Janssen Research & Development *

Statistical Analysis Plan

A Phase 2b, Multicenter, Double-masked, Randomized Study Evaluating the Safety and Clinical Response of Subretinal Administration of CNTO 2476 in Subjects with Visual Acuity Impairment Associated with Geographic Atrophy Secondary to Age Related Macular Degeneration

Protocol CNTO2476MDG2002; Phase 2b

Palucorcel (CNTO 2476)

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Compliance: The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

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AMENDMENT HISTORY

ABBREVIATIONS

AE	adverse event
AMD	age-related macular degeneration
BCVA	best corrected visual acuity
BMI	body mass index
CGIC	Clinician Global Impression of Change
CI	confidence interval
CMH	Cochran Mantel Haenszel
CRO	Contract Research Organization
CSR	Clinical Study Report
CST	central subfield thickness
DA	disc area
DARC	Digital Angiography Reading Center
DSMB	Data Safety Monitoring Board
eCRF	electronic case report form
eDC	electronic data capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FAF	fundus autofluorescence
FDA	Food and Drug Administration
FRI	Functional Reading Index questionnaire
GA	geographic atrophy
ICH	International Conference on Harmonization
IP	investigational product
ITT	Intent-to-Treat
IWRS	interactive web response system
LLBCVA	low luminance BCVA
LLD	low luminance difference
LLT	lowest level term
logMAR	log of the minimum angle of resolution
MedDRA	Medical Dictionary for Regulatory Activities
mITT	modified Intent-to-Treat
NEI-VFQ-25	National Eye Institute Visual Function Questionnaire
OCT	optical coherence tomography
PGIC-Q	Patient Clinician Global Impression of Change – Quality of Life
PGIC-S	Patient Clinician Global Impression of Change – Symptoms
PI	principal investigator
RS	reading speed
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SD-OCT	Spectral-Domain Optical Coherence Tomography
SF-36	Short Form (36) Health Survey
SOC	System Organ Class
SSG	statistical support group
TE	treatment-emergent

1. INTRODUCTION

This statistical analysis plan (SAP) contains definitions of analysis sets, general analysis definitions and statistical methods for analyses planned for the final clinical study report.

1.1. Trial Objectives

Primary Objectives

The primary objective of the Open-label Safety Run-in Phase is to evaluate the safety and performance profile of the suprachoroidal surgical approach and the Delivery System.

Major Secondary Objectives

The major secondary objectives of this study are the following:

- to assess the safety and performance profile of the Delivery System, the safety and tolerability of the suprachoroidal surgical approach, and the safety and tolerability of CNTO 2476 cells in the open-label Safety Run-in Phase
- to assess the effects of CNTO 2476 on anatomic correlates of treatment, including change in the area of geographic atrophy (GA)
- to assess the effects of CNTO 2476 on additional and alternative efficacy outcomes including duration of clinical response.

1.2. Trial Design

This is a multicenter Phase 2b study. A target of approximately 21 subjects will be enrolled in this study. Protocol amendment 3 represents a significant reduction in scope and duration of the study based on the sponsor's decision to discontinue the Palucorcel development program.

The study includes only an initial open-label safety phase.

The target population will be subjects at least 55 years of age and no older than 90 years with a confirmed diagnosis of bilateral GA of the macula secondary to age-related macular degeneration (AMD), with associated vision loss, confirmed within 45 days prior to initial randomization/enrollment by the central reading center using fundus and/or autofluorescence photography. In subjects with neovascular AMD in 1 eye, the eye with GA must be the worse eye. In subjects with bilateral GA and the vision between both eyes is not clinically equal, the eye with the worse vision will be treated in order to minimize risk to the subject's vision. In cases where the best corrected visual acuity (BCVA) of the 2 eyes is clinically equal, the eye with more extensive GA as demonstrated on the imaging studies will become the study eye.

The Safety Run-in Phase consists of approximately 21 subjects (the first 3 subjects at each of approximately 8 sites) who will first be enrolled in an open-label assessment of the safety profile of the procedure and the Delivery System. The first 3 subjects at the first 8 sites (approximately 21 subjects in total) will be the initial Safety Cohort. A minimum of seven different surgeons are required to ensure most of the possible failure modes will be identified. Enrollment will be actively managed to ensure that experience and learning from earlier procedures are promptly

transferred to the subsequent procedures, and to ensure that an appropriate number of subjects are enrolled at the time of the planned safety assessments.

