CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 20-0006
Study Title:
A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults

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STUDY TITLE

Protocol Number Code:	**DMID Protocol: 20-0006**
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Form/Route:	IV
Indication Studied:	COVID-19
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
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This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BEEC	Blinded Endpoint Evaluation Committee
CI	Confidence Interval
CoV / COV	Coronavirus
CRF / eCRF	Case Report Form / Electronic Case Report Form
CSR	Clinical Study Report
DAIDS	Division of AIDS
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
ECMO	Extracorporeal Membrane Oxygenation
FDA	Food and Drug Administration
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
ICH	International Conference on Harmonisation
ITT	Intention to Treat
IV	Intravenous
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
MOP	Manual of Procedures
N	Number (typically refers to subjects)
NEWS	National Early Warning Score
NIH	National Institutes of Health
OP	Oropharyngeal
PCR	Polymerase Chain Reaction
PI	Principal Investigator
PT	Preferred Term / Prothrombin Time
RCD	Reverse Cumulative Distribution
RNA	Ribonucleic Acid

SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SARS	Severe Acute Respiratory Syndrome
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SOC	System Organ Class
US	United States
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults" (DMID Protocol 20-0006) describes and expands upon the statistical information presented in the protocol. This protocol is an adaptive protocol with different stages. Each stage will have a separate SAP. This SAP is for ACTT-1: Remdesivir vs Placebo.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains: a review of the study design, general statistical considerations, comprehensive statistical analysis methods for efficacy and safety outcomes, and a list of proposed tables, figures and listings. Within the table, figure, and listing mock-ups (Appendices 1, 2, and 3), references to CSR sections are included. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

Coronaviruses (CoVs) are positive-sense, single stranded, enveloped RNA viruses, many of which are commonly found in humans and cause mild symptoms. Over the past two decades, emerging pathogenic CoVs capable of causing life-threatening disease in humans and animals have been identified, namely, severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002-2003 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012.

In December 2019, the Wuhan Municipal Health Committee (Wuhan, China) identified an outbreak of viral pneumonia cases of unknown cause. Coronavirus RNA was quickly identified in some of these patients. This novel coronavirus has been designated as SARS-COV-2 and has 89% nucleotide identity with bat SARS-like-CoVZXC21 and 82% with that of human SARS-CoV [reference 1 in protocol]. The human disease caused by SARS-CoV-2 has been designated COVID-19. In most (~80%) cases, COVID-19 presents as a mild-to-moderately severe, self-limited acute respiratory illness with fever, cough, and shortness of breath. Symptoms are thought to appear 2 to 14 days after exposure. COVID-19 can be severe resulting in pneumonia, severe acute respiratory syndrome, kidney failure, and death. The first US COVID-19 death occurred on February 29, 2020.

During the COVID-19 outbreak, incidence of cases has rapidly increased such that on January 5, 2020 there were 59 confirmed cases, 278 cases on January 20, 2118 cases on January 26, and more than 80,000 cases and 2700 deaths as of February 25, 2020 according to various international health reporting agencies. On January 30, 2020, the International Health Regulations Emergency Committee of the World Health Organization (WHO) declared the COVID-19 outbreak a Public Health Emergency of International Concern. On January 31, 2020, the US Department of Health and Human Services declared a public health emergency in the United States. Outbreak forecasting and modeling suggest that these numbers will continue to rise [reference 2 in protocol]. On March 11, 2020, WHO characterized COVID-19 as a pandemic.

Global efforts to evaluate novel antivirals and therapeutic interventions to treat COVID-19 have intensified. There is currently no vaccine to prevent SARS-CoV-2 infection or therapeutic agent to treat COVID-19. Therefore, there is an urgent public health need for rapid development of novel interventions.

2.1. Purpose of the Analyses

This Statistical Analysis Plan (SAP) encompasses all interim analyses and the final analysis of primary and secondary outcome measures. These analyses will assess the efficacy and safety of remdesivir in comparison with Placebo and will be included in the Clinical Study Report. This protocol is an adaptive design and, if the design is modified, the SAP will be amended accordingly. The protocol for DMID 20-0006 calls for a planned interim efficacy analysis once roughly 50% of the targeted number of recoveries have been observed, and ongoing safety analyses. Safety interim analyses occur more frequently to review safety data in the event that the experimental agent inflicts harm. The goal of the efficacy interim analyses is to review endpoint data in order to recommend whether the current study arm should proceed or to stop early for benefit or futility.

The version 3.0 amendment to this SAP was written after the interim analysis results were presented to the DSMB on April 27, 2020. Per DSMB recommendation, the results were then provided to blinded NIAID study leadership. Due to the urgent public health imperative presented by the COVID-19 pandemic, the interim efficacy results were disclosed publicly (NIAID April 29, 2020 News Release). Per discussions with the FDA, the timing of the final analyses was modified from the original plan (see Section 6.2).

As the ACTT1 Interim Analysis DSMB meeting has already occurred, details of the interim analyses for the DSMB meetings are not modified in version 3.0. However, edits have been made to the planned final analyses. A summary of all changes to this document is provided in Section 15.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

Primary Objective

The overall objective of the study is to evaluate the clinical efficacy of different investigational therapeutics relative to the control arm in patients hospitalized with COVID-19 as assessed by the time to recovery up to Day 29.

Secondary Objectives

The key secondary objective is to evaluate the clinical efficacy of different investigational therapeutics relative to the control arm in patients hospitalized with COVID-19 as assessed by the 8-point ordinal clinical status scale at Day 15.

The other secondary objectives are to:

1. Evaluate clinical efficacy of different investigational therapeutics as compared to the control arm as assessed by:
    - Clinical Severity
        - 8-Point Clinical Status Ordinal scale:
            - Time to an improvement of one category and two categories from Day 1 (baseline) on the clinical status 8-point ordinal scale.
            - Subject clinical status using 8-point ordinal scale at Days 3, 5, 8, 11, 15, 22, and 29.
            - Mean change in the clinical status 8-point ordinal scale from Day 1 to Days 3, 5, 8, 11, 15, and 29.
        - National Early Warning Score (NEWS):
            - Time to discharge or to a NEWS of ≤ 2 and maintained for 24 hours, whichever occurs first.
            - Change from Day 1 to Days 3, 5, 8, 11, 15, and 29 in NEWS.
        - Oxygenation:
            - Days requiring oxygen through Day 29.
            - Incidence and duration of new oxygen use through Day 29.
        - Non-invasive ventilation/high flow oxygen:
            - Days of non-invasive ventilation/high flow oxygen through Day 29.
            - Incidence and duration of new non-invasive ventilation or high flow oxygen use through Day 29.
        - Invasive Mechanical Ventilation / extracorporeal membrane oxygenation (ECMO):
            - Days of ventilator/ECMO through Day 29.

    - Incidence and duration of new mechanical ventilation or ECMO use through Day 29.
- Hospitalization
    - Duration of hospitalization (in days) through Day 29.
- Mortality
    - 14-day mortality.
    - 28-day mortality.

2. Evaluate the safety of the intervention through 28 days of follow-up as compared to the control arm as assessed by:
    - Cumulative incidence of SAEs through Day 29
    - Cumulative incidence of Grade 3 and 4 clinical and/or laboratory AEs through Day 29.
    - Discontinuation or temporary suspension of infusions (for any reason).
    - Changes in white cell count (WBC) with differential, hemoglobin, platelets, creatinine, glucose, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and prothrombin time (PT) over time (analysis of lab values in addition to AEs noted above).

Exploratory Objective

The exploratory objective is to evaluate the virologic efficacy of different investigational therapeutics as compared to the control arm as assessed by:

- Percentage of subjects with SARS-CoV-2 detectable in (oropharyngeal) OP sample at Day 3, 5, 8, 11, 15, and 29.
- Quantitative SARS-CoV-2 virus in OP sample at Day 3, 5, 8, 11, 15, and 29.
- Development of resistance of SARS-CoV-2 in OP sample at Day 3, 5, 8, 11, 15, and 29.
- Quantitative SARS-CoV-2 virus in blood at Day 3, 5, 8, and 11.

3.2. Endpoints

Primary Endpoint

Time to recovery, where recovery is defined as clinical status in states 1, 2, or 3 of the 8-point ordinal scale, censored at Day 29.

- Clinical status of a subject (8-point ordinal scale) is defined below:

    8. Death;

    7. Hospitalized, on invasive mechanical ventilation or ECMO;

    6. Hospitalized, on non-invasive ventilation or high flow oxygen devices;

    5. Hospitalized, requiring supplemental oxygen;

4. Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise);

3. Hospitalized, not requiring supplemental oxygen - no longer requiring ongoing medical care;

2. Not hospitalized, limitation on activities and/or requiring home oxygen;

1. Not hospitalized, no limitations on activities

Secondary Endpoints

The key secondary endpoint is clinical status (8-point ordinal scale) on Day 15.

The other secondary endpoints are:

- Ordinal outcome assessed daily while hospitalized and on Days 15, 22, and 29.
- NEWS assessed daily while hospitalized and on Days 15 and 29.
- Days of supplemental oxygen (if applicable).
- Days of non-invasive ventilation/high-flow oxygen (if applicable).
- Days of invasive mechanical ventilation/ECMO (if applicable).
- Days of hospitalization.
- Date and cause of death (if applicable).
- SAEs.
- Grade 3 and 4 adverse events
- WBC with differential, hemoglobin, platelets, creatinine, glucose, total bilirubin, ALT, AST, and PT on Day 1; Days 3, 5, 8, and 11 (while hospitalized); and Days 15 and 29 (if attends in-person visit or still hospitalized).

Exploratory Endpoint

- Qualitative and quantitative polymerase chain reaction PCR for SARS-CoV-2 in OP swab on Day 1; Days 3, 5, 8, and 11 (while hospitalized); and Days 15 and 29 (if attends in-person visit or still hospitalized).
- Qualitative and quantitative PCR for SARS-CoV-2 in blood on Day 1; Days 3, 5, 8, and 11 (while hospitalized).

3.3. Study Definitions and Derived Variables

3.3.1. Baseline Value

For efficacy assessments, the baseline value will be defined as the last value obtained prior to randomization. For safety assessments, the baseline value will be defined as the last value obtained prior to the first dose of study product.

3.3.2. Recovery and Time to Recovery

The primary efficacy outcome measure is the time to recovery. Recovery will be defined as having a value of 1, 2, or 3 on the clinical status 8-point ordinal scale. The time to recovery will be defined as the elapsed time (in days) from randomization to the earliest day at which a subject reaches recovery. Note that since clinical status assessments are recorded as defined in Section 4.3, the day that is being assessed (not necessarily the day the response is collected) will be used to determine the timing of events. For example, a subject with a score of 5 recorded on Days 1 - 3 and a score of 3 recorded on Day 4 will have a time to recovery equal to 3 days. It is also possible that a subject has a clinical status score > 3 reported for a particular day but was subsequently discharged on the same day. For these scenarios where a subject is discharged with no reported clinical score of 1, 2, or 3 will be considered recovered at the time of discharge.

Any subjects that are lost to follow-up or terminated early prior to an observed recovery will be censored at the day of their last observed assessment. Subjects who complete follow-up but do not experience recovery will be censored at the day of their Day 29 visit. All deaths within Day 29 (and prior to recovery) will be considered censored at 28 days. Note that we do not expect many subjects to worsen after discharge.

However, we will evaluate whether any discharged subjects subsequently experience a worse clinical status and sensitivity analyses will be conducted accordingly. For these analyses, subjects who recover but are later re-admitted will not be considered a recovery but will instead be censored at 28 days. Sensitivity analyses will be performed where subjects who were crossover treated with remdesivir (per April 29, 2020 Protocol Administrative Letter) will be censored at the time of remdesivir treatment initiation. In addition, the analyses will be replicated where subjects who were unblinded, regardless of whether they received crossover treatment of remdesivir or not, will be censored at the time of unblinding.

3.3.3. Clinical Status At Specific Timepoints

The key secondary analyses include evaluation of the clinical status score at Day 15. For this outcome, Study Visit Day 15 is the timepoint of interest, not necessarily the actual study day. The score collected at the study visit corresponding to Day 15 will be used for this outcome. For analyses of this outcome, imputation of the clinical score may be performed following the rules described in Section 6.5.

Additional analyses are clinical status at Days 3, 5, 8, 11, 15, 22, and 29. As the with above, the scores that will be used are those collected at the study visits corresponding to those days.

Sensitivity analyses of the key secondary outcome will be performed where subjects who were unblinded and crossover treated with remdesivir prior to Day 15 will have their latest CSO score pre-remdesivir treatment carried forward to Day 15. A similar process will be used for the unblinding sensitivity analysis.

3.3.4. Time to Clinical Status Improvement

Additional analyses will evaluate the time to improvement of at least one point on the clinical status 8-point ordinal scale. That is, improvement will be defined as a decrease of at least one point on the 8-point scale compared to the baseline value (e.g. from 5 to 4; from 5 to 3) and the time to improvement will be defined as the elapsed time (in days) from randomization to the

earliest day of observed improvement. Note that since clinical status assessments are recorded as defined in Section 4.3, the day that is being assessed (not necessarily the day the response is collected) will be used to determine the timing of events.

For analyses of this outcome, imputation of the clinical score may be performed following the rules described in Section 6.5.

Any subjects that are lost to follow-up or terminated early prior to an observed improvement will be censored at the day of their last observed assessment. Subjects who complete follow-up but do not experience improvement will be censored at the day of their Day 29 visit. All deaths within Day 29 (and prior to improvement) will be considered censored at 28 days.

An alternative definition of improvement will also be used where improvement will be defined as a decrease of at least two points on the 8-point scale compared to the baseline value (e.g. from 5 to 3; from 5 to 2). The timing and censoring definitions will follow similarly to the above.

Sensitivity analyses will be performed where subjects who were unblinded and retreated with remdesivir will be censored at the time of remdesivir treatment initiation. A similar process will be used for the unblinding sensitivity analysis.

3.3.5. Time to Discharge or NEWS of ≤ 2

The time to discharge or NEWS of ≤ 2 will be defined as the elapsed time (in days) from baseline to the earliest day at which either of the following occur:

- Discharge from hospital
- Reported NEWS of ≤ 2 which is maintained for 24 hours

For the latter bullet, to meet this criterion, scores of ≤ 2 must be reported on consecutive study visits. The timing of the event will be set to the day of the second assessment.

All deaths that occur before discharge or before an observed NEWS of ≤ 2 will be considered censored at 28 days.

3.3.6. Days of Non-invasive ventilation/high-flow oxygen

Non-invasive ventilation/high flow-oxygen days will be defined as the number of days where the clinical status score is equal to 6. After discharge, the CRF question regarding days of ventilation will be used. The total number of days will be the sum of all reported days, regardless of whether the days occur consecutively or in disjoint intervals. See Section 6.5 for the plan for handling subjects who do not have data through Day 29 or die prior to Day 29.

3.3.7. Days of Ventilation/ECMO

Ventilator / ECMO days will be defined as the number of days where the clinical status score is equal to 7. After discharge, the CRF question regarding days of ventilation will be used. The total number of days will be the sum of all reported days, regardless of whether the days occur consecutively or in disjoint intervals. See Section 6.5 for the plan for handling subjects who do not have data through Day 29 or die prior to Day 29.

3.3.8. Days of Oxygen

Oxygen days will be defined as the number of days where the clinical status score is equal to 5, 6, or 7. After discharge, the CRF question regarding days of oxygenation will be used. The total number of days will be the sum of all reported days, regardless of whether the days occur consecutively or in disjoint intervals. See Section 6.5 for the plan for handling subjects who do not have data through Day 29 or die prior to Day 29.

3.3.9. Days of Hospitalization

Duration (in days) of hospitalization will be defined as the number of days from randomization to discharge. For the secondary outcome, duration of the initial hospitalization will be used only. See Section 6.5 for the plan for handling subjects who do not have data through Day 29 or die prior to Day 29.

3.3.10. Time to Death

For analysis of time to death, the time to death will be defined as the elapsed time (in days) from randomization (or treatment administration for the safety analysis) to death. Any subjects that are lost to follow-up or terminated early prior to death will be censored at the day of their last observed assessment or last captured event (e.g. the end date of an adverse event). If it is learned that a subject who terminated early had subsequently died prior to Day 29, then the subject will be classified as dead. Subjects who complete follow-up will be censored at the earliest of their Day 29 visit and (actual Day 29). Deaths that occur after Day 29 will be censored at Day 29.

Similar censoring methods will be used for the 14-day mortality analyses in that deaths that occur after Day 15 will be censored at Day 15 and subjects who are confirmed alive through Day 15 will be censored at Day 15. Subjects whose last observed assessment or last capture event (e.g. the end date of an adverse event) is prior to Day 15 will be censored at that last observed assessment/event.

Sensitivity analyses will be performed where subjects who were unblinded and retreated with remdesivir will be censored at the time of remdesivir treatment initiation. A similar process will be used for the unblinding sensitivity analysis.

3.3.11. Composite Endpoint of Death, SAEs, Severe AEs, Discontinuation of Study Infusions

A safety composite endpoint will be defined as the occurrence of at least one of the following through Day 29:

1. Death
2. SAE
3. Grade 3 or 4 AE

The time to this composite endpoint will be defined as the elapsed time (in days) from baseline to the earliest date of any of the events. Any subjects that are lost to follow-up or terminated early prior to experiencing any of the events will be censored at the day of their last observed assessment. Subjects who complete follow-up but do not experience any of the events will be censored at the day of their Day 29 visit.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This study is an adaptive, randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of novel therapeutic agents in hospitalized adults diagnosed with COVID-19. The study is a multicenter trial that will be conducted in up to approximately 100 sites globally. The study will compare different investigational therapeutic agents to a control arm. There will be interim monitoring to allow early stopping for futility, efficacy, or safety. If one therapy proves to be efficacious, then this treatment may become the control arm for comparison(s) with new experimental treatment(s). Any such change would be accompanied by an updated sample size. Because background standards of supportive care may evolve/improve over time as more is learned about successful management of COVID-19, comparisons of safety and efficacy will be based on data from concurrently randomized subjects. An independent Data and Safety Monitoring Board (DSMB) will actively monitor interim data to make recommendations about early study closure or changes to study arms.

Recruitment will continue until there are 400 subjects with a "recovered" status (per the primary objective). The primary analysis will be based the total number of subjects enrolled to achieve 400 recoveries. An additional analysis of the moderate severity subgroup (those with baseline status of "Hospitalized, requiring supplemental oxygen" or "Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care") is also of public health importance. Hence, enrollment will be permitted until the date of April 20, 2020 to ensure 400 recoveries and provide additional data about this important subgroup. With recent enrollment rates, the total sample size may be 600 to over 800.

If any additional therapeutic arms are added, the sample size will be recalculated.

Subjects will be assessed daily while hospitalized. If the subjects are discharged from the hospital, they will have a study visit at Days 15, 22, and 29. For discharged subjects, it is preferred that the Day 15 and 29 visits are in person to obtain safety laboratory tests and OP swab and blood (serum only) samples for secondary research as well as clinical outcome data. However, infection control or other restrictions may limit the ability of the subject to return to the clinic. In this case, these visits may be conducted by phone, and only clinical data will be obtained. The Day 22 visit does not have laboratory tests or collection of samples and may also be conducted by phone.

The primary outcome is time to recovery by Day 29. The primary analysis will include data from both severity groups using a stratified log-rank test. A key secondary outcome evaluates treatment-related improvements in the 8-point ordinal scale at Day 15. As little is known about the clinical course of COVID-19, an evaluation of the pooled (i.e., blinded to treatment assignment) proportion recovered will be used to gauge whether the targeted total number of subjects in the recovered categories of the ordinal scale will be achieved with the planned sample size. The analysis of the pilot data will be blinded, allowing for the pilot data to be included in subsequent analyses.

The study will randomize subjects 1:1 to placebo or investigational product. In absence of an established treatment, the use of placebo is justified. If additional arms are added to or dropped from the trial, randomization will proceed with an equal probability of assignment to each of the

remaining arms. Randomization will be stratified by site and severity (severe versus mild-moderate). See Section 4.2.3 for more information on randomization and stratification.

4.2. Selection of Study Population

Male and non-pregnant female adults ≥18 years of age or older with COVID-19 and who meet all eligibility criteria will be enrolled at up to approximately 100 clinical trial sites globally. The target population should reflect the community at large.

Inclusion Criteria

In order to be eligible to participate in this study, a patient must meet all of the following criteria:

1. Admitted to a hospital with symptoms suggestive of COVID-19 infection.
2. Subject (or legally authorized representative) provides informed consent prior to initiation of any study procedures.
3. Subject (or legally authorized representative) understands and agrees to comply with planned study procedures.
4. Male or non-pregnant female adult ≥18 years of age at time of enrollment.
5. Has laboratory-confirmed SARS-CoV-2 infection as determined by PCR or other commercial or public health assay in any specimen, as documented by either of the following:
    - PCR positive in sample collected < 72 hours prior to randomization; OR
    - PCR positive in sample collected ≥ 72 hours prior to randomization, documented inability to obtain a repeat sample (e.g. due to lack of testing supplies, limited testing capacity, results taking > 24 hours, etc.). AND progressive disease suggestive of ongoing SARS-CoV-2 infection.
6. Illness of any duration, and at least one of the following:
    - Radiographic infiltrates by imaging (chest x-ray, CT scan, etc.), OR
    - SpO2 ≤ 94% on room air, OR
    - Requiring supplemental oxygen, OR
    - Requiring mechanical ventilation.
7. Women of childbearing potential must agree to either abstinence or use at least one primary form of contraception not including hormonal contraception from the time of screening through Day 29.
8. Agrees to not participate in another clinical trial for the treatment of COVID-19 or SARS-CoV-2 through Day 29.

Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. ALT/AST > 5 times the upper limit of normal.

2. Estimated glomerular filtration rate (eGFR) < 30 ml/min (including patients receiving hemodialysis or hemofiltration).
3. Pregnancy or breast feeding.
4. Anticipated discharge from the hospital or transfer to another hospital which is not a study site within 72 hours.
5. Allergy to any study medication.

4.2.1. Treatments Administered

Subjects will receive either remdesivir through an IV in a loading (200 mg) dose followed by up to 9 maintenance (100 mg) doses or placebo at an equal volume at the same schedule.

4.2.2. Identity of Investigational Product(s)

Remdesivir is a single diastereomer monophosphoramidate prodrug designed for the intracellular delivery of a modified adenine nucleoside analog GS-441524. In addition to the active ingredient, the lyophilized formulation of remdesivir contains the following inactive ingredients: water for injection, sulfobutylether β-cyclodextrin sodium (SBECD), and hydrochloric acid and/or sodium hydroxide.

