Statistical Analysis Plan

Title: Randomized, Placebo-Controlled, Phase 2 Study of VERU-111 for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Patients at High Risk for Acute Respiratory Distress Syndrome (ARDS)

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Previous SAP Versions

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SAP Amendments before database lock

Version	Issue Date	Section	Revision / Addition	Rationale
1.0	04-JAN-2021			First version
2.0	04-FEB-2021	6.1.3 6.12.1 6.12.2.1 6.12.2.4 6.12.2.5 6.12.2.9 11	ITT population updated to include all randomized subjects. Added responder rate analysis. Updated baseline definition for WHO Ordinal Scale and added note that LOCF will be used for all missing data. Added also sensitivity analysis Added sensitivity analysis. Added responder rate analysis. Added sensitivity analysis. Updated list of outputs with the above additions.	Updates based on FDA feedback on the SAP.
3.0	09-FEB-2021	6.1.5	Updated EE population.	Update during subject evaluability.

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
AE	Adverse Event
ANCOVA	Analysis of Covariance
ARDS	Acute Respiratory Distress Syndrome
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
COVID-19	Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
CSR	Clinical Study Report
CT	Computed Tomography
ECG	Electrocardiogram
ECMO	Extracorporeal Membrane Oxygenation
eCRF	Electronic Case Report Form
ICU	Intensive Care Unit
ITT	Intent-to-Treat
MedDRA	Medical Dictionary of Regulated Activities
mITT	Modified Intent-to-Treat
MMRM	Mixed Model for Repeated Measures
PRN	*Pro re nata* – As Needed
RRT	Renal Replacement Therapy
SAE	Serious Adverse Event
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SpO_2	Capillary Oxygen Saturation
TEAE	Treatment Emergent Adverse Event
WHO	World Health Organization

1 INTRODUCTION

This document details the planned statistical analyses for Veru Inc., protocol "V0211901" study titled "Randomized, Placebo-Controlled, Phase 2 Study of VERU-111 for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Patients at High Risk for Acute Respiratory Distress Syndrome (ARDS)".

The proposed analyses are based on the contents of the final version of the protocol (version 7.0, dated 25-SEP-2020). IND number: 149282.

This study is a multicenter, randomized, double-blind, placebo-control, efficacy and safety study of VERU-111 for the treatment of COVID-19.

This study consists of two treatment arms: VERU-111 18 mg treated group, and Placebo treated Group. Subjects will be randomized in a 1:1 fashion.

Subjects in the VERU-111 treatment group will receive standard of care, plus oral daily VERU-111 18 mg for 21 days or until released from hospital.

Subjects in the Placebo treatment group will receive standard of care, plus a placebo capsule for 21 days or until released from hospital.

VERU-111 18 mg dose will be supplied as capsules containing 18 mg of VERU-111. Capsules will be supplied in bottles containing 21 capsules in each bottle. Subjects will take one VERU-111 capsule per day.

Placebo capsules containing zero (0) mg VERU-111 drug substance will be supplied in bottles containing 21 capsules each. The placebo capsules will contain only anhydrous lactose, USP. These capsules are identically appearing to the VERU-111 capsules. Subjects will take one Placebo capsule per day.

2 STUDY OBJECTIVES

2.1 Primary Objective

To demonstrate the efficacy of VERU-111 in the treatment of SARS-CoV-2 infection by assessing its effect on the proportion of subjects that are alive without respiratory failure at Day 29. Respiratory failure is defined as endotracheal intubation and mechanical ventilation, extracorporeal membrane oxygenation, high-flow nasal cannula oxygen delivery, noninvasive

positive pressure ventilation, clinical diagnosis of respiratory failure with initiation of none of these measures only when clinical decision making is driven solely by resource limitation.

2.2 Secondary Objectives

Secondary objectives of the study are:

1. World Health Organization (WHO) Ordinal Scale for Clinical Improvement (8-point ordinal scale) at Day 15, Day 22, and Day 29
    a. Change in mean WHO Ordinal Scale for Clinical Improvement at Day 15
    b. Change in mean WHO Ordinal Scale for Clinical Improvement at Day 22
    c. Change in mean WHO Ordinal Scale for Clinical Improvement at Day 29
    d. Proportion of subjects that are Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement at Day 15
    e. Proportion of subjects that are Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement at Day 22
    f. Proportion of subjects that are Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement at Day 29
2. Proportion of subjects with normalization of fever and oxygen saturation through Day 15, Day 22, and Day 29
3. Days on mechanical ventilation
4. All-cause mortality at Day 15, Day 22, and Day 29
5. Proportion of subjects alive and free of respiratory failure at Day 15, Day 22
6. Proportion of subjects alive and discharged from the ICU at Day 15, Day 22, and Day 29
7. Proportion of subjects alive and discharged from hospital at Day 15, Day 22, and Day 29
8. Days in Intensive Care Unit (ICU)
9. Days in hospital
10. Proportion of subjects on mechanical ventilation at Day 15, Day 22, and Day 29
11. Assess the pharmacokinetics of VERU-111 on Day 15.

2.3 Safety Objectives

To assess the safety and tolerability of VERU-111.

3 ENDPOINTS

3.1 Primary Endpoint

The primary endpoint for the study is the proportion of subjects that are alive without respiratory failure at Day 29. Respiratory failure is defined as endotracheal intubation and mechanical ventilation, extracorporeal membrane oxygenation, high-flow nasal cannula oxygen delivery, noninvasive positive pressure ventilation, clinical diagnosis of respiratory failure with initiation of none of these measures only when clinical decision making is driven solely by resource limitation.

3.2 Secondary Endpoints

The secondary endpoints on this study are:

1. WHO Ordinal Scale for Clinical Improvement (8-point ordinal scale):

Patient State	**Descriptor**	**Score**
Uninfected	No clinical or virological evidence of infection	0
Ambulatory	No limitation of activities	1
	Limitation of activities	2
Hospitalized, Mild disease	Hospitalized, no oxygen therapy	3
	Oxygen by mask or nasal prongs	4
Hospitalized, Severe disease	Non-invasive ventilation or high-flow oxygen	5
	Intubation and mechanical ventilation	6
	Ventilation + additional organ support – pressors, Renal Replacement Therapy (RRT), Extracorporeal Membrane Oxygenation (ECMO)	7
Death	Death	8