The safety profile of the procedure and the Delivery System will be assessed after the first 21 subjects (the initial Safety Cohort) have been treated with a single dose of 3.0 x 10^5 cells in 50 µL dosing volume and followed for a minimum period of 1 month. An external Data and Safety Monitoring Board (DSMB) will be commissioned for this study. The 2nd Safety Cohort and the randomized double-masked portion of this study were eliminated from the study as of Protocol Amendment 3.

The study will consist of a 12-month acute phase, followed by a 2-year maximum duration follow-up period (3 years total) for all subjects.

The DSMB will monitor study data on an ongoing basis to ensure the continuing safety of the subjects enrolled in this study. The committee will meet periodically to review interim study data. After the review, the DSMB will make recommendations regarding the safety and continuation of the study.

1.3. Statistical Hypotheses for Trial Objectives

The primary hypothesis of the open label safety phase of this study is that the novel subretinal Delivery System is sufficiently safe and usable to deliver cells to the subretinal space. An additional hypothesis is that Palucorcel is safe and well tolerated when delivered as a single dose to the subretinal space.

1.4. Sample Size Justification

The sample size of 21 subjects is based on the number of subjects require to allow for an adequate clinical assessment of the safety and usability of the novel Delivery System.

1.5. Randomization and Masking

Not applicable, because the study only enrolled the initial open-label safety cohort.

2. GENERAL ANALYSIS DEFINITIONS

Analyses will be conducted using SAS Version 9.2 or higher[1]. Continuous variables, including numerical variables assessed on a discrete scale, will be analyzed using descriptive statistics, including number of subjects, mean, median, standard deviation, maximum, and minimum. Minimum and maximum will be reported using the same decimal precision as the corresponding raw data, mean and median will be reported using one more decimal digit than the raw data. Standard deviation will be reported using two more decimal digits than the raw data. For categorical variables, analyses will include counts of subjects and percentages. The treated eye is the eye designated for treatment. The fellow eye is the other eye. Where applicable, results will be summarized by “Treated Eye” or “Fellow Eye” or “Both Eyes”, not left or right eye.

2.1. Study Day

Study Day will be computed relative to the Surgery Date, where the Surgery Date is Day 1. Study Day will be defined as follows:

- (Key Date – Surgery Date + 1), if Key Date is equal or greater than the Surgery Date;
- (Key Date – Surgery Date), if Key Date is prior to Surgery Date;

where Key Date can be a date of assessment, onset of an adverse event, or start of concomitant medication.

2.2. Baseline

For all assessments except for BCVA measurements (i.e., logMAR and total letters correct, both standard and low luminance), baseline will be defined as the most recent value prior to the Surgery Date (and time, if applicable). Thus the baseline could be derived based on Screening or Day 1 pre-op assessments or unscheduled pre-op assessments where applicable.

Baseline BCVA is assessed at an optional pre-screening visit (not recorded on the electronic case report form [eCRF] thus not used for analysis) and at the regular Screening visit (twice at that visit). For BCVA logMAR and total letters correct (both standard and low luminance), the better score at these 2 assessments will be used for baseline. For BCVA logMAR, a lower score is better. For total letters correct, a higher value is better.

Re-screening is allowed per protocol and the subject is not necessarily required to repeat every test during the 2nd screening. When a subject is re-screened, he/she receives a new subject ID. If a baseline value is not present for the current subject ID for this type of subject, it will be necessary to use the screening/baseline value captured in the 1st screening visit for that subject (captured using their previous subject ID) as the baseline value.

2.3. Visit Windows

All "by-visit" analyses will be presented by scheduled study visit as recorded on the eCRF; no visit windows will be used. Unscheduled assessments will be presented in by-subject data listings.

2.4. Pooling Algorithm for Analysis Centers

Not applicable. Data from all investigative sites (centers) will be combined together for analysis irrespective of the site in which the subject undergoes evaluations.

2.5. Analysis Sets

The initial Safety Cohort is defined as the first 21 subjects enrolled in the Open-label Safety Run-in Phase of the study who received surgery. Results will be presented as treatment group "CNTO 2476 3.0x10^5 cells".

