Statistical Analysis Plan

Title: Phase 3, Randomized, Placebo-Controlled, Efficacy and Safety 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)

Protocol Number: V3011902

Protocol Version: 1.0 (08-MAR-2021), 2.0 (27-APR-2021), 3.0 (12-MAY-2021), 4.0 (03-AUG-2021), 5.0 (10-SEP-2021), 6.0 (09-JAN-2022), 7.0 (18-MAR-2022)

SAP Version 5.0

SAP Issue Date: 30-JUN-2022

SAP Author: [redacted]

Previous SAP Versions

Version 1.0 (11-FEB-2022), Version 2.0 (16-MAR-2022), Version 3.0 (18-MAR-2022), Version 4.0 (07-APR-2022)

SAP Amendments before database lock

Version	Issue Date	Section	Revision / Addition	Rationale
1.0	11-FEB-2022			First Version
2.0	16-MAR-2022	1 and 5	Reworded 'screening' to 'baseline' in randomization strata.	Consistency with the protocol.
		6.11.1, 6.11.3, 6.11.5.2	Allow model to include country as covariate instead of study site.	To allow model modification i.e. if model does not converge.
		6.11.1	Updated SAS code for imputation model. Added clarifications for study site variable. Added clarifications for DISCHARGE and DISCONT variables.	FDA request.
		6.14.1	Updated TEAE definition.	FDA request.
		6.14.1, 11.1	Added tables for TEAEs leading to treatment modification, TEAEs leading to treatment discontinuation and Fatal TEAEs.	FDA request.
3.0	18-MAR-2022	1	Added new version of the protocol.	Protocol update. Sample size changed from 300 to 210.
		4	Updated for new sample size.	Protocol update.
4.0	07-APR-2022	6.11.1, 6.11.3, 6.11.5.2	In the statistical models allowing also region as covariate	Some countries h[redacted] only very few subjects so

				model fitting might have issues.
		6.11.3, 6.11.5.2, 11.1	Added subgroup analyses for primary endpoint	FDA request
5.0	30-JUN-2022	6.2.1	Updated baseline definition to match protocol.	Clarifications during output production.
		6.2.2	Allow study day derivation to use randomization date for those subjects who were not treated.	Clarifications during output production.
		6.2.4	Added imputation for COVID-19 vaccines.	Clarifications during output production.
		6.2.10	Updated handling of discharge, early termination and unscheduled visits.	Clarifications during output production.
		6.11	Small clarifications in the text.	Clarifications during output production.
		6.12	Added formulas for geometric mean, SD and CV.	Clarifications during output production.
		6.14.2	Added normalization of lab values to make results from different labs comparable.	Clarifications during output production.

		6.14.6 11	Added section for chest x-ray. Updated TFLs as needed.	Clarifications during output production. Clarifications during output production.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ANCOVA	Analysis of Covariance
ARDS	Acute Respiratory Distress Syndrome
AUC	Area Under Curve
ATC	Anatomic Therapeutic Chemical
COVID-19	SARS-CoV-2 infection
CS	Clinically Significant
CSR	Clinical Study Report
CV	Coefficient of Variation
ECMO	Extracorporeal Membrane Oxygenation
eCRF	electronic Case Report Form
ICU	Intensive Care Unit
IDMC	Independent Data Monitoring Committee
ITT	Intent-to-Treat (Analysis Set)
LLOQ	Lower Limit of Quantification
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary of Regulated Activities
mITT	Modified Intent-to-Treat (Analysis Set)
MMRM	Mixed Model for Repeated Measures
NCS	Not Clinically Significant
RRT	Renal Replacement Therapy
SAF	Safety Analysis Set
SAP	Statistical Analysis Plan
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
TEAE	Treatment-Emergent Adverse Event
WHO	World Health Organization

1 INTRODUCTION

This document details the planned statistical analyses for Veru Inc., protocol "V3011902" study titled "Phase 3, Randomized, Placebo-Controlled, Efficacy and Safety 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 (dated 08-MAR-2021), and amendments 1 (dated 27-APR-2021), 2 (12-MAY-2021), 3 (03-AUG-2021), 4 (10-SEP-2021), 5 (09-JAN-2022), 6 (18-MAR-2022).

This randomized, placebo-control clinical study consists of two treatment arms: VERU-111 9 mg treated group, and Placebo treated group. Subjects will be randomized in a 2:1 fashion to the VERU-111 treated group and Placebo treated group, respectively.

All patients will receive standard of care for the treatment of SARS-CoV-2 infection (COVID-19).

Randomization will be stratified by baseline WHO Ordinal Scale score of 4, 5 and 6 such that subjects with a WHO Ordinal Scale of 4, 5 and 6 at baseline are approximately equally distributed between the treatment groups.

The study will require that each subject in the study receive 9 mg daily oral dose of VERU-111 or placebo for up to 21 days (Day 21) or until the patient is discharged from the hospital with efficacy and safety follow up continuing to Day 60 of the study. The total duration of the study for a subject in the study from screening to follow-up visit (approximately Day 60 on study) will be approximately 62 days.

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 die on study (up to Day 60).

2.2 Secondary Objectives

The secondary objectives/endpoints on this study are:

1. The proportion of subjects that are alive without respiratory failure at Day 15, Day 22, and Day 29. Day 29 is the key secondary endpoint. 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. Days in Intensive Care Unit (ICU)
3. WHO Ordinal Scale for Clinical Improvement change from baseline to Day 15, Day 22, and Day 29.

