CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 20-0013
Study Title:
A Multicenter Platform Trial of Putative Therapeutics for the Treatment of COVID-19 in Hospitalized Adults

NCT04583956, NCT04583969, NCT04988035

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STUDY TITLE

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This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

ACTIV	Accelerating COVID-19 Therapeutic Interventions and Vaccines
ACTT	Adaptive COVID-19 Treatment Trial
AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BET	Big Effect Trial
BLOQ	Below the Limit of Quantitation
CI	Confidence Interval
cm	Centimeters
CoV	Coronavirus
COVID-19	Coronavirus Disease 2019
CRF	Case Report Form
CRP	C-Reactive Protein
CSR	Clinical Study Report
HLT	High-Level Term
DAIDS	Division of AIDS
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
ECMO	Extracorporeal Membrane Oxygenation
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
eGRF	Estimated Glomerular Filtration Rate
ERC	Endpoint Review Committee
Hgb	Hemoglobin
INR	International Normalized Ratio
ITT	Intent-to-Treat
JAK	Janus kinase
kg	Kilograms

List of Abbreviations *(continued)*

LDH	Lactate Dehydrogenase
LLOD	Lower Limit of Detection
LLOQ	Lower Limit of Quantification
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities
MI	Multiple Imputation
mL	Milliliter
N	Number (typically refers to subjects)
NAAT	Nucleic Acid Amplification Test
NEWS	National Early Warning Score
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
OP	Oropharyngeal
OR	Odds Ratio
PBMC	Peripheral Blood Mononuclear Cells
PCR	Polymerase Chain Reaction
PK	Pharmacokinetic
PLT	Platelet
PT	Preferred Term
Q1	First Quartile
Q3	Third Quartile
RR	Respiratory Rate
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard Deviation
SOC	System Organ Class
SpO2	Blood Oxygen Saturation
TEAE	Treatment-Emergent Adverse Events

List of Abbreviations *(continued)*

TLF	Tables, Listings, and Figures
TNF	Tumor Necrosis Factor
ULOQ	Upper Limit of Quantification
US	United States
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

A novel coronavirus designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in December 2019 in Wuhan, China, and has since spread globally, resulting in an ongoing pandemic of Coronavirus Disease 2019 (COVID-19). Currently, remdesivir is the only FDA approved antiviral for the treatment of patients hospitalized with COVID-19, but even with this antiviral the mortality of COVID-19 remains high. Multiple putative therapeutics involving repurposed agents (licensed or in late development) have been proposed for treating COVID-19, but there is no way to evaluate many of these agents due to lack of suitable animal models that replicate human disease. There is an urgent need for rapid development and testing of interventions to treat COVID-19 in hospitalized patients. An adaptive platform trial is one approach to allow for accelerated testing and selection of promising therapeutic agents in order to meet ongoing public health needs. Each new intervention represents a new stage. Default elements are described in this Master Statistical Analysis Plan (SAP) and align closely with BET-A study. Any stage-specific elements will be detailed in the respective stage-specific appendix of the SAP, and these supersede the corresponding elements described in this Master SAP.

2. INTRODUCTION

2.1. Purpose of the Analyses

This Statistical Analysis Plan (SAP) encompasses all interim analyses and the final analysis of primary, secondary and some exploratory outcome measures. These analyses will assess the efficacy and safety of different investigational therapeutic agents relative to a common control arm and will be included in each investigational therapeutic Clinical Study Report (CSR). The protocol for ACTIV – 5 DMID BET 20-0013 – v6.0 calls for a planned interim efficacy analysis once approximately 50 subjects per treatment arm reach Study Day 8 or discontinue the trial early. If a stage is planned to have a total sample size greater than 200 subjects, then an additional planned futility analysis may be conducted. The details of the additional futility analysis will be described in the stage-specific SAP, if applicable.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

The overall objective of the study is to evaluate the clinical efficacy and safety of different investigational therapeutics relative to the control arm among hospitalized adults who have COVID-19.

3.1.1. Primary Objective

The default primary objective for the different stages in this platform trial is to evaluate the clinical efficacy and safety of different investigational therapeutics relative to the control arm in adults hospitalized with COVID-19 according to clinical status (8-point ordinal scale) at Study Day 8. In each stage-specific appendix, the primary endpoint most applicable to the intervention in that stage will be identified.

3.1.2. Secondary Objectives

3.1.2.1. Key Secondary Objectives

1. To evaluate the clinical efficacy of different investigational therapeutics, as assessed by time to sustained recovery, compared to the control arm up to and including Study Day 60.
2. To evaluate the clinical efficacy of different investigational therapeutics, as assessed by whether subjects are alive and without respiratory failure (ordinal score < 7), compared to the control arm up to and including Study Day 29, among those with an ordinal score of 5 or 6 at baseline.

If the key secondary objective is different than what is covered in the master SAP, it will be highlighted for each individual investigational intervention in the corresponding stage-specific appendix.

3.1.2.2. Other Secondary Objectives

1. To evaluate the 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 1 category and 2 categories from Study Day 1 (baseline) up to and including Study Day 60 using clinical status,
            - Clinical status using 8-point ordinal scale at Study Days 1, 3, 5, 8, 11, 15, 22, and 29,
        - Mean change in the ordinal score from Study Day 1 to Study Days 3, 5, 8, 11, 15, 22, and 29
        - Oxygenation:
            - Supplemental oxygen use up to and including Study Day 29.
        - Non-invasive ventilation/high-flow oxygen:
            - Non-invasive ventilation/high-flow oxygen use up to and including Study Day 29,
            - Incidence and duration of new non-invasive ventilation or high-flow oxygen use up to and including Study Day 29 (i.e., a subject with a baseline ordinal score of 5 who worsens to an ordinal score of 6, 7, or 8).

- Invasive Mechanical Ventilation/ extracorporeal membrane oxygenation (ECMO):
  - Ventilator/ECMO use up to and including Study Day 29,
  - Incidence and duration of new mechanical ventilation or ECMO use up to and including Study Day 29 (i.e., a subject with a baseline ordinal score of 5 or 6 who worsens to an ordinal score of 7).
- Proportion of subjects alive and without respiratory failure at Day 29

- Hospitalization:
  - Duration of hospitalization (days) up to and including Study Day 29.
- Mortality:
  - 14-day mortality (up to an including Day 15),
  - 28-day mortality (up to and including Day 29),
  - 59-day mortality (up to and including Day 60),
  - Time to death up to and including Day 29.
- Markers of inflammation and coagulation.

2. To evaluate the safety of different investigational therapeutics as compared to the control arm as assessed by:
   - Cumulative incidence of serious adverse events (SAEs) up to and including Study Day 60,
   - Cumulative incidence of Grade 3 and 4 clinical and/or laboratory adverse events (AEs) up to and including Study Day 60,
   - Discontinuation or temporary suspension of study product administration (for any reason),
   - Changes in white blood cell (WBC) count with differentials, hemoglobin, platelets, creatinine, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), estimated glomerular filtration rate (eGFR) and international normalized ratio (INR) over time.

If other secondary objectives are different than what is covered in the master SAP, it will be highlighted for each individual investigation intervention in the corresponding stage-specific appendix.

3.1.3. Exploratory Objectives

1. To evaluate the virologic efficacy of different investigational therapeutics as compared to the control arm as assessed by:
   - Percent of subjects with SARS-CoV-2 detectable in saliva (or best technology) sample at Study Days 3, 5, 8, 11, 15, and 29,
   - Quantitative SARS-CoV-2 virus in saliva (or best technology) sample at Study Days 3, 5, 8, 11, 15, and 29,
   - Percent of subjects with SARS-CoV-2 detectable in blood sample at Study Days 3, 5, 8, and 11,
   - Quantitative SARS-CoV-2 virus in blood at Study Days 3, 5, 8, and 11.
2. To evaluate the impact of study interventions on markers of inflammation and immune response.

3. To evaluate post-baseline usage of key concomitant COVID-19 treatments (e.g., steroids) in investigational therapeutic arms as compared to the control arm.

If the exploratory objectives are different than what is covered in the master SAP, it will be highlighted for each individual investigational intervention in the corresponding stage appendix. If data is not available for some of the exploratory endpoints at the time of the CSR, those endpoints will be reported in a separate CSR addendum.

3.2. Endpoints

Primary Endpoint

The default primary endpoint is clinical status (8-point ordinal scale) on Study Day 8:

1. Not hospitalized, no new or increased limitations on activities;
2. Not hospitalized, but new or increased limitation on activities and/or requiring new or increased home oxygen, CPAP, or BiPAP;
3. Hospitalized, not requiring new or increased supplemental oxygen - no longer requires ongoing medical care;
4. Hospitalized, not requiring new or increased supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise);
5. Hospitalized, requiring new or increased supplemental oxygen;
6. Hospitalized, requiring new or increased non-invasive ventilation or high-flow oxygen devices;
7. Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO);
8. Death.

Key Secondary Endpoints

One of the key secondary endpoints is time to sustained recovery (up to and including Study Day 60) and is defined as the first day on which the subject satisfies 1 of the following 3 categories from the clinical status ordinal scale (and does not return to a score of ≥ 4 up to and including Study Day 60):

1. Not hospitalized, no new or increased limitations on activities;
2. Not hospitalized, but new or increased limitation on activities and/or requiring new or increased home oxygen, CPAP, or BiPAP;
3. Hospitalized, not requiring new or increased supplemental oxygen - no longer requires ongoing medical care.

The other key secondary endpoint is whether the subject did not satisfy one of the following two categories from the ordinal scale up to and including Study Day 29. This analysis will only be completed for those subjects with baseline ordinal score of 5 or 6:

7. Hospitalized, on invasive mechanical ventilation or ECMO;
8. Death.

If the key secondary endpoints are different than what is covered in this master SAP, it will be highlighted for each individual investigational intervention in the corresponding stage-specific appendix.

Other Secondary Endpoints

The other secondary endpoints are:

Efficacy

- Time (days) from Study Day 1 to the first day for which a subject is assessed to be at least 1 category lower (improvement) than the subject's baseline ordinal score up to and including Study Day 60;
- Time (days) from Study Day 1 to the first day for which a subject is assessed to be at least 2 categories lower (improvement) than the subject's baseline ordinal score up to and including Study Day 60;
- Clinical status assessed using ordinal scale on Study Days 1, 3, 5, 8, 11, 15, 22, and 29;
- Change in clinical status using change in ordinal scale from Study Day 1 to Study Days 3, 5, 8, 11, 15, 22, and 29;
- Days of supplemental oxygen or worse (i.e., ordinal score of 5, 6, 7, 8) up to and including Study Day 29;
- Days of non-invasive ventilation/high-flow oxygen or worse (i.e., ordinal score of 6, 7, 8) up to and including Study Day 29;
- Whether a subject who has a baseline ordinal score of 5 requires new non-invasive oxygen use or worse (i.e., ordinal score of 6, 7, 8) during the study up to and including Study Day 29 (incidence);
- Days a subject who has a baseline ordinal score of 5 has an ordinal score of 6 or greater up to and including Study Day 29;
- Days of invasive mechanical ventilation/ECMO or worse (i.e., an ordinal score of 7 or 8) up to and including Study Day 29;
- Whether subject who has a baseline ordinal score of 5 or 6 requires new invasive ECMO use or worse (i.e., ordinal score of 7 or 8) during study up to and including Study Day 29 (incidence);
- Days a subject who has a baseline ordinal score of 5 or 6 has an ordinal score > 6 up to and including Study Day 29;
- Whether a subject is alive and without respiratory failure (ordinal score < 7) at Study Day 29;
- Time (days) to ventilation or death from Study Day 1 up to and including first 29 days of being on study.
- Days of hospitalization from date of admission up to and including Study Day 29.
- Values of C-reactive protein (CRP), ferritin, D-dimer, lactate dehydrogenase (LDH), and fibrinogen on Study Days 1, 3, 5, 8, and 11 (while hospitalized); and Study Days 15 and 29 (if attends in-person visit or still hospitalized).

Safety

- Whether a subject died from Day 1 up to and including Study Day 15.
- Whether a subject died from Day 1 up to and including Study Day 29.
- Whether a subject died from Day 1 up to and including Study Day 60.
- Time (days) to death from Study Day 1 up to and including Study Day 29.

- Whether a subject experienced at least one SAE up to and including Study Day 60.
- Whether a subject experienced at least one Grade 3 or Grade 4 AE up to and including Study Day 60.
- Episodes of early discontinuation or interruption of study product administration.
- Values of WBC with differential, hemoglobin, platelets, creatinine, eGFR, total bilirubin, ALT, AST, and INR on Study Days 1, 3, 5, 8, and 11 (while hospitalized); and Study Days 15 and 29 (if attends in-person visit or still hospitalized).

Exploratory Endpoints

The exploratory endpoints are:

- Whether a subject used concomitant COVID-19 treatments (e.g., steroids) post-baseline up to and including Study Day 29.

Details for the exploratory endpoints listed below are not provided in this master SAP will be provided in a separate SAP addendum and reported in a separate CSR addendum.

- Whether a subject has detectable SARS-CoV-2 according to polymerase chain reaction (PCR) in saliva from oropharyngeal (OP) swab (or best technology) on Study Day 1; Study Days 3, 5, 8, and 11 (while hospitalized); and Study Days 15, and 29 (if subject attends in-person visits or is still hospitalized);
- Quantitative polymerase chain reaction (PCR) for SARS-CoV-2 in saliva from OP swab on Study Days 1, 3, 5, 8, and 11 (while hospitalized); and Study Days 15 and 29 (if subject attends in-person visit or is still hospitalized);
- Whether a subject has detectable SARS-CoV-2 in blood at Study Days 1, 3, 5, 8, and 11 (while hospitalized);
- Quantitative PCR for SARS-CoV-2 in blood on Study Days 1, 3, 5, 8, and 11 (while hospitalized);
- Proteomic analysis of plasma cytokines and markers of inflammation;
- Transcription, epigenetic, and molecular profiles of mRNA in peripheral blood mononuclear cells (PBMC);
- Phenotypic and responsiveness markers in PBMC.

3.3. Study Definitions and Derived Variables

3.3.1. Definition of Study Day

Study day will be calculated from the first dosing date of study product and derived as follows:

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

Therefore, Study Day 1 is the day of first dose of study product administration. If subjects are not treated with study product, then their Study Day 1 will be their randomization date.

3.3.2. Analysis Visit Windows

The nominal visit as recorded in the electronic data capture (EDC) or within the permitted visit window as specified by the Schedule of Assessments will be used when data are summarized by visit (see Table 1 and Table 2). Any data relating to unscheduled visits will not be assigned to a particular visit or time point. However, the following exceptions will be made:

- An unscheduled visit prior to the first dose of study product may be included in the calculation of baseline value, if applicable.

Table 1: Clinical Status Study Day Windows

Analysis Visit Day	Nominal Day	Target day	Visit Window
Screening	Screening	-1 to 1	<1
Baseline	Day 1 (Hospitalized)	1	1
Day 3	Day 3 (Hospitalized)	3	3
Day 5	Day 5 (Hospitalized)	5	5
Day 8	Day 8 (Hospitalized)	8	8
Day 8	Day 8 (Discharged)	8	6-10
Day 11	Day 11 (Hospitalized)	11	11
Day 15	Day 15 (Discharged)	15	13-17
Day 22	Day 22 (Discharged)	22	19-25
Day 29	Day 29 (Discharged)	29	26-32
Day 60	Day 60 (Discharged)	60	57-63

Table 2: Lab Sample Collection Study Day Windows

Analysis Visit Day	Nominal Day	Target day	Visit Window
Screening	Screening	-1 to 1	<1
Baseline	Day 1 (Hospitalized)	1	1
Day 3	Day 3 (Hospitalized)	3	2-4*
Day 5	Day 5 (Hospitalized)	5	4-6*
Day 8	Day 8 (Hospitalized)	8	7-9
Day 11	Day 11 (Hospitalized)	11	10-12
Day 15	Day 15 (Hospitalized)	15	14-16
Day 15	Day 15 (Discharged)	15	13-17
Day 29	Day 29 (Hospitalized)	29	28-30
Day 29	Day 29 (Discharged)	29	26-32

*For windows that overlap, the priority will be given to the earlier date. For example, a lab sample drawn on Study Day 4 will be used as a Study Day 3 lab sample draw if there isn't a lab sample drawn for Study Days 2 or 3, regardless of whether a Study Day 5 lab is drawn.

In general, the Study Day 1 (baseline) value will be the last non-missing value prior to the administration of the first dose. If multiple measurements occur on the same day, the last non-missing value prior to first dose will be considered as the baseline value. If these multiple measurements are recorded on Day 1 but the time is

not available, the average of these measurements (for continuous data) will be considered the Study Day 1 value. For categorical measurements, if there are multiple records with the same time or no time recorded on the same day prior to the first dose, the value with the lowest severity will be selected as baseline (i.e., normal will be selected over abnormal).

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a platform trial to conduct a series of randomized, double-blind, placebo-controlled trials using common assessments and endpoints in hospitalized adults diagnosed with COVID-19. This is a proof-of-concept study with the intent of identifying promising treatments to enter a more definitive study (such as Adaptive COVID-19 Treatment Trial [ACTT], Accelerating COVID-19 Therapeutic Interventions and Vaccines [ACTIV], industry sponsored trials etc.). The study will be conducted at up to 70 domestic sites and 5 international sites. The study will compare different investigational therapeutic agents to a common control arm and determine which have relatively large treatment effects. In order to maintain the double blind, each intervention will have a matched placebo. However, the control arm will be shared between stages/interventions and may include participants receiving the matched placebo for a different stage/intervention.

The general goal of the stages included in this platform trial is not to determine clear statistical significance for an intervention, but rather to determine which products yield clinical data suggestive of efficacy and should be moved quickly into larger studies. However, clinical or drug development priorities may arise that require a larger sample size and a plan for a more definitive study. Estimates produced from this trial will provide an improved basis for designing the larger trial, in terms of sample size and endpoint selection. Products with little indication of significant efficacy will be dropped on the basis of interim evaluations. In addition, some interventions may be discontinued on the basis of interim futility or efficacy analyses.

The study will include one Master Protocol (DMID Protocol 20-0013: ACTIV-5/Big Effect Trial) and an additional "stage" for each investigational intervention included in the study. Stage-Specific Appendices will be provided, detailing the protocol interventions and any specific exceptions to the Master Protocol. One or more interventions/stages may be started at any time. The number of interventions/stages enrolling concurrently are programmatic decisions and will be based on the number of sites and the pace of enrollment. At the time of enrollment, subjects will be randomized to a stage, and then to either the active arm of that stage or the matching placebo. There will be approximately 100 subjects in each active arm of the platform trial (though this may be modified as specified in each stage-specific appendix to accommodate special circumstances). A given site will generally have no more than 3 interventions/stages at once.

See the schedule of assessments in each stage-specific appendix for assessment details. The schedule is similar to Adaptive COVID-19 Treatment Trial (ACTT) to allow evaluation of endpoints used in the larger study. Subjects will be assessed daily while hospitalized. Once subjects are discharged from the hospital, they will have a study visit on Study Days 8, 15, 22, 29 and 60 as an outpatient. The outpatient Study Days 8, 22 and 60 visits do not have laboratory tests or collection of samples and may be conducted by phone. Days 15 and 29 visits are preferred to be in person in order to collect safety laboratory testing, stored samples, and virologic assessments. However, if infection control considerations and other restrictions limit the ability to have visits at Study Days 15 and 29 in person, they may also be conducted by phone and only clinical data will be obtained.

4.2. Discussion of Study Design, Including the Choice of Control Groups

This study utilizes an adaptive platform design that increases efficiency to identify safe and efficacious therapeutic agents for subjects with COVID-19 during the current outbreak. The platform design allows rapid addition of new therapeutic agents as they are identified and ready for testing in clinical trials. As the study is a multicenter, randomized, controlled study, we will be able to acquire rigorous data about the safety and efficacy of investigational therapeutic agents for COVID-19 that will lead to generalizable evidence. The trial

is designed to stop quickly if the agents are unlikely to have a large effect (odds ratio around 1) and will identify those with a large effect (e.g., odds ratio 2 or above). This trial is not designed for definitive determination of efficacy, but rather to identify agents for testing in larger definitive studies.

Subject assignment to study intervention will be randomized, which is essential for providing evidence for efficacy of these new therapeutic agents. Finally, collecting clinical and virologic data on enrolled subjects using a standardized timeline and collection instruments should provide valuable information about the clinical course of and morbidities associated with COVID-19 in a diverse group of hospitalized adults.

4.3. Selection of Study Population

This trial will study putative therapeutics in a hospitalized adult population (≥18 years old) with COVID-19. The platform trial will have common inclusion criteria with modifications appropriate for each stage. Additional stage-specific criteria are included in the stage-specific appendices. Exclusion criteria are described in each stage-specific appendix.

Inclusion Criteria:

1. Admitted to a hospital with symptoms suggestive of COVID-19 and requires ongoing medical care.
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. Illness of any duration and has laboratory-confirmed SARS-CoV-2 infection as determined by PCR or other commercial or public health assay (e.g., Nucleic Acid Amplification Test [NAAT], antigen test) in any respiratory specimen or saliva <14 days prior to randomization.
6. Illness of any duration, and requiring, just prior to randomization, supplemental oxygen (any flow), mechanical ventilation or ECMO (ordinal scale category 5, 6, or 7).
7. Women of childbearing potential must agree to either abstinence or use at least one acceptable method of contraception (duration will be study product defined).

   **Acceptable methods included barrier contraceptives (condoms or diaphragm) with spermicide, intrauterine devices (IUDs), hormonal contraceptives, oral contraceptive pills, and surgical sterilization. When applicable, stage-specific contraception requirements are included in each stage-specific appendix.*
8. Agrees not to participate in another blinded clinical trial (both pharmacologic and other types of interventions) for the treatment of COVID-19 through Day 29.

Exclusion Criteria:

See specific exclusion criteria described in each stage-specific appendix.

Specific Populations:

The inclusion of vulnerable subjects and exclusion of specific populations need to be customized according to each stage or intervention and its corresponding controls with the current understanding of epidemiology and clinical disease. Inclusion and exclusion of specific populations will be described for each stage in the stage-specific appendices.

4.4. Treatments

4.4.1. Treatments Administered

Each stage in this platform trial may have different study products. Information about the study product(s) for a given stage can be found in the study protocol stage-specific appendix.

4.4.2. Identity of Investigational Product(s)

See stage-specific protocol for details of study product formulation.

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

Randomization will be stratified by study site and severity measured by baseline ordinal score (baseline ordinal score of 5 versus a baseline ordinal score of 6 or 7).

Subjects will first be randomized to 1 of the stages to which they are eligible with equal allocation. Then patients are randomized to the active intervention or placebo version of that stage with allocation k:1, where k is the number of interventions for which a subject is eligible. For example, if a subject is eligible for 3 active interventions or stages that the site is currently randomizing, the subject will be randomized to 1 stage with a 1:1:1 allocation to the 3 stages, then randomized to the selected intervention's or stage's active or placebo arm with a 3:1 allocation of active versus placebo. This process results in equal allocation of the 3 active intervention arms and the pooled placebo arm.

Differing entry criteria across interventions adds complexity to this process. Subjects who are eligible for all 3 interventions will be randomized to A, B, or C in the first randomization step, and then have a 25% chance of randomization to placebo in the second step. However, the subject who is not eligible for C will first be randomized to stages with A or B with equal probability, and will have a 33% chance of randomization to placebo in the second step, leading to equal size A, B, and pooled placebo groups for this stratum of subjects. Ultimately, evaluation of A versus placebo would need to only include subjects that were eligible to be randomized to A.

The previous paragraph refers to a scenario in which the interventions have largely overlapping study populations. However, at some point the trial might study agents for non-overlapping cohorts. For example, there might be one or multiple interventions that are only appropriate for subjects who have a baseline ordinal score of 5, and a completely different set of interventions that are only appropriate for subjects who have a baseline ordinal score of 6 or 7. Since these interventions would occur in non-overlapping cohorts, they can be viewed as two different studies. Thus, the randomization process described above would be implemented separately in the two cohorts (baseline ordinal score groups). If there were two interventions in the first cohort, randomization would follow as above with k=2, and if there was one intervention in the second cohort, randomization would follow in that cohort as above with k=1. Since the study populations and interventions would not overlap, all analyses would be conducted completely separately by cohort.

4.4.4. Selection of Doses in the Study

All subjects in this study will be receiving remdesivir in addition to the investigational drug or placebo. The dose of remdesivir used in this study will be the same dose shown to be efficacious in the ACTT-1 clinical trial and are the US FDA approved doses. The duration of dosing may be adjusted by the site according to clinical severity. The maximum number of doses to be given during hospitalization is ten doses. This includes the loading dose and all maintenance doses given during the study and pre-study if applicable.

Refer to the stage-specific appendix for details of doses of study products administered in each stage.

4.4.5. Selection and Timing of Dose for Each Subject

Each stage in this platform trial may have different timing of dose. Information about the timing of dose for each study product(s) for a given stage can be found in the stage-specific appendix.

4.4.6. Blinding

The interventions the study subjects are eligible for and the intervention each subject is randomized to in the first randomization step will be known and collected on CRF. The treatment arm each subject is randomized to in the second step of randomization will be blinded (see Section 4.4.3). 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 utilize the unblinded pharmacist role within the Premier Interactive Response Technology (IRT) system to perform the Treatment Arm Lookup task to determine the treatment for subjects. No other user roles have access to this information within the system.

4.4.7. Prior and Concomitant Therapy

Each stage in this platform trial may have different permitted therapies that need to be customized according to each intervention. Information about the study permitted therapies for a given stage can be found in its stage-specific appendix.

4.4.8. Treatment Compliance

Each dose of study product will be administered by a blinded member of the clinical research team who is qualified and licensed to administer the study product. Administration date and time, and whether any doses were slowed, halted or missed will be entered into the electronic case report form (eCRF).

4.5. Efficacy and Safety Variables

For each study day while the subject is hospitalized and follow-up visits, the clinical status will be recorded on an 8- point ordinal scale. The clinical status scale is defined as follows:

1. Not hospitalized, no new or increased limitations on activities;
2. Not hospitalized, but new or increased limitation on activities and/or requiring new or increased home oxygen, CPAP or BiPAP;
3. Hospitalized, not requiring new or increased supplemental oxygen* - no longer requires ongoing medical care;
4. Hospitalized, not requiring new or increased supplemental oxygen* - requiring ongoing medical care (COVID-19 related or otherwise);
5. Hospitalized, requiring new or increased supplemental oxygen*;
6. Hospitalized, requiring new or increased non-invasive ventilation or high flow oxygen devices;
7. Hospitalized, on invasive mechanical ventilation or ECMO;
8. Death.

The National Early Warning Score (NEWS) has demonstrated an ability to discriminate subjects at risk of poor outcomes [1]. This score is based on 7 clinical parameters (see Table 3). The NEWS is collected at baseline as a measure of ordinal score. It can be performed concurrently with the Ordinal Scale.

The 7 parameters can be obtained from the hospital chart or electronic medical record (EMR) 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). The NEWS is recorded for the day on which it is obtained. ECMO and mechanical ventilated subjects should be assigned a score of 3 for respiratory rate (RR<8) regardless of the ventilator setting. Subjects on ECMO should get a score of 3 for heart rate since they are on cardiopulmonary bypass.

Table 3: National Early Warning Score (NEWS)

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

Level of consciousness = alert (A), and non-alert and arousable only to voice (V) or pain (P), and unresponsive (U).

Oxygenation, non-invasive ventilation/high flow oxygen, invasive mechanical ventilation/extracorporeal membrane oxygenation (ECMO) will be assessed using results of the 8-point ordinal scale. Hospitalization duration will be assessed using admittance and discharge dates. Mortality will be assessed using results from the electronic case report form (eCRF) serious adverse events (SAEs) form. That is, the number of days from Study Day 1 to the date of death.

Safety will be assessed by the following:

- Cumulative incidence of SAEs up to and including Study Day 60.
- Cumulative incidence of Grade 3 and 4 clinical and/or laboratory AEs up to and including Study Day 60.
- Discontinuation or temporary suspension of study product administration (for any reason).
- Changes in WBC count with differential, hemoglobin, platelets, creatinine, total bilirubin, ALT, AST, eGFR, and INR over time (analysis of lab values in addition to AEs noted above).

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

Exploratory endpoints for post-baseline usage of key concomitant COVID-19 treatments (e.g., steroids) summarized by investigational therapeutic and control arms. The details of analyses for all virology and PK exploratory endpoints will be included in a separate analysis plan(s).

The schedule of study assessments is provided in each stage-specific appendix of the SAP.

5. SAMPLE SIZE CONSIDERATIONS

We have chosen a sample size of 100 per arm for the proof of concept stages. The power can be computed for the Study Day 8 ordinal score on the basis of an odds ratio representing clinical improvement. The odds ratio represents the odds of improvement in the ordinal scale for treatment relative to placebo. The sample size to detect a given odds ratio for 1:1 randomization using a 2-tailed test at level α is given by

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

where λ 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, $z_{\alpha/2}$and z_{β} are the $1 - \alpha/2$ and $1 - \beta$ quantiles, respectively, of the standard normal distribution.

However, to fully understand all aspects of the testing procedure, we have simulated the probabilities of an intervention: a) being declared futile after 50 subjects per arm, b) being declared efficacious after 50 subjects per arm, and c) being declared promising by 100 subjects per arm.

The interim analysis will find an intervention futile if its point estimate for the primary endpoint has an odds ratio <1. An intervention can be declared efficacious early after 50 subjects per arm if two-sided p<0.001 and OR>1. If the intervention continues to 100 subjects, it will be declared promising if the final p-value is <0.20 and OR>1, and statistically significant if the final p-value is <0.05. More details are provided in Interim Analysis Section.

Table 4 displays the outcome probabilities in the control arm for sample size determination; this uses preliminary unpublished data from the remdesivir arm in ACTT study. The categories of the 8-point ordinal scale are described in Section 3.2.

