CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 20-0006
Study Title:
A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults (ACTT-4)

NCT04640168

ACTT-4 Version 2.0

DATE: 09-June-2021

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 20-0006 (ACTT-4)**
Development Phase:	Phase 3
Products:	Baricitinib + IV Placebo + Remdesivir PO Placebo + Dexamethasone + Remdesivir
Form/Route:	IV (Remdesivir, Dexamethasone/Placebo) and Oral Tablet (Baricitinib/Placebo)
Indication Studied:	COVID-19
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	December 1, 2020
Clinical Trial Completion Date:	Trial Ongoing
Date of the Analysis Plan:	June 9, 2021
Version Number:	2.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

ACTT	A Multicenter, Adaptive Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults (Adaptative COVID-19 Treatment Trial)
AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
CI	Confidence Interval
CoV / COV	Coronavirus
CRF / eCRF	Case Report Form / Electronic Case Report Form
CRP	C-reactive protein
CSR	Clinical Study Report
DAIDS	Division of AIDS
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
ECMO	Extracorporeal Membrane Oxygenation
FDA	Food and Drug Administration
ICH	International Conference on Harmonisation
IV	Intravenous
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mITT	Modified Intention-to-Treat
MOP	Manual of Procedures
N	Number (typically refers to subjects)
NIH	National Institutes of Health
OP	Oropharyngeal
PBO	Placebo
PCR	Polymerase Chain Reaction
PI	Principal Investigator
PO	"Per os", by mouth
PT	Preferred Term / Prothrombin Time

RCD	Reverse Cumulative Distribution
RDV	Remdesivir
RMST	Restricted Mean Survival Time
RNA	Ribonucleic Acid
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SARS	Severe Acute Respiratory Syndrome
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SOC	System Organ Class
SQ	Subcutaneous
US	United States
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults" (DMID Protocol 20-0006) describes and expands upon the statistical information presented in the protocol. This protocol is an adaptive protocol with different stages. Each stage will have a separate SAP. This SAP is for the study's 4th stage "ACTT-4": Baricitinib + Placebo + Remdesivir vs. Placebo + Dexamethasone + Remdesivir.

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

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

2. INTRODUCTION

Data from ACTT-1 showed that hospitalized adults with COVID-19 who were randomized to receive remdesivir alone resulting in the U.S. Food and Drug Administration (FDA) issuing an Emergency Use Authorization (EUA) to permit the use of remdesivir for treatment of suspected or laboratory-confirmed COVID-19 in adults and children hospitalized with severe disease. Remdesivir has also received, full or conditional approval in several other countries. On August 28, 2020, the FDA expanded the scope of the EUA to include hospitalized patients with suspected or laboratory-confirmed mild or moderate COVID-19 based on final data from ACTT-1 and two other clinical studies.

While remdesivir is considered the standard antiviral for COVID-19, significant morbidity and mortality still occur despite its use. Early in the outbreak, it was observed that COVID-19 patients who developed severe respiratory disease including acute respiratory distress syndrome (ARDS) had increased levels of cytokines consistent with that seen in patients infected with other pathogenic coronaviruses (e.g., SARS). It is postulated that this dysregulated inflammatory immune response contributes to the excessive mortality and targeting this response would further improve outcomes. While multiple strategies have been proposed to counter the hyper-inflammation, to date only two anti-inflammatory strategies have demonstrated efficacy in large randomized trials – dexamethasone and baricitinib.

In ACTT-2, subjects receiving the combination treatment of baricitinib and remdesivir had a shorter median time-to-recovery of 7 days (95% confidence interval (CI), 6 to 8 days) when compared with patients who received remdesivir and placebo (8 days; 95% CI, 7 to 9 days) with control [rate ratio for recovery [RRR] 1.16, 95% CI 1.01 to 1.32; P=0.03)]. Patients who received combination treatment were 30% more likely to have clinical improvement by day 15 than those in the control arm (odds ratio [OR] 1.3; 95%CI 1.0 to 1.6). The patients who benefited the most from combination treatment were those requiring high-flow oxygen or non-invasive ventilation at enrollment with a median of 10 days to recovery compared with 18 days in control group (RRR 1.5, 95% CI 1.1 to 2.1) and the best clinical improvement by day 15 (OR 2.2; 95% CI 1.4 to 3.6). Baricitinib also showed benefit to those on low flow oxygen with a median of 5 days to recovery compared with 6 days in control group (RRR 1.17, 95% CI 0.98 to 1.39) and the clinical improvement by day 15 (OR 1.2; 95% CI 0.9 to 1.6). Patients who received combination treatment with baricitinib and remdesivir and those in the control arm had a similar incidence of adverse and serious adverse events including infections and venous thromboembolic events (VTE).

The Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial is a controlled, open- label randomized trial, involving all major hospitals in the UK. The trial compared a range of possible treatments in patients who were hospitalized with COVID-19. Included, was a treatment arm assigned to receive oral or intravenous dexamethasone (at a dose of 6 mg once daily for up to 10 days) or to received usual care alone. Overall, 22.9% in the dexamethasone group and 25.7% in the usual care group died within 28 days after randomization (age-adjusted rate ratio, 0.83; 95% confidence interval [CI], 0.75 to 0.93; P<0.001). In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and among those receiving supplemental oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94) but not among those who were receiving no supplemental oxygen respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.91 to 1.55). Remdesivir was not used routinely in the RECOVERY trial.

The ACTT-2 and RECOVERY trials are very different and direct comparison is difficult (see Protocol Appendix D Section 2.2.1) However, the relative risk ratios also suggest these two anti-inflammatory strategies may be optimal in different inpatient populations, with baricitinib having the larger effect in the

high flow or low flow oxygen group and dexamethasone having the largest effect in those on mechanical ventilation.

For this reason, direct comparison of these two anti-inflammatory interventions is important. ACTT-4 will evaluate patients hospitalized with COVID-19 and requiring oxygen and determine if baricitinib or dexamethasone (both in addition to remdesivir) is superior or if they are comparable.

2.1. Purpose of the Analyses

This SAP encompasses all interim analyses and the final analysis of primary and secondary outcome measures. These analyses will assess the efficacy and safety of baricitinib + remdesivir in comparison with dexamethasone + remdesivir and will be included in the Clinical Study Report. This protocol is an adaptive design and, if the design is modified, the SAP will be amended accordingly. Safety interim analyses will occur on an ongoing basis to review safety data in the event that the experimental agents inflicts harm. A single interim efficacy analysis will be conducted if enrollment of 1/3 of all subjects is not completed within 1.5 months of study activation. More rapid enrollment will obviate the interim analysis since only a small fraction of remaining enrollment would be impacted by resulting decisions. The goal of the efficacy interim analyses is to review endpoint data in order to recommend whether the current study arm should proceed or to stop early for benefit or futility.

This SAP describes the planned analysis to be conducted by the Investigational New Drug (IND) sponsor NIAID. The analyses in this SAP are intended to be executed to support a Clinical Study Report (CSR) following the last patient's Study Visit Day 60, including all primary and secondary endpoints. Protocol-defined exploratory analyses and additional analyses, if any, performed by the product manufacturer may be pre-specified and described in an addendum to this SAP.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

Primary Objective

To evaluate the clinical efficacy of baricitinib + remdesivir versus dexamethasone + remdesivir as assessed by the **mechanical ventilation free survival** by Day 29.

Secondary Objectives

The key secondary objective is to evaluate the clinical efficacy of baricitinib + placebo + remdesivir versus placebo + dexamethasone + remdesivir according to the clinical status 8-point ordinal scale at Day 15.

The other secondary objectives are to evaluate clinical efficacy of baricitinib + placebo + remdesivir as compared placebo + dexamethasone + remdesivir as assessed by:

- Among subjects with actual baseline Clinical Status ordinal score in Ordinal Score 5, the proportion that do not progress to Clinical Status score 6, 7, or 8 at any time prior to Day 29.
- Mortality
  - Death by Day 15
  - Death by Day 29
- Time to recovery by Day 29.
- Time to an improvement of one category and two categories from Day 1 using the ordinal scale.
- Subject clinical status using 8-point ordinal scale at Days 3, 5, 8, 11, 15, 22, and 29.
- Desirability of Outcome Ranking (DOOR) at Day 15 and Day 29.
- Oxygenation:
  - Oxygenation use up to Day 29.
  - Incidence and duration of new oxygen use through Day 29.
- Non-invasive ventilation/high flow oxygen:
  - Non-invasive ventilation/high flow oxygen use up to Day 29.
  - Incidence and duration of new non-invasive ventilation or high flow oxygen use through Day 29.
- Invasive Mechanical Ventilation / extracorporeal membrane oxygenation (ECMO):
  - Ventilator/ECMO use up to Day 29.
  - Incidence and duration of new mechanical ventilation or ECMO use through Day 29.
- Duration of hospitalization (in days) through Day 29.
- Laboratory Efficacy assessed by d-dimer, and C-reactive protein (CRP) over time

Safety Objectives

Evaluate the safety of baricitinib + remdesivir and dexamethasone + remdesivir through 29 days of follow-up as assessed overall by:

- Cumulative incidence of SAEs through Day 29
- Cumulative incidence of Grade 3 and 4 clinical and/or laboratory AEs through Day 29.
- Discontinuation or temporary suspension of study product administrations (for any reason).
- Changes in white cell count (WBC) with differential, hemoglobin, platelets, creatinine, glucose, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), prothrombin time (PT reported as and INR) over time (analysis of lab values in addition to AEs noted above).

Exploratory Objective

The exploratory objectives are:

1. Evaluate alternate Desirability of Outcome Ranking (DOOR) scales to combine safety and efficacy.
2. To evaluate the virologic efficacy of baricitinib + remdesivir as compared to dexamethasone + remdesivir as assessed by:
   - Percentage of subjects with SARS-CoV-2 detectable in oropharyngeal (OP) sample at Day 3, 5, 8, 11, 15, and 29.
   - Quantitative SARS-CoV-2 virus in OP sample at Day 3, 5, 8, 11, 15, and 29.
   - Quantitative SARS-CoV-2 virus in blood at Day 3, 5, 8, and 11.
3. To evaluate the influence of baricitinib and dexamethasone on SARS-CoV-2 antibody response.
4. To define immunophenotype of subjects by analyzing markers of inflammation, transcriptomics.
5. To describe clinical status of subjects 2 months after treatment, overall and by treatment arm.

3.2. Endpoints

The 8-point ordinal scale is utilized as the principal clinical assessment tool during the study and is the basis for the primary and multiple secondary endpoints. The 8-point ordinal scale is defined as (worst to best):

Category 8: Death;

Category 7: Hospitalized, on invasive mechanical ventilation or ECMO;

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

Category 5: Hospitalized, requiring supplemental oxygen;

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

Category 3: Hospitalized, not requiring supplemental oxygen - no longer requiring ongoing medical care. This would include those kept in hospital for quarantine/infection control, awaiting bed in rehabilitation facility or homecare, etc.;

Category 2: Not hospitalized, but has new or increased limitation on activities and/or new or increased requirement for home oxygen over baseline, pre-COVID-19 status;

Category 1: Not hospitalized, patient is back to their baseline, pre-COVID-19 status, that is, no new or increased limitations on activities and no new or increased oxygen use compared with baseline.

Primary Endpoint

Mechanical ventilation free survival by Day 29 will be assessed as the proportion of subjects not meeting criteria for either of the following categories on the 8-point ordinal scale at any time before or at Day 29.:

Category 8: Death

Category 7: Hospitalized, on invasive mechanical ventilation or ECMO

Secondary Endpoints

The key secondary endpoint is the proportion of subjects meeting criteria for each of the 8-point ordinal scale categories on Day 15.

Other Secondary Endpoints are:

- Proportion of subjects not meeting criteria for one of the following ordinal scale categories at any time by Day 29

  Category 8: Death

  Category 7: Hospitalized, on invasive mechanical ventilation or ECMO

  Category 6: Hospitalized, on non-invasive ventilation or high flow oxygen devices
- Days from randomization and cause of death (if applicable).
- The time to recovery defined as the days from randomization to the first day on which the subject satisfies the criteria for any of the following three categories on the 8-point ordinal scale at any time before or at Day 29:

  Category 3: Hospitalized, not requiring supplemental oxygen - no longer requiring ongoing medical care. This would include those kept in hospital for quarantine/infection control, awaiting bed in rehabilitation facility or homecare, etc.;

  Category 2: Not hospitalized, but has new or increased limitation on activities and/or new or increased requirement for home oxygen over baseline, pre-COVID-19 status;

  Category 1: Not hospitalized, patient is back to their baseline, pre-COVID-19 status, that is, no new or increased limitations on activities and no new or increased oxygen use compared with baseline.
- The time improvement of one category in score defined as the days from randomization to the first day on which the subject satisfies the criteria for a category at least one-step better (e.g., 5 to 4) than their baseline category.
- The time improvement of two categories in score defined as the days from randomization to the first day on which the subject satisfies the criteria for a category at least two-steps better (e.g., 5 to 3) than their baseline category.
- The proportion of subjects meeting the criteria for each of the 8-point ordinal scale categories while hospitalized (Days 3, 5, 8, 11) and on Days 15, 22 and 29.

- Proportion of subjects in each level of the Desirability of Outcome Ranking (DOOR) categories at Day 15 and Day 29. DOOR levels are based on the 8-point ordinal score and the occurrence or absence of SAEs prior to or on the date of the assessment, defined as (best to worst):

  1 - Recovered (Category 1, 2 or 3 Ordinal Score)

  2 - Improved (≥ 1 category improvement in Ordinal Score compared with baseline) & no SAE

  3 - Improved (≥ 1 category improvement in Ordinal Score compared with baseline) & SAE (related or unrelated)

  4 - No change in Ordinal Score from baseline & no SAE

  5 - No change in Ordinal Score from baseline & SAE (related or unrelated)

  6 - Worsening (≥ 1 category worse in Ordinal Score compared with baseline)

  7 - Death

- Days of supplemental oxygen (if applicable) up to Day 29.
- Days of non-invasive ventilation/high-flow oxygen (if applicable) up to Day 29.
- Days of invasive mechanical ventilation/ECMO (if applicable) up to Day 29.
- Days of hospitalization up to Day 29.
- D-dimer and CRP on Day 1, while hospitalized (Days 3, 5, 8, 11), and on Days 15 and 29 (if attends in-person visit or still hospitalized).

Safety Endpoints

Safety endpoints are:

- SAEs
- Grade 3 and 4 treatment emergent adverse events
- Incidence and number of discontinuation or temporary suspension of study product
- WBC with differentials, hemoglobin, platelets, creatinine, glucose, total bilirubin, ALT, AST, INR, on Day 1; Days 3, 5, 8, and 11 (while hospitalized); and Days 15 and 29 (if attends in-person visit or still hospitalized).

Exploratory Endpoints

- Alternate DOOR scales

None of the remaining exploratory endpoints will be described in this SAP, but they include the following:

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

- Immunophenotype endpoints:
  - Proteomic analysis of cytokines, markers of inflammation, and other circulating proteins on Day 1; Days 3, 5, 8, and 11 (while hospitalized) and Day 29.
  - Additionally, in a subset of subjects who consent to genetic testing, transcriptomic analysis of RNA in whole blood and individual immune cells on Days 1, 3, 8, and 29.
- Chronic Clinical Sequelae: Ordinal score, incidence of supplemental oxygen use and physical disability (more than baseline pre-COVID-19 status), readmission to hospital; proportion of subjects with new diagnoses including deep venous thrombosis (DVT), infections, post-traumatic stress disorder (PTSD), anxiety and/or depression.

3.3. Study Definitions and Derived Variables

3.3.1. Baseline Value

For efficacy assessments, the baseline value will be defined as the last value obtained prior to randomization. For safety assessments, the baseline value will be defined as the last value obtained prior to the first on-trial dose of any study product (baricitinib, dexamethasone, remdesivir, or placebo). If the exact time of the assessment or the first dose is not available, but collected on the same date, the assessment will be assumed to have occurred prior to receipt of study product.

A small subset of subjects may receive dexamethasone as standard of care on the same day as but prior to randomization then forgo the dexamethasone / placebo component of the Day 1 study product administration. For these subjects, the baseline value of efficacy assessments will be the last value prior to randomization, as in the preceding paragraph. But, for these subjects, the value of baseline safety assessments will be defined as the last value obtained prior to the dexamethasone dose. If the exact time of the assessment of the pre-randomization dexamethasone or on-trial doses of study product are not available, but collected on the same date, the assessments will be assumed to have occurred prior to receipt of study product and prior to randomization.

3.3.2. Study Day and Time to Event

Use of "Day 29" or "Day 15" are references to actual study days and represent 28 and 14 days post-randomization, respectively. References to visits such as "Study Visit Day 29" and "Study Visit Day 15" pertain to protocol-defined visits which may occur on any day within the defined visit window and not necessarily on Day 29 and Day 15.

Time-to-event endpoints are based on actual study days, e.g., Day 29 or Day 15. Endpoints that are not specifically defined as a time-to-event are based on Study Visits, irrespective of the study day upon which the visit was conducted. As a result, time-to-event endpoints at Day 15 and Day 29 may not match corresponding Clinical Status Ordinal Scores at Study Visit Day 15 and Study Visit Day 29. For example, all subjects with Clinical Status in Category 7 or 8 recorded for Study Visit Day 29 performed on or after Day 31 may not count as events by Day 29 unless there is additional corroborating data (e.g., Death or Supplemental Oxygen Case Report Forms).

3.3.3. Mechanical Ventilation-Free Survival at Day 29

Subjects who do not report an ordinal score in Category 8 (Death) or Category 7 (hospitalized on invasive mechanical ventilation or ECMO) at any point following randomization up to and including Day 29 will be

considered to have survived free from mechanical ventilation. The proportion of subjects who survive through Day 29 free from mechanical ventilation will be estimated using a Kaplan-Meier method, allowing definition of time-to-event and time-to-censoring for all subjects.

The time-to mechanical ventilation or death is defined as the elapsed time in days from randomization to the earliest day at which the subject requires mechanical ventilation or dies. The day the subject requires mechanical ventilation is defined as the first day reporting an ordinal score in Category 7. Note (as in Section 3.3.4), this should be the date the subject is assessed, and not the date the score is reported. The time-to-event for subjects discharged to hospice or other end-of-life care prior to Day 29, but for whom a death date is unknown and with Day 60 data unavailable, will be the number of days from randomization to discharge.

Subjects with Day 29 ordinal score in Categories 6, 5, 4, 3, 2 or 1 will be considered censored on Day 29, if Category 7 was never experienced during the 28 days on study. Subjects completing the Day 29 Study Visit within window, but after Day 29, for which the Day 29 assessment can be completed or confirmed in Categories 6, 5, 4, 3, 2, or 1 will be considered censored on Day 29. Subjects who withdraw from the study or are lost-to-follow-up while hospitalized, prior to reporting a Clinical Status score in Category 7 or 8 will be censored at the date of their last Clinical Status assessment. Subjects who are discharged from hospital (but not to hospice or other end-of-life care) and are not hospitalized at the last contact, who do not have a Day 29 Ordinal Score will be considered censored at Day 29 (i.e., 28 days after randomization). If a subject has a gap in Ordinal Score data available while hospitalized (e.g., the subject is transferred to another hospital or hospice, re-admitted to another facility), the subject may be reviewed by the blinded Endpoint Review Committee to assess whether any data suggests the subject may have progressed to mechanical ventilation in the interim time period. Additionally, if a treated subject terminates early from the study while hospitalized (e.g., due to worsening condition) and without observed progression to mechanical ventilation, the subject's data will be reviewed by the blinded Endpoint Review Committee. Subjects not completing Day 29 or discharged to hospice or other end-of-life care prior to Day 29 with a death date unknown but completing Day 60 will be reviewed by the blinded Endpoint Review Committee to assess whether the Day 60 data impacts handling of the subject for the Day 29 timepoint. Other special cases may also be included for review by the blinded Endpoint Review Committee, as needed.