The supplied matching placebo lyophilized formulation is identical in physical appearance to the active lyophilized formulation and contains the same inactive ingredients. Due to limitations on placebo supplies, normal saline may be given at an equal volume as a placebo in place of the lyophilized formulation.

4.2.3. Method of Assigning Subjects to Treatment Groups (Randomization)

Enrollment and randomization of subjects is done online using the enrollment module of Advantage eClinical®.

Eligible subjects will be randomized and assigned in a 1:1 ratio to either remdesivir or placebo, with stratification by site and disease severity (Mild/Moderate disease or Severe disease). The randomization is based on a variable blocked scheme to provide an approximately balanced allocation to the treatment groups during the study. If arms are added or removed later in the study, randomization will continue in an equal allocation manner.

4.2.4. Selection of Doses in the Study

The dose of remdesivir used in this study will be the same dose that was has been used in the human Ebola clinical trials.

4.2.5. Selection and Timing of Dose for Each Subject

Each subject is randomly assigned to a treatment group as described in Section 4.2.3. Study product is given on Day 1 as a loading dose and daily up to 9 days after as maintenance doses. The dose should be given the same time each day (+/- 2 hours).

4.2.6. Blinding

The treatment will be prepared by the licensed pharmacist and administered by blinded study personnel or hospital staff. All follow-up safety and efficacy evaluations will be performed by blinded clinic staff.

The unblinded pharmacist at each site will refer to the Treatment Key provided for the trial by the SDCC to determine the treatment for the subjects. The pharmacist will maintain an open label code (provided by the SDCC) under locked/secured conditions and will follow the randomization code. Due to limitation on placebo supplies, normal saline may be given at an equal volume as a placebo in place of the lyophilized formulation. In this case, IV bags of study treatment (both Remdesivir and placebo) will be covered to mask the slight color difference between the Remdesivir solution and placebo to maintain the study blind.

After the public disclosure of the interim results, an unblinding procedure was added (per April 29, 2020 Protocol Administrative Letter) in which an investigator could unblind a subject and potentially initiate remdesivir treatment if one of the following criteria is met:

1. Potential remdesivir treatment, only for subjects meeting all of the following criteria:
    a. On study (i.e. have not completed the Day 29 visit)
    b. Hospitalized
    c. It is clinically indicated (i.e., those that are doing poorly)
2. Subject/LAR request, only for subjects meeting one of the following criteria:
    a. Subject is no longer hospitalized and has completed the study (on or after Day 29 visit), or
    b. After death.

4.2.7. Prior and Concomitant Therapy

Therapy prior to enrollment with any other experimental treatment or off-label use of marketed medications that are intended as specific treatment for COVID-10 or the SARS-CoV-2 infection (i.e., post-exposure prophylaxis) are permitted but must be discontinued on enrollment. There is no waiting period between discontinuation of these treatments and infusion of study product. However, these prior treatments and their end date should be documented on the Concomitant Medication form.

If the local standard of care per written policies or guidelines for treatment for COVID-19 or SARS-CoV-2 infection (i.e., not just an individual clinician decision) includes lopinavir/ritonavir (Kaletra), hydroxychloroquine or other agents (e.g. those targeting the host immune response), then continuing these during the study is permitted, but may require additional safety monitoring as determined by the treatment clinician. Additionally, there should be plans on how the concomitant drugs are stopped for additive toxicities (Protocol Section 6.1.4). If there are NO written policies or guidelines for local standard of care, concomitant use of any other experimental treatment or off-label use of marketed medications intended as specific treatment for COVID-10 or SARS-CoV-2 infection are prohibited. This includes medications that target the host immune response.

There is no available data on potential interactions between remdesivir and other anti-SARS-CoV investigational agents. Administering remdesivir concurrently with other agents may lead to antagonism or synergy or may have no effect.

Concomitant medications will be assessed only from 7 days prior to enrollment to Day 11 or upon discharge, whichever comes first.

Of note, acetaminophen is prohibited during the study through Day 15, even if clinically indicated for a subject.

4.2.8. Treatment Compliance

All subjects should receive a loading dose and up to 9 maintenance doses while hospitalized. If a subject is no longer hospitalized, then infusions will no longer be given. Any dose that is missed is not made up; the total course should not exceed 10 calendar days even if an infusion is missed. If the eGFR decreases to an eGFR < 25 ml/min, the study infusion should not be given on that day. The infusion may be resumed on the next day if the eGFR returns to ≥ 30 ml/min. If the subject's renal function worsens to the point that they require hemodialysis or hemofiltration, study product will be discontinued. If the ALT and/or AST increases to > 5 times upper limits of normal, the dose of remdesivir should be held and not be restarted until the ALT and AST ≤ 5 times upper limits of normal.

All doses will be recorded on the appropriate eCRF. Total volume and whether the IV was slowed or halted will be recorded to track compliance.

4.3. Efficacy and Safety Variables

For each study day while the patient is hospitalized, the clinical status will be recorded on an 8-point ordinal scale as follows:

- Day 1 – The clinical assessment at the time of randomization.
- Day 2 - The most severe assessment occurring at any time between randomization and midnight the day of randomization.
- Day 3+ - The most severe assessment occurring from midnight to midnight (00:00 to 23:59) of the prior day (e.g., the value recorded on Day 3 will be the most severe outcome that occurred on Day 2).

where the clinical status scale is defined as follows:

8. Death;

7. Hospitalized, on invasive mechanical ventilation or ECMO;

6. Hospitalized, on non-invasive ventilation or high flow oxygen devices;

5. Hospitalized, requiring supplemental oxygen;

4. Hospitalized, not requiring supplemental oxygen- requiring ongoing medical care (COVID-19 related or otherwise;

3. Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care;

2. Not hospitalized, limitation on activities;

1. Not hospitalized, no limitations on activities

A modified version of the ordinal scale will be used in sensitivity analyses of the primary and secondary outcomes. The modified scale will be as follows:

8. Death;

7. Hospitalized, on invasive mechanical ventilation or ECMO;

6. Hospitalized, on non-invasive ventilation or high flow oxygen devices;

5. Hospitalized, requiring supplemental oxygen;

4. Hospitalized, not requiring supplemental oxygen- requiring ongoing medical care (COVID-19 related or otherwise;

3. Not hospitalized, limitation on activities;

2. Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; or Not hospitalized, no limitations on activities.

That is, category 1 and 3 of the original scale will be combined into the lowest category.

NEWS has demonstrated an ability to discriminate subjects at risk of poor outcomes. This score is based on 7 clinical parameters (see Table 1). This should be evaluated at the first assessment of a given study day and prior to administration of study product. The 7 parameters can be obtained from the hospital chart using the last measurement prior to the time of assessment and a numeric score given for each parameter (e.g., a RR of 9 is one point, oxygen saturation of 92 is two points). This is recorded for the day obtained. i.e., on Day N, the Day N score is obtained and recorded as the Day N score.

Table 1: Categories of the NEWS scale.

PHYSIOLOGICAL PARAMETERS	3	2	1	0	1	2	3
Respiration Rate	≤8		9 - 11	12 - 20		21 - 24	≥25
Oxygen Saturations	≤91	92 - 93	94 - 95	≥96			
Any Supplemental Oxygen		Yes		No			
Temperature	≤35.0		35.1 - 36.0	36.1 - 38.0	38.1 - 39.0	≥39.1	
Systolic BP	≤90	91 - 100	101 - 110	111 - 219			≥220
Heart Rate	≤40		41 - 50	51 - 90	91 - 110	111 - 130	≥131
Level of Consciousness				A			V, P, or U

Oxygenation, Non-invasive ventilation/high flow oxygen, Invasive Mechanical Ventilation / extracorporeal membrane oxygenation (ECMO), hospitalization and mortality will be assessed using results of the 8-point ordinal scale and post discharge eCRF questions.

Safety will be assessed by the following:

- Cumulative incidence of serious adverse events (SAEs) through 28 days of follow-up.
- Cumulative incidence of Grade 3 and 4 AEs.
- Discontinuation or temporary suspension of infusions (for any reason)
- Changes in white cell count, absolute neutrophil count, hemoglobin, platelets, creatinine, glucose, total bilirubin, ALT, AST, and PT over time.

Clinical labs will be drawn on Days 1, 3, 5, 8, 11 and on Day 15 and 29 if the subject is able to return to the clinic or is still hospitalized.

Virologic efficacy is an exploratory endpoint and will be assessed by the following:

- Qualitative and quantitative PCR for SARS-CoV-2 in OP swab on Days 1; 3, 5, 8, 11 (while hospitalized); and Day 15 and 29 (if able to return to clinic or still hospitalized).
- Qualitative and quantitative PCR for SARS-CoV-2 in blood on Days 1; 3, 5, 8, 11 (while hospitalized).

The schedule of study procedures is provided in Table 2 below.

Table 2: Schedule of Study Procedures (from protocol version 3.0)

	Screen	*Baseline*	*Study Intervention Period*	*Follow-up Visits*			
Day +/- Window	**−1 or 1**	**1**	**Daily until hospital discharge**	**15[7] ± 2**	**22[7] ± 3**	**29[7] ± 3**	
ELIGIBILITY							
Informed consent	X						
Demographics & Medical History	X						
Targeted physical exam	X						
Review SARS-CoV-2 results	X						
STUDY INTERVENTION							
Randomization		X					
Administration of remdesivir or control		Daily until discharge or 10 days. No study product given after Day 10.					
STUDY PROCEDURES							
Vital signs including SpO_2		X[4]	Daily until discharge	X[7]	X[7]	X[7]	
Clinical data collection[1]		X[4]	Daily until discharge	X[7]	X[7]	X[7]	
Adverse event evaluation		X[4]	Daily until discharge	X[7]	X[7]	X[7]	
Concomitant medication review		X[4]	From Day -7 to Day 11				
SAFETY LABORATORY							
Safety hematology, chemistry and liver tests	X[2,3]	X[4,5,6]	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized[5,6]	X[7]		X[7]	
Pregnancy test for females of childbearing potential	X[2,3]						
RESEARCH LABORATORY							
Blood for plasma to test for PCR SARS-CoV-2		X[5]	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized				
Oropharyngeal swab[8]		X[5]	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized	X[7]		X[7]	
Blood for serum (for secondary research)		X[5]	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized	X[7]		X[7]	

Notes:
[1] Refer to Section 8.1 of the protocol for details of clinical data to be collected including ordinal score, NEWS, oxygen requirement, mechanical ventilator requirement, etc.
[2] Screening laboratory tests include: ALT, AST, creatinine (and calculate an estimated glomerular filtration rate (eGFR)), and pregnancy test.
[3] Laboratory tests performed in the 48 hours prior to enrollment will be accepted for determination of eligibility.
[4] Baseline assessments should be performed prior to randomization. Laboratory tests performed as part of routine clinical care in the 24 hours prior to first dose will be accepted for the baseline safety laboratory tests. Baseline may be the same as the screening laboratory tests.
[5]Safety laboratory tests include WBC with differential, hemoglobin, platelets, creatinine, glucose, total bilirubin, ALT, AST, and PT.
[6] Any laboratory tests performed as part of routine clinical care within the specified visit window can be used for safety laboratory testing. Window during the 10 days of dosing is ±1 day.
[7] In-person visits are preferred but recognizing quarantine and other factors may limit the subject's ability to return to the site for the visit. In this case, these visits may be conducted by phone

- If still hospitalized at Day 15 and 29 or returns to the site for an in-person visit: Clinical data, vital signs, safety laboratory tests, and research laboratory samples (OP swab and serum only) as able.
- If phone call only on Days 15 and 29 and all Day 22 visits: assess adverse events, clinical status (ordinal scale), readmission to a hospital, and mortality only.

[8] Oropharyngeal swabs are preferred, but if these are not obtainable, nasopharyngeal swabs may be substituted.

5. SAMPLE SIZE CONSIDERATIONS

Sample Size for Primary Analysis

The log-rank test will be used to compare treatment arms with respect to time to recovery. For the log-rank test, the two key determinants of power are the total number of events (i.e., recoveries) E and the treatment-to-control ratio of the rate of recovery. The number of events required for power $1-\beta$ to detect a recovery rate ratio of θ using a two-tailed test at alpha=0.05 is approximately

$$E = \frac{4\left(1.96 + z_\beta\right)^2}{\{\ln(\theta)\}^2},$$

where z_β is the $100(1-\beta)$th percentile of the standard normal distribution.

For 85% power, approximately 320 recoveries are required to detect a 40% increase in the rate of recovery ($\theta = 1.40$) from remdesivir. A recovery rate ratio of 1.40 is similar to, but slightly higher than the figure of 1.31 reported in Cao, Wang, Wen et al. (2020) for a lopinavir/ritonavir trial that used time to improvement by 2 categories as primary endpoint. A total of 400 recoveries is needed for a recovery ratio of 1.35 with 85% power. Table 3 provides power for various recovery rate ratios.

Table 3: Number of recoveries needed for 85% power assuming a type I error rate of 5% for various recovery ratios.

Recovery ratio (θ)	Number of recoveries needed for 85% power
1.25	723
1.30	523
1.35	400
1.40	318

Sample Size for Key Secondary Analysis

The key secondary endpoint of the effect of treatment on Clinical Status at Day 15 will be analyzed using a proportional odds model. In this model, the odds ratio represents the ratio of the odds of a given score or better for the two arms of the study. The sample size to detect a given odds ratio for 1:1 randomization using a 2-tailed test at level alpha (Whitehead 1993) is given by

$$\frac{12\left(z_{\alpha/2} + z_\beta\right)^2}{\theta^2\left(1 - \sum_{i=1}^{K} p_i^3\right)},$$

where θ is the log odds ratio, p_i is the overall probability (combined over both arms) of being in the ith category of the K ordinal outcomes, and $z_{\alpha/2}$ and z_β are the $1-\alpha/2$ and $1-\beta$ quantiles of the standard normal distribution.

Table 4 displays five scenarios considered for outcome probabilities in the placebo arm for sample size determination. There is significant uncertainty with these assumptions given the limited data available.

Table 5 shows a range of sample sizes for odds ratios ranging from 1.25 to 2.5 for 85% power. For 90% power, increase the sample size by 17%.

Table 6 displays the probabilities of being in different categories of the ordinal scale under an odds ratio of 1.75. A total sample size of 396 gives approximately 85% power to detect an odds ratio of 1.75 using a 2-tailed test at level $\alpha = 0.05$.

Table 4: Possible scenarios for the distribution of ordinal outcomes for the control arm at day 15.

	Anticipated	*Different scenarios for control arm*			
	Scenario 1	*Scenario 2*	*Scenario 3*	*Scenario 4*	*Scenario 5*
		more mild disease ⟷ *more severe disease*			
Severity Outcome	outcome (%)	*outcome (%)*	*outcome (%)*	*outcome (%)*	*outcome (%)*
Death	2	*1*	*1*	*2*	*3*
Hospitalized, on mechanical ventilation or ECMO	1	*1*	*1*	*1*	*3*
Hospitalized, on non-invasive ventilation or high flow oxygen devices	2	*1*	*1*	*2*	*4*
Hospitalized, requiring supplemental oxygen	7	*2*	*5*	*5*	*9*
Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise)	8	*5*	*7*	*17*	*23*
Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care	10	*9*	*10*	*20*	*25*
Not hospitalized, limitation on activities and/or requiring home oxygen	30	*36*	*35*	*25*	*18*
Not hospitalized, no limitations on activities	40	*45*	*40*	*28*	*15*

Table 5: Sample size calculations for scenarios in Table 2 for a two-arm study assuming 85% power, a two-sided type I error rate of 5%, and various true odds ratios.

True odds ratio	Total sample size				
	Scenario 1	*Scenario 2*	*Scenario 3*	*Scenario 4*	*Scenario 5*
1.25	2420	*2554*	*2459*	*2293*	*2252*
1.5	744	*786*	*755*	*700*	*684*
1.75	**396**	*419*	*401*	*370*	*360*
2.0	262	*277*	*265*	*243*	*236*
2.25	194	*206*	*196*	*179*	*173*
2.5	154	*163*	*155*	*141*	*136*

Table 6: Treatment ordinal outcome proportions under an odds ratio of 1.75 for five scenarios in Table 5 at day 15.

	Scenario 1		*Scenario 2*		*Scenario 3*		*Scenario 4*		*Scenario 5*	
	Anticipated		*more mild disease* ⟷ *more severe disease*							
Severity Outcome	Control %	Treatment %	*Control %*	*Treatment %*	*Control %*	*Treatment %*	*Control %*	*Treatment %*	*Control %*	*Treatment %*
Death	2	1.2	*1*	*0.6*	*1*	*0.6*	*2*	*1.2*	*3*	*1.7*
Hospitalized, on mechanical ventilation or ECMO	1	0.6	*1*	*0.6*	*1*	*0.6*	*1*	*0.6*	*3*	*1.8*
Hospitalized, on non-invasive ventilation or high flow oxygen devices	2	1.2	*1*	*0.6*	*1*	*0.6*	*2*	*1.2*	*4*	*2.5*
Hospitalized, requiring supplemental oxygen	7	4.3	*2*	*1.2*	*5*	*3.0*	*5*	*3.1*	*9*	*5.8*
Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise)	8	5.3	*5*	*3.1*	*7*	*4.4*	*17*	*11.5*	*23*	*17.4*
Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care;	10	7.2	*9*	*5.9*	*10*	*6.8*	*20*	*16.2*	*25*	*24.4*
Not hospitalized, limitation on activities and/or requiring home oxygen	30	26.5	*36*	*29.3*	*35*	*30.2*	*25*	*25.9*	*18*	*22.7*
Not hospitalized, no limitations on activities	40	53.8	*45*	*58.9*	*40*	*53.8*	*28*	*40.5*	*15*	*23.6*
Note that columns may not sum to exactly 100 due to rounding errors.										

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

This is a double-blind, placebo controlled randomized trial with a two-sided type I error rate of 0.05. Secondary hypotheses have been ordered according to relative importance. These will be described according to the appropriate summary statistics, e.g.

- Percentages/proportions/odds ratios for categorical data. For tabular summaries of percentages/proportions, the denominator (e.g. number of subjects with non-missing data) will be displayed.
- Means, median, and range for continuous data, median for time-to-event data.

Confidence intervals will be generated; for the primary analysis, the confidence level will take into account the group-sequential design of the trial (see Section 6.6 and Section 8.1) whereas 95% confidence intervals will be generated for secondary and exploratory outcomes. For hazard ratio and odds ratio estimates, Wald confidence intervals will be used. For other efficacy outcomes, Wilson or Score confidence intervals will be used. For safety outcomes, exact (e.g. Clopper-Pearson) confidence intervals will be used.

When calculating treatment effects (e.g. differences, hazard ratios, odds ratios) and when using treatment arm as a covariate in regression modeling, the placebo arm will be used as the reference group. For regression modeling that uses strata variables defined in Section 6.4, the first stratum listed for each variable in that section will be used as the reference group.

For the final time-to-event analyses, the following SAS pseudocode will be used to perform stratified analyses to generate stratum-specific median time to event estimates and confidence intervals, stratum-specific Kaplan-Meier curves, and to perform the log-rank test. For any unstratified analyses, code can be used after the removal of the `strata … ;` line.

```
proc lifetest data=dataset plots=(s);
   time TimeVariable * CensorVariable(1);
   strata StrataVariable;
   test TreatmentVariable;
run;
```

Note that the interim efficacy analyses will be performed using R. For all interim and final analyses, the software used will calculate the log rank statistic using the formula in Section 8.1.1.

To perform a stratified Cox proportional hazards model for the final analysis and generate the treatment arm hazard ratio along with its confidence interval, the following pseudocode will be used. For any unstratified analyses, code can be used after the removal of the `strata … ;` line and strata variable in the `class` statement.

```
proc phreg data=dataset;
   class StrataVariable(ref=StrataLabel) TreatmentVariable(ref=PlaceboLabel);
   model TimeVariable * CensorVariable(1) = TreatmentVariable;
   strata StrataVariable;
   hazardratio TreatmentVariable / diff=ref cl=Wald;
   ods output HazardRatios = HRest;
run;
```

The following SAS pseudocode will be used to perform the final proportional odds model with treatment arm and disease severity as covariates and to generate the treatment odds ratio, p-value, and predicted probabilities of the ordinal scale levels by treatment arm and disease severity:

```
proc logistic data=dataset
      plots(only)=effect(x=ResponseVariable
      sliceby=DiseaseSeverityVariable*TreatmentVariable individual connect);
   class DiseaseSeverityVariable(param=ref ref=Mild/ModerateLabel)
         TreatmentVariable(param=ref ref=PlaceboLabel);
   model ResponseVariable = TreatmentVariable StrataVariable;
   oddsratio TreatmentVariable;
   ods output OddsRatiosWald = ORest;
run;
```

6.2. Timing of Analyses

6.2.1. Early Sample Size Reassessment

A blinded estimate of the proportion of recoveries will be computed during the trial to evaluate whether the total sample size will provide the number of recoveries.

6.2.2. Interim analyses

A DSMB will monitor ongoing results to ensure patient well-being and safety as well as study integrity. The DSMB will be asked to recommend early termination or modification only when there is clear and substantial evidence of a treatment difference. More details about the interim analyses are described in Section 6.6.1 and Section 6.6.2 below as well as a separate guidance document for the DSMB.

6.2.3. Final Analyses

After the DSMB meeting on April 27, 2020, the interim results were provided to the sponsor and the interim analyses were performed again on an April 28, 2020 database freeze (unlocked dataset). The results of these analyses were made public on April 29, 2020. Subsequent to this, the plan for the final analyses (and corresponding datasets) was modified to the following:

- A preliminary analysis of the primary, key secondary, and major safety outcomes will be performed on unlocked, partially clean version of data and events that occurred up to April 28, 2020. This preliminary analysis dataset was used for the analyses and summaries included in the "Remdesivir for the Treatment of Covid-19 – Preliminary Report" article published in The New England Journal of Medicine on May 22, 2020 (DOI: 10.1056/NEJMoa2007764) and will be used for the preliminary report, whose summaries will coincide with the summaries provided in the article. This dataset will not be used for any further analyses apart from the preliminary report.
- A fully cleaned and locked version of data and events that occurred up to April 28, 2020 will be denoted as the "early analysis set". Section 7, Section 8, and Section 9 denote which summaries will be provided as part of this report, but will focus largely on primary outcome, key secondary outcome, and mortality.