Table 4: Expected distribution of ordinal outcomes for the control arm at Study Day 8

Severity Outcome	Outcome (%)
1. Not hospitalized, no new or increased limitations on activities	0.0
2. Not hospitalized, but new or increased limitation on activities and/or requiring new or increased home oxygen, CPAP or BiPAP	34.6
3. Hospitalized, not requiring new or increased supplemental oxygen - no longer requires ongoing medical care	1.2
4. Hospitalized, not requiring new or increased supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise)	10.6
5. Hospitalized, requiring new or increased supplemental oxygen	17.1
6. Hospitalized, requiring new or increased non-invasive ventilation or high flow oxygen devices	8.8
7. Hospitalized, on invasive mechanical ventilation or ECMO	24.2
8. Death	3.5

Table 5 provides the probability to detect futility or efficacy given various odds ratios at interim and final analysis based on simulations (with 10,000 replications). An intervention with no effect (an odds ratio of 1)

had 50% chance of stopping at the interim analysis and has only a 10% chance to show promise. An intervention with an odds ratio of 2 has high power to show promise; that is, there is 91% probability that the final p-value will be less than .20 and only a 3% chance it will be stopped at an interim futility test. The powers in Table 5 are slightly lower than what would be determined from the Whitehead formula, because there is some minimal trade-off associated with testing for futility, especially for the alpha=.20 significance threshold. If the primary endpoint is different for a stage, stage-specific power and sample size computations that are relevant to that stage will be included in the stage-specific SAP.

Table 5: Simulated early stopping probabilities at the interim review (n=50/arm), and power calculations for the final study size (n=100/arm) for Study Day 8 Ordinal Score

	Probability of stopping for futility or efficacy at interim analysis for a given true odds ratio		Power at full study enrollment (100 active, 100 control)	
OR	**Futility**	**Efficacy**	**Efficacy w/ alpha=.05**	**Efficacy w/ alpha=.20**
0.75	0.793	0.000	0.001	0.008
1.00	0.502	0.000	0.026	0.096
1.25	0.260	0.004	0.136	0.329
1.50	0.126	0.014	0.348	0.604
1.75	0.060	0.036	0.581	0.802
2.00	0.028	0.070	0.765	0.913
2.25	0.013	0.119	0.879	0.961
2.50	0.006	0.179	0.939	0.984

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

This is a proof of concept double-blind placebo controlled randomized trial testing a superiority hypothesis where interventions with a two-sided p-value < .20 will be declared promising and will be considered statistically significant if the final two-sided p-value is < .05. These data will be summarized by treatment (intervention name versus placebo) and when appropriate by baseline ordinal score. Additionally, data 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 in the specified population) will be displayed.
- Means, standard deviation, median, and/or range for continuous data, median and confidence intervals for time-to-event data.

Confidence intervals will be generated; 95% and 80% confidence intervals will be generated for primary and key secondary outcomes. For hazard ratio and odds ratio estimates, Wald confidence intervals will be used. For confidence intervals of proportions for other efficacy and safety outcomes, Blaker confidence intervals will be used.

In general, all tables will have corresponding listings of data presented unless noted otherwise.

When calculating treatment effects (e.g., differences, hazard ratios, odds ratios) from regression modelling, placebo will be used as the reference group. Subjects on interventions will only be compared to control subjects who could potentially have been randomized to that intervention (i.e., they met eligibility criteria for the intervention and are at a site where the intervention was enrolling at the time of the subject's randomization). Analyses of newly added arm(s) will be performed comparing concurrently enrolled control subjects. For any modeling that uses covariates defined in Section 6.4, the category listed last for each variable in that section will be used as the control group for the interaction analysis and covariate-adjusted analyses.

For the time-to-event analyses, the following SAS pseudocode will be used to generate stratum-specific median time to event estimates and confidence intervals and stratum-specific Kaplan-Meier curves.

```
proc lifetest data=dataset plots=(s);
      time timevariable * censorvariable(1);
      test treatmentvariable;
run;
```

In this approach, `timevariable` represents the time until the event in question (e.g., recovery), `censorvariable` represents the censoring variable (e.g., 0= event observed, 1= event did not occur at the time of withdrawal, discharge, lost-to-followup, etc), and `treatmentvariable` represents the intervention (e.g., 0= remdesivir + placebo, 1= remdesivir + new treatment).

To perform a Cox proportional hazards analysis and generate the treatment hazard ratio along with its Wald confidence interval and p-value from the score test after adjusting for other covariates, the following SAS pseudocode will be used.

```
proc phreg data=dataset;
       class treatmentvariable(ref=placebolabel) othercovariates;
       model timevariable * censorvariable(1) = treatmentvariable othercovariates /
       ties=efron;
       hazardratio treatmentvariable / diff=ref cl=wald;
```

```
       ods output hazardratios = hrest globaltest=pvalue;
run;
```

To assess the assumption of proportional hazards for Cox models, Kaplan-Meier curves for each treatment arm will be produced (PH assumption supported if curves do not cross). Restricted mean survival time along with its 95% CI will be reported to assess whether the results change if the PH assumption is not satisfied.

Proportional Odds analysis without MI:

The following SAS pseudocode will be used to perform the proportional odds analysis with treatment, baseline ordinal score and baseline steroid use as covariates to generate the treatment odds ratio, p-value, and predicted probabilities of the ordinal scale levels by treatment and ordinal score using complete data

```
proc logistic data=dataset out=imp_parms plots(only)=effect(x= ordscore_d8
      sliceby =baseordscorevar*trtvar individual connect);
      class baseordscorevar (param=ref ref=5) basesteroidusevar (param=ref ref=no
steroid use) trtvar (param=ref ref=placebolabel);
       model ordscore_d8 = trtvar baseordscorevar basesteroidusevar;
      oddsratio trtvar;
      ods output oddsratioswald = orest;
run;
```

For the endpoints analyzed by proportional odds, odds ratios between the binary progression strata will be computed, to support data understanding. For example, odds ratio, confidence intervals from logistic regression will be reported for treatment effect for the binary endpoint of OS= 1-7 vs 8, then OS= 1-6 vs 7-8, etc. Similar odds ratios across these 7 2x2 tables will support the proportional odds assumption.

95% Blaker confidence intervals for proportions/percentages:

```
proc freq;
      by analysisvariable;
      table trtvar/alpha=0.05 binomial (cl=blaker);
      ods output binomialcls=outputdsn2;
run;
```

Risk differences and 95% CI Using Miettinen-Nurminen:

```
proc freq data = analysis;tables trtvar*aval/ out=mncidat;run;

proc sort data=mncidat;by  trtvar;run;

ods select  PdiffCLs;
ods output PdiffCLs=mnci_d5v;
proc freq data=mncidat order=data;
    tables trtvar*aval /riskdiff (CL=( MN ));
    weight count;
run;
```

Odds ratios from logistic regression without MI:

```
proc logistic data=dataset out=imp_parms;
      class baseordscorevar (param=ref ref=5) basesteroidusevar (param=ref ref=no
steroid use) trtvar (param=ref ref=placebolabel);
       model aval (event='Yes') = trtvar baseordscorevar basesteroidusevar;
      oddsratio trtvar;
      ods output oddsratioswald = orest;
run;
```

Risk differences from logistic regression using the approach described in Ge et. Al [2]:

```
proc logistic data = dataset outmodel=pout;
      class trtvar ;
      model surv(event='1') = trtvar othercovariates  ;
run;

*Create dataset tempa to contain all subjects and assign them the active treatment and
dataset tempp which include all subjects assigned the placebo treatment;

proc logistic inmodel=pout;
  score data = tempa out=preda(keep=id P_a rename= (P_1=P_a))) ;
run;

proc logistic inmodel=pout;
  score data = tempp out=predp(keep=id P_1 rename= (P_1=P_p)) ;
run;

proc sort data=pred1;by subjectid;run;
proc sort data=pred2;by subjectid;run;

*Combine to obtain risk differences in probabilities for each subject;

data comb;
      merge predp preda;
      by subjectid;
      diff=P_a-P_p;
run;

proc means data=comb;var diff;run;
```

To obtain the CI for the risk difference, use bootstrap with the following steps:

1. Sample with replacement from the dataset.
2. Obtain risk difference estimate for each bootstrap sample.
3. Repeat this step the above step 1000 times and use the 25th and 975th values from the sorted list of the 1000 risk estimates as the limits for the 95% CI for the risk difference. The risk difference estimate from bootstrap can be estimated as the mean of the 1000 risk estimates and should be equal to the risk difference obtained prior to performing bootstrap.

All statistical analyses and summaries will be performed on the mITT, ITT, and/or Safety populations. In general, the efficacy analysis will be performed mITT population and the safety analysis will be conducted on the Safety population. Any exceptions will be stated in the stage-specific appendix.

6.2. Timing of Analyses

6.2.1. Interim Analyses

A Data and Safety Monitoring Board (DSMB) will monitor ongoing results to ensure subject 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. Interim analyses for a given stage will be conducted after each intervention arm and the comparison control arm has approximately 50 subjects with Study Day 8 assessments. The DSMB may use the following guidelines:

- consider an arm futile at the interim evaluation if the odds ratio point estimate for the primary endpoint is <1.
- consider an intervention arm efficacious if the p-value after 50 subjects per arm is <0.001 and OR estimate >1.
- consider to not recommend discontinuing an arm if the p-value is <0.001, if members judge it would be more beneficial to collect more data before announcing the results.

Any time-to-event outcomes for the interim analyses will be analyzed through Study Day 29. The efficacy boundary follows a Haybittle-Peto approach. Given that the statistical adjustment for multiplicity due to this 0.001 boundary would be very minimal, no adjustment to the final p-value will be made, in this proof of concept study.

Safety analyses will evaluate Grade 2 (drug related hypersensitivity only), 3 and 4 AE, AESIs, and SAEs by treatment arm and baseline ordinal score. Safety monitoring will be ongoing (see study protocol Section 10.1.6) and evaluate safety results weekly. The unblinded statistical team will prepare these reports by baseline ordinal score with treatment groups collapsed for review by the DSMB. The unblinded statistical team may also prepare these reports by blinded treatment arm for review by the DSMB, if requested.

The unblinded statistical team will prepare the 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.

6.2.2. Final Analyses

The final analyses of outcomes and planned summaries/listings will be performed on the final locked database through Day 60 and provided in the final report. If data for some of the exploratory endpoints is available, results will also be included in the final report.

6.3. Analysis Populations

The default primary analysis will be based on a modified intention-to-treat (mITT) population, including all subjects who were randomized and received at least one dose of an investigational product administration for all proof of concept stages. If a stage requires a different population for the primary analysis, the appropriate population will be identified in the stage-specific appendix. Safety analyses will be based on the safety population and will use actual treatment received. For some stages an intention-to-treat (ITT) population, which includes all subjects randomized and is analyzed according to the randomized treatment assignment, will be considered. For all populations, actual ordinal score at baseline will be used to classify subjects into baseline ordinal score category.

Stage-specific appendices will denote the appropriate analysis populations to be used if different from the master SAP.

6.3.1. Intention-to-Treat Analysis (ITT) Population

The Intention-to-treat population will include all randomized subjects, and the population will be analyzed using randomized treatment group. Demographics and disposition tables will be based on this population.

6.3.2. Modified Intention-to-Treat (mITT) Population

The mITT population will include all randomized subjects who received at least one dose of an investigational product other than standard of care therapies, and the population will be analyzed using randomized treatment group.

6.3.3. Safety Population

The safety population will include all randomized subjects who received at least one dose of an investigational product other than standard of care therapies, and the population will be analyzed using actual treatment group.

6.4. Covariates and Subgroups

6.4.1. Covariates for the Primary Endpoint

The primary analysis model of ordinal score at Day 8 will use a proportional odds model with baseline steroid use (yes/no) and actual baseline ordinal score (5 vs 6/7) as covariates. A sensitivity analysis of the primary endpoint will include baseline steroid use, actual baseline ordinal score, and categorical variables for sites. Sites will be pooled into categories by grouping sites based on the major US regions (Northeast, Southeast, Midwest, Southwest, and West) groupings include at least 25 subjects who were randomized. A region with less than 25 subjects will be combined with the neighboring region with the fewest subjects. A supplemental analysis of the primary endpoint will include baseline steroid use, actual baseline ordinal score, continuous covariate age, and continuous duration of symptoms prior to enrollment as covariates in the model.

Additional supplemental analyses of the primary endpoint for ordinal score at Day 8 will include baseline steroid use, actual baseline ordinal score, and baseline use (yes/no) of each emerging COVID-19 treatment category listed in Section 6.4.3 as covariates.

A detailed list of covariates and subgroup analyses to be performed for the primary endpoint is also provided in Table 6.

6.4.2. Covariates for Secondary Endpoints

The main analysis for time to sustained recovery will use baseline steroid use and actual baseline ordinal score as covariates in a Cox regression model. P-value from the score test of this adjusted Cox model will be used to compare the covariate adjusted time to sustained recovery between treatment arms. This analysis will be referred to as the primary analysis of the time to sustained recovery endpoint. In the supplemental analysis, time to sustained recovery endpoint will be analyzed using baseline steroid use, actual baseline ordinal score, continuous age, and continuous duration of symptoms prior to enrollment as covariates in the Cox model.

Survival without respiratory failure up to and including Study Day 29 will be analyzed only for subjects with an actual baseline ordinal score of 5 or 6. The main analysis for this endpoint will use a logistic regression model adjusted for baseline ordinal score (5 vs 6/7), baseline dexamethasone use (yes or no), continuous

baseline CRP value, and continuous age as covariates. Additionally, the proportion of subjects who are alive and without respiratory failure up to and including Study Day 29 will be presented by treatment along with 95% and 80% CI estimated from Kaplan Meier. As a sensitivity analysis, survival without respiratory failure will be analyzed using a logistic regression model adjusting for baseline steroid use and actual baseline ordinal score as covariates. A supplemental analysis of this endpoint will use a logistic regression model adjusting for baseline steroid use, actual baseline ordinal, continuous age, and continuous duration of symptoms prior to enrollment.

The analysis of the time to mechanical ventilation or death will include baseline ordinal score (5 vs 6/7), baseline dexamethasone use (yes or no), baseline CRP value and age as covariates in the Cox regression model.

A detailed list of covariates and subgroup analyses to be performed for secondary endpoints is also provided in Table 6.

6.4.3. Subgroups

The following subgroups will be considered for the different subgroup analyses:

- Severity of disease using actual baseline ordinal score
  - Actual baseline ordinal score 5: Hospitalized and requiring supplemental oxygen
  - Actual baseline ordinal score 6 or 7: Hospitalized, on non-invasive ventilation or high-flow oxygen devices; or Hospitalized, on invasive mechanical ventilation or ECMO
- Baseline steroid use (Yes; No)
- Baseline use of emerging COVID-19 treatments (Yes; No): Defined by the sponsor based on a blinded review of WHODrug coded medications.
- Duration of symptoms prior to enrollment
  - Quartiles
  - <= Median; > Median
- Race (White; Black/African American; Asian; Other)
- Ethnicity (Hispanic or Latino; Not Hispanic or Latino)
- Comorbidities
  - None; Any
  - One, Two or more
  - Obese; Non-Obese
- Age (<40; 40-64; 65 and older),
- Sex (Female; Male)

Refer to Table 6 for details of which specific subgroup variables will be considered for a given endpoint.

Interaction tests will be conducted to evaluate whether the effect of treatment is different among subgroups described above for primary and key secondary endpoints. The type III p-value for the interaction term from the primary analysis of the primary endpoint, the primary analysis of the time to sustained recovery endpoint,

and the primary analysis of the survival without respiratory failure endpoint with the addition of the interaction term(s) will be reported.

A review of the concomitant medications will be performed by the study sponsor using the 202003 version of WHODrug to identify emerging COVID-19 treatments focusing on medications that fall into the following categories:

- Other drugs used to treat COVID (off-label, experimental use)
  - Monoclonal antibodies targeting the spike protein of SARS-CoV-2 including casirivimab, imdevimab and bamlanivimab
- Corticosteroids
- Other anti-inflammatory drugs:
  - JAK inhibitors: Tofacitinib, Baricitinib,etc
  - Tyrosine kinase inhibitors: Ruxolitinib, etc
  - Interleukin inhibitors

Additional details regarding covariates used in primary, sensitivity and supplemental analyses along with subgroup analyses to be performed for each endpoint are provided below in Table 6.

Table 6: Covariates and Subgroup Analyses for Each Endpoint

Endpoint	Analysis	Covariates/Subgroups
Primary Endpoint		
1. Ordinal Score at Day 8	Primary	1. Adjust for the following covariates: • Baseline steroid use • Actual baseline ordinal score
	Sensitivity	1. Repeat primary analysis with the following covariates: • Baseline steroid use • Actual baseline ordinal score • Site pooled by geographic regions (Categorical) 2. Repeat primary analysis on ITT population with the following covariates: • Baseline steroid use • Actual baseline ordinal score
	Supplemental	1. Adjust for the following covariates: • Baseline steroid use • Actual baseline ordinal score • Continuous Age • Continuous duration of symptoms prior to enrollment 2. Repeat primary model with the following covariates: • Baseline steroid use • Actual baseline ordinal score • Baseline use of emerging COVID-19 treatment by treatment categories
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatments • Duration of symptoms prior to enrollment • Race • Ethnicity • Comorbidities • Age (categorical) • Sex Baseline steroid use and baseline ordinal score will be included in the subgroup analysis as covariates unless the covariate is the subgroup.
Key Secondary Endpoints		
1. Time to Sustained Recovery	Primary	1. Adjust for the following covariates: • Baseline steroid use • Actual baseline ordinal score
	Supplementary	1. Adjust for the following covariates: • Baseline steroid use • Actual baseline ordinal score • Age (continuous) • Duration of symptoms prior to enrollment (continuous)

Endpoint	Analysis	Covariates/Subgroups
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatments • Duration of symptoms prior to enrollment • Race • Ethnicity • Comorbidities • Age (categorical) • Sex Baseline steroid use and baseline ordinal score should be included in the subgroup analysis as covariates unless the covariate is the subgroup.
2. Survival without respiratory failure up to and including Study Day 29	Primary	1. Adjust for the following covariates: • Baseline dexamethasone use • Actual baseline ordinal score • Baseline CRP value (continuous) • Age (continuous)
	Sensitivity	1. Adjust for the following covariates: • Baseline steroid use • Actual baseline ordinal score
	Supplementary	1. Adjust for the following covariates: • Actual baseline ordinal score • Baseline dexamethasone use • Age (continuous) • Duration of symptoms prior to enrollment (continuous)
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline dexamethasone use • Baseline use of emerging COVID-19 treatments • Duration of symptoms prior to enrollment • Race • Ethnicity • Comorbidities • Age (categorical) • Sex • Baseline CRP <150 Baseline dexamethasone use, baseline CRP, age, and baseline ordinal score will be included in the subgroup analysis as covariates unless the covariate is the subgroup.

Endpoint	Analysis	Covariates/Subgroups
Other Secondary Endpoints: Efficacy		
1. Time to 1-point improvement by Day 60	Primary	Adjust for the following covariates: • Baseline steroid use • Actual baseline ordinal score
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatments • Duration of symptoms prior to enrollment Baseline steroid use and baseline ordinal score will be included in the subgroup analysis as covariates unless the covariate is the subgroup.
2. Time to 2- points improvement by Day 60	Primary	Adjust for the following covariates: • Baseline steroid use • Actual baseline ordinal score
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatments • Duration of symptoms prior to enrollment Baseline steroid use and baseline ordinal score will be included in the subgroup analysis as covariates unless the covariate is the subgroup.
3. Clinical status assessed using ordinal scale on Study Days 1, 3, 5, 8, 11, 15, 22, and 29; Change in clinical status using change in ordinal scale from Study Day 1 to Study Days 3, 5, 8,11, 15, 22 and 29.	Primary	• No covariate adjustment
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score
4. Days of supplemental oxygen by Study Day 29;	Primary	• No covariate adjustment
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatment • Duration of symptoms prior to enrollment (only using the <= Median; > Median classification)
5. Days of non-invasive ventilation/high-flow oxygen by Study Day 29;	Primary	• No covariate adjustment for this analysis
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatment

Endpoint	Analysis	Covariates/Subgroups
		• Duration of symptoms prior to enrollment (only using the <= Median; > Median classification)
6. Incidence of new non-invasive oxygen use (clinical status > 5) during the study up to and including Study Day 29 for subject with baseline clinical status of 5;	Primary	• No covariate adjustment for this analysis
7. Days a subject who has a baseline clinical status of 5 has a clinical status > 5 up to and including Study Day 29;	Primary	• No covariate adjustment for this analysis
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatment • Duration of symptoms prior to enrollment (only using the <= Median; > Median classification)
8. Days of invasive mechanical ventilation/ECMO by Study Day 29;	Primary	• No covariate adjustment for this analysis
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatments • Duration of symptoms prior to enrollment (only using the <= Median; > Median classification)
9. Incidence of new invasive ECMO use through study Day 29 for subjects with baseline clinical status of 5 or 6;	Primary	• No covariate adjustment
10. Days a subject who has a baseline clinical status of 5 or 6 has a clinical status > 6 up to and including Study Day 29;	Primary	• No covariate adjustment
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatment • Duration of symptoms prior to enrollment (only using the <= Median; > Median classification)
11. Proportion of subjects alive and without respiratory failure at Study Day 29;	Primary	• No covariate adjustment
12. Time (days) to death or ventilation up to and Including Day 29	Primary	Adjust for the following covariates: • Baseline dexamethasone use • Actual baseline ordinal score • Baseline CRP value (Continuous) • Age (continuous)

Endpoint	Analysis	Covariates/Subgroups
13. Days of hospitalization from date of admission by Study Day 29.	Primary	• No covariate adjustment for this analysis
	Subgroup	Repeat the primary analysis for this endpoint within each of the following subgroups: • Actual baseline ordinal score • Baseline steroid use • Baseline use of emerging COVID-19 treatment • Duration of symptoms prior to enrollment (only using the <= Median; > Median classification)
Other Secondary Endpoints: Safety		
1. Values of CRP ferritin, D-dimer, LDH, and fibrinogen on Study Day 1: Study Days 3, 5, 8, 11,15 and 29	Primary	• No covariate adjustment
2. 14-day Mortality	Primary	1. Adjust for the following covariates: • Actual baseline ordinal score • Baseline steroid use
3. 28-day Mortality	Primary	1. Adjust for the following covariates: • Actual baseline ordinal score • Baseline steroid use
4. 59-day Mortality	Primary	1. Adjust for the following covariates: • Actual baseline ordinal score • Baseline steroid use
	Sensitivity	1. Adjust for the following covariates: • Actual baseline ordinal score • Baseline steroid use
5. Time to death by Day 29	Primary	• No covariate adjustment
	Sensitivity	• No covariate adjustment
6. SAEs by Day 60	Primary	• No covariate adjustment
7. Grade 3 or 4 AE by Day 60	Primary	• No covariate adjustment
8. Time to Death, SAE or Grade 3 or 4 TEAE	Primary	• No covariate adjustment
9. Episodes of early discontinuation or interruption of study product administration;	Primary	• No covariate adjustment
10. Values of WBC with differential, hemoglobin, platelets, creatinine, total bilirubin, ALT, AST, and INR on Study Day 1; Study Days 3, 5, 8, and 11 (while hospitalized); and Study Days 15 and 29 (if	Primary	• No covariate adjustment

Endpoint	Analysis	Covariates/Subgroups
attends in-person visit or still hospitalized).		
Exploratory Endpoints		
1. Concomitant COVID-19 treatments (e.g., steroids) post-baseline up to and including Study Day 29.	Primary	• No covariate adjustment

6.5. Missing Data

6.5.1. General Guidelines Regarding Handling of Missing Data

All attempts will be made to collect all data per the protocol. Efforts to minimize loss-to-follow-up will be considerable. Chart review will be performed for lost-to-follow-up subjects to obtain data related to the subjects' clinical status, oxygen use, or death status after discharge. However, small amounts of missing data may occur. In order to conduct mITT and ITT analyses for primary and secondary outcomes, missing data will be imputed in the manners described below in Table 7. Prior to applying the imputation rules described in Table 7, an endpoint review committee (ERC) may meet to adjudicate the primary endpoint and the key secondary endpoints for each study stage, such as Day 8 ordinal scores for subjects discharged to hospice, another hospital, or long-term care facilities. Any ERC reviews will be performed prior to database lock and all committee members will be blinded to treatment assignments. If an ERC is used, an ERC charter will be prepared prior to any reviews.

For the primary analysis of ordinal score at Day 8, the following imputations will be performed prior to multiple imputation:

- If a subject is discharged from the hospital to another location other than LTAC, hospice care or other hospital, has intermittent missing ordinal score and reported an ordinal score of 1 or 2 after the missing score then:
    - The intermittent missing ordinal score is imputed as 1 if the scores reported before and after the missing value are both 1 and no change in oxygen use or hospitalization status after discharge to a location other than hospice, long term acute care or other hospital.
    - The intermittent missing ordinal score is imputed as 2 after discharge to a location other than hospice, long term acute care or other hospital if the subject doesn't fall into the category above and subject is not hospitalized at the time point.
- LOCF will be used for remaining intermittent missingness of ordinal scores for the next planned assessment.
- All missing scores after death will be assigned an ordinal score of 8.
- Subjects that terminated from the study with known discharge to a location other than hospice, LTAC or other hospital at their last assessment will be assigned a score of 2 for all timepoints after last assessment.

Remaining missing ordinal scores for subjects that terminated early from the study and were still hospitalized at the time of their last assessment or with discharge to a location of hospice, LTAC or other hospital at the time of last contact will be imputed using multiple imputation. A sensitivity analysis of this analysis will be

performed using multiple imputation for all subjects missing ordinal after their last assessment regardless of their discharge status at the last assessment. Details of multiple Imputation are provided in Section 6.5.2.

Some analyses of ordinal score such as those reported in Table 17, Table 18, Table 20, Table 21, Table 24, Table 25, Table 26, Table 27, Table 34, Table 35, Figure 4, Figure 5, Figure 6, Figure 7, and Figure 18 will be based on complete ordinal score data created using the following steps:

- If a subject is discharged from the hospital to a location other than LTAC, Hospice care or other hospital, has intermittent missing ordinal score and reported an ordinal score of 1 or 2 after the missing score then:
  - Impute the intermittent missing ordinal score as 1 if the scores reported before and after the missing value are both 1 and no change in oxygen use or hospitalization status after discharge to a location other than hospice, long term acute care or other hospital.
  - Impute the intermittent missing ordinal score as 2 after discharge to a location other than hospice, long term acute care or other hospital if the subject doesn't fall into the category above and subject is not hospitalized at the time point.
- LOCF will be used for remaining intermittent missingness of ordinal scores for the next planned assessment.
- All missing scores after death will be assigned an ordinal score of 8.
- Subjects discharged from the hospital to a location other than LTAC, hospice care or other hospital at their last assessment will be assigned a score of 2 for all timepoints after last assessment.
- Impute all remaining missing data after last assessment using last observation carried forward.

Analysis of time to event endpoints (i.e., sustained recovery, time to improvement, time to mechanical ventilation or death) will be based on observed ordinal score without imputation along with discharge and death information. Refer to Table 7 for additional details regarding censoring and handling of missing data for all endpoints. As handling of missing data might differ for different stages of this study, stage-specific SAPs will provide additional details if handling of missing data for an endpoint for that stage differ from what is in the master SAP.

Table 7: Imputation Method for Each Endpoint and Analysis Type

Endpoint	Analysis	Imputation Method
Primary Endpoint		
1. Ordinal Score at Day 8	Primary	• If a subject is discharged from the hospital to another location other than LTAC, hospice care or other hospital, has intermittent missing ordinal score and reported an ordinal score of 1 or 2 after the missing score then: o Impute the intermittent missing ordinal score as 1 if the scores reported before and after the missing value are both 1 and no change in oxygen use or hospitalization status after discharge to a location other than hospice, long term acute care or other hospital. o Impute the intermittent missing ordinal score as 2 after discharge to a location other than hospice, long term acute care or other hospital if the subject doesn't fall into the category above and subject is not hospitalized at the time point. • LOCF will be used for remaining intermittent missingness of ordinal scores for the next planned assessment. • All missing scores after death will be assigned an ordinal score of 8.

Endpoint	Analysis	Imputation Method
		• Subjects discharged from the hospital to a location other than LTAC, hospice care or other hospital at their last assessment will be assigned a score of 2 for all timepoints after last assessment. • Multiple imputation will be used to impute missing ordinal scores after last assessment for subjects still hospitalized or discharged to hospice, other hospital, or long-term care facility at their last assessment. See Section 6.5.2 for more details.
	Primary with Sensitivity Imputation 1	• Use similar imputation methods for intermittent missingness and missing data after death. • Multiple Imputation will be used for all subjects missing data after last assessment regardless of their discharge status at the last assessment.
	Primary with Sensitivity Imputation 2	**Use complete data defined as follow:** • If a subject is discharged from the hospital to another location other than LTAC, hospice care or other hospital, has intermittent missing ordinal score and reported an ordinal score of 1 or 2 after the missing score then: o Impute the intermittent missing ordinal score as 1 if the scores reported before and after the missing value are both 1 and no change in oxygen use or hospitalization status after discharge to a location other than hospice, long term acute care or other hospital. o Impute the intermittent missing ordinal score as 2 after discharge to a location other than hospice, long term acute care or other hospital if the subject doesn't fall into the category above and subject is not hospitalized at the time point. • LOCF will be used for remaining intermittent missingness of ordinal scores for the next planned assessment. • All missing scores after death will be assigned an ordinal score of 8 • Subjects discharged from the hospital to a location other than LTAC, hospice care or other hospital at their last assessment will be assigned a score of 2 for all timepoints after last assessment. • Impute all remaining missing data after last assessment using last observation carried forward.
	Sensitivity	• Same imputation as the primary analysis
	Supplemental	• Same imputation as the primary analysis
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint.
Key Secondary Endpoints		
1. Time to Sustained Recovery	Primary	• Use the complete data for ordinal score to derive sustained recovery. • Subjects whose last assessment in the study is prior to Day 57 (beginning of Day 60 window) will be considered not recovered and censored at the date of their last assessment. • Death prior to recovery will be considered not recovered and censored at expected study Day 60.
	Primary with Sensitivity Imputation 1	• Use the complete data for ordinal score to derive sustained recovery. • Subjects whose last assessment in the study is prior to Day 57 (beginning of Day 60 window) after discharge from the hospital to a location other than LTAC, hospice care or other hospital will be treated as recovered by Day 60. Their time to recovery will be the day of their first observed/imputed recovery score (i.e., 1, 2, 3) or the day of discharge, whichever comes first. • Subjects whose last assessment in the study is prior to Day 57 (beginning of Day 60 window) without being discharged from the hospital to a location other than LTAC, Hospice care or other hospital at their last assessment will be considered not recovered and censored at the date of their last assessment.