3.3.4. Clinical Status Ordinal Score at Specific Timepoints

The Primary Endpoint, Key Secondary Endpoint, and several other Secondary Endpoints rely on evaluation of the Clinical Status ordinal score at specific days. For these endpoints, the Study Visit Day is the timepoint of interest, not the actual study day (e.g., Study Visit Day 29 as opposed to study day 29). The Clinical Status Score collected at the Study Visit corresponding to the specific endpoint will be used for the outcome. Specifically, results from Study Visit Day 29 will be used for the Primary Endpoint and results from Study Visit Day 15 will be used for the Key Secondary Endpoint, with these and other Study Visit Days (3, 5, 8, 11, 22) used for other Secondary Endpoints. For analyses involving Clinical Status at specific timepoints, imputation of missing scores may be performed following the rules described in Section 6.5.

3.3.5. Progression to Clinical Status Category 6, 7, or 8 by Day 29

This Secondary Endpoint will be assessed similarly to Mechanical Ventilation-free survival (Section 3.3.2), but the event of interest is any report of a Clinical Status ordinal score in Category 8 (Death), Category 7 (invasive mechanical ventilation or ECMO), or Category 6 (non-invasive ventilation or high-flow oxygen device). This endpoint will only be assessed in those with actual baseline Clinical Status in Category 5 (hospitalized, requiring supplement oxygen).

3.3.6. Time to Death

For analysis of time to death, the time to death will be defined as the elapsed time (in days) from randomization to death. For the safety analysis, this will be elapsed time (in days) from the first dose of study treatment (baricitinib, dexamethasone, remdesivir, or placebo).

Any subjects that are lost to follow-up or terminated early prior to death will be censored at the day of their last observed assessment or last captured event (e.g. the end date of an adverse event). Subjects who complete follow-up will be censored at the earliest of their Study Visit Day 29 and (actual) Day 29. Deaths that occur after Day 29 will be censored at Day 29.

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

3.3.7. Recovery and Time to Recovery

A Secondary Endpoint measure requires the time to recovery assessed through Study Visit Day 29. Recovery will be defined as having a value of 1, 2, or 3 on the 8-point ordinal Clinical Status score. The time to recovery will be defined as the elapsed time (in days) from randomization to the earliest day at which a subject reaches recovery. Note that since clinical status assessments are recorded as defined in Section 4.3, the day that is being assessed (not necessarily the day the response is collected) will be used to determine the timing of events. For example, a subject with a score of 5 recorded on study days 1-3 and a score of 3 recorded on study day 4 will have a time to recovery equal to 3 days. It is also possible that a subject has a clinical status ordinal score > 3 reported for a particular day but was subsequently discharged on the same day. If a subject is discharged to a location other than hospice or another hospital the subject will be considered recovered at the time of discharge but may be reviewed by the Endpoint Review Committee, if other data suggests the subject may not be recovered (e.g., the subject is re-admitted). If a subject is discharged to hospice or another hospital, re-admitted, or is a special case where recovery handling may be unclear , the subject's data will be reviewed by the Endpoint Review Committee to make the determination of whether the subject should be considered recovered 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 and care), and any information regarding readmittance. Additional information may be solicited to assess recovery.

Any subjects that are lost to follow-up or terminated early prior to an observed recovery will be censored at the day of their last observed assessment. Subjects who complete follow-up but do not experience recovery will be censored at the day of their Study Visit Day 29. All deaths that occur on or before Study Visit Day 29 (and prior to any observed recovery) will be considered censored at Day 29. Note that we do not expect many subjects to worsen after discharge. However, we will evaluate whether any discharged subjects subsequently experience a worse clinical status and sensitivity analyses will be conducted accordingly. For these analyses, subjects who recover but are later re-admitted for COVID-19 will not be considered a recovery but will instead be censored at 28 days.

3.3.8. Time to Clinical Status Improvement

Several Secondary Endpoints involve evaluation of the time to improvement of at least one or two points on the clinical status 8-point ordinal scale. The time to improvement will be defined as the elapsed time (in days)

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

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

Any subjects that are lost to follow-up or terminated early prior to an observed improvement will be censored at the day of their last observed Clinical Status score. Subjects who complete follow-up but do not experience improvement will be censored at the day of their Study Visit Day 29. All deaths that occur on or before Study Visit Day 29 (and prior to any observed improvement) will be considered censored at Day 29.

3.3.9. Desirability of Outcome Ranking (DOOR)

The DOOR is based on categorization of the 8-point ordinal Clinical Status score, changes in the score, or combination with the occurrence (or absence) of SAEs. The DOOR category will be determined by the Clinical Status score at Baseline and at the Study Visit Day (15 and 29), and any SAEs that have occurred up to and including the respective Study Visit Day. Since this endpoint involving Clinical Status at specific timepoints, imputation of missing scores may be performed following the rules described in Section 6.5.

3.3.10. Days of Oxygen

Oxygen days will be defined as the number of days where the Clinical Status score is equal to 5, 6, or 7. The Post-Discharge Supplemental Oxygen CRF question 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. Individual subject of post-discharge oxygen use will be generated (Listing 28). The total number of days will be the sum of all reported days, regardless of whether the days occur consecutively or in disjoint intervals. See Section 6.5 for the plan for handling subjects who do not have data through Day 29 or die prior to Day 29.

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

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

3.3.12. Days of Invasive Mechanical Ventilation/ECMO

Invasive Mechanical Ventilator / ECMO days will be defined as the number of days where the Clinical Status score is equal to 7. 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. The total number of days will be the sum of all reported days, regardless of whether the days occur consecutively or in disjoint intervals. See Section 6.5 for the plan for handling subjects who do not have data through Day 29 or die prior to Day 29.

3.3.13. Days of 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.

3.3.14. Composite Endpoint of Death, SAEs, Severe AEs

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

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

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

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

ACTT-4 will evaluate the combination of baricitinib and remdesivir compared to dexamethasone and remdesivir. Subjects will be assessed daily while hospitalized. After the subjects are discharged from the hospital, they will have a study visit at Days 15, 22, and 29 (as applicable). For discharged subjects, it is preferred that the Day 15 and 29 visits are in person to obtain safety laboratory tests and OP swab, plasma (Day 29) and serum samples for secondary research as well as clinical outcome data. However, infection control or other restrictions may limit the ability of the subject to return to the clinic. In this case, these visits may be conducted by phone, and only clinical data will be obtained. The Day 22 visit does not have laboratory tests or collection of samples and is conducted by phone.

Additionally, subjects will be contacted by phone at 2 months (Day 60) to assess long term efficacy and safety outcomes as an exploratory outcome. A chart review/extraction of data through Day 60 may be done if the subject is not available for the phone contact.

4.2. Selection of Study Population

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

See Section 5.1 and 5.2 of Appendix D of the study protocol for the full list of inclusion and exclusion criteria.

4.2.1. Treatments Administered

Dosing of the medications does not need to occur at the same time. All subjects receive remdesivir as a 200 mg intravenous (IV) loading dose on Day 1, followed by a 100 mg once-daily IV maintenance dose for the duration of the hospitalization up to a 10-day total course. If subjects already received the loading dose prior to study enrollment, then start at 100 mg/day on Day 1. Any doses of remdesivir given prior to enrollment will be counted, so the total duration of remdesivir (i.e. pre-enrollment + on this trial) is 10 days (i.e., a maximum of 10 total infusions). Any doses of remdesivir were administered prior to study enrollment should be documented in Advantage eClinical as a concomitant medication given prior to Day 1. The duration of dosing may be adjusted by the site similar to what is described in the package insert and based on a subject's clinical course and ultimate disease severity.

For the baricitinib component, subjects receive either active product or placebo as follows:

- Baricitinib will be administered as a 4 mg orally (po) (two 2mg tablets) or dissolved for NG tube, daily for the duration of the hospitalization up to a 14-day total course.
- A placebo will be given as two tablets po or dissolved for NG tube, daily for the duration of the hospitalization up to a 14-day total course.
    - Any pre-study dexamethasone (max 1 dose per inclusion criteria) is not counted towards the 10-day course.

For dexamethasone component, subjects receive either active product or placebo as follows:

- Dexamethasone administered as a 6 mg slow IV push over 3 to 5 minutes daily for the duration of the hospitalization up to a 10-day total course.

- A placebo will be given as an equal volume normal saline, as a slow IV push daily for the duration of the hospitalization up to a 10-day total course.
- If site local standards use other means of administration (such as IV infusion), these may be used for both active and placebo after approval of the sponsor.
- Any pre-study dexamethasone (max 1 dose per inclusion criteria) is not counted towards the 10 day course.

Duration of therapy:

- IV remdesivir – up to 10 days while hospitalized (i.e., maximum of 10 total infusions pre-enrollment and during study).
- Oral baricitinib (or oral placebo) – 14 days while hospitalized (i.e., maximum of 14 total doses).
- IV dexamethasone (or IV placebo) – 10 days while hospitalized (i.e., maximum of 10 total doses).
- All study medications stop on discharge from hospital.
    - Of note, if a subject is retained in the hospital for non-COVID-19 related issues and no longer requires supplemental oxygen and ongoing medical care (i.e., ordinal scale category 3), the PI may decide to discontinue all medications.
- If readmitted after discharge, see Appendix D Section 7.4 of the study protocol.

4.2.2. Identity of Investigational Product(s)

See Section 6.1.1 of Appendix D of the study protocol.

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

Randomization will be stratified by:

- Site
- Clinical Status at enrollment (by ordinal scale)
    - Category 6: Hospitalized, on non-invasive ventilation or high flow oxygen devices, OR
    - Category 5: Hospitalized, requiring supplemental oxygen

4.2.4. Selection of Doses in the Study

The dose of remdesivir used in this study is the same dose used in previous ACTT studies, and is the US FDA approved dosage. 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. This study will use the same dose and duration of baricitinib that was evaluated in ACTT-2. The 4 mg daily dose of baricitinib was originally selected for use in this population of adults hospitalized with COVID-19 based on clinical data showing an inhibitory effect on cytokine signaling. This study will use the same dose and duration of dexamethasone that was evaluated in the RECOVERY trial, the largest and most influential study of dexamethasone in COVID-19.

4.2.5. Selection and Timing of Dose for Each Subject

See Sections 6.1.2 through 6.1.5 of Appendix D of the study protocol.

4.2.6. Blinding

As both arms are receiving remdesivir, the remdesivir product is not blinded and study infusions can be labeled accordingly. The baricitinib/placebo component is blinded. Baricitinib and placebo tablets are identical in appearance. The dexamethasone/placebo IV component is blinded. Dexamethasone and intravenous placebo are identical in appearance.

Unblinding of the study will occur after all subjects enrolled have reached the end of study, these visits are monitored, and data is cleaned or if the DSMB recommends unblinding. Data through Day 29 will be locked prior to the completion and lock of Day 60 data. DMID and the SDCC will be unblinded after the Day 29 database lock. Clinical sites will not be unblinded to subject-level treatment assignments until after the Day 60 database lock.

If a subject's clinical status worsens to require mechanical ventilation (ordinal 7), the treating clinician may request unblinding in order to use the prior treatment assignment to inform future treatment. See protocol Appendix D Section 6.3.2.2.

If a Serious Adverse Event occurs, that is thought to be related to the study drug, and the treating clinician believes that knowledge of the treatment arm may change the therapy provided to the patient, the individual subject can be unblinded. If unblinded for SAE, the investigator may decide to have the blinded study product and/or remdesivir infusions discontinued based on the adverse event that led to unblinding and the benefit-risk analysis. See protocol Appendix D Section 6.3.2.3.

4.2.7. Prior and Concomitant Therapy

See Section 6.5.1 of Appendix D of the study protocol for permitted concomitant therapy and procedures. See Section 6.5.2 of Appendix D of the study protocol for prohibited concomitant therapies.

4.2.8. Treatment Compliance

See Section 6.1.4 of Appendix D of the study protocol for details on dose modifications.

Each dose of study product will be administered by a member of the clinical research team who is qualified and licensed to administer the study product. Administration date and time will be entered into the case report form (CRF).

4.3. Efficacy and Safety Variables

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

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

where the clinical status scale is defined as follows:

Category 8: Death;

Category 7: Hospitalized, on invasive mechanical ventilation or ECMO;

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

Category 5: Hospitalized, requiring supplemental oxygen;

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

Category 3: Hospitalized, not requiring supplemental oxygen - no longer requiring ongoing medical care. This would include those kept in hospital for quarantine/infection control, awaiting bed in rehabilitation facility or homecare, etc.;

Category 2: Not hospitalized, but has new or increased limitation on activities and/or new or increased requirement for home oxygen over baseline, pre-COVID-19 status;

Category 1: Not hospitalized, patient is back to their baseline, pre-COVID-19 status, that is, no new or increased limitations on activities and no new or increased oxygen use compared with baseline.

A modified version of the ordinal scale will be used in sensitivity analyses of the Key Secondary and Other Secondary Endpoints of time-to-recovery and time-to-improvement.

The "Modified Recovery" ordinal scale combines Category 1 and 3 of the original Clinical Status scale and is defined as follows:

Category 8: Death;

Category 7: Hospitalized, on invasive mechanical ventilation or ECMO;

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

Category 5: Hospitalized, requiring supplemental oxygen;

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

Category 3: Not hospitalized, but new or increased limitation on activities and/or requiring new or increased home oxygen;

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

Desirability of outcomes response (DOOR) is an ordinal scale combining current clinical status with SAEs. SAE may be related or unrelated to study product. Any SAE occurring after study product administration through Day 15 (or through Day 29) will be counted:

1- Recovered (Ordinal Score Category 1,2,3)

2- Improved by at least 1 Ordinal Score from baseline & no SAE

3- Improved by at least 1 Ordinal Score Category from baseline & SAE

4- No change in Ordinal Score Category from baseline & no SAE

5- No change in Ordinal Score Category from baseline & SAE

6- Worsened by at least 1 Ordinal Score Category from baseline

7- Death (Ordinal Score Category 8)

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

Safety will be assessed by the following:

- Cumulative incidence of serious adverse events (SAEs) through 28 days of follow-up.
- Cumulative incidence of Grade 3 and 4 treatment-emergent AEs.
- Discontinuation or temporary suspension of study product administration (for any reason).
- Changes in white cell count, hemoglobin, platelets, creatinine, total bilirubin, ALT, AST, and INR, d-dimer, C-reactive protein over time. Note D-dimer and CRP are not graded.
- Time to the Composite Endpoint of the first of death, SAE, or Severe AE from the day of first dose of study treatment to the earliest date of any of these events.

Clinical labs will be drawn on Days 1, 3, 5, 8, 11 and on Day 15 and 29 if the subject is able to return to the clinic or is still hospitalized. CRP values from sites using a high-sensitivity assay will be excluded from all CRP summaries and any analyses that use CRP values.

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

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

The schedule of study procedures is provided in Section 1.2 of Appendix D of the study protocol.

5. SAMPLE SIZE CONSIDERATIONS

Sample Size for Primary Analysis

The primary hypothesis will be a test of the difference in proportions surviving without requiring invasive mechanical ventilation between the two treatment arms by Day 29. Estimating the expected treatment effect of baricitinib relative to dexamethasone is difficult given the differences between the ACTT-2 and RECOVERY studies as discussed above. In Table 1 the first row of treatment effects is based on estimates from the ACTT-2 and RECOVERY results amongst the cohort that most closely resembles the ACTT-4 target population (those in ordinal 5 and 6). In the second row, the relative findings were changed to assume a gradual improvement in standard of care. This corresponds to a sample size of 1382 subjects. Sample size calculations were based on an exact unconditional score test of proportions using StatXact v11.1.0. Assuming 8% lost to follow-up, the sample size is planned to be approximately 1500 subjects.

The remaining lines demonstrate the power of the proposed sample size. There is good power of this trial for multiple scenarios unless the proportions surviving without invasive mechanical ventilation is much higher than anticipated (thought to be unlikely) or the difference in the proportions is smaller than anticipated (possible, but difficult to anticipate given the data available).

The protocol defined primary analyses were to be based on Kaplan-Meier estimates of the proportion of patients surviving without mechanical ventilation by Day 29 using a large sample normal approximation with Greenwood's variance formula. Accordingly, power for the final analysis is assumed to be equal or slightly higher than the power for the exact score as seen below.

Table 1: Sample Size Estimates and Study Power

	Total Sample Size	Proportion Dex Arm Surviving Through Day 29 Without Mechanical Ventilation	Proportion Bari Arm Surviving Through Day 29 Without Mechanical Ventilation	Power (unconditional exact score)	Power (KM + Greenwood)
- Baricitinib from ACTT-2 (OS 5 and 6) - Dexamethasone relative efficacy (only those on oxygen) from RECOVERY applied to ACTT-2 placebo arm	1342	0.814	0.87	80.9%	80.6%
Estimate of the above proportion applied to current outcomes given gradual improvement in care	**1382**	0.85	0.9	80%	80.5%
Other scenarios showing study power for the sample size of 1382	1382	0.9	0.95	94.5%	94.9%
	1382	0.9	0.925	37.0%	37.5%
	1382	0.85	0.925	99.4%	99.4%
	1382	0.8	0.875	96.6%	96.6%
	1382	0.8	0.85	68.2%	68.9%
Note: two-sided type I error rate 5%; Exact unconditional score test of proportions.					

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

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

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

Confidence intervals will be generated; for the primary analysis, the confidence level will take into account the group-sequential design of the trial (see Section 6.6 and Section 8.1) whereas 95% confidence intervals will be generated for secondary and exploratory outcomes. Proportions will be estimated using the Kaplan-Meier Day 29 survival estimate with Wald-type confidence intervals assuming large-sample normality with standard errors estimated using Greenwood's formula for variance. For hazard ratio and odds ratio estimates, Wald confidence intervals will also be used. For other efficacy outcomes (e.g. proportions), Wilson or Score confidence intervals will be used. For safety outcomes, exact (e.g. Clopper-Pearson) confidence intervals will be used.

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

For the final comparison of Day 29 mechanical ventilation free survival, the following SAS pseudocode will be used to obtain Kaplan-Meier survival estimates, standard errors and confidence intervals, for each treatment within strata. Survival estimates and standard errors will be used to calculate the test statistic and compared to a standard normal distribution as in Section 8.1.1.

