue haematoma	10043959
Tongue haemorrhage	10049870
Tonsillar haemorrhage	10057450
Tooth pulp haemorrhage	10072228
Tooth socket haemorrhage	10064946
Tracheal haemorrhage	10062543
Traumatic haematoma	10044522
Traumatic haemorrhage	10053476

MedDRA Preferred Term	PT Code
Traumatic haemothorax	10074487
Traumatic intracranial haematoma	10079013
Traumatic intracranial haemorrhage	10061387
Tumour haemorrhage	10049750
Ulcer haemorrhage	10061577
Umbilical cord haemorrhage	10064534
Umbilical haematoma	10068712
Umbilical haemorrhage	10045455
Upper gastrointestinal haemorrhage	10046274
Urethral haemorrhage	10049710
Urinary bladder haemorrhage	10046528
Urogenital haemorrhage	10050058
Uterine haematoma	10063875
Uterine haemorrhage	10046788
Vaccination site bruising	10069484
Vaccination site haematoma	10069472
Vaccination site haemorrhage	10069475
Vaginal haematoma	10046909
Vaginal haemorrhage	10046910
Varicose vein ruptured	10046999
Vascular access site bruising	10077767
Vascular access site haematoma	10077647
Vascular access site haemorrhage	10077643
Vascular access site rupture	10077652
Vascular graft haemorrhage	10077721
Vascular pseudoaneurysm ruptured	10053949
Vascular purpura	10047097
Vascular rupture	10053649
Vein rupture	10077110
Venous haemorrhage	10065441
Venous perforation	10075733
Ventricle rupture	10047279
Vertebral artery perforation	10075735
Vessel puncture site bruise	10063881
Vessel puncture site haematoma	10065902
Vessel puncture site haemorrhage	10054092
Vitreous haematoma	10071936
Vitreous haemorrhage	10047655
Von Willebrand's disease	10047715
Von Willebrand's factor antibody positive	10066358
Von Willebrand's factor multimers abnormal	10055165
Vulval haematoma	10047756
Vulval haematoma evacuation	10047757
Vulval haemorrhage	10063816
White nipple sign	10078438
Withdrawal bleed	10047998
Wound haematoma	10071504
Cerebral cyst haemorrhage	10082099
Pituitary apoplexy	10056447
Haematoma muscle	10055890
Battle's sign	10082307
Puncture site bruise	10082035
Haemorrhagic cholecystitis	10082088
Puncture site haematoma	10081957
Subendocardial haemorrhage	10082459
Acute haemorrhagic oedema of infancy	10070599
Wound haemorrhage	10051373

Appendix 4. Hypersensitivity Medical Search Term

Note: The list presented below is based on a SMQ in MedDRA Version 22.0. The actual list will be up-versioned to the MedDRA version used at the time of database finalization.

MedDRA Preferred Term	PT Code
Acute respiratory failure	10001053
Alveolitis	10001889
Anaphylactic reaction	10002198
Anaphylactic shock	10002199
Anaphylactoid reaction	10002216
Anaphylaxis treatment	10002222
Angioedema	10002424
Application site dermatitis	10003036
Application site rash	10003054
Asthma	10003553
Asthma late onset	10003559
Atopy	10003645
Auricular swelling	10003800
Blepharitis allergic	10005149
Blister	10005191
Blood immunoglobulin A abnormal	10005584
Blood immunoglobulin A increased	10005586
Blood immunoglobulin E abnormal	10005589
Blood immunoglobulin E increased	10005591
Blood immunoglobulin G abnormal	10005594
Blood immunoglobulin G increased	10005596
Blood immunoglobulin M abnormal	10005599
Blood immunoglobulin M increased	10005601
Bromoderma	10006404
Bronchospasm	10006482
Bullous impetigo	10006563
Charcot-Leyden crystals	10008413
Cheilitis	10008417
Choking	10008589
Choking sensation	10008590
Circulatory collapse	10009192
Conjunctival oedema	10010726
Conjunctivitis	10010741
Conjunctivitis allergic	10010744
Contrast media reaction	10010836
Corneal oedema	10011033
Cutaneous vasculitis	10011686
Dermatitis	10012431
Dermatitis acneiform	10012432
Dermatitis allergic	10012434
Dermatitis atopic	10012438
Dermatitis bullous	10012441
Dermatitis contact	10012442
Dermatitis exfoliative	10012455
Dermatitis exfoliative generalised	10012456
Dermatitis herpetiformis	10012468
Dermatitis infected	10012470
Drug eruption	10013687
Drug hypersensitivity	10013700
Ear swelling	10014025
Eczema	10014184
Eczema infantile	10014198
Eczema nummular	10014201
Encephalopathy allergic	10014627
Eosinophil count increased	10014945
Eosinophilia	10014950
Eosinophilia myalgia syndrome	10014952
Eosinophilic pneumonia	10014962
Epidermolysis bullosa	10014989
Epiglottic oedema	10015029
Erythema	10015150
Erythema multiforme	10015218
Erythema nodosum	10015226
Eye allergy	10015907