Endpoint	Analysis	Imputation Method
		• Death prior to recovery will be considered not recovered and censored at expected study Day 60.
	Supplementary	• Same imputation method as primary analysis for time to sustained recovery.
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint.
2. Survival without respiratory failure up to and including Study Day 29	Primary	• Subjects who complete follow-up without mechanical ventilation or death or who have the event after Day 29 will be considered non-events and censored at Day 29. • Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and before experiencing death or progression to mechanical ventilation will be considered non-events and censored at the last assessment. • Subjects whose last assessment in the study is before Day 29 but within window for Day 29 (i.e., Day 26, 27, 28) and before experiencing death or progression to mechanical ventilation will be considered non-events regardless of their discharge status and censored at Day 29.
	Primary with Sensitivity Imputation	• Subjects who complete follow-up without mechanical ventilation or death or who have the event after Day 29 will be considered non-events and censored at Day 29. • Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and before experiencing death or progression to mechanical ventilation and were discharged to a location other than LTAC, hospice care, or other hospital will be considered non-events and censored at Day 29. • Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and before experiencing death or progression to mechanical ventilation without being discharged to a location other than LTAC, hospice care, or other hospital will be considered non-events and censored at the last assessment. • Subjects whose last assessment in the study is before Day 29 but within window for Day 29 (i.e., Day 26, 27, 28) and before experiencing death or progression to mechanical ventilation will be considered non-events regardless of their discharge status and censored at Day 29.
	Sensitivity	• Same imputation method as primary analysis of this endpoint
	Supplementary	• Same imputation method as primary analysis of this endpoint
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint
Other Secondary Endpoints: Efficacy		
1. Time to 1-point improvement by Day 60	Primary	• Use the complete data for ordinal score to define time to improvement. • Subjects whose last assessment in the study is prior to an observed improvement will be censored at the day of their last assessment. • Subjects who complete follow-up but do not experience improvement will be censored at the day of their Study Day 60. • Death prior to improvement will be considered not improved and censored at expected study Day 60.
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint.
2. Time to 2-points improvement by Day 60	Primary	• Use the complete data for ordinal score to define time to improvement. • Subjects whose last assessment in the study is prior to an observed improvement will be censored at the day of their last assessment. • Subjects who complete follow-up but do not experience improvement will be censored at the day of their Study Day 60.

Endpoint	Analysis	Imputation Method
		• Death prior to improvement will be considered not improved and censored at expected study Day 60.
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint.
3. Clinical status assessed using ordinal scale on Study Days 1, 3, 5, 8, 11, 15, 22, and 29;Change in clinical status using change in ordinal scale from Study Day 1 to Study Days 3, 5, 8,11, 15, 22 and 29.	Primary	• Use complete data for ordinal score.
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint.
4. Days of supplemental oxygen by Study Day 29;	Primary	• If the subject's clinical status scale is 6 or above at the last observed assessment, then the subject will be considered to be on supplemental oxygen use 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's clinical status is less than 6 at the last observed assessment, then the subject will be considered to not be on supplemental oxygen use for the remainder of follow-up. Thus, no additional imputed days will be added to the number of days recorded on available assessments.
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint.
5. Days of non-invasive ventilation/high-flow oxygen by Study Day 29;	Primary	• If the subject's clinical status scale is 6 or above 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's clinical status is less than 6 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.
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint.
6. Incidence of new non-invasive oxygen use (clinical status > 5) during the study up to and including Study Day 29 for subject with baseline clinical status of 5	Primary	• If the subject's clinical status scale is 6 or above 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's clinical status is less than 6 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.
7. Days a subject who has a baseline clinical status of 5 has a clinical status > 5 up to and including Study Day 29;	Primary	• Use complete data for ordinal score to define this endpoint.
	Subgroup	• Use complete data for ordinal score to define this endpoint.
8. Days of invasive mechanical ventilation/ECMO by Study Day 29;	Primary	• If the subject's clinical status scale is 7 or above at the last observed assessment, then the subject will be considered to be on invasive mechanical 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's clinical status is less than 7 at the last observed assessment, then the subject will be considered to not be on invasive ventilation/ECMO for the remainder of follow-up. Thus, no additional imputed days will be added to the number of days recorded on available assessments.
	Subgroup	• Repeat analysis for each subgroup using same imputation as primary analysis for this endpoint.

Endpoint	Analysis	Imputation Method
9. Incidence of new invasive ECMO use through study Day 29 for subjects with baseline clinical status of 5 or 6;	Primary	• If the subject's clinical status scale is 7 or above at the last observed assessment, then the subject will be considered to be on invasive mechanical 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's clinical status is less than 7 at the last observed assessment, then the subject will be considered to not be on invasive ventilation/ECMO for the remainder of follow-up. Thus, no additional imputed days will be added to the number of days recorded on available assessments.
10. Days a subject who has a baseline clinical status of 5 or 6 has a clinical status > 6 up to and including Study Day 29;	Primary	• Use complete data for ordinal score to define this endpoint.
	Subgroup	• Repeat analysis for each subgroup using the complete dataset for ordinal score.
11. Proportion of subjects alive and without respiratory failure at Study Day 29;	Primary	• Use the complete data for ordinal score to define survival without respiratory failure. • Subjects will be considered events at Day 29 if they are dead or are on invasive mechanical ventilation/ECMO anytime between Day 26 and Day 32 (Window for Day 29) regardless of their baseline ordinal score. • All subjects who died before Day 26 (beginning of Day 29 visit window) will be considered events. • All subjects who died after Day 32 or those who were not on invasive mechanical ventilation/ECMO between Day 26 and Day 32 will be considered non-events.
12. Time (days) to ventilation or death up to and Including Day 29;	Primary	• Use the complete data for ordinal score to define survival without respiratory failure. • All subjects whose last assessment in the study is before Day 26 and before progression to mechanical ventilation or death will be considered non-events and censored at the date of their last observed assessment. • Subjects who complete follow-up without mechanical ventilation or death will be censored at the expected study Day 29. • Subjects whose last assessment in the study is before Day 29 but within window for Day 29 (i.e., Day 26, 27, 28) and before experiencing death or progression to mechanical ventilation will be considered non-events regardless of their discharge status at Day 29.
	Primary with Sensitivity Imputation	• Use the complete data for ordinal score to define survival without respiratory failure. • Subjects whose last assessment in the study is before Day 26 and were discharged to a location other than LTAC, hospice care or other hospital, or progressed to mechanical ventilation or death after Day 29 will be considered non-events and censored at Day 29. • Subjects whose last assessment in the study is before Day 26 and before progression to mechanical ventilation or death and without being discharged to a location other than LTAC, hospice care or other hospital at their last assessment will be considered non-events and censored at the date of their last observed assessment. • Subjects who complete follow-up without mechanical ventilation or death will be censored at the expected study Day 29.
13. Days of hospitalization from date of admission by Study Day 29.	Primary	• If a subject is discharged and no further hospitalization data are available, consider the subject as not readmitted, no additional imputed days will be added. • If a subject dies while hospitalized, the number of days of hospitalization will be imputed as the number of days between the date of admission and the expected date of subject's Study Day 29 visit+1.
	Subgroup	• Use complete data for ordinal score to define this endpoint.

Endpoint	Analysis	Imputation Method
Other Secondary Endpoints: Safety		
1. Values of CRP, ferritin, D-dimer, LDH, and fibrinogen on Study Day 1: Study Days 3, 5, 8, 11,15 and 29	Primary	• If results are not available for any visit day(s) but are available for visits before or after that visit, the average of the two nearest visits will be imputed for all missing visits between them. • If a subject dies or is otherwise terminated early from the study, their last available observation will be carried forward. If baseline is missing, another pre-treatment dose will be used, or the earliest post treatment dose will be used.
2. 14-day Mortality	Primary	• Subjects whose last assessment in the study is before Day 13 (beginning of Day 29 window) and before death will be considered not dead and censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 15. • Deaths that occur after Day 15 will be censored at Day 15.
	Primary with Sensitivity Imputation	• Subjects whose last assessment in the study is before Day 13 (beginning of Day 15 window) and were discharged to a location other than LTAC, hospice care or other hospital, or subjects died after Day 15 will be considered non-events and censored at Day 15. • Subjects whose last assessment in the study is before Day 13 (beginning of Day 15 window) and before death and without being discharged to a location other than LTAC, hospice care or other hospital at their last assessment will be considered non-events and censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 15.
3. 28-day Mortality	Primary	• Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and before death will be considered not dead and censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 29. • Deaths that occur after Day 29 will be censored at Day 29.
	Primary with Sensitivity Imputation	• Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and were discharged to a location other than LTAC, hospice care or other hospital, or subjects died after Day 29 will be considered non-events and censored at Day 29. • Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and before death and without being discharged to a location other than LTAC, hospice care or other hospital at their last assessment will be considered non-events and censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 29.
4. 59-day Mortality	Primary	• Subjects whose last assessment in the study is before Day 57 (beginning of Day 60 window) and before death will be considered not dead and censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 60. • Deaths that occur after Day 60 will be censored at Day 60.
	Primary with Sensitivity Imputation	• Subjects whose last assessment in the study is before Day 57 (beginning of Day 60 window) and were discharged to a location other than LTAC, hospice care or other hospital, or subjects died after Day 60 will be considered non-events and censored at Day 60. • Subjects whose last assessment in the study is before Day 57 (beginning of Day 60 window) and before death and without being discharged to a location other than LTAC, hospice care or other hospital at their last assessment will be considered non-events and censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 60.

Endpoint	Analysis	Imputation Method
5. Time to death by Day 29	Primary	• Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and before death will be considered not dead and censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 29. • Deaths that occur after Day 29 will be censored at Day 29.
	Primary with Sensitivity Imputation	• Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and were discharged to a location other than LTAC, hospice care or other hospital, or subjects died after Day 29 will be considered non-events and censored at Day 29. • Subjects whose last assessment in the study is before Day 26 (beginning of Day 29 window) and before death and without being discharged to a location other than LTAC, hospice care or other hospital at their last assessment will be considered non-events and censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 29.
6. SAEs by Day 60	Primary	• No imputation of missing data will be performed.
7. Grade 3 or 4 AE by Day 60	Primary	• No imputation of missing data will be performed.
8. Time to Death, SAE or Grade 3 or 4 TEAE by Day 60	Primary	• Subjects whose last assessment in the study is prior to death or SAE or Grade 3 or 4 TEAE will be censored at the date of their last observed assessment. • Subjects who complete follow-up will be censored at Day 60. • Deaths that occur after Day 60 will be censored at Day 60.
9. Episodes of early discontinuation or interruption of study product administration;	Primary	• No imputation of missing data will be performed.
10. Values of WBC with differential, hemoglobin, platelets, creatinine, total bilirubin, ALT, AST, and INR on Study Day 1; Study Days 3, 5, 8, and 11 (while hospitalized); and Study Days 15 and 29 (if attends in-person visit or still hospitalized).	Primary	• No imputation of missing data will be performed.
Exploratory Endpoints		
1. Concomitant COVID-19 treatments (e.g., steroids) post-baseline up to and including Study Day 29.	Primary	• No imputation of missing data will be performed. Details regarding imputation of missing dates are provided in Table 8.

6.5.2. Multiple Imputation

Multiple imputation will be performed for the primary endpoint of the Day 8 ordinal score for subjects whose last assessment in the study is before Day 8 and missing ordinal scores after their last assessment for the following two scenarios:

- For the primary analysis of the primary endpoint, assign a score of 2 for subjects missing Day 8 score after last assessment for subjects with a good discharge status (i.e., discharged to a location other than LTAC, hospice care, other hospital) at last assessment and use multiple imputation to impute missing data at Day 8 only for subjects without a good discharge status (i.e., subjects with no post baseline data or still hospitalized or those discharged to LTAC, hospice care, or other hospital) at their last assessment

- As a sensitivity analysis of the primary endpoint, use multiple imputation to impute missing ordinal scores for all subjects missing Day 8 ordinal scores after last assessment regardless of their good discharge status at last assessment.

For analyses based on multiple imputation, remaining missing ordinal scores will be imputed for Day 8 using the PROC MI procedure in SAS. Treatment group (trtvar), baseline ordinal score (basesteroidusevar), baseline steroid use (basesteroidvar), duration of symptoms prior to randomization (dursymp), age, indicator for black or Hispanic ethnicity (blackhispfl), presence of 2 or more comorbidities (comorb2fl), baseline CRP (basescrp), and indicator for discharge to a location other than long term care facility (LTAC), hospice care or another hospital (i.e., good discharge status) at the last assessment of the subject being imputed will be included as covariates in the multiple imputation model for ordinal scores at each timepoint using monotone logistic regression. The good discharge status variable at last assessment variable (goodischstat) will vary from subject to subject and will be defined as the discharge status for all subjects at the last assessed timepoint of the subject being imputed. For example, if the subject being imputed had their last assessment at Day 5, the good discharge status variable for all subjects will be defined as their discharge status at Day 5. The timing for the discharge status variable will be defined according to the last assessment timepoint of the subjects being imputed. The treatment group variable (trtvar) represents the randomized treatment group. Each imputation model will include all subjects with complete data plus all subject with missing ordinal score at Day 8 to be imputed who have the same last assessment day. The procedure will loop through all possible last assessment days (i.e., day 1 through day 8) imputing data for subjects missing data who were last assessed on the same day.

Since missing data in any of these baseline characteristics may cause issues with the monotone missing data patterns, the following methods will be used to fill in missing baseline covariates data:

- For continuous baseline covariates (age, CRP, duration of symptoms), mean imputation will be used to replace missing values with the overall mean value from all randomized subjects for the given covariate.
- For indicator variables of baseline steroid use, black or Hispanic ethnicity, and presence of two or more comorbidities, subjects with missing values will be given the value with the greatest number of subjects among all randomized subjects.
- We do not anticipate any missing data for actual baseline ordinal score.

Twenty imputation sets will be generated, and final results from these 20 imputed datasets will be aggregated.

Pseudocode:

- Define `ordscore_d8` as the ordinal score:
- DEFINE `ordscore_d8` as the ordinal score value at Day 8.
- DEFINE j: as the last time assessment for the subjects being imputed used to define the good discharge status variable in the model. Possible values for j are from 1 to 8.
- DEFINE jMax= Maximum time of last assessment observed during the study.
- DEFINE g&j=analysis dataset containing predictors and ordinal score for complete data subjects as well as subjects missing Day 8 score who were last assessed on the same day.
- DEFINE &&modelVars = list of covariates to be used in the imputation model: trtvar baseordscorevar basesteroidusevar dursymp age blackhispfl comorb2fl basecrp goodischstat_j.

- DEFINE imp_g&j = g&j with 20 imputed values for the missing ordinal score added by PROC MI.

```
%do j=1 %to &jMax;

proc mi data=g&j out= imp_g&j impute=20 seed = 300&j noprint;
      class trtvar baseordscorevar basesteroidusevar  blackhispfl comorb2fl
      goodischstat_j ordscore_d8;
      var trtvar baseordscorevar basesteroidusevar dursymp age blackhispfl comorb2fl
      basecrp goodischstat_j ordscore_d8;
      monotone logistic(ordscore_d8 = trtvar baseordscorevar basesteroidusevar dursymp
      age blackhispfl comorb2fl basecrp goodischstat_j;
run;
 %end;
```

imp_g&j will be subset to contain only rows for the subjects with imputed ordinal scores and merged together with data from subjects with complete data to form twenty complete multiply imputed datasets. The final dataset imp_g will contain 20 replicates for complete subjects and data from the 20 imputation datasets for imputed subjects.

Proportional Odds analysis with multiple imputation:

The following SAS pseudocode will be used to perform the proportional odds analysis with treatment, baseline ordinal score and baseline steroid use as covariates to generate the treatment odds ratio, p-value, and predicted probabilities of the ordinal scale levels by treatment and ordinal score using data from multiple imputation:

```
proc logistic data=imp_g out=imp_parms plots(only)=effect(x= ordscore_d8
      sliceby =baseordscorevar*trtvar individual connect);
      by _imputation_;
      class baseordscorevar (param=ref ref=5) basesteroidusevar (param=ref ref=no
steroid use) trtvar (param=ref ref=placebolabel);
       model ordscore_d8 = trtvar baseordscorevar basesteroidusevar;
      oddsratio trtvar;
      ods output oddsratioswald = orest parameterestimates=pars;
run;

*Keep only estimates for the treatment variable;
data pars1;set pars;where Variable='Treatment variable';run;
*Combine estimates;
PROC MIANALYZE DATA=pars1;
      ODS OUTPUT PARAMETERESTIMATES= logor;
      MODELEFFECTS estimate ;
      STDERR stderr ;
RUN;
*Transform estimates from the log(OR) scale to the OR scale;
data OR;
      SET logor;
      OR_estimate = EXP(ESTIMATE);
      OR_LCL_95 =OR_estimate*EXP(-1.96*STDERR);
      OR_UCL_95 =OR_estimate*EXP(+1.96*STDERR);
      OR_LCL_80 =OR_estimate*EXP(-1.28*STDERR);
      OR_UCL_80 =OR_estimate*EXP(+1.28*STDERR);

RUN;
```

Similar pseudocode for odds ratio between the binary progression strata will use used for the Day 8 ordinal score endpoint analyzed by proportional odds using multiple imputation.

If the primary analysis results are at least borderline significant with a p-value < 0.10 and more than 5% of subjects have missing primary endpoint data, additional analyses will be performed to evaluate the effect of the missing data assumptions on the results. Using a tipping point strategy, these analyses will vary the Day 8 ordinal score independently across groups to determine if there is a distribution of missing data that would result in a change of conclusion.

6.6. Data Handling and Transformations

By-subject listings will be presented and sorted by treatment group, actual baseline ordinal score, subject number, and study day (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order and alphabetical order using the preferred term within subject. The intervention stage and treatment arm to which subjects were randomized will be used in the listings.

In general, age (in years) on the date of Study Day 1 will be used for analyses and presentation in demographic data listings. If an enrolled subject was not dosed with study product at all, the date baseline assessment was conducted will be used instead of the first dosing date of study product. For screen failures, the date the informed consent was signed will be used for age calculation. If only the birth year is collected on the case report form (CRF), “01 January” will be used for the unknown birthday and month for the purpose of age calculation, unless age is captured on the CRF.

The conventions for missing dates (adverse event [AE], concomitant medication [CM], medical history [MH]) are provided in Table 8.

Table 8: Partial Date Imputation for Adverse Events (AEs), Concomitant medications (CMs), and Medical History (MH)

Type of Date	Scenario			Impute strategy
	Month	Day	Year	
AE Dates				
AE Start Date	UNK	UNK	UNK	IMPUTE with FIRST_DOSE; Default to making AE start date/time a treatment emergent event and earliest possible date. Impute with randomization date if not treated, or informed consent date for other subjects. In case that imputed start date is after stop date, impute as stop date.
AE Start Date	UNK	UNK	YYYY	IMPUTE with 01/01/YYYY, or FIRST_DOSE (or randomization date if not treated) date if in same year. In case that imputed start date is after AE stop date, impute as stop date.
AE Start Date	MM	UNK	YYYY	IMPUTE with MM/01/YYYY, or FIRST_DOSE (or randomization date if not treated) if it is in same month/year. In case that imputed start date is after AE stop date, impute as stop date.
AE Stop Date	UNK	UNK	UNK	IMPUTE with discharge date, or last assessment date if never discharged or last assessment is after discharge date
AE Stop Date	UNK	UNK	YYYY	If discharge date or last assessment date is YYYY, IMPUTE with discharge date if discharged, or last assessment date if never discharged. If discharge date or last assessment date is YYYY+1 then IMPUTE AE Stop date as 12/31/YYYY.
AE Stop Date	MM	UNK	YYYY	IMPUTE with last day of MM/YYYY or last assessment day if never discharged or last assessment month/year is the same as MM/YYYY
CM Dates				
CM Start Date	UNK	UNK	UNK	IMPUTE with FIRST_DOSE date; Default = make CM start date/time a CM with earliest possible date; Impute with randomization date if not treated, or informed consent date for other subjects. In cases with imputed start date after stop date, impute start date as stop date.
CM Start Date	UNK	UNK	YYYY	IMPUTE with 01/01/YYYY, or FIRST_DOSE date (or randomization date if not treated) if in same year; if first dose is later in that year, start date= 01/01/YYYY. In cases with imputed start date after CM stop date, impute start date as stop date.
CM Start Date	MM	UNK	YYYY	IMPUTE with MM/01/YYYY, or FIRST_DOSE (or randomization date if not treated) if it is in same month/year. In case that imputed start date is after CM stop date, impute start date with stop date.
CM Stop Date	UNK	UNK	UNK	IMPUTE with discharge date, or last assessment date if never discharged or last assessment date is after discharge date
CM Stop Date	UNK	UNK	YYYY	If discharge date or last assessment date is YYYY, IMPUTE with discharge date if discharged, or last assessment date if never discharged. If discharge date or last assessment date is YYYY+1 then IMPUTE AE Stop date as 12/31/YYYY.
CM Stop Date	MM	UNK	YYYY	IMPUTE with last day of MM/YYYY or last assessment day if never discharged or last assessment month/year is the same as MM/YYYY
MH Dates				
MH Start Date	UNK	UNK	UNK	IMPUTE with FIRST_DOSE date; Default = make MH start date/time a MH with earliest possible date. Impute with randomization date if not treated, or informed consent date for other subjects. In case that imputed start date is after stop date, impute start date with stop date.
MH Start Date	UNK	UNK	YYYY	IMPUTE with 01/01/YYYY
MH Start Date	MM	UNK	YYYY	IMPUTE with MM/01/YYYY
MH Stop Date	UNK	UNK	UNK	IMPUTE with discharge date, or last assessment date if never discharged or last assessment date is after discharge date
MH Stop Date	UNK	UNK	YYYY	IMPUTE with 12/31/YYYY
MH Stop Date	MM	UNK	YYYY	IMPUTE with last day of MM/YYYY

Listings should not present imputed dates; listings should present partial dates or "." if date is entirely missing.

6.7. Multicenter Studies

Data will be pooled across all clinical sites. Center effects are not anticipated because the sites are using standardized procedures for collection of data.

Nevertheless, to guard against the potential for regional differences, a sensitivity analysis for the primary endpoint will adjust for site effects pooling sites together based on their geographic region.

6.8. Multiple Comparisons/Multiplicity

Analyses related to primary and key secondary endpoints will be conducted without adjustment for multiple endpoints and multiple arms. That is, all planned analyses will be conducted without statistical adjustment for multiplicity, with the main focus on the primary and secondary endpoints for each intervention versus placebo comparison.

However, a possible set of supplementary analyses described in the remainder of this section adjusting for multiplicity might be performed, but only if their inclusion appears likely to be helpful in interpreting the primary and secondary analyses results.

For this approach, adjusted p-values for multiple endpoints (primary and secondary continuous and binary endpoints) will be computed using the Westfall-Young permutation approach (specifically, the free step-down resampling method procedure that produces adjusted p-values that preserves the order of the endpoints for the unadjusted p-values) and results will be reported in Table 44. Two analyses will be performed both based on complete data, one treating Day 8 ordinal score as a continuous variable and the other excluding Day 8 endpoint from the Westfall-Young analysis. Time-to-event endpoints will be excluded from both models.

A third analysis will provide adjusted P-values using Hochberg method. This analysis will include p-values from endpoints and will use p-value from multiple imputation where applicable. Results will be reported in Table 45.

An additional global analysis will calculate Z-scores for all primary and secondary efficacy endpoints applicable to all subjects in the analysis population [3] and a global p-value will be calculated from the permutation test using z-scores from the linear model for continuous endpoints, cox model for time-to-event data, logistic regression for binary, and ordinal logistic regression model for continuous. For the logistic and log-rank test, the z-score can be calculated as the square root of the chi-square statistic of the treatment group variable from the adjusted model. A global test statistic vector will be constructed where each element is a Z score calculated from an endpoint in Table 9.

The mean of the z-scores for all the endpoints will be calculated. A global p-value can then be obtained through a permutation test. Results of this global test will be reported in Table 45.

Table 9: Endpoints to be included in the global analysis

Endpoint type	Endpoint
Primary	Ordinal score at Study Day 8
Key Secondary	Time (days) to sustained recovery
Key Secondary	Sustained survival without respiratory failure (binary: 1=Yes or 0=No)
Secondary	Time (days) to at least 1 units improvement from baseline/Time (days) to at least 2 units improvement from baseline
Secondary	Difference from baseline ordinal score at Days 3, 5, 8, 11, 15, 22, 29
Secondary	Number of days ordinal score > 4
Secondary	Number of days ordinal score > 5
Secondary	Number of days ordinal score > 6
Secondary	Number of days of hospitalization
Secondary	Value of CRP, ferritin, D-dimer, LDH, fibrinogen
Secondary (safety)	14-Day mortality, 28-Day mortality,59-Day morality (binary: 1=Yes or 0=No)
Secondary (safety)	Time (days) to death

Pseudocode:

Method 1: Obtain Adjusted P-values from Westfall-Young for Continuous and Binary Endpoints using observed data

```
proc multtest data=dataset perm stepboot n=100000 seed=1234;
      class trt;
      test  mean (C1 C2 C3/uppertailed) ;
             test  mean (C4 C5 … Cx/lowertailed) ;
      test fisher(B1 B2 B3 B4/lowertailed);
      test fisher(B5 B6 … Bx/uppertailed);
      contrast 'Trt vs Placebo' -1 1;
      ods output pValues=pvals;
run;
```

Where `C1 C2 … Cx` is a list of all continuous covariates `and C1 C2 … Cx` is the list of all binary covariates. The contrast should be updated as needed so that the placebo group is the reference. Note that the variables are grouped depending on the direction of the hypothesis test.

Method 2: Obtain Adjusted P-values using Hochberg method: Use raw p-values as input from the primary analysis for all the endpoints in Table 9.

```
proc multtest data=rawpvalues hoc out=adj_pvals;
run;
```

7. STUDY SUBJECTS

7.1. Disposition of Subjects

A summary of subject disposition and study milestones will be provided by treatment and actual baseline ordinal score in Table 13. This summary will present the number of subjects screened, enrolled, randomized, completed all infusions of investigational agents, had any investigational infusions slowed or stopped, completed all expected blood draws, completed all expected NP swabs, completed Study Day 8, completed Study Day 15 visit, completed Study Day 22 visit, completed Study Day 29 visit, completed Study Day 60, and the number of subjects in each of the categories listed below.

- Safety Population
- ITT Population
- mITT Population
- Discontinuation of Treatment with reasons for discontinuation
- Completed the Study
- Did not complete the study with reasons for discontinuation of study

The denominator for the percentage calculation will be the total number of subjects who were in the analysis population corresponding to that treatment and ordinal score category.

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 actual baseline ordinal score (ordinal scale 5, 6, 7).

A listing will be provided by subject number, treatment assignment, actual baseline ordinal score, completion status and reasons for discontinuation of study product or study (Listing 1).

A listing of subjects who failed screening and reasons that subjects were screened but not randomized is provided in Listing 2.

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be provided by treatment and actual baseline ordinal score (Table 11). Summaries will include the reason for the deviation and the deviation category for all subjects. All subject-specific protocol deviations and non-subject specific protocol deviations will be included in listings (Listing 3 and Listing 4).

7.3. Investigational Product Exposure and Compliance

The number of subjects with halted, slowed, or missed investigational doses will be summarized for the investigational product by treatment and actual baseline ordinal score (Table 12).

For subjects with doses missed, halted or slowed, a listing of treatment exposure will be provided by subject number, treatment start/end dates, treatment duration in days, volume administered, and the number of missed, halted or slowed doses as well as the corresponding reasons (Listing 10). Total duration of exposure will be defined as last dosing date of investigational product – first dosing date of investigational product + 1, regardless of any temporary interruptions in study product administration, and will be expressed in days using up to 1 decimal place (e.g., 5.5 days).

8. EFFICACY EVALUATION

All efficacy analyses will be summarized and performed on the mITT and/or ITT populations by treatment and baseline ordinal score. Each stage will be summarized and listed separately. If the handling of any subject's primary or key secondary endpoint data is unclear, the subject's data may be reviewed by a blinded endpoint review committee (ERC), see Section 6.5 for more details on the ERC.

8.1. Primary Efficacy Analysis

Analysis of the primary endpoint, clinical status (8-point ordinal scale) on Study Visit (not necessarily actual) Study Day 8, will be analyzed using a proportional odds model with baseline steroid use and baseline ordinal score as covariates (primary analysis of the primary endpoint) after multiple imputation. See Section 6.5 for details regarding handling of missing ordinal score data.

The null hypothesis for active treatment over control is:

H_0: OR =1

and the alternative hypothesis is:

H_A: OR $\neq$ 1

where:

OR = common odds ratio

The treatment odds ratio at Day 8 estimated from the model will be presented along with the corresponding 95% and 80% confidence intervals, and the p-value (Table 16). Subjects in the shared control arm can only be used in comparison of any given intervention 'A', if they were eligible for 'A' and consented to randomization to 'A'; thus controls randomized at clinics where 'A' is not currently being studied are not compared to subjects in the 'A' arm. Odds ratios between the binary progression strata from the proportional odds model are reported in Table 22 for mITT population and Table 23 for ITT population at Day 8.

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

Results of the sensitivity, supplemental and subgroup analyses for ordinal score at Day 8 are provided in Table 16. Adjusted odds ratios of inferior clinical status at Day 8 along with their 95% CIs and 80% CIs are presented overall ad within each subgroup in Figure 2 and Figure 3. These analyses will be repeated for the ITT population and results will be in Table 19.

Individual listing of ordinal score and its components will be provided in Listing 13.