- The final analyses of all outcomes and planned summaries/listings will be performed on the final full locked database and provided in an addendum to the final report. This is the fully cleaned and locked version of all data and events that occurred at any time during this trial and will be denoted as the "full analysis dataset".

6.3. Analysis Populations

Summaries and analysis of safety data will be presented for the Treated Population. Summaries and analysis of efficacy data will be presented for the intent-to-treat (ITT) population and a Treated population.

6.3.1. Intention-to-Treat (ITT) and Treated Populations

The intent-to-treat (ITT) population includes all subjects who were randomized.

The treated population includes all randomized subjects who received any study drug infusion, even if the infusion was halted or slowed.

For the main analyses of the primary and secondary efficacy outcomes, subjects in both populations will be classified by the treatment arm and disease severity stratum to which they were randomized. For safety, subgroup, and sensitivity analyses, subjects may be classified by their randomized or actual disease severity and placebo subjects who cross over and are treated with remdesivir will be censored/excluded as described in Section 3 and Section 8.

6.4. Covariates and Subgroups

Subgroup analyses for the main efficacy outcomes (i.e. the primary and key secondary analyses) will evaluate the treatment effect across the following subgroups:

- Geographic region:
  - US sites; Non-US sites
  - North American sites; Asian sites; European sites
- Duration of symptoms prior to enrollment
  - Quartiles
  - <= 10 days; > 10 days
  - <= Median; > Median
- Race (White; Black/African American; Asian; Other)
- Comorbidities
  - None; Any
  - None, One, Two or more
  - Obese; Non-Obese
- Age (<40; 40-64; 65 and older),
- Sex (Female; Male),

- Severity of disease
  - Randomization stratification: Mild/Moderate; Severe.
  - Actual disease severity at baseline: Mild/Moderate; Severe
  - Baseline ordinal scale category: 4; 5; 6; 7

Additionally, main analyses of all secondary outcomes will evaluate the treatment effect across the following subgroups:

- Duration of symptoms prior to enrollment (<= Median; > Median)
- Severity of disease
  - Randomization stratification: Mild/Moderate; Severe.
  - Actual disease severity at baseline: Mild/Moderate; Severe
  - Baseline ordinal scale category: 4; 5; 6; 7

The analyses of time to improvement will also be repeated in the subset of the randomized subjects who enrolled with a baseline clinical score of 7. As part of these analyses, the sensitivity analyses described in Section 3.3.4 regarding unblinded and retreated subjects will be performed in this subset, as well.

There will also be a sensitivity analysis of the primary, key secondary, and mortality outcomes to evaluate the effect of concomitant therapy including experimental treatment and off-label use of marketed medications that are intended as treatment for COVID-19 and are given to patient prior to and during the study. Subjects who report use of the following categories of therapies/treatments will be censored at the time of the earliest start date of any of the therapies/treatments:

- Protease inhibitors
- Polymerase inhibitors
- Other drugs used to treat COVID (off-label, experimental use)
- Corticosteroids
- Other anti-inflammatory drugs:
  - JAK inhibitors
  - Tyrosine kinase inhibitors
  - TNF inhibitors
  - Interleukin inhibitors
  - Interferons
  - Plasma
  - Immunoglobulins
  - T-cell therapies (anti-PD-1 monoclonal antibodies)

- Selective T-cell co-stimulation blockers
- B-cell therapies (CD 20 monoclonal antibodies)

For the recovery analyses, if a subject recovered prior to use of any of the medications/therapies, then the subject will still be counted as a recovery in the sensitivity analysis. For the analysis of the key secondary outcome, if a subject reports use of any of the medications/therapies prior to their Day 15 assessment, then the subject's last clinical status score prior to medication/therapy use will be used as their Day 15 outcome. For the mortality analyses, subjects will be censored at the time of medication/therapy initiation. Additional modeling of efficacy/mortality outcomes using restricted medication use as a covariate may be investigated in exploratory analyses.

In addition, the effect of treatment on the primary and key secondary efficacy outcomes will be explored via regression modeling controlling for age and duration of symptoms prior to enrollment as continuous covariates.

6.5. Missing Data

All attempts will be made to collect all data per protocol. Any data point that appears to be erroneous or inexplicable based on clinical judgment will be investigated as a possible outlier. If data points are identified as outliers, sensitivity analyses may be performed to examine the impact of including or excluding the outliers. Any substantive differences in these analyses will be reported.

For time to event outcomes, subjects who are lost to follow-up or terminate the study prior to Day 29 and prior to observing/experiencing the event will be censored at the time of their last observed assessment. Subjects who die prior to observing/experiencing the event will be censored at Day 29.

For the analysis of the key secondary outcome, subjects who are discharged but are subsequently re-admitted prior to Day 15 without a reported clinical score, their clinical score will be imputed at 7, which is the highest value for a hospitalized subject.

For the analyses of the secondary outcomes that involve clinical score (i.e. the key secondary outcome and time to improvement), if a subject is discharged from the hospital without a previously or concurrently reported clinical score of 1 or 2, then their clinical score at the time of discharge will be imputed as 2, which is the highest value for a non-hospitalized subject.

For the modified version of the ordinal score described in Section 4.3, if a subject is discharged from the hospital without a previously or concurrently reported clinical score of 2 or 3, then their clinical score at the time of discharge will be imputed as 3, which is the highest value for a non-hospitalized subject.

For the analyses of the secondary outcomes described in Section 3.3, the following imputation rules will be used for subjects who are lost to follow-up, terminate early from the study, or do not have further outcome data available after discharge for any reason:

- Days of Non-invasive ventilation/high-flow oxygen:
  - If the subject's clinical status scale is 6 at the last observed assessment, then the subject will be considered to be on non-invasive ventilation/high-flow oxygen

through Day 29. The endpoint will be total days when assessments are available plus all imputed days following the last observed assessment.

- If the subject is not on non-invasive ventilation/high-flow oxygen at the last observed assessment, then the subject will be considered to not be on non- invasive ventilation/high-flow oxygen for the remainder of follow-up. Thus, no additional imputed days will be added to the number of days recorded on available assessments.

- Days of ventilation/ECMO:
  - If the subject's clinical status scale is 7 at the last observed assessment, then the subject will be considered to be on ventilation/ECMO through Day 29. The endpoint will be total days when assessments are available plus all imputed days following the last observed assessment.
  - If the subject is not on ventilation/ECMO at the last observed assessment, then the subject will be considered to not be on ventilation/ECMO through Day 29. Thus, no additional imputed days will be added to the number of days recorded on available assessments.
- Days of Oxygen:
  - If the subject's clinical status score is 5, 6, or 7 at the last observed assessment, then the subject will be considered to be on oxygen through Day 29. The endpoint will be total days when assessments are available plus all imputed days following the last observed assessment.
  - If the subject is not on oxygen at the last observed assessment, then the subject will be considered to not be on oxygen through Day 29. Thus, no additional imputed days will be added to the number of days recorded on available assessments.
- Days of Hospitalization
  - If the subject is discharged and no further hospitalization data are available, then the subject will be assumed to not have been readmitted. Thus, no additional imputed days will be added to the number of days recorded on available assessments. If a subject dies while hospitalized, the number of days of hospitalization will be imputed as 28 days.

6.6. Interim Analyses and Data Monitoring

6.6.1. Interim Safety Analyses

Interim safety data will be available electronically in real time. No formal interim safety analyses are planned.

6.6.2. Interim Efficacy Review

Interim efficacy analyses will be conducted after at approximately 50% of total information. The information fraction at an interim analysis will be computed as $t = r/400$, where r is the number of recoveries by the time of the data freeze date for the interim analysis. The Lan-DeMets spending function analog of the O'Brien-Fleming boundary will be used to monitor the

primary endpoint using an overall two-sided type-I error rate of 0.05. Specifically, two one sided boundaries are constructed at level 0.025 using the spending function

$$\alpha^*(t) = 2[1 - \Phi\{2.241/t^{\frac{1}{2}}\}],$$

where Φ is the standard normal distribution function. Lan-DeMets software from the University of Wisconsin, now available in the R package `ldbounds', will be used to calculate boundaries.

Conditional power will be presented as an additional guide to the DSMB. Conditional power allows computation of the probability of obtaining a statistically significant result by the end of the trial given the data accumulated thus far, incorporating and assuming a hypothesized treatment effect (e.g., the treatment effect assumed for sample size determination) thereafter. If conditional power is less than 20% under the original trial assumptions, consideration should be given to stopping the trial.

The unblinded statistical team will prepare these closed reports for DSMB review and recommendations. Analyses will be presented with blinded codes for treatment arms to protect against the possibility that the DSMB report may fall into the wrong hands. A DSMB charter will further describe procedures and membership. An additional document on statistical issues related to monitoring will be provided to the DSMB prior to interim analyses.

Section 6.2.3 describes the plan for the final analyses of the early and final analysis sets.

6.7. Multicenter Studies

Data will be pooled across all clinical sites. Secondary analyses of the primary outcome will account for site via stratification by geographic region as noted in Section 6.4.

A sensitivity analysis of the primary outcome will be performed to assess the impact of individual sites on the observed treatment effect. Letting M be the total number of sites, the primary analysis will be repeated by excluding a single clinical site and performing the analyses on the remaining M-1 sites. This process will be repeated so that estimates are generated for each of the M-1 subset datasets. Presentations from these analyses are described in Section 8.1.2.

6.8. Multiple Comparisons/Multiplicity

There is only one primary outcome measure. The study utilizes a group-sequential design to control the overall type I error rate while allowing for formal interim analyses of the primary outcome measure (as described in Section 6.6 and Section 8.1). There is no planned adjustment for multiple comparisons in any secondary or exploratory analyses.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

A summary of the reasons that subjects were screened but not enrolled will be tabulated (Table 7).

The composition of analysis populations, including reasons for subject exclusion will be summarized by treatment group and disease severity (Table 8). The summaries will be provided for both the early and full analysis sets. A subject listing of analysis population eligibilities for the early and full analysis sets will be generated (Listing 1).

The disposition of subjects will be tabulated by treatment group, disease severity and site (Table 9). Study milestones included in the table will be the total number of subjects that were screened, randomized, received a loading dose, received all expected maintenance doses, completed all expected blood draws, completed Study Day 15 visit, completed Study Day 22 visit, and completed Study Day 29 visit. In addition, the number of subjects who were unblinded to their treatment and the number of subjects with crossover remdesivir treatment will be summarized. For the calculation of percentages, subjects who die will not be included in the denominators for visits/assessments beyond their death. The number of subjects unblinded and crossover treated at each site will also be summarized (Table 10).

Treatment compliance (number of subjects who had their required infusions halted/slowed and the number of subjects with missed doses) will be summarized by treatment group (Table 11).

A flowchart showing the disposition of study subjects, adapted from the Consort Statement [4] will be generated (Figure 1). This figure will present the number of subjects screened, randomized, lost to follow-up, and analyzed, by treatment group and disease severity. This figure will be generated for both the early and full analysis sets.

A listing of subjects who discontinued dosing or terminated study follow-up and the reason will be generated (Listing 2).

7.2. Protocol Deviations

Subject-specific protocol deviations will be summarized by the reason for the deviation, the deviation category, treatment group, disease severity and (separately) site for all subjects (Table 12 and Table 13). All subject-specific protocol deviations and non-subject specific protocol deviations will be included in listings (Listing 3 and Listing 4).

8. EFFICACY EVALUATION

8.1. Primary Efficacy Analysis

8.1.1. Primary Analyses

All the summaries described in this section will be generated for both the early and the full analysis sets.

The primary analysis uses the stratified log rank test to compare treatment to control through Day 29 with respect to time to recovery, as defined in Section 3.3. Stratification is based on mild/moderate versus severe disease at baseline. As noted in Section 3.3, all deaths within 29 days will be considered censored at Day 29 with respect to time to recovery. Conceptually, a death corresponds to an infinite time to recovery, but censoring at any time greater than or equal to Day 29 gives the same answer as censoring at Day 29; both correspond to giving deaths the worst rank.

Let MM and S denote the Mild/Moderate and Severe subgroups, respectively. The z-score associated with the stratified log rank test is

$$Z = \frac{\sum_{MM}(O_i - E_i) + \sum_{S}(O_i - E_i)}{\sqrt{\sum_{MM} V_i + \sum_{S} V_i}}.$$

The sums are over recovery times t_i in the mild/moderate and severe subgroups, O_i is the number of treatment arm participants recovering at time t_i, and E_i and V_i are the null expected value and variance of the number of treatment recoveries calculated using the hypergeometric distribution. Specifically, if n_{Ti} and n_{Ci} denote the numbers of patients `at risk' in the two arms in a given stratum at t_i, and r_i is the total number of recoveries at t_i, then $E_i = r_i n_{Ti}/(n_{Ti} + n_{Ci})$ and $V_i = r_i(n_i - r_i)n_{Ti}n_{Ci}/[n_i^2(n_i - 1)]$, where $n_i = n_{Ti} + n_{Ci}$. The $O_i, E_i, and\ V_i$ are computed separately within the mild/moderate and severe strata.

As noted in Section 6.6.2, to maintain an overall two-sided type-I error rate of 0.05, the Lan-DeMets spending function analog of the O'Brien-Fleming boundary will be used to derive the cumulative error spending and boundaries for the interim analyses.

The log rank test will be performed using the pseudocode provided in Section 6.1. The following pseudocode can be used to compute the bounds for the final analyses and compare to the calculated log-rank statistic. The `Boundaries` dataset will contain the updated boundaries calculated from the interim analyses using the actual information levels observed at the interim analyses.

```
data Parms_LogR;
   set logrankp(rename=(Statistic=Estimate));
   if Variable='TreatmentVariable';
   _Scale_='Score';
   _Stage_= AnalysisNumber;
   keep Variable _Scale_ _Stage_ StdErr Estimate;
run;

proc seqtest Boundary=Boundaries
             Parms(Testvar=TreatmentVariable)=Parms_LogR
```

```
            infoadj=prop
            boundaryscale=score
            ;
   ods output Test=FinalResults ParameterEstimates = LogHRest;
run;
```

If the trial is stopped at the interim analysis, then to derive the p-value, hazard ratio estimate, and confidence interval for the early and final analysis sets, stage-wise ordering of the sample space will be used [5]. The resulting p-value, median unbiased estimate, and confidence interval will be presented in the final report. If the trial is not stopped early, then the fixed sample estimates of the statistics using an alpha level of 5% will be computed and reported for the early and final analysis sets. The SAS pseudocode above provides estimates for the log hazard ratio and so the estimates will be exponentiated and reported.

The primary analysis will be performed in the ITT analysis population. The treatment hazard ratio estimate and confidence interval and p-value from the stratified log rank test will be presented (Table 14). The median time to event and 95% confidence interval will be summarized by treatment arm and disease severity. In addition, stratum-specific estimates of the treatment hazard ratio from Cox models run within each of the disease severity strata will be presented. Kaplan-Meier curves for each treatment arm will be presented, supplemented with the hazard ratio estimate, p-value, and the number of subjects at risk in each arm and severity stratum at Days 1, 3, 5, 7, 11, 15, 22, and 29 (Figure 2).

Subject listings of the ordinal scale results by day will be generated (Listing 5).

8.1.2. Supplemental and Sensitivity Analyses

For all supplemental and sensitivity analyses of the primary outcome, p-values will not be reported, and 95% confidence levels will be used for confidence interval estimates.

The primary analysis will be repeated in the Treated analysis population where subjects who are ineligible at baseline will be censored at enrollment. The tabular and graphical summaries described in the previous section will be replicated for this Treated analysis.

Sensitivity analyses will be performed using Cox proportional hazards models to estimate the hazard ratio. First, an ITT analysis will be performed in which subjects who die prior to recovering are treated as experiencing a competing risk in the Fine-Gray proportional hazards regression model. Second, a Cox model will be fit with binary indicators for treatment group and disease severity (Mild/Moderate vs. Severe [separate models for randomized stratum and actual stratum]) as well as a treatment * disease severity interaction term. The models will be fit to the ITT analysis population. The treatment group hazard ratios and CIs will be reported for both sets of models and the interaction term p-value will be reported for the interaction models.

The primary analysis will also be repeated using the other subgroups defined in Section 6.4 in place of disease severity. Each subgroup will be considered separately and the tabular and graphical summaries described in the previous section will be replicated for each subgroup. The tabular summary will also include results from an analysis of time to recovery controlling for age and duration of symptoms as continuous covariates. A forest plot will be generated to display the overall treatment hazard ratio estimate and CI from each of the within-stratum analyses (Figure 6). These analyses will be performed in the ITT and Treated populations.

In addition, a forest plot will be generated for the "leave one out" sensitivity analyses described in Section 6.7; hazard ratio estimates and CIs will be provided for each subgroup that leaves a single site out.

An additional sensitivity analysis will evaluate the effect of recoveries that were not sustained as indicated in Section 3.3.2.

As noted in Section 6.4, analyses that take into account concomitant medication will be performed. The primary analysis will be repeated, where subjects who take prohibited medications will be treated as treatment failures and will be censored at the time of medication use.

As noted in Section 3.3.2, an analysis of the primary outcome where placebo subjects has crossover treatment with remdesivir are censored at the time of retreatment will be performed. To support this sensitivity analysis, a summary of the clinical status scores assessed on the day of retreatment and the following day will be provided (Table 21). A spaghetti plot of the clinical status scores by study day will be provided for all placebo subjects, where the subjects who are retreated will be highlighted (Figure 9).

Two corroborative summaries will also be generated. A summary of the number and percentage of subjects in each treatment group who recovered (and are alive), did not recover (and are alive), and died by Day 29 will be summarized. The summary will also include the numbers and percentages, grouping deaths and non-recoveries together(Table 23). The summaries will also be provided by the duration of symptoms categorizations specified in Section 6.4.

Other censoring techniques and additional analyses of the primary outcome may be performed.

8.2. Secondary Efficacy Analyses

This section describes the planned analyses for the secondary efficacy outcome measures. Where applicable, refer to Section 6.1 for SAS pseudocode. Analyses of mortality will be described in Section 9.4.

Analyses of the key secondary outcome measure will be explored in the specified subgroups described in Section 6.4. Analyses of the other secondary outcome measures will be performed by treatment arm only and repeated for specified subgroups described in Section 6.4 and Section 6.7 via stratified analyses. As with the analyses described in Section 8.1.2, tabular summaries will follow the structure of the main tabular summaries planned for each outcome with the modification that stratified estimates will be provided in separate rows. Forest plots will display confidence intervals of outcomes/estimates across subgroups, where applicable.

All secondary efficacy analyses will be performed in the ITT population. Treated analyses will be explored to investigate consistency of results compared to the ITT analyses.

8.2.1. Ordinal Scale Outcomes (Key Secondary Outcome Measure)

For the analysis of the key secondary outcome measure, the distribution of the 8-point ordinal clinical status scale with 8 categories at Study Visit Day 15 (not necessarily actual study day 15), the outcome will be analyzed using a proportional odds model with treatment arm and disease severity as covariates. The treatment odds ratio estimated from the model will be presented along

with the p-value (Table 24). Predicted individual probabilities of scale levels by treatment arm and disease severity will be summarized graphically (Figure 10).

As noted in Section 3.3, sensitivity analyses will be performed to account for subjects who are unblinded as well as placebo subjects who are unblinded and crossover treated with remdesivir. These analyses will be performed in the ITT population.

Multiple supplemental analysis of this key secondary outcome will be performed. Time to improvement by at least one category in the clinical status 8-point scale (see Section 3.3). The log rank test will be performed using a Cox proportional hazards model to test whether the curves differ between treatment arms. The median time to event and CI in each treatment group will be summarized along with the treatment hazard ratio estimate and log rank p-value (Table 26). Differences in time-to-event endpoints by treatment arm will be summarized with Kaplan-Meier curves (Figure 11). Number at risk, hazard ratio and log rank p-values will be presented on the figures. The analyses (and tabular and graphical summaries) will be repeated using the outcome of time to improvement in two categories of the ordinal scale defined in Section 3.3. Both time to improvement (one and two categories) analyses will be repeated using the censoring plan described in Section 3.3 for subjects who are retreated with remdesivir (Table 28). In addition, a subgroup analysis time to improvement among subjects enrolled with a clinical score of 7 will be performed using the retreatment censoring plan (Table 29).

The above analyses will be repeated with the following modification to the ordinal scale described in Section 4.3 (Table 29).

The number and proportion of subjects along with 95% confidence intervals by category of clinical status will be presented by treatment arm at Study Visit (not necessarily actual) Days 1, 3, 5, 8, 11, 15 and 29 (Table 34). A figure will present stacked bar charts by day with side by side bars for each treatment arm (Figure 13). Histograms will be generated to display the ordinal scale value distributions over time in each treatment group (Figure 14).

8.2.2. NEWS

The median time to discharge or to a NEWS of ≤ 2 and CI will be summarized by treatment group (Table 36). The hazard ratio and log rank p-values will be provided with the summaries. Differences in time-to-event endpoints by treatment arm will be summarized with Kaplan-Meier curves. Number at risk, hazard ratio and log rank p-values will be included on the figures (Figure 15).

The mean, standard deviation (SD), median, minimum, and maximum NEWS at Baseline and Study Visit (not necessarily actual) Days 3, 5, 8, 11, 15 and 29 will be presented by treatment arm as well as change from baseline at each post-Day 1 visit (Table 39). A figure with mean and SD over time will also be presented by treatment arm (Figure 16).

Subject listings of NEWS responses (overall and individual components) by day will be generated (Listing 6).

8.2.3. Days of Oxygenation

Duration of oxygenation days will be summarized in a table using medians and quartiles by treatment arm (Table 41). This will only include subjects in category 5, 6, or 7 at enrollment. Analyses will be performed in the ITT population, Treated population, and a subset of the

Treated population of treated subjects only as subjects who are not treated are terminated from the study immediately and are included in the ITT/Treated analyses with a count of 1 day. Bee swarm plots of oxygen days by treatment arm will be generated, where subject whose days are imputed to the maximum of 28 days due to death are grouped separately from subjects who do not die (Figure 17).

8.2.4. Incidence of New Oxygen use

The incidence and duration of new oxygen use will be analyzed by treatment arm. This will only include subjects in category 4 at enrollment. New use will be identified by a post-enrollment score of at least 5; the number of subjects reporting new use and the incidence rate (and CI) will be reported.