2.6. Definition of Subgroups

Not applicable.

3. INTERIM ANALYSIS AND DATA MONITORING COMMITTEE REVIEW

A DSMB will be established to monitor data on an ongoing basis to ensure the continuing safety of the subjects enrolled in this study. The DSMB will consist of at least 1 medical expert in the relevant therapeutic area, and at least 1 statistician. The committee will meet periodically to review interim data. After the review, the DSMB will make recommendations regarding the continuation of the study.

The first formal safety data review will take place when 1-month safety follow-up data are available for the 21 subjects in the initial Safety Cohort. In addition, the DSMB charter will specify rules for interrupting the study enrollment in the event of device- or procedure-related safety events prior to the completion of the initial Safety Cohort. Events of special interest are choroidal hemorrhage, endophthalmitis or infections, retinal detachments, leakage of cells into the vitreous/need for vitrectomy, significant loss of vision defined as ≥15 letters lost compared to baseline (at the Week 4 post-surgery follow-up visit only), and failure to deliver cells/device failure.

Since no additional subjects are to be enrolled as of Protocol Amendment 3, there will be no further DSMB meetings and DSMB will be disbanded. Janssen retains the option to reform the DSMB should the need arise.

The DSMB's responsibilities, authorities, and procedures, will be documented in a separate charter.

The statistical analyses planned for the DSMB are provided in a separate DSMB SAP.

4. SUBJECT INFORMATION

4.1. Demographics and Baseline Characteristics

The following characteristics will be summarized: age (both as a continuous variable and with frequency counts for the following age groups: <65, ≥65 to <75, ≥75 years), sex, race, ethnicity, baseline weight, baseline height, baseline body mass index (BMI), tobacco substance usage; and the following baseline characteristics for both the treated and fellow eye: axial length, BCVA logMAR score, BCVA total letters correct, optical coherence tomography (OCT) central subfield thickness (CST) in microns (μ), total area of GA by fundus autofluorescence (FAF) in mm^2, and square root of total area of GA by FAF in mm.

Demographics and baseline characteristics for individual subjects will be presented in a data listing.

4.2. Medical History

General Medical History and Ocular Medical History will be summarized. The number and percentage of subjects with abnormalities recorded in the general medical history will be

tabulated by system organ class (SOC) and preferred term (PT). The number and percentage of subjects with ophthalmic disorders recorded in ocular medical history (which includes both past and ongoing) will be tabulated by SOC, PT and eye (treated, fellow, or both).

General Medical History and Ocular Medical History for individual subjects will be presented in data listings.

4.3. Disposition Information

The number of subjects will be tabulated for the following disposition categories: received open-label surgery, completed 6 months of follow-up, discontinued prior to month 6, completed 12 months of follow-up, discontinued prior to month 12, completed total study follow-up, and discontinued after month 12 prior to end of study. Reasons for discontinuation will also be tabulated for subjects who discontinue prior to month 6, prior to month 12 or prior to end of study.

Subject disposition information for individual subjects will be presented in a data listing.

4.4. Treatment Compliance

Not applicable for this study as the investigational product will be administered subretinally as a single dose by the retinal surgeon. The administration of the investigational product will take place in an operating room using the Delivery System. Compliance will not require any activity by the subject.

4.5. Extent of Exposure

The number of subjects who received cells (investigational product [IP] was delivered to the subretinal space) will be tabulated as part of the Summary of Surgery and Delivery System.

4.6. Protocol Deviations

All Major Protocol Deviations will be documented in the study database.

The number of subjects with major protocol deviations during the study will be summarized by category. Subjects with more than one deviation will be counted in all applicable categories.

Major protocol deviations for individual subjects will be presented in a data listing.

4.7. Prior and Concomitant Medications

Prior and concomitant medications will be coded using the WHO Drug dictionary. Medication stopped prior to the Surgery Date will be considered as prior. Medications that are not considered prior, i.e., taken on or after the Surgery Date, will be considered concomitant medications. Missing or incomplete medications' start and end dates will be handled as described in Attachment 1 in order to determine whether the medications are concomitant or not.

Prior and concomitant ocular medications will be tabulated by medication class and standardized medication name. Prior and concomitant non-ocular medications will be tabulated separately. A

subject taking the same prior/concomitant medication multiple times will only be counted once for that prior/concomitant medication.