8.2. Secondary Efficacy Analyses

8.2.1. Key Secondary Efficacy Analyses

Recovery will be defined as having a value of 1, 2, or 3 on the clinical status 8-point ordinal scale. The time to sustained recovery will be defined as the elapsed time (in days) from Study Day 1 to the day prior to the earliest recorded day at which a subject reaches recovery or hospital discharge and doesn't worsen (ordinal score > 3) up to and including Study Day 60. For example, a hospitalized subject with an ordinal score of 3 on Study Day 7 and doesn't worsen up to and including Day 60 will have a time to sustained recovery of 6 days, since ordinal score is reflective of the prior 24-hours.

For the primary analysis of sustained recovery endpoint, any subjects whose last assessment in the study is prior to an observed recovery will be censored at the day of their last observed assessment. For the sensitivity analysis of this endpoint, subjects whose last assessment in the study is prior to an observed recovery before Day 57 (beginning of Day 60 window) and who were discharged to a location other than LTAC, hospice care, or other hospital will be considered recovered and censored at Day 60. For both primary and sensitivity analysis of this endpoint, subjects who complete follow-up but do not experience sustained recovery will be censored at the day of their Study Day 60. All deaths that occur on or before Study Visit Day 60 will be considered not recovered and censored at Day 60. Note that we do not expect many subjects to worsen after discharge.

If a subject's last assessment is before Day 57 and is discharged to a location other than hospice, another hospital, or long-term care facilities, the subject will be considered recovered at the time of discharge for the sensitivity analysis but may be reviewed by the Endpoint Review Committee, if other data suggests the subject may not be recovered (e.g., to a location other than a private residence or discharged on high flow oxygen). If a subject is discharged to hospice or another hospital, or is a special case where recovery handling may be unclear, the subject's data may be reviewed by the Endpoint Review Committee to make the determination of whether the subject should be considered to have sustained recovery and, if so, at what time point in the analyses. Subject data to be reviewed as part of this determination will include the reported clinical status scores while hospitalized, where the subject was discharged to (e.g., private residence, rehabilitation facility, long-term care/nursing home, comfort care), and any information regarding readmittance. Additional information may be solicited to assess recovery.

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

The main analysis of the first key secondary endpoint (time to sustained recovery up to and including Study Day 60) conducts a score test to compare treatment to control up to and including Study Day 60. The treatment median survival time, confidence intervals and p-value from the score test will be presented (Table 28). Restricted mean recovery time estimates will be provided for each treatment group and actual baseline ordinal score stratum as well as the difference in restricted mean recovery time between treatment groups within each of the baseline ordinal score strata (Table 29).

Kaplan-Meier curves for each treatment arm will be presented and supplemented with the hazard ratio estimate, p-value, and the number of subjects at risk in each treatment at Study Day (not necessarily actual Study Days 1, 3, 5, 8, 11, 15, 22, 29, and 60) (Figure 8).

If the key secondary endpoint is different than what is covered in this SAP, it will be highlighted for each individual stage in the corresponding stage-specific appendix along with the subsequent analysis.

Each subgroup from Table 6 will be considered separately, and the tabular and graphical summaries described above will be replicated for each subgroup (Table 20). A forest plot will be generated to display 95% and 80% CIs for hazard ratios from each of the subgroup analyses (Figure 16, Figure 17).

Proportion of Subjects Alive and Without Respiratory Failure up to and Including Study Day 29

Any subjects whose last assessment is prior to death or progression to respiratory failure and prior to Day 26 (beginning of Day 29 window) will be censored at the date of their last observed assessment. For the sensitivity analysis of this endpoint, subjects whose last assessment is prior to obtaining the event and who were discharged to a location other than LTAC, hospice care, or other hospital will be considered recovered and censored at Day 29. For both primary and sensitivity analysis of this endpoint, subjects who complete follow-up will be censored Day 29. Events that occur after Day 29 will be censored at Day 29.

Kaplan-Meier estimates for the proportion of subjects with baseline ordinal score 5 or 6, who are alive and without respiratory failure up to and including Study Day 29 will be presented by treatment along with 95% CI from Kaplan-Meier (Table 30). Odds ratios and a p-value from an adjusted logistic regression model adjusting for covariates [2] detailed in Table 6 will be presented in Table 30. Risk differences and corresponding CIs obtained through bootstrap will also be generated using the approach discussed in [2] and results will be reported in Table 30. This analysis will be referred to as the primary analysis for the survival without respiratory failure endpoint.

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

Results of the primary, sensitivity, and subgroup analyses for this endpoint are reported in Table 30.

8.2.2. Other Secondary Efficacy Analyses

This section describes the planned analyses for the secondary efficacy outcome measures. Analyses of mortality will be described in Section 9.4 and analyses of markers of inflammation and coagulation will be described in Section 9.7.

Analyses of the other secondary outcome measures will be performed by treatment only and repeated for specified subgroups described in Table 6. As with the analyses described in Section 8.2.1, tabular summaries will mimic 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.

Ordinal Scale Outcomes

Analyses will evaluate the time to improvement of at least one point on the clinical status 8-point ordinal scale. The time to 1 point improvement (at least 1 point drop from baseline) will be defined as the elapsed time (in days) from Study Day 1 to the day prior to the earliest recorded day at which a subject reaches at least a 1-point improvement up to and including Study Day 60. Any subjects whose last assessment in the study is prior to an observed improvement will be censored at the day of their last observed Clinical Status score. Subjects who complete follow-up but do not experience improvement will be censored at the day of their Study Day 60. All deaths that occur on or before Study Day 60 (and prior to any observed improvement) will be considered censored at Day 60.

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

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 a strategy similar to the above one-point improvement.

The Cox proportional hazards model will be performed to test whether the survival curves differ between treatments (with respect to improvement endpoints). The median time to event and CI in each treatment group will be summarized along with the treatment hazard ratio estimate and p-value (Table 32). Differences in time-to-event endpoints by treatment will also be summarized with Kaplan-Meier curves (Figure 9). Number at risk, hazard ratio and log rank test 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 (Table 33, Figure 10).

The number and proportion of subjects in each ordinal score by baseline ordinal score will be presented by treatment at Baseline and Study Visit (not necessarily actual) Study Days 3, 5, 8, 11, 15, 22, 29, 60 (Table 35). Additionally, the change from baseline in ordinal scale (e.g., proportion who have a 1-, 2-, 3-, or 4-point improvement or 1-, 2-, 3-, or 4-point worsening), or no change, will be presented at all post-dose Study Visit Days (Table 34). Figures by study day visits will present grouped bar charts by point changes with side-by-side bars for each treatment (Figure 18).

The mean change from baseline at Study Days 3, 5, 8, 11, 15, 22, 29, and 60 will be summarized by treatment (Table 35).

The main analysis of the primary endpoint will be repeated using the ordinal score on Study Days 15 and 29 instead of Day 8 using complete data, adjusting for baseline severity and steroid use. The analysis will be repeated for baseline severity of disease, baseline steroid use, baseline use of emerging COVID-19 treatments, and duration of symptoms subgroups. Each subgroup will be considered separately, and the estimated treatment odds ratio from the proportional odds model with corresponding 95% and 80% confidence intervals and the p-value will be presented for each subgroup. A forest plot will be generated to display the overall treatment odds ratio and CI from each of the within-stratum analyses. Results for Day 15 will be presented in Table 17, Figure 4, and Figure 5 while results for Day 29 will be presented in Table 18, Figure 6, and Figure 7. These analyses will be repeated for the ITT population and results will be presented in Table 20 and Table 21. Odds ratios between the binary progression strata from the proportional odds model are reported in Table 24, Table 25, Table 26, Table 27 for mITT population and ITT population for Study Days 15 and 29.

Oxygenation

Oxygen days will be defined as the number of days where the ordinal score > 4 up to and including Study Day 29. The total number of days will be the sum of all reported days, regardless of whether the days occur consecutively or in disjoint intervals. For planned gaps between study days, the day of the qualifying Study Day and the days to the next planned Study Day will be included in the total number of days. The Post-Discharge Supplemental Oxygen CRF questions regarding days of oxygenation (including ECMO, invasive ventilation, non-invasive ventilation, high-flow oxygen devices, and all other oxygen delivery devices) will be used for any time period the subject is not hospitalized at the study hospital. See Section 6.5 for the plan for handling subjects who do not have data through Study Day 29 or die prior to Study Day 29.

Duration of oxygenation days will be summarized in a table using medians and quartiles by treatment (Table 36). Bee swarm plots of oxygen days by treatment will be generated (Figure 19).

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

Non-Invasive Ventilation/High-Flow Oxygen

Non-invasive ventilation/high flow-oxygen days or worse will be defined as the number of days where the ordinal score is > 5 up to and including Study Day 29. The total number of days will be the sum of all reported days, regardless of whether the days occur consecutively or in disjoint intervals. For planned gaps between study days, the day of the qualifying Study Day and the days to the next planned Study Day will be included in the total number of days. The Post-Discharge Supplemental Oxygen CRF questions regarding days of non-invasive ventilation or high-flow oxygen will be used for any time period the subject is not hospitalized at the study hospital. See Section 6.5 for the plan for handling subjects who do not have data through Study Day 29 or die prior to Study Day 29.

Duration of non-invasive ventilation/high flow oxygen days or worse will be summarized in a table using medians and quartiles by treatment (Table 37). Bee swarm plots of non-invasive ventilation/high flow oxygen days by treatment will be generated (Figure 20).

The incidence and duration of new Non-Invasive Ventilation/High-Flow Oxygen use or worse will be analyzed by treatment (Table 40). The numerator will include only subjects in category 5 or below at enrollment who change to a category 6, 7, or 8. The denominator will only include subjects with an actual baseline ordinal score of 5 or below at enrollment. The number of subjects reporting new use of Non-Invasive Ventilation/High-Flow Oxygen and the incidence rate along with 95% and 80% CIs estimated using the Blaker method will be reported.

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

Invasive Mechanical Ventilation/ECMO

Ventilator / ECMO days will be defined as the number of days where the ordinal score > 6 up to and including Study Day 29. The total number of days will be the sum of all reported days, regardless of whether the days occur consecutively or in disjoint intervals. For planned gaps between study days, the day of the qualifying Study Day and the days to the next planned Study Day will be included in the total number of days. The Post-Discharge Supplemental Oxygen CRF questions regarding days of ECMO or invasive ventilation will be used for any time period the subject is not hospitalized at the study hospital. See Section 6.5 for the plan for handling subjects who do not have data through Study Day 29 or die prior to Study Day 29.

Duration of Invasive Mechanical Ventilation/ECMO days will be summarized in a table using medians and quartiles by treatment (Table 38). Bee swarm plots of Invasive Mechanical Ventilation/ECMO days, and days hospitalized by treatment will be generated (Figure 21).

The incidence of new Invasive Mechanical Ventilation/ECMO use will be analyzed by treatment (Table 41). The numerator will only include subjects in category 6 or below at enrollment who change to a category 7 or 8. The denominator will include subjects with a baseline ordinal score of 6 or below. The number of subjects reporting new use of Invasive Mechanical Ventilation/ECMO and the incidence rate along with 95% and 80% CIs estimated using the Blaker method will be reported.

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

Proportion of Subjects Alive and Without Respiratory Failure at Study Day 29

The proportion of subjects alive and without respiratory failure at Study Day 29 will be defined as the proportion of subjects with an ordinal score < 7 at any time between Day 26 through Day 32 (Visit window for Study Day 29 Visit). The proportion of subjects with respiratory Failure or death at Day 29 will also be provided. These proportions will be presented by treatment along with 95% and 80% Blaker CIs. Treatment differences will be evaluated using a logistic regression and the p-value will be presented (Table 31).

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

Time to Mechanical Ventilation or Death up to and Including Day 29

The time to mechanical ventilation or death up to and including Day 29 will be defined as the elapsed time (in days) from Study Day 1 to date of mechanical ventilation or death. Any subjects whose last assessment is prior to obtaining the event and prior to Day 26 (beginning of Day 29 window) will be censored at the date of their last observed assessment. For the sensitivity analysis of this endpoint, subjects whose last assessment is

prior to obtaining the event and who were discharged to a location other than LTAC, hospice care, or other hospital will be considered recovered and censored at Day 29. For both primary and sensitivity analysis of this endpoint, subjects who complete follow-up will be censored Day 29. Events that occur after Day 29 will be censored at Day 29. A table will present median time to event along with corresponding 95% and 80% confidence intervals for each treatment along with the hazard ratio estimate and score test p-value from a Cox-proportional hazard model (Table 42). The Cox model will include as covariates baseline ordinal score, baseline CRP value, continuous age, and baseline dexamethasone use. Differences in time-to-event endpoints by treatment will be summarized with Kaplan-Meier curves (Figure 11). Analyses will be performed on the mITT population for those subjects who at baseline have an ordinal score of 5 or 6, CRP<150 mg/L, and age<85 years and results will be reported in Table 42. This analysis will be repeated for all subjects in the mITT population and results will be reported in Table 43.

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

Hospitalization

Duration (in days) of hospitalization will be defined as the number of days subject is hospitalized for COVID-19-related reasons starting from the date of randomization. It will be calculated as the total number of days hospitalized, including readmissions for COVID-19-related reasons. It will also be calculated as the total number of days hospitalized, including any readmissions regardless of cause. See Section 6.5 for the plan for handling subjects who do not have data through Day 29 or die prior to Day 29.

Duration of hospitalization days will be summarized in a table using medians and quartiles by treatment (Table 39). Bee swarm plots of days hospitalized by treatment will be generated, where subjects whose days are imputed due to death are grouped separately from subjects who do not die (Figure 22).

Refer to Table 6 for a list of covariates and subgroup analyses for this endpoint. Refer to Table 7 for imputation methods to be applied to this endpoint.

Individual listing of all primary and secondary endpoints is provided in Listing 14.

8.3. Exploratory Efficacy Analyses

Key Concomitant COVID-19 Treatments

The post-baseline usage, onset, and duration of treatment of key concomitant COVID-19 treatments will be summarized by treatment for each concomitant medication/therapy category (Table 78). If no concomitant COVID-19 treatment has been applied up to Study Day 60, day of onset will be censored at Study Day 60 for descriptive statistics (means, medians). Duration will be defined as the number of days between day of onset and end of medication. For ongoing medication at the end of the study, the medication end date will be imputed based on rules in Table 8.

Steroid Usage

Steroid usage and steroid type for indications other than COVID-19 post-baseline will be summarized by treatment group (Table 87). If no concomitant COVID-19 treatment has been applied up to Study Day 60, day of onset will be censored at Study Day 60 for descriptive statistics (means, medians). Duration will be defined as the number of days between day of onset and end of medication. For ongoing medication at the end of the study, the medication end date will be imputed based on rules in Table 8.

Details of analyses for virology and markers of inflammation and immune response will be covered in a separate SAP.

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Subject demographic variables (i.e., age, sex, race, and ethnicity) will be summarized by treatment and overall using descriptive statistics for age, and using number and percentage of subjects for sex, race, and ethnicity (Table 14). Age at Study Day 1 is calculated in years at the first dosing date of study product and will be rounded down to an integer. Age group (<40; 40-64; 65 or older) will be summarized by using summary statistics for categorical variables. If a subject did not receive study product after enrollment, the subject's age will be calculated from the date of randomization unless stated otherwise in a stage-specific appendix.

A demographic listing, including the informed consent date, will be provided Listing 5.

Baseline characteristics include body weight (in kg), height (in cm), body mass index (BMI; in kg/m^2), duration of symptoms prior to enrollment, steroid use, baseline viral measures and ordinal score. These baseline characteristics will be summarized by the treatment group and overall using descriptive statistics for continuous variables and using number and percentage of subjects for categorical variables (Table 15). No formal statistical testing is planned.

A listing of baseline characteristics will be provided (Listing 5).

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 signs and symptoms.
- Prior enrollment in ACTIV-5/BET.
- History of vaccinations within 4 weeks prior to screening, including SARS-CoV-2 vaccination.
  - Exclusionary vaccine history includes any live vaccine (that is, live attenuated) within 4 weeks prior to screening
- History of chronic medical conditions including chronic oxygen requirement prior to onset of COVID-19.
- History of medication allergies.
- Medications and therapies for this current illness taken in the 7 days prior to Study Day 1.
- Whether subject is participating in another clinical trial or plan to enroll in another clinical trial in the next 30 days.

Medical history is limited to the following conditions: asthma, cancer, cardiac vascular disease, chronic kidney disease, chronic liver disease, chronic oxygen requirement, chronic respiratory disease, coagulopathy, congestive heart failure, coronary artery disease, current nicotine consumption, diabetes type I and II, hypertension, immune deficiency, and obesity. Summaries of subjects' medical history will be presented by treatment group and overall (Table 14, Table 15).

A listing of medical history will be provided by subject number. Additional medial history other than the diagnoses listed above will be included in the listing (Listing 6).

9.1.2. Prior and Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHODrug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs.

Prior medications are defined as any medications begun and stopped before a subject took the first dose of study product. If a partial stop date is entered, the month and year (if day is missing) or year (if day and month are missing) of the stop date are prior to the first dosing date will be considered prior (See Table 8).

Concomitant medications are defined as medications taken while a subject took study product. Therefore, any medications started prior to or during the first dosing date of study product and continued after the first dosing date or started after the first dosing date will be considered concomitant medications. If a partial start date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) after the date of first study product administration will be included in the concomitant medication summary. Medications with completely missing start and stop dates will be included in the concomitant medication summary (Table 8).

Prior and concomitant medications reported on the concomitant medication form will be summarized separately WHO Drug Level 1 and 2 Codes, actual baseline ordinal score, and treatment group using the number and percentage of subjects for each treatment, actual baseline ordinal score, and overall (Table 84, Table 85). Concomitant COVID-19 treatments are reported in Table 86 while steroids used for indications other than COVID-19 are reported in Table 87. A subject reporting the same medication more than once will be counted only once when calculating the number and percentage of subjects who received that medication. The summary will be ordered alphabetically by WHO Drug level 1code then by WHO Drug level 2 code in order of descending overall frequency within each WHO Drug level code. For drugs with the same frequency, sorting will be done alphabetically.

Summaries of prior and concomitant medications will be based on the Safety population and individual subject listing of all prior and concomitant medications including those reported on the SAE form is provided in Listing 9, Listing 10 for steroids, and Listing 11 for other medication of interest.

9.2. Measurements of Treatment Compliance

Section 7 provides the descriptions of summaries of key treatment compliance milestones/variables. Individual subject listings will be presented for all subjects who discontinued dosing (Listing 1). Individual subject listings will be presented for all subjects who missed, halted or slowed any dose (Listing 12).

9.3. Adverse Events

All safety analyses will be summarized and performed on the Safety population by treatment and ordinal score, as appropriate.

Clinical and laboratory adverse events (AEs) will be coded using the version 23.0 of MedDRA. System organ class (SOC) and preferred term (PT) will be provided in the AE dataset.

AEs are graded by the investigator as Grade 2 (moderate), Grade 3 (severe), Grade 4 (severe/potentially life-threatening), or Grade 5 (fatal/death) according to the NIAID Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Corrected Version 2.1 [5].The severity grade of events for which the investigator did not record severity will be categorized as “missing” for tabular summaries and data listings. The missing category will be listed last in summary presentation.

The relationship of an adverse event to the component of the investigational product should be assessed using clinical judgment by the investigator, describing the event as either unrelated or related. Events for which the investigator did not record relationship to study product will be considered related to study product for summary purposes. However, data listings will show relationship as missing. Relationship to COVID-19 and other medical conditions is also collected and will be reported in data listings.

Treatment-emergent adverse events (TEAEs) are defined as any AE with an onset date on or after the study product start date.

If the onset date of the AE is incomplete and the AE stop date is not prior to the first dosing date of study product, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent. The event is considered treatment emergent if the AE onset is the same as or after the month and year (or year) of the first dosing date of study product.

An AE with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dosing date of study product, will be considered to be treatment emergent. In addition, an AE with the onset date missing and incomplete stop date with the same or later month and year (or year alone if month is not recorded) as the first dosing date of study product will be considered treatment emergent. For additional details on imputation of partial or missing dates, see Table 8.

For the calculation of incidence of TEAEs each subject will only be counted once per category (Any TEAEs, Any SOC, Any PT within SOC) and any repetitions of TEAEs within a subject will be ignored; the denominator will be the number of subjects in the Safety population.

An overall summary of TEAEs by treatment, actual baseline ordinal score, severity, and relatedness of TEAEs will be presented in Table 46 and will include subjects with at least one:

- TEAE
- Grade ≥3 TEAE
- TEAE related to study treatment
- Grade ≥3 TEAE related to study treatment
- Treatment-emergent SAE
- Treatment-emergent SAE related to study treatment
- TEAE leading to early termination of study product
- TEAE leading to study discontinuation
- TEAE leading to death.

The following summaries for TEAEs will be presented by MedDRA system organ class, preferred term, severity and relatedness (when applicable) of TEAE, ordinal score and treatment:

- Subject listing of non-serious AEs (Listing 15);
- Bar chart of non-serious related AEs by severity and MedDRA system organ class (beginning at Figure 23 and continuing through Figure 30);

The proportion of subjects reporting at least one TEAE will be summarized by MedDRA system organ class and preferred term for each treatment (Table 47), by baseline ordinal score (Table 48), by baseline steroid use (Table 49), by baseline use of Emerging COVID-19 treatments (Table 50), and by duration of symptoms prior to enrollment (Table 51). Denominators for percentages are the number of subjects in the Safety population.

Similarly, the proportion of subjects reporting at least one treatment-emergent SAE will be summarized by MedDRA system organ class and preferred term for each treatment, ordinal score and overall (Table 52, Table 53).

Separate listings of non-serious TEAEs, all TEAEs, related TEAEs, treatment-emergent SAEs, and TEAEs leading to early termination of study product, TEAEs leading to study discontinuation or death will be presented (beginning at Listing 15 and continuing through Listing 21).

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

The time to death up to and including Day 60 will be defined as the elapsed time (in days) from Study Day 1 to date of death. Any subjects whose last assessment is prior to death will be censored at the date of their last observed assessment. For the sensitivity analysis of this endpoint, subjects discharged to a location other than LTAC, hospice care, or other hospital will be considered non-events and censored at Day 60. For both analyses, subjects who complete follow-up will be censored at Day 60. Deaths that occur after Day 60 will be censored at Day 60. The Kaplan-Meier estimates of mortality rates along with corresponding 80% CI and 95% CI will be presented by treatment group and baseline ordinal score. Difference in Kaplan-Meier estimates of mortality rates between treatment arms along with corresponding 80% CI, 95% CI will be presented. Additionally, hazard ratios along with corresponding 80% CI, 95% CI and score test p-value calculated from the Cox proportional hazard model adjusted from baseline ordinal score and baseline steroid use will be presented (Table 54).

This analysis will be repeated for deaths through Day 15 and deaths through Day 29 and results will be reported in Table 54. Restricted mean mortality time estimates will be provided for each treatment group and actual baseline ordinal score stratum as well as the difference in restricted mean mortality time between treatment groups within each of the baseline ordinal score strata (Table 55).

Differences in time-to-event endpoints by treatment will be summarized with Kaplan-Meier curves (Figure 12, Figure 13, Figure 14). Analyses of mortality will be performed on the Safety population at risk.

A safety composite endpoint will be defined as the occurrence of at least one of the following up to and including Study Day 60:

1. Death
2. Treatment-emergent SAE
3. Grade 3 or 4 TEAE

The time to this composite endpoint will be defined as the elapsed time (in days) from Study Day 1 to the earliest date of any of the events. Any subjects whose last assessment in the study is 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 expected date of their Study Day 60 visit.

Rates death, SAE, and Grade $\geq$ 3 TEAEs occurrence up to and including expected date of the Study Day 60 visit will be presented for each treatment arm. Further, the composite endpoint of the occurrence of death, treatment-emergent SAE, or Grade 3 or 4 TEAE will be analyzed as a time-to-event outcome. A table will present Kaplan-Meier estimates of the event rates along with corresponding 80%, 95% confidence intervals for each treatment. Difference in event rates along with corresponding 80%, 95% confidence intervals will also be presented. Hazard ratio estimates and score test p-value from the Cox model will also be presented (Table 56). Differences in time-to-event endpoints by treatment will also be summarized with Kaplan-Meier curves (Figure 18).

9.5. Pregnancies

For any subjects in the Safety 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 clinical study report (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 beginning at Listing 22 and continuing through Listing 26.

9.6. Clinical Laboratory Evaluations

Clinical safety laboratory AEs are collected Study Days 1, 3, 5, 8, and 11 (while hospitalized); and outpatient Study Days 15 and 29 (if attends in-person visit or still hospitalized). Parameters evaluated include WBC, differential, Hgb, PLT, creatinine, (and calculate an estimated glomerular filtration rate (eGFR); the formula used is determined by the sites, but should be consistent throughout the study), total bilirubin, AST, ALT, and INR. Additional laboratory parameters may be summarized based on each intervention's safety profile. Laboratory safety parameters will be graded according to the NIAID Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Corrected Version 2.1 (July 2017).

The distribution of Grade 3 and 4 chemistry and hematology laboratory results by maximum severity, time point, ordinal score and treatment group will be presented in Table 62 through Table 66 for chemistry and Table 76 through Table 81 for hematology. Absolute values and change from baseline of laboratory values will be summarized by mean, SD, median, minimum, and maximum results at Study Days 1, 3, 5, 8, 11, 15 and 29 in Table 57, through Table 61 for chemistry and Table 67 through Table 75 for hematology. Individual laboratory results are provided in Listing 27 for chemistry and hematology and Listing 29 for urine pregnancy results.

Markers of inflammation and coagulation results for CRP, ferritin, d-dimer, LDH, and fibrinogen will be summarized by mean, SD, median, minimum, and maximum results at Study Day 1 and Study Visit (not necessarily actual) Study Days 3, 5, 8, 11, 15 and 29 by treatment as well as change from baseline at each post-Study Day 1 visit (Table 82). Figures with mean and SD over time will also be presented by treatment (Figure 31, Figure 32, Figure 33, Figure 34, Figure 35). Individual results for markers of inflammation are presented in Listing 28.

9.7. Vital Signs and Physical Evaluations

Vital sign measurements include pulse, systolic blood pressure, respiratory rate, blood oxygen saturation (SpO_2) and oral temperature. Vital signs were assessed as part of the NEW score at baseline and will be listed (Listing 7). Descriptive statistics for baseline vital signs (i.e., NEWS components) collected will be presented by treatment (Table 83).

Targeted physical examinations are performed at Study 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 8).

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHODrug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs.

Summaries of prior and concomitant medications will be based on the Safety population and are provided in Table 84, Table 85, Table 86, and Table 87. An individual subject listing of all concomitant medications is provided in Listing 9.

9.9. Other Safety Measures

No additional safety analyses are planned.

10. PHARMACOKINETICS

Details for PK analysis will be provided in a separate SAP.

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, confidence intervals, median, IQR, and other statistics will be reported to 1 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 <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than 0.5% but < 1% will be presented as "<1"; values greater than 99.5% but less than 100% will be reported as ">99".

For all other estimators, the NEJM statistical reporting guidelines will be followed: results will be presented with no more precision than is of scientific value and is meaningful. For example, measures of association, such as odds ratios, will be reported to two or three significant digits. Results derived from models will be limited to the appropriate number of significant digits.

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

15.1. Changes from Planned analyses for BET-B

The BET-B protocol and SAP inadvertently did not include analysis of Day 8 ordinal score endpoint. As this endpoint is the primary endpoint for BET-A and BET-C, the BET-B planned analyses are updated as described in this section to include Day 8 ordinal score as a secondary endpoint for BET-B. The Day 8 ordinal score analysis will only be based on complete data only, without the use of multiple imputation. Imputations for intermittent missingness described in Section 6.5 will be used. Subjects missing Day 8 score after last assessment for subjects with a good discharge status (i.e., discharged to a location other than LTAC, hospice care, other hospital) at last assessment will be assigned a score of 2 and last observation carried forward will be used for subjects missing data at Day 8 without a good discharge status (i.e., subjects with no post baseline data or still hospitalized or those discharged to LTAC, hospice care, or other hospital) at their last assessment.

Tables similar to Table 16, Table 22 will be presented for the primary subgroup (ITT Population with Baseline Ordinal Score of 5 or 6, CRP<150 mg/L, and age<85 years) and for the full ITT population. Only complete data and subgroup rows from Table 22 will be presented. Results will also be presented graphically in a figure similar to Figure 2 using complete data.

15.2. Changes from Version 1.0 to Version 2.0 of the Master SAP

- Version 1.0 of the SAP was written by Social & Scientific Systems, Inc. Version 2.0 of the SAP was updated by Emmes and revised to follow Emmes standard formats.
- The SAP was updated to clarify the statistical methods and imputations to be used including clear details regarding multiple imputation and multiplicity testing.
- For the analysis of primary endpoint and key secondary endpoints, baseline ordinal score and baseline steroid use were updated to be used as the covariates instead of the stratification variables.
- For time to event endpoints, the analyses were updated to report the p-value from the score test in the adjusted Cox model instead of unadjusted p-value from the log rank test.
- For the analysis of proportion alive and without respiratory failure through Day 29, the analysis was updated to use an adjusted regression model to match what is being done for BET-B.
- For binary endpoints, the analyses were updated to report a p-value from a logistic regression instead of a p-value from the Chi-square test.
- Updated language for time to recovery to use time to sustained recovery.
- Updated language throughout the SAP to use baseline ordinal score for disease severity at baseline instead of using moderate, severe categories.
- Major formatting updates to TFL shells and clarification changes
- Removed PK and virology exploratory endpoints from the master SAP. These endpoints will be covered in a separate SAP.
- Added a table and figure for LDH.
- Ethnicity was added as a subgroup.

- Added an endpoint review committee to review and adjudicate if a subject's primary or key secondary endpoint data is unclear.
- The SAP was updated to note that the DSMB report will not be done by a blinded team.
- The method for multiplicity adjustment was updated to use Westfall-Young only for binary and continuous endpoints using complete data. An additional analysis was added to use the Hochberg approach to adjust p-values from all endpoints.