8.2.5. Days of Non-Invasive Ventilation/High-Flow Oxygen

Duration of non-invasive ventilation/high flow oxygen days will be summarized in a table using medians and quartiles by treatment arm. This will only include subjects in category 6 or 7 at enrollment. Analyses will be performed in the ITT population, Treated population, and a subset of the Treated population of treated subjects only as subjects who are not treated are terminated from the study immediately and are included in the ITT/Treated analyses with a count of 1 day. Bee swarm plots of non-invasive ventilation/high flow oxygen days by treatment arm will be generated, where subject whose days are imputed to the maximum of 28 days due to death are grouped separately from subjects who do not die.

8.2.6. Incidence of New Non-Invasive Ventilation/High-Flow Oxygen

The incidence and duration of new Non-Invasive Ventilation/High-Flow Oxygen use will be analyzed by treatment arm. This will only include subjects in category 4 or 5 at enrollment. The incidence of new oxygen use will be analyzed by treatment arm. This will only include subjects in category 4 at enrollment. New use will be identified by a post-enrollment score of at least 6. The number of subjects reporting new use and the incidence rate (and CI) will be reported.

8.2.7. Days of Invasive Mechanical Ventilation/ECMO

Duration of invasive Mechanical Ventilation/ECMO days will be summarized in a table using medians and quartiles by treatment arm. This will only include subjects in category 7 at enrollment. Analyses will be performed in the ITT population, Treated population, and a subset of the Treated population of treated subjects only as subjects who are not treated are terminated from the study immediately and are included in the ITT/Treated analyses with a count of 1 day. Bee swarm plots of invasive Mechanical Ventilation/ECMO days, and days hospitalized by treatment arm will be generated, where subject whose days are imputed to the maximum of 28 days due to death are grouped separately from subjects who do not die.

8.2.8. Incidence of New Non-Invasive Ventilation/High-Flow Oxygen

The incidence and duration of new Non-Invasive Ventilation/High-Flow Oxygen use will be analyzed by treatment arm. This will only include subjects in category 4, 5, or 6 at enrollment. The incidence of new oxygen use will be analyzed by treatment arm. This will only include

subjects in category 4 at enrollment. New use will be identified by a post-enrollment score of 7. The number of subjects reporting new use and the incidence rate (and CI) will be reported.

8.2.9. Days of Hospitalization

Duration of hospitalization days will be summarized in a table using medians and quartiles by treatment arm (Table 47). Incidence of readmittance will also be summarized. Analyses will be performed in the ITT population, Treated population, and a subset of the Treated population of treated subjects only as subjects who are not treated are terminated from the study immediately and are included in the ITT/Treated analyses with a count of 1 day. Bee swarm plots of days hospitalized by treatment arm will be generated, where subject whose days are imputed to the maximum of 28 days due to death are grouped separately from subjects who do not die.

8.3. Exploratory Efficacy Analyses

Analyses of exploratory outcome measures are not covered in this SAP.

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, height, weight, BMI, ethnicity, and race will be presented by treatment group as well as geographic region, duration of symptoms prior to enrollment, and disease severity (Table 49 and Table 50). Ethnicity will be categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option. Both demographic tables will be repeated to assess baseline differences between remdesivir subjects, placebo subjects who are not retreated with remdesivir, and placebo subjects who are retreated with remdesivir (Table 51 and Table 52).

Individual subject listings will be presented for all demographics and baseline characteristics (Listing 7).

9.1.1. Prior and Concurrent Medical Conditions

Focused medical history is obtained at the screening visit that includes the following:

- Day of onset of COVID-19 symptoms
- History of chronic medical conditions related to inclusion and exclusion criteria
- Medication allergies
- Review medications and therapies for this current illness.

Medical history is limited to the following conditions: asthma, cancer, chronic kidney disease, chronic liver disease, chronic oxygen requirement, chronic respiratory disease, congestive heart failure, coronary artery disease, diabetes I and II, hypertension, immune deficiency, and obesity. All current illnesses and past pre-existing medical conditions will be MedDRA® coded using MedDRA dictionary version 22.0 or higher. Summaries of subjects' pre-existing medical conditions will be presented by treatment group (Table 53).

Individual subject listings will be presented for all medical conditions (Listing 8).

9.1.2. Prior and Concomitant Medications

Medication history (concomitant medications) includes a review of all current medications and medications taken within 7 days prior to enrollment through approximately Day 11 or early termination (if Day 11), whichever occurs first.

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by WHO Drug Terms 2 and 3 and treatment group (Table 54). Summaries of overall use of prohibited medications/therapies listed in Section 6.4 as well as use by select study days will also be generated (Table 55 and Table 56).

Individual subject listings will be presented for all concomitant medications (Listing 9).

9.2. Measurements of Treatment Compliance

The subject disposition table will summarize the number of subjects that were screened, randomized, received a loading dose, received all maintenance doses, each maintenance dose, completed all blood draws, and completed Study Day 29 visit. In addition, the number of subjects with halted, slowed, or missed doses will be summarized by treatment arm (See Section 7).

Individual subject listings will be presented for all subjects who discontinued dosing (Listing 2).

Individual subject listings will be presented for all subjects who missed, halted or slowed any doses (Listing 10).

9.3. Adverse Events

For the calculation of incidence of adverse events (i.e., on a per subject basis), each subject will only be counted once and any repetitions of adverse events within a subject will be ignored; the denominator will be the number of subjects in the Treated population. All adverse events reported will be included in the summaries and analyses.

An overall summary by treatment arm and disease severity of adverse events is presented that includes subjects with at least one event, at least one related event, at least one SAE, at least one related SAE and at least one AE leading to early termination (Table 57).

Adverse events occurring in 5% of subjects (by MedDRA preferred term) in any treatment group will be presented (Table 58).

The proportion of subjects reporting at least one adverse event will be summarized by MedDRA system organ class and preferred term for each treatment arm, disease severity and overall. Denominators for percentages are the number of subjects in the Treated population.

The following summaries for adverse events will be presented by MedDRA system organ class, preferred term, disease severity and treatment group:

- Subject listing of non-serious adverse events (Listing 11);
- Bar chart of non-serious related adverse events by severity and MedDRA system organ class (Figure 21);
- Bar chart of non-serious related adverse events by maximum severity and MedDRA system organ class (Figure 22);

All the summaries described in this section will be generated for both the early and the full analysis sets.

9.4. Deaths, Serious Adverse Events and other Significant Adverse Events

A listing of death and other serious adverse events will be presented, including Subject ID, treatment group, Adverse Event Description, Associated Dose Number, Number of Days Post Dose (Duration), Number of Days Post Dose the Event Became Serious, Reason Reported as an SAE, Severity, Relationship to Treatment, Alternate Etiology if not Related, Action Taken with

Study Treatment, Subject Discontinuation, Outcome, MedDRA SOC, and MedDRA PT (Listing 12 and Listing 13).

The number of subjects who die by Day 15 and Day 29 will be presented by treatment arm. The 14- and 28-day crude mortality rate, which will use the number of subjects in the treatment group and analysis population as the denominator, will be presented (Table 59). The analysis will be repeated censoring placebo subjects who were retreated with remdesivir at the time of retreatment.

Mortality through Day 15 and 29 will also be analyzed as a time to event endpoint (see Section 3.3). A table will present median time to event along with 95% confidence intervals overall for each treatment arm along with the hazard ratio estimate and log rank p-values (Table 61). Differences in time-to-event endpoints by treatment will be summarized with Kaplan-Meier curves (Figure 23). Analyses of mortality will be performed in the ITT and the Treated analysis populations and will be performed on both the early and the full analysis sets.

The ITT tabular summaries will be repeated censoring placebo subjects who were retreated with remdesivir at the time of retreatment. Similarly, the summaries will be repeated censoring subjects who were unblinded at the time of unblinding.

Rates of Grade 3 and 4 AE occurrence will be compared between treatment arms using Barnard's exact test and presented (Table 63). Rates of SAE occurrence will also be compared between treatment arms using Barnard's exact test and presented. Further, the composite endpoint of the occurrence of death, SAE, or Grade 3 or 4 AE described in Section 3.3 will be analyzed as a time to event outcome. A table will present median time to event along with 95% confidence intervals overall for each treatment arm along with the hazard ratio estimate and log rank p-values (Table 64). Differences in time-to-event endpoints by treatment will be summarized with Kaplan-Meier curves (Figure 24).

9.5. Pregnancies

For any subjects in the Treated population who become pregnant during the study, every attempt will be made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. Note that the CSR will not be delayed to wait for outcomes of any pregnancies; an addendum to the CSR would be provided in such a scenario. A set of listings of pregnancies and outcomes will be presented (Listing 14, Listing 15, Listing 16 , Listing 17, Listing 18).

9.6. Clinical Laboratory Evaluations

Clinical safety laboratory adverse events are collected Day 1, 3, 5, 8, 11 and Day 15 and 29 if able to return to clinic or still hospitalized. Parameters evaluated include white blood cell count, absolute neutrophil count, eGFR, platelet count, hemoglobin concentration, creatinine, glucose, total bilirubin, ALT, AST, and PT/INR. Laboratory safety parameters will be graded according to the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, version 2.1 (July 2017).

The distribution of Grade 3 and 4 chemistry and hematology laboratory results by maximum severity, time point, disease severity and treatment group will be presented (Table 65).

Descriptive statistics including mean, median, standard deviation, maximum, and minimum values and change from baseline by time point, for all and each chemistry and hematology laboratory parameter will be summarized by disease severity and treatment arm (Table 66). Changes in chemistry and hematology laboratory values will be presented in line graphs over time with mean and SD plotted by disease severity and treatment arm (Figure 25).

Listings will provide a complete listing of individual chemistry and hematology laboratory results with applicable reference ranges (Listing 19).

9.7. Vital Signs and Physical Evaluations

Vital sign measurements include pulse, systolic blood pressure, respiratory rate, SpO_2 and oral temperature. Vital signs were assessed as part of the NEW score (assessed daily while hospitalized and on Day 15) and will be listed in Listing 6.

Targeted Physical examinations are performed at Day 1 and are performed post-baseline only when needed to evaluate possible adverse events. At the screening visit, the targeted physical examination is focused on lung auscultation. Physical exam findings per subject will be detailed in a listing (Listing 20).

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. Concomitant medication use will be presented in a subject listing (Listing 20). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code, disease severity and treatment group for the Treated population (Table 54). The summaries will be repeated for the subgroups defined in Section 6.4.

9.9. Other Safety Measures

No additional safety analyses are planned.

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

Not applicable.

12. OTHER ANALYSES

Not applicable.

13. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to 3 decimal places; p-values less than 0.0005 will be reported as "<0.001" and p-values greater than 0.9995 will be reported as ">0.999".

The mean, standard deviation, and other statistics will be reported to1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data.

Proportions will be presented as 2 decimal places; values greater than zero but <0.005 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than zero but < 0.5% will be presented as "<1"; values greater than 99.5% but less than 100% will be reported as >99.

Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

14. TECHNICAL DETAILS

SAS version 9.4 or above, or R language and environment for statistical computing 3.6.1 or above, will be used to generate all tables, figures and listings.

15. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

The following are the changes in the SAP from version 2.0 to 3.0:

Throughout document/multiple sections:

- Typos and errors were fixed and clarifications to text were added where necessary.
- This plan was updated to describe the two sets of final analyses to be performed: the early data set and the final data set. Language was added to Section 6.2, Section 7, Section 8, and Section 9 regarding which summaries would be provided for both the early and the final data sets.
- The Treated analysis population was added which replaced the MITT and safety analysis populations.
- Sensitivity analyses that explore placebo subjects who were unblinded and treated with remdesivir while on study were added.

Section 2.1:

- A description of the interim analysis and public disclosure of interim results was added.

Section 3.3.1:

- It was clarified that for efficacy data, the last value obtained prior to randomization would be defined as the baseline value, whereas for safety data, the last value obtained prior to the first received dose would be the baseline value.

Section 3.3.3:

- It was clarified that for clinical status analysis at specified days, the data used for those analyses would be the data collected at the study visit corresponding to that day and not necessarily the actual study day. Corresponding language was updated throughout Section 8.

Section 3.3.10:

- The definition of time to death by Study Day 15 and 29 was clarified and a description of the censoring plan was added.

Section 4:

- Language was updated throughout to match the language in version 3.0 of the protocol.

Section 4.3:

- Language describing the modified ordinal scale was moved from Section 8 to this section.

Section 6.4:

- Additional subgroups to be explored were added.
- The specific list of restricted concomitant therapies/treatments to be explored in the sensitivity analyses was added.

Section 6.5:

- Details of imputation methods that were left out of the previous version of the SAP were added.

Section 6.7:

- An additional analysis to explore the effect of clinical site on the primary outcome was added. Corresponding language was added to Section 8.1.2.

Section 8.1.2:

- The description of the analyses that control for age and duration of symptoms was moved from Section 6.4 to this section.

Section 9.1.1:

- The section was fixed to denote that summaries would be provided for each of the solicited comorbidities and summaries would not be provided by MedDRA SOC/PT.

Section 9.3:

- As no solicited adverse events are not collected, the term "unsolicited" was removed throughout the section and corresponding shells.

Section 9.4:

- It was clarified that the mortality rate to be estimated and reported will be the crude mortality rate that uses the total number of subjects in the analysis population as the denominator.
- It was clarified that mortality estimates would be provided for both the ITT and treated analysis populations.
- The time-to-event analysis of death by Day 15 was erroneously left out of the plan; this analysis was added.

Section 9.6:

- Duplicative summaries were removed.

Section 9.7:

- As vital signs will be listed as part of the NEWS listing, the separate vital signs listing was removed.

Table, figure, and listing shells:

- Table and figure shells were provided for planned sensitivity analyses.
- Tables and listings that provided duplicative results/summaries were removed from the list of shells.
- Where possible, tables were combined in order to present related summaries together (e.g. the within-stratum hazard ratio estimates for the time to recovery analyses were inserted into the primary time to recovery tables and the separate within-stratum hazard ratio tables were removed).

- Multiple table, figure, and listing shells and/or their programming notes were modified to fix errors, provide clarifications, or provide a more concise or more appropriate presentation of the results.

16. REFERENCES

1. Schoenfeld, D. 1981. The asymptotic properties of nonparametric tests for comparing survival distributions. Biometrika. 68 (1): 316–319.
2. Cao, Wang, Wen et al. 2020. A trial of lopinavir–ritonavir in adults hospitalized with severe covid-19. New DOI: 10.1056/NEJMoa2001282.
3. Whitehead, J. 1993. Sample size calculations for ordered categorical data. Statistics in Medicine 12, 2257-2271.
4. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15):2006-2007.
5. Jennison C., Turnbull B.W. 2000. Group sequential methods with applications to clinical trials. Chapman & Hall, Boca Raton.

17. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3.

The formatting of the final version of a table, figure, or listing may differ from what is presented in the shell or the presentation of the results may be changed, however the key content will remain unchanged. Additional summaries/data points may be included in the final version of a table, figure, or listing, as well. Additional tables, figures, and listings may be generated to supplement the planned output.

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

Table 7: Ineligibility Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
All Subjects	Total number of subjects failing any eligibility criterion or were eligible but not enrolled	x	100
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	xx
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx
Eligible but Not Enrolled		x	xx

[a] More than one criterion may be marked per subject.
[b] Denominator for percentages is the total number of screen failures.

Programming Notes;

Protocol Version 3.0 included an additional inclusion criteria; footnote the addition of the inclusion/exclusion criteria based on protocol version and specify date it occurred and how many subjects were under the previous version of the criteria.

Subjects who are eligible but not enrolled will be counted in the denominator.

Table 8: Analysis Population Eligibilities by Treatment Group and Disease Severity

		Remdesivir (N=X)				Placebo (N=X)				All Subjects (N=X)			
Analysis Population	Inclusion / Reason for Exclusion	Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)	
		n	%	n	%	%	n	n	%	n	%	n	%
Intention-to-Treat Population	Included in Population	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx
Treated Population	Included for Population	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx
	Excluded from Population	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx
	Did Not Receive at least one Infusion	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx
N = Number of subjects randomized to the specified arm/disease severity stratum													

Table 9: Subject Disposition by Treatment Group and Disease Severity

	Remdesivir (N=X)				Placebo (N=X)				All Subjects (N=X)			
	Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)	
Subject Disposition	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Randomized	x	100	x	100	x	100	x	100	x	100	x	100
Received Loading Dose	x	xx	x	xx	x	Xx	x	xx	x	xx	x	xx
Completed All Blood Draws	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed All OP swab collections	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 8)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 11)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 15)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 22)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 29)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Unblinded during follow-up	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Retreated with Remdesivir during follow-up	-	-	-	-	x	xx	x	xx	x	xx	x	xx
N= Number of subjects enrolled												

Programming Notes:

To count a subject as completing all blood draws, a subject had to have the following questions from the visit CRFs answered as a Yes or NA (not required) up through their discharge/death:

- Was blood collected for hematology, chemistry, and/or liver tests?
- Was blood drawn for PCR assays?

  Note: in LB – there should be a result in LBSTRESN for each visit or LBSTAT=NOT DONE and LBREASND = Not required.

To count a subject as completing all OP swab collections, a subject had to have the following question from the visit CRFs answered as a Yes or N/A (not required) up through their discharge/death.

- Was oropharyngeal swab collected?
- Was a swab collected for viral load and/or shedding

To count a subject for each Study Day, the subject had to complete the visit for that day. Study Day 8 = VISITNUM=108, Study Day 11 = VISITNUM=111, Study Day 15 = VISITNUM=115, Study Day 22 = VISITNUM=122, Study Day 29 = VISITNUM=129

Table 10: Subject Unblinding and Crossover Treatment by Site

Site	Number of Subjects Unblinded	Number of Subjects Crossover Treated
Site 1	x	x
Site 2	x	x
Site 3	x	x
Site 4	x	x
Site 5	x	x
…	…	…

Programming Notes: Only sites with at least one unblinded subject will be included in the table.

Table 11: Treatment Compliance by Treatment Group

Disposition	Remdesivir (N=X)			Placebo (N=X)			All Subjects (N=X)			Proportion Difference	
	n	%	95%CI[a]	n	%	95%CI	n	%	95%CI	%	95%CI
Received Loading Dose	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x	x	x.x, x.x
Completed all 10 Infusions	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x	x	x.x, x.x
Completed less than 10 Infusions due to Discharge	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x	x	x.x, x.x
Completed less than 10 Infusions due to Death	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x	x	x.x, x.x
Had Any Infusions Halted or Slowed	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x	x	x.x, x.x
Missed Any Maintenance Dose	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x	x	x.x, x.x

N = Number of subject enrolled
A required infusion is counted as complete even if it was halted or slowed. A required full infusion is counted as completed as long as it was not halted nor slowed.
95% CI for proportions obtained by Clopper-Pearson
95% CI for difference in proportions obtained by the exact method

Programming Notes:

Received Loading Dose: Subjects received the first treatment: EC.ECTPT = DOSE 1, EC.ECPSTRG=200, ECADJ is missing.

Had any infusions halted or slowed: EC.ECADJ is not missing through day 10 or through discharge from hospital or death.

Missed any maintenance dose: EC.ECOCCUR=N through day 10 or through discharge from hospital or death.

95% CI for proportions obtained by Clopper-Pearson:

```
proc freq;
      Table treatment*analysisvariable / binomial;
      ods output binomialcls=outputdsn;
run;
```

95% CI for difference in proportions obtained by the exact method:

```
proc freq;
      Table treatment*analysisvariable / riskdiff (cl=exact);
run;
```

Table 12: Distribution of Protocol Deviations by Category, Type, Treatment Group, and Disease Severity

Category	Deviation Type	Remdesivir (N=X)				Placebo (N=X)				All Subjects (N=X)			
		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)	
		# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x	x	x	x	x	x	x
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x
	ICF not signed prior to study procedures	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x
Treatment administration schedule	Any type	x	x	x	x	x	x	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x	x	x	x
	Missed treatment administration	x	x	x	x	x	x	x	x	x	x	x	x
	Delayed treatment administration	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x
Protocol procedure/assessment	Any type	x	x	x	x	x	x	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x	x	x	x	x	x	x
	Blood not collected	x	x	x	x	x	x	x	x	x	x	x	x
	Oropharyngeal swab not collected	x	x	x	x	x	x	x	x	x	x	x	x
	Other specimen not collected	x	x	x	x	x	x	x	x	x	x	x	x
	Specimen result not obtained	x	x	x	x	x	x	x	x	x	x	x	x
	Required procedure not conducted	x	x	x	x	x	x	x	x	x	x	x	x

Category	Deviation Type	Remdesivir (N=X)				Placebo (N=X)				All Subjects (N=X)			
		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)	
		# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x
Treatment administration	Any type	x	x	x	x	x	x	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x
Blinding policy/procedure	Any type	x	x	x	x	x	x	x	x	x	x	x	x
	Treatment unblinded	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x
N = number of subjects enrolled													

Tables with similar format:

Table 13: Distribution of Protocol Deviations by Category, Type, and Site

Table 14: Time to Recovery by Treatment Group and Disease Severity

Analysis Population	Treatment Group	Disease Severity	n	Median Time to Recovery		HR		P-value
				Estimate	95% CI	Estimate	95% CI	
ITT Population	**Remdesivir (N=X)**	**Mild/Moderate**	x	x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Placebo (N=X)		x	x.x	x.x, x.x			
	Remdesivir (N=X)	**Severe**	x	x.x	x.x, x.x	x.x	x.x, x.x	
	Placebo (N=X)		x	x.x	x.x, x.x			
	Remdesivir (N=X)	**Any Severity**	x	x.x	x.x, x.x	x.x	x.x, x.x	
	Placebo (N=X)		x	x.x	x.x, x.x			
Repeat for the Treated Population.								

N= Number of subjects in the specified treatment group, disease severity, and analysis population.
n = Number of recovered subjects.
HR for the 'Any Severity' group is the hazard ratio from the stratified Cox Model.
P-value calculated using the stratified log-rank test

Tables with similar format:

Table 15: Time to Recovery by Treatment Group and Disease Severity: Fine-Gray and Interaction Modeling

Table 16: Time to Recovery by Treatment Group within Subgroups – ITT Population

Table 17: Time to Recovery by Treatment Group within Subgroups – Treated Population

Table 18: Time to Recovery by Treatment Group and Disease Severity: Readmittance Sensitivity Analysis – ITT Population

Table 19: Time to Recovery by Treatment Group and Disease Severity: Concomitant Medication Sensitivity Analysis – ITT Population

Table 20: Time to Recovery by Treatment Group and Disease Severity: Unblinding and Crossover Treatment Sensitivity Analysis – ITT Population

Programming Notes for Table 15:

The "Analysis Population" column will be replaced by a "Model" column. For the Fine-Gray estimates, the column will display "Fine-Gray", for the interaction model, the columns will display "Treatment-Severity Interaction (Randomized Severity)" and "Treatment-Severity Interaction (Actual Severity)", respectively. For the interaction model, the p-value for the interaction term will be provided in a foonote reading "The p-value for the treatment by disease severity interaction term was 0.xxxx.".