2. Proportion of subjects that are Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement at Day 15

3. Proportion of subjects that are Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement at Day 22
4. Proportion of subjects that are Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement at Day 29
5. Change in mean WHO Ordinal Scale for Clinical Improvement at Day 15
6. Change in mean WHO Ordinal Scale for Clinical Improvement at Day 22
7. Change in mean WHO Ordinal Scale for Clinical Improvement at Day 29
8. Proportion of subjects with normalization of fever and oxygen saturation through Day 15. This will be a composite of fever normalization maintained for at least 24 hours AND peripheral capillary oxygen saturation (SpO_2) >94% sustained for 24 hours.
9. Proportion of subjects with normalization of fever and oxygen saturation through Day 22. This will be a composite of fever normalization maintained for at least 24 hours AND peripheral capillary oxygen saturation (SpO_2) >94% sustained for 24 hours.
10. Proportion of subjects with normalization of fever and oxygen saturation through Day 29. This will be a composite of fever normalization maintained for at least 24 hours AND peripheral capillary oxygen saturation (SpO_2) >94% sustained for 24 hours.
11. Days on mechanical ventilation
12. All-cause mortality at Day 15
13. All-cause mortality at Day 22
14. All-cause mortality at Day 29
15. Proportion of subjects alive and free of respiratory failure at Day 15
16. Proportion of subjects alive and free of respiratory failure at Day 22
17. Proportion of subjects alive and discharged from the ICU at Day 15
18. Proportion of subjects alive and discharged from the ICU at Day 22
19. Proportion of subjects alive and discharged from the ICU at Day 29
20. Proportion of subjects alive and discharged from hospital at Day 15
21. Proportion of subjects alive and discharged from hospital at Day 22
22. Proportion of subjects alive and discharged from hospital at Day 29
23. Days in ICU
24. Days in hospital
25. Proportion of subjects on mechanical ventilation at Day 15
26. Proportion of subjects on mechanical ventilation at Day 22
27. Proportion of subjects on mechanical ventilation at Day 29
28. Pharmacokinetics of VERU-111 on Day 15.

4 SAMPLE SIZE

In the Phase 2, there are no power calculations done to determine the sample size. The Phase 2 study is intended as a proof-of-concept study only.

5 RANDOMIZATION

Approximately, 40 subjects are planned to be randomized at a 1:1 ratio into two treatment arms (20 subjects in the VERU-111 treated group and 20 subjects in the Placebo treated group).

The subjects with documented evidence of COVID-19 infection (by standard diagnostic method) with symptoms for less than 8 days will be enrolled. Subjects will be at high risk for the development of ARDS.

6 PLANNED ANALYSES

No statistical analysis plan (SAP) prepared in advance of the data can be absolutely definitive and the final Clinical Study Report (CSR) may contain additional tables or statistical tests if warranted by the data obtained. The justification for any such additional analyses will be fully documented in the final CSR.

6.1 Analysis Populations

Subjects excluded from the analysis populations and the reason for their exclusion will be listed in Appendix 16.2 of the CSR.

6.1.1 Enrolled Population

All subjects who gave informed consent.

6.1.2 Randomized Population

All enrolled subjects who were randomized to study treatment.

6.1.3 Intent-to-Treat (ITT) Population

All randomized subjects regardless whether the subject took the study drug or not. The ITT population will be used as the safety population.

6.1.4 Modified Intent-to-Treat (mITT) Population

All enrolled subjects who have taken at least 7 doses of study drug.

6.1.5 Efficacy Evaluable (EE) Population

All ITT subjects excluding those subjects who were identified as non-compliant to study procedures. These subjects will be identified together with reason for exclusion in the subject evaluability form which will be signed prior to the database lock.

6.2 Derived Data

This section describes the derivations required for statistical analysis. Unless otherwise stated, variables derived in the source data will not be re-calculated.

6.2.1 Baseline

Baseline is defined as the last non-missing value (either scheduled, unscheduled or repeat) before the subject receives the first dose of study drug.

6.2.2 Duration / Study Day / Time

Study day will be calculated as the number of days from first dose of study drug.

- date of event – date of first dose of study drug + 1, for events on or after first dose
- date of event – date of first dose of study drug, for events before first dose

6.2.3 Conventions for Missing and Partial Dates

All rules explained below for partial / missing dates will be followed unless contradicted by any other data recorded on the electronic Case Report Form (eCRF).

All dates presented in the individual subject listings will be as recorded on the eCRF (i.e., not completed as per the below rules).

6.2.4 Missing / Partial Start / Stop Date of Concomitant Medications

Missing and partial start and stop date will be imputed for analysis purposes as follows.

Partial or missing stop date will be imputed as follows:

If the stop date is completely missing and the event has resolved, or the subject has stopped taking the concomitant medication, the stop date will be imputed as the date of the subject's last clinic visit in the study.

- If only the year is known, the stop date will be imputed as "31-Dec" of that year or as the date of the subject's last clinic visit in the study if in the same year.

- If the month and year are known, the stop date will be imputed as the last day of that month unless the stop date corresponds to the same month as the subject's last clinic visit in which case the date of subject's last clinic visit in the study will be used instead.

Missing start date will be imputed as follows:

- If the stop date occurs on or after the start of study drug or the event / concomitant medication is ongoing, the start date will be imputed as the date of the first dose of study drug.
- If the stop date occurs before the start of study drug, the start date of the event / concomitant medication will be imputed as the subject's screening date or the stop date of the event / concomitant medication whichever the earlier.

Partial start date (year present, but month and day missing)

- If the stop date occurs on or after the start of study drug or the event / concomitant medication is ongoing, and the year is the same as the year of first dosing the start date will be imputed as "01-Jan" of the same year or the date of the first dose of study drug whichever is latest. If the year is different from the year of first dosing "01-Jan" will be used.
- If the stop date occurs before the start of study drug, the start date of the event / concomitant medication will be imputed as the "01-Jan" of the same year.

Partial start date (month and year present, but day missing)

- If the stop date occurs on or after the start of study drug or the event / concomitant medication is ongoing, the start date will be imputed as the first day of the same month and year unless this partial start date is in same month as the first dose of study drug in which case the date of first dose of study drug will be used.
- If the stop date occurs before the start of study drug, the start date will be imputed as the first day of the month and year of the partial stop date.

If the start time is missing it will be imputed only in the case where the start date of the concomitant medication / event corresponds to the date of the first dose of study drug. The time will be imputed as the same time as the first dose of study drug. In all other cases the time will not be imputed.

6.2.5 Missing Last Dates of Study Drug Dosing

Missing dates for study drug dosing will not be imputed.

6.2.6 Missing Diagnosis Dates

If the month and year are present but the day is missing, the diagnosis date will be set to first day of the relevant month. If only the year is recorded the diagnosis date will be set as "01-Jan" for that year.

6.2.7 Exposure to Study Drug

Exposure to study drug will be calculated as the date of last dosing minus the first day of dosing + 1. The exposure calculation will not take into account breaks in therapy.