15.3. Changes from Version 2.0 to Version 3.0 of the Master SAP

- All analyses of time to events (e.g., time to sustained recovery, time to death, time to mechanical ventilation or death) endpoints were updated to censor subjects without events at last assessment.
- A sensitivity analysis was added for time to recovery endpoint that considers subjects whose last assessment in the study is prior to Day 60 after discharge from the hospital to a location other than LTAC, hospice care or other hospital as recovered by Day 60. Their time to recovery will be the day the time of their first observed/imputed recovery score (i.e., 1, 2, 3) or the day of discharge, whichever comes first.
- A sensitivity analysis was added for survival without respiratory failure and time to mechanical ventilation or death that considers subjects lost to follow-up before Day 26 (beginning of Day 29 window) before event who were discharged to a location other than LTAC, hospice care, or other hospital as non-events and censors them at Day 29.
- The analyses for mortality were updated to use Kaplan Meier estimates instead of crude estimates for mortality rates. All subjects lost to follow up before death were censored at their last assessment.
- A sensitivity analysis was added for the 14-day mortality and time to death through Day 15 endpoints that consider subjects lost to follow-up before Day 13 (beginning of Day 15 window) before event who were discharged to a location other than LTAC, hospice care, or other hospital as non-events and censors them at Day 15. Similar sensitivity analyses were added for 28-day mortality, 59-day mortality, time to death by Day 29, and time to death by Day 60 endpoints.
- The definition for survival without respiratory failure at Day 29 was updated count respiratory failure events and deaths that occurred within the Day 29 visit window (Day 26 through Day 32) and to count all deaths that occurred before Day 29.
- The method for handling ties in time to event analyses was updated from Breslow to the Efron method for analyses based on Cox regression model.
- Tables for laboratory parameters without grading ranges (Eosinophils, monocytes, basophils) were removed.
- The previous SAP version used a subject-specific multiple imputation approach that only used covariates with non-missing values. This MI method was updated to first impute continuous covariates (baseline CRP, baseline duration of symptoms, age) with missing values using the overall mean among all randomized subjects and impute indicator variables of baseline steroid use, black or Hispanic ethnicity, and presence of two or more comorbidities, subjects with missing values using the value with the greatest number of subjects among all randomized subjects. Moreover, this updated multiple imputation will use one model to impute all subjects missing Day 8 ordinal score and with the same last assessment time in the study. The number of MI models fit will correspond to the number of observed last assessment times prior to Day 8.

16. REFERENCES

1. G. B. Smith, D. R. Prytherch, P. E. Schmidt and P. I. Featherstone, "The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, death.," *Resuscitation,* pp. 465-470, 2013.
2. M. Ge, L. K. Durham, R. D. Meyer, W. Xie and N. Thomas, "Covariate-Adjusted difference in proportions from clincal trials using logistic regression and weighted risk differences.," *Ther Innov Regul Sci,* vol. 45, pp. 481-493, 2011.
3. Pocock SJ, Geller NL, Tsiatis AA. The analysis of multiple endpoints in clinical trials. *Biometrics*. 1987 Sep;43(3):487-98. PMID: 3663814.
4. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. *JAMA.* 2001; 285(15):2006-2007.
5. Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Corrected Version 2.1," U.S. Department of Health and Human Services, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Division of AIDS, 2017.[Online].Available: https://rsc.niaid.nih.gov/sites/default/files/daidsgadingcorrectedv21.pdf. [Accessed July 2020].

17. LISTING OF TABLES, FIGURES, AND LISTINGS

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

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

Tables below will be presented for final reports of all stages. Additional stage-specific tables will be added to each stage-specific SAP appendix as needed.

LIST OF TABLES

9.5.1 Efficacy and Safety Measurements Assessed and Flow Chart

Table 10: Schedule of Study Procedures

	Screen	*Baseline*	*Study Intervention Period*	*Follow-up Visits*				
Day +/- Window	**−1 or 1**	**1[15]**	**Daily until hospital discharge (up to Day 29)**	**8[10] ± 2**	**15[6] ± 2**	**22[10] ± 3**	**29[6] ± 3**	**60[10] ± 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 investigational agent		• Risankizumab or placebo: one infusion on Day 1 • Remdesivir: IV daily for 5-10 days or until discharge.						
STUDY PROCEDURES								
Vital sign and NEWS score [1]		X[3]						
Clinical data collection[1]		X[3]	Daily until discharge	X	X	X	X	X[13]
Adverse event evaluation		X[3]	Daily until discharge	X	X	X	X	X
Concomitant medication review[12]		X[3]	Day -7 until discharge	X	X	X	X	
SAFETY LABORATORY								
Safety hematology, chemistry, and liver tests[4]	X[2]	X[3]	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized[5]		X		X	
Pregnancy test for females of childbearing potential	X[2]							
RESEARCH LABORATORY[16]								
Oropharyngeal swab[7]		X[3]	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized		X		X	
Blood draw for serum and plasma. Specific testing is as follows:		X[3]	Day 3, 5, 8, 11 (all ± 1 day) if hospitalized		X		X	
PCR SARS-CoV-2		*X[3]*	*Day 3, 5, 8, 11 (all ± 1 day) if hospitalized*					
Proteomic analysis (including specifically for Risankizumab IL-17A, IL-22, and IL-1b)		*X[3]*	*Day 3, 8, (all ± 1 day) if hospitalized*		*X*		*X*	
Risankizumab pharmacokinetics[11]		*X[8]*	*Day 5 (± 1 day) if hospitalized*		*X*		*X*	
Risankizumab immunogenicity[11]		*X[8]*					*X*	
Serum for secondary research		*X[3]*	*Day 3, 5, 8, 11 (all ± 1 day) if hospitalized.*		*X*		*X*	
Blood for RNA		X[3]	Day 3, 8 (all ± 1 day) if hospitalized		X		X	
Blood for PBMC[11]		X[3]	Day 3, 8 (all ± 1 day) if hospitalized		X		X	

[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) the formula used is determined by the sites, but should be consistent throughout the study), and urine or serum pregnancy test for females of child-bearing potential. Laboratory tests performed as part of routine clinical care in the 48 hours prior to enrollment will be accepted for determination of eligibility.

[3] Baseline assessments should be performed prior to first infusion. 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 if obtained in the 24 hours prior to first dose.

[4] Safety laboratory tests include WBC with differential, hemoglobin, platelets, creatinine, total bilirubin, ALT, AST, and INR.

[5] Any laboratory tests performed as part of routine clinical care within the specified visit window can be used for safety laboratory testing.

[6] 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, the visit may be performed by phone.

- *If still hospitalized at Day 15 and 29 or returns to the site for an in-person visit: assess adverse events, collect clinical data, vital signs, safety laboratory tests, and research laboratory samples (OP swab and blood) as able.*
- *If phone call only on Days 15 and 29 and all Day 22 and Day 60 visits: assess adverse events, clinical status (ordinal scale), readmission to a hospital, and mortality only.*

[7] Oropharyngeal swabs are preferred, but if these are not obtainable, saliva or nasopharyngeal or nasal swabs may be substituted.
[8] Pre-dose serum sample collections for PK and immunogenicity.
[9] To include markers of inflammation and coagulation: CRP, ferritin, fibrinogen, LDH, d-dimer.
[10] Day 8, 22 and 60 visits performed by phone if discharged from the site hospital: assess adverse events, clinical status (ordinal scale), readmission to a hospital, and mortality only.
[11] Only collected at selected sites capable of processing.
[12] Steroids and other concomitant therapies intended as specific treatment of COVID-19, as well as all biologics, will be assessed from 7 days prior to enrollment to Day 29. All other concomitant medications will be assessed from 7 days prior to enrollment to Day 15 or upon discharge, whichever comes first.
[13] Ordinal score only.
[14] Vital signs include temperature, systolic blood pressure, heart rate, respiratory rate, O2 saturation and level of consciousness. In addition, height and weight are obtained only at baseline (height can be self-reported). Vital signs collected as part of standard care may be used.
[15] Day 1 is defined as the calendar day of randomization.
[16] Blood draws for research labs may be omitted on any given study day if inappropriate for a subject's clinical status per site investigator judgment.

10.2 Protocol Deviations

Table 11: Protocol Deviations—mITT Population

Category	Deviation Type	Treatment A (N=X)								Treatment B (N=X)							
		Baseline Ordinal Score[a]								Baseline Ordinal Score[a]							
		5 (N=x)		6 (N=x)		7 (N=x)		Any BOS[b] (N=x)		5 (N=x)		6 (N=x)		7 (N=x)		Any BOS[b] (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.	# of Subj.	# of Dev.	# of Subj.	# of Dev.
Major Deviations																	
Eligibility/randomization	Any type	x	x	x	x	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	x	x	x	x
	Met exclusion criterion	x	x	x	x	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	x	x	x	x
	Other	x	x	x	x	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	x	x	x	x
	Out of window visit	x	x	x	x	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	x	x	x	x
	Missed treatment administration	x	x	x	x	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	x	x	x	x
	Other	x	x	x	x	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	x	x	x	x
	Out of window visit	x	x	x	x	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	x	x	x	x
	Other	x	x	x	x	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	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	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	x	x	x	x

Category	Deviation Type	Treatment A (N=X)								Treatment B (N=X)							
		Baseline Ordinal Score[a]								Baseline Ordinal Score[a]							
		5 (N=x)		6 (N=x)		7 (N=x)		Any BOS[b] (N=x)		5 (N=x)		6 (N=x)		7 (N=x)		Any BOS[b] (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.	# of Subj.	# of Dev.	# of Subj.	# of Dev.
	Oropharyngeal swab not collected	x	x	x	x	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	x	x	x	x
	Specimen result not obtained	x	x	x	x	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	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	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	x	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Stratification error	x	x	x	x	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	x	x	x	x
Treatment administration	Any type	x	x	x	x	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	x	x	x	x
	Study product temperature excursion	x	x	x	x	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	x	x	x	x
Blinding policy/procedure	Any type	x	x	x	x	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	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Repeat for Minor Deviations																	

BOS= Baseline Ordinal Score.
N=Number of subjects in the modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria.
[a] There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.

Table 12: Treatment Exposure and Compliance by Baseline Ordinal Score — Safety Population

	Treatment A (N=X)				Treatment B (N=X)			
	Baseline Ordinal Score[a]				Baseline Ordinal Score[a]			
	5 (N=X)	6 (N=X)	7 (N=X)	Any BOS[b] (N=X)	5 (N=X)	6 (N=X)	7 (N=X)	Any BOS[b] (N=X)
Number of Subjects Halted, Missed, or Slowed Doses								
Number of Subjects with Halted Doses	xx	xx	xx	xx	xx	xx	xx	xx
Number of Subjects with Slowed Doses	xx	xx	xx	xx	xx	xx	xx	xx
Number of Subjects with Missed Doses[c]	xx	xx	xx	xx	xx	xx	xx	xx

BOS= Baseline Ordinal Score.
N=Number of subjects in the Safety population.
[a] Baseline Ordinal Score defined as: 5 (Moderate), 6 or 7 (Severe).
[b] There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.
[c] Missed doses refer to intermittent missing doses and do not include doses missed after treatment discontinuation.

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 13: Subject Disposition by Baseline Ordinal Score – ITT Population

	Treatment A (N=X)								Treatment B (N=X)								All Subjects (N=X)							
	5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)	
Subject Disposition	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
Randomized/Enrolled[b]	x/x	100	x/x	100	x/x	100	x/x	100	x/x	100	x/x	100	x/x	100	x/x	100	x/x	100	x/x	100	x/x	100	x/x	100
Safety Population[c]	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Discharged from Hospital	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Died During Follow-up	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Completed Follow-up (Study Day 1) – Hospitalized Subjects in Study[f]	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Ordinal Scale Data Available	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Safety Laboratory Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Secondary Research Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	
OP Swab Collection	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
PCR or Proteomic Assays Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Serum Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Repeat for Days 3, 5, 8, 11																								
Completed Follow-up (Study Day 15) – All Subjects in Study[f]	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Ordinal Scale Data Available	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x

	Treatment A (N=X)								**Treatment B** (N=X)								**All Subjects** (N=X)							
	5 (N=X)		**6 (N=X)**		**7 (N=X)**		**Any BOS[a] (N=X)**		**5 (N=X)**		**6 (N=X)**		**7 (N=X)**		**Any BOS[a] (N=X)**		**5 (N=X)**		**6 (N=X)**		**7 (N=X)**		**Any BOS[a] (N=X)**	
Subject Disposition	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
Safety Laboratory Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Secondary Research Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	
OP Swab Collection	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
PCR or Proteomic Assays Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Serum Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
RNA Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
PBMC Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Completed Follow-up (Study Day 22) – All Subjects in Study	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Ordinal Scale Data Available	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Completed Follow-up (Study Day 29) – All Subjects in Study[f]	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Ordinal Scale Data Available	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Safety Laboratory Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Secondary Research Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
OP Swab Collection	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
PCR or Proteomic Assays Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Serum Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x

	Treatment A (N=X)								Treatment B (N=X)								All Subjects (N=X)							
	5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)	
Subject Disposition	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
RNA Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
PBMC Blood Draw	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Completed Follow-up (Study Day 60) – All Subjects in Study[f]	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Ordinal Scale Data Available	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Treatment Completion																								
Discontinued Treatment[d]	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Reasons for Discontinuation of Treatment[e]																								
XXXX	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
XXXX	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Study Completion																								
Completed Study	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Did not Complete Study	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
Reasons for Discontinuation of Study																								
XXXX	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x
XXXX	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	xx	x/x	x

BOS= Baseline Ordinal Score.
N=Number of subjects randomized/enrolled and in study for visits 1, 15, 22, 29, 60 and the number of subjects hospitalized and in study for visits 3,5, 8, and 11. Subjects that died or terminated early from the study on or prior to the study visit are not included in the denominators. n= Number of unique subjects that satisfy the row criteria.
[a]There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.
[b] Represents the number of subjects who were randomized to either treatment arm.
[c] Represents the number of subjects who received any amount of investigational agent.
[d] Refers to the discontinuation of the investigational agent or placebo.
[e]Refer to Listing 1 for the individual reasons subjects discontinued or terminated early.
[f] Visit completion is as completing a visit for that day or another day that is in window for the corresponding visit.

Programming

- Update milestones for each visit based on stage-specific schedule of events.
- Had any infusions stopped or slowed: if the question "Was full infusion administered successfully?" is marked "slowed or stopped" for either treatment, subject will be counted in this row.
- Completed all Required Investigational Infusions: if treatment was not discontinued, then subject will be counted in this row.
- Completed all Blood Draws: If there are not any blood draws that were "Not done", then subject will be counted in this row.

14.1.2 Demographic Data by Study Group

Table 14: Categorical Demographics and Medical History – ITT Population

Demographic Category	Characteristic	Treatment A (N=X)								Treatment B (N=X)								All Subjects (N=X)							
		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Age	<40 years old	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	40-64 years old	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	≥65 years old	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Sex	Male	x	x	x	x	x	x	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	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	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	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	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	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	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	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	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	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	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	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	x	x	x	x	x	x
Baseline Ordinal Score	4	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	5	x	x	x	x	x	x	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	x	x	x	x	x	x
	7	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Any BOS	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Demographic Category	Characteristic	Treatment A (N=X)								Treatment B (N=X)								All Subjects (N=X)							
		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Steroid Use	Yes	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	No	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Comorbidities	History of Medication Allergies	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Diabetes Type I	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Diabetes Type II	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Obesity	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Chronic Kidney Disease	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Chronic Liver Disease (e.g., chronic hepatitis, cirrhosis)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Chronic Respiratory Disease (e.g., COPD, emphysema)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Respiratory Support (e.g., CPAP, BiPAP)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Asthma	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Current Nicotine Consumption (any amount daily)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Chronic Oxygen Requirement	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Coronary Artery Disease	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Cardiac Valvular Disease	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Hypertension	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Congestive Heart Failure	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Cancer	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Immune Deficiency (acquired or innate)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Coagulopathy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Demographic Category	Characteristic	Treatment A (N=X)								Treatment B (N=X)								All Subjects (N=X)							
		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)		5 (N=X)		6 (N=X)		7 (N=X)		Any BOS[a] (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Participating in another clinical trial or plan to enroll in another trial in next 30 days	Yes	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	No	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Baseline NEW Score	0	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	2	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	3	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	[Add the rest of observed NEW score values]	x	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 enrolled subjects in the ITT population.
n = Number of subjects that satisfy the row criteria.
[a] There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.

Table 15: Continuous Demographics and Medical History – ITT Population

Variable	Statistic	Treatment A (N=X)				Treatment B (N=X)				All Subjects (N=X)			
		5 (N=X)	6 (N=X)	7 (N=X)	Any BOS[a] (N=X)	5 (N=X)	6 (N=X)	7 (N=X)	Any BOS[a] (N=X)	5 (N=X)	6 (N=X)	7 (N=X)	Any BOS[a] (N=X)
Age (years)	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Height (cm)	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Weight (kg)	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
BMI (kg/m^2)	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x

Variable	Statistic	Treatment A (N=X)				Treatment B (N=X)				All Subjects (N=X)			
		5 (N=X)	**6 (N=X)**	**7 (N=X)**	**Any BOS[a] (N=X)**	**5 (N=X)**	**6 (N=X)**	**7 (N=X)**	**Any BOS[a] (N=X)**	**5 (N=X)**	**6 (N=X)**	**7 (N=X)**	**Any BOS[a] (N=X)**
Duration of Symptoms Prior to Randomization (days)	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Baseline CRP	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Baseline Ferritin	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Baseline D-Dimer	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x

Variable	Statistic	Treatment A (N=X)				Treatment B (N=X)				All Subjects (N=X)			
		5 (N=X)	**6 (N=X)**	**7 (N=X)**	**Any BOS[a] (N=X)**	**5 (N=X)**	**6 (N=X)**	**7 (N=X)**	**Any BOS[a] (N=X)**	**5 (N=X)**	**6 (N=X)**	**7 (N=X)**	**Any BOS[a] (N=X)**
Baseline Fibrinogen	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Baseline LDH	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x

SD=Standard Deviation. BMI=Body Mass Index. LDH= Lactate Dehydrogenase. CRP=C-Reactive Protein.
N=Number of subjects in the ITT population. n=number of subjects with a non-missing assessment.

14.2 Efficacy Data

Table 16: Global Odds Ratios for Inferior Clinical Status Score at Study Visit Day 8 Using a Proportional Odds Model — mITT Population

Analysis/Subgroup	Category	Treatment A (N=x)	Treatment B (N=x)	Odds Ratio			P-value
		n	n	Estimate	95% CI	80% CI	
Initial model, MI for subjects without a discharge to a location other than LTAC, hospice or other hospital[a]	-	x	X	x.x	x.x, x.x	x.x, x.x	0.xxx
Sensitivity/Supplemental Analyses							
Primary with Sensitivity Imputation 1: MI for All Subjects with Missing Data[b]	-	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
Primary with Sensitivity Imputation 2: Complete Data[c]	-	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
Sensitivity Analysis 1: Impact of Investigational site, MI[d]	-	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
Supplemental Analysis 1: Impact of age and duration of symptoms prior to enrollment, MI[e]	-	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
Supplemental Analysis 2: Baseline Use of Emerging Covid-19 Treatment, MI[f]							
Any Baseline Use of Emerging Covid-19 Treatments	-	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
Corticosteroids Use	-	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
Monoclonal Antibodies Use	-	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
Other Anti-Inflammatory Drugs Use	-	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
Subgroup Analyses, Complete Data[g]							
Baseline Ordinal Score	5	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	6 or 7	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Baseline Use of Steroid	Yes	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	No	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Baseline Use of Emerging Covid-19 Treatments	Yes	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	No	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]	x	x				0.xxx

Analysis/Subgroup	Category	Treatment A (N=x)	Treatment B (N=x)	Odds Ratio			P-value
		n	n	Estimate	95% CI	80% CI	
Duration of Symptoms Prior to Enrollment Group 1	≤ Median	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	> Median	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Duration of Symptoms Prior to Enrollment Group 2	< 25th percentile	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	25<75th percentile	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	≥75th percentile	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Race	White	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Black/African American	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Asian	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Other	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Ethnicity	Hispanic or Latino	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Not Hispanic or Latino	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Comorbidities Group 1	None	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Any	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Comorbidities Group 2	One	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Two or More	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Comorbidities Group 3	Obese	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Non-obese	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]			x.x	x.x, x.x	x.x, x.x	0.xxx

Analysis/Subgroup	Category	Treatment A (N=x)	Treatment B (N=x)	Odds Ratio			P-value
		n	n	Estimate	95% CI	80% CI	
Age Group	< 40	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	41-64	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	65 and older	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx
Sex	Male	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Female	x	x	x.x	x.x, x.x	x.x, x.x	0.xxx
	P-value for interaction[h]						0.xxx

CI=Confidence Internals. OR=Odds Ratios. NA=Not applicable. MI=Multiple Imputation.
N=Number of subjects in the modified-intent-to-treat (mITT) population.
n=Number of subjects with non-missing Day 8 ordinal score for each treatment group.
[a] Odds Ratios calculated for the odds of moving down the ordinal score using a proportional odds model where the clinical status (8- point ordinal scale) is the dependent variable, odds ratios compare Active treatment vs Placebo. Subjects discharged to a location other than LTAC, hospice or other hospital at their last assessment were assigned a score of 2 for all timepoints after last assessment, and MI will be used to impute data for remaining subjects missing ordinal score data without a good discharge status after their last assessment.
[b] Primary with Sensitivity Imputation 1: Multiple imputation was used to impute missing data after last assessment for all subjects. The model described in [a] was used to estimate the OR, 95% CI, 80% CI and p-values.
[c] Primary with Sensitivity Imputation 2: The model described in [a] was used to estimate the OR, 95% CI, 80% CI and p-values using complete data.
[d] Sensitivity Analysis 1 (impact of investigational site): In addition to the variable included in the model described in [a], the investigational site was added to the model when estimating the OR, 95% CI and p-values using the same multiple imputation approach as the primary analysis in [a].
[e] Supplemental Analysis 1 (age and duration of symptoms prior to enrollment): In addition to the variable included in the model described in [a], age and duration of symptoms prior to enrollment as additional covariates were added to the model when estimating the OR, 95% CI, 80% CI, and p-values using the same multiple imputation approach as the primary analysis in [a].
[f] Supplemental Analysis 2 (by Baseline COVID-19 treatment category): In addition to the variable included in the model described in [a], baseline use of COVID-19 treatment as additional covariates were added to the model when estimating the OR, 95% CI, 80% CI, and p-values using the same multiple imputation approach as the primary analysis in [a]. Additional models using use of each COVID-19 treatment category as a covariate separately.
[g] For the subgroup analyses, the model described in [a] using complete data was performed for each level of the subgroup.
[h] P-Value for treatment difference or P-value from interaction Type III test in subgroup analysis where the interaction between subgroup and treatment is being added to the model.

Tables with similar format:

[Implementation notes: For analyses using Day 15 and Day 29, perform all the analyses using complete data. Delete Primary with Sensitivity Imputation 1 and Primary with Sensitivity Imputation 2 analyses.]

Table 17: Global Odds Ratios for Inferior Clinical Status Score at Study Visit Day 15 Using a Proportional Odds Model — mITT Population

Table 18: Global Odds Ratios for Inferior Clinical Status Score at Study Visit Day 29 Using a Proportional Odds Model — mITT Population

Table 19: Global Odds Ratios for Inferior Clinical Status Score at Study Visit Day 8 Using a Proportional Odds Model — ITT Population

Table 20: Global Odds Ratios for Inferior Clinical Status Score at Study Visit Day 15 Using a Proportional Odds Model — ITT Population

Table 21: Global Odds Ratios for Inferior Clinical Status Score at Study Visit Day 29 Using a Proportional Odds Model — ITT Population

Table 22: Proportional Odds Model for Clinical Status Score at Study Visit 8 – Odds Ratios Between the Binary Progression Strata with Multiple Imputation — mITT Population

OS Table Comparison	Treatment	Lower OS		Higher OS		Odds Ratio OR (80% CI)	Odds Ratio OR (95% CI)	P-value X^2	P-value Fisher's Exact
		n	%	n	%				
1 vs 2-8	Treatment A (N=X)	x	xx.x	x	xx.x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	0.xxx	0.xxx
	Treatment B (N=X)	x	xx.x	x	xx.x				
1-2 vs 3-8	Treatment A (N=X)	x	xx.x	x	xx.x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	0.xxx	0.xxx
	Treatment B (N=X)	x	xx.x	x	xx.x				
1-3 vs 4-8	Treatment A (N=X)	x	xx.x	x	xx.x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	0.xxx	0.xxx
	Treatment B (N=X)	x	xx.x	x	xx.x				
1-4 vs 5-8	Treatment A (N=X)	x	xx.x	x	xx.x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	0.xxx	0.xxx
	Treatment B (N=X)	x	xx.x	x	xx.x				
1-5 vs 6-8	Treatment A (N=X)	x	xx.x	x	xx.x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	0.xxx	0.xxx
	Treatment B (N=X)	x	xx.x	x	xx.x				
1-6 vs 7-8	Treatment A (N=X)	x	xx.x	x	xx.x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	0.xxx	0.xxx
	Treatment B (N=X)	x	xx.x	x	xx.x				
1-7 vs 8	Treatment A (N=X)	x	xx.x	x	xx.x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	0.xxx	0.xxx
	Treatment B (N=X)	x	xx.x	x	xx.x				

OS= Ordinal Score. CI= Confidence Interval. N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria.

Tables with similar format

[Implementation note: *For analyses using Day 15 and Day 29, repeat the analysis using complete data.*]

Table 23: Proportional Odds Model for Clinical Status Score at Study Visit 8 – Odds Ratios Between the Binary Progression Strata with Multiple Imputation — ITT Population

Table 24: Proportional Odds Model for Clinical Status Score at Study Visit 15 – Odds Ratios Between the Binary Progression Strata without Multiple Imputation — mITT Population

Table 25: Proportional Odds Model for Clinical Status Score at Study Visit 15 – Odds Ratios Between the Binary Progression Strata without Multiple Imputation — ITT Population

Table 26: Proportional Odds Model for Clinical Status Score at Study Visit 29 – Odds Ratios Between the Binary Progression Strata without Multiple Imputation — mITT Population

Table 27: Proportional Odds Model for Clinical Status Score at Study Visit 29 – Odds Ratios Between the Binary Progression Strata without Multiple Imputation — ITT Population

Table 28: Time to Sustained Recovery through Day 60 — mITT Population

Analysis/Subgroup	Treatment	Number of Recovered Subjects		Median Time Until Recovery			Hazard Ratio		P-value[e]
		n	%	Estimate	80% CI	95% CI	Estimate	95% CI	
Initial Model [a]	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Sensitivity Analyses									
Primary with Sensitivity Imputation 1: Imputation for good discharges[b]	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Supplemental Analysis 1: Impact of age and duration of symptoms[c]	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Subgroup Analyses[d]									
Baseline Ordinal Score									
5	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
6 or 7	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx
Baseline Steroid Use									
Yes	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
No	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx
Baseline Use of Emerging Covid-19 Treatments									
Yes	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
No	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			

Analysis/Subgroup	Treatment	Number of Recovered Subjects		Median Time Until Recovery			Hazard Ratio		P-value[e]
		n	%	Estimate	80% CI	95% CI	Estimate	95% CI	
	P-value for interaction[e]								0.xxx
Duration of Symptoms Prior to Enrollment Group 1									
≤ Median	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
> Median	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx
Duration of Symptoms Prior to Enrollment Group 2									
< 25th percentile	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
25 ≤ 75th percentile	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
≥ 75th percentile	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]	x	x.x						0.xxx
Race									
White	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Black/African American	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Asian	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Other	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx

Analysis/Subgroup	Treatment	Number of Recovered Subjects		Median Time Until Recovery			Hazard Ratio		P-value[e]
		n	%	Estimate	80% CI	95% CI	Estimate	95% CI	
Ethnicity									
Hispanic or Latino	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Not Hispanic or Latino	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx
Comorbidities Group 1									
None	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Any	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx
Comorbidities Group 2									
One	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Two or More	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								
Comorbidities Group 3									
Obese	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Non-obese	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx

Analysis/Subgroup	Treatment	Number of Recovered Subjects		Median Time Until Recovery			Hazard Ratio		P-value[e]
		n	%	Estimate	80% CI	95% CI	Estimate	95% CI	
Age Group									
< 40	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
41-64	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
65 and older	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx
Sex									
Male	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
Female	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x			
	P-value for interaction[e]								0.xxx

CI=Confidence Intervals. N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique recovered subjects that satisfies the row criteria.

[a] Hazard Ratio (HR) is the hazard ratio calculated from the Cox Proportional Hazard Model comparing Active treatment vs Placebo. All subjects lost to follow-up before recovery are censored at last assessment date.

[b] Primary with Sensitivity Imputation 1: Subjects discharged to a location other than LTAC, hospice care, or other hospital are considered recovered at Day 60. The rest of lost to follow-up subjects are censored at last assessment date. Model [a] was fit to estimate the HR, 95% CI and p-values.

[c] Supplemental Analysis 1 (age and duration of symptoms prior to enrollment): In addition to the variable included in the model described in [a], age and duration of symptoms prior to enrollment as additional covariates were added to the model when estimating the HR, 95% CI and p-values. Same censoring as in model [a].

[d] For the subgroup analyses, the model described in [a] was performed for each level of the subgroup.

[e] P-value is based on the Cox adjusted model or P-value from interaction Type III test in subgroup analysis where the interaction between subgroup and treatment is being added to the Cox Proportional Hazard Model.