MedDRA Preferred Term	PT Code
Eye swelling	10015967
Eyelid oedema	10015993
Face oedema	10016029
Fixed eruption	10016741
Flushing	10016825
Generalised oedema	10018092
Genital rash	10018175
Giant papillary conjunctivitis	10018258
Gingival swelling	10018291
Henoch-Schonlein purpura	10019617
Hereditary angioedema	10019860
Hypersensitivity	10020751
Hypersensitivity vasculitis	10020764
Idiopathic urticaria	10021247
Immunoglobulins abnormal	10021497
Immunoglobulins increased	10021500
Injection site dermatitis	10022056
Injection site hypersensitivity	10022071
Injection site rash	10022094
Injection site urticaria	10022107
Interstitial lung disease	10022611
Laryngeal oedema	10023845
Laryngospasm	10023891
Laryngotracheal oedema	10023893
Lip oedema	10024558
Lip swelling	10024570
Mouth ulceration	10028034
Mucocutaneous ulceration	10028084
Mucosa vesicle	10028103
Mucosal ulceration	10028124
Multiple allergies	10028164
Nephritis allergic	10029120
Neurodermatitis	10029263
Nikolsky's sign	10029415
Occupational dermatitis	10030012

MedDRA Preferred Term	PT Code
Oculomucocutaneous syndrome	10030081
Oedema mouth	10030110
Oedema mucosal	10030111
Orbital oedema	10031051
Oropharyngeal spasm	10031111
Oropharyngeal swelling	10031118
Panniculitis	10033675
Penile swelling	10034319
Perioral dermatitis	10034541
Periorbital oedema	10034545
Pharyngeal oedema	10034829
Photosensitivity reaction	10034972
Pneumonitis	10035742
Prurigo	10037083
Pruritus	10037087
Pulmonary eosinophilia	10037382
Radioallergosorbent test positive	10037789
Rash	10037844
Rash erythematous	10037855
Rash follicular	10037857
Rash generalised	10037858
Rash macular	10037867
Rash maculo-papular	10037868
Rash morbilliform	10037870
Rash neonatal	10037871
Rash papulosquamous	10037879
Rash pruritic	10037884
Rash pustular	10037888
Rash scarlatiniform	10037890
Rash vesicular	10037898
Reaction to azo-dyes	10037973
Reaction to colouring	10037974
Reaction to food additive	10037977
Red man syndrome	10038192
Respiratory arrest	10038669