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

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

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

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

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

```
proc logistic data=dataset
      plots(only)=effect(x=ResponseVariable sliceby= actualbaselinestrata
      *TreatmentVariable individual connect);
   class actualbaselinestrata(param=ref ref=category5)
         TreatmentVariable(param=ref ref=RemdesivirLabel);
   model ResponseVariable = TreatmentVariable StrataVariable;
   oddsratio TreatmentVariable;
   ods output OddsRatiosWald = ORest;
run;
```

6.2. Timing of Analyses

6.2.1. Interim Analyses

A DSMB will monitor ongoing results to ensure patient well-being and safety as well as study integrity. The DSMB will be asked to recommend early termination or modification only when there is clear and substantial evidence of a treatment difference. More details about the interim analyses are described in Section 6.6.1 and Section 6.6.3 below. The summaries to be generated for the interim analysis are provided in the separate DSMB shell report.

The separate Futility Analysis Plan describes the methods for the Futility Analysis conducted in April 2021.

6.2.2. Final Analyses

The final analyses of all outcomes and planned summaries/listings will be performed on the final full locked database through Day 29 and provided in the final report. If substantial Day 60 data is available, results from Day 60 may also be included in the final report and this SAP amended appropriately. In addition, the final report may be amended to include the totality of the Day 60 data when locked.

6.3. Analysis Populations

Summaries and analysis of safety data will be presented for the As Treated Population. Summaries and analysis of efficacy data will be presented for the modified intention-to-treat (mITT) population and As Treated population.

6.3.1. Intention-to-Treat (ITT) Population

The intention-to-treat (ITT) population includes all subjects who were randomized. ITT subjects will be classified by their randomized treatment assignment and randomized disease severity stratum (i.e., the stratum to which the subject randomized at enrollment, which is not necessarily equivalent to their baseline ordinal score if the subject was mis-stratified).

6.3.2. Modified Intention-to-Treat (mITT) and As Treated Populations

The modified intention-to-treat (mITT) population includes all subjects who were randomized. mITT subjects will be classified by their randomized treatment assignment and actual baseline ordinal score ordinal stratum (i.e., the stratum corresponding to their baseline ordinal score, not necessarily the stratum within which the subject was randomized at enrollment).

The As Treated population includes all randomized subjects who received the study product, even if only one dose was administered.

For As Treated analyses of efficacy outcomes, subjects will be classified by their actual treatment assignment and their actual baseline ordinal score, unless otherwise specified in the table or figure shell. Note that if no subjects are administered the incorrect treatment and all subjects receive at least one dose of baricitinib/placebo, dexamethasone/placebo, the As Treated efficacy analysis will not be performed as they will be identical to the mITT analyses.

For As Treated analyses of safety outcomes, concomitant medications, and medical history, subjects will be classified by their actual treatment assignment and actual baseline ordinal score stratum.

6.4. Covariates and Subgroups

As additional secondary analysis, the primary efficacy outcome will be summarized within each of the baseline actual ordinal score subgroups (5 and 6). Analysis of all secondary outcomes will be performed in subgroups based on the baseline actual ordinal score.

Further subgroup analyses for the primary and key secondary efficacy outcomes will evaluate the treatment effect within the following subgroups:

- Prior Corticosteroid use
  - Yes / No
  - Dexamethasone on the day of randomization / not
  - Number of on-study dexamethasone/placebo infusion (9 vs 10). Some subjects who received dexamethasone on the day of randomization may skip their first post-randomization, on-study dexamethasone / placebo infusion and therefore receive only 9, rather than the expected 10, on-study infusions.
- Geographic region
  - US sites; Non-US sites
  - North American sites; Asian sites; European sites
- Duration of symptoms prior to randomization
  - Quartiles
  - <= 10 days; > 10 days
  - <= Median; > Median
- Race (White; Black/African American; Asian; Other)
- Comorbidities
  - None; Any
  - None, One, Two or more
  - Obese; Non-Obese
- Age (<40; 40-64; 65 and older)
- Sex (Female; Male)

- Randomized strata
  - 5 or 6 (separately) on ordinal scale used for randomization

  Note: separate analyses for randomized/actual severity will only be performed if at least one subject is erroneously randomized into the incorrect baseline ordinal score stratum.

Additionally, analyses of all remaining secondary efficacy outcomes and the time to death by Day 15/29 outcomes will evaluate the treatment effect within the following subgroups (among subjects enrolled with baseline ordinal score of 5 or 6 only):

- Duration of symptoms prior to randomization (<= Median; > Median)
- Severity of disease
  - Randomization stratification: 5 or 6 (separately) on ordinal scale.
  - Actual ordinal score at baseline: 5 or 6 (separately) on ordinal scale.

  Note: separate analyses for randomized/actual severity will only be performed if at least one subject is erroneously randomized into the incorrect baseline ordinal score stratum.

There will also be a sensitivity analysis of the primary, secondary, and mortality outcomes to evaluate the effect of concomitant therapy including experimental treatment and off-label use of marketed medications that are intended as treatment for COVID-19 and are given to patient prior to and during the study. A blinded review of the concomitant medication data will be performed by the medical monitor to identify medications that fall into any of the following categories of "Medications of Interest":

- Vaccine for SARS-CoV-2 (Pfizer, Moderna, or other) including 1 or 2 doses received
- Antivirals
  - Protease inhibitors
  - Polymerase inhibitors
- Other Potential Treatments for COVID-19
  - Aplidin® (plitidepsin)
  - Colchicine (Colcrys)
  - Monoclonal antibodies targeting the spike protein of SARS-CoV-2 including casirivimab, imdevimab and bamlanivimab
  - Ivermectin (stromectol, Soolantra, Sklice)
- Corticosteroids
- Renin-angiotensin system (RAS) Inhibitors and HMG-CoA reductase inhibitors (statins)
- Other anti-inflammatory drugs
  - Monoclonal Antibodies Targeting Cytokines
  - Other Biologic Therapies

Summaries of subjects who report use of the categories and subcategories of therapies/treatments will be provided. Note that after the blinded review of the medications, additional categories/sub-categories may be defined and/or categories/sub-categories may be combined.

In addition, the sensitivity analyses will consider the following categories (individually):

- Any Medication of Interest
- Vaccines to SARs-CoV-2
- Antivirals
- COVID-19 treatments
- Monoclonal antibody treatments for COVID-19
- Corticosteroids
- RAS Inhibitors and HMG-CoA reductase inhibitors (statins)
- Other Anti-Inflammatory Drugs

Three initiation and duration groups will be constructed for each of the above categories:

1. Prior and During: Subjects taking medication of interest before randomization and during study (on or after Day 1).
2. Prior Only: Subjects taking medications of interest prior to randomization but stopping prior to randomization.
3. During Only: Subjects initiating mediations of interest during the study (on or after Day 1).

For the analysis of mechanical ventilation free survival, subjects will be censored at the time of medication/therapy initiation. For the analysis of the key secondary outcome, if a subject reports use of any of the medications/therapies prior to their Day 15 assessment, then the subject's last clinical status score prior to medication/therapy use will be used as their Day 15 outcome. For the mortality analyses, subjects will be censored at the time of medication/therapy initiation. For the analysis of the proportion of subjects that do not progress to Clinical Status Ordinal Score of 6, 7, or 8 by Day 29, subjects will be censored at the time of medication / therapy initiation. For the recovery analyses, subjects will be censored at the time of medication/therapy initiation. If a subject recovered prior to use of any of the medications/therapies, then the subject will still be counted as a recovery in the sensitivity analysis.

The effect of on-study treatment on select efficacy outcomes will also be explored among subjects who reported use of HMG-CoA reductase inhibitors (statins), angiotensin receptor blockers (ARBs), or angiotensin converting enzyme inhibitors (ACEIs) via subgroup analyses.

Lastly, the effect of treatment on the primary and key secondary efficacy outcomes will be explored via regression modeling controlling for age, duration of symptoms prior to randomization, baseline d-dimer, and baseline CRP values as continuous covariates.

6.5. Missing Data

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

For time to event outcomes, subjects who are lost to follow-up or terminate the study prior to Day 29 and prior to observing/experiencing the event will be censored at the time of their last observed assessment. Other rules for censoring are listed for the specific endpoint in Section 3.3.

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

For the analyses of the secondary outcomes that involve clinical score (i.e. the key secondary outcome and time to improvement), if a subject is discharged from the hospital (but not to hospice or other end-of-life care) without a previously or concurrently reported clinical score of 1 or 2, then their clinical score at the time of discharge will be imputed as 2, which is the highest value for a non-hospitalized subject. If a subject terminates early from the study while they are hospitalized or completes the study while still hospitalized, the last observed clinical score assessment will be used as their final assessment.

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

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

- Days of Non-Invasive Ventilation/High-Flow Oxygen:
  - If the subject's clinical status scale is 6 at the last observed assessment, then the subject will be considered to be on non-invasive ventilation/high-flow oxygen through Day 29. The endpoint will be total days when assessments are available plus all imputed days following the last observed assessment.
  - If the subject is not on non-invasive ventilation/high-flow oxygen at the last observed assessment, then the subject will be considered to not be on non- invasive ventilation/high-flow oxygen for the remainder of follow-up. Thus, no additional imputed days will be added to the number of days recorded on available assessments.
- Days of Ventilation/ECMO:
  - If the subject's clinical status scale is 7 at the last observed assessment, then the subject will be considered to be on ventilation/ECMO through Day 29. The endpoint will be total days when assessments are available plus all imputed days following the last observed assessment.
  - If the subject is not on ventilation/ECMO at the last observed assessment, then the subject will be considered to not be on ventilation/ECMO through Day 29. Thus, no additional imputed days will be added to the number of days recorded on available assessments.
- Days of Oxygen:
  - If the subject's clinical status score is 5, 6, or 7 at the last observed assessment, then the subject will be considered to be on oxygen through Day 29. The endpoint will be total days when assessments are available plus all imputed days following the last observed assessment.
  - If the subject is not on oxygen at the last observed assessment, then the subject will be considered to not be on oxygen through Day 29. Thus, no additional imputed days will be added to the number of days recorded on available assessments.
- Days of Hospitalization

- If the subject is discharged and no further hospitalization data are available, then the subject will be assumed to not have been readmitted. Thus, no additional imputed days will be added to the number of days recorded on available assessments. If a subject dies while hospitalized, the number of days of hospitalization will be imputed as 28 days.

- Lab Efficacy (d-dimer and CRP)
  - 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 lost to follow-up, 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.

6.6. Interim Analyses and Data Monitoring

6.6.1. Planned Interim and Early Analyses

A 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.

6.6.2. Interim Safety Review

Safety analyses will evaluate Grade 3 and 4 AE and SAEs by treatment arm. Safety monitoring will be ongoing with the DSMB reviewing safety data approximately every one to two weeks during the study. The unblinded statistical team will prepare these reports for review by the DSMB.

6.6.3. Interim Efficacy Review

The time of the interim efficacy analysis for ACTT-4 will be assessed by enrollment 1.5 months after the first enrollment:

- If the study reaches or exceeds 1/3 of total enrollment within 1.5 months (assumes slightly slower enrollment at the beginning), no interim efficacy analysis will be performed.
- If the study does not reach 1/3 of total enrollment within 1.5 months, an interim analysis will occur after the first third of enrolled subjects have reached Day 29.

If an interim efficacy analysis is performed, the Lan-DeMets spending function analog of the O'Brien-Fleming boundaries will be used to monitor the primary endpoint as a guide for the DSMB with an overall two-sided type-I error rate of 0.05.

Specifically, two one sided boundaries are constructed at level 0.025 using the spending function

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

where Φ is the standard normal distribution function. Lan-DeMets software from the University of Wisconsin, now available in the R package `ldbounds', will be used to calculate boundaries. The planned boundaries at 33% and 100% of information on the z-scale are +/- 3.7307 (nominal p = 0.00019153) and 1.9605 (nominal p = 0.049937).

All available data at the time of lock will be included in the Interim Efficacy data. Subjects who are on-study but have not yet completed the Day 29 study visit will also be included but will be censored at their last assessment unless they have progressed to mechanical ventilation or died.

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

The unblinded statistical team will prepare these closed session 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.

6.7. Multicenter Studies

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

A sensitivity analysis of the primary outcome will be performed to assess the impact of individual sites on the observed treatment effect. Letting *M* be the total number of sites, the primary analysis will be repeated by excluding a single clinical site and performing the analyses on the remaining *M-1* sites. This process will be repeated so that estimates are generated for each of the *M-1* subset datasets. Presentations from these analyses are described in Section 8.2.1.

6.8. Multiple Comparisons/Multiplicity

A fixed sequence testing scheme will control the overall family-wise Type I error rate at a two-sided α level of 0.05. If the primary hypothesis is rejected at two-sided $\alpha < 0.05$, hypothesis testing will proceed to four key secondary endpoints. Hypothesis testing will follow the fixed ordering below (Figure 1):

Figure 1: Elements of the fixed-sequence hierarchical testing procedure

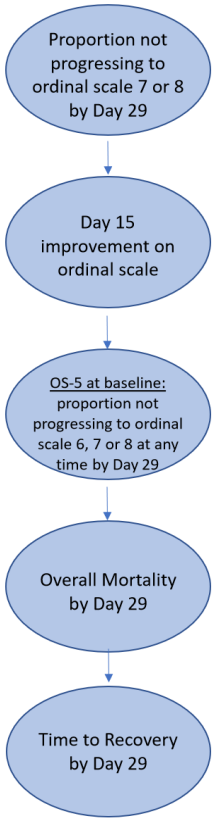
1) Mechanical Ventilation-Free Survival by Day 29 (i.e., Proportion not progressing to ordinal scale 7 or 8)

2) Day 15 Clinical Status Ordinal Score;

3) Proportion not progressing to ordinal scale 6, 7 or 8 (amongst actual baseline Clinical Status ordinal scale 5 only);

4) Overall mortality (Day 29); and

5) Time to recovery (Day 29).



Hypothesis testing will continue at the next endpoint with $\alpha = 0.05$ only if the previous hypothesis is rejected at $\alpha=0.05$. This method of carrying forward the α -level from the previous test is described in the FDA guidance on Multiple Endpoints in Clinical Trials [https://www.fda.gov/regulatory-information/search-fda-guidance-documents/multiple-endpoints-clinical-trials-guidance-industry]. See Section 8.1.2 for details on the sequence of hierarchical analyses.

There is no planned multiplicity adjustment for the evaluation of safety (Section 9) or additional sensitivity or additional secondary efficacy (Section 8.2) or exploratory (Section 8.3) analyses.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

A summary of the reasons that subjects were screened but not randomized will be tabulated (Table 2).

The composition of analysis populations, including reasons for subject exclusion will be summarized by treatment group and actual baseline ordinal score (Table 3). A subject listing of subjects excluded from the As Treated Population will be generated (Listing 1).

The disposition of subjects will be tabulated by treatment group and actual baseline ordinal score (Table 4). Study milestones included in the table will include, but not limited to: the total number of subjects that were randomized, completed expected blood draws, completed Study Visit Day 15, completed Study Visit Day 22, and completed Study Visit Day 29. For the calculation of percentages, subjects who die will not be included in the denominators for visits/assessments beyond their death. Subject status at study termination will be summarized by treatment group and baseline ordinal score (Table 5).

Treatment exposure will be summarized by treatment group (Table 6, Table 7, and Table 8). Summaries of prior remdesivir treatment, prior remdesivir, and prior dexamethasone treatment by treatment group and actual baseline ordinal score will also be provided (Table 9, Table 10, and Table 11).

A flowchart showing the disposition of study subjects, adapted from the Consort Statement [1] will be generated (Figure 2). 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,). The number of subjects that terminated early by hospitalization status at the time of the last ordinal score collection will be summarized graphically (Figure 3).

A listing of subjects who discontinued dosing or terminated study follow-up and the reason will be generated (Listing 2). A listing of subjects who received incorrect treatment and a listing of subjects who were randomized to the incorrect stratum will also be generated (Listing 5 and Listing 6).

The disposition of subjects at Day 60 will be tabulated by treatment group and actual baseline ordinal score (Table 12).

7.2. Protocol Deviations

Subject-specific protocol deviations will be summarized by the reason for the deviation, the deviation category, treatment group, and actual baseline ordinal score (Table 13). A summary of major deviations will also be generated (Table 14). All subject-specific protocol deviations and non-subject specific protocol deviations will be included in listings (Listing 3 and Listing 4).

8. EFFICACY EVALUATION

8.1. Primary Efficacy Analysis

8.1.1. Primary Analysis of Mechanical Ventilation-Free Survival

The primary efficacy analysis will be performed in the mITT population and is a test of superiority of the proportion of participants with invasive mechanical ventilation free survival, between the two treatment groups at Day 29 (Table 15). The test statistic will be a large sample test of the difference in Kaplan-Meier estimates of the 28-day probability of mechanical ventilation free survival with a two-sided type I error rate of 0.05. The test of difference will assume asymptotic normality and use Greenwood's variance formula. The primary analysis will utilize a test statistic adjusting by actual baseline Clinical Status ordinal score strata [2] (Klein 2007) and be based on the weighted complementary log-log transformation of the Kaplan-Meier estimator. The two primary baseline Clinical Status strata will be patients with baseline ordinal score 5 or baseline ordinal score 6.

The primary analysis will utilize a test statistic adjusting by actual baseline ordinal score ordinal score strata (Klein 2007) and be based on the complementary log-log transformation of the Kaplan-Meier estimator.

The test statistic to be used is, as in Klein 2007:

$$X^2_{\text{STRAT}} = \frac{\left(\sum_{s=1}^{3} \hat{w}_s(\log\left(-\log\left(\hat{S}_{1s}(t)\right)\right) - \log\left(-\log\left(\hat{S}_{2s}(t)\right)\right))\right)^2}{\sum_{s=1}^{3} \hat{w}_s^2(\hat{V}\left(\log\left(-\log\left(\hat{S}_{1s}(t)\right)\right)\right) + \hat{V}\left(\log\left(-\log\left(\hat{S}_{2s}(t)\right)\right)\right))}$$

Where $\hat{V}(\cdot)$ is the estimated variance of the transformed survival function which is equal to $\hat{\sigma}_{ks}(t)^2 / \left(\log\left(\hat{S}_{is}(t)\right)\right)^2$ for the treatment group k and strata s and where $\hat{\sigma}_{ks}(t)^2$ is estimated using Greenwood's formula:

$$\hat{\sigma}_{ks}(t)^2 = \sum_{t_{ksi} \le t} \frac{d_{ksi}}{Y_{ksi}(Y_{ksi} - d_{ksi})}$$

And $k = 1, 2$ is the treatment group, $s = 1, 2$ is the actual baseline Clinical Status strata, $\hat{S}_{ks}(t)$ is the estimated survival at time $t = 28$ and $\hat{w}_s$ is inverse variance of the difference divided by the sum of inverse variances of the difference.

This test-statistic follows a Chi-square distribution with 1-degree of freedom or, alternatively, the square-root follows a standard-normal distribution.

As noted in Section 6.6.3, to maintain an overall two-sided type-I error rate of 0.05, the Lan-DeMets spending function analog of the O'Brien-Fleming boundary will be used to derive the cumulative error spending and boundaries for the interim analysis.

For the final analysis, square-root of the test statistic and p-value from a standard normal distribution function will be calculated using the pseudocode and formulae provided in Section 6.1 and compared to the final boundary and nominal p-value as determined using the 'ldlbound' package listed in Section 6.6.3.

If the trial is stopped at the interim analysis, then to derive the p-value and confidence intervals for the early and final analysis sets, stage-wise ordering of the sample space will be used [3]. The resulting p-value, proportions, and confidence interval will be presented in the final report.