Table 29: Time to Sustained Recovery through Day 60 by Treatment Group, Actual Baseline Ordinal Score, and Analysis Population: Restricted Mean Survival Time Analysis

Analysis Population	Treatment Group	Actual Baseline Ordinal Score	n	Tau[a]	Restricted Mean Recovery Time (Days)			Difference		
					Estimate	95% CI	80% CI	Estimate	95% CI	80% CI
mITT	Treatment A (N=X)	5	x	x	x.x	x.x, x.x	x.x, x.x	x.xx	x.xx, x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x	x.x	x.x, x.x	x.x, x.x			
	Treatment A (N=X)	6	x	x	x.x	x.x, x.x	x.x, x.x	x.xx	x.xx, x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x	x.x	x.x, x.x	x.x, x.x			
	Treatment A (N=X)	7	x	x	x.x	x.x, x.x	x.x, x.x	x.xx	x.xx, x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x	x.x	x.x, x.x	x.x, x.x			
	Treatment A (N=X)	Any BOS	x	x	x.x	x.x, x.x	x.x, x.x	x.xx	x.xx, x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x	x.x	x.x, x.x	x.x, x.x			
ITT	Treatment A (N=X)	5	x	x	x.x	x.x, x.x	x.x, x.x	x.xx	x.xx, x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x	x.x	x.x, x.x	x.x, x.x			
	Treatment A (N=X)	6	x	x	x.x	x.x, x.x	x.x, x.x	x.xx	x.xx, x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x	x.x	x.x, x.x	x.x, x.x			
	Treatment A (N=X)	7	x	x	x.x	x.x, x.x	x.x, x.x	x.xx	x.xx, x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x	x.x	x.x, x.x	x.x, x.x			
	Treatment A (N=X)	Any BOS	x	x	x.x	x.x, x.x	x.x, x.x	x.xx	x.xx, x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x	x.x	x.x, x.x	x.x, x.x			

N = Number of subjects in the specified treatment group, actual baseline ordinal score, and analysis population.
n = Number of recovered subjects.
Difference is the difference in the restricted mean recovery time between active treatment to placebo.
[a] Tau is the truncation time point for the Restricted Mean Survival Time analysis and is equal to the minimum of the largest observed times in each group.

Programming

Within an actual baseline ordinal score stratum:

```
proc lifetest data=enrevent plots=(rmst) method=breslow rmst(cl);
by stratum;
time evntday * Censor(1);
strata trtcode /diff=all;
ods output  rmst=rmst;
run;
```

Table 30: Proportion of Subjects Alive and Without Respiratory Failure through Day 29 — mITT Population

Analysis/Subgroup	Category	Treatment A (N=x)		Treatment B (N=x)		Odds Ratio			Risk Difference[g]			P-value[h]
		n	% (95%CI)[f]	n	% (95%CI)[f]	Estimate	95% CI	80% CI	Estimate	95% CI	80% CI	
Initial model, Age, Baseline OS, Dexamethasone Use, and CRP[a]	-	x	x.x (x.x, x.x)	X	x.x (x.x, x.x)	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
Primary with Sensitivity Imputation 1[b]	-	x	x.x (x.x, x.x)	X	x.x (x.x, x.x)	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
Sensitivity Analysis 1: Baseline OS and Steroid Use[c]	-	x	x.x (x.x, x.x)	x	x.x (x.x, x.x)	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
Supplemental Analysis 1: Impact of age and duration of symptoms prior to enrollment[d]	-	x	x.x (x.x, x.x)	x	x.x (x.x, x.x)	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
Subgroup Analyses[e]												
Baseline Ordinal Score	5	x	x.x (x.x, x.x)	x	x.x (x.x, x.x)	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	6 or 7	x	x.x (x.x, x.x)	x	x.x (x.x, x.x)	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
Repeat for all subgroups from Table 6		x	x.x (x.x, x.x)	x	x.x (x.x, x.x)	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx

CI=Confidence Internals. OR=Odds Ratios. NA=Not applicable.
N=Number of subjects in the modified-intent-to-treat (mITT) population. n=Number of subjects without respiratory failure or death through Day 29.
[a] Odds Ratios of Active treatment vs Placebo calculated from the logistic regression model adjusted for baseline dexamethasone use, baseline OS, age, and baseline CRP. Subjects lost to follow-up before Day 26 (beginning of Day 29 window) and before experiencing death or progression to mechanical ventilation will be considered non-events and censored at the last assessment.
[b] Primary with Sensitivity Imputation 1: Subjects lost to follow-up before Day 26 (beginning of Day 29 window) and before experiencing death or progression to mechanical ventilation who were discharged to a location other than LTAC, hospice care, or other hospital were considered non-events and censored at Day 29 while those still hospitalized or discharged to LTAC, hospice care, or other hospital were censored at the last assessment.
[c] Sensitivity Analysis 1: Same analysis as in the initial model but only using baseline ordinals score and baseline steroid use as covariates in the logistic regression model.
[d] Supplemental Analysis 1 (age and duration of symptoms prior to enrollment): In addition to the variable included in the model described in [a], age and duration of symptoms prior to enrollment as additional covariates were added to the model when estimating the OR, 95% CI and p-values
[e] For the subgroup analyses, the model described in [a] was performed for each level of the subgroup.
[f] Kaplan-Meier estimates and confidence intervals are reported. All subjects whose last assessment in the study is before Day 29 and before experiencing death or progression to mechanical ventilation were considered non-events and censored at last assessment.
[g] Risk Differences calculated using the approach described in Ge.et al [2]. CIs calculated using bootstrap.
[h] P-Value from the logistic regression model.

Table 31: Proportion of Subjects Alive and Without Respiratory Failure at Study Day 29 — mITT Population

Status	Treatment A (N=X)				Treatment B (N=X)				P-value
	n	%	80% CI	95% CI	n	%	80% CI	95% CI	
Initial Analysis[a]									
Alive and Without Respiratory Failure	x	xx	x.x, x.x	x.x, x.x	x	xx	x.x, x.x	x.x, x.x	
Respiratory Failure or Death	x	xx	x.x, x.x	x.x, x.x	x	xx	x.x, x.x	x.x, x.x	0.xxx
Subgroup Analyses: Alive and Without Respiratory Failure[b]									
Baseline Ordinal Score									
5	x	xx	x.x, x.x	x.x, x.x	x	xx	x.x, x.x	x.x, x.x	0.xxx
6 or 7	x	xx	x.x, x.x	x.x, x.x	x	xx	x.x, x.x	x.x, x.x	0.xxx
Repeat for the subgroups presented in Table 6									

CI= Confidence Interval. N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria.
[a] The table includes 80% and 95% Blaker confidence intervals and p-value from the logistic regression with treatment group as the only covariate.
[b] For the subgroup analyses, only the values for the "Alive and Without Respiratory Failure" are presented and analyses similar to those in [a] were performed.

Table 32: Time to Improvement by at Least One Category through Day 60 in the 8-point Ordinal Scale — mITT Population

Analysis/Subgroup	Treatment	Number of Recovered Subjects		Median Time to Recovery			Hazard Ratio			P-value[c]
		n	%	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	
Initial Model[a]	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
Subgroup Analyses[b]										
Baseline Ordinal Score										
5	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
6 or 7	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
Other	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
Baseline Steroid Use										
Yes	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
No	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
Baseline Use of Emerging Covid-19 Treatments										
Yes	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
No	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
Duration of Symptoms Prior to Enrollment Group 1										
≤ Median	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
> Median	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				

Analysis/Subgroup	Treatment	Number of Recovered Subjects		Median Time to Recovery			Hazard Ratio			P-value[c]
		n	%	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	
Duration of Symptoms Prior to Enrollment Group 2										
< 25th percentile	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
25 ≤ 75th percentile	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
≥ 75th percentile	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				

CI=Confidence Intervals. Improvement is defined by an Improvement by at least One Category in the 8-point Ordinal Scale. N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria.
[a] Hazard Ratio (HR) is the hazard ratio calculated from the Cox Proportional Hazard Model comparing Active treatment to placebo adjusting for baseline ordinal score and baseline steroid use.
[b] For the subgroup analyses, the model described in [a] was performed for each level of the subgroup. The subgroup variable was removed from the model where applicable.
[c] P-value is based on the Score test from Cox model.

Table with similar format:

Table 33: Time to Improvement by at Least Two Categories through Day 60 in the 8-point Ordinal Scale — mITT Population

Table 34: Summary of Change from Baseline of Ordinal Score by Study Day — mITT Population

Subgroup	Study Day	Treatment	Categories Worsening						Same		Category Improvement							
			3		2		1				1		2		3		4	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Primary analysis	Day 3	Treatment A (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Treatment B (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Day X	Treatment A (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Treatment B (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	X	x.x	x	x.x	x	x.x
Subgroup Analysis																		
Baseline Ordinal Score																		
5	Day 3	Treatment A (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Treatment B (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Day X	Treatment A (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Treatment B (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Repeat the above rows for Change from Baseline and Study Days 5, 8, 11, 15, 22, 29, and 60. Repeat for all subgroups specified in Table 6.																		
N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria.																		

Table 35: Disease Severity Distribution as Measured by Ordinal Score for Study Day — mITT Population

Subgroup	Study Day	Treatment	Ordinal Score[a]															
			8		7		6		5		4		3		2		1	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Primary Analysis	Day 3	Treatment A (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Treatment B (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Day X	Treatment A (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Treatment B (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	X	x.x	x	x.x	x	x.x
Subgroup Analysis																		
Baseline Ordinal Score																		
5	Day 3	Treatment A (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Treatment B (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Day X	Treatment A (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Treatment B (N=X)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Repeat the above rows for Study Days 5, 8, 11, 15, 22, 29, and 60, Repeat for each subgroup as shown in Table 6																		

N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria with non-missing data.

Table 36: Summary of Continuous Secondary Outcomes through Day 29 – Oxygen Days — mITT Population

Outcomes	Treatment	n	%	Minimum	25th Percentile	Median	75th Percentile	Maximum
Primary Analysis	Treatment A (N=X)	x	x	x	x.x	x.x	x.x	x
	Treatment B (N=X)	x	x	x	x.x	x.x	x.x	x
Subgroup Analyses								
Baseline Ordinal Score								
5	Treatment A (N=X)	x	x	x	x.x	x.x	x.x	x
	Treatment B (N=X)	x	x	x	x.x	x.x	x.x	x
Repeat for each subgroup analyses as shown in Table 6.								
N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria with non-missing data.								

Tables with similar format:

Table 37: Summary of Continuous Secondary Outcomes through Day 29 – Non-Invasive Ventilation/High Flow Oxygen Free Days or Worse — mITT Population

Table 38: Summary of Continuous Secondary Outcomes through Day 29 – Ventilator/ECMO Days or Worse — mITT Population

Table 39: Summary of Continuous Secondary Outcomes through Day 29 – Duration of Hospitalization — mITT Population

[Implementation note: For duration of hospitalization, remove rows for multiple imputation.]

Table 40: Incidence of Secondary Outcomes – Non-Invasive Ventilation/High Flow Oxygen Free Days or Worse through Day 29 — mITT Population

Outcomes	Treatment	Population at Risk[a]		New Cases[b]		Incidence Rate		
		n	%	n	%	Estimate[c]	95% CI[d]	80% CI[d]
Primary Analysis	Treatment A (N=X)	x	x.x	x	x.x	x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
	Treatment B (N=X)	x	x.x	x	x.x	x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
Subgroup Analysis								
Repeat for each sensitivity and subgroup category as detailed in Table 6 and Table 7.								

N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria.
[a] Population at risk is defined as all subjects with a baseline ordinal score of 5 or below.
[b] New cases are defined as subjects with a baseline ordinal score of 5 or below that progress to an ordinal score of 6, 7, or 8.
[c] The incidence rate is the proportion of the population at risk that have new cases.
[d] Confidence intervals for the incidence rate estimated using Blaker method.

Table 41: Incidence of Secondary Outcomes – Ventilator/ECMO Days or Worse through Day 29 — mITT Population

Outcomes	Treatment	Population at Risk[a]		New Cases[b]		Incidence Rate		
		n	%	n	%	Estimate[c]	95% CI[d]	80% CI[d]
Primary Analysis	Treatment A (N=X)	x	x.x	x	x.x	x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
	Treatment B (N=X)	x	x.x	x	x.x	x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
Subgroup Analysis								
Repeat for each sensitivity and subgroup category as detailed in Table 6 and Table 7.								

N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects that satisfies the row criteria.
[a] Population at risk is defined as all subjects with a baseline ordinal score of 6 or below.
[b]New cases are defined as subjects with a baseline ordinal score of 6 or below that progress to an ordinal score of 7 or 8.
[c]The incidence rate is the proportion of the population at risk that have new cases.
[d] Confidence intervals for the incidence rate estimated using Blaker method.

Table 42: Time to Mechanical Ventilation or Death through Day 29 — mITT Population with Baseline Ordinal Score of 5 or 6, CRP<150 mg/L, and age<85 years

Analysis/Subgroup	Treatment	Number of Subjects to Mechanical Ventilation or Death[d]		Median Time Until Event			Hazard Ratio			P-value[e]
		n	%	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	
Initial Model[a]	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
Primary with Sensitivity Imputation[b]	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
Subgroup Analyses[c]										
Baseline Ordinal Score										
5	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
6	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
5 or 6	Treatment A (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	x	x.x	x.x	x.x, x.x	x.x, x.x				
Repeat for the rest of the subgroups in Table 6.										

CI=Confidence Intervals.
N=Number of subjects in modified intent-to-treat (mITT) population. n= Number of unique subjects who progressed to mechanical ventilation or death that satisfies the row criteria.
[a] Hazard Ratio (HR) is the hazard ratio calculated from the Cox Proportional Hazard Model comparing Active treatment vs Placebo and adjusting for the baseline dexamethasone use (yes, no), Baseline Ordinal Score (5, 6 or 7), age, and baseline CRP as covariates. All subjects whose last assessment was before Day 29 and were missing the event were censored at the date of last assessment.
[b] Primary with Sensitivity Imputation: Same analysis as the initial model but subjects missing event and whose last assessment is before Day 29 are non-events for good discharges and censored at Day 29 or at last assessment for subjects still hospitalized or discharged to LTAC, hospice care, or other hospital.
[c] For the subgroup analyses, the model described in [a] was performed for each level of the subgroup.
[d] Number of subjects who progressed to a clinical status of 7 or 8 through Day 29.
[e] P-value is based on the adjusted cox model.

Table with similar format:

Table 43: Time to Mechanical Ventilation or Death through Day 29 — mITT Population

[Implementation note: Add subgroup category for baseline ordinal score 7 and baseline ordinal score '6 or 7' to Table 43.]

Table 44: Z-Scores and Westfall-Young Permutation P-Value Adjustment — mITT Population

[Implementation note: This analysis is option and will be performed only if its inclusion appears likely to be helpful in interpreting the primary and secondary analyses results.]

Endpoint	Raw P-value	Westfall-Young Adjusted P-Value
Analysis Including Day 8 OS as a Continuous Endpoint		
Clinical Status at Study Day 8	0.xxx	0.xxx
Sustained Survival Without Respiratory Failure	0.xxx	0.xxx
Difference from Baseline Clinical Status at Days 3	0.xxx	0.xxx
Difference from Baseline Clinical Status at Days 5	0.xxx	0.xxx
Difference from Baseline Clinical Status at Days 8	0.xxx	0.xxx
Difference from Baseline Clinical Status at Days 11	0.xxx	0.xxx
Difference from Baseline Clinical Status at Days 15	0.xxx	0.xxx
Difference from Baseline Clinical Status at Days 22	0.xxx	0.xxx
Difference from Baseline Clinical Status at Days 29	0.xxx	0.xxx
Number of Days Clinical Status >4	0.xxx	0.xxx
Number of Days Clinical Status>5	0.xxx	0.xxx
Number of Days Clinical Status>6	0.xxx	0.xxx
Value of CRP	0.xxx	0.xxx
Value of Ferritin	0.xxx	0.xxx
Value of D-dimer	0.xxx	0.xxx
Value of Fibrinogen	0.xxx	0.xxx
Value of LDH	0.xxx	0.xxx
14-Day Mortality	0.xxx	0.xxx
28-Day Mortality	0.xxx	0.xxx
59-Day Mortality	0.xxx	0.xxx
Repeat above analyses excluding the Day 8 OS endpoint		
Note: This analysis will be based on complete data.		

Table 45: Hochberg P-Value Adjustment — mITT Population

[Implementation note: This analysis is option and will be performed only if its inclusion appears likely to be helpful in interpreting the primary and secondary analyses results.]

Endpoint	Raw P-value[a]	Hochberg Adjusted P-Value	Z-Scores	Global P-Value
Clinical Status at Study Day 8	0.xxx	0.xxx	x.xx	0.xxx
Time (days) to Sustained Recovery	0.xxx	0.xxx	x.xx	
Sustained Survival Without Respiratory Failure	0.xxx	0.xxx	x.xx	
Time (days) to at least 1 point Improvement from Baseline	0.xxx	0.xxx	x.xx	
Time (days) to at least 2 point Improvement from Baseline	0.xxx	0.xxx	x.xx	
Difference from Baseline Clinical Status at Days 3	0.xxx	0.xxx	x.xx	
Difference from Baseline Clinical Status at Days 5	0.xxx	0.xxx	x.xx	
Difference from Baseline Clinical Status at Days 8	0.xxx	0.xxx	x.xx	
Difference from Baseline Clinical Status at Days 11	0.xxx	0.xxx	x.xx	
Difference from Baseline Clinical Status at Days 15	0.xxx	0.xxx	x.xx	
Difference from Baseline Clinical Status at Days 22	0.xxx	0.xxx	x.xx	
Difference from Baseline Clinical Status at Days 29	0.xxx	0.xxx	x.xx	
Number of Days Clinical Status >4	0.xxx	0.xxx	x.xx	
Number of Days Clinical Status>5	0.xxx	0.xxx	x.xx	
Number of Days Clinical Status>6	0.xxx	0.xxx	x.xx	
Value of CRP	0.xxx	0.xxx	x.xx	
Value of Ferritin	0.xxx	0.xxx	x.xx	
Value of D-dimer	0.xxx	0.xxx	x.xx	
Value of Fibrinogen	0.xxx	0.xxx	x.xx	
Value of LDH	0.xxx	0.xxx	x.xx	
14-Day Mortality	0.xxx	0.xxx	x.xx	
28-Day Mortality	0.xxx	0.xxx	x.xx	
59-Day Mortality	0.xxx	0.xxx	x.xx	
Time (days) to Death	0.xxx	0.xxx	x.xx	

[a] Raw p-values and Z-scores will come from analysis of these endpoints using multiple imputation for Day 8 Ordinal Score and using complete data for the rest of the endpoints.

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 46: Overall Summary of Treatment Emergent Adverse Events by Baseline Ordinal Score — Safety Population

Adverse Event Categories	Treatment A (N=X)												Treatment B (N=X)											
	Baseline Ordinal Score												Baseline Ordinal Score											
	5			6			7			Any BOS[a]			5			6			7			Any BOS[a]		
	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
At least one TEAE	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
At least one TEAE grade ≥ 3	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
At least one related TEAE	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
At least one related TEAE grade ≥ 3	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
At least one treatment-emergent SAE	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
At least one TEAE leading to early termination of study	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
At least one TEAE leading to study drug discontinuation	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
Death	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx

BOS= Baseline Ordinal Score.
TEAE= Treatment-emergent Adverse Event. N=Number of subjects in the Safety population. n= Number of unique subjects that satisfies the row criteria.
[a] There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.

Table 47: Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Treatment Group — Safety Population

MedDRA Classification		Treatment A (N=X)			Treatment B (N=X)			Risk Difference	
System Organ Class	**Preferred Term**	**n**	**%**	**Events**	**n**	**%**	**Events**	**Estimate**	**95% CI[a]**
Any SOC	Any PT	x	x.x	xxx	x	x.x	xxx	x.x	x.x
SOC 1	Any PT	x	x.x	xxx	x	x.x	xxx	x.x	x.x
	PT 1	x	x.x	xxx	x	x.x	xxx	x.x	x.x
	PT 2	x	x.x	xxx	x	x.x	xxx	x.x	x.x
SOC 2	Any PT	x	x.x	xxx	x	x.x	xxx	x.x	x.x
	PT 1	x	x.x	xxx	x	x.x	xxx	x.x	x.x
	PT 2	x	x.x	xxx	x	x.x	xxx	x.x	x.x

TEAE= Treatment-emergent Adverse Event. n= Number of unique subjects that satisfies the row criteria. N=Number of subjects in the Safety population. n= Number of unique subjects that satisfies the row criteria.
Denominators are the number of subjects in the Safety population.
If a subject has multiple occurrences of an adverse event, the subject is counted only once in the preferred term/system organ class category.
All adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0.
[a] 95% CI for risk differences calculated using the Miettinen-Nurminen method.

Table 48: Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Baseline Ordinal Score — Safety Population

MedDRA Classification		Treatment A (N=X)												Treatment B (N=X)											
		Baseline Ordinal Score												Baseline Ordinal Score											
		5			6			7			Any BOS[a]			5			6			7			Any BOS[a]		
System Organ Class	Preferred Term	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Any SOC	Any PT	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
SOC 1	Any PT	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
	PT 1	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
	PT 2	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
SOC 2	Any PT	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
	PT 1	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
	PT 2	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx

TEAE= Treatment-emergent Adverse Event. n= Number of unique subjects that satisfies the row criteria. N=Number of subjects in the Safety population.
Denominators are the number of subjects in the Safety population.
If a subject has multiple occurrences of an adverse event, the subject is counted only once in the preferred term/system organ class category.
All adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0.
[a] There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.

Table with similar format:

Table 49: Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Baseline Steroid Use — Safety Population

Table 50: Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Baseline Use of Emerging Covid-19 Treatments — Safety Population

Table 51: Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Duration of Symptoms Prior to Enrollment — Safety Population

Table 52: Treatment Emergent Serious Adverse Events by System Organ Class, Preferred Term and Treatment Group — Safety Population

MedDRA Classification		Treatment A (N=X)			Treatment B (N=X)			Risk Difference	
System Organ Class	Preferred Term	n	%	Events	n	%	Events	Estimate	95% CI[a]
Any SOC	Any PT	x	x.x	xxx	x	x.x	xxx	x.x	x.x
SOC 1	Any PT	x	x.x	xxx	x	x.x	xxx	x.x	x.x
	PT 1	x	x.x	xxx	x	x.x	xxx	x.x	x.x
	PT 2	x	x.x	xxx	x	x.x	xxx	x.x	x.x
SOC 2	Any PT	x	x.x	xxx	x	x.x	xxx	x.x	x.x
	PT 1	x	x.x	xxx	x	x.x	xxx	x.x	x.x
	PT 2	x	x.x	xxx	x	x.x	xxx	x.x	x.x

TEAE= Treatment-emergent Adverse Event. n= Number of unique subjects that satisfies the row criteria. N=Number of subjects in the Safety population.
Denominators are the number of subjects in the Safety population.
If a subject has multiple occurrences of an adverse event, the subject is counted only once in the preferred term/system organ class category.
All adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0.
[a] 95% CI for risk differences calculated using the Miettinen-Nurminen method.

Table 53: Treatment Emergent Serious Adverse Events by System Organ Class, Preferred Term, and Baseline Ordinal Score — Safety Population

MedDRA Classification		Treatment A (N=X)												Treatment B (N=X)											
		Baseline Ordinal Score												Baseline Ordinal Score											
		5			6			7			Any BOS[a]			5			6			7			Any BOS[a]		
System Organ Class	Preferred Term	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Any SOC	Any PT	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
SOC 1	Any PT	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
	PT 1	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
	PT 2	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
SOC 2	Any PT	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
	PT 1	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx
	PT 2	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx	x	x.x	xxx

TEAE= Treatment-emergent Adverse Event. n= Number of unique subjects that satisfies the row criteria. N=Number of subjects in the Safety population.
Denominators are the number of subjects in the Safety population.
If a subject has multiple occurrences of an adverse event, the subject is counted only once in the preferred term/system organ class category.
All adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0.
[a] There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.

Table 54: Mortality Rates — Safety Population

Analysis Type	Baseline Ordinal Score	Treatment Group	Number of Deaths		Mortality Rate (CI)[c]			Difference in Mortality Rates at the Specified Time Point[d]			HR[e]			P-value[f]
			n	%	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	
Time to Death by Day 15														
Primary[a]	5	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	6	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	7	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	Any BOS	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
Primary with Sensitivity Imputation[b]	5	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	6	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	7	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	Any BOS	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
Time to Death by Day 29														
Primary[a]	5	Treatment A (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	6	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	7	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx

Analysis Type	Baseline Ordinal Score	Treatment Group	Number of Deaths		Mortality Rate (CI)[c]			Difference in Mortality Rates at the Specified Time Point[d]			HR[e]			P-value[f]
			n	%	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	Any BOS	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
Primary with Sensitivity Imputation[b]	5	Treatment A (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	6	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	7	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	Any BOS	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
Time to Death by Day 60														
Primary[a]	5	Treatment A (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	6	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	7	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	Any BOS	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
Primary with Sensitivity Imputation[b]	5	Treatment A (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	6	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	7	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx

Analysis Type	Baseline Ordinal Score	Treatment Group	Number of Deaths		Mortality Rate (CI)[c]			Difference in Mortality Rates at the Specified Time Point[d]			HR[e]			P-value[f]
			n	%	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
	Any BOS	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
		Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							

CI= Confidence Intervals. N=Number of subjects in the Safety population. n= Number of unique subjects that satisfies the row criteria.

[a] For the primary endpoint, all subjects whose last assessment was before the corresponding timepoint (Day 15 Visit, Day 29 Visit, Day 60 Visit) and were missing the event were censored at the date of last assessment.

[b] Primary with Sensitivity Imputation: Same analysis as the initial model but subjects missing event and whose last assessment is before the corresponding timepoint (Day 15 Visit, Day 29 Visit, Day 60 Visit) are non-events for good discharges and censored at Day 15, Day 29, Day 60 respectively or at last assessment for subjects still hospitalized or discharged to LTAC, hospice care, or other hospital.

[c] Mortality Rates are the Kaplan-Meier estimates.

[d] Difference in mortality rates (80%, 95% CI) obtained from Kaplan Meier.

[e] HR is the hazard ratio from the Cox Proportional Hazard Model adjusted for baseline ordinal score and baseline steroid use.

[f] P-value is based on the Cox adjusted model.

Table 55: Time to Death through Day 15, 29, or 60 by Treatment Group: Restricted Mean Survival Time Analysis — Safety Population

Study Day	Treatment Group	Actual Baseline Ordinal Score	n	Restricted Mean Mortality Time (Days)		Difference	
				Estimate	95% CI	Estimate	95% CI
Day 15	Treatment A (N=X)	5	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x.x	x.x, x.x		
	Treatment A (N=X)	6	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x.x	x.x, x.x		
	Treatment A (N=X)	7	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x.x	x.x, x.x		
	Treatment A (N=X)	Any BOS	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	Treatment B (N=X)		x	x.x	x.x, x.x		
Repeat for Day 29 and Day 60							

N= Number of subjects in the specified treatment group, actual baseline ordinal score, and analysis population.
n = Number of subjects who died by the specified study day.
Difference is the difference in the restricted mean mortality time between Active treatment and Placebo.

Table 56: Time to Death, SAE or Grade ≥3 TEAEs through Day 60 — Safety Population

Baseline Ordinal Score	Treatment Group	Number of Deaths or Grade >3 TEAEs		Event Rate (CI)[a]			Difference in Event Rates at the Specified Time Point[b]			HR[c]			P-value[d]
		n	%	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	Estimate	80% CI	95% CI	
5	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
6	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
7	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							
Any BOS	Treatment A (N=X)	X	x.x	x.x	x.x, x.x	x.xxx	x.x	x.x, x.x	x.x, x.x	x.x	x.x, x.x	x.x, x.x	0.xxx
	Treatment B (N=X)	X	x.x	x.xx	x.x, x.x	x.xxx							

CI= Confidence Intervals. N=Number of subjects in the Safety population. n= Number of unique subjects that satisfies the row criteria.
[a] Event rates are the Kaplan-Meier estimates.
[b] Difference in event rates (80%, 95% CI) obtained from Kaplan Meier.
[c] HR is the hazard ratio from the Cox Proportional Hazard Model adjusted for baseline ordinal score and baseline steroid use.
[d] P-value is based on the Cox adjusted model.

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 57: Summary of ALT Results Values and Change from Baseline by Study Days — Safety Population

Study Day	Treatment Group	Value at Visit						Change from Baseline					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Day 1	Treatment A (N=X)	x	x.x	x.xx	x.x	x.x	x.x	-	-	-	-	-	-
	Treatment B (N=X)	x	x.x	x.xx	x.x	x.x	x.x	-	-	-	-	-	-
Repeat Rows for Study Days 3, 5, 8, 11, 15, and 29		x	x.xx	x.xx	x.xx	x.x	x.x	x	x.x	x.xx	x.x	x.x	x.x
		x	x.xx	x.xx	x.xx	x.x	x.x	x	x.x	x.xx	x.x	x.x	x.x
SD= Standard Deviation. Min- Minimum. Max= Maximum. N=Number of subjects in the Safety population.													

Tables with similar format:

Table 58: Summary of AST Results Values and Change from Baseline by Study Days — Safety Population

Table 59: Summary of Bilirubin Results Values and Change from Baseline by Study Days — Safety Population

Table 60: Summary of Creatinine Values and Change from Baseline by Study Days — Safety Population

Table 61: Summary of eGFR Results Values and Change from Baseline by Study Days — Safety Population

[Implementation note: Add footnote that eGFR values reported as >60 are analyzed as 61 and those reported as >90 are analyzed as 91.]

Table 62: ALT Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Study Day	Baseline Ordinal Score	N	Severity[a]						
			None-Grade 2		Grade 3		Life Threatening/ Grade 4		Missing
			n	%	n	%	n	%	n
Baseline									
Treatment A	5	x	x	x.x	x	x.x	x	x.x	x
	6								
	7	x	x	x.x	x	x.x	x	x.x	x
	Any BOS	x	x	x.x	x	x.x	x	x.x	x
Treatment B	5	x	x	x.x	x	x.x	x	x.x	x
	6								
	7	x	x	x.x	x	x.x	x	x.x	x
	Any BOS	x	x	x.x	x	x.x	x	x.x	x
Repeat Rows or Study Days 3, 5, 8, 11, 15, 29									
Maximum Severity Post Baseline									
Treatment A	5	x	x	x.x	x	x.x	x	x.x	x
	6								
	7	x	x	x.x	x	x.x	x	x.x	x
	Any BOS	x	x	x.x	x	x.x	x	x.x	x
Treatment B	5	x	x	x.x	x	x.x	x	x.x	x
	6								
	7	x	x	x.x	x	x.x	x	x.x	x
	Any BOS	x	x	x.x	x	x.x	x	x.x	x

N=Number of subjects in the Safety population with a non-missing lab value at the respective time point. n= Number of unique subjects that satisfies the row criteria and have the corresponding lab severity. The "Maximum Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.

[a] Severity as per NIAID Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Corrected Version 2.1 (July 2017).