Programming Notes for Tables 16 and 17:

The "Disease Severity" column will be replaced by a "Subgroup" column. These tables will not display the "Any…" rows. For the analysis controlling for age and symptom duration as continuous covariates, the elements for the "Subgroup" column will state "Age and Duration of Symptoms as Continuous Covariates". The elements for the "n" and "Median Time to Recovery" columns will display "-".

Programming Notes for Table 20:

The "Analysis Population" column will be replaced by a column titled "Unblinding/Crossover Remdesivir Treatment". The first set of summaries will be for the "Unblinding" sensitivity analyses, and the second set will be for the "Crossover Remdesivir Treatment" sensitivity analyses.

Table 21: Summary of Clinical Status Score Assessed the Day of and the Day following Remdesivir Treatment – Placebo Subjects treated with Remdesivir

Placebo Subjects Retreated with Remdesivir (N)						
	Day of Retreatment			Day following Retreatment		
Ordinal Scale Measure	n	%	95% CI	N	%	95% CI
Death at or before Study Visit (8)	-	-	-	X	x	x.x, x.x
Hospitalized, on invasive mechanical ventilation or ECMO (7)	x	x	x.x, x.x	X	x	x.x, x.x
Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	x	x	x.x, x.x	X	x	x.x, x.x
Hospitalized, requiring supplemental oxygen (5)	x	x	x.x, x.x	X	x	x.x, x.x
Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	x	x	x.x, x.x	X	x	x.x, x.x
Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	x	x	x.x, x.x	X	x	x.x, x.x
Not hospitalized, limitation on activities and/or requiring home oxygen (2)	-	-	-	X	x	x.x, x.x
Not hospitalized, no limitations on activities (1)	-	-	-	X	x	x.x, x.x
No clinical status score reported	x	x	x.x, x.x	X	x	x.x, x.x
Denominator for percentages is the number of retreated subjects (N)						

Table 22: Summary of Recoveries and Deaths by Day 29 – ITT Population

Treatment Group	Grouping Variable	Subgroup	Recovered		Did Not Recover		Deaths		Not Recovered or Died	
			n	%	n	%	n	%	n	%
Remdesivir (N=X)	**Disease Severity**	**Mild/Moderate**	x	x	x	x	x	x	x	x
Placebo (N=X)			x	x	x	x	x	x	x	x
Remdesivir (N=X)		**Severe**	x	x	x	x	x	x	x	x
Placebo (N=X)			x	x	x	x	x	x	x	x
Remdesivir (N=X)		**Any Severity**	x	x	x	x	x	x	x	x
Placebo (N=X)			x	x	x	x	x	x	x	x
Continue for duration of symptoms categories in Section 6.4										
N= Number of subjects in the ITT Population.										

Implementation Note: For the symptom categorizations, the Grouping Variable column will display "Duration of Symptoms prior to enrollment".

Table 23: Odds Ratio for Inferior Clinical Status Score at Study Visit Day 15 by Treatment Using a Proportional Odds Model – ITT Population

Covariate	Treatment Group	Odds Ratio		P-value
		Estimate	95% CI	
Disease Severity	Remdesivir (N=X)			
	Placebo (N=X)	x.x	x.x, x.x	0.xxx
[Continue for each Section 6.4 subgroups]	Remdesivir (N=X)			
	Placebo (N=X)	x.x	x.x, x.x	0.xxx
The specified covariates were included individually in separate models.				

Table with similar format:

Table 24: Odds Ratio for Inferior Clinical Status Score at Study Visit Day 15 by Treatment Using a Proportional Odds Model – Treated Population

Table 25: Odds Ratio for Inferior Clinical Status Score at Study Visit Day 15 by Treatment Using a Proportional Odds Model – Unblinding and Crossover Treatment Sensitivity Analysis – ITT Population

Table 26: Time to Improvement on the 8-Point Ordinal Scale by Treatment Group

Analysis Population	Treatment Group	n	Median Time		HR		P-value
			Estimate	95% CI	Estimate	95% CI	
Improvement by at least One Category							
ITT Population	**Remdesivir (N=X)**	x	x.x	x.x, x.x			
	Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx
Treated Population	**Remdesivir (N=X)**	x	x.x	x.x, x.x			
	Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx
Improvement by at least Two Categories							
ITT Population	**Remdesivir (N=X)**	x	x.x	x.x, x.x			
	Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx
Treated Population	**Remdesivir (N=X)**	x	x.x	x.x, x.x			
	Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx

N = Number of subjects in the specified treatment group and analysis population.
n = Number of subjects with improvement.
HR is the hazard ratio from the Cox Model
P-value calculated using the Log-rank test

Tables with similar format:

Table 27: Time to Improvement on the 8-Point Ordinal Scale by Treatment Group: Remdesivir Retreatment Sensitivity Analysis

Table 28: Time to Improvement on the 8-Point Ordinal Scale by Treatment Group – Remdesivir Retreatment Sensitivity Analysis on Subjects with Clinical Status Score of 7 at Enrollment

Table 29: Time to Improvement by at least Two Clinical Status Categories on the 8-Point Ordinal Scale by Treatment Group: Alternate Ordinal Scale

Table 30: Time to Improvement by at least One Clinical Status Category on the 8-Point Ordinal Scale by Treatment Group within Subgroups – ITT Population

Table 31: Time to Improvement by at least One Clinical Status Category on the 8-Point Ordinal Scale by Treatment Group within Subgroups – Treated Population

Table 32: Time to Improvement by at least Two Clinical Status Categories on the 8-Point Ordinal Scale by Treatment Group within Subgroups – ITT Population

Table 33: Time to Improvement by at least Two Clinical Status Categories on the 8-Point Ordinal Scale by Treatment Group within Subgroups – Treated Population

Programming notes for Tables 30 – 33:

Instead of the "Analysis Population" column, a column titled "Grouping Variable" will be to the left of Treatment Group. Rows will be generated for each subgroup.

Table 34: Clinical Status Scores by Treatment Group and Study Visit – ITT Population

Study Visit	Ordinal Scale Measure	Remdesivir (N=X)			Placebo (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
Day 1	Death at or before Study Visit (8)	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	Hospitalized, requiring supplemental oxygen (5)	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	Not hospitalized, no limitations on activities (1)	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	No clinical status score reported – Hospitalized subjects	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
	No clinical status score reported – Discharged subjects	x	x	x.x, x.x	x	x	x.x, x.x	x	x	x.x, x.x
[Repeat for Study Visit Days 3, 5, 8, 11, 15, 22, and 29]										

N = Number of Subject in the ITT Population.
n = Number of subjects who reported the respective score
95% CI calculated using Wilson Cis

Programming Notes:

```
proc freq;
      Table treatment*analysisvariable / binomial(wilson);
      ods output binomialcls=outputdsn;
run;
```

Table with similar format:

Table 35: Clinical Status Scores by Treatment Group and Study Visit – Treated Population

Table 36: Time to Discharge or to a NEWS of ≤ 2 by Treatment Group

Analysis Population	Treatment Group		Median Time		HR		
		n[a]	Estimate	95% CI	Estimate	95% CI	P-value
ITT Population	**Remdesivir (N=X)**	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx
	Placebo (N=X)	x	x.x	x.x, x.x			
Treated Population	**Remdesivir (N=X)**	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx
	Placebo (N=X)	x	x.x	x.x, x.x			

N= Number of subjects in the specified treatment group and analysis population.
n = Number of subjects who discharged or had a NEWS of ≤ 2 prior to Day 29.
HR is the hazard ratio from the Cox Model
P-value calculated using the Log-rank test

Table with similar format:

Table 37: Time to Discharge or to a NEWS of ≤ 2 by Treatment Group within Subgroups – ITT Population

Table 38: Time to Discharge or to a NEWS of ≤ 2 by Treatment Group within Subgroups – Treated Population

Programming notes for Tables 36 – 37:

A "Grouping Variable" column will replace the "Analysis Population" column to the left of "Treatment Group". Rows will be repeated for each subgroup.

Table 39: Change from Baseline of NEWS by Treatment Group and Study Visit – ITT Population

Study Visit	Statistic	Remdesivir (N=X)	Placebo (N=X)	All Subjects (N = X)
Day 3	n	x	x	x
	Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)
	Median	x.x	x.x	x.x
	Range (Min, Max)	x, x	x, x	x, x
	Change from Baseline Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)
[Repeat for Study Visit Days 5, 8, 11, 15, 22, 29 and Change from Baseline at each]				
n = Number of subjects with an assessment at both baseline and the time point being summarized. SD = Standard deviation.				

Table with similar format:

Table 40: Change from Baseline of NEWS by Treatment Group and Study Visit – Treated Population

Table 41: Oxygen Use by Treatment Group

Analysis Population	Oxygen Use	Statistic	Treatment Group	
			Remdesivir	Placebo
ITT Population	**On Oxygen at Baseline (N = x)**			
	Days on Oxygen	Q1	x.x	x.x
		Median	x.x	x.x
		Q3	x.x	x.x
	Not on Oxygen at Baseline (N = x)			
	New Oxygen Use	n	x	x
		Incidence Rate	x.x	x.x
		Incidence Rate CI	x.x, x.x	x.x, x.x
	Days on Oxygen	Q1	x.x	x.x
		Median	x.x	x.x
		Q3	x.x	x.x
Continue for Treated population…				
N = Number of subjects in the specified analysis population and oxygen use category. Q1 and Q3 are the first and third quartiles, respectively.				

Tables with similar format:

Table 42: Oxygen Use by Treatment Group within Subgroups

Table 43: Non-invasive Ventilation/High-Flow Oxygen Use by Treatment Group

Table 44: Non-invasive Ventilation/High-Flow Oxygen Use by Treatment Group within Subgroups

Table 45: Ventilation/ECMO Use by Treatment Group

Table 46: Ventilation/ECMO Use by Treatment Group within Subgroups

Programming notes for Tables 41, 43, 45:

"Analysis Population" will be replaced by "Grouping Variable" column. Summaries will only be generated for ITT population.

Table 47: Hospitalization by Treatment Group

Analysis Population	Hospitalization Summary	Statistic	Treatment Group	
			Remdesivir	Placebo
ITT Population	Days of Initial Hospitalization	N	x	x
		Q1	x.x	x.x
		Median	x.x	x.x
		Q3	x.x	x.x
	Readmittance	n	x	x
		Percentage	x	x
		Percentage CI	x.x, x.x	x.x, x.x
Continue for Treated population…				
N = Number of subjects in the specified analysis population. Q1 and Q3 are the first and third quartiles, respectively. Denominator of readmittance percentages is the number of subjects in the specific analysis population.				

Table with similar format:

Table 48: Hospitalization by Treatment Group within Subgroups

Programming notes for Table 47:

"Analysis Population" will be replaced by "Grouping Variable" column. Summaries will only be generated for ITT population

Table 49: Categorical Demographic and Baseline Characteristics by Disease Severity and Treatment Group – ITT Population

Demographic Category	Characteristic	Remdesivir						Placebo						All Subjects					
		Mild-Moderate (N=X)		Severe (N=X)		All Subjects (N=X)		Mild-Moderate (N=X)		Severe (N=X)		All Subjects (N=X)		Mild-Moderate (N=X)		Severe (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sex	Male	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Female	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Ethnicity	Not Hispanic or Latino	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Hispanic or Latino	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Not Reported	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Race	American Indian or Alaska Native	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Asian	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Native Hawaiian or Other Pacific Islander	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Black or African American	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	White	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Multi-Racial	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Geographic Region	Region 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	…Continue for all region categorizations	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Age	< 40	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	40-64	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	>=65	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Baseline Clinical Status	7	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	6	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	…continue for other scores	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Demographic Category	Characteristic	Remdesivir						Placebo						All Subjects					
		Mild-Moderate (N=X)		Severe (N=X)		All Subjects (N=X)		Mild-Moderate (N=X)		Severe (N=X)		All Subjects (N=X)		Mild-Moderate (N=X)		Severe (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Duration of Symptoms prior to enrollment	Categorization 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	…Continue for all symptom categorizations	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Comorbidities	List of individual comorbidities…	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Also categorizations: 0, 1, 2+	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
N = Number of subjects enrolled.																			

Table 50: Continuous Demographic and Baseline Characteristics by Disease Severity and Treatment Group – ITT Population

Variable	Statistic	Remdesivir			Placebo			All Subjects		
		Mild-Moderate (N=X)	Severe (N=X)	All Subjects (N=X)	Mild-Moderate (N=X)	Severe (N=X)	All Subjects (N=X)	Mild-Moderate (N=X)	Severe (N=X)	All Subjects (N=X)
Age (years)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x
Height (cm)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x
Weight (Kg)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x
BMI	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x
Duration of Symptoms prior to Enrollment (Days)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x

Variable	Statistic	Remdesivir			Placebo			All Subjects		
		Mild-Moderate (N=X)	Severe (N=X)	All Subjects (N=X)	Mild-Moderate (N=X)	Severe (N=X)	All Subjects (N=X)	Mild-Moderate (N=X)	Severe (N=X)	All Subjects (N=X)
	Minimum	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x

Tables with similar format:

Table 51: Categorical Demographic and Baseline Characteristics by Disease Severity and Treatment Group and Remdesivir Retreatment – ITT Population

Table 52: Continuous Demographic and Baseline Characteristics by Disease Severity and Treatment Group and Remdesivir Retreatment – ITT Population

Programming notes for Tables 50 and 51:

The three major columns for these tables will be “Remdesivir”, “Placebo (Not Retreated)”, and “Placebo (Retreated)” instead of “Remdesivir”, “Placebo”, and “All Subjects”

Table 53: Summary of Subjects with Pre-Existing Medical Conditions Treatment Group - Treated Population

Condition	Remdesivir (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
None	x	xx	x	xx	x	xx
Any Condition	x	xx	x	xx	x	xx
Diabetes I	x	xx	x	xx	x	xx
Diabetes II	x	xx	x	xx	x	xx
…continue for all solicited conditions…	…	…	…	…	…	…

N = Number of subjects in the Treated Population;
n = Number of subjects reporting the condition

Table 54: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification, Disease Severity, and Treatment Group – Treated Population

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Remdesivir (N=X)				Placebo (N=X)				All Subjects (N=X)			
		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 – 2]	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N = Number of subjects in the Treated Population.
n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

Table 55: Number and Percentage of Subjects Reporting Use of Prohibited Medications by Disease Severity, and Treatment Group – Treated Population

	Remdesivir (N=X)				Placebo (N=X)				All Subjects (N=X)			
	Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)	
Medication/Therapies	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Medication/Therapy	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Protease inhibitors	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Polymerase inhibitors	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Other drugs used to treat COVID-19	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Corticosteroids	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Other anti-inflammatory drugs	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N = Number of subjects in the Treated Population.
n=Number of subjects reporting taking at least one medication in the specified category.

Table 56: Prohibited Medication Use by Study Day, Disease Severity, and Treatment Group – Treated Population

	Remdesivir (N=X)				Placebo (N=X)				All Subjects (N=X)			
	Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Mild-Moderate (N=X)		Severe (N=X)	
Study Day	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Day 1	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 3	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 5	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 8	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 11	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N = Number of subjects in the Treated Population.
n=Number of subjects reporting taking at least one prohibited medication by the specified study day.

Programming Notes: If the start date of the prohibited medication is on or before the specified (actual) study day, then the subject will be denoted as taking the med for that Study Day.

Table 57: Overall Summary of Adverse Events – Treated Population

	Remdesivir (N=X)						Placebo (N=X)						All Subjects (N=X)					
	Mild-Moderate (N=X)		Severe (N=X)		Any Severity (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Any Severity (N=X)		Mild-Moderate (N=X)		Severe (N=X)		Any Severity (N=X)	
Subjects[a] with	N	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
At least one adverse event	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one related adverse event	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Life-threatening (Grade 4)	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Death (Grade 5)	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one related serious adverse event	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to early termination[b]	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one Unanticipated Problem	X	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

N = Number of subjects in the Treated Population
[a]Subjects are counted once for each category regardless of the number of events.
[b]As reported on the Adverse Event eCRF.
All Grade 3 and 4 AEs are captured as AEs. In addition, any Grade 2 or higher suspected drug-related hypersensitivity reaction is reported as an AE.

Table 58: Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - Treated Population

Preferred Term	MedDRA System Organ Class	Remdesivir (N=X)			Placebo (N=X)			All Subjects (N=X)		
		n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events										
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc.	Etc.	x	x	x	x	x	x	x	x	x
Other (Non-serious) Adverse Events										
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc	Etc	x	x	x	x	x	x	x	x	x

N = number of subjects in the Treated Population (number of subjects at risk).
n = number of subjects reporting event.
Events = total frequency of events reported.

Programming Notes:

Select all preferred terms/System organ classes where the % for any treatment group or overall is >= 5%. Sort preferred terms by descending order of frequency.

Table 59: Deaths by Day 15 or Day 29 by Treatment Group

Analysis Population	Study Day	Remdesivir (N=X)			Placebo (N=X)		
		n	Mortality Rate	Rate 95% CI	n	Mortality Rate	Rate 95% CI
ITT Population	Day 15	x	x.x	x.x, x.x	x	x.x	x.x, x.x
	Day 29	x	x.x	x.x, x.x	x	x.x	x.x, x.x
Treated Population	Day 15	x	x.x	x.x, x.x	x	x.x	x.x, x.x
	Day 29	x	x.x	x.x, x.x	x	x.x	x.x, x.x

N = Number of Subject in the specified treatment group and analysis population.
n = Number of subjects in a given treatment group who died by the given timepoint

Table with similar format:

Table 60: Deaths by Day 15 or Day 29 by Treatment Group – Unblinding and Crossover Treatment Sensitivity Analysis

Programming Notes: The "Analysis Population" column will be replaced by a column titled "Unblinding/Crossover Remdesivir Treatment". The first set of summaries will be for the "Unblinding" sensitivity analyses, and the second set will be for the "Crossover Remdesivir Treatment" sensitivity analyses.

Table 61: Time to Death through Day 15 and 29 by Treatment Group

Analysis Population	Study Day	Treatment Group		Median Time		HR		
			n	Estimate	95% CI	Estimate	95% CI	P-value
ITT Population	**Day 15**	**Remdesivir (N=X)**	x	x.x	x.x, x.x			
		Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx
	Day 29	**Remdesivir (N=X)**	x	x.x	x.x, x.x			
		Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx
Treated Population	**Day 15**	**Remdesivir (N=X)**	x	x.x	x.x, x.x			
		Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx
	Day 29	**Remdesivir (N=X)**	x	x.x	x.x, x.x			
		Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx

N= Number of subjects in the specified treatment group and analysis population.
n = Number of subjects who died by the specified study day.
HR is the hazard ratio from the Cox Model
P-value calculated using the Log-rank test

Table with similar format:

Table 62: Time to Death through Day 15 and 29 by Treatment Group – Unblinding and Crossover Treatment Sensitivity Analysis

Programming Notes: The "Analysis Population" column will be replaced by a column titled "Unblinding/Crossover Remdesivir Treatment". The first set of summaries will be for the "Unblinding" sensitivity analyses, and the second set will be for the "Crossover Remdesivir Treatment" sensitivity analyses.

Table 63: Subjects Experiencing Grade 3 or 4 AEs and SAEs through Day 29 by Treatment Group– Treated Population

Safety Event Outcome	Remdesivir (N=X)			Placebo (N=X)			P-value
	n	%	95% CI	n	%	95% CI	
Grade 3 or 4 AE	x	x	x.x, x.x	x	x	x.x, x.x	0.xxx
SAE	x	x	x.x, x.x	x	x	x.x, x.x	0.xxx

N = Number of Subject in the Treated Population.
n = Number of subjects in a given treatment group who experienced the specified safety event outcome.
95% CI calculated using C-P/Blaker method
P-value calculated using Barnard's Exact Test

Table 64: Analysis of Time to Death, SAEs, or Grade 3 or 4 AEs by Treatment Group – Treated Population

Treatment Group	n	Median Time		HR		P-value
		Estimate	95% CI	Estimate	95% CI	
Remdesivir (N=X)	x	x.x	x.x, x.x			
Placebo (N=X)	x	x.x	x.x, x.x	x.x	x.x, x.x	x.xxx

N= Number of subjects in the Treated Population.
n = Number of subjects who died or experienced SAEs, Grade 3 or 4 AEs, or Discontinuation of Study Infusions.
HR is the hazard ratio from the Cox Model
P-value calculated using the Log-rank test

Table 65: Abnormal Laboratory Results of Grade 3 or 4 by Parameter, Maximum Severity, Time Point, and Treatment Group – Treated Population

Laboratory Parameter	Time Point	Treatment Group	N	Severe/ Grade 3		Life Threatening/ Grade 4	
				n	%	n	%
Any Parameter	Baseline	Remdesivir	x	x	x	x	x
		Placebo	x	x	x	x	x
	Day 3	Remdesivir	x	x	x	x	x
		Placebo	x	x	x	x	x
	Day 5	Remdesivir	x	x	x	x	x
		Placebo	x	x	x	x	x
	Day 8	Remdesivir	x	x	x	x	x
		Placebo	x	x	x	x	x
	Day 11	Remdesivir	x	x	x	x	x
		Placebo	x	x	x	x	x
	Day 15	Remdesivir	x	x	x	x	x
		Placebo	x	x	x	x	x
	Day 29	Remdesivir	x	x	x	x	x
		Placebo	x	x	x	x	x
	Maximum Severity Post Baseline	Remdesivir	x	x	x	x	x
		Placebo	x	x	x	x	x
Each parameter will be summarized individually similar to the above…							
The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. N = Number of subjects in the Treated Population							

Table 66: Summary Statistics of Laboratory Results by Parameter, Study Visit Day, and Treatment Group – Treated Population

Laboratory Parameter	Study Visit Day	Treatment Group	Absolute					Change from Baseline				
			N	Mean	SD	Median	Min, Max	N	Mean	SD	Median	Min, Max
Parameter 1	Baseline	Remdesivir	x	xx.x	xx.x	xx.x	xx.x, xx.x	---	---	---	---	---
		Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x	---	---	---	---	---
	Day 3	Remdesivir	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Day 5	Remdesivir	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Day 8	Remdesivir	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Day 11	Remdesivir	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Day 15	Remdesivir	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Day 29	Remdesivir	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x	xx.x	xx.x, xx.x
Continue for all parameters…												
N = Number of subjects in the Treated Population with laboratory data available for the parameter at the specified study visit.												