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

4. Days on mechanical ventilation
5. Days in hospital

6. Proportion of subjects that die on study at Day 15, Day 22, and Day 29.
7. Change from baseline in viral load (baseline to Day 9).

2.3 Safety Objective

To assess the safety, tolerability, and risk/benefit of VERU-111.

3 ENDPOINTS

3.1 Primary Endpoint

The primary endpoint for the study is the proportion of subjects that die on study (up to Day 60).

3.2 Secondary Endpoints

The secondary endpoints on this study are:

1. The proportion of subjects that are alive without respiratory failure at Day 15, Day 22, and Day 29. Day 29 is the key secondary endpoint. 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. Days in ICU
3. WHO Ordinal Scale for Clinical Improvement change from baseline to Day 15, Day 22, and Day 29
4. Days on mechanical ventilation
5. Days in hospital
6. Proportion of subjects that die on study at Day 15, Day 22, and Day 29.
7. Change from baseline in viral load (baseline to Day 9)

4 SAMPLE SIZE

Approximately 210 subjects are planned to be randomized at a 2:1 ratio into two treatment arms (approximately 140 subjects in the VERU-111 treated group and approximately 70 subjects in the Placebo treated group).

5 RANDOMIZATION

Randomization will be stratified by baseline WHO Ordinal Scale score of 4, 5 and 6 such that subjects with a WHO Ordinal Scale of 4, 5 and 6 at baseline are approximately equally distributed between the treatment groups.

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 Sets

Subjects excluded from the analysis sets and the reason for their exclusion will be summarized and listed.

6.1.1 Enrolled Set

All subjects who gave informed consent.

6.1.2 Intent-to-Treat (ITT) Analysis Set

All randomized subjects will be included in this analysis set.

6.1.3 Modified Intent-to-Treat (mITT) Analysis Set

All randomized subjects who completed the efficacy portion of the trial and who do not have any major protocol violations will be included in the mITT Analysis Set. Subjects who were randomized but did not receive study medication will be excluded from the mITT Analysis Set.

All protocol deviations will be assessed and documented on a case-by-case basis before the database lock, and deviations considered to have a serious impact on the efficacy results will lead to the relevant subject being excluded from the mITT. Exclusion of subjects who were randomized using incorrect WHO scores will be evaluated. Also, exclusion of subjects who were randomized under original protocol (WHO strata 5 and 6) will be evaluated.

Before database lock, potential subject exclusions from mITT will be reviewed by the Sponsor and documented in a subject evaluability document.

6.1.4 Safety (SAF) Analysis Set

All randomized subjects who received at least one dose of study medication (VERU-111 or Placebo) will be included in this analysis set.

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

The Day 1 visit assessment will serve as the baseline assessments.

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.

If subject does not get study drug then 'Day 1' visit date (or randomization date) can be used instead of the date of first dose of study drug.

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

For COVID-19 vaccines missing/partial dates will be imputed as follows:

- Completely missing dates will be imputed using 01JAN2021
- If month and day are missing then imputed using 01JAN of the year
- If only day is missing then imputed using the first of the month.

If reported COVID-19 vaccine was a single shot then missing end date will be set to equal to start date.

For other 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.

For pharmacokinetic data values below lower limit of quantification (LLOQ) will be handled as follows in summary tables:

- If value collected before first dose of study treatment then set to 0.
- If value collected on or after the first dose of study treatment then set to LLOQ/2.

6.2.9 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 60 using trapezoidal rule. For each subject all available measurements up to

study day 60 are included in the calculations. If subject does not have record on Day 60 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 60. If the patient is discharged as a 2 on Day 5 then they would be a 2 from Day 5 to Day 60. Actual collection times will be used in the calculations.

6.2.10 Discharge, Early Termination and Unscheduled Visits

Only scheduled post-baseline values will be tabulated. Discharge, early termination and unscheduled visits will be mapped to the closest scheduled post-baseline time point. If subject then having more than one record mapped for specific visit then the closest value to the scheduled time point will be used in the analysis.

All collected data will be presented in subject data listings.

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 9 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 4 decimal places. P-values < 0.0001 will be presented as p<0.0001.

6.4 Subject Disposition

Subject disposition will be summarized as follows:

- The number of enrolled subjects overall in Enrolled Set.
- The number of screen failures overall in Enrolled Set.
- The number of subjects with inclusion/exclusion criteria violations overall in Enrolled Set.
- Number of subjects in each Analysis Set by treatment group and overall in Enrolled Set.
- The reasons for exclusion from the mITT Analysis Set will be summarized by treatment group and overall.
- Study completion, early treatment withdrawal with reason, early study termination with reason and other disposition by treatment group and overall in ITT Analysis Set.

6.5 Protocol Deviations

Protocol deviations will be summarized and listed.

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 Safety Analysis Set and mITT Analysis Set:

- 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 Baseline
- Height (cm) at Baseline
- Body Mass Index (BMI) (kg/m2) at Baseline
- WHO Ordinal Scale for Clinical Improvement (descriptive statistics and frequencies for each score category).

The following baseline conditions will be summarized:

- Comorbidities, n (%)
  - Cancer
  - Diabetes
  - Hypertension
  - History of Heart Failure
  - Pneumonia, Renal Issues
  - Respiratory Issues
  - Asthma (subset of Respiratory Issues)
- Oxygen Saturation (SpO2) (%)
- Creatinine Clearance (mL/min)
- Time from Admission to Randomization (days).

6.7 Medical History

Separate tabulations of previous and ongoing conditions at screening will be presented by randomized treatment group and overall for the Safety Analysis Set.

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 24.0) 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 Safety Analysis Set. 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.