Prior and concomitant ocular and non-ocular medications for individual subjects will be presented in a data listing.

5. SAFETY

The verbatim terms used in the eCRF by investigators to identify adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). All reported AEs with onset from the surgery start date and onwards (i.e., treatment-emergent (TE) AEs, and AEs that have worsened since baseline) will be included in the analysis. Note that after Month 12, only serious AEs and ocular AEs are collected as per protocol. Missing or incomplete AE onset dates will be handled as described in Attachment 1.

5.1. Ocular AEs

Ocular TE AEs include those with system organ class (SOC) = "Eye Disorders" or those with eye specified on the eCRF. The number and percentage of subjects who experienced at least 1 ocular TE AE will be presented in summary tables by preferred term according to MedDRA terminology as well as by affected eyes (events occurring in the treated eye only, in the fellow eye only, and in both eyes).

Serious ocular TE AEs will be summarized similarly.

Ocular TE AEs will be summarized by severity, and by relationship indicated on the eCRF (study treatment, device, and surgical procedure).

Ocular TE AEs will also be summarized by timing: for those with onset on or before the Week 4 visit date, and those with onset after the Week 4 visit date.

Individual subject ocular AEs will be presented in a data listing.

5.2. All AEs

The number and percentage of subjects who experienced at least 1 TE AE will be presented in summary tables by SOC and preferred term according to MedDRA terminology.

Serious TE AEs will be summarized and presented in a data listing.

Individual subject non-ocular AEs will be presented in a data listing.

5.3. Events of Special Interest

The events of special interest and how they are defined as per data captured in the clinical database are listed below.

- Retinal Detachment: A TE AE in the treated eye with preferred term "Retinal detachment" or a lowest level term (LLT) of "Rhegmatogenous retinal detachment",

"Central serous retinal detachment", "Haemorrhagic detachment of retinal pigment epithelium", "Detachment of macular retinal pigment epithelium", "Haemorrhagic detachment of retinal pigment epithelium" or "Vitreoretinal detachment".

- Significant choroidal hemorrhage: A TE AE in the treated eye with preferred term "Choroidal haemorrhage" or "Retinal haemorrhage" or LLT of "Choroidal bleeding", "Choroidal haemorrhage and rupture", "Expulsive choroidal haemorrhage", "Haemorrhagic choroidal detachment", "Retinal bleeding", "Bleeding intraretinal", "Retinal dot and blot haemorrhages", "Retinal blot haemorrhages", "Retinal haemorrhage spotted", "Subretinal haemorrhage", "Preretinal haemorrhage", or "Retinal nerve fiber layer hemorrhage". For these terms, the severity must be greater than mild (must be indicated as moderate or severe).
- Leakage of cells or need for vitrectomy: A "Yes" response to the Surgery and Delivery Device Details eCRF item "Was any IP visible in the vitreous after delivery?" on either surgery attempt (either the 1st or the 2nd attempt) or the text "vitrectomy" present in the Procedures eCRF item "Therapeutic or Diagnostic Procedures" with a start date/time on or after the date of surgery.
- Failure to deliver cells: A "No" response to the Surgery and Delivery Device Details eCRF item "Was the IP delivered to the target delivery location?" or a Surgical Deviation of "Dose of IP not fully administered". The response must be on the last surgery attempt for the subject (i.e., if there was a 2nd surgery attempt, the response must be on the 2nd attempt for that subject).
- Endophthalmitis: A TE AE in the treated eye with preferred term "Endophthalmitis" or LLT of "Acute endophthalmitis", "Chronic endophthalmitis", "Sterile endophthalmitis", "Aseptic endophthalmitis". "Infectious endophthalmitis", "Purulent endophthalmitis" or "Mycotic endophthalmitis".
- Significant loss of vision: defined as a decrease of ≥ 15 BCVA letters from baseline in the treated eye at the Week 4 visit. Unscheduled BCVA assessments after surgery prior to the Week 4 visit and assessments after Week 4 will not be considered here.

The Events of Special Interest will be summarized for the Safety Cohort. For each event, the count and percentage of subjects who had the event and the Exact Binomial 95% CI will be presented. Individual subject events will be presented in a data listing.

5.4. Surgery and Delivery System

The Surgery and Delivery System details captured on the eCRFs will be summarized. Individual subject data will be presented in a data listing.