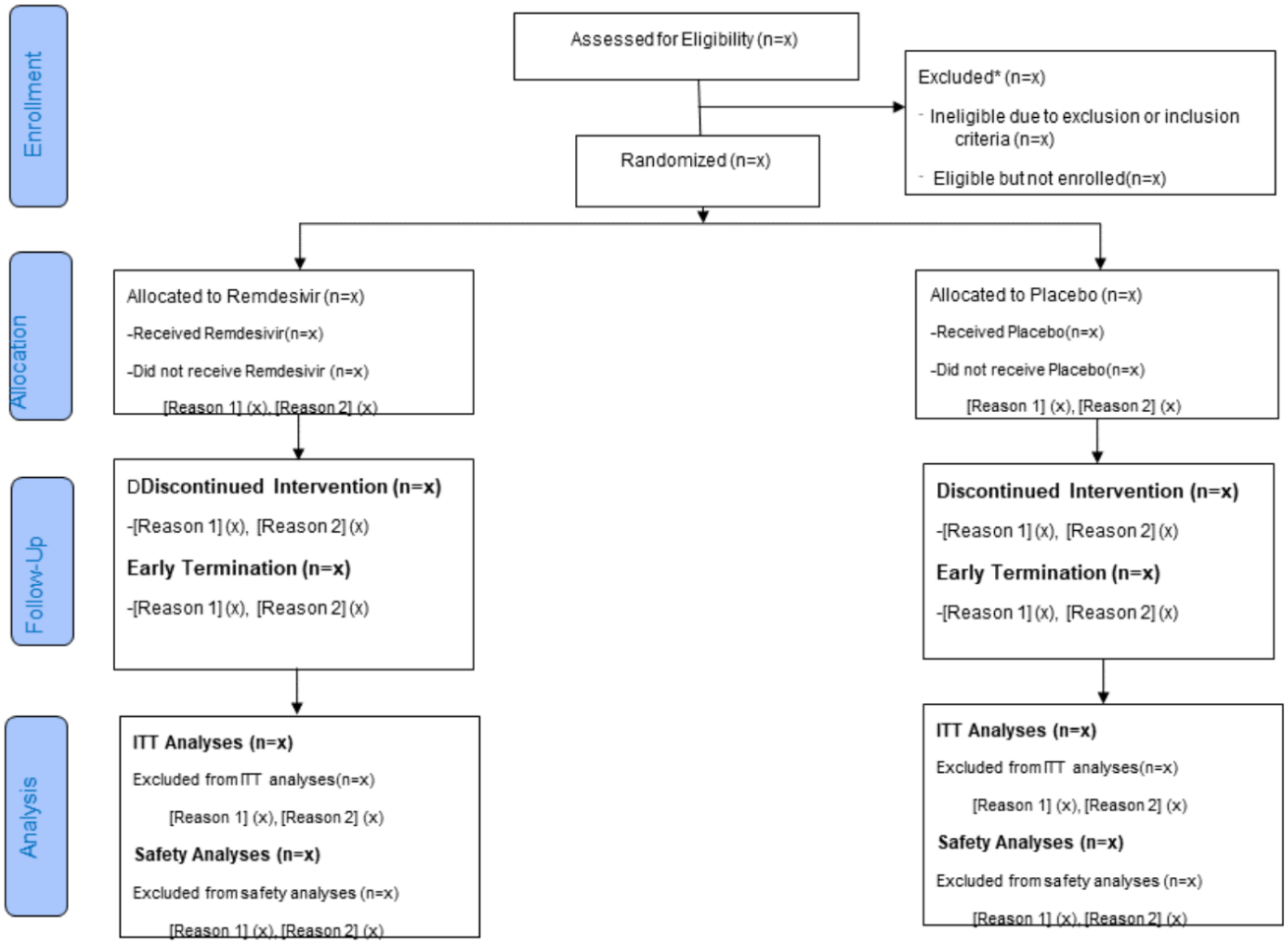
APPENDIX 2. FIGURE MOCK-UPS

General Programming Notes for figures:

- Use the same color for a treatment on the different graphs:
  - Remdesivir = Blue
  - Placebo = Red
- For severity graphs:
  - Mild = yellow
  - Moderate = orange
  - Severe = light red
  - Life-threatening = red
  - Death = black

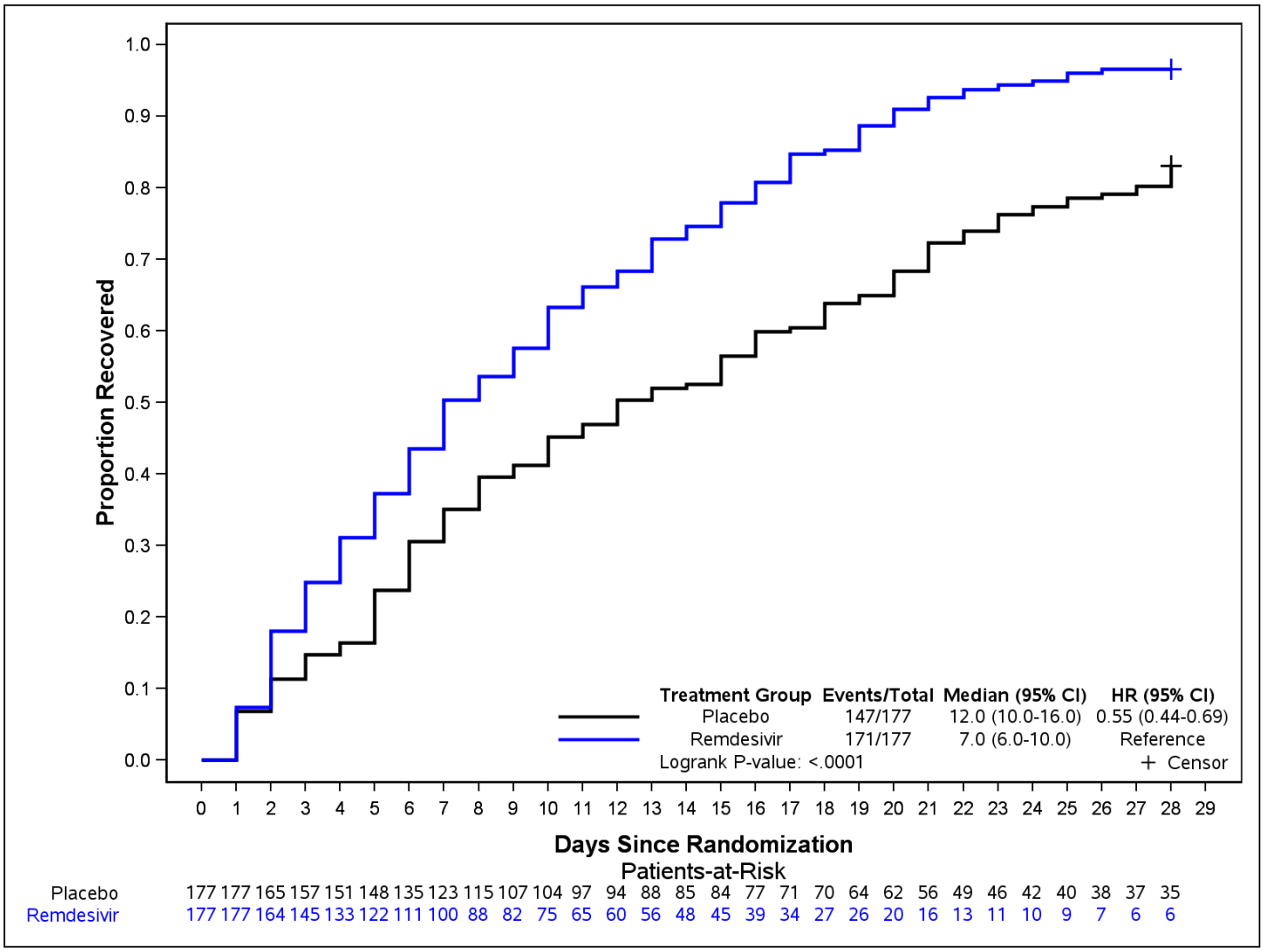
LIST OF FIGURES

Figure 1: CONSORT Flow Diagram



Implementation Note: Disease Stratum boxes will be included in the final CONSORT diagram.

Figure 2: Kaplan-Meier Curves of Time to Recovery by Treatment Group – ITT Population



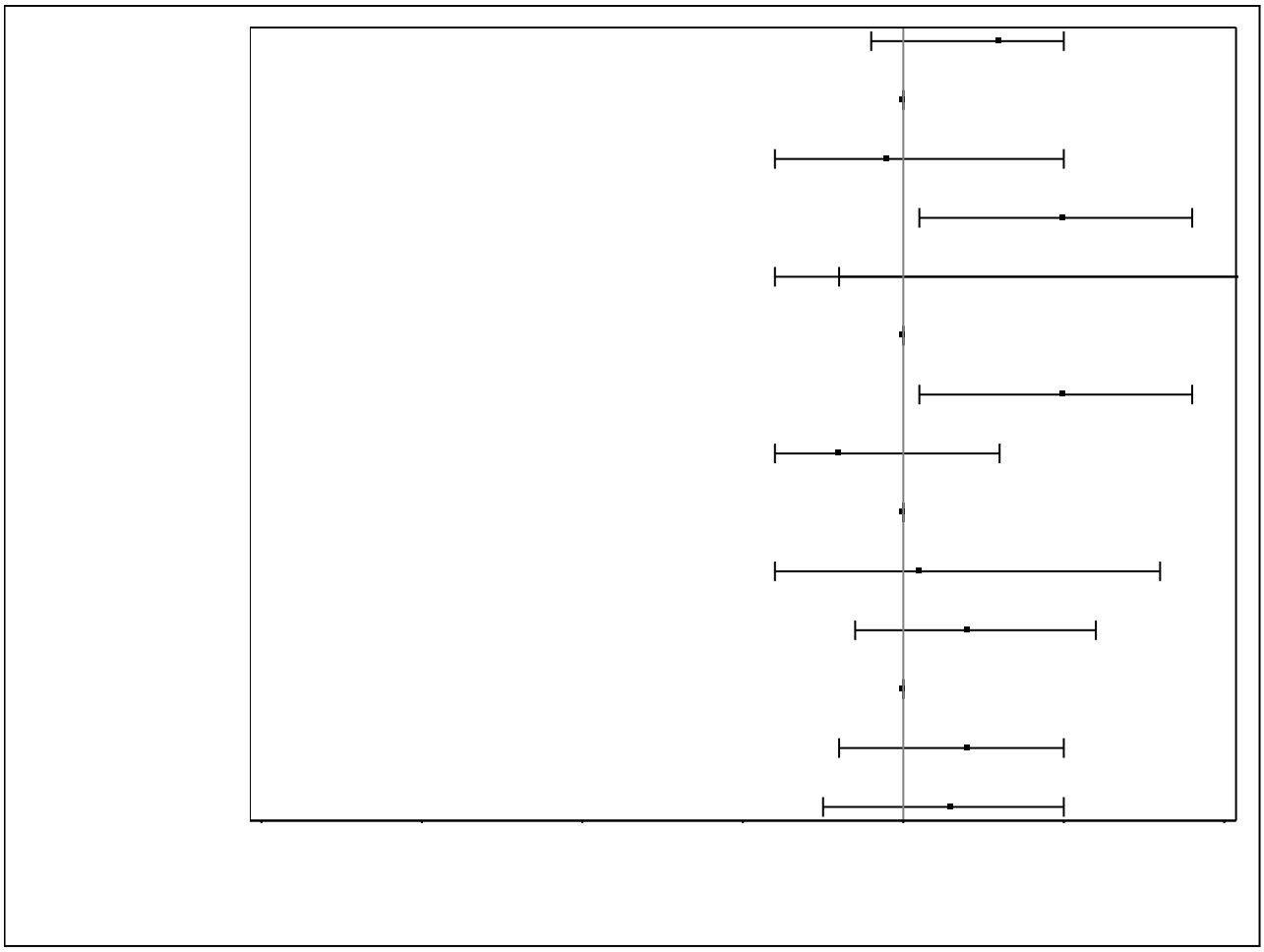
Figures with similar format:

Figure 3: Kaplan-Meier Curve of Time to Recovery by Treatment Group – Treated Population

Figure 4: Kaplan-Meier Curve of Time to Recovery by Treatment Group and Disease Severity – ITT Population

Figure 5: Kaplan-Meier Curve of Time to Recovery by Treatment Group and Disease Severity – Treated Population

Figure 6: Forest Plot of Hazard Ratios of Time to Recovery by Subgroup - ITT Population



Figures with similar format:

Figure 7: Forest Plot of Hazard Ratios of Time to Recovery by Subgroup - Treated Population

Figure 8: Forest Plot of Hazard Ratios of Time to Recovery: Leave One Site Out Sensitivity Analysis - ITT Population

Figure 9: Clinical Status Scores by Study Day – Placebo Recipients

[Shell not provided. The figure will be a spaghetti plot of clinical status scores by actual study day (of the assessment). Lines for subjects who are not retreated with remdesivir will be a muted gray color while the lines for subjects who are retreated with remdesivir will be a bold red or black color].

Figure 10: Predicted Probabilities of Scale Rating at Day 15 by Treatment Group and Disease Severity – ITT Population

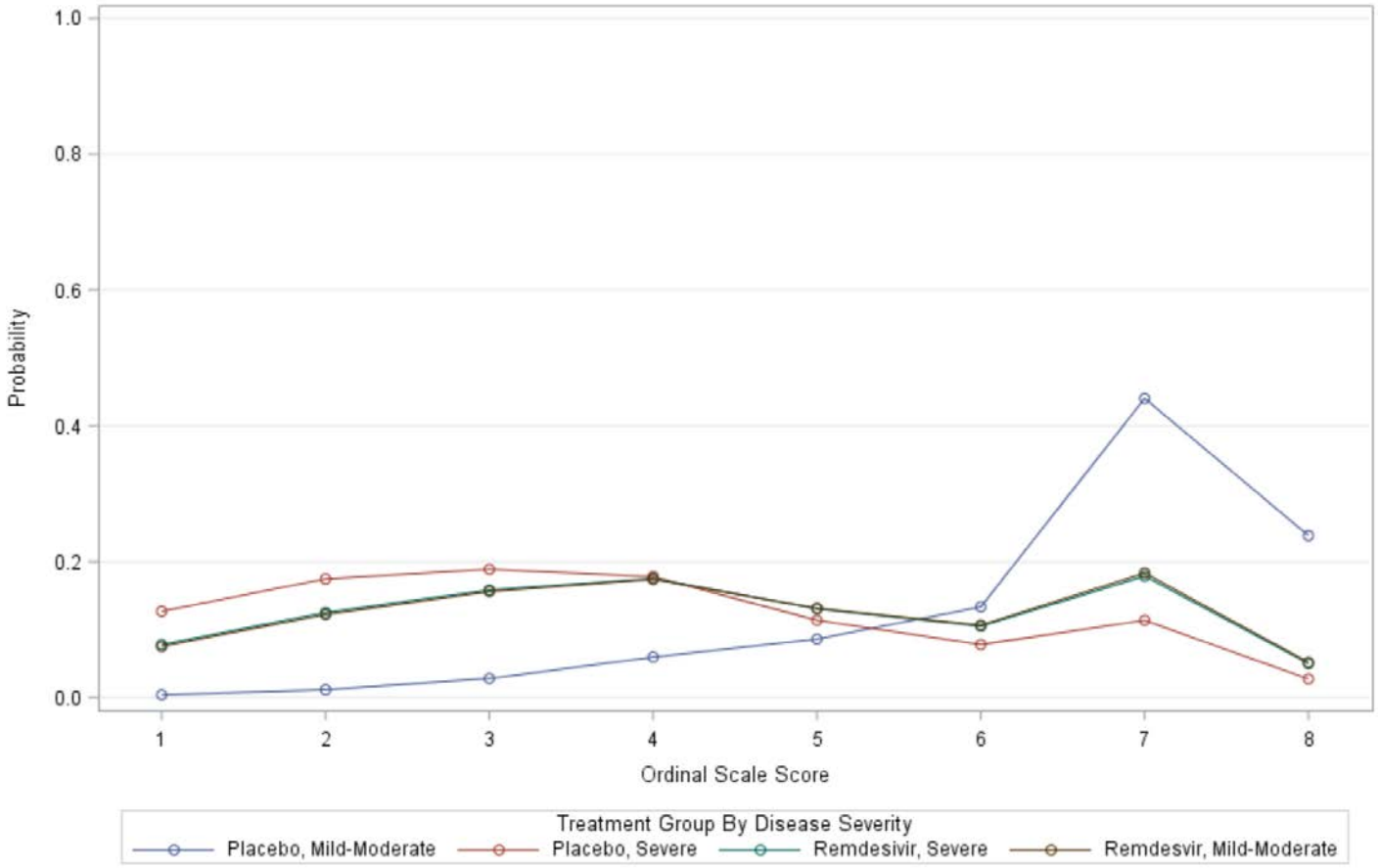


Figure 11: Kaplan-Meier Curves of Time to Improvement by at least One Category of Clinical Status Score by Treatment Group – ITT Population

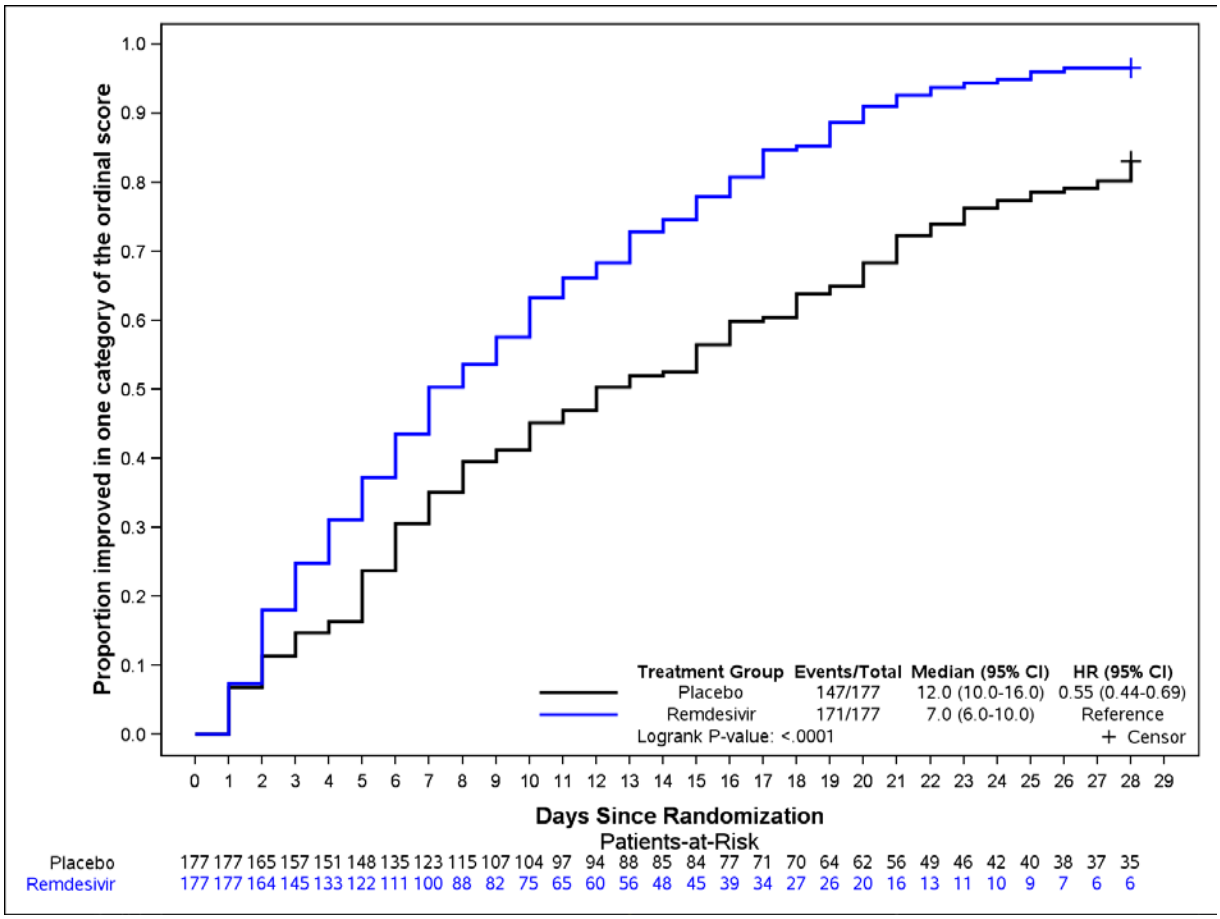
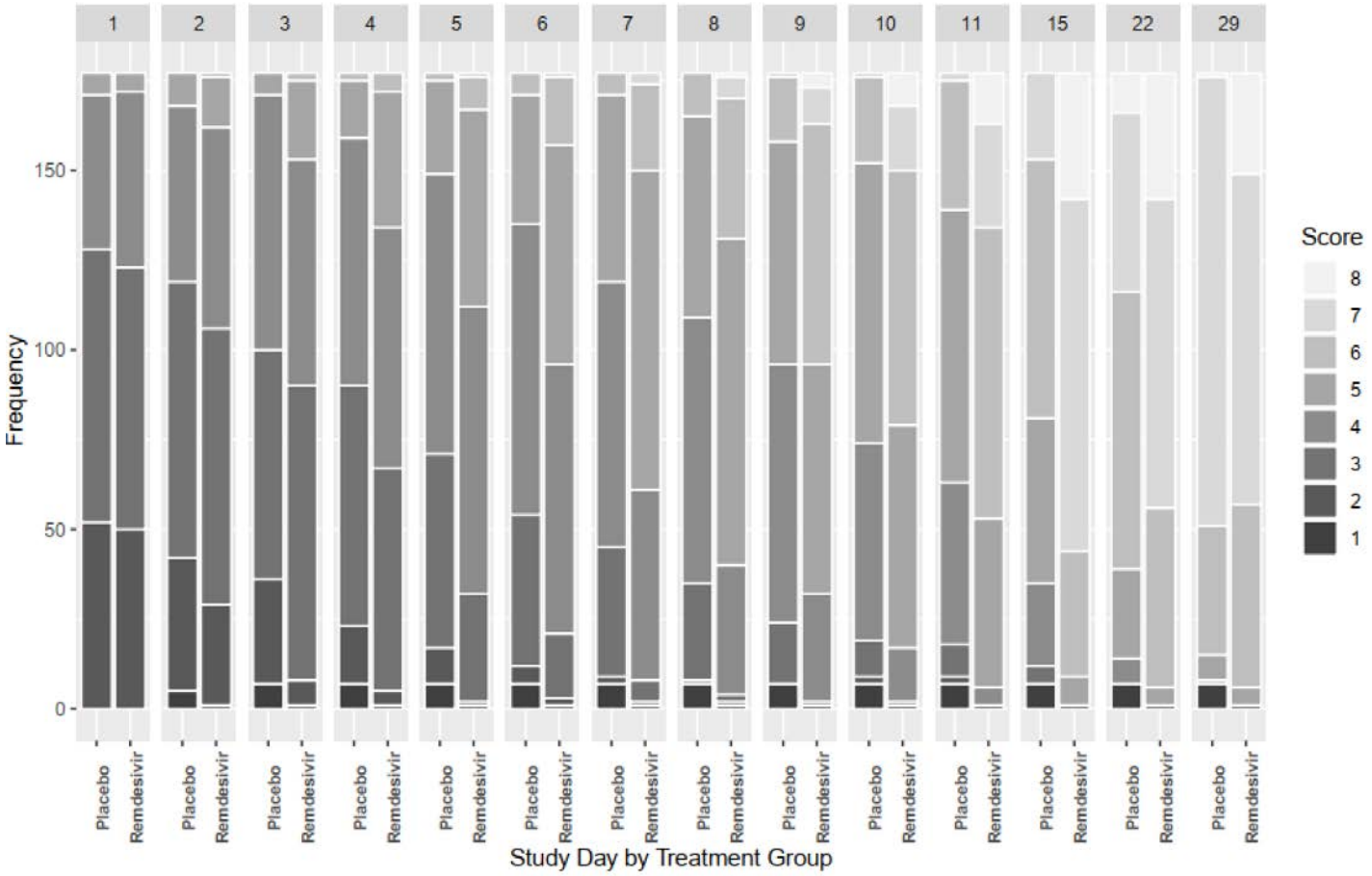