Concomitant medications will be summarized using Anatomic Therapeutic Chemical (ATC) Level 2 and Drug Reference Names using the WHO dictionary (version B3 Mar 2021).

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 Safety Analysis Set.

6.10 Treatment Compliance

All subjects will receive standard of care plus oral daily VERU-111 or Placebo. Subjects will take one capsule 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%', '80-120%' and '>120%' 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 – date of first dose +1.

6.11 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.

6.11.1 Primary Efficacy Analysis

The primary endpoint for the study will be the proportion of subjects that die on study (up to Day 60). Responders are subjects who are alive at Day 60.

The number and percentage of deaths will be summarized by treatment group.

Mortality rates will be analyzed using a logistic regression model. The model will include treatment as a factor and gender, study site (or country or region), remdesivir use (No/Yes), dexamethasone use (No/Yes) and WHO Ordinal Scale strata used in randomization as covariates. The model will be fitted using logit link function. 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 analysis set and the ITT data scope regardless of patient's use of rescue medications, protocol violations or investigational product discontinuation consistent with the treatment policy strategy. Every effort will be made to collect vital status up to the end of the study period. Missing data for subjects who are lost to follow up will be imputed using multiple imputation methods.

Example SAS code for imputation is as follows:

```
proc mi data=xxx out=imputed1 seed=1234 nimpute=50;
class treatment sex site discharge discont remdesivir dexamethasone whostrata
      imputedresponse;
fcs logistic(imputedresponse / details likelihood=augment);
var treatment sex site discharge discont remdesivir dexamethasone whostrata
    imputedresponse;
run;
```

where IMPUTEDRESPONSE is the response variable to be imputed, TREATMENT is the randomized treatment group (veru/placebo), SEX is sex of the subject (male/female), SITE is study site (if there are issues fitting imputation model then this might be replaced with country or region), DISCHARGE is whether the subject was discharged from the hospital at any time during the study

(no/yes, populated as 'no' for subjects who were not discharged from the hospital prior to withdrawing from the study before Day 60), DISCONT is whether subject discontinued treatment early (no/yes), REMDESIVIR is the use of remdesivir at baseline (no/yes), DEXAMETHASONE is the use of dexamethasone at baseline (no/yes) and WHOSTRATA is the WHO Ordinal Scale strata used in randomization. If the imputation model does not converge when both DISCHARGE and DISCONT variables are included then will be checked if either of them alone can be included in the model. If model converges with DISCHARGE or DISCONT alone but the model with both DISCHARGE and DISCONT does not converge, then imputation model will include only DISCHARGE.

The imputed data sets will be analyzed separately for each imputation using the logistic regression model. If all subjects have the mortality status at Day 60 then the imputation part above will not be used and observed data will be analyzed as such. Example SAS code for logistic regression is as follows:

```
proc logistic data=imputed1 order=internal descending;
by _imputation_;
class imputedresponse treatment sex site remdesivir dexamethasone whostrata
      / param=glm;
model imputedresponse = treatment sex site remdesivir dexamethasone whostrata
      / clodds=both firth;
estimate 'Treatment A vs. Treatment B' treatment 1 -1 / cl e exp;
lsmeans treatment / cl exp diff;
ods output modelanova=imputed_modelanova1
           lsmeans=imputed_lsmeans1
           diffs=imputed_diffs1
           parameterestimates=imputed_parmest1;
run;
```

If there are enough deaths to perform analysis without FIRTH option then it might be dropped out. Note that variable _IMPUTATION_ identifies each of the imputations created by PROC MI.

Finally, results from individual imputations are pooled via Rubin's rules using PROC MIANALYZE. Example SAS code for pooling log(odds) for each treatment group is as follows:

```
proc mianalyze data=imputed_lsmeans1;
by trt01pn;
modeleffects estimate;
stderr stderr;
ods output parameterestimates=combined_odds1;
```

```
run;
```

Example SAS code for pooling log(odds ratio) for each treatment group is as follows:

```
proc mianalyze data=imputed_diffs1;
modeleffects estimate;
stderr stderr;
ods output parameterestimates=combined_diffs1;
run;
```

6.11.2 Sensitivity Analysis for the Primary Endpoint

A sensitivity analysis using the tipping-point approach will be conducted to assess the robustness of the primary analysis approach. This analysis will be performed only if primary efficacy analysis shows significant difference between treatment groups and at least some subjects have missing mortality status as Day 60.

Missing endpoints will be re-assigned in a series of analyses that are progressively more in favor of placebo.

The tipping point analysis will consider the full range of possible response rates in the subjects with missing data in the primary analysis. This will be done by systematically changing assumed response rates from 0% to 100% in a stepwise manner. The imputation will be performed independently within the two treatment groups so that, in the most extreme case, the imputed response rate in the VERU-111 arm will be 0% and 100% in the placebo arm.

Multiple imputation will be used for each pair of response rates under consideration. Both the imputation model and the analysis model will incorporate the covariates as used in the primary analysis.

The following algorithm will be used for the imputation;

Step 1: Use efficacy data to identify subjects classed as non-responders due to missing data.

Step 2: 121 pairs of response rates for VERU-111 and placebo in the table below will be used for the imputation.