MedDRA Preferred Term	PT Code
Respiratory distress	10038687
Respiratory failure	10038695
Rhinitis allergic	10039085
Rhinitis perennial	10039094
Scrotal oedema	10039755
Scrotal swelling	10039759
Serum sickness	10040400
Serum sickness-like reaction	10040402
Shock	10040560
Shock symptom	10040581
Skin erosion	10040840
Skin exfoliation	10040844
Skin necrosis	10040893
Skin reaction	10040914
Skin test positive	10040934
Sneezing	10041232
Solar urticaria	10041307
Solvent sensitivity	10041316
Status asthmaticus	10041961
Stevens-Johnson syndrome	10042033
Stomatitis	10042128
Stridor	10042241
Suffocation feeling	10042444
Swelling face	10042682
Swelling of eyelid	10042690
Swollen tongue	10042727
Throat tightness	10043528
Tongue oedema	10043967
Toxic epidermal necrolysis	10044223
Tracheal obstruction	10044291
Tracheal oedema	10044296
Tracheostomy	10044320
Type I hypersensitivity	10045240
Urticaria	10046735
Urticaria cholinergic	10046740
Urticaria contact	10046742
Urticaria papular	10046750
Urticaria physical	10046751
Urticaria pigmentosa	10046752
Urticaria vesiculosa	10046755
Vaginal ulceration	10046943
Vasculitic rash	10047111
Vulval oedema	10047763
Vulval ulceration	10047768
Wheezing	10047924
Acute generalised exanthematous pustulosis	10048799
Urticarial vasculitis	10048820
Seasonal allergy	10048908
Localised oedema	10048961
Allergic sinusitis	10049153
Gingival oedema	10049305
Rash maculovesicular	10050004
Application site eczema	10050099
Application site urticaria	10050104
Vulvovaginal ulceration	10050181
Allergic pharyngitis	10050639
Cytokine storm	10050685
Anti-neutrophil cytoplasmic antibody positive vasculitis	10050894
Complement factor C3 decreased	10050981
Complement factor C4 decreased	10050983
Scleritis allergic	10051126
Allergic cystitis	10051394
Complement factor C1 decreased	10051552
Complement factor C2 decreased	10051555
Generalised erythema	10051576
Infusion related reaction	10051792
Kaposi's varicelliform eruption	10051891
Cytokine release syndrome	10052015
Iodine allergy	10052098

MedDRA Preferred Term	PT Code
Eye oedema	10052139
Eosinophil percentage increased	10052222
Circumoral oedema	10052250
Catheter site rash	10052271
Catheter site urticaria	10052272
Laryngeal dyspnoea	10052390
Urticaria chronic	10052568
Pruritus generalised	10052576
Allergic bronchitis	10052613
Eosinophilic pneumonia acute	10052832
Eosinophilic pneumonia chronic	10052833
Epidermolysis	10053177
Skin swelling	10053262
Injection site photosensitivity reaction	10053396
Type IV hypersensitivity reaction	10053613
Type III immune complex mediated reaction	10053614
Allergic cough	10053779
Streptokinase antibody increased	10053797
Anti-insulin antibody positive	10053814
Anti-insulin antibody increased	10053815
Type II hypersensitivity	10054000
Allergy to fermented products	10054929
Allergy to vaccine	10055048
Eczema weeping	10055182
Allergy test positive	10056352
Encephalitis allergic	10056387
Periorbital swelling	10056647
Mucocutaneous rash	10056671
Bronchial oedema	10056695
Palpable purpura	10056872
Septal panniculitis	10056876
Palatal oedema	10056998
Allergic keratitis	10057380
Scleral oedema	10057431

MedDRA Preferred Term	PT Code
Toxic skin eruption	10057970
Rash rubelliform	10057984
Gastrointestinal oedema	10058061
Eosinophil percentage abnormal	10058133
Dermatitis psoriasiform	10058675
Skin oedema	10058679
Eczema vesicular	10058681
Application site photosensitivity reaction	10058730
Hand dermatitis	10058898
Stoma site rash	10059071
Epidermal necrosis	10059284
Allergic colitis	10059447
Haemorrhagic urticaria	10059499
Laryngeal obstruction	10059639
Infusion site rash	10059830
Alpha tumour necrosis factor increased	10059982
Allergic oedema	10060934
Complement factor decreased	10061048
Eosinophil count abnormal	10061125
Immunology test abnormal	10061214
Mucosal erosion	10061297
Antibody test abnormal	10061425
Antibody test positive	10061427
Arthritis allergic	10061430
Allergic otitis media	10061557
Allergy to chemicals	10061626
Reversible airways obstruction	10062109
Heparin-induced thrombocytopenia	10062506
Necrotising panniculitis	10062579
Dennie-Morgan fold	10062918
Mesenteric panniculitis	10063031
Anaphylactoid shock	10063119
Blood immunoglobulin D increased	10063244
Pruritus allergic	10063438
Allergic respiratory symptom	10063527