Figure with similar format:

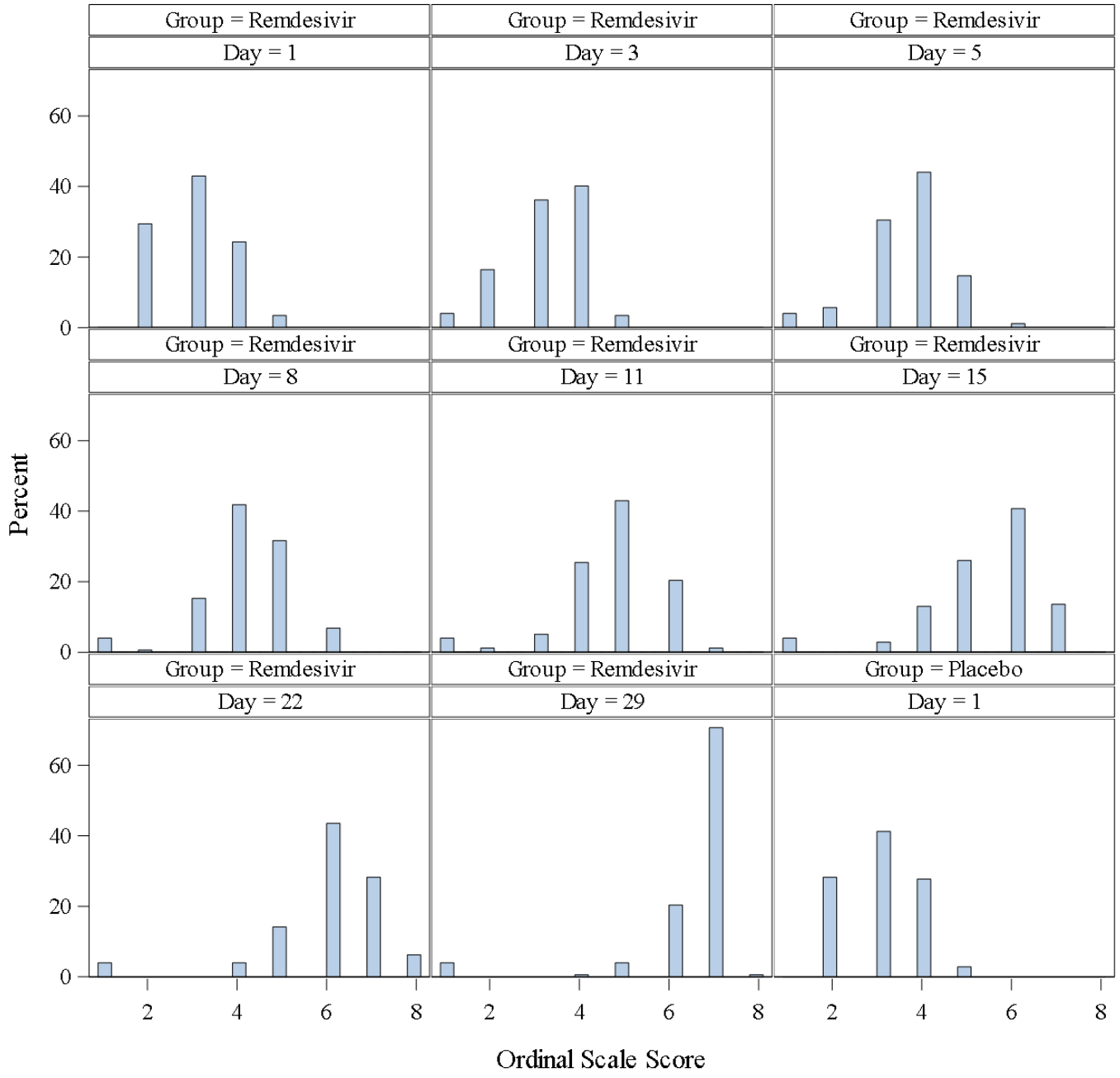
Figure 12: Kaplan-Meier Curves of Time to Improvement by at least Two Categories of Clinical Status Score by Treatment Group – ITT Population

Figure 13: Distribution of Clinical Status Scores By Day by Treatment Group – ITT Population



Implementation Note: Heat map coloring will be used for the clinical score scale.

Figure 14: Bar Plots of Clinical Status Scores by Study Day and Treatment Group – ITT Population



Implementation Note: Each panel will contain bars for Remdesivir and Placebo.

Figure 15: Kaplan-Meier Curves of Time to Discharge or NEWS ≤ 2 by Treatment Group – ITT Population

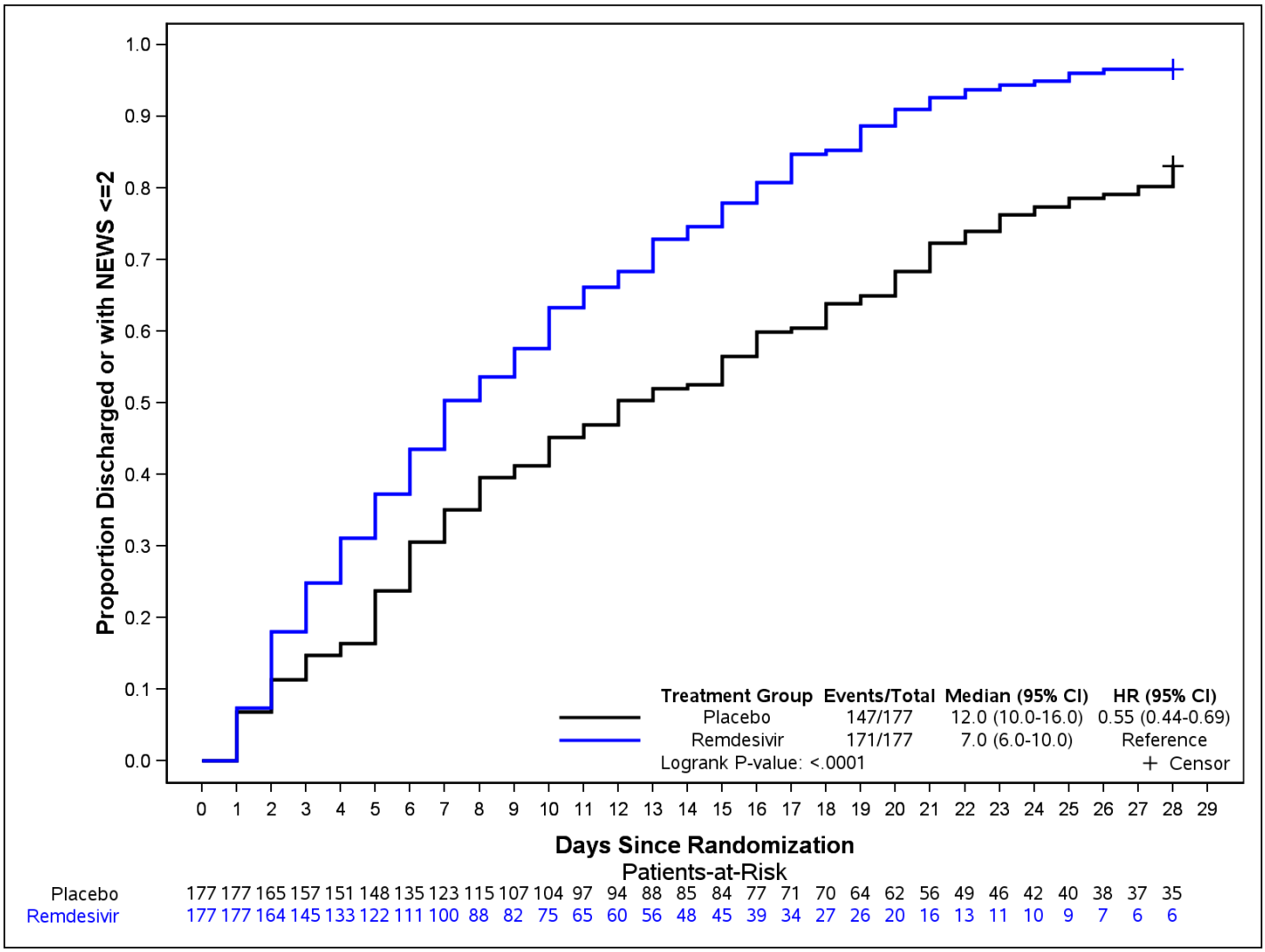


Figure 16: Mean NEWS by Day and Treatment Group – ITT Population

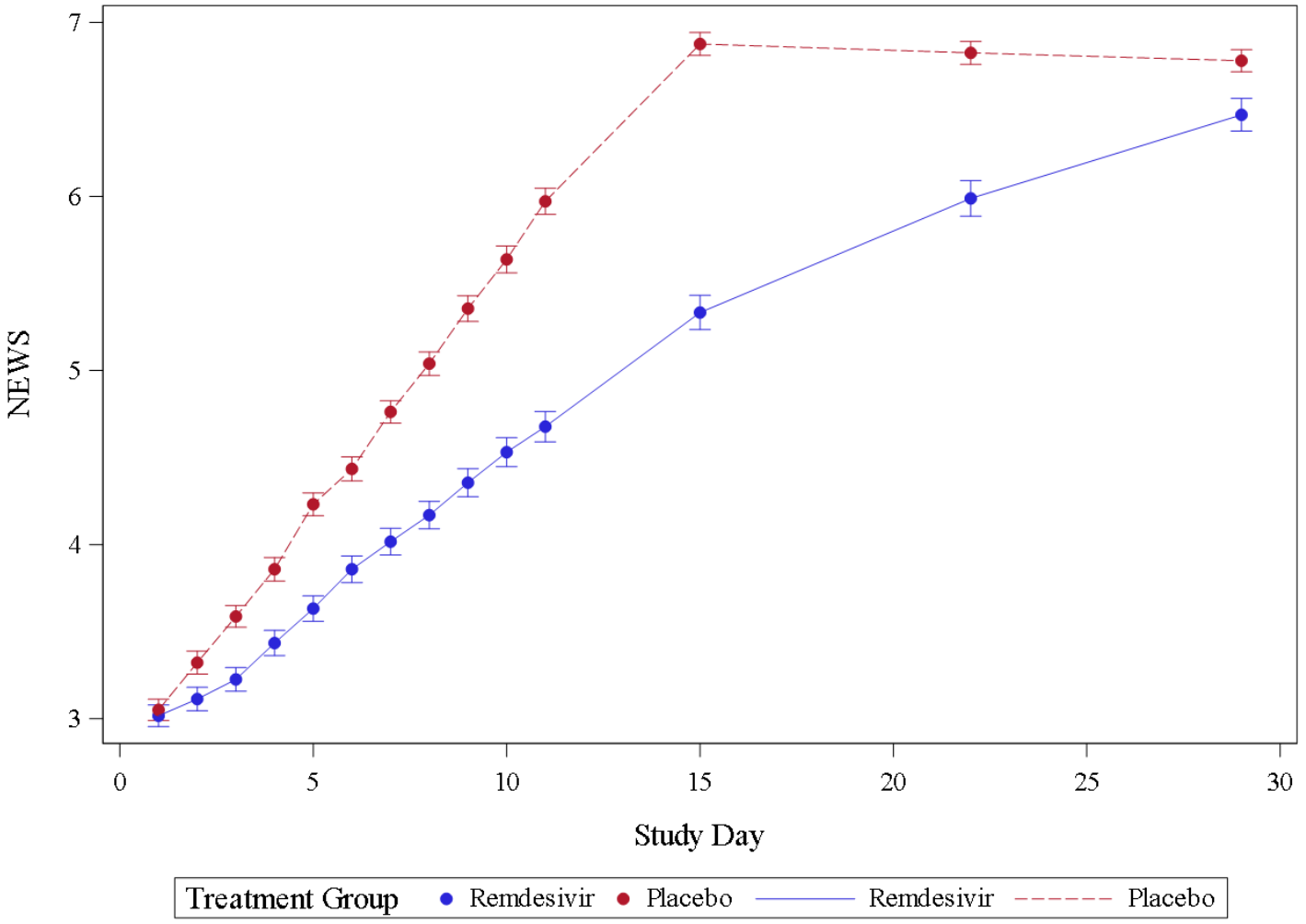
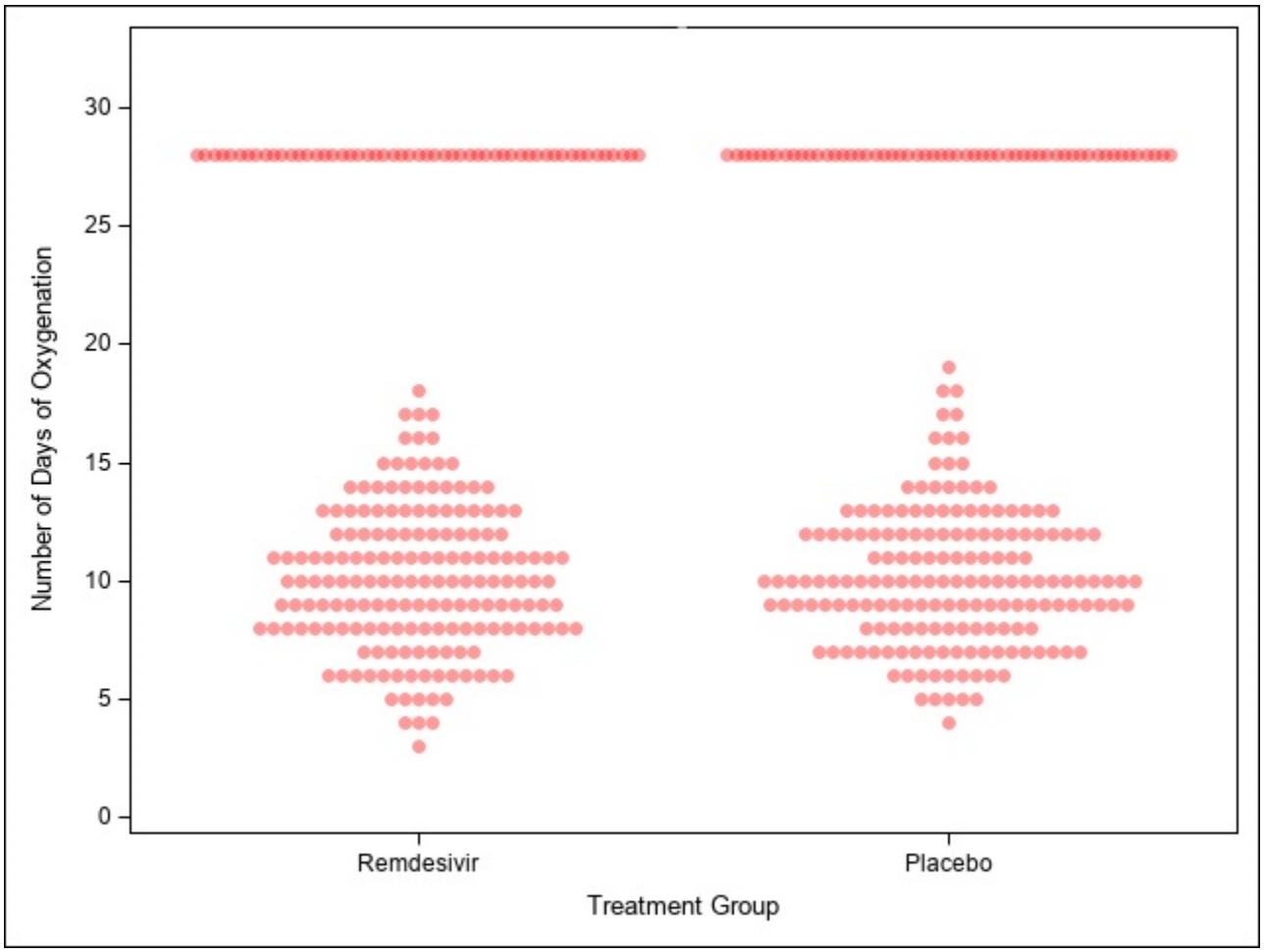


Figure 17: Bee Swarm Plot of Oxygen Days by Treatment Group – ITT Population



Implementation Note: Death swarm will be presented as a circle or similar shape instead of a line.

Figures with similar format:

Figure 18: Bee Swarm Plot of Non-invasive Ventilation/High-Flow Oxygen Days by Treatment Group – ITT Population

Figure 19: Bee Swarm Plot of Invasive Mechanical Ventilation/ECMO Days by Treatment Group – ITT Population

Figure 20: Bee Swarm Plot of Hospitalization Days by Treatment Group – ITT Population

Figure 21: Frequency of Non-Serious Related Unsolicited Adverse Events by MedDRA System Organ Class, Severity, and Treatment Group - Treated Population

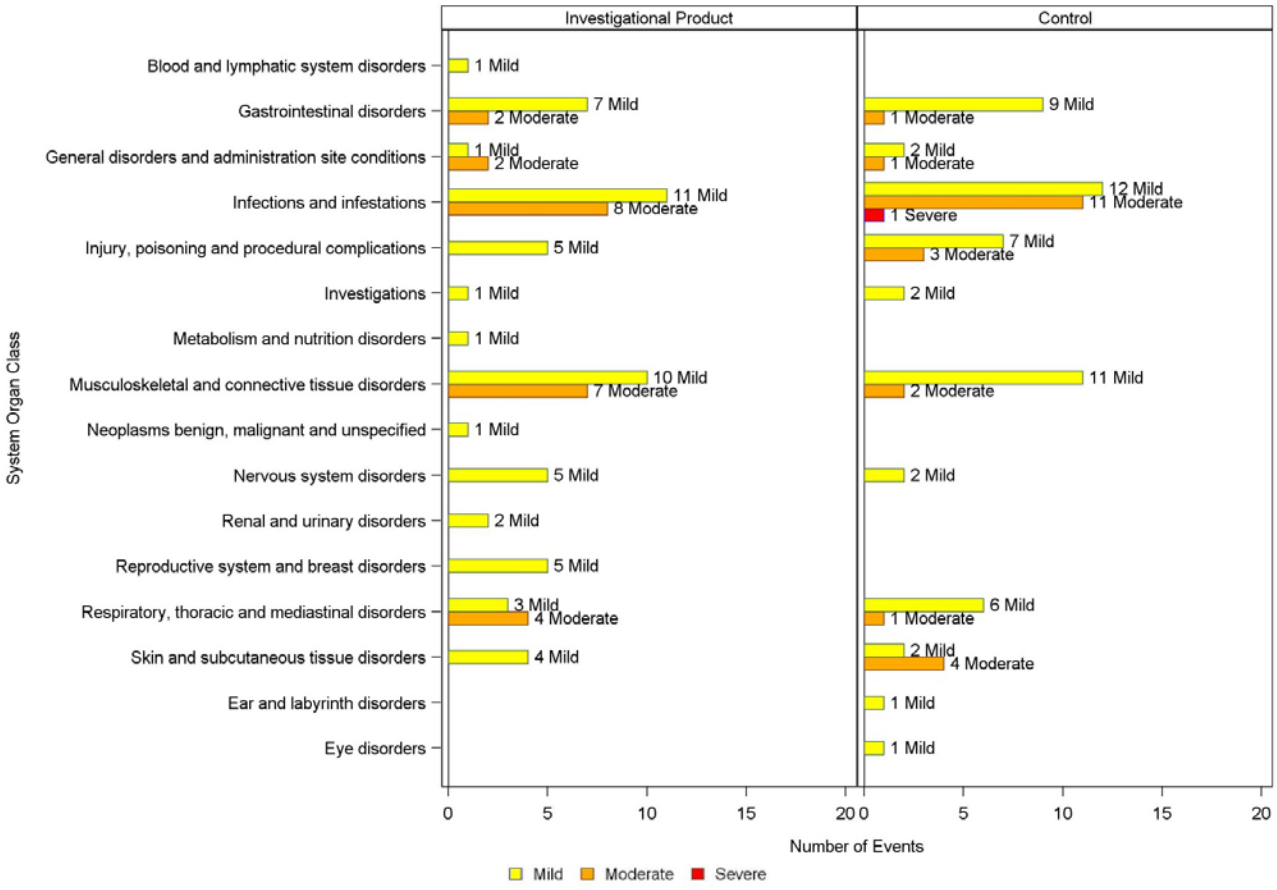


Figure 22: Incidence of Non-Serious Related Unsolicited Adverse Events by MedDRA System Organ Class, Severity, and Treatment Group - Treated Population