	Placebo Response Rate										
	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0

VERU-111 9 mg Response Rate	0	1	2	3	4	5	6	7	8	9	10	11
	0.1	12	13	14	15	16	17	18	19	20	21	22
	0.2	23	24	25	26	27	28	29	30	31	32	33
	0.3	34	35	36	37	38	39	40	41	42	43	44
	0.4	45	46	47	48	49	50	51	52	53	54	55
	0.5	56	57	58	59	60	61	62	63	64	65	66
	0.6	67	68	69	70	71	72	73	74	75	76	77
	0.7	78	79	80	81	82	83	84	85	86	87	88
	0.8	89	90	91	92	93	94	95	96	97	98	99
	0.9	100	101	102	103	104	105	106	107	108	109	110
	1.0	111	112	113	114	115	116	117	118	119	120	121

For each of the 121 pairs of response rates in the table above, (e.g. for pair number 46, response rate for Placebo = 0.1, while response rate for VERU-111 = 0.4.):

- For each subject identified in Step 1, generate a continuous response score between 0 (non-response) and 1 (response) using SAS PROC MI adjusting for the same covariates as in the primary analysis. Example SAS code is as follows:

```
proc mi data=a out=xxx seed=1234 nimpute=50
        minimum=. . . . . . . . 0 maximum=. . . . . . . . 1;
class treatment sex site discharge discont remdesivir dexamethasone
whostrata;
fcs reg(imputedresp / details);
var treatment sex site discharge discont remdesivir dexamethasone
whostrata imputedresp;
run;
```

- Assign the imputed response (1=response, 0=non-response) based on the response score and the current tipping point. Using the example values above:
  - Given a VERU-111 tipping point response rate of 0.1, subjects in the VERU-111 group with a response score ≥ 0.9 would be imputed as responders and non-responders otherwise.
  - Given a placebo tipping point response rate of 0.4, subjects in the placebo group with a response score ≥ 0.6 would be imputed as responders and non-responders otherwise.
- Then same model as in primary analysis will be run for each pair of response rates and p-values reported in the table. From the table the robustness of results can be evaluated.

6.11.3 Secondary Analyses for the Primary Endpoint

The primary endpoint, mortality rate at Day 60, will also be assessed in the subset of mITT patients and Safety Analysis Set (all treated subjects).

Additionally, similar analysis to primary analysis will be performed in subgroups for region, standard of care, WHO Ordinal Scale at baseline and vaccination status.

To obtain risk differences between treatment groups, the same analysis as described above for primary efficacy analysis will be performed except identity link function will be used. Example SAS code is as follows:

```
proc genmod data=a order=internal;
class treatment sex site remdesivir dexamethasone whostrata;
model response=treatment sex site remdesivir dexamethasone whostrata
      / type3 dist=bin link=identity;
lsmeans treatment / e diff exp cl;
run;
```

Additionally, mortality rates will be summarized using Kaplan-Meier (KM) survival curves and equality of treatment groups will be tested using log-rank test. Hazard ratios will be calculated using the Cox proportional hazards model including terms for treatment, gender, study site (or country or region), remdesivir use (No/Yes), dexamethasone use (No/Yes) and WHO Ordinal Scale strata used in randomization. Any subjects for whom survival status is not available at day 60 will be censored at the day of their last observed assessment or last captured event.

Example SAS code for log-rank test is as follows:

```
proc lifetest data=XXX outsurv=surv1
              plots=survival(atrisk=0 to 60 by 1);
time time*cens(1);
strata treatment;
run;
```

Example SAS code for proportional hazards model is as follows:

```
proc phreg data=XXX;
class treatment sex site remdesivir dexamethasone whostrata;
model time*cens(1)=treatment sex site remdesivir dexamethasone
whostrata;
```

```
hazardratio treatment;
assess ph / resample seed=1234;
 run;
```

6.11.4 Exploratory Analysis for the Primary Endpoint

Not applicable.

6.11.5 Secondary Efficacy Analyses

6.11.5.1 The proportion of subjects that are alive without respiratory failure at Day 15, Day 22, and Day 29.

This analysis will compare subjects that are alive without respiratory failure on the visit (responder) to subjects who died before the visit or had respiratory failure (non-responder) on the visit.

Responders are subjects who are alive and have Grade 0-4 on the WHO Ordinal Scale for Clinical Improvement on the visit. If subject was discharged from the hospital prior to the visit and WHO Ordinal Scale for Clinical Improvement is not collected at the specific visit then the last available observation before or at the time of discharge will be used. If subject's vital status is not known then missing information will be imputed using multiple imputation.

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

The number and percentage of responders will be summarized by treatment group and visit.

Responders will be analyzed using the same methodology as for the primary endpoint (separate analysis will be performed for each visit):

- Multiple imputation + logistic regression model

6.11.5.2 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 60. In this analysis the worst possible endpoint will be assigned to those subjects who died at any time up to Day 60. For subjects who died the days in ICU will be set to 60. Even for those who were never in the ICU. If

subject did not report any days in the ICU then their days will be set to zero except for those who died.

Same analysis will be performed in subgroups for region, standard of care and WHO Ordinal Scale at baseline.

A sensitivity analysis will be performed using the actual number of days in ICU. If subject was never in the ICU then days in ICU will be set to 0 even if subject died.