6.2.8 Inexact Values

In the case where a variable is recorded as "> x", "≥ x", "< x" or "≤ x", a value of x will be taken for analysis purposes.

6.2.9 Unscheduled Visits

Only scheduled post-baseline values will be tabulated. Post-baseline repeat / unscheduled assessments will be disregarded, although these post-baseline assessments will be listed in the relevant appendices to the CSR.

6.3 Conventions

All data listings, summaries, figures and statistical analyses will be generated using SAS version 9.4 or higher[1].

Summaries will be presented by treatment group. Treatment group labels will be displayed as follows:

- VERU-111 18 mg
- Placebo

Listings will be sorted in the following order treatment group, subject, parameter, and visit unless otherwise stated. All data will be listed, subjects who were not randomized will be displayed after the randomized treatment groups.

Continuous variables will be summarized by the number of non-missing observations, mean, median, standard deviation, and minimum and maximum.

Categorical variables will be summarized by presenting the frequency and percent. Percentages will be based on the number of non-missing observations or the subject population unless otherwise specified. For each variable, all categories will be shown. Zero frequencies (but not the percent) within a category will be presented.

6.3.1 Decimal Places

Decimal places for derived data described in section 6.2 will be determined by the scale of measurement unless otherwise stated. No decimal places will be displayed if the smallest calculated value is ≥ 100; 1 decimal place will be displayed when the smallest value is within the interval (10, 100), with 10 being inclusive; 2 decimal places will be displayed when the smallest value is within (1, 10), with 1 being inclusive; and so on for even smaller scales of measurement.

Derived data where it is known in advance the result will be an integer for example day, month, year, number of days and total scores (for rating scales) will be presented with zero decimal places.

Means, medians and percentiles will be displayed to one more decimal place than the data**,** dispersion statistics (e.g. standard deviation) will have two more decimal places, and the minimum and maximum will be displayed to the same number of decimal places as reported in the raw data. Percentages will be displayed with one decimal place.

P-values will be quoted to 3 decimal places. P-values < 0.001 will be presented as p<0.001. Where this value is less than 0.05, 0.01 or 0.001, attention will be drawn to this fact using the conventional "*", "**" or "***" annotation, respectively.

6.4 Subject Disposition

Subject disposition will be summarized as follows:

- The number of subjects, who entered the study, were randomized and who are in each analysis population will be summarized by treatment group and overall for the enrolled population.
- The number of subjects who failed screening and the reasons for failure will be tabulated for enrolled population.
- The number of early withdrawals and the reasons for withdrawals will be tabulated by treatment group and overall for the ITT population.
- The number of subjects present at each scheduled visit will be summarized by treatment group for the ITT population.

6.5 Protocol Deviations

Protocol deviations will be summarized and listing of protocol deviations will be provided within Appendix 16.2 of the CSR.

6.6 Baseline Comparability

The comparability of treatment groups with respect to subject demographics and baseline characteristics will be assessed in a descriptive manner, but no formal statistical testing will be performed.

Standard continuous or categorical variable summaries will be presented by randomized treatment group for the following variables based on the ITT population:

- Age (years) at Informed Consent
- Age category (<60 years, >=60 years)
- Sex (Female, Male)
- Fertility Status for Women (Childbearing Potential, Post-menopausal, Surgically Sterile)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White)
- Weight (kg) at Screening
- Height (cm) at Screening
- Body Mass Index (BMI) (kg/m^2) at Screening.

6.7 Medical History

Separate tabulations of previous and ongoing conditions will be presented by randomized treatment group and overall for the ITT population. Previous conditions are all conditions which ended before the first dose of study drug. Ongoing conditions are all conditions which were ongoing at the time of the first dose of study drug.

Conditions will be presented by Medical Dictionary of Regulated Activities (MedDRA, version 23.0 updated) primary system organ class and preferred term.

6.8 Prior and Concomitant Medications

Separate tabulations will be produced for prior and concomitant medications presented by randomized treatment group and overall for the ITT population. Prior medications are defined as all medications ending before the date of first dose of study drug. Concomitant medications are defined as medications taken on or after the date of first dose of study drug.

Prior and Concomitant medication verbatim terms (as recorded on the CRFs) will be mapped to Anatomical Therapeutic Chemical (ATC) Level 2 and Drug Reference Names using the WHO dictionary (version B3 Mar 2020).

Concomitant medications will be summarized using ATC Level 2 and preferred term.

6.9 Exposure to Study Drug

Extent of exposure (number of days of exposure to study drug) will be presented by randomized treatment group for the ITT population.

6.10 Treatment Compliance

All subjects will receive standard of care plus oral daily VERU-111 or Placebo. Subjects will take one capsules per day.

Overall study drug compliance (%) will be summarized using descriptive statistics by treatment group and overall. Additionally, compliance (%) will be summarized as frequencies in '<80%' and '>=80%' categories.

Overall study drug compliance will be calculated as follows:

$$100 * \frac{number\ of\ capsules\ taken}{planned\ total\ number\ of\ capsules}$$

where planned number of capsules is 1 capsules/day in both VERU-111 and placebo groups. Planned number of capsules will be calculated as last dose date – randomization date +1.

6.11 Dosing of Standard of Care

The number and percentage of subjects using remdesivir or dexamethasone (or both) will be summarized by treatment group.

All standard of care information will be listed.

6.12 Efficacy Analyses

All statistical tests will be performed using a two-tailed 5% overall significance level, unless otherwise stated. All comparisons between treatments will be reported with 95% confidence intervals for the difference.

6.12.1 Primary Endpoint

The primary endpoint for the study is the proportion of subjects that are alive without respiratory failure at Day 29. Respiratory failure is defined as endotracheal intubation and mechanical ventilation, extracorporeal membrane oxygenation, high-flow nasal cannula oxygen delivery, noninvasive positive pressure ventilation, clinical diagnosis of respiratory failure with initiation of none of these measures only when clinical decision making is driven solely by resource limitation.

This analysis will compare the percentage of subjects that are alive without respiratory failure on Day 29 (responder).

Responders are subjects who have Grade 0-4 on the WHO Ordinal Scale for Clinical Improvement on Day 29. If subject was discharged from the hospital prior to Day 29 and WHO Ordinal Scale for Clinical Improvement is not collected at Day 29 then the last available observation before or at the time of discharge will be carried forward.

Non-responders are subjects who died before Day 29 or has Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement on Day 29.

The number and percentage of responders will be summarized by treatment group. Responders will be analyzed using a logistic regression model. This model will include treatment as a factor, and study site, remdesivir use (No/Yes), dexamethasone use (No/Yes) and WHO Ordinal Scale for Clinical Improvement at baseline as a covariates. Odds ratios, standard errors, 95% confidence intervals and p-values for the treatment difference will be presented.