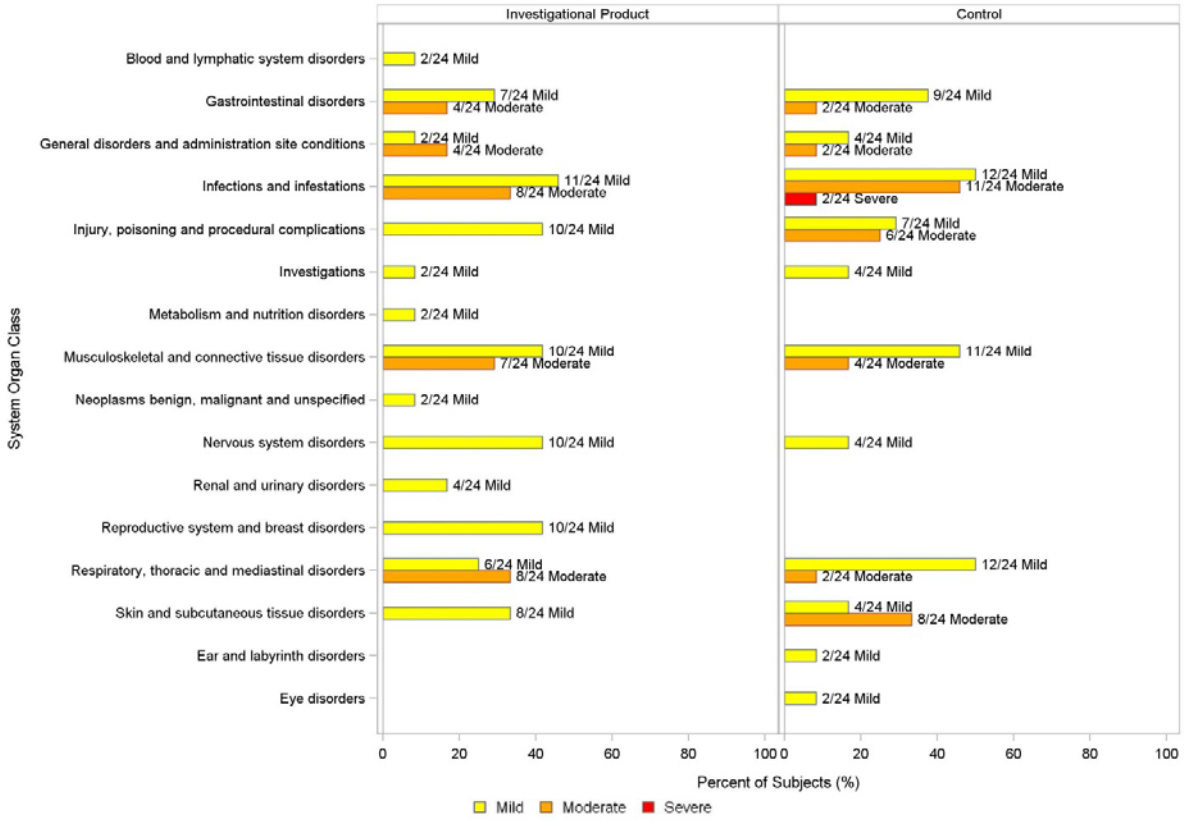


Figure 23: Kaplan-Meier Curve of Time to Death through Day 29 by Treatment Group – Treated Population

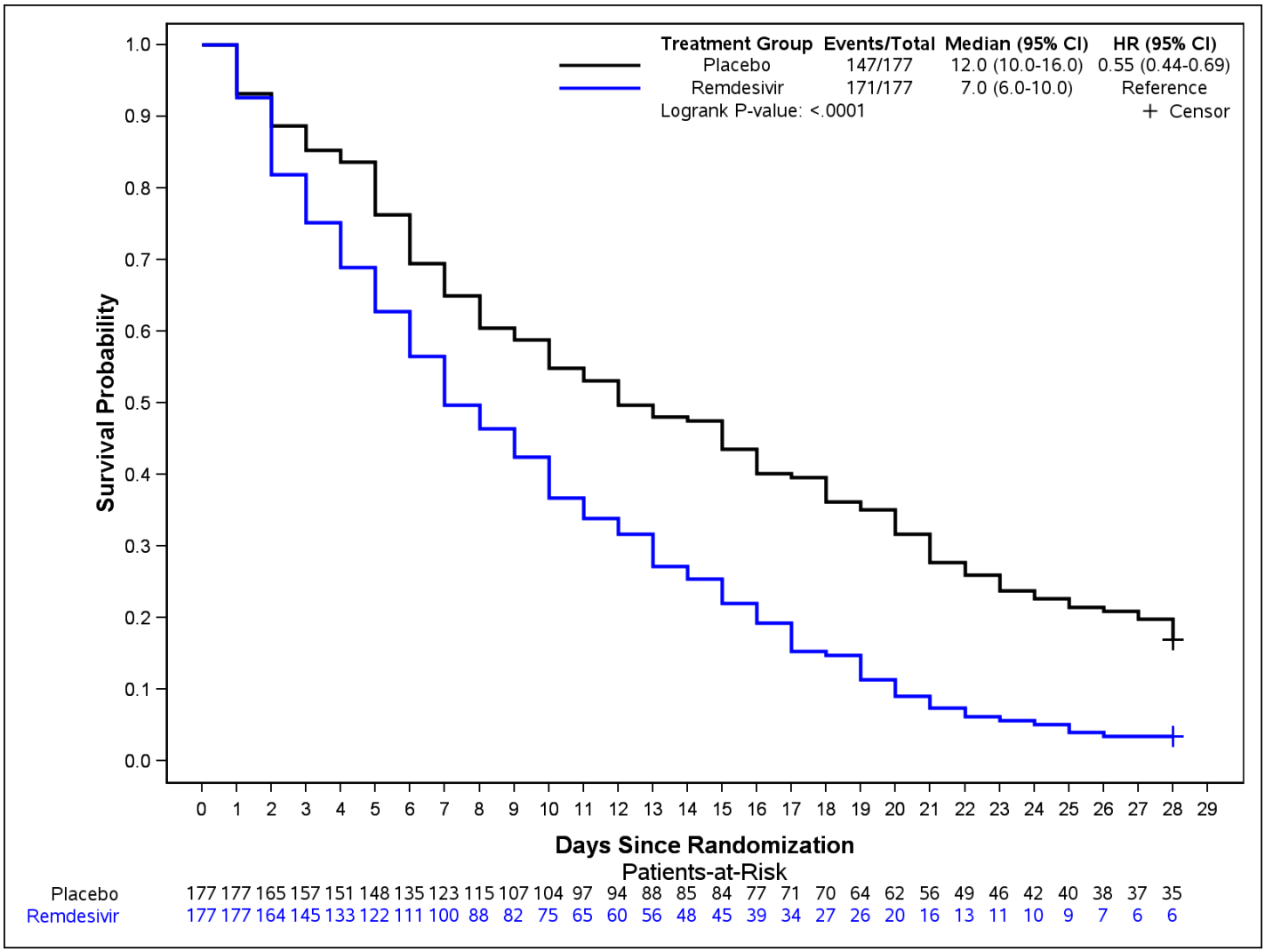


Figure 24: Kaplan-Meier Curve of Time to Death, SAE, Discontinuation of Study Infusions or Grade 3 or 4 AE through Day 29 by Treatment Group – Treated Population

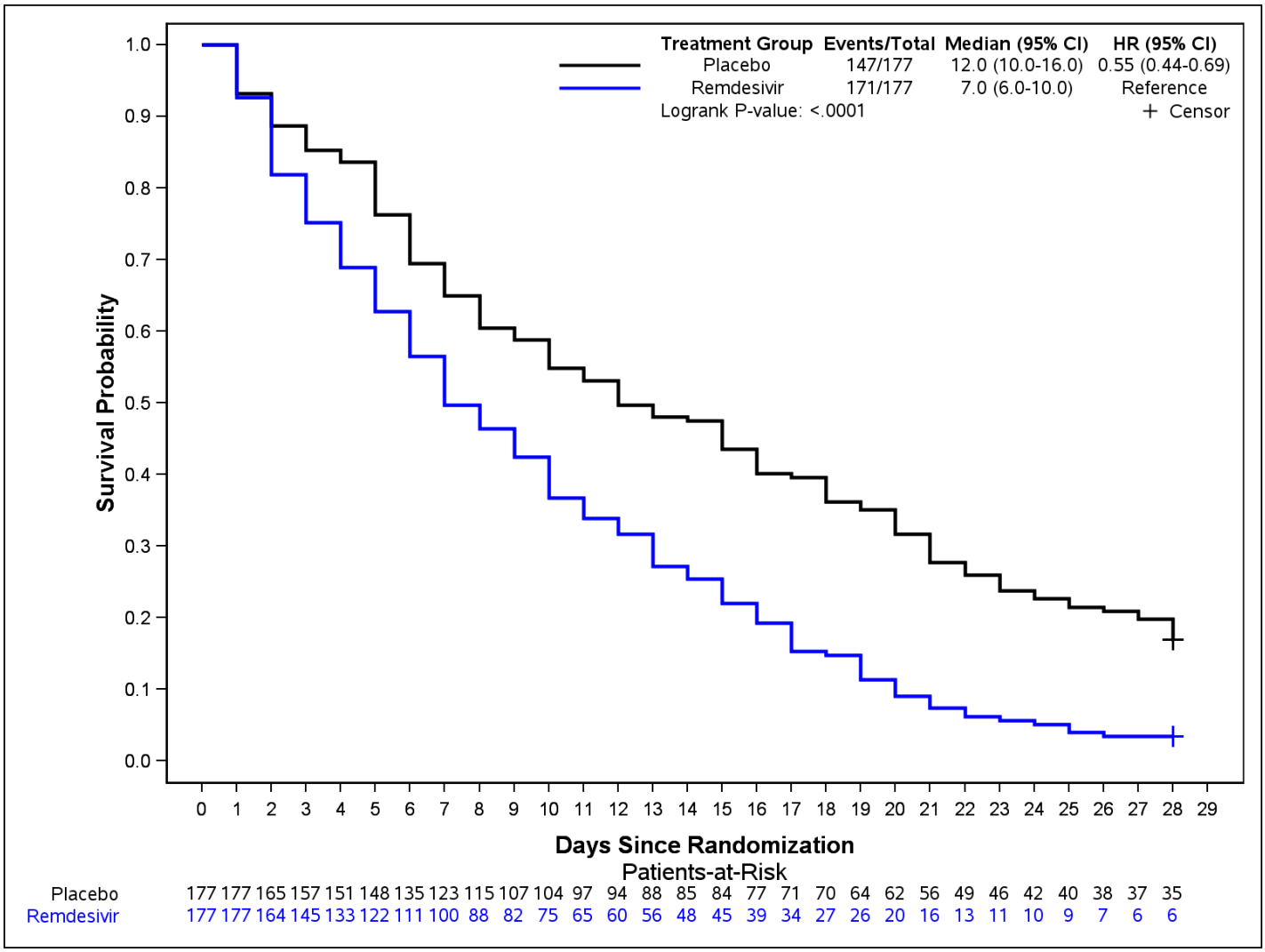
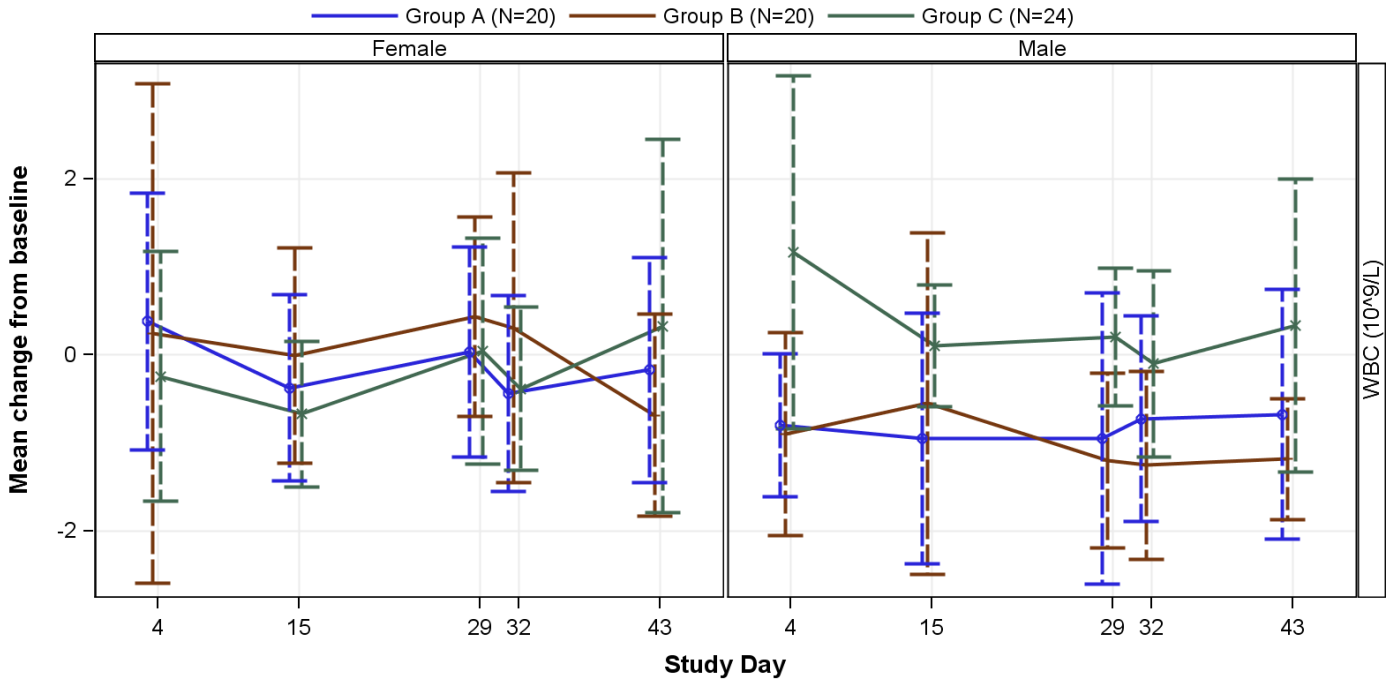


Figure 25: [Parameter X] Results by Scheduled Visits: Mean Changes from Baseline by Treatment Group – Treated Population



APPENDIX 3. LISTINGS MOCK-UPS

TABLE OF LISTINGS

Listing 1: Analysis Population Inclusions/Exclusions for Randomized Subjects

Treatment Group	Subject ID	Analysis Population	Included in Population?	Reason Subject Excluded	Included in Early Analysis Set?
Remdesivir/Placebo	XXXXX	Intent-to-Treat	Yes/No	NA/xxxxxxxxx	Yes
		Treated	Yes/No	NA/xxxxxxxxx	

Programming Notes: Include randomized subjects only. Sort Order = Treatment Group, USUBJID. If subject was included in the early analysis set, then display "Yes". Otherwise do not display anything.

Listing 2: Subjects who Early Terminated or Discontinued Treatment

Treatment Group	Subject ID	Category	Reason for Early Termination or Treatment Discontinuation	Study Day
Remdesivir/Placebo	XXXXX	Early Termination/Treatment Discontinuation	xxxxxx	xxxx

Programming Notes: Sort Order = Treatment Group, USUBJID, category where Treatment discontinuation is sorted prior to Early termination. If the subject discontinued treatment because they were unblinded and crossover treated with remdesivir, then the reason for discontinuation will display "Treated with Remdesivir".

Listing 3: Subject-Specific Protocol Deviations

Treatment Group	Disease Severity	Subject ID	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Comments
Remdesivir/Placebo	Mild/Moderate / Severe	xxxxx	xx	xxx	xxx	x	xxxx	Yes/No	Yes/No	Yes/No	xxxx

Programming Notes: Sort Order = Treatment Group, USUBJID, Deviation Number

Listing 4: Non-Subject-Specific Protocol Deviations

Site	Start Date	End Date	Deviation	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Category	Comments
Xxxx	xxxx	xxxx	xxxx	xxxx	Yes/No	Yes/No	xxxx	xxxxx

Programming Notes: Sort Order = Site, start date, deviation

Listing 5: Individual Efficacy Response Data: Clinical Status Score Data

Treatment Group	Disease Severity	Subject ID	Study Visit Day of Assessment	Actual Study Day of Assessment	Clinical Status Score	Clinical Status	Included in Early Analysis Set?
Remdesivir/Placebo	Mild/Moderate / Severe	xxxxx	xx	xx	xx	xxxxx	Yes

Programming Notes: Sort Order = Treatment Group, USUBJID, Study Day. Clinical status should match the wording of the scale definitions in Section 4.3. If the record was included in the early analysis set, then display "Yes". Otherwise do not display anything.

Listing 6: Individual Efficacy Response Data: NEWS

Treatment Group	Disease Severity	Subject ID	Study Visit Day	Actual Study Day	Respiratory Rate Score	O_2 Saturation Score	Any Supplemental O_2 Score	Temperature Score	Systolic BP Score	Heart Rate Score	Level of Consciousness Score	Total Score
Remdesivir/Placebo	Mild/Moderate / Severe	xxxxx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Programming Notes: Sort Order = Treatment Group, USUBJID, Study Day

Listing 7: Demographic Data

Treatment Group	Disease Severity	Subject ID	Geographic Region	Sex	Age at Enrollment (years)	Ethnicity	Race	Duration of Symptoms prior to Enrollment	Weight (Kg)	Height (Cm)	BMI	Included in Early Analysis Set?
Remdesivir/Placebo	Mild/Moderate / Severe	xxxxx	xxx	xxx	xx	xxx	xxx	xxx	xx	xx	xxx	Yes

Programming Notes: Sort Order = Treatment Group, USUBJID. If subject was included in the early analysis set, then display "Yes". Otherwise do not display anything.

Listing 8: Pre-Existing and Concurrent Medical Conditions

Treatment Group	Subject ID	MH Number	Medical History Term	MedDRA System Organ Class	MedDRA Preferred Term
Remdesivir/Placebo	xxx	xx	xxxxx	xxxx	xxxx

Programming Notes: Sort Order = Treatment Group, USUBJID, MH Number

Listing 9: Concomitant Medications

Treatment Group	Subject ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)	Prohibited Medication?
Remdesivir/Placebo	xxx	xx	xxxx	x	x	xxxx	Yes/No	Yes/No	xxxx / xxxx	Yes/No

Programming Notes: Sort Order = Treatment Group, USUBJID, CM number

Note: If medication started prior to enrollment and there is no date, then Medication Start Day = Prior to Enrollment
If medication is ongoing at end of study, the Medication End Day = Ongoing

The "Prohibited Medication?" column refers to whether the medication falls under one of the categories of prohibited medications listed in Section 6.4.

Listing 10: Compliance Data

Category	Number of Doses	Reason for Missing, Halting or Slowing any doses	Study Day of Discharge	Study Day of Death
Treatment Group: , Subject ID:				
Received	xx	--	Xxx/NA	Xxx/NA
Missed	xx	xxxxxx		
Halted/Slowed	xx	xxxxxx		

Programming Notes: Sort Order = Treatment Group, USUBJID.

Listing 11: Listing of Non-Serious Adverse Events

Adverse Event	Study Day	Duration	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term	Included in Early Analysis Set?
Treatment Group: Subject ID: , Disease Severity: , AE Number:											
xxx	xx	x	xxx	Related/Not Related	xxxx	xxx	Yes/No	xxxx	xxxx	xxxx	Yes
Comments: xxxx											

Programming Note: Sort order will be Treatment Group, USUBJID, AE Number. If the event was included in the early analysis set, then display "Yes". Otherwise do not display anything.

Listing 12: Listing of Non-Fatal Serious Adverse Events

Adverse Event	Study Day	Duration	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term	Included in Early Analysis Set?
Treatment Group: Subject ID: , AE Number:													
xxxx	x	x	x	xxxxx	xxx	Related/Not Related	xxxx	xxxx	Yes/No	xxxxx	xxxxx	xxxxx	Yes
Comments: xxxx													

Programming Note: Sort order will be Treatment Group, USUBJID, AE Number. If the event was included in the early analysis set, then display "Yes". Otherwise do not display anything.

Listing 13: Listing of Deaths

Adverse Event	Study Day	Duration	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	MedDRA System Organ Class	MedDRA Preferred Term	Included in Early Analysis Set?
Treatment Group: Subject ID: , AE Number:												
xxxx	x	x	x	xxxxx	xxx	Related/Not Related	xxxx	xxxx	Yes/No	xxxxx	xxxxx	Yes
Comments: xxxx												

Programming Note: If the event was included in the early analysis set, then display "Yes". Otherwise do not display anything.

Listing 14: Pregnancy Reports – Maternal Information

Treatment Group	Subject ID	Pregnancy Number	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?
Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.											

Listing 15: Pregnancy Reports – Gravida and Para

			Live Births												
Subject ID	**Pregnancy Number**	**Gravida**	**Extremely PB[a]**	**Very Early PB[a]**	**Early PB[a]**	**Late PB[a]**	**Early TB[b]**	**Full TB[b]**	**Late TB[b]**	**Post TB[b]**	**Still Births**	**Spontaneous Abortion/ Miscarriage**	**Elective Abortions**	**Therapeutic Abortions**	**Major Congenital Anomaly with Previous Pregnancy?**
Gravida includes the current pregnancy, para events do not.															

[a] Preterm Birth
[b] Term Birth

Listing 16: Pregnancy Reports – Live Birth Outcomes

Subject ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score, 1 minute	Apgar Score, 5 minutes	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?
Congenital Anomalies are included in the Adverse Event listing.												

Listing 17: Pregnancy Reports – Still Birth Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?

Listing 18: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion

Listing 19: Clinical Laboratory Results

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Toxicity Grade)	Reference Range Low	Reference Range High
Remdesivir/Placebo	xxx	xx	xx	xx	x	xxx (xxx)	xxx (xxxx)	xxxx	xxxx

Listing 20: Physical Exam Findings

Treatment Group	Subject ID	Planned Study Day	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)
Remdesivir/Placebo	xxx	xx	xx	xxxx	xxxxxx	Yes/No/NA

Implementation Note: For respiratory findings denoted as 'Yes' on the Physical Exam CRF, denote the Body System as "Respiratory Finding' and denote the Abnormal Finding as the symptom name; e.g. if Wheezing is reported, the Abnormal Finding will be 'Wheezing'. The Reported as an AE cell will be denoted as 'NA' for respiratory findings. Each reported respiratory finding will appear in its own row.

Sort order will be treatment group, subject ID, planned time point, and body system.