Treatment comparison will be based on analysis of covariance (ANCOVA) model including treatment as a factor, and study site (or country or region), remdesivir use (No/Yes), dexamethasone use (No/Yes) and WHO Ordinal Scale strata used in randomization 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 whostrata /
                ddfm=kr;
lsmeans trt01pn / cl diff;
ods output tests3=tests lsmeans=lsmeans diffs=diffs
run;
```

6.11.5.3 WHO Ordinal Scale for Clinical Improvement change from baseline to Day 15, Day 22, and Day 29

WHO Ordinal Scale for Clinical Improvement will be summarized in frequency table by visit and treatment group.

Additionally, response status for each subject will be defined based on WHO Ordinal Scale for Clinical Improvement. This analysis will compare subjects that have WHO score 0 or 1 (responder) on the visit to subjects who have WHO score >=2 (non-responder) on the visit.

Baseline for WHO Ordinal Scale is the last available record up to and including Day 1. If subject 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. If subject dies then following time points will be set to the worst possible outcome (score=8).

The number and percentage of responders will be summarized by treatment group and visit.

Responders will be analyzed using similar logistic regression model except not planning multiple imputation as the above algorithm provides responder status for all subjects.

6.11.5.4 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 defined using two different algorithms similarly to 'Days in ICU'.

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

6.11.5.5 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 defined using two different algorithms similarly to 'Days in ICU'.

'Days in hospital' will be analyzed using the same methodology as for 'Days in ICU' and the same sensitivity analysis will be performed except the subgroup analyses will not be performed.

6.11.5.6 The proportion of subjects that die on study 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 (separate analysis will be performed for each visit):

- Multiple imputation + logistic regression model
- Risk differences between treatment groups (using identity link function).

6.11.5.1 Change from baseline in viral load (baseline to Day 9)

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. For viral load post-BL time points for summary and analysis will be 'Last On-Study' and 'Day 9 only'.

Change from baseline in viral load will be analyzed using the same methodology as for 'Days in ICU' but including also viral load at baseline as covariate.

6.11.6 Exploratory Efficacy Analyses

AUC of WHO Ordinal Scale for Clinical Improvement will be summarized using descriptive statistics by treatment group.

6.11.7 Multiplicity

Holm (1979) step-down procedure will be used to control multiplicity for selected key secondary endpoints (days in ICU and days on mechanical ventilation).

If the primary analysis of the primary endpoint is significant at the <0.05 level key secondary endpoints days in ICU and days on mechanical ventilation will be tested using the Holm step-down procedure. In this way an overall type 1 (false-positive) error rate of 5% will be maintained so that no statistical significance for the key secondary efficacy endpoints will be claimed unless the principal analysis of the primary efficacy endpoint using the ITT set is statistically significant at the 5% level.

Holm procedure will be applied as follows:

1. If the p-value for primary endpoint >= 0.05 then testing will stop and key secondary endpoints will not be tested. If p-value <0.05 then testing continues to key secondary endpoints.
2. P-values for key secondary endpoints will be sorted from smallest to greatest (ascending order).
3. The smallest p-value for key secondary endpoints will be compared to 0.025.
4. If the smallest p-value yields significant result at 0.025 level then sequential testing continues to the next largest p-value and adjusted alpha value of 0.05. Otherwise the testing will stop.

Data from all analyses, regardless of the level of significance, will be presented for review.

6.12 Pharmacokinetic Analyses

Pharmacokinetic concentration data will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum and maximum) at each time point. Also CV%, geometric mean, geometric SD and geometric CV% will be presented.

Geometric mean is calculated as

$$\mu_g = \sqrt[n]{x_1 x_2 x_3 \dots x_n},$$

where n is the number of observations and x_i are the observed data. This can be expressed also in the following form

$$\mu_g = \exp\left(\frac{\sum_{i=1}^{n} \ln x_i}{n}\right),$$

which is easier for the practical calculation. This would simply be the exponent of the arithmetic mean from logarithmically transformed data.

Geometric standard deviation (SD)

Geometric SD is calculated as

$$\sigma_g = \exp\left(\sqrt{\frac{\sum_{i=1}^{n}\left(\ln x_i - \ln \mu_g\right)^2}{n}}\right).$$

This would simply be the exponent of the arithmetic standard deviation from logarithmically transformed data.

Geometric coefficient of variation (CV)

Geometric CV is calculated as

$$CV_g = \sqrt{e^{(\ln \sigma_g)^2} - 1},$$

where ln σ_g is the arithmetic standard deviation from logarithmically transformed data. Geometric CV can be multiplied by 100 if CV displayed in percentage.

6.13 Pharmacodynamic Analyses

Not applicable.

6.14 Safety Analyses

The safety analyses will be presented by the treatment received for the Safety Analysis Set.

6.14.1 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.