MedDRA Preferred Term	PT Code
Allergic respiratory disease	10063532
Application site hypersensitivity	10063683
Implant site rash	10063786
Implant site urticaria	10063787
Vaginal oedema	10063818
Implant site dermatitis	10063855
Implant site hypersensitivity	10063858
Antiallergic therapy	10064059
Eosinophilic oesophagitis	10064212
Lip exfoliation	10064482
Vaginal exfoliation	10064483
Penile exfoliation	10064485
Mucosal exfoliation	10064486
Oral mucosal exfoliation	10064487
Tongue exfoliation	10064488
Corneal exfoliation	10064489
Exfoliative rash	10064579
Immune complex level increased	10064650
Leukotriene increased	10064663
Reaction to preservatives	10064788
Asthmatic crisis	10064823
Laryngitis allergic	10064866
Neutralising antibodies positive	10064980
Non-neutralising antibodies positive	10064982
Perivascular dermatitis	10064986
Infusion site dermatitis	10065458
Infusion site hypersensitivity	10065471
Infusion site photosensitivity reaction	10065486
Infusion site urticaria	10065490
Antiendomysial antibody positive	10065514
Eosinophilic bronchitis	10065563
Visceral oedema	10065768
Eczema vaccinatum	10066042
Bronchial hyperreactivity	10066091
Allergic transfusion reaction	10066173

MedDRA Preferred Term	PT Code
Injection site eczema	10066221
Penile oedema	10066774
Injection site recall reaction	10066797
Gleich's syndrome	10066837
Contrast media allergy	10066973
Anaphylactic transfusion reaction	10067113
Haemolytic transfusion reaction	10067122
Immediate post-injection reaction	10067142
Oculorespiratory syndrome	10067317
Contact stomatitis	10067510
Genital swelling	10067639
Upper airway obstruction	10067775
HLA marker study positive	10067937
Oropharyngeal blistering	10067950
Interstitial granulomatous dermatitis	10067972
Mucosal necrosis	10067993
Injection site vasculitis	10067995
Anti-insulin receptor antibody positive	10068225
Anti-insulin receptor antibody increased	10068226
Oral allergy syndrome	10068355
Capillaritis	10068406
Mechanical urticaria	10068773
Palisaded neutrophilic granulomatous dermatitis	10068809
Vaccination site hypersensitivity	10068880
Kounis syndrome	10069167
Henoch-Schonlein purpura nephritis	10069440
Vaccination site dermatitis	10069477
Vaccination site rash	10069482
Vaccination site exfoliation	10069489
Vaccination site urticaria	10069622
Vaccination site vesicles	10069623
Administration related reaction	10069773
Limbal swelling	10070492
Distributive shock	10070559

MedDRA Preferred Term	PT Code
Immune tolerance induction	10070581
Respiratory tract oedema	10070774
Reactive airways dysfunction syndrome	10070832
Occupational asthma	10070836
Injection related reaction	10071152
Administration site rash	10071156
Allergic hepatitis	10071198
Vulvovaginal swelling	10071211
Chronic hyperplastic eosinophilic sinusitis	10071380
Chronic eosinophilic rhinosinusitis	10071399
Vulvovaginal rash	10071588
Device allergy	10072867
Incision site dermatitis	10073168
Blister rupture	10073385
Incision site rash	10073411
Implant site photosensitivity	10073415
Drug reaction with eosinophilia and systemic symptoms	10073508
Instillation site hypersensitivity	10073612
Instillation site rash	10073622
Instillation site urticaria	10073627
Catheter site dermatitis	10073992
Catheter site eczema	10073995
Catheter site hypersensitivity	10073998
Catheter site vasculitis	10074014
Allergy to immunoglobulin therapy	10074079
Pathergy reaction	10074332
Drug provocation test	10074350
Palatal swelling	10074403
Stoma site hypersensitivity	10074509
Immune thrombocytopenic purpura	10074667
Noninfective conjunctivitis	10074701
Infusion site eczema	10074850
Infusion site vasculitis	10074851
Caffeine allergy	10074895

MedDRA Preferred Term	PT Code
Transplantation associated food allergy	10075008
Allergic otitis externa	10075072
Aspirin-exacerbated respiratory disease	10075084
Administration site dermatitis	10075096
Administration site eczema	10075099
Administration site hypersensitivity	10075102
Administration site urticaria	10075109
Allergic eosinophilia	10075185
Mouth swelling	10075203
Airway remodelling	10075289
Allergic gastroenteritis	10075308
Perineal rash	10075364
Allergy alert test positive	10075479
Medical device site dermatitis	10075572
Medical device site eczema	10075575
Medical device site hypersensitivity	10075579
Medical device site rash	10075585
Medical device site urticaria	10075588
Nodular rash	10075807
Administration site photosensitivity reaction	10075961
Administration site recall reaction	10075964
Administration site vasculitis	10075969
Application site recall reaction	10076024
Application site vasculitis	10076027
Infusion site recall reaction	10076085
Medical device site photosensitivity reaction	10076137
Medical device site recall reaction	10076140
Vaccination site eczema	10076161
Vaccination site photosensitivity reaction	10076186
Vaccination site recall reaction	10076188
Vaccination site vasculitis	10076191
Intestinal angioedema	10076229
Documented hypersensitivity to administered product	10076470