Tables with similar format:

Table 63: AST Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Table 64: Bilirubin Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Table 65: Creatinine Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Table 66: eGFR Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

[Implementation note: Add footnote that eGFR values reported as >60 are analyzed as 61 and those reported as >90 are analyzed as 91.]

14.3.5.1 Hematology Results

Table 67: Summary of White Blood Cells Results Values and Change from Baseline by Study Days — Safety Population

Study Day	Treatment Group	Value at Visit						Change from Baseline					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Day 1	Treatment A (N=X)	x	x.xx	x.xx	x.xx	x.x	x.x	-	-	-	-	-	-
	Treatment B (N=X)	x	x.xx	x.xx	x.xx	x.x	x.x	-	-	-	-	-	-
Repeat Rows for Study Days 3, 5, 8, 11, 15, and 29		x	x.xx	x.xx	x.xx	x.x	x.x	x	x.x	x.xx	x.x	x.x	x.x
		x	x.xx	x.xx	x.xx	x.x	x.x	x	x.x	x.xx	x.x	x.x	x.x
SD= Standard Deviation. Min- Minimum. Max= Maximum. N=Number of subjects in the Safety population.													

Tables with similar format:

Table 68: Summary of Platelets Results Values and Change from Baseline by Study Days — Safety Population

Table 69: Summary of Hemoglobin Results Values and Change from Baseline by Study Days — Safety Population

Table 70: Summary of INR Results Values and Change from Baseline by Study Days — Safety Population

Table 71: Summary of Neutrophils Results Values and Change from Baseline by Study Days — Safety Population

Table 72: Summary of Eosinophils Results Values and Change from Baseline by Study Days — Safety Population

[Implementation note: Add footnote that Eosinophils values reported as <0.03 are analyzed as 0.02.]

Table 73: Summary of Basophils Results Values and Change from Baseline by Study Days — Safety Population

Table 74: Summary of Lymphocytes Results Values and Change from Baseline by Study Days — Safety Population

Table 75: Summary of Monocytes Results Values and Change from Baseline by Study Days — Safety Population

Table 76: White Blood Cell Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Study Day	Baseline Ordinal Score	N	Severity[a]						
			None-Grade 2		Grade 3		Life Threatening/ Grade 4		Missing
			n	%	n	%	n	%	n
Baseline									
Treatment A	5	x	x	x.x	x	x.x	x	x.x	x
	6								
	7	x	x	x.x	x	x.x	x	x.x	x
	Any BOS	x	x	x.x	x	x.x	x	x.x	x
Treatment B	5	x	x	x.x	x	x.x	x	x.x	x
	6								
	7	x	x	x.x	x	x.x	x	x.x	x
	Any BOS	x	x	x.x	x	x.x	x	x.x	x
Repeat Rows or Study Days 3, 5, 8, 11, 15, 29									
Maximum Severity Post Baseline									
Treatment A	5	x	x	x.x	x	x.x	x	x.x	x
	6								
	7	x	x	x.x	x	x.x	x	x.x	x
	Any BOS	x	x	x.x	x	x.x	x	x.x	x
Treatment B	5	x	x	x.x	x	x.x	x	x.x	x
	6								
	7	x	x	x.x	x	x.x	x	x.x	x
	Any BOS	x	x	x.x	x	x.x	x	x.x	x

N=Number of subjects in the Safety population. n= Number of unique subjects that satisfies the row criteria.
[a] Severity as per NIAID Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Corrected Version 2.1 (July 2017).

Tables with similar format:

Table 77: Platelets Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Table 78: Hemoglobin Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Table 79: INR Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Table 80: Neutrophils Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Table 81: Lymphocytes Results by Baseline Ordinal Score, Severity and Study Days — Safety Population

Table 82: Summary of Continuous Markers of Inflammation and Immune Response by Study Day — Safety Population

Study Day	Immune Response Measure	Treatment A (N=X)						Treatment B (N=X)					
		n	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max	P-value[a]
Day 3	C-reactive protein	xx	x.x	x.xx	x.x	x	x	x.x	x.xx	x.x	x	x	0.xxx
	Ferritin	xx	x.x	x.xx	x.x	x	x	x.x	x.xx	x.x	x	x	0.xxx
	D-Dimer	xx	x.x	x.xx	x.x	x	x	x.x	x.xx	x.x	x	x	0.xxx
	Fibrinogen	xx	x.x	x.xx	x.x	x	x	x.x	x.xx	x.x	x	x	0.xxx
	LDH	xx	x.x	x.xx	x.x	x	x	x.x	x.xx	x.x	x	x	0.xxx
Rows should be repeated for Study Days 1, 5, 8, 11, 15, and 29													

SD= Standard Deviation. Min= Minimum. Max= Maximum. N=Number of subjects in Safety population.
Values of D-Dimer reported as <220 were analyzed as 219 and values of CRP reported as <3.0 were analyzed as 2.9.
[a] P-value of tests of two sample means.

14.3.6 Displays of Vital Signs

Table 83: Summary Statistics of Baseline Vital Signs by Actual Baseline Ordinal Score and Treatment Group — Safety Population

Variable	Statistic	Treatment A (N=X)				Treatment B (N=X)				All Subjects (N=X)			
		BOS 5 (N=X)	BOS 6 (N=X)	BOS 7 (N=X)	Any BOS[a] (N=X)	BOS 5 (N=X)	BOS 6 (N=X)	BOS 7 (N=X)	Any BOS[a] (N=X)	BOS 5 (N=X)	BOS 6 (N=X)	BOS 7 (N=X)	Any BOS[a] (N=X)
Pulse	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Diastolic Blood Pressure	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Respiratory Rate	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x
Blood oxygen Saturation	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Median	x	x	x	x	x	x	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x

Variable	Statistic	Treatment A (N=X)				Treatment B (N=X)				All Subjects (N=X)			
		BOS 5 (N=X)	BOS 6 (N=X)	BOS 7 (N=X)	Any BOS[a] (N=X)	BOS 5 (N=X)	BOS 6 (N=X)	BOS 7 (N=X)	Any BOS[a] (N=X)	BOS 5 (N=X)	BOS 6 (N=X)	BOS 7 (N=X)	Any BOS[a] (N=X)
Oral Temperature	n	x	x	x	x	x	x	x	x	x	x	x	x
	Mean	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
	Minimum	x	x	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x	x	x

N=Number of subjects in the Safety population. n=number of subjects with a non-missing assessment.
[a] There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.

14.4 Summary of Concomitant Medications

Table 84: Number and Percentage of Subjects with Prior Medications by WHO Drug Classification, Actual Baseline Ordinal Score, and Treatment Group — Safety Population

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Treatment A (N=X)								Treatment B (N=X)								All Subjects (N=X)							
		BOS 5 (N=X)		BOS 6 (N=X)		BOS 7 (N=X)		Any BOS[a] (N=X)		BOS 5 (N=X)		BOS 6 (N=X)		BOS 7 (N=X)		Any BOS[a] (N=X)		BOS 5 (N=X)		BOS 6 (N=X)		BOS 7 (N=X)		Any BOS[a] (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	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	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Any ATC 2	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	ATC 2	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
ATC 1	ATC 2	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Any ATC 2	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	ATC 2	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
ATC 1	ATC 2	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Prior medications are defined as any medications begun before a subject took the first dose of study product. Medications are coded using the WHO Drug Dictionary version 202003.
ATC=Anatomical Therapeutic Chemical.
BOS= Baseline Ordinal Score.
N=Number of subjects in the Safety population.
n= Number of subjects reporting taking at least one medication in the specific ATC Class.
[a] There were X additional subjects with an Actual Baseline Ordinal Score of 4 that are included in the 'Any BOS' summaries.

Table with similar format:

Table 85: Number and Percentage of Subjects with Concomitant Medications by WHO Drug Classification, Actual Baseline Ordinal Score, and Treatment Group — Safety Population

[Implementation note: Update the footnote to state 'Concomitant medications are defined as any medications that begun after a subject took the first dose of study product or that begun before the first dose and continued after the subject took the first dose of study product.']

Table 86: Summary of Concomitant COVID-19 Treatments — Safety Population

Type	Summary Measure	Treatment A (N=X)						Treatment B (N=X)					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
[COVID-19 Treatment 1]	Number of Subjects	x	-	-	-	-		x	-	-	-	-	-
	Study Day Onset[a]	x	x.x	x.xx	x.x	x	x	x	x.x	x.xx	x.x	x	x
	Duration (days)	x	x.x	x.xx	x.x	x	x	x	x.x	x.xx	x.x	x	x

Concomitant COVID-19 Treatments are defined as medications that started before dose 1 of study product and continued throughout the study or those started after a subject took study product.
SD=Standard Deviation. Min=Minimum. Max=Maximum.
N=Number of subjects in the Safety population.
n=Number of subjects reporting at least one of the concomitant COVID-19 treatments. Refer to Section 6.4 for a list of COVID-19 treatments of interest.
[a] Study day onset is defined as the start day of the concomitant medication.

Table 87: Summary of Steroid Usage for Indications Other than COVID-19 by Treatment of Indication — Safety Population

Type	Summary Measure	Treatment A (N=X)						Treatment B (N=X)					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
[COVID-19 Treatment 1]	Number of Subjects	x	-	-	-	-		x	-	-	-	-	-
	Study Day Onset[a]	x	x.x	x.xx	x.x	x	x	x	x.x	x.xx	x.x	x	x
	Duration (days)	x	x.x	x.xx	x.x	x	x	x	x.x	x.xx	x.x	x	x

Concomitant Steroid Treatments are defined as steroids for indications other than COVID-19 that started before dose 1 of study product and continued throughout the study or those started after a subject took study product.
SD=Standard Deviation. Min=Minimum. Max=Maximum.
N=Number of subjects in the Safety population.
n=Number of subjects reporting steroid usage for indications other than COVID-19. Refer to Section 6.4 for a list of steroids of interest.
[a] Study day onset is defined as the start day of the concomitant medication.

APPENDIX 2. FIGURE MOCK-UPS

General Programming Notes for figures:

- Treatment group labeling will vary by stage. Abbreviations will be used if the treatment group labels need to be abbreviated to improve fit.
- All figures will be based on complete data analyses without multiple imputation.
- Use the same color for a treatment on the different graphs (SAS standard colors):
  - Active Treatment = Blue
  - Placebo = Red
- For severity graphs (SAS standard colors):
  - 5 = green
  - 6 = blue
  - 7 = red
  - Death = black

LIST OF FIGURES

10.1 Disposition of Subjects

Figure 1: CONSORT Flow Diagram

[Implementation note: Update final CONSORT diagram to include only the two treatment groups applicable to each stage.]

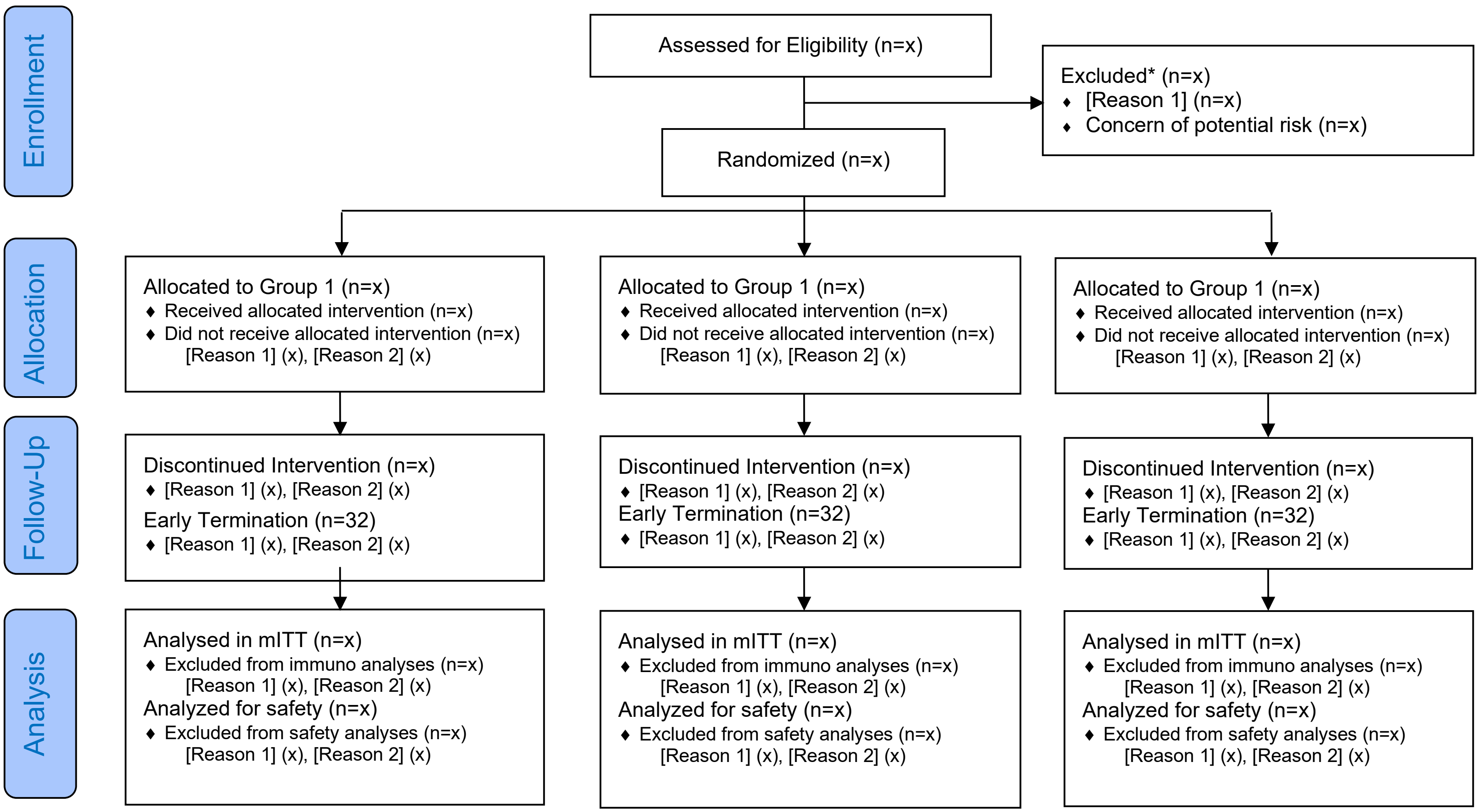
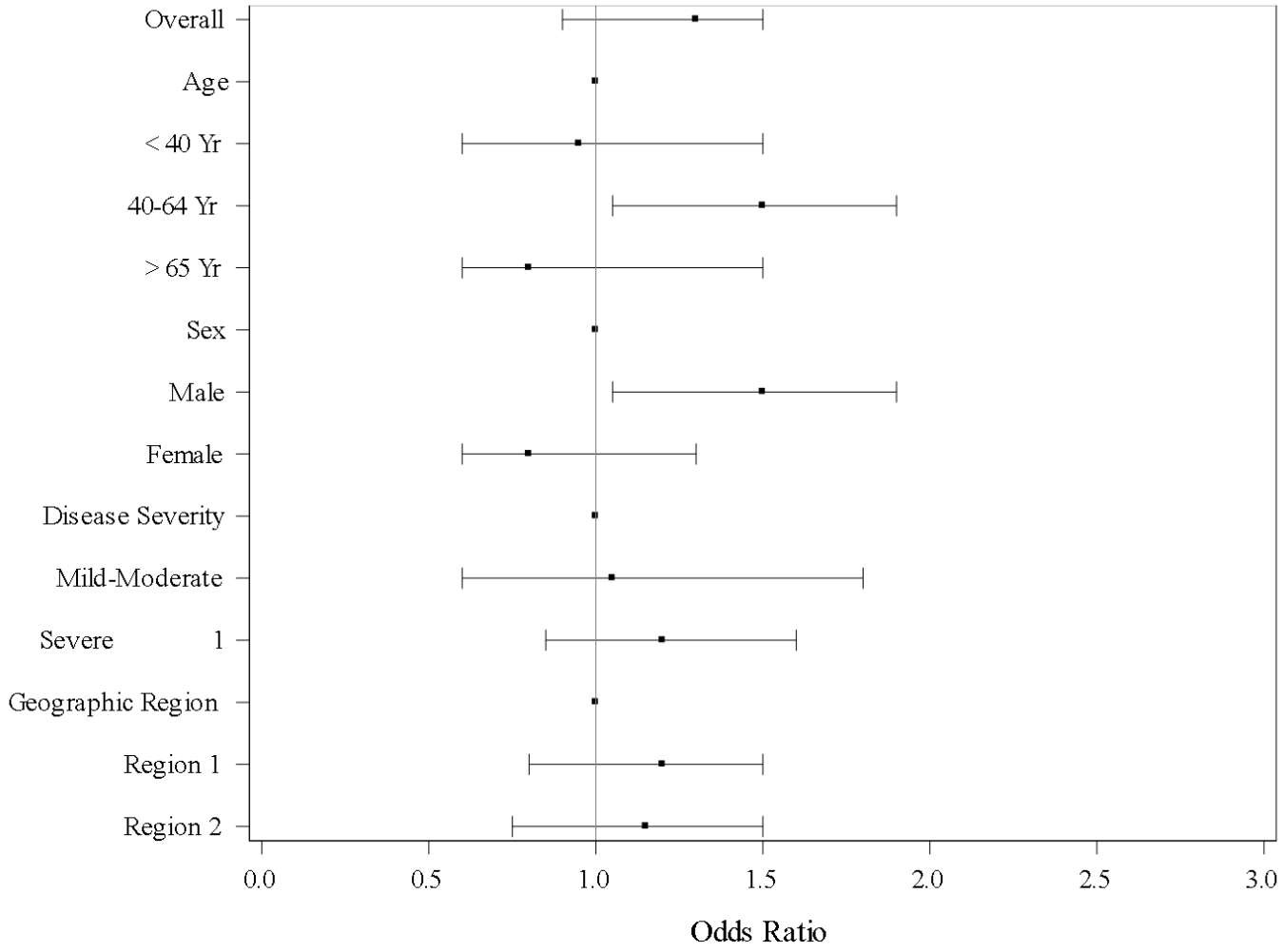


Figure 2: Adjusted Odds Ratios and 95% Confidence Interval of Inferior Clinical Status Score at Study Visit Day 8 Using a Proportional Odds Model: Overall and for each Subgroup — mITT Population

[Implementation note: The reference group for odds ratio calculation is the placebo group.]



Figures with similar format:

Figure 3: Adjusted Odds Ratios and 80% Confidence Interval of Inferior Clinical Status Score at Study Visit Day 8 Using a Proportional Odds Model: Overall and for each Subgroup — mITT Population

Figure 4: Adjusted Odds Ratios and 95% Confidence Interval of Inferior Clinical Status Score at Study Visit Day 15 Using a Proportional Odds Model: Overall and for each Subgroup — mITT Population

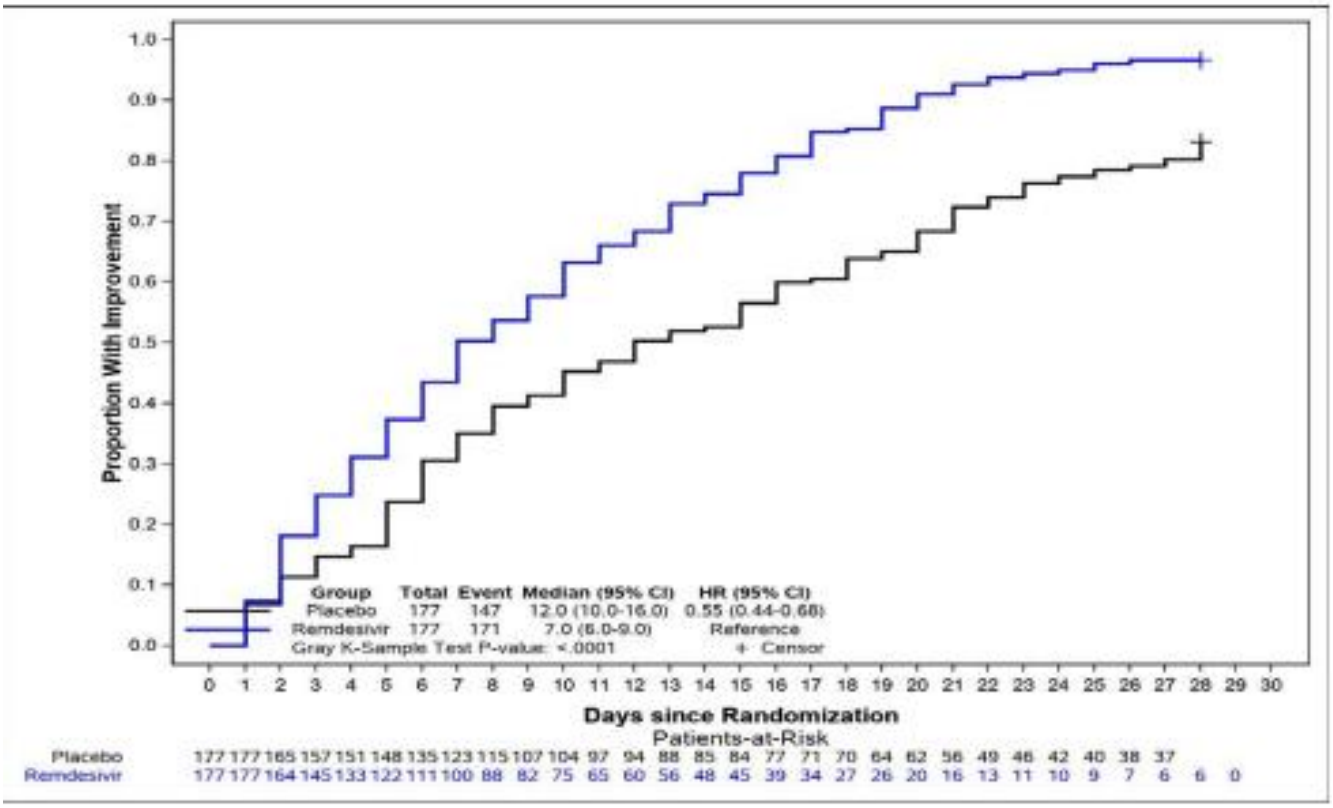
Figure 5: Adjusted Odds Ratios and 80% Confidence Interval of Inferior Clinical Status Score at Study Visit Day 15 Using a Proportional Odds Model: Overall and for each Subgroup — mITT Population

Figure 6: Adjusted Odds Ratios and 95% Confidence Interval of Inferior Clinical Status Score at Study Visit Day 29 Using a Proportional Odds Model: Overall and for each Subgroup — mITT Population

Figure 7: Adjusted Odds Ratios and 80% Confidence Interval of Inferior Clinical Status Score at Study Visit Day 29 Using a Proportional Odds Model: Overall and for each Subgroup — mITT Population

Figure 8: Kaplan-Meier Plot for Time to Sustained Recovery through Day 60 defined by 8-point Ordinal Scale — mITT Population

[Implementation note: For time to sustained recovery, create individual figures 8A through 8F for all subjects, baseline steroid use=Yes, No and baseline ordinals score=5,6,7]



Figures with Similar Format:

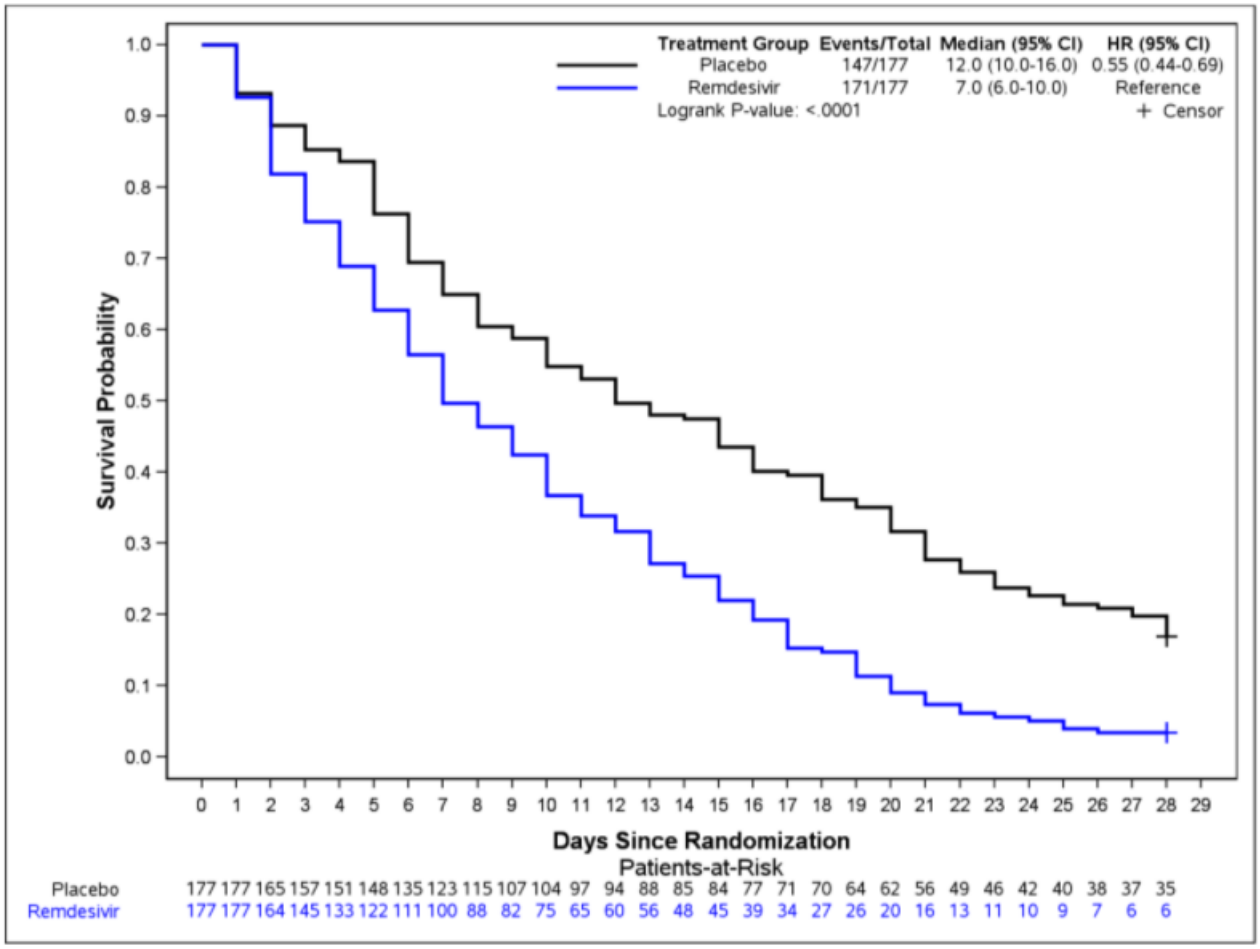
Figure 9: Kaplan-Meier Plot for Time to Improvement by at least One Category in the Ordinal Scale through Day 60 — mITT Population

Figure 10: Kaplan-Meier Plot for Time to Improvement by at least Two Categories in the Ordinal Scale through Day 60 — mITT Population

[Implementation note: For time to improvement KM figures, create one figure for all subjects in the analysis population.]

Figure 11: Kaplan-Meier Plot for Time to Mechanical Ventilation or Death through Day 29 — mITT Population

[Implementation note: For time to mechanical ventilation or death, create individual figures 11A through 11F for all baseline dexamethasone use=Yes, No and Baseline ordinal score=5,6,7.]



Figures with similar format:

[Implementation note: For the figures below, create only one figure for all subjects in the analysis population.]