A graphical hierarchical design will be used to control the study-wide alpha as described in Section 6.8. This will not change the construction of p-values or their interpretation for the primary analysis, but will influence secondary analyses listed in Section 8.1.2.

Kaplan-Meier curves (Figure 4) and p-values with estimates of mechanical ventilation-free survival at 28 days will be calculated and accompanied by confidence intervals adjusted to be consistent with the nominal alpha level at the interim or final analysis and constructed using the complementary log-log transformation.

8.1.2. Hierarchical Sequence of Secondary Endpoints Analyses

Analyses described in this section will be subject to the fixed-sequence hierarchical testing procedure described in Section 6.8. Any reference to p-values in this section is conditional on preceding hypothesis tests in the hierarchy.

If a superior test fails to reject the null hypothesis, the analyses will still be performed to provide estimated effects with confidence intervals for relevant statistics and associated confidence-interval by-arm, but p-values will not be generated. Confidence intervals for all analyses of secondary endpoints, will be 95% confidence intervals.

8.1.2.1. Clinical Status Ordinal Scale at Day 15

In the mITT population, the distribution of the 8-point Clinical Status ordinal score at Study Visit Day 15 (not necessarily actual study day 15), will be analyzed using a proportional odds model with treatment arm and actual baseline ordinal score (baseline ordinal score 5 or baseline ordinal score 6) as covariates. The treatment odds ratio estimated from the model will be presented along with the p-value, (Table 21). This analysis will be repeated for the As Treated population (Table 22). The Study Visit Day 15 clinical status score will be depicted graphically using shifted bar plots; the outcomes will be presented by actual baseline ordinal score and treatment group (Figure 13).

8.1.2.2. Proportion of Subjects Not Progressing to Clinical Status 6, 7, or 8 by Day 29

In the mITT population and among only those with an actual baseline ordinal score of 5, the proportion of subjects not progressing to ordinal score 6, 7, or 8 by Day 29 (see Section 3.3.4) will be analyzed using the same modeling approach as the primary outcome and described in Section 8.1.1. Kaplan-Meier curves (Figure 31) and p-values with estimates of proportions at the Day 29 study visit will be calculated and accompanied by confidence intervals (Table 23).

8.1.2.3. Mortality by Day 29

Mortality through Day 29 will be analyzed as a time to event endpoint (see Section 3.3.5). A table will present median time to event along with 95% confidence intervals overall for each treatment arm along with the hazard ratio estimate and log rank p-values. Differences in time-to-event endpoints by treatment will be summarized with Kaplan-Meier curves (Figure 27).

8.1.2.4. Time to Recovery

In the mITT population, the time to recovery, as defined in Section 3.3, will be analyzed using a stratified log rank test to compare treatment to control through Day 29. Stratification is based on actual baseline Status ordinal score (ordinal score 5, ordinal score 6). As noted in Section 3.3, all deaths within 29 days will be considered censored at Day 29 with respect to time to recovery. Conceptually, a death corresponds to an

infinite time to recovery, but censoring at any time greater than or equal to Day 29 gives the same answer as censoring at Day 29; both correspond to giving deaths the worst rank.

The treatment hazard ratio estimate and confidence interval and p-value from the stratified log rank test will be presented (Table 28). The median time to event and 95% confidence intervals will be summarized by treatment group and actual baseline Clinical Status ordinal score. Kaplan-Meier curves will also be generated by treatment arm (Figure 15, Figure 16, Figure 17).

8.2. Additional Secondary Efficacy and Sensitivity Analyses

This section describes the planned sensitivity analyses for the Primary Efficacy analysis and for the secondary efficacy outcome measures that will be executed outside of the hierarchical testing procedure governing the study-wide type 1 error described in the preceding section. Results described here are considered supportive and corroborative to the primary analysis from Section 8.1.

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

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

8.2.1. Sensitivity and Corroborative Analyses of the Primary Endpoint

The primary analysis will be repeated in the As Treated analysis population and in the ITT analysis population. The tabular and graphical summaries described in the previous section will be replicated for this As Treated analysis (Figure 5) and by baseline ordinal score (Figure 6 and Figure 7).

Sensitivity analyses will be performed using Cox proportional hazards models to estimate the hazard ratio or progression to mechanical-ventilation or death (Table 16). A Cox model will be fit with binary indicators for treatment group and actual baseline Clinical Status ordinal score (5 or 6) as well as a treatment * actual baseline Clinical Status score interaction terms. The models will be fit to the mITT analysis population. The treatment group hazard ratios and CIs will be reported for both sets of models and the interaction term p-value will be reported for the interaction models. The tabular summary will also include results from an analysis of time to death or mechanical ventilation controlling for age and duration of symptoms as continuous covariates and baseline d-dimer and CRP values as continuous covariates.

The primary analysis will also be repeated using the other subgroups defined in Section 6.4 in place of actual baseline Clinical Status. Each subgroup will be considered separately, and the tabular and graphical summaries described in the previous section will be replicated for each subgroup. A forest plot (Figure 8, Figure 9, Figure 10, Figure 11) will be generated to display the overall treatment hazard ratio estimate and CI from each of the within-subgroup analyses (Table 17).

As noted in Section 6.4, analyses that take into account concomitant medication will be performed (Table 18 and Table 19).

In addition, a forest plot will be generated for the “leave one out” sensitivity analyses described in Section 6.7 (Figure 12); estimated proportions and CIs will be provided for each subgroup that leaves a single site out.

Two corroborative summaries will also be generated. A summary of the number and percentage of subjects in each treatment group who:

- recovered (and are alive),
- did not recover and did not require mechanical ventilation or ECMO (and are alive),
- did not recover and required mechanical ventilation or ECMO (and are alive), and
- dead by Day 29.

The summary will also include the numbers and percentages, grouping deaths and ventilation required together (Table 20). The summaries will also be provided by the duration of symptoms categorizations specified in Section 6.4.

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

8.2.2. Additional Analyses of Clinical Status Ordinal Scale at Day 15

Analysis of the key secondary outcome measure, the distribution of the Clinical Status 8-point ordinal score at Study Visit Day 15 will be repeated in the subgroups defined in Section 6.4 (Table 21).

In addition to the subgroup analyses, the main analysis will be repeated including a treatment * baseline ordinal score interaction term, where the interaction term p-value will be reported for the interaction model (Table 21).

8.2.3. Additional Analyses of Failure to Progress to Clinical Status 6, 7, or 8

Additional analyses as described for the mechanical ventilation free survival (Section 8.2.1) will be performed (Table 24, Table 25, Table 26, and Table 27).

8.2.4. Additional Analyses of Mortality

Analyses of mortality will be performed in the mITT and the As Treated analysis populations and at Day 15 (Table 67 and Table 68). As a supplemental analysis, a Cox model will be fit with binary indicators for treatment group and actual baseline ordinal score as well as a treatment * actual baseline ordinal score interaction term. The model will be fit in the mITT and As Treated analysis populations (Table 74). The treatment group hazard ratios and CIs and the interaction term p-value will be reported. Finally, the results of the subgroup and sensitivity time-to event analyses described in Section 6.4 will be presented in a table. A restricted mean survival time analysis of mortality will be performed as an exploratory analysis. The restricted mean mortality time estimates will be provided for each treatment group and randomized 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 75).

8.2.5. Additional Analyses of Time-to-Recovery

The analysis of Time-to-Recovery will be repeated in the mITT population but including only subjects with actual baseline Clinical Status scores in ordinal score 5 or 6 (excluding those with any other baseline score) and in the As-Treated population. The analysis will also be repeated using the Modified Recovery ordinal scale described in Section 4.3 (Table 29).

Sensitivity analyses will be performed using Cox proportional hazards models to estimate the hazard ratio (Table 29). First, a mITT analysis will be performed in which subjects who die prior to recovering are treated as experiencing a competing risk in the Fine-Gray proportional hazards regression model. Second, a Cox

model will be fit with binary indicators for treatment group and baseline ordinal score (5 or 6) as well as a treatment * baseline ordinal score (as a continuous variable) interaction terms. The models will be fit to the mITT analysis population. The treatment group hazard ratios and CIs will be reported for both sets of models and the interaction term p-value will be reported for the interaction models. The tabular summary will also include results from an analysis of time to recovery controlling for age and duration of symptoms as continuous covariates and baseline d-dimer and CRP values as continuous covariates.

The time-to-recovery analysis will also be repeated using the other subgroups defined in Section 6.4 in place of actual baseline ordinal score. Each subgroup will be considered separately, and the tabular and graphical summaries described in the previous section will be replicated for each subgroup. Forest plots (Figure 18 and Figure 19) will be generated to display the overall treatment hazard ratio estimate and CI from each of the within-subgroup analyses (Table 30).

As noted in Section 6.4, analyses that take into account concomitant medication will be performed (Table 32). An additional sensitivity analysis will evaluate the effect of recoveries that were not sustained as indicated in Section 3.3.2 (Table 31).

A restricted mean survival time analysis will be performed as an exploratory analysis. The 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 34).

Two corroborative summaries will also be generated. A summary of the number and percentage of subjects in each treatment group who recovered (and are alive), did not recover (and are alive), and died by Day 29 will be summarized. The summary will also include the numbers and percentages, grouping deaths and non-recoveries together (Table 35). The summaries will also be provided by the Modified Recovery ordinal scale (Table 33) and the duration of symptoms categorizations specified in Section 6.4.

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

8.2.6. Time-to Improvement in Clinical Status

Time to improvement by at least one category in the clinical status 8-point scale (see Section 3.3). The log rank test will be performed using a Cox proportional hazards model to test whether the curves differ between treatment arms. The median time to event and CI in each treatment group will be summarized along with the treatment hazard ratio estimate and log rank p-value (Table 36). Differences in time-to-event endpoints by treatment arm will be summarized with Kaplan-Meier curves (Figure 14). Number at risk, hazard ratio and log rank p-values will be presented on the figures. The analyses (and tabular and graphical summaries) will be repeated using the outcome of time to improvement in two categories of the ordinal scale defined in Section 3.3.

The above analyses will be repeated with the modification to the ordinal scale described in Section 4.3 (Table 37). The only subgroup analysis that will be performed for time to improvement will be an analysis that classifies subjects by the duration of symptoms at baseline subgroups (above/below the median) (Table 38).

8.2.7. Clinical Status Ordinal Scale While Hospitalized, Day 22, Day 29

The number and proportion of subjects along with 95% confidence intervals by category of clinical status will be presented by treatment arm at Study Visit (not necessarily actual) Days 1, 3, 5, 8, 11, 15 and 29 (Table 39).

Change from baseline will also be summarized at Days 3, 5, 8, 11, 15, 22, and 29 (Table 39) and by subgroup (Table 40). Individual subject listings of clinical status scores will be presented (Listing 5).

8.2.8. Desirability of Outcomes Response (DOOR)

Proportions of subjects in each category of DOOR response (1 through 7) and 95% confidence intervals will be presented by treatment arm at Study Visit 15 and 29 (Table 41) in the mITT population. DOOR score will be summarized at Day 3, 5, 8, 11, 15, 22, and 29 mITT population (Table 42). The treatment arms will be compared at Day 15 and Day 29 using a Mann-Whitney U-statistic. Additionally, the mean DOOR score by Day and treatment group will be displayed in Figure 20. Individual subject listings of DOOR scores will be presented (Listing 6).

8.2.9. Days of Oxygenation

Duration of oxygenation use will be summarized in a table using means, standard deviations, medians and quartiles by treatment arm (Table 43). Analyses will be performed in the mITT and As Treated populations, and by duration of symptoms at baseline (Table 44). Bee swarm plots of oxygen days by treatment arm will be generated, where subjects whose days are imputed to the maximum of 28 days due to death are grouped separately from subjects who do not die (Figure 21).

8.2.10. Incidence of New Oxygen Use

The incidence and duration of new oxygen use will be analyzed by treatment arm. This will only include subjects in category 4 at randomization. New use will be identified by a post-randomization score of at least 5; the number of subjects reporting new use and the incidence rate (and CI) will be reported (Table 43).

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

Duration of non-invasive ventilation/high flow oxygen use will be summarized in a table using means, standard deviations, medians, and quartiles by treatment arm (Table 45). Analyses will be performed in the mITT and As Treated populations and by duration of symptoms at baseline (Table 46). Bee swarm plots of non-invasive ventilation/high flow oxygen days by treatment arm will be generated, where subjects whose days are imputed to the maximum of 28 days due to death are grouped separately from subjects who do not die (Figure 22).

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

The incidence and duration of new Non-Invasive Ventilation/High-Flow Oxygen use will be analyzed by treatment arm. This will only include subjects in category 5 or 6 at randomization. New use will be identified by a post-randomization score of 6. The number of subjects reporting new use and the incidence rate (and CI) will be reported (Table 45).

8.2.13. Days of Invasive Mechanical Ventilation/ECMO

Duration of Invasive Mechanical Ventilation/ECMO use will be summarized in a table using means, standard deviations, medians, and quartiles by treatment arm (Table 47). Analyses will be performed in the mITT and As Treated populations and by duration of symptoms at baseline (Table 48). Bee swarm plots of Invasive Mechanical Ventilation/ECMO days by treatment arm will be generated, where subjects whose days are imputed to the maximum of 28 days due to death are grouped separately from subjects who do not die (Figure 23).

8.2.14. Incidence of New Invasive Mechanical Ventilation/ECMO

The incidence and duration of new Invasive Mechanical Ventilation/ECMO use will be analyzed by treatment arm. New use will be identified by a post-randomization score of 7. The number of subjects reporting new use and the incidence rate (and CI) will be reported (Table 47).

8.2.15. Days of Hospitalization

Duration of hospitalization will be summarized in a table using means, standard deviations, medians, and quartiles by treatment arm. Incidence of readmittance will also be summarized (Table 49). A listing of subjects who were readmitted will be generated (Listing 29). Analyses will be performed in the mITT and As Treated population and by duration of symptoms at baseline (Table 50). Bee swarm plots of days hospitalized by treatment arm will be generated, where subjects whose days are imputed to the maximum of 28 days due to death are grouped separately from subjects who do not die (Figure 24).

8.3. Exploratory Efficacy Analyses

Only Day 60 exploratory outcome measures are covered in this SAP.

8.3.1. Clinical Status Ordinal Scale at Day 60

The number and proportion of subjects along with 95% confidence intervals by category of clinical status will be presented by treatment arm and actual ordinal score for Day 60 (Table 52). Change from Day 29 to Day 60 will be summarized categorically (e.g., maintained recovery, worsened) at Day 60 (Table 53).

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, height, weight, BMI, ethnicity, and race will be presented by treatment group as well as geographic region, comorbidities, duration of symptoms prior to randomization, and actual baseline ordinal score (Table 54 and Table 55). Ethnicity will be categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option.

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

9.1.1. Prior and Concurrent Medical Conditions

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

- History of chronic medical conditions related to inclusion and exclusion criteria
- Review medications and therapies for this current illness.

Medical history is limited to the following conditions: asthma, autoimmune hepatitis, cancer, cardiac arrythmia, cardiac valvular disease, chronic kidney disease, chronic liver disease, chronic oxygen requirement, chronic respiratory disease, coagulopathy, congestive heart failure, coronary artery disease, current nicotine consumption, depression or psychotic disorder, diabetes I and II, epilepsy/seizure, hypertension, immune deficiency, obesity, systemic lupus erythematosus, and thyroid disease. History and risk factors for DVT/PE, major surgery in the past month, prolonged immobility, delivery in the past 6 weeks, pre-COVID oxygen use, blood type, and COVID-19 vaccination are also collected. All current illnesses and past pre-existing medical conditions will be MedDRA® coded using MedDRA dictionary version 23.0 or higher. Summaries of subjects' pre-existing medical conditions will be presented by treatment group (Table 56).

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

9.1.2. Prior and Concomitant Medications

Medication history (concomitant medications) includes a review of all current medications and medications taken within 7 days prior to enrollment through approximately Day 15 or early termination (if Day 15), whichever occurs first.

Summaries of medications that were started prior to dosing and continued at the time of dosing or started after dosing while on study will be presented by WHO Drug Level 1 and 2 Codes, actual baseline ordinal score, and treatment group (Table 57). Summaries of overall use of medications/therapies of interest listed in Section 6.4 that were started prior to dosing and continued at the time of dosing or started after dosing while on study as well as use by select study days will also be generated (Table 58 and Table 59).

Individual subject listings will be presented for all concomitant medications (Listing 9), corticosteroid use (Listing 10), and medications of interest (Listing 11).

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 2). Individual subject listings will be presented for all subjects who missed, halted or slowed any dose (Listing 12).

9.3. Adverse Events

For the calculation of incidence of adverse events (i.e., on a per subject basis), each subject will only be counted once and any repetitions of adverse events within a subject will be ignored; the denominator will be the number of subjects in the As Treated population. All adverse events reported and treatment emergent will be reported in tables and listings; treatment emergent events are adverse events or events increasing in severity anytime following the initiation of administration with any study product (baricitinib, dexamethasone, remdesivir, or any placebo).

An overall summary by treatment arm and actual baseline ordinal score of adverse events is presented that includes, but not limited to: subjects with at least one event, at least one related event, at least one SAE, at least one related SAE and at least one AE leading to early termination for all subjects (Table 60 and Table 61).

Adverse events occurring in 5% of subjects (by MedDRA preferred term) in any treatment group will be presented (Table 63).

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

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

- Renal adverse events by preferred term (Table 64);
- Hepatic adverse events by preferred term (Table 65)
- Related adverse events by MedDRA system organ class and preferred term (Table 66);
- Subject listing of non-serious adverse events (Listing 13) and listing of related adverse events (Listing 14);
- Bar chart of non-serious related adverse events by actual baseline ordinal score and MedDRA system organ class (Figure 25, Figure 26);

A table of new diagnoses between the Day 29 visit and the Day 60 visit will be summarized by condition, treatment arm, actual baseline ordinal score and overall (Table 67). Conditions reported at the Day 60 visit will be listed (Listing 30).

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

Serious adverse events will be summarized by MedDRA system organ class and preferred term (Table 62). Listings of death and other serious adverse events will be presented, including Subject ID, treatment group, Adverse Event Description, Number of Days Post Dose (Duration), Number of Days Post Dose the Event Became Serious, Reason Reported as an SAE, Severity, Relationship to Treatment, Alternate Etiology if not Related, Action Taken with Study Treatment, Subject Discontinuation, Outcome, MedDRA SOC, and MedDRA PT (Listing 15 and Listing 17).

The number of subjects who die by Day 15 and Day 29 will be presented by treatment arm. The 14-, 28-and exploratory 60- day mortality rate, which will use Kaplan-Meier estimator, will be presented (Table 69). Differences in time-to-event endpoints by treatment will be summarized with Kaplan-Meier curves (Figure 28, Figure 29, Figure 30).

Mortality through Day 15 and 29 will also be analyzed as a time to event endpoint (see Section 3.3). A table will present median time to event along with 95% confidence intervals overall for each treatment arm along with the hazard ratio estimate and log rank p-values (Table 70). Differences in time-to-event endpoints by treatment will be summarized with Kaplan-Meier curves (Figure 27). Analyses of mortality will be performed in the mITT and the As Treated analysis populations (Table 71). As a supplemental analysis, a Cox model will be fit with binary indicators for treatment group and actual baseline ordinal score as well as a treatment * actual baseline ordinal score interaction term (Table 74). The model will be fit in the mITT and As Treated analysis populations. The treatment group hazard ratios and CIs and the interaction term p-value will be reported. Finally, the results of the subgroup and sensitivity time-to event analyses described in Section 6.4 will be presented in a table (Table 72 and Table 73). A restricted mean survival time analysis of mortality will be performed as an exploratory analysis. The restricted mean mortality time estimates will be provided for each treatment group and randomized actual baseline ordinal score stratum as well as the difference in restricted mean recovery time between treatment groups within each of the actual baseline ordinal score strata (Table 75).