- Any pre-existing AE that has worsened in severity on or after the first dose of study drug.

A treatment-related AE is defined as an AE with causality collected as 'POSSIBLY RELATED', 'PROBABLY RELATED' or 'RELATED' in the CRF.

The intent is to collect all data, in a rare cases data might be incomplete for AE relationship and/or standard toxicity grade. This is not anticipated to cause any issues in the analysis and in these cases values will be imputed using worst-case scenario for analysis as follows:

- 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. This is not worst case but more meaningful to impute as severe compared to life-threatening or death.

AEs will be summarized according to the MedDRA (version 24.0) 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
  - TEAEs leading to treatment modification (drug interrupted / dose increased / dose reduced)

- TEAEs leading to treatment discontinuation (drug withdrawn)
- Fatal 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 event 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.

6.14.2 Laboratory Data

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

Even when same units are used in different labs the normal ranges can vary within each lab parameter. Also in these cases normalization of the data need to be performed.

Laboratory data shift tables (low/normal/high) will be done based on the original ranges used in the local laboratories.

For descriptive statistics, local laboratory results are normalized using location-scale normalization or scale normalization formulas given by Karvanen (2003).

Result Normalization

Location-scale normalization is used when both central lab and local lab have both lower and upper limits for normal specified in the data:

$$s_{\text{location-scale}} = L_S + (x - L_X)\frac{(U_S - L_S)}{(U_X - L_X)}$$

If location-scale normalization reaches negative value for a parameter then for that parameter scale normalized value will be used instead (giving priority for value using upper normal limit). Scale normalization is used when either central lab or local lab have and only lower or upper limits for normal specified in the data (or location-scale normalization reaches negative value):

$$s_{\text{scale(upper)}} = x\frac{U_S}{U_x} \quad \text{or} \quad s_{\text{scale(lower)}} = x\frac{L_S}{L_x}$$

The notation in the above formulas are as follows:

s	normalized result
x	local laboratory result
L_X	lower normal limit in local lab
U_X	upper normal limit in local lab
L_S	lower normal limit in central lab
U_S	upper normal limit in central lab.

As this study does not have central laboratory then the most common range will be used instead of central lab values in the formula above. This keeps the number of normalized values as low as possible.

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. Listings will show the normalized values.

6.14.3 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 (%)

When study day has more than one record (i.e. vital sign log data) 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.

6.14.4 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 = Not Clinically Significant, CS = Clinically Significant.

All physical examination data will be listed.

6.14.5 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.

6.14.6 Chest X-Ray

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

All chest X-ray data will be listed.

7 INTERIM ANALYSIS

Interim analyses are described in separate IDMC SAP.

8 INDEPENDENT DATA MONITORING COMMITTEE (IDMC) ANALYSIS

Independent Data Monitoring Committee (IDMC) analyses and interim analyses are described in separate IDMC analysis plan.

9 CHANGES TO PLANNED PROTOCOL ANALYSIS

Original protocol stated that randomization will be stratified by WHO scores 5 and 6 but it was updated to include WHO scores 4, 5 and 6 in protocol version 3.0 (amendment 2)(dated 12-MAY-2021).

In the protocol WHO score was planned to be analyzed as continuous variable using MMRM. However this was changed into responder type of analysis in the SAP.

Holm step-down procedure was added to control multiplicity for primary endpoint and key secondary endpoints.

10 REFERENCES

1. SAS Institute Inc., Cary, NC, 27513, USA
2. Holm SA. A simple sequentially rejective multiple test procedure. Scandanavian Journal of Statistics 1979; 6: 65-70.
3. Karvanen J. The Statistical Basis of Laboratory Data Normalization. Drug Information Journal, Vol. 37, pp. 101–107, 2003, 0092-8615/2003

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 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)

11.1 Tables

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.1.1.1	Subject Enrollment Enrolled Set	IP	
14.1.1.2	Screen Failures Enrolled Set	IP	
14.1.1.3	Inclusion/Exclusion Criteria Violations Enrolled Set	IP	
14.1.1.4	Analysis Sets and Subject Disposition ITT Set	IP	
14.1.1.5	Protocol Deviations ITT Set	IP	
14.1.1.6	Reasons for Exclusion from Per-Protocol Set ITT Set	IP	
14.1.1.7	Randomization by Country and Site ITT Set	IP	
14.1.2.1	Demographics ITT Set	IP	
14.1.2.2	Demographics Safety Set	IP	

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.1.2.3	Demographics mITT Set	IP	14.1.2.1
14.1.2.4	Baseline Condition ITT Set	IP	
14.1.2.5	Baseline Condition Safety Set	IP	
14.1.2.6	Baseline Condition mITT Set	IP	14.1.2.3
14.1.3.1	Previous Medical History by System Organ Class and Preferred Term ITT Set	IP	
14.1.3.2	Ongoing Medical History by System Organ Class and Preferred Term ITT Set	IP	14.1.3.1