MedDRA Preferred Term	PT Code
Mast cell degranulation present	10076606
Dialysis membrane reaction	10076665
Asthma-chronic obstructive pulmonary disease overlap syndrome	10077005
Vessel puncture site rash	10077117
Allergy to surgical sutures	10077279
Immune-mediated adverse reaction	10077665
Vessel puncture site vesicles	10077813
Eosinophilic granulomatosis with polyangiitis	10078117
Symmetrical drug-related intertriginous and flexural exanthema	10078325
Nasal crease	10078581
Oropharyngeal oedema	10078783
Allergic reaction to excipient	10078853
Allergic stomatitis	10079554
Therapeutic product cross-reactivity	10079645
Reaction to excipient	10079925
Vulvovaginitis allergic	10080783
Procedural shock	10080894
Hereditary angioedema with C1 esterase inhibitor deficiency	10080955
Vernal keratoconjunctivitis	10081000
Hypersensitivity myocarditis	10081004
Acquired C1 inhibitor deficiency	10081035
Scrotal exfoliation	10081178
Childhood asthma	10081274
Atopic cough	10081492
Circumoral swelling	10081703
Hypersensitivity pneumonitis	10081988
Human anti-hamster antibody increased	10082107
Human anti-hamster antibody positive	10082109
Pharyngeal swelling	10082270
Urticarial dermatitis	10082290
Immune-mediated pneumonitis	10082452

Appendix 5. Cytopenia Medical Search Term

Note: The list presented below is based on MedDRA Version 22.0. The actual list will be up-versioned to the MedDRA version used at the time of database finalization.

MedDRA Preferred Term	PT Code
Acquired amegakaryocytic thrombocytopenia	10076747
Megakaryocytes decreased	10027119
Mononuclear cell count decreased	10082036
Platelet count decreased	10035528
Platelet maturation arrest	10035537
Platelet production decreased	10035540
Platelet toxicity	10059440
Thrombocytopenia	10043554
Febrile neutropenia	10016288
Neutropenia	10029354
Neutrophil count decreased	10029366
Agranulocytosis	10001507
Autoimmune neutropenia	10055128
Transfusion-related alloimmune neutropenia	10081503
Granulocytopenia	10018687
Idiopathic neutropenia	10051645
Neutropenic colitis	10062959
Neutropenic infection	10059482
Neutropenic sepsis	10049151
Neutrophil count abnormal	10061313
Band neutrophil count decreased	10057950
Band neutrophil percentage decreased	10059130
Neutrophil percentage abnormal	10058134
Neutrophil percentage decreased	10052223
Granulocyte count decreased	10018681
Granulocytes abnormal	10018685
Anaemia macrocytic	10002064
Aplasia pure red cell	10002965

MedDRA Preferred Term	PT Code
Aplastic anaemia	10002967
Erythroblast count decreased	10058505
Erythroid maturation arrest	10015279
Erythropenia	10015287
Hypoplastic anaemia	10021074
Microcytic anaemia	10027538
Proerythroblast count decreased	10060229
Red blood cell count decreased	10038153
Reticulocyte count decreased	10038790
Reticulocytopenia	10038795
Anaemia	10002034
Anaemia neonatal	10002068
Erythroblast count abnormal	10058508
Erythropoiesis abnormal	10049467
Foetal anaemia	10077577
Haematocrit abnormal	10049221
Haematocrit decreased	10018838
Haemoglobin abnormal	10018879
Haemoglobin decreased	10018884
Leukoerythroblastic anaemia	10053199
Normochromic anaemia	10029782
Normochromic normocytic anaemia	10029783
Normocytic anaemia	10029784
Proerythroblast count abnormal	10060227
Red blood cell count abnormal	10038151
Reticulocyte count abnormal	10038788
Reticulocyte percentage decreased	10059921
Autoimmune aplastic anaemia	10071576
Bicytopenia	10058956

MedDRA Preferred Term	PT Code
Bone marrow failure	10065553
Cytopenia	10066274
Febrile bone marrow aplasia	10053213
Full blood count decreased	10017413
Gelatinous transformation of the bone marrow	10078097
Pancytopenia	10033661
Panmyelopathy	10050026

Appendix 6. Cardiac arrhythmia Medical Search Term

Note: The list presented below is based on MedDRA Version 22.0. The actual list will be up-versioned to the MedDRA version used at the time of database finalization.