The primary analysis will be performed on the ITT population. A sensitivity analysis will be performed repeating the analysis on the EE population.

Example SAS code for the analysis is as follows:

```
proc logistic data=XXX order=internal;
class response trt01pn site remdesivir dexamethasone;
model response=trt01pn site remdesivir dexamethasone who_base /
                clodds=both firth;
estimate 'Treatment A vs. Treatment B' trt01pn 1 -1 / cl e exp;
lsmeans trt01pn / cl exp diff;
ods output modelanova=modelanova1 lsmeans=lsmeans1 diffs=diffs1;
run;
```

Responder rates and differences between treatment groups in responder rates will be calculated as sensitivity analysis for primary endpoint. Wald method will be used for 95% confidence intervals and testing of treatment differences.

Example SAS code for the analysis is as follows:

```
proc freq data=XXX order=internal;
tables avisitn*trt01pn*avalc / riskdiff(column=2 equal var=null cl=wald);
exact riskdiff barnard(column=2);
ods output riskdiffcol2=riskdiff1 pdiffcls=waldci1 pdifftest=waldtest1
barnardstest=barnard1;
run;
```

6.12.2 Secondary Endpoints

6.12.2.1 Change in mean WHO Ordinal Scale for Clinical Improvement at Day 15, Day 22 and Day 29

The mean change in WHO Ordinal Scale for Clinical Improvement from baseline to Day 15, Day 22 and Day 29 will be assessed.

Baseline for WHO Ordinal Scale is the last available record up to and including Day 1. If subject died or was discharged from the hospital prior to Day 15, 22 or 29 and WHO Ordinal Scale for Clinical Improvement is not collected or record is otherwise missing at those timepoints then the last available observation before or at the time of death/discharge will be carried forward.

Analysis will be performed using two different approaches, including the LOCF values and excluding LOCF values. Further, these analyses will be repeated using separate baseline definition. As the time of WHO Ordinal Scale is collected it cannot be definitely confirmed if Day 1 record was taken before or after start of study treatment. Sensitivity analysis will be performed using the WHO Ordinal Scale from Screening record.

Descriptive statistics (n, mean, standard deviation, median, minimum and maximum) will be summarized for absolute values and change from baseline by treatment group and visit.

Change from baseline will be analyzed using mixed model for repeated measures (MMRM) including treatment, visit and treatment-by-visit interaction as fixed effects, and study site, remdesivir use (No/Yes), dexamethasone use (No/Yes) and WHO Ordinal Scale for Clinical Improvement at baseline as covariates. The resulting F-tests will be based on Kenward-Roger's adjusted degrees of freedom. Subject effect will be assumed to be random and an unstructured covariance structure will be used for within subject variation. If this model does not converge then the following covariance matrices will be used in order until the model converges: Toeplitz, first-order autoregressive, and compound symmetry. Least squares means, standard errors, 95% confidence intervals and p-values for treatments and treatment differences at each visit (study days 15, 22, 29, 45 and 60) will be presented.

Example SAS code for the analysis is as follows:

```
proc mixed data=XXX order=internal;
class usubjid trt01pn avisitn siteid remdesivir dexamethasone;
model response=trt01pn avisitn trt01pn*avisitn site remdesivir
                dexamethasone who_base / ddfm=kr;
repeated avisitn / type=un subject=usubjid;
lsmeans trt01pn trt01pn*avisitn / diff cl e;
ods output tests3=tests lsmeans=lsmeans diffs=diffs
convergencestatus=converge;
run;
```

6.12.2.2 Proportion of subjects that are Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement at Day 15, Day 22, and Day 29

As the primary endpoint will be using WHO scale to define responders/non-responders this analysis specified in the protocol would be corresponding to the primary endpoint. Primary endpoint analysis table will include Days 15, 22 and 29 which makes this analysis redundant. Therefore this secondary endpoint will be dropped out.

6.12.2.3 Proportion of subjects with normalization of fever and oxygen saturation through Day 15, Day 22, and Day 29.

The percentage of subjects with normalization of fever and oxygen saturation through Day 15, Day 22 and Day 29 (inclusive) will be summarized. A subject will be considered as a treatment success if fever normalization (body temperature < 37.0 °C) maintained for at least 24 hours AND peripheral capillary oxygen saturation (SpO_2) >94% sustained for 24 hours is observed.

This analysis will compare the percentage of subjects that meet the composite endpoint at Day 15, Day 22, and Day 29.

Evaluation of the responder status will include all vital sign data and vital sign log data, and responder status will be evaluated at study days 15, 22 and 29 by checking if subject had normal temperature and SpO_2 at least for the last 24 hours.

Responders are subjects who have fever normalization maintained for at least 24 hours AND peripheral capillary oxygen saturation (SpO_2) >94% sustained for 24 hours is observed at the time of the visit.

Non-responders are subjects who died before the visit or do not meet both criteria of the endpoint (fever normalization and SpO_2>94%) at the time of the visit.

These endpoints will be analyzed using the same methodology as for the primary endpoint.

Separate analysis will be performed for each visit.

6.12.2.4 Days on mechanical ventilation

Mechanical ventilation is defined as subject having 'Intubation and mechanical ventilation' or 'Ventilation + additional organ support – pressors, RRT, ECMO'.

'Days on mechanical ventilation' will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum and maximum) by treatment group.

'Days on mechanical ventilation' will be the number of days on mechanical ventilation up to Day 29. If subject dies early in the study and was on mechanical ventilation at the time of the death then it is assumed that subject was on mechanical ventilation up to Day 29. A sensitivity analysis will be performed assigning the worst possible endpoint score for deaths (i.e., considered to be on mechanical ventilation from baseline up to Day 29 and setting days on mechanical ventilation to 29).

Treatment comparison will be based on analysis of covariance (ANCOVA) model including treatment as a factor, and study site, remdesivir use (No/Yes), dexamethasone use (No/Yes) and WHO Ordinal Scale for Clinical Improvement at baseline as covariates. Treatment difference, standard error, 95% confidence interval and p-value will be presented.

Example SAS codes for the analysis are as follows:

```
proc mixed data=XXX order=internal;
class trt01pn site remdesivir dexamethasone;
model response=trt01pn site remdesivir dexamethasone who_base /
                ddfm=kr;
lsmeans trt01pn / cl diff;
ods output tests3=tests lsmeans=lsmeans diffs=diffs
run;
```

6.12.2.5 All-cause mortality at Day 15, Day 22, and Day 29

The number and percentage for all-cause mortality will be summarized by treatment group and visit.