14.1.4.1	Prior Medications by ATC Level 2 and Preferred Term ITT Set	IP	
14.1.4.2	Concomitant Medications by ATC Level 2 and Preferred Term ITT Set	IP	14.1.4.1
14.1.4.3	Background Standard of Care by Country ITT Set	IP	
14.1.5.1	Treatment Exposure Safety Set	IP	
14.1.5.2	Treatment Compliance Safety Set	IP	
14.2.1.1	Proportion of Subjects Alive by Visit ITT Set	IP	
14.2.1.2	Logistic Regression for Proportion of Subjects Alive by Visit ITT Set	Stat IP	

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.2.1.3	Proportion of Subjects Alive by Visit Safety Set	IP	14.2.1.1
14.2.1.4	Logistic Regression for Proportion of Subjects Alive by Visit Safety Set	Stat IP	14.2.1.2
14.2.1.5	Proportion of Subjects Alive by Visit mITT Set	IP	14.2.1.1
14.2.1.6	Logistic Regression for Proportion of Subjects Alive by Visit mITT Set	Stat IP	14.2.1.2
14.2.1.7	Tipping Point Analysis for Proportion of Subjects Alive at Day 60 ITT Set	Stat IP	
14.2.1.8	Logistic Regression for Proportion of Subjects Alive by Visit - Identity Link ITT Set	Stat IP	14.2.1.2
14.2.1.9	Kaplan-Meier Estimates for Overall Mortality ITT Set	Stat IP	
14.2.1.10	Cox Proportional Hazards Model for Overall Mortality ITT Set	Stat IP	
14.2.1.11	Proportion of Subjects Alive by Region, Country and Site, and Visit ITT Set	IP	14.2.1.1
14.2.1.12	Logistic Regression for Proportion of Subjects Alive by Region and Visit ITT Set	Stat IP	14.2.1.2
14.2.1.13	Proportion of Subjects Alive by Standard of Care and Visit ITT Set	IP	14.2.1.1
14.2.1.14	Logistic Regression for Proportion of Subjects Alive by Standard of Care and Visit ITT Set	Stat IP	14.2.1.2

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.2.1.15	Proportion of Subjects Alive by WHO Ordinal Scale at BL and Visit ITT Set	IP	14.2.1.1
14.2.1.16	Logistic Regression for Proportion of Subjects Alive by WHO Ordinal Scale at BL and Visit ITT Set	Stat IP	14.2.1.2
14.2.1.17	Proportion of Subjects Alive by Vaccination Status (All Vaccinated (at Least One Shot) vs. All Unvaccinated) and Visit ITT Set	IP	14.2.1.1
14.2.1.18	Proportion of Subjects Alive by Vaccination Status (All Vaccinated with US Acceptable Vaccine vs. the Rest of the Population) and Visit ITT Set	IP	14.2.1.1
14.2.1.19	Proportion of Subjects Alive by Vaccination Status (All Vaccinated with at Least One Shot within 6 Months of the First Dose on V3011902 vs. the Rest of the Population) and Visit ITT Set	IP	14.2.1.1
14.2.2.1	Proportion of Subjects Alive and Free of Respiratory Failure by Visit ITT Set	IP	14.2.1.1
14.2.2.2	Logistic Regression for Proportion of Subjects Alive and Free of Respiratory Failure by Visit ITT Set	Stat IP	14.2.1.2
14.2.3.1	Descriptive Statistics for Days in Intensive Care Unit (ICU) - Death Assigned to Worst Possible Outcome ITT Set	IP	
14.2.3.2	Analysis of Covariance (ANCOVA) for Days in Intensive Care Unit (ICU) - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.2.3.3	Descriptive Statistics for Days in Intensive Care Unit (ICU) by Region - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.3.4	Analysis of Covariance (ANCOVA) for Days in Intensive Care Unit (ICU) by Region - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.3.5	Descriptive Statistics for Days in Intensive Care Unit (ICU) by Standard of Care - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.3.6	Analysis of Covariance (ANCOVA) for Days in Intensive Care Unit (ICU) by Standard of Care - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.3.7	Descriptive Statistics for Days in Intensive Care Unit (ICU) by WHO Ordinal Scale at BL - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.3.8	Analysis of Covariance (ANCOVA) for Days in Intensive Care Unit (ICU) by WHO Ordinal Scale at BL - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.3.9	Descriptive Statistics for Days in Intensive Care Unit (ICU) - Actual Days ITT Set	IP	14.2.3.1
14.2.3.10	Analysis of Covariance (ANCOVA) for Days in Intensive Care Unit (ICU) - Actual Days ITT Set	Stat IP	14.2.3.2
14.2.4.1	Frequencies for WHO Ordinal Scale for Clinical Improvement by Visit ITT Set	IP	
14.2.4.2	WHO Ordinal Scale for Clinical Improvement Responders by Visit ITT Set	IP	

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.2.4.3	Logistic Regression for WHO Ordinal Scale for Clinical Improvement Responders by Visit ITT Set	Stat IP	14.2.4.1
14.2.5.1	Descriptive Statistics for Days on Mechanical Ventilation - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.5.2	Analysis of Covariance (ANCOVA) for Days on Mechanical Ventilation - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.5.3	Descriptive Statistics for Days on Mechanical Ventilation by Region - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.5.4	Analysis of Covariance (ANCOVA) for Days on Mechanical Ventilation by Region - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.5.5	Descriptive Statistics for Days on Mechanical Ventilation by Standard of Care - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.5.6	Analysis of Covariance (ANCOVA) for Days on Mechanical Ventilation by Standard of Care - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.5.7	Descriptive Statistics for Days on Mechanical Ventilation by WHO Ordinal Scale at BL - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.5.8	Analysis of Covariance (ANCOVA) for Days on Mechanical Ventilation by WHO Ordinal Scale at BL - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.2.5.9	Descriptive Statistics for Days on Mechanical Ventilation - Actual Days ITT Set	IP	14.2.3.1