Figure 12: Kaplan-Meier Plot for Time to Death through Day 15 — Safety Population

Figure 13: Kaplan-Meier Plot for Time to Death through Day 29 — Safety Population

Figure 14: Kaplan-Meier Plot for Time to Death through Day 60 — Safety Population

Figure 15: Kaplan-Meier Plot for Time to Death, SAE or Grade ≥3 TEAEs through Day 60 — Safety Population

Figure 16: Adjusted Hazard Ratios and 95% Confidence Intervals of Time to Sustained Recovery through Study Visit Day 60 Using a Cox Proportional Hazard Model Overall and for each Subgroup — mITT Population

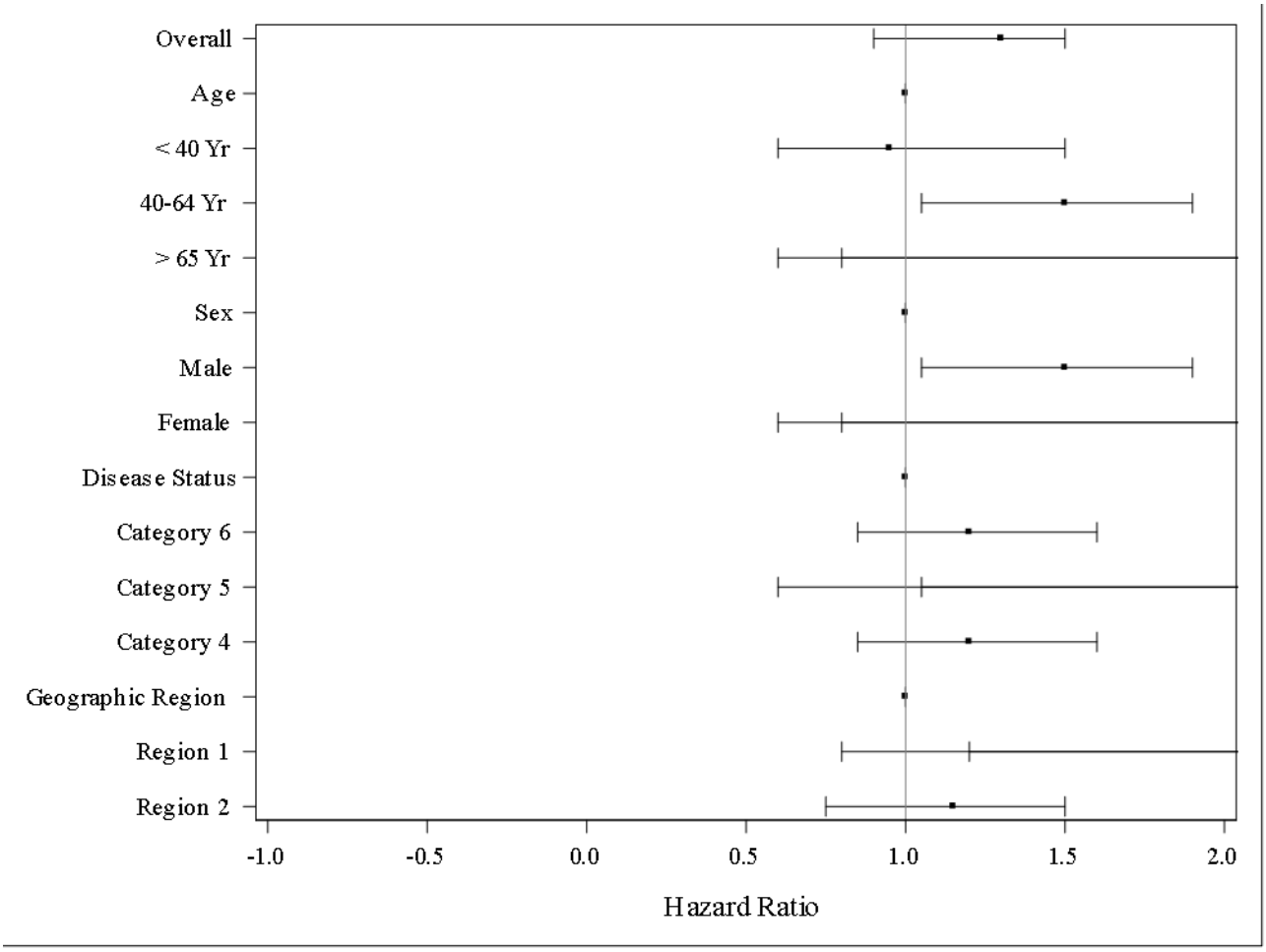


Figure with Similar Format:

Figure 17: Adjusted Hazard Ratios and 80% Confidence Interval of Time to Sustained Recovery through Study Visit Day 60 Using a Cox Proportional Hazard Model Overall and for each Subgroup — mITT Population

Figure 18: Distribution of Ordinal Scores by Study Days — mITT Population

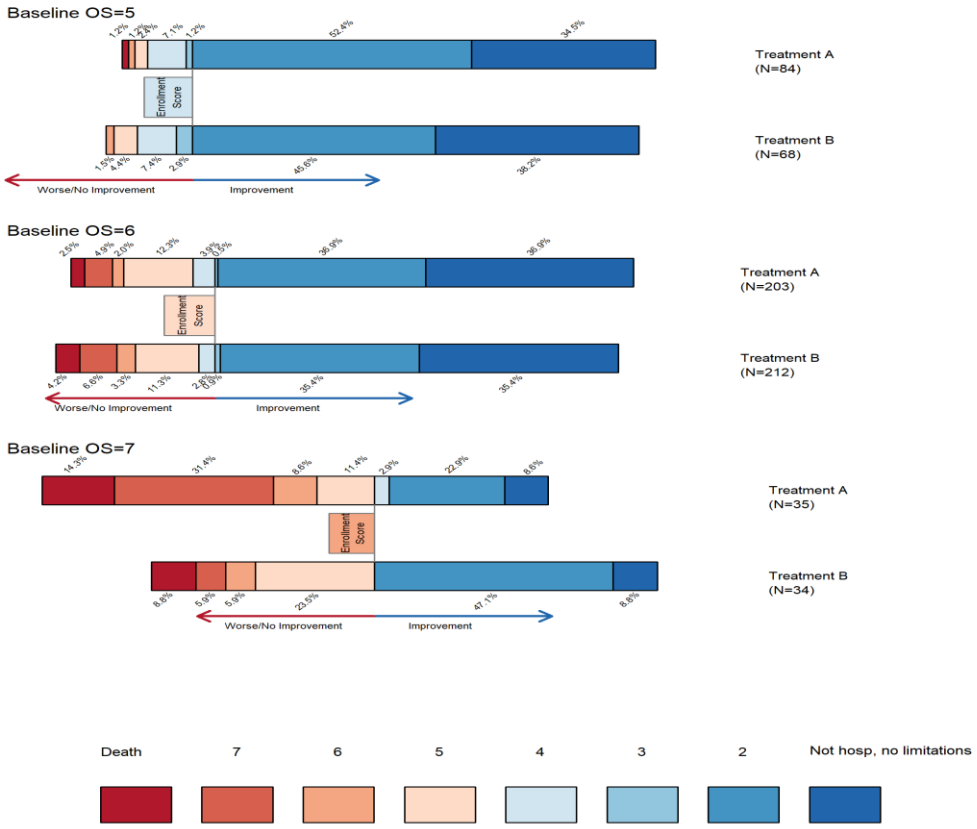
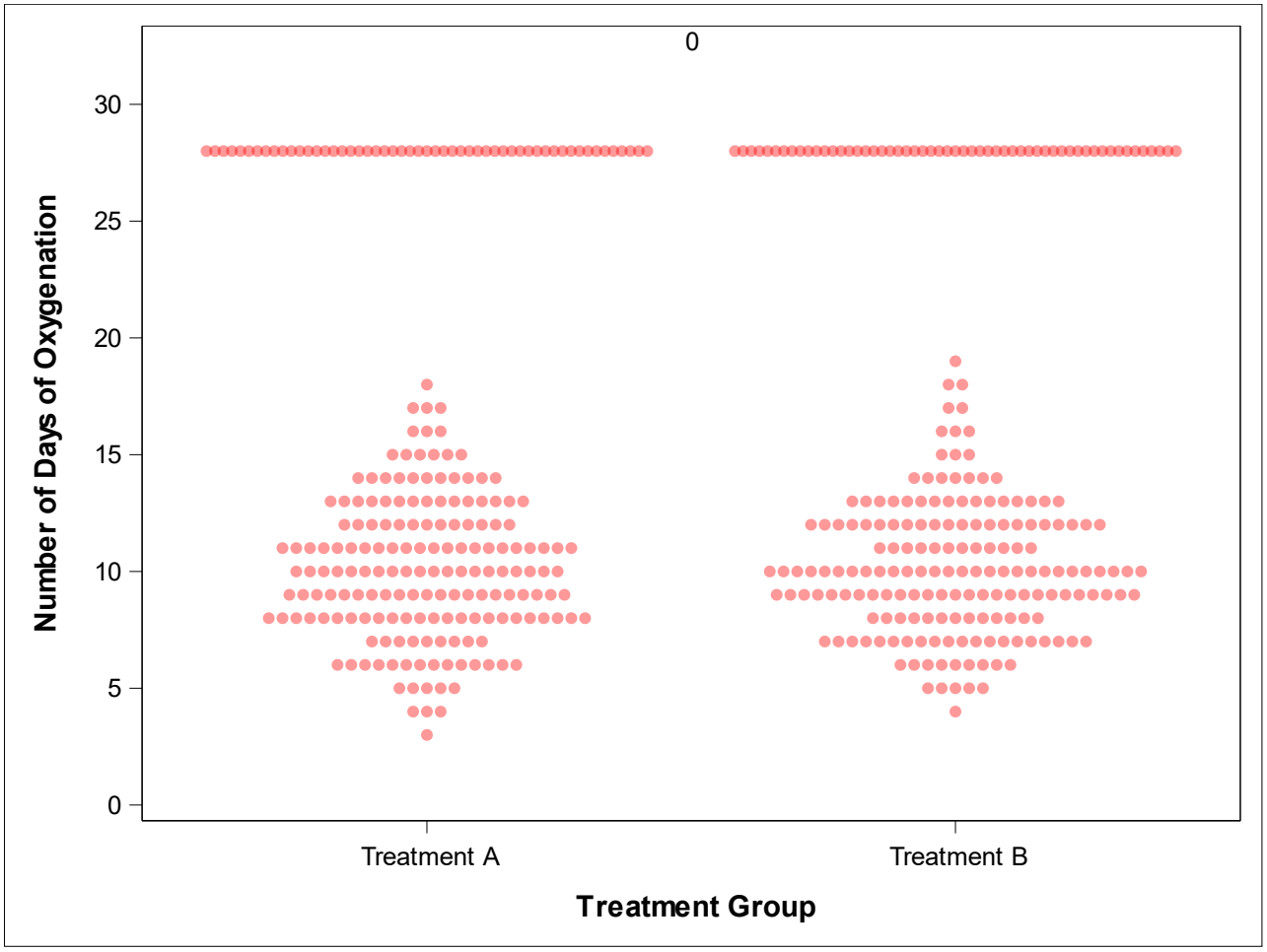


Figure 19: Bee Swarm Plot of Oxygenation Days through Day 29 — mITT Population

[Implementation note: Update colors for treatment groups to match colors used for KM curves.]



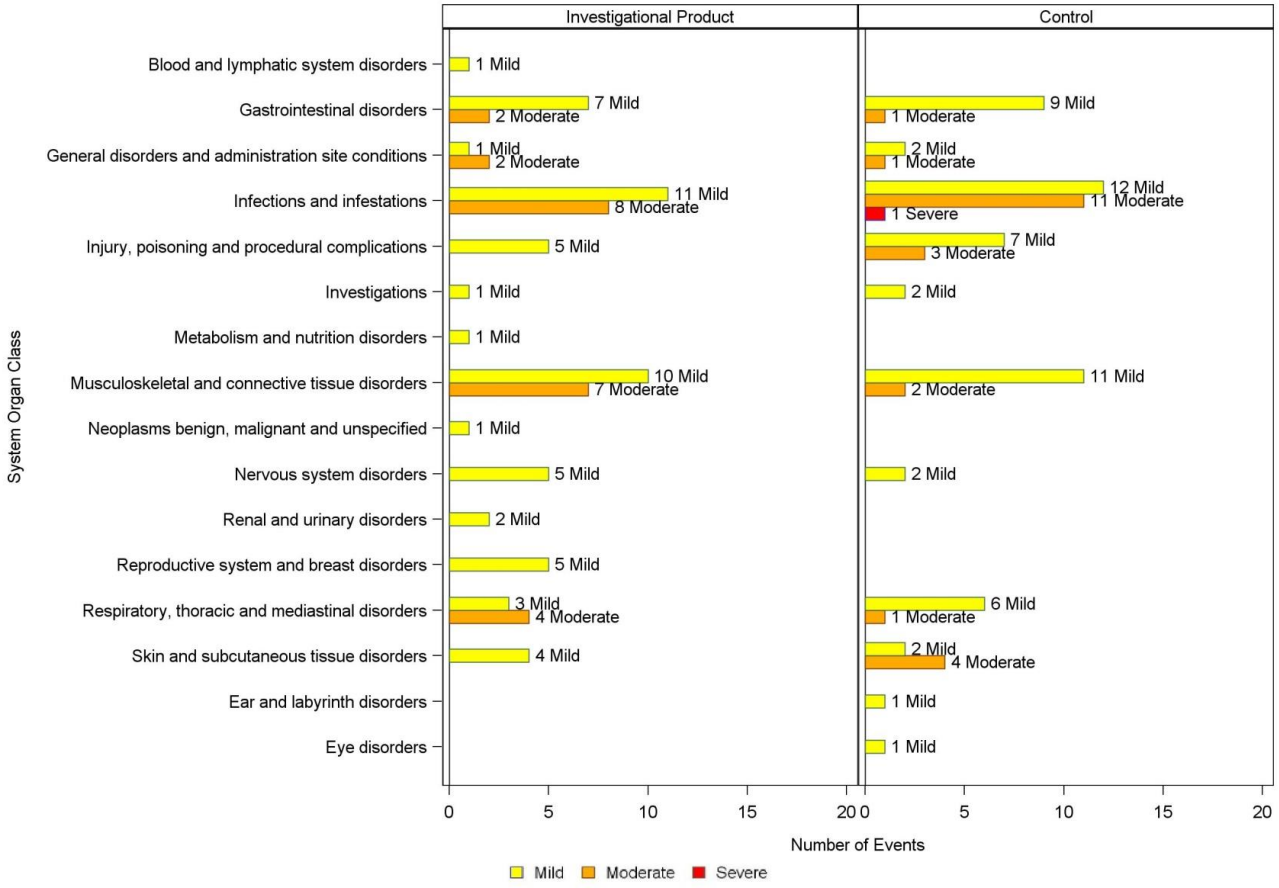
Figures with similar format:

Figure 20: Bee Swarm Plot of Non-Invasive/High-Flow Oxygen Days through Day 29 — mITT Population

Figure 21: Bee Swarm Plot of Invasive Mechanical Ventilation/ECMO Days through Day 29 — mITT Population

Figure 22: Bee Swarm Plot of Hospitalization Days through Day 29 — mITT Population

Figure 23: Frequency of Non-Serious Related AEs by MedDRA System Organ Class and Severity — Safety Population, All Subjects



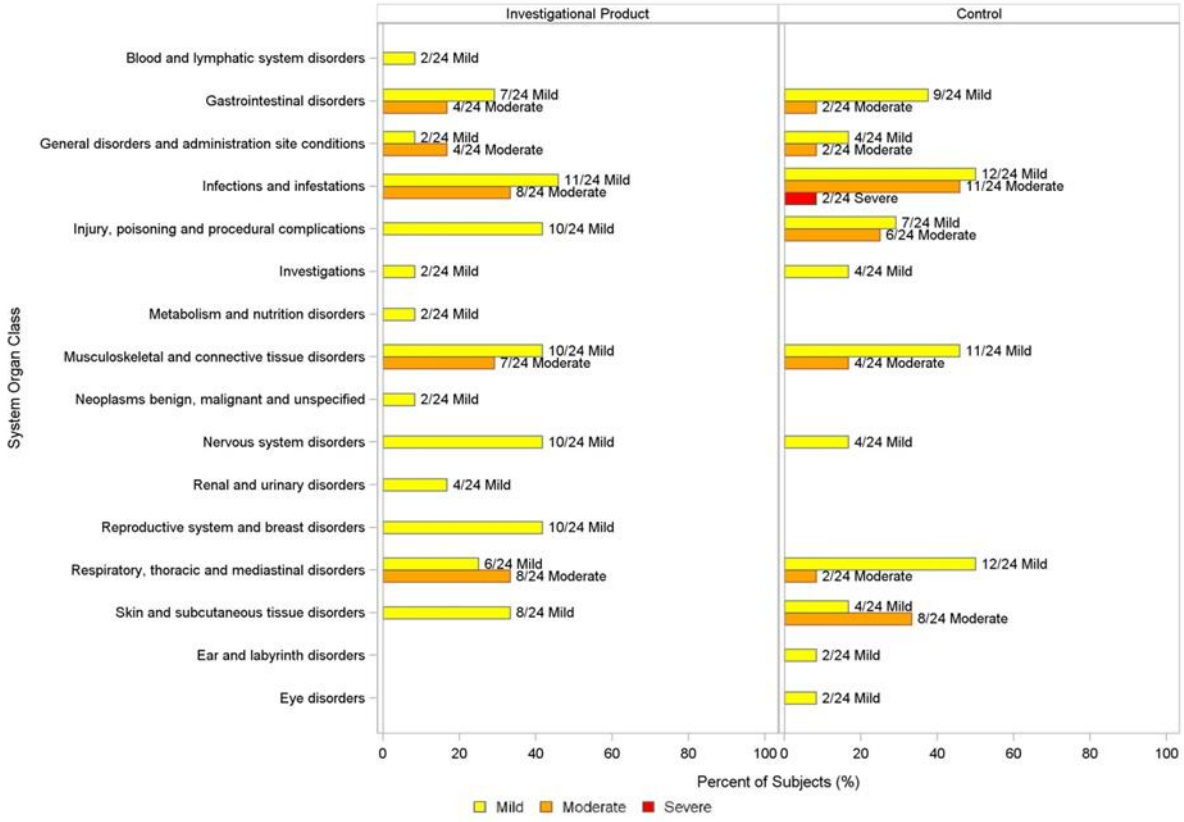
Figures with similar format:

Figure 24: Frequency of Non-Serious Related AEs by MedDRA System Organ Class and Severity — Safety Population, Actual Baseline Ordinal Score 5

Figure 25: Frequency of Non-Serious Related AEs by MedDRA System Organ Class and Severity — Safety Population, Actual Baseline Ordinal Score 6

Figure 26: Frequency of Non-Serious Related AEs by MedDRA System Organ Class and Severity — Safety Population, Actual Baseline Ordinal Score 7

Figure 27: Incidence of Non-Serious Related AEs by MedDRA System Organ Class and Severity — Safety Population, All Subjects



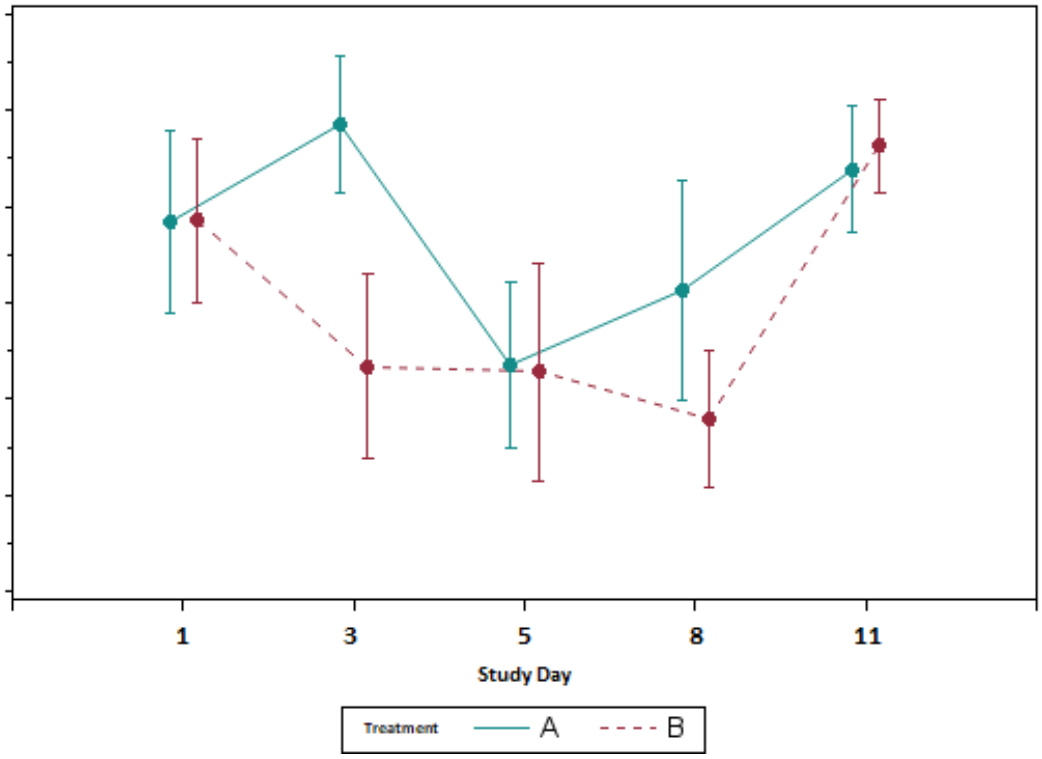
Figures with similar format:

Figure 28: Incidence of Non-Serious Related AEs by MedDRA System Organ Class and Severity — Safety Population, Actual Baseline Ordinal Score 5

Figure 29: Incidence of Non-Serious Related AEs by MedDRA System Organ Class and Severity — Safety Population, Actual Baseline Ordinal Score 6

Figure 30: Incidence of Non-Serious Related AEs by MedDRA System Organ Class and Severity — Safety Population, Actual Baseline Ordinal Score 7

Figure 31: Mean and Standard Deviations of CRP by Study Days — Safety Population



Figures with similar format:

Figure 32: Mean and Standard Deviations of Ferritin by Study Days — Safety Population

Figure 33: Mean and Standard Deviations of D-Dimer by Study Days — Safety Population

Figure 34: Mean and Standard Deviations of Fibrinogen by Study Days — Safety Population

Figure 35: Mean and Standard Deviations of LDH by Study Days — Safety Population

APPENDIX 3. LISTINGS MOCK-UPS

LIST OF LISTINGS

Listing 1: Subjects Who Early Terminated or Discontinued Treatment

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Study Day	Last Date of Study Treatment	Category	Treatment Discontinued	Reason for Early Termination or Treatment Discontinuation
Treatment A or B	7/6/5	XXXXX	xxxx		Early Termination/Treatment Discontinuation	NA/Infusions/RDV/ Risankizumab	xxxxx

Programming

Include randomized subjects only.

Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, category where Treatment discontinuation is sorted prior to Early termination. If there are multiple treatment discontinuations (i.e., distinct dates for each product type) the order will be sorted by Study day. If both treatments were discontinued at the same time "Infusions + Injections" will be displayed in the Treatment Discontinued column. If subjects were randomized and not dosed are categorized as "Not Treated" and sorted after PBO + Dexamethasone + RDV if applicable.

Listing 2: Screen Failures — Screen Failed Subjects

Subject ID	Inclusion/Exclusion Not Met
XXXXX	

Programming

Include screen failure subjects only. Sort Order = USUBJID.

Listing 3: Subject-Specific Protocol Deviations

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	DV Number	Deviation	Deviation Classification	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Planned or Unplanned?
Treatment A or B	7/6/5	Xxxxx	xx	xxx	Major/Minor	xxx	x	xxxx	Yes/No	Yes/No	Yes/No	Planned, Approved/ Planned, Not Approved /Not Planned

Programming

Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, Deviation Number. Concatenate all the specify fields as appropriate. If the columns do not fit within the eCTD specified margins, then Actual Treatment Group, Actual Baseline Ordinal Score, Subject ID will be placed in a header row as in the AE listings.

Listing 4: Non Subject-Specific Protocol Deviations

Site	Start Date	End Date	Deviation	Deviation Classification	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Category	Planned or Unplanned?
xxxx	xxxx	xxxx	xxxx	Major/Minor	xxxx	Yes/No	Yes/No	xxxx	Planned, Approved/ Planned, Not Approved /Not Planned

Programming

Sort Order = Site (use site name and not the 5 alphanumeric site code), start date, deviation. Concatenate all the specify fields as appropriate.

Listing 5: Demographics and Baseline Characteristics

Actual Treatment Group	Randomized Treatment Group	Baseline Ordinal Score	Subject ID	Site ID	Sex	Age (years)	Ethnicity	Race	Eligibility	Date of Informed Consent
xx	Treatment A or B	7/6/5	xxxxx	xx	xxx	xx	xxx	xxx	xx	DDMMMYYYY

Programming

Sort Order = Actual Treatment Group, Baseline Ordinal Score (descending order, i.e., 6, then 5, then 4), USUBJID.

For date of informed consent, use the date the subject signed the informed consent for corresponding stage being analyzed.

Listing 6: Medical History

Subject ID	Screen Date	Date of Onset COVID-19 Symptoms	List of Comorbidities	Concomitant Medications for Any Comorbidities 7 Days Prior to Enrollment	Concomitant Medications for Current SARS-CoV-2 Infection 7 Days Prior to Enrollment	Relevant Medical History
xx						
Medications were coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary (WHODRUG) version 202003.						

Programming

Sort Order = USUBJID, Screen Date, Comorbidities.

Listing 7: NEW Score Individual Components and Overall NEW Score for Study Day 1 (Baseline)

Actual Treatment Group	Baseline Ordinal Score	Subject ID	Assessment Date (Day)	Respiratory Rate (bpm)	O_2 Saturation (%)	Any Supplemental O_2	Temperature (°C)	Systolic BP (mmHg)	Heart Rate (bpm)	Level of Consciousness	Total NEW Score
Treatment A or B	7/6/5	xx	DDMMYYYY (xx)	xx	xx	Yes/No	xx.x	xxx	xx	A/N	xx

Programming

Sort Order = Actual Treatment Group, Baseline Ordinal Score (descending order, i.e., 6, then 5, then 4), USUBJID, Assessment Date.

Listing 8: Physical Examinations

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Study Day	Date (Day) of Assessment	Body System	Abnormal Finding
Treatment A or B	7/6/5/4	xxx	xx	DDMMYYYY (xx)	xxxx	xxxxxx

Programming

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'. Each reported respiratory finding will appear in its own row.

Sort order will be Treatment Group, Actual Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, Study Day, and Body System.

Listing 9: Prior and Concomitant Medications

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Medication Number	Medication	Start Date (Day)	Stop Date (Day)	Indication	Taken for a condition on Medical History? (MH Description; Number)	Taken for AE? (AE Description; Number)	ATC Level 1 (ATC Level 2)
Treatment A or B	7/6/5/4	xxx	xx	xxxx	DDMMYYYY (xx)	DDMMYYY (xx)	xxxxx	Yes/No	Yes/No	xxxx

Programming

Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, CM number

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

Listing 10: Steroid Use

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Medication Number	Medication	Medication Start Day	Medication End Day	Dose / Route	Frequency	Indication	Taken for an AE? (AE Description; Number)
Treatment A or B	7/6/5/4/	xxx	xx	xxxx	x	x	xx / xx	xx	xxxx	Yes/No

Programming Notes: Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, CM number. 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

Listing 11: Medications of Interest

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Medication Number	Medication	Medication Start Day	Medication End Day	Indication	Medication of Interest Category	Medication of Interest Subcategory	ATC Level 1 (ATC Level 2)
Treatment A or B	7/6/5/4/	xxx	xx	xxxx	x	x	xxxx	xxxx	xxxx	xxxx / xxxx

Programming Notes: Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), 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

If the medication does not have an applicable subcategory, then display 'N/A'

Listing 12: Treatment Exposure

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Treatment Administration Start Date (day)	Treatment Administration End Date (day)	Treatment Duration (days)	Dose Status	Reason for Halting/Slowing/Missing
Treatment A or B	7/6/5/4	xxxx	DDMMYYYY (xx)	DDMMYYYY (xx)	xx	Halted/Slowed/Missing	xxxxx

Programming

Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, Treatment Administration Start Date.

Listing 13: Individual Components and Ordinal Score

Treatment Group	Actual Baseline Ordinal Score	Subject ID	Visit Number	Study Visit Date (day) of Assessment	Death Date (day)	Hospitalization Date	Reason for Hospitalization	If Hospitalized: New or Increased Supplemental Oxygen	If Not Hospitalized: Increased Limitation of Physical Activities	If Not Hospitalized: New or Increased Home Oxygen	Ordinal Score
Treatment A or B	7/6/5/4	xxxx	xx	DDMMYYYY (xx)	DDMMYYYY (xx)	DDMMYYYY (xx)					

Programming

Sort Order = Treatment Group, Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, Visit Number.

Listing 14: Primary and Secondary Efficacy Endpoints

Treatment Group	Baseline Ordinal Score	Subject ID	Visit Number	Study Visit Date (day) of Assessment	Parameter	Result	Change from Baseline	Analysis Type	Analysis Flag 01
Treatment A or B	7/6/5/4	xxxx	xx	DDMMYYYY (xx)					
Analysis Flag identified the record used in the analysis in case of more than one record is present by parameter and visit.									

Programming

Sort Order = Treatment Group, Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, Study Day.

Listing 15: Non-Serious Treatment Emergent Adverse Events

Start Date (day)	End Date (day)	Adverse Event Number	Adverse Event Reported Term	MedDRA System Organ Class	MedDRA Preferred Term	Severity	Relationship to Study Treatment	Relationship to COVID-19	Relationship to Other Medical Conditions	Subject Discontinued Due to AE	Action Taken with Study Treatment
Subject ID: , Treatment Group: , Baseline Ordinal Score:											
DDMMYYYY (xx)	DDMMYYYY (xx)					xxxx	Not Related/Related	Related/Not Related	Related/Not Related	Yes/No	For each of Remdesivir, Risankizumab, or Placebo

Programming

Sort order will be Treatment Group, Actual Baseline Ordinal Score (descending order, i.e., 6, then 5 then 4), USUBJID, AE Number. For relationship to study treatment, list either Not Related or each study treatment it is related to. For Action taken, separately list actions for each treatment.

Listings with similar format:

Listing 16: Treatment Emergent Adverse Events Leading to Early Termination of Study Drug

Listing 17: Treatment Emergent Adverse Events Resulting in Death

Listing 18: All Treatment Emergent Adverse Events

Listing 19: Related Treatment Emergent Adverse Events

Listing 20: Serious Treatment Emergent Adverse Events

Listing 21: Treatment Emergent Adverse Events Leading to Early Termination of Study

Listing 22: Pregnancy Reports - Maternal Information

Actual Treatment Group	Actual Baseline Ordinal Score	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?
Treatment A or B	7/6/5/4	xxxx	xx									
Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.												

Programming notes:

Sort order will be Treatment Group, Actual Baseline Ordinal Score, USUBJID, Pregnancy Number.

Listing 23: Pregnancy Reports - Gravida and Para

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?
Treatment Group: , Actual Baseline Ordinal Score: , Subject ID: , Pregnancy Number:													
Gravida includes the current pregnancy, para events do not. [a] Preterm Birth [b] Term Birth													

Programming notes:

Sort order will be Treatment Group, Actual Baseline Ordinal Score, USUBJID, Pregnancy Number.

Listing 24: Pregnancy Reports - Live Birth Outcomes

Treatment Group	Actual Baseline Ordinal Score	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?
Treatment A or B														
Congenital Anomalies are included in the Adverse Event listing.														

Listing 25: Pregnancy Reports - Still Birth Outcomes

Treatment Group	Actual Baseline Ordinal Score	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?
Treatment A or B													

Listing 26: Pregnancy Reports - Spontaneous, Elective, or Therapeutic Abortion Outcomes

Treatment Group	Actual Baseline Ordinal Score	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
Treatment A or B								

Listing 27: Clinical Laboratory Test Results

Treatment Group	Actual Baseline Ordinal Score	Subject ID	Planned Study Day	Actual Study Day	Date (Day) of Sample	Laboratory Parameter (Units)	Result (Toxicity Grade)	Change from Baseline	Reference Range Low	Reference Range High
Treatment A or B	7/6/5/4	xxx	xx	xx	DDMMMYYYY (xx)	xxx (xxx)	xxx (xxxx)	xxx	xxxx	xxxx

Programming notes:

Sort order will be Treatment Group, Baseline Ordinal Score, USUBJID, Planned Study Day. If subjects were randomized and not dosed "Not Treated" will be used for the actual treatment category and will be sorted after PBO + Dexamethasone + RDV. All parameters will be included in the listing.

Listings with similar format:

Listing 28: Markers of Inflammation and Coagulation Test Results

Listing 29: Urine Pregnancy Test Results