These endpoints will be analyzed using the same methodology as for the primary endpoint.

Responders are subjects who are alive at the time of the visit.

Non-responders are subjects who died before the visit.

Separate analysis will be performed for each visit.

Responder rates and differences between treatment groups in responder rates will be calculated as sensitivity analysis using the same methodology as for the primary endpoint.

6.12.2.6 Proportion of subjects alive and free of respiratory failure at Day 15, and Day 22

These endpoints will be analyzed using the same methodology as for the primary endpoint.

Separate analysis will be performed for each visit.

This will be the same analysis as for primary endpoint but just repeated for days 15 and 22.

6.12.2.7 Proportion of subjects alive and discharged from the ICU at Day 15, Day 22, and Day 29

The percentage of subjects alive and discharged from the ICU through Day 15, Day 22 and Day 29 (inclusive) will be summarized.

This analysis will compare the percentage of subjects that are alive and discharged from the ICU (responder) at Day 15, Day 22, and Day 29.

Responders are subjects who are alive and have been discharged from the hospital or not in the ICU at the time of the visit.

Non-responders are subjects who died before the visit or are in the ICU at the time of the visit.

This endpoint will be analyzed using the same methodology as for the primary endpoint.

Separate analysis will be performed for each visit.

6.12.2.8 Proportion of subjects alive and discharged from hospital at Day 15, Day 22, and Day 29

The percentage of subjects alive and discharged from the hospital through Day 15, Day 22 and Day 29 (inclusive) will be summarized.

This analysis will compare the percentage of subjects that are alive and discharged from the hospital (responder) at Day 15, Day 22, and Day 29.

Responders are subjects who are alive and have been discharged from the hospital at the time of the visit.

Non-responders are subjects who died before the visit or are in the hospital at the time of the visit.

This endpoint will be analyzed using the same methodology as for the primary endpoint.

Separate analysis will be performed for each visit.

6.12.2.9 Days in ICU

'Days in ICU' will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum and maximum) by treatment group.

'Days in ICU' will be the number of days in ICU up to Day 29. If subject dies early in the study and is in the ICU at the time of the death then it is assumed that subject was in the ICU up to Day 29.

'Days in ICU' will be analyzed using the same methodology as for 'Days in mechanical ventilation' and the same sensitivity analysis will be performed.

6.12.2.10 Days in hospital

'Days in hospital' will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum and maximum) by treatment group.

'Days in hospital' will be the number of days in hospital up to Day 29. If subject dies early in the study and is in the hospital at the time of the death then it is assumed that subject was in the hospital up to Day 29.

'Days in hospital' will be analyzed using the same methodology as for 'Days in mechanical ventilation'.

6.12.2.11 Proportion of subjects on mechanical ventilation at Day 15, Day 22, and Day 29

The percentage of subjects on mechanical ventilation through Day 15, Day 22 and Day 29 (inclusive) will be summarized.

This analysis will compare the percentage of subjects that are NOT on mechanical ventilation (responder) at Day 15, Day 22, and Day 29.

Responders are subjects who have been discharged from the hospital or are not on mechanical ventilation at the time of the visit.

Non-responders are subjects who died before the visit or are on the mechanical ventilation at the time of the visit.

This endpoint will be analyzed using the same methodology as for the primary endpoint.

Separate analysis will be performed for each visit.

6.12.3 Exploratory Endpoints

6.12.3.1 Area under curve (AUC) of WHO Ordinal Scale for Clinical Improvement

Area under curve (AUC) of WHO Ordinal Scale for Clinical Improvement will be calculated from baseline up to Day 15 using trapezoidal rule. For each subject all available measurements up to study day 15 are included in the calculations. If subject does not have record on Day 15 then the last observation carried forward (LOCF) will be used. If a patient dies on Day 10, then they would be an 8 from Day 10 to Day 15. If the patient is discharged as a 2 on Day 5 then they would be a 2 from Day 5 to Day 15.

Actual collection times will be used in the calculations.

AUC will be summarized by treatment group and listed together with WHO Ordinal Scale for Clinical Improvement.

6.12.3.2 Oxygen Use

Oxygen use will be summarized by treatment group as shift (decrease, no change, increase) from baseline (last oxygen dose prior to the date of treatment start) at study days 3, 9, 15, 22 and 29. This information will be derived from concomitant medication data for oxygen.

6.12.4 Multiplicity

All secondary endpoints and the supportive analyses will be considered as descriptive evidence of efficacy and will be analyzed without any procedures to account for multiple comparisons.

6.13 Pharmacokinetic Analyses

The pharmacokinetics of VERU-111 will be assessed on Day 15. Plasma samples for pharmacokinetic assessment will be taken at baseline (prior to dosing on Day 15) and at 4 hours (±2 hours), 12 hours (±2 hours) after dosing on Day 15, and at 24 hours (±2 hours) after dosing on Day 15 (prior to dosing on Day 16).

The following parameters will be estimated through standard methodology with this limited sampling schedule:

- AUC_{0-t} Area Under Concentration Curve from time 0 to time t.
- C_{max} Maximum Concentration
- T_{max} Time to C_{max}
- k_{el} Elimination Rate Constant

- Cl/F Clearance
- $T_{½}$, Half-Life
- V_d/F Volume of Distribution

The limited sampling schedule is used due to limitations on study personnel entering the subject's room during the day. If the sample is missed due to restrictions in entering the room, then this sample will be listed as missing.

PK concentrations will be summarized using descriptive statistics (n, mean, standard deviation, CV(%), geometric mean, median, minimum and maximum) for absolute values by treatment group and visit. Mean plots by treatment and individual subject curves will be displayed on linear and semi-logarithmic scale (time on linear scale, concentration on logarithmic scale) for concentration data.

PK parameters will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum and maximum) for absolute values by treatment group.

All PK concentration and PK parameter data will be listed.

6.14 Pharmacodynamic Analyses

Not applicable.

6.15 Safety Analyses

The safety analyses will be presented by the treatment received for the ITT Population.

6.15.1 Adverse Events

A treatment emergent adverse event (TEAE) is defined as:

- Any AE that has an onset on or after the first dose of study drug and before last dose of study drug + 7 days.
- Any pre-existing AE that has worsened in severity on or after the first dose of study drug and before the last dose of study drug + 7 days.

A treatment-related AE is defined as an AE with causality collected as 'POSSIBLY RELATED', 'PROBABLY RELATED' or 'RELATED' in the CRF. If an AE has missing relationship it is assumed to be 'RELATED' to the study drug for analysis purposes.

If an AE has missing standard toxicity grade it is assumed to be 'GRADE 3 (SEVERE)' for analysis purposes.