Data from the 1st and 2nd (if applicable) surgical attempt will be summarized separately.

The count and percentage of subjects with surgical deviations will be presented, and individual subjects will be presented in a data listing.

5.5. Clinical Laboratory Tests

Clinical laboratory data will be summarized by type of lab test. Descriptive statistics will be presented for each laboratory test at baseline and at each scheduled follow-up time point, and for the change from baseline.

Frequency tabulations of subjects with TE abnormal clinical laboratory results will be presented for each test for each scheduled follow-up time point. TE abnormal low results are defined as those below the laboratory normal range where baseline was not below the normal range low value. TE abnormal high results are those defined as those above the laboratory normal range where baseline was not above the normal range high value. An overall tabulation will also be presented for subjects with at least 1 occurrence of a TE abnormal result at any follow-up time point for that test. A listing of subjects' laboratory results (all results at scheduled and unscheduled time points) will be provided, with flags for TE abnormal results.

5.6. Vital Signs

Descriptive statistics of temperature, pulse/heart rate, respiratory rate, and blood pressure (systolic and diastolic) values and changes from baseline will be summarized at each scheduled time point.

Frequency tabulations of subjects with TE abnormal vital signs results will be presented for each test for each follow-up time point. TE abnormal low results are defined as those below the reference range value where baseline was not below the reference range low value. TE abnormal high results are defined as those above the reference range where baseline was not above the reference range high value. An overall tabulation will also be presented for subjects with at least 1 occurrence of a TE abnormal result at any follow-up time point for that test. A listing of subjects' vital signs results (all results at scheduled and unscheduled follow-up time points) will be provided, with flags for values outside the reference ranges.

Table 5: Vital Signs Reference Ranges

Test	Reference Range Low	Reference Range High
Temperature (C)	36	38
Pulse (beats/min)	50	120
Systolic Blood Pressure (mm HG)	90	180
Diastolic Blood Pressure (mm HG)	50	105

6. EFFICACY

6.1. BCVA

The primary efficacy measure will be the BCVA testing performed after refraction and under standardized photopic lighting conditions and distance using an ETDRS logMAR chart.

If the BCVA assessment was done, but total letters correct is missing because neither the 4m nor the 1m assessments could be done, (i.e., only highest degree of vision was done), the BCVA total letters correct will be assigned a value of 0 and BCVA logMAR score will be assigned a value of 1.7 (using the formula logMAR = 1.7 – [0.02 x total letters correct]).

Descriptive statistics will be presented for BCVA (letters and logMAR) at baseline and at each scheduled follow-up time point, and for the change from baseline, for the treated and fellow eye.

The count and percentage of BCVA responders at each follow-up time point (responder=yes for subjects who have BCVA change from baseline >=15 letters) will be summarized for the treated and fellow eye.

BCVA data for individual subjects will be presented in a data listing.

6.2. Imaging Results

Certain parameters obtained from OCT assessments will be evaluated by 2 or 3 image readers interpreting the same image. For such parameters, two readers provide their assessments initially. If their assessments do not agree to a certain degree, a third reader provides an additional evaluation. For the purposes of statistical summaries, in the case of numerical measurements, a median value across the readers will be used. In the case of categorical parameters, a category provided by majority (two readers) will be used.

OCT measurements may be obtained post-surgery on study day 1 and/or on follow-up study day 2 to assist in surgery training purposes. These data will not be included in statistical summaries or analyses but will be included in any subject data listings provided.

Descriptive statistics will be presented for OCT CST, total area of GA by FAF in mm^2, and square root of total area of GA by FAF in mm, at baseline and at each scheduled follow-up time point and for the change from baseline, for the treated and fellow eye.

The yearly rate of change in GA area at an assessment is calculated as the change from baseline in the square root of total area of GA by FAF in mm, divided by the number of days of follow-up for that assessment, multiplied by 365. The number of days of follow-up for a given assessment time point is calculated as that visit date – surgery date + 1. This measurement will be summarized using descriptive statistics at the 3- , 6- and 12-month follow-up time points for the treated eye, and at the 3- and 12-month follow-up time points for the fellow eye. Note for the fellow eye, scans are only read by the central reader for a subset of time points.

Imaging data for individual subjects will be presented in a data listing.