Rates of Grade 3 and 4 AE occurrence will be summarized by treatment arm (Table 76). Rates of SAE occurrence will also be compared between treatment arms using Barnard's exact test and presented. Further, the composite endpoint of the occurrence of death, SAE, or Grade 3 or 4 AE described in Section 3.3 will be analyzed as a time to event outcome. A table will present median time to event along with 95% confidence intervals overall for each treatment arm along with the hazard ratio estimate and log rank p-values (Table 77). Differences in time-to-event endpoints by treatment will be summarized with Kaplan-Meier curves (Figure 33).

A summary of the infection culture results will be summarized by treatment group and AE severity (Table 78). The anatomical location(s) of the infection and causative pathogen(s) determined by culture will be summarized (Table 79, Table 81, Table 83). A listing of culture results will be generated (Listing 16). Infections considered to be opportunistic, as identified by the sponsor, will also be included in the summaries (Table 80, Table 82, Table 84). Both summaries will be repeated by Dexamethasone use prior to enrollment (Table 85 and Table 86).

A summary of venous thromboembolisms, comprised of deep vein thrombosis and pulmonary embolisms by Treatment Group, will be included (Table 87).

9.5. Pregnancies

For any subjects in the Treated population who become pregnant during the study, every attempt will be made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. Note that the CSR will not be delayed to wait for outcomes of any pregnancies; an addendum to the CSR would be provided in such a scenario. A set of listings of pregnancies and outcomes will be presented (Listing 18, Listing 19, Listing 20, Listing 21, and Listing 22).

9.6. Clinical Laboratory Evaluations

Clinical safety laboratory adverse events are collected Day 1, 3, 5, 8, 11 and Day 15 and 29 if able to return to clinic or still hospitalized. Parameters evaluated include white blood cell count, absolute neutrophil count, eGFR, platelet count, hemoglobin concentration, creatinine, glucose, total bilirubin, ALT, AST, INR, d-dimer, and CRP. Laboratory safety parameters will be graded according to the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, version 2.1 (July 2017). For sites that do not

report an upper (lower) limit for the value of a laboratory parameter, the median of the reported upper (lower) limits across the other sites will be used. Medians and calculated LLN/ULN used if any, will be documented in the ADaM documentation. Vitamin D is collected on Day 1 and is not graded, but results will be summarized.

The distribution of Grade 3 and 4 chemistry and hematology laboratory results by maximum severity, time point, actual baseline ordinal score and treatment group will be presented (Table 88). Treatment-emergent laboratory abnormalities will be summarized by parameter and grade (Table 89).

Descriptive statistics including mean, median, standard deviation, maximum, and minimum values and change from baseline by time point, for all and each chemistry and hematology laboratory parameter will be summarized by actual baseline ordinal score and treatment arm (Table 51 and Table 90). Changes in chemistry and hematology laboratory values will be presented in line graphs over time with median, Q1 and Q3 plotted by actual baseline ordinal score and treatment arm (Figure 34).

Listings will provide a complete listing of individual chemistry and hematology laboratory results with applicable reference ranges (Listing 23).

9.7. Vital Signs and Physical Evaluations

Vital sign measurements include pulse, systolic blood pressure, respiratory rate, SpO_2 and oral temperature. Vital signs were assessed as part of the NEW score (assessed at Day 1) and will be listed in Listing 24.

Targeted Physical examinations are performed at Day 1 and may be 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 25).

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. Concomitant medication and corticosteroid use will be presented in subject listings (Listing 9 and Listing 10). The use of concomitant medications during the study (regardless of whether the medications were started prior to enrollment or after enrollment) will be summarized by ATC1, ATC2 code, actual baseline ordinal score and treatment group for the As Treated population (Table 55).

9.9. Other Safety Measures

No additional safety analyses are planned.

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

Not applicable.

12. OTHER ANALYSES

Not applicable.

13. REPORTING CONVENTIONS

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

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

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. Test Statistic for Primary Endpoint of Time to Mechanical Ventilation or ECMO

The test statistic in Section 8.1.1 was modified to account for unequal weighting in each stratum. The weighting is based on the inverse variance of the difference of the complementary log-log transformation of the Kaplan-Meier estimator at Day 29. The version of the formula reported in Klein 2007 gave equal weight to each stratum. As rationale for the modification, consider the extreme scenario where the difference in Kaplan-Meier Estimators is 10% in one stratum and -10% in the other stratum. However, the first stratum has n=10,000 and the second stratum has n=100. Using the original formula, both strata would be equally weighted and show no difference. By adding a weighting to the formula, the strata with the higher information will be given more weight in computing the final test statistic.

15.2. AE Reporting of Clinical Laboratory Results for eGFR, Creatinine, INR and Glucose

The DAIDS Toxicity Table will be applied to clinical laboratory results and the corresponding grade 3 or 4 AEs reported based on these laboratory results, with the below clarifications for AE reporting.

15.2.1. eGFR and Creatinine Grading

The DAIDS Toxicity Table has two grading options for eGFR and Creatinine, “Change from baseline” or “absolute value”. The absolute values will be used for AE reporting.

15.2.2. Glucose Grading

No change to the grading per the DAIDS Toxicity Table. However, a baseline condition of diabetes mellitus will be factored into reporting of grade 3 or grade 4 adverse events, as follows:

- If a subject has no history of any type of diabetes mellitus and baseline glucose levels are normal, grade 1 or grade 2, then any grade 3 or 4 glucose spike will be reported as an AE.
- If a subject has a history of any type of diabetes mellitus, then:
  - All grade 4 glucose elevations will be reported as AEs.
  - If baseline glucose levels are normal, grade 1, grade 2 and there are two or more consecutive elevations of glucose to grade 3, this will be reported as an AE.
  - If baseline glucose levels are normal, grade 1 or grade 2, a single elevation of glucose to grade 3 will not be reported as an AE or reported as related to Dexamethasone.

15.2.3. INR Grading

The DAIDS Toxicity Table includes grading for subjects not on anticoagulant therapy. As many of the subjects will be on anticoagulant therapy, these subjects’ INR values will not be graded. Additionally, reporting of AEs will be based on the following guidelines:

- If a subject is on anticoagulant therapy, INR in the 2.0-<3.0 times the upper limit of normal is expected and an AE does not need to be reported. However, an INR 3.0 or more times the upper limit of normal is reported in the context of a clinical syndrome.

- If a subject is not on anticoagulant therapy or on Low Molecular Weight Heparin (LMWH) like Enoxaparin (Lovenox) and has any INR values at least 2.0 times the upper limit of normal (grade 3+) then an AE for INR should be reported. Note that abnormal INR values should be reported as part of a clinical syndrome (e.g., coagulopathy secondary to sepsis; GI bleed; multi-organ failure, etc.) and not reported as a separate AE.

15.3. Changes to the SAP from Version 1.0 to Version 2.0

The below summarizes the changes made to the SAP from version 1.0 to version 2.0.

- As described in Section 15.1, the primary analysis was updated to use a weighted test statistic.
- As described in Section 15.2, text was added to describe reporting of AEs for eGFR, Creatinine, Glucose and INR.
- It was decided that the Day 60 analyses would be included in the final study report, rather than an addendum. The SAP was amended to include data through Day 60.
- At the time of the SAP update, all subjects were enrolled and there was only one known stratification error where a subject was neither ordinal score 5 nor 6 at baseline. Since only one subject fell into the "other" category in SAP version 1.0, tables were updated to include the one stratification error in the overall summaries but exclude the subject from subgroup analyses and modeling with adjustments for baseline strata. The SAP was left flexible enough to handle any additional stratifications errors identified prior to database lock.
- Modeling including baseline strata was updated to only be run based on handling the baseline ordinal score as continuous since there are only two levels included (i.e., baseline ordinal score 5 or 6).
- SAP version 1.0 table title "Infections by Treatment Group" was updated to be "Culture Results by Treatment Group and AE Severity". Additional tables of infections by MedDRA preferred term were added.
- Section 3.3.3, the following sentence was removed: "Subjects who are randomized but do not initiate treatment will be censored at time 0." Additionally, the following sentence was added: "Subjects not completing Day 29 or discharged to hospice or other end-of-life care prior to Day 29 with a death date unknown but completing Day 60 will be reviewed by the blinded Endpoint Review Committee to assess whether the Day 60 data impacts handling of the subject for the Day 29 timepoint."
- Throughout the document:
  - Typos and errors introduced via copying/pasting language from other sections were corrected.
  - Clinical Status was updated to be "Ordinal Score" in the tables for consistency with language used in prior ACTT clinical study reports.
  - Titles for tables and figures were updated to include "by Day 29", where applicable, to distinguish from Day 60 outcomes.

16. REFERENCES

1. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15):2006-2007.
2. Klein JP, Logan B, Harhoff M, Andersen PK. Analyzing survival curves at a fixed point in time. Stat Med. 2007;26(24):4505-19.
3. Jennison C., Turnbull B.W. 2000. Group sequential methods with applications to clinical trials. Chapman & Hall, Boca Raton.

17. LISTING OF TABLES, FIGURES, AND LISTINGS

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

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

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

Table 2: Ineligibility Summary of Screen Failures

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

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

Programming Note: Subjects who are eligible but not randomized will be counted in the denominator.

Table 3: Analysis Population Eligibilities by Treatment Group and Actual Baseline Ordinal Score

		Baricitinib + PBO + RDV			PBO + Dexamethasone + RDV		
Analysis Population	**Inclusion / Reason for Exclusion**	**Baseline Ordinal Score 5**	**Baseline Ordinal Score 6**	**All Subjects[d]**	**Baseline Ordinal Score 5**	**Baseline Ordinal Score 6**	**All Subjects[d]**
		n	**n**	**n**	**n**	**n**	**n**
Intent-to-Treat Population (Randomized Strata)[a]	Included in Population	x	x	x	x	x	x
Modified Intent-to-Treat Population (Actual Baseline Clinical Status) [b]	Included in Population	x	x	x	x	x	x
As Treated Population[c]	Included in Population	x	x	x	x	x	x
	Excluded from Population	x	x	x	x	x	x
	Did Not Receive Dose of Baricitinib/Placebo	x	x	x	x	x	x
	Did Not Receive Dose of Dexamethasone/Placebo						

[a] Counts are the numbers of subjects randomized to the specified treatment group with the randomized baseline ordinal score.
[b] Counts are the numbers of subjects randomized to the specified treatment group with the actual baseline ordinal score.
[c] Counts are the numbers of subjects who received the specified treatment with the actual baseline ordinal score.
[d] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Programming Notes:

If at least one subject received the incorrect treatment, then a footnote will be added which reads "XX subject[s] [was/were] randomized to [insert randomized treatment] but was administered [insert actual treatment]. In addition, a row under "Included in Population" and "Excluded from Population" will be added for the As Treated Population section with the label "Randomized to [insert randomized treatment] but administered [insert actual treatment]."

Table 4: Subject Disposition by Treatment Group and Actual Baseline Ordinal Score – mITT Population

	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N = X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X) [a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X) [a]	
Subject Disposition	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**	**n/N**	**%**
Randomized	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
Terminated Early from 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
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
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
Completed Follow-up (Study Day 1) – Hospitalized 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
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
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
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
PCR 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
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
Repeat for Days 3, 5, 8, 11																		
Completed Follow-up (Study Day 15) – 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
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
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
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
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
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
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
Completed Follow-up (Study Day 29) – 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
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

	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N = X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X) [a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X) [a]	
Subject Disposition	**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
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
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

N = Number of subjects randomized and in study for visits 1, 15, 22 and 29 and the number of subjects hospitalized and in study for visits 3, 5, 8 and 11. Subjects that died or terminated from the study on or prior to the study visit are not included in the denominators.

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 5: Subject Status at Study Termination by Treatment Group and Actual Baseline Ordinal Score – mITT Population

Baseline Ordinal Score	Category	Status at Termination	Baricitinib + PBO + RDV			PBO + Dexamethasone + RDV		
			N	n	%	N	n	%
All Subjects[a]	Any Status	Any Status	x	x	x	x	x	x
	Recovery	Recovered	x	x	x	x	x	x
		Not Recovered	x	x	x	x	x	x
	Hospitalization	Hospitalized	x	x	x	x	x	x
		Not Hospitalized	x	x	x	x	x	x
	Relative to Day 15	Prior to Day 15	x	x	x	x	x	x
		On or After Day 15	x	x	x	x	x	x
Continue for Baseline Ordinal Score 5, 6	…	…	…	…	…	…	…	…

N = Number of subjects in the mITT Population with the baseline ordinal score.
Status at termination based on the time of the last ordinal score collection.
[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 6: Baricitinib / PO Placebo Exposure by Treatment Group and Actual Baseline Ordinal Score – mITT Population

	Baricitinib + PBO + RDV (N = X)			PBO + Dexamethasone + RDV (N = X)		
	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]
Number of Doses Received						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Q1, Q3	x, x	x, x	x, x	x, x	x, x	x, x
Min, Max	x, x	x, x	x, x	x, x	x, x	x, x
Number of Subjects by Doses Received						
1 Dose	x	x	x	x	x	x
2 Doses	x	x	x	x	x	x
3 Doses	x	x	x	x	x	x
4 Doses	x	x	x	x	x	x
5 Doses	x	x	x	x	x	x
6 Doses	x	x	x	x	x	x
7 Doses	x	x	x	x	x	x
8 Doses	x	x	x	x	x	x
9 Doses	x	x	x	x	x	x
10 Doses	x	x	x	x	x	x
11 Doses	x	x	x	x	x	x
12 Doses	x	x	x	x	x	x
13 Doses	x	x	x	x	x	x
14 Doses	x	x	x	x	x	x
Number of Subjects Treatment Temporarily Held	x	x	x	x	x	x
Number of Subjects by Reason for Hold	x	x	x	x	x	x
[Reason 1]	x	x	x	x	x	x
[Reason 2]	x	x	x	x	x	x
Etc…	x	x	x	x	x	x
Number of Subjects Discontinuing Treatment	x	x	x	x	x	x
Number of Subjects by Reason for Discontinuation	x	x	x	x	x	x
[Reason 1]	x	x	x	x	x	x
[Reason 2]	x	x	x	x	x	x
Etc…	x	x	x	x	x	x

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 7: Dexamethasone / IV Placebo Exposure by Treatment Group and Actual Baseline Ordinal Score – mITT Population

	Baricitinib + PBO + RDV (N = X)			PBO + Dexamethasone + RDV (N = X)		
	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]
Number of Doses Received						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Q1, Q3	x, x	x, x	x, x	x, x	x, x	x, x
Min, Max	x, x	x, x	x, x	x, x	x, x	x, x
Number of Subjects who Received Dexamethasone Prior to Enrollment	x	x	x	x	x	x
Number of Subjects by Doses Received						
1 Dose	x	x	x	x	x	x
2 Doses	x	x	x	x	x	x
3 Doses	x	x	x	x	x	x
4 Doses	x	x	x	x	x	x
5 Doses	x	x	x	x	x	x
6 Doses	x	x	x	x	x	x
7 Doses	x	x	x	x	x	x
8 Doses	x	x	x	x	x	x
9 Doses	x	x	x	x	x	x
10 Doses	x	x	x	x	x	x
Number of Subjects Discontinuing Treatment	x	x	x	x	x	x
Number of Subjects by Reason for Discontinuation	x	x	x	x	x	x
[Reason 1]	x	x	x	x	x	x
[Reason 2]	x	x	x	x	x	x
Etc…	x	x	x	x	x	x

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 8: Remdesivir Exposure by Treatment Group and Actual Baseline Ordinal Score – mITT Population

	Baricitinib + PBO + RDV (N = X)			PBO + Dexamethasone + RDV (N = X)		
	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]
Number of Doses Received						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Q1, Q3	x, x	x, x	x, x	x, x	x, x	x, x
Min, Max	x, x	x, x	x, x	x, x	x, x	x, x
Number of Subjects who Received RDV Prior to Enrollment	x	x	x	x	x	x
Number of Subjects by Doses Received						
1 Dose	x	x	x	x	x	x
2 Doses	x	x	x	x	x	x
3 Doses	x	x	x	x	x	x
4 Doses	x	x	x	x	x	x
5 Doses	x	x	x	x	x	x
6 Doses	x	x	x	x	x	x
7 Doses	x	x	x	x	x	x
8 Doses	x	x	x	x	x	x
9 Doses	x	x	x	x	x	x
10 Doses	x	x	x	x	x	x
Number of Subjects Treatment Temporarily Held	x	x	x	x	x	x
Number of Subjects by Reason for Hold	x	x	x	x	x	x
[Reason 1]	x	x	x	x	x	x
[Reason 2]	x	x	x	x	x	x
Etc…	x	x	x	x	x	x
Number of Subjects Discontinuing Treatment	x	x	x	x	x	x
Number of Subjects by Reason for Discontinuation	x	x	x	x	x	x
[Reason 1]	x	x	x	x	x	x
[Reason 2]	x	x	x	x	x	x
Etc…	x	x	x	x	x	x

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 9: Subjects Reporting Prior Remdesivir Treatment by Actual Baseline Ordinal Score and Treatment Group – mITT Population

Prior RDV Treatment Summary	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)		
	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]
Received RDV Treatment Prior to Enrollment – n (%)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Number of Doses of RDV Received Prior to Enrollment						
Number of Subjects with Number of Doses Available	x	x	x	x	x	x
Mean (STD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x.x	x.x	x.x	x.x	x.x	x.x
IQR	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Range (Min, Max)	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 10: Subjects Reporting Prior Baricitinib Treatment by Actual Baseline Ordinal Score and Treatment Group – mITT Population

Prior RDV Treatment Summary	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)		
	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]
Received baricitinib Treatment Prior to Enrollment – n (%)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Number of Doses of Baricitinib Received Prior to Enrollment						
Number of Subjects with Number of Doses Available	x	x	x	x	x	x
Mean (STD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x.x	x.x	x.x	x.x	x.x	x.x
IQR	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Range (Min, Max)	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 11: Subjects Reporting Prior Dexamethasone Treatment by Actual Baseline Ordinal Score and Treatment Group – mITT Population

Prior RDV Treatment Summary	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)		
	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects (N=X)[a]
Received Dexamethasone Treatment Prior to Enrollment – n (%)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Number of Doses of Dexamethasone Received Prior to Enrollment						
Number of Subjects with Number of Doses Available	x	x	x	x	x	x
Mean (STD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x.x	x.x	x.x	x.x	x.x	x.x
IQR	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Range (Min, Max)	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 12: Day 60 Subject Disposition by Treatment Group and Actual Baseline Ordinal Score – mITT Population

Subject Disposition	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
	Ordinal Score 5 (N=X)		Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Ordinal Score 5 (N=X)		Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Ordinal Score 5 (N=X)		Ordinal Score 6 (N=X)		All Subjects[a] (N = X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Visit Occurred	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Type of Visit[b]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Inpatient/In-person Visit																		
Phone Visit																		
Chart Review																		
Subject Deceased After the Day 29 Visit Window																		
Was the Subject Seen by a Doctor, Outside a Hospital Re-Admission after Day 29/Last Study Contact?																		
Was the Subject Re-Admitted after Day 29/Last Study Contact?																		
If Seen by a Doctor or Re-Admitted after Day 29/Last Study Contact, Was the Reason Due to a Worsening or Exacerbated Pre-Existing Condition?																		