AEs will be summarized according to the MedDRA (version 23.0 updated) system organ class and preferred term.

The following tables will be presented for AEs:

- Overall incidence and the number of events in the following categories:
  - TEAEs
  - Treatment-Related TEAEs
  - Serious TEAEs
  - Treatment-Related Serious TEAEs
- For the above AE categories tables including incidence and number of events will be presented by system organ class and preferred term
- TEAEs by system organ class, preferred term and maximum toxicity grade (incidence, no event counts)
- TEAEs by system organ class, preferred term and strongest relationship grade (incidence, no event counts)
- Listing of Deaths (presented in the Table section of the appendices)
- Listing of Serious TEAEs (presented in the Table section of the appendices).

In counting the number of AEs reported, a continuous event (i.e. reported more than once and which did not cease), will be counted only once; non-continuous AE reported several times by the same subject will be counted as multiple events.

All AEs will be listed.

6.15.2 Laboratory Data

Laboratory data will be collected in local labs and the units need to be made consistent before presenting in summary tables.

Descriptive statistics of the observed values and change from baseline (continuous data) will be presented by treatment group and visit for each chemistry, hematology and urinalysis parameter.

Each measurement (continuous data) will be classed as below, within, or above normal range, based on ranges supplied by the laboratory used. Shift tables in relation to the normal range from baseline to each timepoint will be presented.

A listing of any clinically significant laboratory measurements recorded throughout the study will be presented in tables section.

All laboratory data will be listed.

6.15.3 Vital Signs

Descriptive statistics for observed values and changes from baseline in the following vital signs will be presented by treatment group and visit:

- Systolic blood pressure (mmHg)
- Diastolic blood pressure (mmHg)
- Pulse rate (bpm)
- Respiration rate (breath / min)
- Body weight (kg)
- Body temperature (degrees Celsius)
- SpO_2 (%)

Vital Signs log will be collected every 12 hours during study days 1-21. When study day has more than one record then summary table will use the average within the day.

Data for body temperature and SpO_2 log will be presented in plot where individual subjects will be overlaid in one figure (spaghetti plot) by treatment group.

All vital sign data will be listed.

6.15.4 Physical Examination

Shift tables for each body system from baseline to worst post-baseline record will be presented (Normal, Abnormal NCS and Abnormal CS). NCS = Abnormal Not Clinically Significant, CS = Clinically Significant.

All physical examination data will be listed.

6.15.5 Electrocardiogram Data

Descriptive statistics for observed values and changes from baseline in the following ECG variables will be tabulated at each follow-up visit:

- Heart rate (bpm)
- PR interval (ms)

- RR interval (ms)
- QRS duration (ms)
- QT interval (ms)
- QTc interval (ms)
- QTc interval (ms) [Bazett's formula - QTcB]
- QTc interval (ms) [Fridericia's formula - QTcF]

Shift tables in relation to the overall interpretation (Normal, Abnormal NCS and Abnormal CS) from baseline to worst post-baseline record will be presented.

All ECG data will be listed.

6.15.6 Chest X-Ray / Computed Tomography (CT)

Shift tables for chest X-ray / CT from baseline to each timepoint will be presented (Normal, Abnormal).

All chest X-ray / CT data will be listed.

6.15.7 Pregnancy Test

Pregnancy test data will be listed only.

7 INTERIM ANALYSIS

Interim analysis was planned in the protocol but will not be performed.

8 DATA SAFETY MONITORING BOARD ANALYSIS

Data safety monitoring board (DSMB) will meet on a bi-weekly basis to:

- Review aggregate and individual subject data related to safety, data integrity and overall conduct of the trial.
- Provide recommendations to continue or terminate the trial depending upon these analyses.

9 CHANGES TO PLANNED PROTOCOL ANALYSIS

In the statistical models the use of remdesivir and dexamethasone were added as covariates.

Secondary endpoint 'Proportion of subjects that are Grade 5, 6, 7, or 8 on the WHO Ordinal Scale for Clinical Improvement at Day 15, Day 22, and Day 29' will be excluded from the SAP as it would be the same as primary endpoint and corresponding endpoints for Days 15 and 22.

Interim analysis will not be performed.

ITT Population was updated to include all randomized subjects regardless whether the subject too study drug or not. This will not have impact on the populations as all randomized subjects were treated.

Efficacy Evaluable (EE) Population was added.

10 REFERENCES

1. SAS Institute Inc., Cary, NC, 27513, USA

11 LIST OF TABLES, FIGURES AND LISTINGS

The following table includes details of the tables, figures and listings to be included within each section of the eCTD. The eCTD section is shown in bold. The following validation methods maybe used:

- Independent programming of numbers and manual review of format (IP)
- Independent programming by statistician of numbers and manual review of format (Stat IP)
- Manual review (MR)
- Code review (CR)

Table Number	Table Title	Included in Preliminary Analysis	Included in DSMB (Table No.)	Validation Method	Shell Number (if repeat)
14.1	**Demographics Data**				
14.1.1	**Disposition**				
14.1.1.1	Subject Enrollment (Enrolled Population)		Yes (O1, S1)	IP	
14.1.1.2	Screen Failures (Enrolled Population)			IP	
14.1.1.3	Inclusion/Exclusion Criteria Violations (Enrolled Population)			IP	
14.1.1.4	Analysis Populations (Enrolled Population)			IP	
14.1.1.5	Subject Disposition (Randomized Population)		Yes (S2)	IP	
14.1.1.6	Protocol Deviations (ITT Population)		Yes (S3)	IP	
14.1.2	**Demographics**				
14.1.2.1	Demographics (ITT Population)		Yes (S4)	IP	
14.1.2.2	Demographics (EE Population)			IP	14.1.2.1
14.1.2.3	Baseline Condition (ITT Population)		Yes (S5)	IP	
14.1.2.4	Baseline Condition (EE Population)			IP	14.1.2.3
14.1.3-14.1.4	**Baseline Characteristics**				
14.1.3.1	Previous Medical History by System Organ Class and Preferred Term (ITT Population)			IP	
14.1.3.2	Ongoing Medical History by System Organ Class and Preferred Term (ITT Population)			IP	14.1.3.1
14.1.4.1	Prior Medications by ATC Level 2 and Preferred Term (ITT Population)			IP	
14.1.4.2	Concomitant Medications by ATC Level 2 and Preferred Term (ITT Population)			IP	14.1.4.1
14.1.5	**Extent of Exposure, Dosage Information, And Compliance**				
14.1.5.1	Treatment Exposure (ITT Population)			IP	
14.1.5.2	Treatment Compliance (ITT Population)			IP	