The microperimetry and specialized OCT image analysis data will be examined by expert specialty laboratory reviewers. Analysis of microperimetry data is beyond the scope of this document and no statistical tables are planned for this effort.

6.3. Low Luminance BCVA

Low Luminance BCVA (LLBCVA) indicates the best possible vision that an eye can achieve with the use of trial frames/lenses following refraction and visual assessment under low luminance conditions.

If the LLBCVA assessment was done, but total letters correct is missing because neither the 4m nor the 1m assessments could be done, (i.e., only highest degree of vision was done), the total letters correct will be assigned a value of 0 and logMAR will be assigned a value of 1.7 (using the formula logMAR = 1.7 – [0.02 x total letters correct]).

Low Luminance Difference (LLD) is defined as the difference between standard photopic BCVA total letters correct and LLBCVA total letters correct.

The results for LLBCVA (letters and logMAR) and LLD (letters) at baseline and at each follow-up time point, and for the change from baseline, will be summarized with descriptive statistics for the treated eye and fellow eye.

LLBCVA data for individual subjects will be presented in a data listing.

6.4. Contrast Sensitivity

The Pelli-Robson test measures contrast sensitivity using a single large letter size with contrast varying across groups of letters. The chart uses letters (6 per line), arranged in groups whose contrast varies from high to low. Subjects read the letters, starting with the highest contrast level (log contrast level 0.00), until they are unable to read two or three letters in a single group. Each group has three letters of the same contrast level. The number of letters read correctly at each log contrast level is recorded on the eCRF. The subject is assigned a threshold score based on the log contrast of the last group in which two or three letters were correctly read. A threshold score of 2.0 indicates normal contrast sensitivity of 100 percent. Scores of less than 2.0 signify poorer contrast sensitivity. A score of less than 1.5 is consistent with visual impairment and a score of less than 1.0 represents visual disability.

Descriptive statistics will be presented for contrast sensitivity threshold scores at baseline and each scheduled follow-up time point and for the change from baseline for the treated eye and fellow eye.

Contrast sensitivity data for individual subjects will be presented in a data listing.

7. PHARMACOKINETICS/PHARMACODYNAMICS

Not applicable.

8. IMMUNOGENICITY

Immunogenicity data including the sample ADA (anti-drug antibodies) status and mean result FACS (fluorescence activated cell sorting) screen for individual subjects will be presented in a data listing.

9. HEALTH ECONOMICS AND HEALTH OUTCOMES

Not applicable. Since PROs and questionnaire results (NEI-VFQ-25, SF-36, and Near Vision Subscale, FRI, PGIC-S, PGIC-Q, CGIC) are not included as study objectives as of Protocol Amendment 3, these data will not be summarized in tables or listings for the CSR.

REFERENCES

1. SAS Institute Inc. Version 9.2, Cary, NC.

ATTACHMENTS

1. DATA HANDLING RULES FOR MISSING OR PARTIAL DATES

Onset/Start Date

If only the day part of the event onset/start date is missing and occurs in the same month and year as the Surgery Date, then the Surgery Date will be used as the onset/start date of the event.

Otherwise, if only the day part of the event onset date is missing, the first day of the month will be used to complete the onset/start date of the event.

If only the day and the month parts of the event onset/start date are missing and the event occurs in the same year as the Surgery Date, then the Surgery Date will be used as the onset/start date of the event. Otherwise, if only the day and the month parts of the event onset/start date are missing, January 1st will be used to complete the onset/start date of the event.

If the event onset/start date is equal to the Surgery Date, but the clock time is missing, then the event will be considered treatment emergent; i.e., as if onset/start time was during or after surgery.

If the time of onset of an event is missing, no imputation will be made.

Stop Date

If only the day part of the event stop date is missing, the last day of the month will be used to complete the stop date of the event.

If only the day and the month parts of the event stop date are missing, December 31st will be used.

If the stop date is completely missing and the ongoing status is also missing, the event will be considered as ongoing.

Any medication which is ongoing will be considered concomitant.

The imputed onset and stop dates will be verified to ensure that the onset date is prior or equal to the stop date.

The imputed dates will be used to determine the treatment-emergent status of the AE or the concomitant/prior status of medications, and to calculate study day and/or duration as needed.

medications, and to calculate study day and/or duration as needed.