N = Number of subjects in the mITT Population.
n = Number of subjects meeting the criteria.
[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]
[b] Percentage based on the number of subjects with a visit. Visits may be conducted by more than one method (e.g., inpatient and chart review).

Table 13: Distribution of Subject Specific Protocol Deviations by Category, Type, Treatment Group, and Actual Baseline Ordinal Score - mITT Population

		Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]	
Category	Deviation Type	# 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.	# of Subj.	# of Dev.
Eligibility/ randomization	Any type	x	x	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	x	x
	Met exclusion criterion	x	x	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	x	x
	Other	x	x	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	x	x
	Out of window visit	x	x	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	x	x
	Missed treatment administration	x	x	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	x	x
	Other	x	x	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	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Category	Deviation Type	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]	
		# 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.	# of Subj.	# of Dev.
	Missed visit/visit not conducted	x	x	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	x	x
Protocol procedure/ assessment	Any type	x	x	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	x	x
	Blood not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Oropharyngeal swab not collected	x	x	x	x	x	x	x	x	x	x	x	x	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	x	x
	Specimen result not obtained	x	x	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	x	x
	Required procedure done incorrectly	x	x	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	x	x
	Specimen temperature excursion	x	x	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	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

		Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N=X)[a]	
Category	**Deviation Type**	**# 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.**	**# of Subj.**	**# of Dev.**
Treatment administration	Any type	x	x	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	x	x
	Study product temperature excursion	x	x	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	x	x
Blinding policy/procedure	Any type	x	x	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	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table with similar format:

Table 14: Distribution of Major Subject Specific Protocol Deviations by Category, Type, Treatment Group, and Actual Baseline Ordinal Score – mITT Population

Table 15: Mechanical Ventilation-free Survival by Day 29 by Treatment Group and Actual Baseline Ordinal Score

Analysis Population	Treatment Group	Actual Baseline Ordinal Score	Number Subjects requiring Mechanical Ventilation by Day 29	Number Subjects Dying by Day 29	Day 29 Mechanical Ventilation-Free Survival		HR		P-value
					Estimate	95% CI	Estimate	95% CI	
mITT Population	Baricitinib + PBO + RDV (N=X)	5	x	x	x.x	x.x, x.x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x	x	x.x	x.x, x.x			
	Baricitinib + PBO + RDV (N=X)	6	x	x	x.x	x.x, x.x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x	x	x.x	x.x, x.x			
	Baricitinib + PBO + RDV (N=X)	Baseline Clinical Status 5 or 6	x	x	x.x	x.x, x.x	x.xx	x.xx, x.xx	0.xxx
	PBO + Dexamethasone + RDV (N=X)		x	x	x.x	x.x, x.x			
	Baricitinib + PBO + RDV (N=X)	Any Baseline Ordinal Score	x	x	x.x	x.x, x.x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x	x	x.x	x.x, x.x			
Repeat for the As Treated Population and ITT population.									

N= Number of subjects in the specified treatment group, actual baseline ordinal score, and analysis population.
n = Number of subjects.
Mechanical Ventilation-Free Survival are Kaplan-Meier Estimates at Day 29 study visit
HR is the ratio of the hazard of mechanical ventilation or death in each treatment group estimated from the Cox model. The ratio is to PBO + Dexamethasone + RDV to Baricitinib + PBO + RDV.
HRs for the 'combined ordinal score groups are the hazard ratio from the stratified Cox Model.
P-value calculated using a stratified Chi-square test as in Klein 2007
[a] [X] additional subjects are included in the 'Any Baseline Ordinal Score' row that were enrolled with an actual baseline ordinal score of 4. [Include as applicable]

Programming note: Subject may be listed in both Mechanical Ventilation by Day 29 and Dying by Day 29 columns if they required ventilation at any point prior to death. If Dying without ventilation, not included in both.

Table 16: Mechanical Ventilation Free Survival by Day 29 by Treatment Group and Actual Baseline Ordinal Score: Sensitivity and Exploratory Analyses – mITT Population, Actual Baseline Ordinal Score 5 or 6

Model	Treatment Group	Actual Baseline Ordinal Score	HR		Interaction P-value[a]
			Estimate	95% CI	
Covariate-Adjusted	Baricitinib + PBO + RDV (N=X)	Baseline Ordinal Score 5 or 6	x.xx	x.xx, x.xx	0.xxx
	PBO + Dexamethasone + RDV (N=X)		x.xx	x.xx, x.xx	
Treatment Arm-Baseline Ordinal Score Interaction	Baricitinib + PBO + RDV (N=X)	5	x.xx	x.xx, x.xx	0.xxx
	PBO + Dexamethasone + RDV (N=X)				
	Baricitinib + PBO + RDV (N=X)	6	x.xx	x.xx, x.xx	
	PBO + Dexamethasone + RDV (N=X)				
	Baricitinib + PBO + RDV (N=X)	Baseline Ordinal Score 5 or 6	x.xx	x.xx, x.xx	
	PBO + Dexamethasone + RDV (N=X)				

HR is the ratio of the hazard of mechanical ventilation or death in each treatment group estimated from the indicated model. The ratio is PBO + Dexamethasone + RDV to Baricitinib + PBO + RDV.
HR for the Baseline Ordinal Score 5 or 6' group is the hazard ratio from the stratified Cox Model.
Covariate adjustment is by age, duration of symptoms prior to randomization, baseline d-dimer, and baseline CRP values as continuous covariates. High-sensitivity CRP values are excluded from this analysis.
Estimates are HR and CIs from interaction Cox models. For the interaction models, HRs are calculated at the level of each individual ordinal score category.
a P-values are from the likelihood ratio test.

Programming Notes:

For the "Treatment Arm-Actual Baseline Ordinal Score Interaction", the ordinal score covariate will be treated as a categorical variable.

Tables with similar format:

Table 17: Mechanical Ventilation Free Survival by Day 29 by Treatment Group within Subgroups – mITT Population, Actual Baseline Ordinal Score 5 or 6

Table 18: Mechanical Ventilation Free Survival by Day 29 by Treatment Group: Prior Corticosteroid Use – mITT Population, Actual Baseline Ordinal Score 5 or 6

Table 19: Mechanical Ventilation Free Survival by Day 29 by Treatment Group: Medications of Interest Sensitivity Analysis – mITT Population, Actual Baseline Ordinal Score 5 or 6

Programming Notes for Table 17:

A "Subgroup" column will replace the "Model" column to the left of the "Treatment Group" column. Actual baseline ordinal score subgroups, prior corticosteroid use and medications of interest will not be included in this table. This table will include all other subgroups (see Section 6.4). P-values will not be included in this table.

Programming Notes for Table 18 and Table 19:

P-values will not be included in these tables.

A "Subgroup" column will replace the "Model" column to the left of the "Treatment Group" column. Actual Baseline Ordinal Score subgroups will not be included in this table.

A "Subgroup" column will replace the "Model" column to the left of the "Treatment Group" column. Actual Baseline Ordinal Score subgroups will not be included in this table. Separate models will be fit with censoring based on the first date of use for each of the following categories of medications (see Section 6.4).

- Any Medication of Interest
- Antivirals
- COVID-19 Vaccination
- Treatments for COVID-19
- Monoclonal antibodies targeting the spike protein of SARS-CoV-2 including casirivimab, imdevimab, and bamlanivimab.
- Renin-angiotensin system (RAS) Inhibitors and HMG-CoA reductase inhibitors (Statins)
- Corticosteroids
- Other Anti-Inflammatory Drugs

The table will include the following footnote: “In this analysis, subjects that reported use of the specified medications of interest are censored at time of medication receipt.”

Table 20: Summary of Recoveries, Ventilator/ECMO Requirement, and Deaths by Day 29 – mITT Population

Grouping Variable	Actual Baseline Ordinal Score	Treatment Group	Recovered		Not Recovered and do not Require Mechanical Ventilation or ECMO		Require ECMO		Require Mechanical Ventilation		Require Mechanical Ventilation or ECMO		Deaths	
			n	%	n	%	n	%	n	%	n	%	n	%
Actual Baseline Ordinal Score	5	Baricitinib + PBO + RDV (N=X)	x	x	x	x	x	x	x	x	x	x	x	x
		PBO + Dexamethasone + RDV (N=X)	x	x	x	x	x	x	x	x	x	x	x	x
	6	Baricitinib + PBO + RDV (N=X)	x	x	x	x	x	x	x	x	x	x	x	x
		PBO + Dexamethasone + RDV (N=X)	x	x	x	x	x	x	x	x	x	x	x	x
	Baseline Ordinal Score 5 or 6	Baricitinib + PBO + RDV (N=X)	x	x	x	x	x	x	x	x	x	x	x	x
		PBO + Dexamethasone + RDV (N=X)	x	x	x	x	x	x	x	x	x	x	x	x
	Any Baseline Ordinal Score[a]	Baricitinib + PBO + RDV (N=X)	x	x	x	x	x	x	x	x	x	x	x	x
		PBO + Dexamethasone + RDV (N=X)	x	x	x	x	x	x	x	x	x	x	x	x
Repeat for duration of symptoms categories in Section 6.4														

N= Number of subjects in the mITT Population.
[a] [X] additional subjects are included in the 'Any Baseline Ordinal Score' row that were enrolled with an actual baseline clinical status of 4. [Include as applicable]

Programming Note: For the categories of "Recovered", "Did Not Recover […]" and "Deaths", subjects who recover but subsequently die will be classified under "Recovered" and "Deaths". If there are cases of this, a footnote will be added that states "Counts of recoveries and deaths include X subjects who recovered but subsequently died."

Table 21: Odds Ratio for Better (Lower) Clinical Status Score at Study Visit Day 15 by Treatment Using a Proportional Odds Model, Baricitinib + PBO + RDV Relative to PBO + Dexamethasone + RDV – mITT Population, Actual Baseline Ordinal Score 5 or 6

Analysis/Subgroup	Treatment Group	Odds Ratio		P-value
		Estimate	95% CI	
Main Analysis of Key Secondary Endpoint				
Analysis of Key Secondary Endpoint[a]	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	0.xxx
	PBO + Dexamethasone + RDV (N=X)			
Subgroup Analyses of Key Secondary Endpoint				
[Repeat for each Section 6.4 subgroups]	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
Medications of Interest Subgroup Analyses				
Any Medication of Interest	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
Antivirals	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
COVID-19 Vaccination	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
Treatments for COVID-19	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
Monoclonal Antibodies to COVID-19 spike protein	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
RAS inhibitors and HMG-CoA reductase inhibitors	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
Corticosteroids	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
Other Anti-Inflammatory Drugs	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
Covariate-Adjusted Model				
Covariate-Adjusted	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)			
Interaction Models				
Treatment-Continuous Actual Baseline Ordinal Score (5 or 6) Interaction	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)	x.xx	x.xx, x.xx	

[a]Analysis of key secondary endpoint using those subjects in the mITT Population with actual baseline ordinal score of 5 or 6 with actual baseline ordinal score as a model covariate.
Odds ratios for interaction models are calculated at the level of each actual baseline ordinal score.

Programming Notes:

For the Main Analysis, the p-value will only be reported if the p-value from the primary analysis mechanical ventilation free survival is significant. If the p-value will not be reported, then the columns will be removed.

P-value of treatment comparison will only be displayed for the main analysis. For the interaction models, the p-value for the interaction term will be provided in a footnote reading "The p-value for the treatment by actual baseline ordinal score interaction term was 0.xxx." or "The p-value for the treatment by continuous baseline ordinal score interaction term was 0.xxx.".

For the covariate-adjusted model, the model will be run with age, duration of symptoms prior to randomization, baseline d-dimer, and baseline CRP values included as continuous covariates. High sensitivity CRP values are excluded from this analysis (denote this in a footnote).

Table with similar format:

Table 22: Odds Ratio for Better (Lower) Clinical Status Score at Study Visit Day 15 by Treatment Using a Proportional Odds Model, Baricitinib + PBO + RDV Relative to PBO + Dexamethasone + RDV – As Treated Population, Actual Baseline Ordinal Score 5 or 6

Programming Note: P-value of treatment comparison will only be displayed for the main analysis. For the interaction models, the p-value for the interaction term will be provided in a footnote reading "The p-value for the treatment by actual baseline ordinal score interaction term was 0.xxx." or "The p-value for the treatment by continuous baseline ordinal score interaction term was 0.xxx.".

Table 23: Proportion of Subjects Not Progressing to Clinical Status Ordinal Score 6, 7, or 8 by Day 29 by Treatment Group, Actual Baseline Ordinal Score 5

Analysis Population	Treatment Group	Actual Baseline Ordinal Score	Number Subjects Progressing to Clinical Status Ordinal Score 6, 7, or 8 by Day 29	Number Subjects Dying by Day 29	Proportion Not Progressing to Clinical Status 6, 7, or 8 by Day 29		HR		P-value
					Estimate	95% CI	Estimate	95% CI	
mITT Population	Baricitinib + PBO + RDV (N=X)	5	x	x	x.x	x.x, x.x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x	x	x.x	x.x, x.x			
Repeat for the As Treated Population.									

N= Number of subjects in the specified treatment group, actual baseline ordinal score, and analysis population.
n = Number of subjects.
Proportions Not Progressing to Clinical Status 6, 7, or 8 by Day 29 are Kaplan-Meier Estimates at Day 29 study visit
HR is the ratio of the hazard of mechanical ventilation or death in each treatment group estimated from the Cox model. The ratio is to PBO + Dexamethasone + RDV to Baricitinib + PBO + RDV.
P-value calculated using a stratified Chi-square test as in Klein 2007

Programming Notes:

If performed, the p-value is from the stratified Chi-square test as in Klein 2007, and will only be reported contingent on results from the hierarchical testing procedure (see Section 6.8).

Table 24: Proportion of Subjects Not Progressing to Clinical Status Ordinal Score 6, 7, or 8 by Day 29 by Treatment Group and Actual Baseline Ordinal Score: Sensitivity and Exploratory Analyses – mITT Population, Actual Baseline Ordinal Score 5

Model	Treatment Group	HR		Interaction P-value[a]
		Estimate	95% CI	
Covariate-Adjusted	Baricitinib + PBO + RDV (N=X)	x.xx	x.xx, x.xx	0.xxx
	PBO + Dexamethasone + RDV (N=X)	x.xx	x.xx, x.xx	

HR is the ratio of the hazard of high flow oxygen, ventilation or death in each treatment group estimated from the indicated model. The ratio is PBO + Dexamethasone + RDV to Baricitinib + PBO + RDV.
Covariate adjustment is by age, duration of symptoms prior to randomization, baseline d-dimer, and baseline CRP values as continuous covariates. High-sensitivity CRP values are excluded from this analysis.
Estimates are HR and CIs interaction Cox models.
[a] P-values are from the likelihood ratio test.

Tables with similar format:

Table 25: Proportion of Subjects Not Progressing to Clinical Status Ordinal Score 6, 7, or 8 by Day 29 by Treatment Group within Subgroups – mITT Population, Actual Baseline Ordinal Score 5

Table 26: Proportion of Subjects Not Progressing to Clinical Status Ordinal Score 6, 7, or 8 by Day 29 by Treatment Group: Prior Corticosteroid Use – mITT Population, Actual Baseline Ordinal Score 5

Table 27: Proportion of Subjects Not Progressing to Clinical Status Ordinal Score 6, 7, or 8 by Day 29 by Treatment Group: Medications of Interest Sensitivity Analysis – mITT Population, Actual Baseline Ordinal Score 5

Programming Notes for Table 25:

A "Subgroup" column will be replace the "Model" to the left of the "Treatment Group" column. Actual baseline ordinal score subgroups will not be included in this table. This table will allsubgroups (see Section 6.4) other than actual baseline ordinal score, corticosteroids and medications of interest. P-values will not be included in this table. baseline ordinal scoreSubGroups of prior Corticosteroid Use (Section 6.4) will be presented in Table 25.

Programming Notes for Table 26 and Table 27

P-values will not be included in these tables.

A "Subgroup" column will be replace the "Model" to the left of the "Treatment Group" column. Actual Baseline Ordinal Score subgroups will not be included in this table.

A "Subgroup" column will replace the "Model" to the left of the "Treatment Group" column. Clinical Status subgroups will not be included in this table. Separate models will be fit with censoring based on the first date of use for each of the following categories of medications (see Section 6.4).

- Any Medication of Interest
- Antivirals
- COVID-19 Vaccination
- Treatments for COIVD-19
- Monoclonal antibodies targeting the spike protein of SARS-CoV-2 including casirivimab, imdevimab, and bamlanivimab
- Renin-angiotensin system (RAS) Inhibitors and HMG-CoA reductase inhibitors (Statins)
- Corticosteroids
- Other Anti-Inflammatory Drugs

The table will include the following footnote: “In this analysis, subjects that reported use of the specified medications of interest are censored at time of medication receipt.”

Table 28: Time to Recovery by Day 29 by Treatment Group and Actual Baseline Ordinal Score

Analysis Population	Treatment Group	Actual Baseline Ordinal Score	n	First Quartile Time to Recovery (Days)		Median Time to Recovery (Days)		Third Quartile Time to Recovery (Days)		HR		P-value
				Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	
mITT Population	Baricitinib + PBO + RDV (N=X)	5	x	x.x	x.x, x.x	x.x	x.x, x.x	x.x	x.x, x.x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x	x.x	x.x, x.x	x.x	x.x, x.x	x.x	x.x, x.x			
	Baricitinib + PBO + RDV (N=X)	6	x	x.x	x.x, x.x	x.x	x.x, x.x	x.x	x.x, x.x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x	x.x	x.x, x.x	x.x	x.x, x.x	x.x	x.x, x.x			
	Baricitinib + PBO + RDV (N=X)	Baseline Clinical Status 5 or 6	x	x.x	x.x, x.x	x.x	x.x, x.x	x.x	x.x, x.x	x.xx	x.xx, x.xx	0.xxx
	PBO + Dexamethasone + RDV (N=X)		x	x.x	x.x, x.x	x.x	x.x, x.x	x.x	x.x, x.x			
	Baricitinib + PBO + RDV (N=X)	Any Baseline Ordinal Score[a]	x	x.x	x.x, x.x	x.x	x.x, x.x	x.x	x.x, x.x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x	x.x	x.x, x.x	x.x	x.x, x.x	x.x	x.x, x.x			
Repeat for the As Treated Population.												

N= Number of subjects in the specified treatment group, actual baseline ordinal score, and analysis population.
n = Number of recovered subjects.
HR is the ratio of the hazard of recovery in each treatment group estimated from the Cox model. The ratio is PBO + Dexamethasone + RDV to Baricitinib + PBO + RDV.
HRs for the 'Baseline Clinical Status 5 or 6' and 'Any Baseline Clinical Status' groups are the hazard ratios from the stratified Cox Model.
P-value calculated using the stratified log-rank test
[a] [X] additional subjects are included in the 'Any Baseline Ordinal Score' row that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Programming Notes:

The p-value for the stratified log-rank test in the (5 or 6) subgroup will only be reported if the p-value for the "Baseline Ordinal Score 5 or 6" analysis is significant (see Section 6.8).