Table Number	Table Title	Included in Preliminary Analysis	Included in DSMB (Table No.)	Validation Method	Shell Number (if repeat)
14.1.5.3	Standard of Care (ITT Population)			IP	
14.2	**Efficacy Data**				
14.2.1	**Primary Efficacy Endpoint**				
14.2.1.1	Proportion of Subjects Alive and Free of Respiratory Failure by Visit (ITT Population)	Yes		IP	
14.2.1.2	Logistic Regression for Proportion of Subjects Alive and Free of Respiratory Failure by Visit (ITT Population)	Yes		Stat IP	
14.2.1.2a	Responder Rates for Proportion of Subjects Alive and Free of Respiratory Failure by Visit (ITT Population)			Stat IP	
14.2.1.3	Proportion of Subjects Alive and Free of Respiratory Failure by Visit (EE Population)			IP	14.2.1.1
14.2.1.4	Logistic Regression for Proportion of Subjects Alive and Free of Respiratory Failure by Visit (EE Population)			Stat IP	14.2.1.2
14.2.2-14.2.11	**Secondary Efficacy Endpoints**				
14.2.2.1	Descriptive Statistics for WHO Ordinal Scale for Clinical Improvement by Visit - With LOCF values (ITT Population)	Yes		IP	
14.2.2.2	Mixed Model for Repeated Measures (MMRM) for Change from Baseline in WHO Ordinal Scale for Clinical Improvement - With LOCF values (ITT Population)	Yes		Stat IP	
14.2.2.3	Descriptive Statistics for WHO Ordinal Scale for Clinical Improvement by Visit - Without LOCF values (ITT Population)			IP	14.2.2.1
14.2.2.4	Mixed Model for Repeated Measures (MMRM) for Change from Baseline in WHO Ordinal Scale for Clinical Improvement - Without LOCF values (ITT Population)			Stat IP	14.2.2.2
14.2.2.5	Descriptive Statistics for WHO Ordinal Scale for Clinical Improvement by Visit - With LOCF values - Screening as Baseline (ITT Population)	Yes		IP	14.2.2.1
14.2.2.6	Mixed Model for Repeated Measures (MMRM) for Change from Baseline in WHO Ordinal Scale for Clinical Improvement - With LOCF values - Screening as Baseline (ITT Population)	Yes		Stat IP	14.2.2.2
14.2.2.7	Descriptive Statistics for WHO Ordinal Scale for Clinical Improvement by Visit - Without LOCF values - Screening as Baseline (ITT Population)			IP	14.2.2.1
14.2.2.8	Mixed Model for Repeated Measures (MMRM) for Change from Baseline in WHO Ordinal Scale for Clinical Improvement - Without LOCF values - Screening as Baseline (ITT Population)			Stat IP	14.2.2.2
14.2.2.9	Area Under Curve of WHO Ordinal Scale for Clinical Improvement (ITT Population)			IP	
14.2.3.1	Proportion of Subjects with Fever Normalization and SpO_2>94% by Visit (ITT Population)			IP	14.2.1.1

Table Number	Table Title	Included in Preliminary Analysis	Included in DSMB (Table No.)	Validation Method	Shell Number (if repeat)
14.2.3.2	Logistic Regression for Proportion of Subjects with Fever Normalization and SpO_2>94% by Visit (ITT Population)			Stat IP	14.2.1.2
14.2.3.3	Shift from Baseline in Oxygen Use (ITT Population)			IP	
14.2.4.1	Descriptive Statistics for Days on Mechanical Ventilation (ITT Population)	Yes		IP	
14.2.4.2	Analysis of Covariance (ANCOVA) for Days on Mechanical Ventilation (ITT Population)	Yes		Stat IP	
14.2.4.3	Descriptive Statistics for Days on Mechanical Ventilation - Death Assigned to Worst Possible Outcome (ITT Population)	Yes		IP	
14.2.4.4	Analysis of Covariance (ANCOVA) for Days on Mechanical Ventilation - Death Assigned to Worst Possible Outcome (ITT Population)	Yes		Stat IP	
14.2.5.1	Frequency Table for All-Cause Mortality by Visit (ITT Population)			IP	14.2.1.1
14.2.5.2	Logistic Regression for All-Cause Mortality by Visit (ITT Population)			Stat IP	14.2.1.2
14.2.5.2a	Responder Rates for All-Cause Mortality by Visit (ITT Population)			Stat IP	14.2.1.2a
14.2.6.1	Proportion of Subjects Alive and Discharged from the ICU by Visit (ITT Population)			IP	14.2.1.1
14.2.6.2	Logistic Regression for Proportion of Subjects Alive and Discharged from the ICU by Visit (ITT Population)			Stat IP	14.2.1.2
14.2.7.1	Proportion of Subjects Alive and Discharged from the Hospital by Visit (ITT Population)	Yes		IP	14.2.1.1
14.2.7.2	Logistic Regression for Proportion of Subjects Alive and Discharged from the Hospital by Visit (ITT Population)	Yes		Stat IP	14.2.1.2
14.2.8.1	Descriptive Statistics for Days in ICU (ITT Population)	Yes		IP	14.2.5.1
14.2.8.2	Analysis of Covariance (ANCOVA) for Days in ICU (ITT Population)	Yes		Stat IP	14.2.5.2
14.2.8.3	Descriptive Statistics for Days in ICU - Death Assigned to Worst Possible Outcome (ITT Population)	Yes		IP	14.2.5.1
14.2.8.4	Analysis of Covariance (ANCOVA) for Days in ICU - Death Assigned to Worst Possible Outcome (ITT Population)	Yes		Stat IP	14.2.5.2
14.2.9.1	Descriptive Statistics for Days in Hospital (ITT Population)			IP	14.2.1.1
14.2.9.2	Analysis of Covariance (ANCOVA) for Days in Hospital (ITT Population)			Stat IP	14.2.5.2
14.2.10.1	Proportion of Subjects on Mechanical Ventilation by Visit (ITT Population)			IP	14.2.1.1
14.2.10.2	Logistic Regression for Proportion of Subjects on Mechanical Ventilation by Visit (ITT Population)			Stat IP	14.2.1.2
14.3	**Safety Data**				
14.3.1	**Displays of Adverse Events**				