MedDRA PreferredTerm	PT Code
Accelerated idioventricular rhythm	10049003
Neonatal bradyarrhythmia	10082054
Neonatal tachyarrhythmia	10082055
Congenital supraventricular tachycardia	10082343
Frederick's syndrome	10082089
Accessory cardiac pathway	10067618
Adams-Stokes syndrome	10001115
Agonal rhythm	10054015
Anomalous atrioventricular excitation	10002611
Arrhythmia	10003119
Arrhythmia neonatal	10003124
Arrhythmia supraventricular	10003130
Arrhythmogenic right ventricular dysplasia	10058093
Atrial conduction time prolongation	10064191
Atrial fibrillation	10003658
Atrial flutter	10003662
Atrial parasystole	10071666
Atrial tachycardia	10003668
Atrioventricular block	10003671
Atrioventricular block complete	10003673
Atrioventricular block first degree	10003674
Atrioventricular block second degree	10003677
Atrioventricular conduction time shortened	10068180
Atrioventricular dissociation	10069571
Atrioventricular node dispersion	10077893
Bifascicular block	10057393
Bradyarrhythmia	10049765
Brugada syndrome	10059027
Bundle branch block	10006578
Bundle branch block bilateral	10006579
Bundle branch block left	10006580
Bundle branch block right	10006582
Cardiac fibrillation	10061592
Cardiac flutter	10052840
Chronotropic incompetence	10068627
Conduction disorder	10010276
Defect conduction intraventricular	10012118
Electrocardiogram delta waves abnormal	10014372
Electrocardiogram PQ interval prolonged	10053656
Electrocardiogram PQ interval shortened	10075328
Electrocardiogram PR prolongation	10053657
Electrocardiogram PR shortened	10014374
Electrocardiogram QRS complex prolonged	10014380
Electrocardiogram QT prolonged	10014387
Electrocardiogram repolarisation abnormality	10052464
Electrocardiogram U wave present	10057913
Electrocardiogram U wave inversion	10062314
Electrocardiogram RR interval prolonged	10067652
Electrocardiogram U-wave abnormality	10055032
Extrasystoles	10015856
Foetal arrhythmia	10016847
Foetal heart rate disorder	10061158
Foetal tachyarrhythmia	10077575

MedDRA PreferredTerm	PT Code
Heart alternation	10058155
Heart block congenital	10019263
Heart rate irregular	10019304
Junctional ectopic tachycardia	10074640
Lenegre's disease	10071710
Long QT syndrome	10024803
Long QT syndrome congenital	10057926
Lown-Ganong-Levine syndrome	10024984
Nodal arrhythmia	10029458
Nodal rhythm	10029470
Pacemaker generated arrhythmia	10053486
Pacemaker syndrome	10051994
Parasystole	10033929
Paroxysmal arrhythmia	10050106
Paroxysmal atrioventricular block	10077503
Pulseless electrical activity	10058151
Reperfusion arrhythmia	10058156
Rhythm idioventricular	10039111
Sinoatrial block	10040736
Sinus arrest	10040738
Sinus arrhythmia	10040739
Sinus bradycardia	10040741
Sinus node dysfunction	10075889
Sinus tachycardia	10040752
Sudden cardiac death	10049418
Supraventricular extrasystoles	10042602
Supraventricular tachyarrhythmia	10065342
Supraventricular tachycardia	10042604
Tachyarrhythmia	10049447
Torsade de pointes	10044066
Trifascicular block	10044644
Ventricular arrhythmia	10047281
Ventricular asystole	10047284
Ventricular dyssynchrony	10071186
Ventricular extrasystoles	10047289
Ventricular fibrillation	10047290
Ventricular flutter	10047294
Ventricular parasystole	10058184
Ventricular pre-excitation	10049761
Ventricular tachyarrhythmia	10065341
Ventricular tachycardia	10047302
Wandering pacemaker	10047818
Withdrawal arrhythmia	10047997
Wolff-Parkinson-White syndrome	10048015
Wolff-Parkinson-White syndrome congenital	10049291
Bradycardia	10006093

Appendix 7. Rash Medical Search Term

Note: The list presented below is based on MedDRA Version 22.0. The actual list will be up-versioned to the MedDRA version used at the time of database finalization.