14.2.5.10	Analysis of Covariance (ANCOVA) for Days on Mechanical Ventilation - Actual Days ITT Set	Stat IP	14.2.3.2
14.2.6.1	Descriptive Statistics for Days in Hospital - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.6.2	Analysis of Covariance (ANCOVA) for Days in Hospital - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.6.3	Descriptive Statistics for Days in Hospital by Region - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.6.4	Analysis of Covariance (ANCOVA) for Days in Hospital by Region - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.6.5	Descriptive Statistics for Days in Hospital by Standard of Care - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.6.6	Analysis of Covariance (ANCOVA) for Days in Hospital by Standard of Care - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2
14.2.6.7	Descriptive Statistics for Days in Hospital by WHO Ordinal Scale at BL - Death Assigned to Worst Possible Outcome ITT Set	IP	14.2.3.1
14.2.6.8	Analysis of Covariance (ANCOVA) for Days in Hospital by WHO Ordinal Scale at BL - Death Assigned to Worst Possible Outcome ITT Set	Stat IP	14.2.3.2

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.2.6.9	Descriptive Statistics for Days in Hospital - Actual Days ITT Set	IP	14.2.3.1
14.2.6.10	Analysis of Covariance (ANCOVA) for Days in Hospital - Actual Days ITT Set	Stat IP	14.2.3.2
14.2.7.1	Viral Load Descriptive Statistics ITT Set	IP	
14.2.7.2	Analysis of Covariance (ANCOVA) for Change from Baseline in Viral Load ITT Set	Stat IP	14.2.3.2
14.2.8.1	Area Under Curve of WHO Ordinal Scale for Clinical Improvement ITT Set	IP	
14.2.9.1	Summary of Primary and Key Secondary Efficacy Endpoints (Holm Step-down Procedure) ITT Set	Stat IP	
14.3.1.1.1	Overall Summary of Adverse Events Safety Set	IP	
14.3.1.2.1	TEAEs by System Organ Class and Preferred Term Safety Set	IP	
14.3.1.2.2	Treatment-Related TEAEs by System Organ Class and Preferred Term Safety Set	IP	14.3.1.2.1
14.3.1.2.3	Serious TEAEs by System Organ Class and Preferred Term Safety Set	IP	14.3.1.2.1
14.3.1.2.4	Treatment-Related Serious TEAEs by System Organ Class and Preferred Term Safety Set	IP	14.3.1.2.1

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.3.1.2.5	TEAEs Leading to Treatment Modification (drug interrupted / dose increased / dose reduced) by System Organ Class and Preferred Term Safety Set	IP	14.3.1.2.1
14.3.1.2.6	TEAEs Leading to Treatment Discontinuation (drug withdrawn) by System Organ Class and Preferred Term Safety Set	IP	14.3.1.2.1
14.3.1.2.7	Fatal TEAEs by System Organ Class and Preferred Term Safety Set	IP	14.3.1.2.1
14.3.1.3.1	TEAEs by System Organ Class, Preferred Term and Maximum Toxicity Grade Safety Set	IP	
14.3.1.3.2	TEAEs by System Organ Class, Preferred Term and Strongest Relationship to Study Treatment Safety Set	IP	
14.3.2.1	Listing of Deaths Safety Set	IP	
14.3.2.2	Listing of Serious TEAEs Safety Set	IP	14.3.2.1
14.3.4.1	Listing of Abnormal Laboratory Values Safety Set	IP	
14.3.5.1.1	Hematology Descriptive Statistics Safety Set	IP	14.2.7.1
14.3.5.1.2	Hematology Shift Table Safety Set	IP	
14.3.5.2.1	Chemistry Descriptive Statistics Safety Set	IP	14.2.7.1
14.3.5.2.2	Chemistry Shift Table Safety Set	IP	14.3.5.1.2

Table Number	Table Title	Validation Method	Shell Number (if repeat)
14.3.5.3.1	Urinalysis Descriptive Statistics (Continuous) Safety Set	IP	14.2.7.1
14.3.5.3.2	Urinalysis Descriptive Statistics (Categorical) Safety Set	IP	14.2.1.1
14.3.5.3.3	Urinalysis Shift Table Safety Set	IP	14.3.5.1.2
14.3.6.1.1	Vital Signs Descriptive Statistics Safety Set	IP	14.2.7.1
14.3.7.1.1	Physical Examination Shift Table Safety Set	IP	14.3.5.1.2
14.3.8.1.1	ECG Descriptive Statistics Safety Set	IP	14.2.7.1
14.3.8.1.2	ECG Shift Table Safety Set	IP	14.3.5.1.2
14.3.9.1.1	Chest X-Ray / CT Shift Table Safety Set	IP	14.3.5.1.2
14.4.1.1	Descriptive Statistics for Pharmacokinetic Concentrations of Veru-111 (ng/mL) Safety Set	IP	

11.2 Figures

Figure Number	Figure Title	Validation Method	Shell Number (if repeat)
14.2.1.1	Time to Death ITT Set	IP	
14.2.2.1	Mean Profile for WHO Ordinal Scale for Clinical Improvement - with LOCF Values ITT Set	IP	
14.2.2.2	Mean Change from Baseline Profile for WHO Ordinal Scale for Clinical Improvement - with LOCF Values ITT Set	IP	14.2.1.1
14.3.1.1	Mean Profile for Body Temperature ITT Set	IP	14.2.2.1
14.3.2.1	Mean Profile for SpO2 ITT Set	IP	14.2.2.1

11.4 Listings

Listing Number	Listing Title	Validation Method	Shell Number (if repeat)
16.2.1.1	Screen Failures Enrolled Set	IP	
16.2.1.2	Inclusion/Exclusion Criteria Violations Enrolled Set	IP	
16.2.1.3	Treatment Completion Safety Set	IP	
16.2.1.4	Study Completion ITT Set	IP	
16.2.2.1	Protocol Deviations ITT Set	IP	
16.2.3.1	Analysis Sets Enrolled Set	IP	
16.2.4.1	Demographics ITT Set	IP	
16.2.4.2	Medical History ITT Set	IP	
16.2.4.3	Prior and Concomitant Medications ITT Set	IP	
16.2.5.1	Drug Accountability ITT Set	IP	
16.2.5.2	Dosing ITT Set	IP	
16.2.5.3	Standard of Care ITT Set	IP	
16.2.5.4	Pharmacokinetic Concentrations Safety Set	IP	

Listing Number	Listing Title	Validation Method	Shell Number (if repeat)
16.2.6.1	Responder Endpoints ITT Set	IP	
16.2.6.2	WHO Ordinal Scale for Clinical Improvement ITT Set	IP	
16.2.6.3	Time-to-Event and 'Days on/in' Endpoints ITT Set	IP	
16.2.6.4	Viral Load ITT Set	IP	
16.2.7.1	Adverse Events ITT Set	IP	
16.2.8.1	Hematology ITT Set	IP	
16.2.8.2	Serum Chemistry ITT Set	IP	
16.2.8.3	Urinalysis ITT Set	IP	
16.2.8.4	Pregnancy Test ITT Set	IP	
16.2.8.5	Vital Signs ITT Set	IP	
16.2.8.6	Physical Examination ITT Set	IP	
16.2.8.7	ECG ITT Set	IP	
16.2.8.8	Chest X-Ray ITT Set	IP	