Table Number	Table Title	Included in Preliminary Analysis	Included in DSMB (Table No.)	Validation Method	Shell Number (if repeat)
14.3.1.1.1	Overall Summary of Adverse Events (ITT Population)		Yes (S6)	IP	
14.3.1.2.1	TEAEs by System Organ Class and Preferred Term (ITT Population)		Yes (S7)	IP	
14.3.1.2.2	Treatment-Related TEAEs by System Organ Class and Preferred Term (ITT Population)		Yes (S8)	IP	14.3.1.2.1
14.3.1.2.3	Serious TEAEs by System Organ Class and Preferred Term (ITT Population)		Yes (S9)	IP	14.3.1.2.1
14.3.1.2.4	Treatment-Related Serious TEAEs by System Organ Class and Preferred Term (ITT Population)		Yes (S10)	IP	14.3.1.2.1
14.3.1.3.1	TEAEs by System Organ Class, Preferred Term and Maximum Toxicity Grade (ITT Population)			IP	
14.3.1.3.2	TEAEs by System Organ Class, Preferred Term and Strongest Relationship to Study Treatment (ITT Population)			IP	14.3.1.3.1
14.3.2	**Listings of Deaths, Other Serious and Significant Adverse Events**				
14.3.2.1	Listing of Deaths (ITT Population)		Yes (S11)	IP	
14.3.2.2	Listing of Serious TEAEs (ITT Population)			IP	14.3.2.1
14.3.3	**Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events**				
	Not applicable				
14.3.4	**Abnormal Laboratory Values**				
14.3.4.1	Listing of Abnormal Laboratory Values (ITT Population)			IP	
14.3.5	**Laboratory Data**				
14.3.5.1.1	Hematology Descriptive Statistics (ITT Population)		Yes (S12)	IP	14.2.2.1
14.3.5.1.2	Hematology Shift Table (ITT Population)			IP	
14.3.5.2.1	Chemistry Descriptive Statistics (Safety Population)		Yes (S13)	IP	14.2.2.1
14.3.5.2.2	Chemistry Shift Table (ITT Population)			IP	14.3.5.1.2
14.3.5.3.1	Urinalysis Descriptive Statistics (Continuous) (ITT Population)		Yes (S14)	IP	14.2.2.1
14.3.5.3.2	Urinalysis Descriptive Statistics (Categorical) (ITT Population)		Yes (S15)	IP	
14.3.5.3.3	Urinalysis Shift Table (ITT Population)			IP	14.3.5.1.2
14.3.6	**Vital Signs**				
14.3.6.1.1	Vital Signs Descriptive Statistics (ITT Population)			IP	14.2.2.1
14.3.7	**Physical Examination**				
14.3.7.1.1	Physical Examination Shift Table (ITT Population)			IP	14.3.5.1.2
14.3.8	**ECG**				
14.3.8.1.1	ECG Descriptive Statistics (ITT Population)			IP	14.2.2.1
14.3.8.1.2	ECG Shift Table (ITT Population)			IP	14.3.5.1.2
14.3.9	**Other Safety**				
14.3.9.1.1	Chest X-Ray / CT Shift Table (ITT Population)			IP	14.3.5.1.2
14.4	**Pharmacokinetics**				

Table Number	Table Title	Included in Preliminary Analysis	Included in DSMB (Table No.)	Validation Method	Shell Number (if repeat)
14.4.1.1	Pharmacokinetic Concentrations Descriptive Statistics (ITT Population)			IP	
14.4.2.1	Pharmacokinetic Parameters Descriptive Statistics (ITT Population)			IP	

Figure Number	Figure Title	Included in DSMB	Validation Method	Shell Number (if repeat)
14.2	**Efficacy Figures**			
14.2.1.1	Mean Profile for WHO Ordinal Scale for Clinical Improvement (ITT Population)		IP	
14.2.1.2	Mean Change from Baseline Profile for WHO Ordinal Scale for Clinical Improvement (ITT Population)		IP	14.2.1.1
14.3	**Safety Figures**			
14.3.1.1	Individual Body Temperature versus Time by Treatment Group (ITT Population)		IP	
14.3.2.1	Individual SpO_2 versus Time by Treatment Group (ITT Population)		IP	14.3.1.1
14.4	**Pharmacokinetic Figures**			
14.4.1.1	Pharmacokinetic Concentrations, Individual Profiles on Linear and Semi-Logarithmic Scales (ITT Population)		IP	
14.4.1.2	Pharmacokinetic Concentrations, Mean Profiles on Linear and Semi-Logarithmic Scales (ITT Population)		IP	

Listing Number	Listing Title	Included in DSMB	Validation Method	Shell Number (if repeat)
16.2	**Subject Data Listings**			
16.2.1	**Discontinued Subjects**			
16.2.1.1	Screen Failures (Enrolled Population)		IP	
16.2.1.2	Inclusion/Exclusion Criteria Violations (Enrolled Population)		IP	
16.2.1.3	Study Completion (ITT Population)		IP	
16.2.2	**Protocol Deviations**			
16.2.2.1	Protocol Deviations (ITT Population)	Yes (LS7)	IP	
16.2.3	**Subjects Excluded from The Efficacy Analyses**			
16.2.3.1	Analysis Populations (ITT Population)		IP	
16.2.4	**Demographic Data**			
16.2.4.1	Demographics (ITT Population)	Yes (LS1)	IP	
16.2.4.2	Medical History (ITT Population)	Yes (LS2)	IP	
16.2.4.3	Prior and Concomitant Medications (ITT Population)		IP	
16.2.5	**Compliance and / or Drug Concentration Data**			
16.2.5.1	Drug Accountability (ITT Population)		IP	
16.2.5.2	Dosing (ITT Population)		IP	
16.2.5.3	Standard of Care (ITT Population)		IP	16.2.4.3
16.2.5.4	Pharmacokinetic Concentrations (ITT Population)		IP	
16.2.5.5	Pharmacokinetic Parameters (ITT Population)		IP	
16.2.6	**Individual Efficacy Response Data**			
16.2.6.1	Responder Endpoints (ITT Population)		IP	
16.2.6.2	WHO Ordinal Scale for Clinical Improvement (ITT Population)		IP	
16.2.6.3	'Days on/in' Endpoints (ITT Population)		IP	
16.2.7	**Adverse Event Listings**			
16.2.7.1	Adverse Events (ITT Population)	Yes (LS3)	IP	
16.2.8	**Individual Laboratory Measurements and Other Safety**			
16.2.8.1	Hematology (ITT Population)	Yes (LS4)	IP	
16.2.8.2	Serum Chemistry (ITT Population)	Yes (LS5)	IP	
16.2.8.3	Urinalysis (ITT Population)	Yes (LS6)	IP	
16.2.8.4	Pregnancy Test (ITT Population)		IP	
16.2.8.5	Vital Signs (ITT Population)		IP	
16.2.8.6	Physical Examination (ITT Population)		IP	
16.2.8.7	ECG (ITT Population)		IP	
16.2.8.8	Chest X-Ray / CT (ITT Population)		IP	