MedDRA Term Name	PT Code
Acute generalised exanthematous pustulosis	10048799
Angina bullosa haemorrhagica	10064223
Autoimmune dermatitis	10075689
Blister	10005191
Blister rupture	10073385
Butterfly rash	10067982
Cervical bulla	10050019
Dermatitis exfoliative	10012455
Dermatitis exfoliative generalised	10012456
Dermatosis	10048768
Drug eruption	10013687
Drug reaction with eosinophilia and systemic symptoms	10073508
Eosinophilic pustular folliculitis	10052834
Epidermolysis	10053177
Epidermolysis bullosa	10014989
Eruptive pseudoangiomatosis	10068095
Erythema multiforme	10015218
Erythema nodosum	10015226
Erythrosis	10056474
Exfoliative rash	10064579
Fixed eruption	10016741
Flagellate dermatitis	10075467
Interstitial granulomatous dermatitis	10067972
Lichenoid keratosis	10064000
Macule	10025421
Mucocutaneous rash	10056671
Mucocutaneous ulceration	10028084
Mucosa vesicle	10028103

MedDRA Term Name	PT Code
Necrolytic migratory erythema	10060821
Neurodermatitis	10029263
Oculomucocutaneous syndrome	10030081
Oral mucosal blistering	10030995
Oropharyngeal blistering	10067950
Palmar-plantar erythrodysaesthesia syndrome	10033553
Palmoplantar pustulosis	10050185
Palpable purpura	10056872
Papule	10033733
Paraneoplastic rash	10074687
Pemphigoid	10034277
Pemphigus	10034280
Penile blister	10052898
Prurigo	10037083
Rash	10037844
Rash erythematous	10037855
Rash follicular	10037857
Rash generalised	10037858
Rash macular	10037867
Rash maculo-papular	10037868
Rash maculovesicular	10050004
Rash morbilliform	10037870
Rash papular	10037876
Rash papulosquamous	10037879
Rash pruritic	10037884
Rash pustular	10037888
Rash rubelliform	10057984
Rash scarlatiniform	10037890
Rash vesicular	10037898

MedDRA Term Name	PT Code
Seborrhoeic dermatitis	10039793
Skin disorder	10040831
Skin plaque	10067723
Skin reaction	10040914
Skin toxicity	10059516
Stevens-Johnson syndrome	10042033
Symmetrical drug-related intertriginous and flexural exanthema	10078325
Toxic epidermal necrolysis	10044223
Toxic erythema of chemotherapy	10074982
Toxic skin eruption	10057970
Umbilical erythema	10055029
Urticarial vasculitis	10048820
Vaginal exfoliation	10064483
Vasculitic rash	10047111
Viral rash	10047476
Skin lesion inflammation	10081154
Target skin lesion	10081998
Plethoric face	10081808
Vulvovaginal rash	10071588

Appendix 8. List of Laboratory Tests for Safety Summary

Serum Chemistry	Hematology
Albumin	WBC
Alkaline phosphatase	Hemoglobin
ALT	Hematocrit
Amylase	Platelet Count
AST	Basophils
Bicarbonate	Monocytes
BUN	Eosinophils
Calcium	Neutrophils
Chloride	Lymphocytes
Creatinine[a]	Red Blood Cells
GGT	
Glucose[b]	
LDH	
Lipase	
Potassium	
Sodium	
Total bilirubin	
Total Protein	
Uric Acid	

a Both creatinine and creatinine clearance rate will be included in the safety summary. Estimated creatinine clearance rate will be calculated based on the Cockcroft-Gault formula

b If fasting status is not unknown, non-fasting criteria will be applied for toxicity grading.

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ELECTRONIC SIGNATURES

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PPD	Clinical Research eSigned	04-Mar-2021 01:56:25
PPD	Biostatistics eSigned	05-Mar-2021 07:32:28