Table 29: Time to Recovery by Day 29 by Treatment Group and Baseline Ordinal Score: Sensitivity and Exploratory Analyses – mITT Population, Actual Baseline Ordinal Score 5 or 6

Model	Treatment Group	Actual Baseline Ordinal Score	HR		Interaction P-value[a]
			Estimate	95% CI	
Fine-Gray	Baricitinib + PBO + RDV (N=X)	5	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)				
	Baricitinib + PBO + RDV (N=X)	6	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)				
	Baricitinib + PBO + RDV (N=X)	Baseline Ordinal Score 5 or 6	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)				
Covariate-Adjusted	Baricitinib + PBO + RDV (N=X)	Baseline Ordinal Score 5 or 6	x.xx	x.xx, x.xx	0.xxx
	PBO + Dexamethasone + RDV (N=X)		x.xx	x.xx, x.xx	
Treatment Arm-Continuous Actual Baseline Status Interaction	Baricitinib + PBO + RDV (N=X)	5	x.xx	x.xx, x.xx	0.xxx
	PBO + Dexamethasone + RDV (N=X)				
	Baricitinib + PBO + RDV (N=X)	6	x.xx	x.xx, x.xx	
	PBO + Dexamethasone + RDV (N=X)				

HR is the ratio of the hazard of recovery in each treatment group estimated from the indicated model. The ratio is PBO + Dexamethasone + RDV to Baricitinib + PBO + RDV.
HR for the 'Baseline Ordinal Score 5 or 6) group is the hazard ratio from the stratified Cox Model.
For the Fine-Gray model, subjects who die prior to any observed recovery as coded as experiencing a competing risk.
Covariate adjustment is by age, duration of symptoms prior to randomization, baseline d-dimer, and baseline CRP values as continuous covariates. High-sensitivity CRP values are excluded from this analysis.
Estimates are HR and CIs from Fine-Gray or interaction Cox models. For the interaction models, HRs are calculated at the level of each individual actual baseline ordinal score.
[a] P-values are from the likelihood ratio test.

Programming Notes:

For the "Treatment Arm-Actual Baseline Ordinal Score Interaction", the covariate will be treated as a categorical variable.

Tables with similar format:

Table 30: Time to Recovery by Day 29 by Treatment Group within Subgroups – mITT Population, Actual Baseline Ordinal Score of 5 or 6

Table 31: Time to Recovery by Day 29 by Treatment Group and Actual Baseline Ordinal Score: Readmittance Sensitivity Analysis – mITT Population, Actual Baseline Ordinal Score of 5 or 6

Table 32: Time to Recovery by Day 29 by Treatment Group and Actual Baseline Ordinal Score: Medications of Interest Sensitivity Analysis – mITT Population, Actual Baseline Ordinal Score of 5 or 6

Table 33: Time to Recovery by Day 29 by Treatment Group using Modified Recovery Scale Sensitivity Analysis – mITT Population, Actual Baseline Ordinal Score of 5 or 6

Programming Notes for Table 30:

The "Actual Baseline Ordinal Score" and "Analysis Population" columns will be removed. A "Subgroup" column will be inserted to the left of the "Treatment Group" column. This table will not display the "Any…" rows. The elements for the "n" and "Median Time to Recovery" columns will display "-". This table will include subgroups (see Section 6.4), except for actual baseline ordinal score.

Programming Notes for Table 31 and Table 32:

P-values will not be included in these tables.

Table 31 will include a column to the left of the "n" column titled "m". The corresponding footnote will read "m = Number of subjects readmitted for COVID-19." Table will include the following footnote: "In this analysis, subjects that recover and are subsequently readmitted for COVID-19 are censored at 28 days".

Table 32 will include a column to the left of the "n" column titled "m". The corresponding footnote will read "m = Number of subjects reporting use of a medication of interest." The "Analysis Population" column will be replaced by a column labeled "Medication of Interest". Separate models will be fit with censoring based on the first date of use for each of the following categories of medications (see Section 6.4):

- Any Medication of Interest
- Antivirals
- COVID-19 Vaccination
- Treatments for COVID-19
- Monoclonal antibodies targeting the spike protein of SARS-CoV-2 including casirivimab, imdevimab, and bamlanivimab
- Renin-angiotensin system (RAS) Inhibitors and HMG-CoA reductase inhibitors (Statins)

- Corticosteroids
- Other Anti-Inflammatory Drugs

The table will include the following footnote: “In this analysis, subjects that reported use of the specified medications of interest are censored at time of medication receipt.”

Table 34: Time to Recovery by Day 29 by Treatment Group and Actual Baseline Ordinal Score: Restricted Mean Survival Time Analysis, Actual Baseline Ordinal Score 5 or 6

Analysis Population	Treatment Group	Actual Baseline Ordinal Score	n	Tau[a]	Restricted Mean Recovery Time (Days)		Difference	
					Estimate	95% CI	Estimate	95% CI
mITT Population	Baricitinib + PBO + RDV (N=X)	5	x	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)		x	x	x.x	x.x, x.x		
	Baricitinib + PBO + RDV (N=X)	6	x	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)		x	x	x.x	x.x, x.x		
	Baricitinib + PBO + RDV (N=X)	Baseline Ordinal Score 5 or 6	x	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)		x	x	x.x	x.x, x.x		
Repeat for the As Treated Population.								

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 PBO + Dexamethasone + RDV to Baricitinib + PBO + RDV.
[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 Notes:

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;
```

Stratified by actual Baseline Ordinal Score ("Baseline Ordinal Score 5 or 6" row).

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

Table 35: Summary of Recoveries and Deaths by Day 29 – mITT Population

Grouping Variable	Actual Baseline Ordinal Score	Treatment Group	Recovered[b]		Did Not Recover		Deaths[b]		Died or Not Recovered	
			n	%	n	%	n	%	n	%
Actual Baseline Ordinal Score	5	Baricitinib + PBO + RDV (N=X)	x	x	x	x	x	x	x	x
		PBO + Dexamethasone + RDV (N=X)	x	x	x	x	x	x	x	x
	6	Baricitinib + PBO + RDV (N=X)	x	x	x	x	x	x	x	x
		PBO + Dexamethasone + RDV (N=X)	x	x	x	x	x	x	x	x
	Baseline Ordinal Score 5 or 6	Baricitinib + PBO + RDV (N=X)	x	x	x	x	x	x	x	x
		PBO + Dexamethasone + RDV (N=X)	x	x	x	x	x	x	x	x
	Any Baseline Ordinal Score[a]	Baricitinib + PBO + RDV (N=X)	x	x	x	x	x	x	x	x
		PBO + Dexamethasone + RDV (N=X)	x	x	x	x	x	x	x	x
Repeat for duration of symptoms categories in Section 6.4										

N= Number of subjects in the mITT Population.
[a] [X] additional subjects are included in the 'Any Baseline Ordinal Score' row that were enrolled with a baseline ordinal score of 4. [Include as applicable]
[b] [Number] subjects recovered but subsequently died. These X subjects are included in both the recoveries and also in the deaths counts.

Programming Note: For the categories of "Recovered", "Did Not Recover" and "Deaths", subjects who recover but subsequently die will be classified under "Recovered" and "Deaths". If there are cases of this, footnote b will be added.

Table 36: Time to One or Two Category Improvement on the 8-Point Ordinal Scale by Treatment Group, Actual Baseline Ordinal Score 5 or 6

Analysis Population	Treatment Group	n	Median Time		HR	
			Estimate	95% CI	Estimate	95% CI
	Improvement by at Least One Category					
mITT Population	Baricitinib + PBO + RDV (N=X)	x	x.x	x.x, x.x		
	PBO + Dexamethasone + RDV (N=X)	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
As Treated Population	Baricitinib + PBO + RDV (N=X)	x	x.x	x.x, x.x		
	PBO + Dexamethasone + RDV (N=X)	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	Improvement by at Least Two Categories					
mITT Population	Baricitinib + PBO + RDV (N=X)	x	x.x	x.x, x.x		
	PBO + Dexamethasone + RDV (N=X)	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
As Treated Population	Baricitinib + PBO + RDV (N=X)	x	x.x	x.x, x.x		
	PBO + Dexamethasone + RDV (N=X)	x	x.x	x.x, x.x	x.xx	x.xx, x.xx

N = Number of subjects in the specified treatment group, analysis population, and actual baseline ordinal score of 5 or 6.
n = Number of subjects with improvement.
HR is the ratio of the hazard of improvement in each treatment group estimated from the Cox model. The ratio is Baricitinib + PBO + RDV to PBO + Dexamethasone + RDV.

Tables with similar format:

Table 37: Time to Improvement on the 8-Point Ordinal Scale by Treatment Group: Modified Ordinal Scale, Actual Baseline Ordinal Score 5 or 6

Table 38: Time to Improvement on the 8-Point Ordinal Scale by Treatment Group and Duration of Symptoms at Baseline – mITT Population, Actual Baseline Ordinal Score 5 or 6

Programming notes for Table 37:

The table will include the footnote: This analysis used the modified version of the ordinal scale where the categories “Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care” and “Not hospitalized, no limitations on activities” were classified together and given a score of 2 while the category “Not hospitalized, but new or increased limitation on activities and/or requiring new or increased home oxygen” was given the score 3.

Programming notes for Table 38:

The “Analysis Population” column will be re-labeled “Duration of Symptoms at Baseline”. The “Actual Baseline Ordinal Score” column will be removed. Rows will be generated for each subgroup defined by duration above/below the median. Only subjects with baseline ordinal score 5 or 6 will be included in the table. The footnote for “N” will read “N = Number of subjects in the specified treatment group and analysis population with an actual baseline ordinal score of 5 or 6.”

Table 39: Clinical Status Scores by Treatment Group and Study Visit, Imputed – mITT Population, Actual Baseline Ordinal Score 5 or 6

Study Visit	Ordinal Scale Measure	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)			Risk Difference	
		n	%	95% CI	n	%	95% CI	%	95% CI
Day 1	Death at or before Study Visit (8)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	Hospitalized, requiring supplemental oxygen (5)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	Not hospitalized, but new or increased limitation on activities and/or requiring new or increased home oxygen (2)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	Not hospitalized, no limitations on activities (1)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
[Repeat for Study Visit Days 3, 5, 8, 11, 15, 22, and 29]									

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

Programming Note: If necessary, a row for "No clinical status score reported – Completed study without reporting score" will be added as the last row for each day.

Table 40: Summary of Clinical Status Score by Treatment Group and Study Visit – mITT Population, Actual Baseline Ordinal Score 5 or 6

Study Visit	Statistic	Baricitinib + PBO + RDV (N=X)	PBO + Dexamethasone + RDV (N=X)	Difference
Baseline	Number of reported clinical scores	x	x	--
	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Median	x.x	x.x	x.x (x.x, x.x)
	Range (Min, Max)	x, x	x, x	--
Day 3	Number of reported clinical scores	x	x	--
	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Median	x.x	x.x	x.x (x.x, x.x)
	Range (Min, Max)	x, x	x, x	--
	Change from Baseline Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	--
Continue for Days 5, 8, 11, 15, 22, 29				
N = Number of subjects in the mITT Population. Missing values were imputed using Last Observation Carried Forward. Clinical scores of 8 were carried forward from the date of death for subjects who died.				

Table 41: DOOR Category by Treatment Group and Study Visit, Imputed – mITT Population, Actual Baseline Ordinal Score 5 or 6

Study Visit	DOOR Category	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)			Risk Difference	
		n	%	95% CI	n	%	95% CI	%	95% CI
Day 15	1 - Recovered (Category 1, 2 or 3 Clinical Status)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	2 - Improved (≥ 1 category improvement in Clinical Status compared with baseline) & no SAE	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	3 - Improved (≥ 1 category improvement in Clinical Status compared with baseline) & SAE (related or unrelated)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	4 - No change in Clinical Status from baseline & no SAE	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	5 - No change in Clinical Status from baseline & SAE (related or unrelated)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	6 - Worsening (≥ 1 category worse in Clinical Status compared with baseline)	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
	7 - Death	x	x	x.x, x.x	x	x	x.x, x.x	x.x	x.x, x.x
[Repeat for Study Visit Day 29]									

N = Number of Subject in the mITT Population.
n = Number of subjects with the respective score
95% CI calculated using Wilson CIs

Table 42: Summary of DOOR by Treatment Group and Study Visit, Imputed – mITT Population, Actual Baseline Ordinal Score 5 or 6

Study Visit	Statistic	Baricitinib + PBO + RDV (N=X)	PBO + Dexamethasone + RDV (N=X)	Difference	P-value
Day 15	n	x	x	--	
	Mean (95% CI)	x.x (x.x, x.x)	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)	
	Range (Min, Max)	x, x	x, x	--	
Day 29	n	x	x	--	
	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	
	Median	x.x	x.x	x.x (x.x, x.x)	
	Range (Min, Max)	x, x	x, x	--	
[Repeat for Study Visit Days 5, 8, 11, 15, 22, 29 and Change from Baseline at each]					
n = Number of subjects with an assessment at the time point being summarized.					

Programming Notes:

P-value calculated using a Mann-Whitney U statistic

Table 43: Oxygen Use Through Day 29 by Treatment Group – Actual Baseline Ordinal Score of 5 or 6

Analysis Population	Oxygen Use	Statistic	Treatment Group	
			Baricitinib + PBO + RDV	PBO + Dexamethasone + RDV
mITT Population	**On Oxygen at Baseline (N = x)**			
	Days on Oxygen (Including imputations for subjects who died)	N	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)
		Q1	x.x	x.x
		Median	x.x	x.x
		Q3	x.x	x.x
		Difference in Medians (95% CI)	x.x (x.x, x.x)	
	Days of Oxygen (Among subjects who did not die)	N	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)
		Q1	x.x	x.x
		Median	x.x	x.x
		Q3	x.x	x.x
		Difference in Medians (95% CI)	x.x (x.x, x.x)	
	Not on Oxygen at Baseline (N = x)			
	New Oxygen Use	N	x	x
		n	x	x
		Incidence Rate	x.x	x.x
		Incidence Rate 95% CI	x.x, x.x	x.x, x.x
		Difference in Rates (95% CI)	x.x (x.x, x.x)	
	Days on Oxygen (Including imputations for subjects who died)	N	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)
		Q1	x.x	x.x
		Median	x.x	x.x
		Q3	x.x	x.x
		Difference in Medians (95% CI)	x.x (x.x, x.x)	
	Days of Oxygen (Among subjects who did not die)	N	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)
		Q1	x.x	x.x
		Median	x.x	x.x
		Q3	x.x	x.x
		Difference in Medians (95% CI)	x.x (x.x, x.x)	
Repeat for As Treated Population.				

N = Number of subjects in the specified analysis population and oxygen use category.
Q1 and Q3 are the first and third quartiles, respectively.

Programming Note: For the "Days on Oxygen" statistics within the "Not on Oxygen at Baseline" subgroup, only summarize days for subjects who reported new use.

Tables with similar format:

Table 44: Oxygen Use Through Day 29 by Treatment Group and Duration of Symptoms at Baseline – Actual Baseline Ordinal Score of 5 or 6

Table 45: Non-invasive Ventilation/High-Flow Oxygen Use Through Day 29 by Treatment Group – Actual Baseline Ordinal Score of 5 or 6

Table 46: Non-invasive Ventilation/High-Flow Oxygen Use Through Day 29 by Treatment Group and Duration of Symptoms at Baseline – Actual Baseline Ordinal Score of 5 or 6

Table 47: Ventilation/ECMO Use Through Day 29 by Treatment Group – Actual Baseline Ordinal Score of 5 or 6

Table 48: Ventilation/ECMO Use Through Day 29 by Treatment Group and Duration of Symptoms at Baseline – Actual Baseline Ordinal Score of 5 or 6

Programming notes for Table 44, Table 46, and Table 48:

"Analysis Population" will be replaced by "Duration of Symptoms at Baseline" column. The tables will consider the duration above/below median subgroup. Summaries will only be generated for mITT population.

Programming notes for Table 47, Table 48:

The "On Ventilation/ECMO at Baseline" section of the table will not be generated.

Programming notes for Table 43 and Table 44:

The "New Use" section of the table will not be generated.

Programming notes for Tables 43, 44, 45, 46, 47, 48

When subjects died without new use of the specified oxygen type, split the "N" row for the "Days on Oxygen (including imputations for subjects who died" into:

- "N (Observed New Use)" which includes subjects who were observed to have new use
- "Deaths (imputed No new use Observed)" including the subjects who died without observed new use.

Table 49: Hospitalization Through Day 29 by Treatment Group – Actual Baseline Ordinal Score of 5 or 6

Analysis Population	Summary	Statistic	Treatment Group	
			Baricitinib + PBO + RDV	PBO + Dexamethasone + RDV
mITT Population	Number of Subjects	N	x	x
	Days of Hospitalization (including imputation for subjects who died)	Mean (SD)	x.x (x.x)	x.x (x.x)
		Q1	x.x	x.x
		Median	x.x	x.x
		Q3	x.x	x.x
		Difference in Medians (95% CI)	x.x (x.x, x.x)	
	Days of Hospitalization (among subjects who did not die)	Q1	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)
		Median	x	x
		Q3	x.x, x.x	x.x, x.x
		Difference in Medians (95% CI)	x.x (x.x, x.x)	
	Readmittance for COVID-19	N	x	x
		n	x	x
		Percentage	x	x
		Percentage 95% CI	x.x, x.x	x.x, x.x
		Difference in Percentages (95% CI)	x.x (x.x, x.x)	
	Readmittance for Any Reason	N	x	x
		n	x	x
		Percentage	x	x
		Percentage 95% CI	x.x, x.x	x.x, x.x
		Difference in Percentages (95% CI)	x.x (x.x, x.x)	
Continue for As Treated Population….				
N = Number of subjects in the specified analysis population. Q1 and Q3 are the first and third quartiles, respectively. Denominator of readmittance percentages is the number of subjects in the specific analysis population that discharged				

Table with similar format:

Table 50: Hospitalization Through Day 29 by Treatment Group and Duration of Symptoms at Baseline – Actual Baseline Ordinal Score of 5 or 6

Programming Note for Table 50:

"Analysis Population" will be replaced by "Duration of Symptoms at Baseline" column. The table will consider the duration above/below median subgroup. Summaries will only be generated for mITT population

Table 51: Summary Statistics of Laboratory Efficacy Results by Study Visit Day, and Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5 or 6

Laboratory Parameter	Study Visit Day	Treatment Group	Absolute					Change from Baseline				
			N	Mean	95% CI	Median	Min, Max	N	Mean	95% CI	Median	Min, Max
D-dimer	Baseline	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	---	---	---	---	---
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	---	---	---	---	---
	Day 3	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 5	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 8	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 11	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 15	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 29	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
CRP	Baseline	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	---	---	---	---	---
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	---	---	---	---	---
	Day 3	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 5	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 8	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 11	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x

Laboratory Parameter	Study Visit Day	Treatment Group	Absolute					Change from Baseline				
			N	Mean	95% CI	Median	Min, Max	N	Mean	95% CI	Median	Min, Max
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 15	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 29	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x

N = Number of subjects in the As Treated Population with laboratory data available for the parameter at the specified study visit.
High-sensitivity CRP values are excluded from the summaries.

Programming notes:

Use imputed results for missing data, see Section 6.5.

Table 52: Day 60 Ordinal Scores by Treatment Group and Actual Baseline Ordinal Score – mITT Population

	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)	
Subject Ordinal Score	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Death at or before Study Visit (8)	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Hospitalized, on invasive mechanical ventilation or ECMO (7)	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Hospitalized, requiring supplemental oxygen (5)	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Not hospitalized, but new or increased limitation on activities and/or requiring new or increased home oxygen (2)	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Not hospitalized, no limitations on activities (1)	x	xx	x	Xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N = Number of subjects in the mITT Population with a Day 60 ordinal score.
n = Number of subjects with the reported ordinal score at Day 60.
[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 53: Day 60 Change in Ordinal Score from Day 29 by Treatment Group and Actual Baseline Ordinal Score – mITT Population

Status at Day 29	Ordinal Score Change at Day 60	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Recovered	Maintained Recovery Status (OS 1, 2 or 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Worsened to OS 4	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Worsened to OS 5	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Worsened to OS 6	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Worsened to OS 7	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Died	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Not Recovered	Recovered (OS 1, 2 or 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Recovered but Improved by 1 or More OS Categories	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	No Change from Last Observed OS	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Worsened by 1 or More OS Categories	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Died	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
All Subjects	Recovered (OS 1, 2, 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Progressed to OS 7	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Died	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N = Number of subjects in the mITT Population with a Day 60 ordinal score.
n = Number of subjects meeting the criteria.
[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 54: Categorical Demographic and Baseline Characteristics by Actual Baseline Ordinal Score and Treatment Group – mITT Population

Demographic Category	Characteristic	Baricitinib + PBO + RDV						PBO + Dexamethasone + RDV						All Subjects					
		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sex	Male	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Female	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Ethnicity	Not Hispanic or Latino	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Hispanic or Latino	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Not Reported	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Race	American Indian or Alaska Native	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Asian	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Native Hawaiian or Other Pacific Islander	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Black or African American	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	White	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Multi-Racial	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Geographic Region	Region 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	…Continue for all region categorizations	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Country	Country 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	…Continue for all countries	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Age	< 40	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	40-64	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	>=65	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Demographic Category	Characteristic	Baricitinib + PBO + RDV						PBO + Dexamethasone + RDV						All Subjects					
		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Blood Type	A+	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	A-	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	…Continue for all blood types	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Duration of Symptoms prior to randomization	Categorization 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	…Continue for all symptom categorizations	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Comorbidities	Comorbidity 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Comorbidity 2	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	…Continue for all comorbidities	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Comorbidities Group X	…Continue for all comorbidity categorizations	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
COVID Vaccination	Yes	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
Pre-COVID-19 Use of Supplemental Oxygen	Yes	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

[a] [X] additional subjects are included in the 'Any Clinical Status' row that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 55: Continuous Demographic and Baseline Characteristics by Actual Baseline Ordinal Score and Treatment Group – mITT Population

Variable	Statistic	Baricitinib + PBO + RDV			PBO + Dexamethasone + RDV			All Subjects		
		Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects[a] (N=X)	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects[a] (N=X)	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects[a] (N=X)
Age (years)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	IQR	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x
Height (cm)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	IQR	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	X
	Maximum	x	x	x	x	x	x	x	x	X
Weight (Kg)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	IQR	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	X
	Maximum	x	x	x	x	x	x	x	x	X
BMI	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	IQR	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	X

Variable	Statistic	Baricitinib + PBO + RDV			PBO + Dexamethasone + RDV			All Subjects		
		Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects[a] (N=X)	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects[a] (N=X)	Baseline Ordinal Score 5 (N=X)	Baseline Ordinal Score 6 (N=X)	All Subjects[a] (N=X)
	Maximum	x	x	x	x	x	x	x	x	X
Duration of Symptoms prior to Randomization (Days)	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	IQR	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	X
	Maximum	x	x	x	x	x	x	x	x	X

[a] [X] additional subjects are included in the 'Any Baseline Ordinal Score' row that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 56: Summary of Subjects with Pre-Existing Medical Conditions Treatment Group - As Treated Population

	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)	
Condition	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Any Condition	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Diabetes I	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Diabetes II	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
…continue for all solicited conditions…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…

N = Number of subjects in the As Treated Population;
n = Number of subjects reporting the condition. Subjects who report 'unknown' for a condition are assumed to not have the condition.
[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Programming Note: "None" and "Any Condition" will be the first two rows. The remainder of the rows will be sorted in order of prevalence, with the condition most reported among All Subjects being displayed first.

Table 57: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification, Actual Baseline Ordinal Score, and Treatment Group – As Treated Population

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects (N = X)	
		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
[ATC Level 1 - 1]	Any [ATC 1 – 1]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 – 2]	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Programming Note: Only include medications with missing end dates (i.e. ongoing) or end dates on or after the enrollment date.

Table 58: Number and Percentage of Subjects Reporting On-Study Use of Medications of Interest by Actual Baseline Ordinal Score, and Treatment Group – As Treated Population

	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)	
Medication/Therapies	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Statins/ARBs/ACEIs	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Protease inhibitors	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Polymerase inhibitors	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Potential Treatments for COVID-19	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Chloroquine/Hydroxychloroquine	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Aplidin (plitidepsin)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Colchicine (Colcyrs)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Ivermectin (stromectol, Soolantra, Sklice)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Monoclonal antibodies targeting the spike protein of SARS-CoV-2 including casirivimab, imdevimab, and bamlanivimab	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Other	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Corticosteroids	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
RAS Inhibitors and HMG-CoA reductase inhibitors	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Other anti-inflammatory drugs	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Monoclonal Antibodies Targeting Cytokines	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Other Biologic Therapies	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N = Number of subjects in the As Treated Population.
n=Number of subjects reporting taking at least one medication in the specified category.
[a] [X] addtional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Programming Note: only include medications where the end date is missing (i.e. ongoing) or end date is on or after enrollment date

Table 59: On-Study Use of Medications of Interest by Study Day, Actual Baseline Ordinal Score, and Treatment Group – As Treated Population

	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N=X)	
Study Day	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Statins/ARBs/ACEIs																		
Day 1	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 3	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 5	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 8	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Day 11	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
…Repeat for all categories and sub-categories of the medications in Section 6.4																		

N = Number of subjects in the As Treated Population.
n = Number of subjects reporting taking at least one prohibited medication by the specified study day.
[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

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

Table 60: Overall Summary of Adverse Events – As Treated Population

	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[c] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[c] (N=X)	
Subjects[a] with	n	%	n	%	n	%	n	%	n	%	n	%
At least one adverse event	x	x	x	x	x	x	x	x	x	x	x	x
At least one Severe or Life-threatening (Grade 3 or 4) adverse event	x	x	x	x	x	x	x	x	x	x	x	x
At least one related adverse event[b]	x	x	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x	x	x
Life-threatening (Grade 4)	x	x	x	x	x	x	x	x	x	x	x	x
Severe or Life-Threatening (Grade 3 or 4)	x	x	x	x	x	x	x	x	x	x	x	x
Death (Grade 5)	x	x	x	x	x	x	x	x	x	x	x	x
At least one not related adverse event[b]	x	x	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x	x	x
Life-threatening (Grade 4)	x	x	x	x	x	x	x	x	x	x	x	x
Death (Grade 5)	x	x	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event with fatal outcome	x	x	x	x	x	x	x	x	x	x	x	x
At least one related serious adverse event[b]	x	x	x	x	x	x	x	x	x	x	x	x
At least one related serious adverse event with fatal outcome[b]	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to study drug temporary hold[b]	x	x	x	x	x	x	x	x	x	x	x	x
At least one related adverse event leading to study drug temporary hold[b]	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to study drug discontinuation[b]	x	x	x	x	x	x	x	x	x	x	x	x
At least one related adverse event leading to study drug discontinuation[b]	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to early termination[b]	x	x	x	x	x	x	x	x	x	x	x	x
At least one Unanticipated Problem	x	x	x	x	x	x	x	x	x	x	x	x

	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[c] (N=X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[c] (N=X)	
Subjects[a] with	n	%	n	%	n	%	n	%	n	%	n	%

N = Number of subjects in the actual baseline ordinal score stratum and As Treated Population
[a] Subjects are counted once for each category regardless of the number of events.
All Grade 3 and 4 AEs are captured as AEs. In addition, any Grade 2 or higher suspected drug-related hypersensitivity reaction is reported as an AE.
[b] Relationship, discontinuation and drug hold are defined as occurring for any study product (remdesivir, baricitinib/placebo or dexamethasone/placebo).
[c] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 61: Subject-Level Rates of Adverse Events and Differences between Treatment Groups – As Treated Population

	Baricitinib + PBO + RDV (N=X)		PBO + Dexamethasone + RDV (N=X)		
Subjects[a] with at least one:	n	%	n	%	Risk Difference (95% CI)
AE	x	x	x	x	x.x (x.x, x.x)
Related AE[b]	x	x	x	x	x.x (x.x, x.x)
Grade 3-4 AE	x	x	x	x	x.x (x.x, x.x)
Grade 3-4 Related AE[b]	x	x	x	x	x.x (x.x, x.x)
SAE	x	x	x	x	x.x (x.x, x.x)
Related SAE[b]	x	x	x	x	x.x (x.x, x.x)
SAE with fatal outcome	x	x	x	x	x.x (x.x, x.x)
Related SAE with fatal outcome[b]	x	x	x	x	x.x (x.x, x.x)
AE leading to discontinuation of study drug[b]	x	x	x	x	x.x (x.x, x.x)
Related AE leading to discontinuation of study drug[b]	x	x	x	x	x.x (x.x, x.x)

N = Number of subjects in the As Treated Population.
[a] Subjects are counted once for each category regardless of the number of events.
[b] Relationship and discontinuation are defined as occurring for any study product (remdesivir, baricitinib/placebo or dexamethasone/placebo).

Table 62: Serious Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group - As Treated Population

MedDRA System Organ Class	Preferred Term	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)			Risk Difference	
		n	%	Events	n	%	Events	%	95% CI
SOC1	PT1	x	x	x	x	x	x	x.x	x.x, x.x
Etc.	Etc.	x	x	x	x	x	x	x.x	x.x, x.x

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

Table 63: Non-Serious Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - As Treated Population

MedDRA System Organ Class	Preferred Term	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)			Risk Difference	
		n	%	Events	n	%	Events	%	95% CI
SOC1	PT1	x	x	x	x	x	x	x.x	x.x, x.x
Etc.	Etc.	x	x	x	x	x	x	x.x	x.x, x.x

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

Programming Note: Select all preferred terms/system organ classes among non-serious AEs where the % for any treatment group or overall is >= 5%. For both sections, sort preferred terms by descending order of frequency.

Table 64: Renal Adverse Events by Preferred Term and Treatment Group – As Treated Population

Preferred Term	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)			Risk Difference	
	n	%	Events	n	%	Events	%	95% CI
Any renal adverse event	**x**	**x**	**x**	**x**	**x**	**x**	**x.x**	**x.x, x.x**
PT 1	x	x	x	x	x	x	x.x	x.x, x.x
PT 2	x	x	x	x	x	x	x.x	x.x, x.x
Etc.	x	x	x	x	x	x	x.x	x.x, x.x

N = Number of subjects in the As Treated Population.
n = Number of subjects reporting event.
Events = Total frequency of events reported.
Renal adverse events determined through a Standardized MedDRA Query (SMQ) of acute renal failures.

Table with similar format:

Table 65: Hepatic Adverse Events by Preferred Term and Treatment Group – As Treated Population

Programming Note:

Update footnote to be: Hepatic adverse events determined through a Standardized MedDRA Query (SMQ) of hepatic disorders.

Table 66: Related Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group - As Treated Population

Related Study Product	MedDRA System Organ Class	Preferred Term	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)			Risk Difference	
			n	%	Events	n	%	Events	%	95% CI
Remdesivir	Any SOC	Any PT	x	x	x	x	x	x	x.x	x.x, x.x
	SOC1	PT1	x	x	x	x	x	x	x.x	x.x, x.x
	Etc.	Etc.	…	…	…	…	…	…	…	…
Repeat for Dexamethasone/Placebo, Baricitinib/Placebo, Any Study Product (Remdesivir, Dexamethasone/Placebo or Baricitinib/Placebo)										
N = number of subjects in the As Treated Population (number of subjects at risk). n = number of subjects reporting event. Events = total frequency of events reported.										

Table 67: Day 60 New Diagnoses Since Day 29 by Treatment Group and Actual Baseline Ordinal Score – As Treated Population

Condition	Baricitinib + PBO + RDV (N=X)						PBO + Dexamethasone + RDV (N=X)						All Subjects (N=X)					
	Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)		Baseline Ordinal Score 5 (N=X)		Baseline Ordinal Score 6 (N=X)		All Subjects[a] (N = X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Infection	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Chronic Respiratory Disease	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Pulmonary Emboli	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Deep Venous Thrombosis	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Cardiac Arrhythmia	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Myocardial Infarction	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Stroke	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Major Depression	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Anxiety	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Post-traumatic Stress Disorder	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Other New Diagnosis	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

N = Number of subjects in the As Treated Population with a Day 60 visit.
n = Number of subjects reporting the condition.
[a] [X] additional subjects are included in the 'All Subjects' column that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 68: Deaths by Day 15, Day 29, or Day 60 by Treatment Group and Actual Baseline Ordinal Score – mITT Population

Study Day	Actual Baseline Clinical Status	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)		
		n	Mortality Rate[a]	Rate 95% CI	n	Mortality Rate[a]	Rate 95% CI
Day 15	5	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
	Baseline Ordinal Score 5 or 6	X	x.x	x.x, x.x	x	x.x	x.x, x.x
	Any Baseline Ordinal Score[b]	X	x.x	x.x, x.x	x	x.x	x.x, x.x
Day 29	5	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
	Baseline Ordinal Score 5 or 6	X	x.x	x.x, x.x	x	x.x	x.x, x.x
	Any Baseline Ordinal Score[b]	X	x.x	x.x, x.x	x	x.x	x.x, x.x
Day 60	5	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
	Baseline Ordinal Score 5 or 6	X	x.x	x.x, x.x	x	x.x	x.x, x.x
	Any Baseline Ordinal Score[b]	X	x.x	x.x, x.x	x	x.x	x.x, x.x

N = Number of subjects in the specified treatment group and analysis population.
n = Number of subjects in a given treatment group who died by the given timepoint
[a] Mortality Rate is the Kaplan-Meier estimate.
[b] [X] additional subjects are included in the 'Any Baseline Ordinal Score' row that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table with similar format:

Table 69: Deaths by Day 15 or Day 29 by Treatment Group and Actual Baseline Ordinal Score – As Treated Population

Table 70: Time to Death through Day 15 and 29 by Treatment Group and Actual Baseline Ordinal Score – mITT Population

Study Day	Treatment Group	Actual Baseline Ordinal Score	n	HR		P-value
				Estimate	95% CI	
Day 15	Baricitinib + PBO + RDV (N=X)	5	x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x			
	Baricitinib + PBO + RDV (N=X)	6	x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x			
	Baricitinib + PBO + RDV (N=X)	Baseline Ordinal Score 5 or 6	x	x.xx	x.xx, x.xx	x.xxx
	PBO + Dexamethasone + RDV (N=X)		x			
	Baricitinib + PBO + RDV (N=X)	Any Baseline Ordinal Score[a]	x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x			
Day 29	Baricitinib + PBO + RDV (N=X)	5	x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x			
	Baricitinib + PBO + RDV (N=X)	6	x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x			
	Baricitinib + PBO + RDV (N=X)	Baseline Ordinal Score 5 or 6	x	x.xx	x.xx, x.xx	x.xxx
	PBO + Dexamethasone + RDV (N=X)		x			
	Baricitinib + PBO + RDV (N=X)	Any Baseline Ordinal Score[a]	x	x.xx	x.xx, x.xx	--
	PBO + Dexamethasone + RDV (N=X)		x			

N= Number of subjects in the specified treatment group and analysis population.
n = Number of subjects who died by the specified study day.
HR is the ratio of the hazard of Death in each treatment group estimated from the Cox model. The ratio is Baricitinib + PBO + RDV to PBO + Dexamethasone + RDV.
HR for the 'Baseline Ordinal Score 5 or 6 and 'Any Baseline Ordinal Score' group is the hazard ratio from the stratified Cox Model.
P-value calculated using the stratified Log-rank test.
[a] [X] additional subjects are included in the 'Any Baseline Ordinal Score' row that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Programming Notes:

The p-value for the stratified log-rank test for the 'Any Baseline Ordinal Score' will only be reported if the p-value from the preceding elements of the hierarchical testing procedure are all < 0.05. Otherwise the p-value from the analysis including the 6 subgroup will be reported.

Tables with similar format:

Table 71: Time to Death through Day 15 and 29 by Treatment Group and Actual Baseline Ordinal Score – As Treated Population

Table 72: Time to Death through Day 15 and 29 by Treatment Group within Subgroups – mITT Population, Actual Baseline Ordinal Score 5 or 6

Table 73: Time to Death through Day 15 and 29 by Treatment Group: Medications of Interest Sensitivity Analysis – mITT Population, Actual Baseline Ordinal Score 5 or 6

Table 74: Time to Death through Day 15 and 29 by Treatment Group: Interaction Modeling – mITT Population, Actual Baseline Ordinal Score 5 or 6

Programming notes for Table 72:

Log-rank p-values will not be included in this table so the column will be removed. The Actual Baseline Ordinal Score column will be removed and to the left of the Study Day column, a column titled "Analysis/Subgroup" will be inserted. Rows will be generated for each subgroup. Actual baseline ordinal score will be excluded from this table.

Programming notes for Table 73:

Log-rank p-values will not be included in this table so the column will be removed. The table will include a column to the left of the "n" column titled "m". The corresponding footnote will read "m = Number of subjects reporting use of the medication of interest." The Actual Baseline Ordinal Score column will be removed and a "Medication of Interest" column will be inserted to the left of Study Day. Separate models will be fit with censoring based on the first date of use for each of the following categories of medications (see Section 6.4):

- Any Medication of Interest
- Antivirals
- COVID-19 Vaccination
- Treatments for COVID-19
- Monoclonal antibodies targeting the spike protein of SARS-CoV-2 including casirivimab, Imdevimab, and bamlanivimab
- Renin-angiotensin system (RAS) Inhibitors and HMG-CoA reductase inhibitors (Statins)
- Corticosteroids

- Other Anti-Inflammatory Drugs

The table will include the following footnote: “In this analysis, subjects that reported use of the specified medications of interest (Section 6.4) are censored at time of medication receipt.”

Programming notes for Table 74:

This table will only include the Treatment Group and HR columns only as well as a column to the left of Treatment Group titled “Interaction”. The following models will be run:

- “Treatment – Continuous Actual Baseline Ordinal Score” will include a treatment* baseline ordinal score interaction term.

For each interaction model, the p-value for the interaction term will be provided in a footnote reading “The p-value for the treatment by continuous baseline ordinal score interaction term was 0.xxxx.”.

Table 75: Time to Death through Day 15 and 29 by Treatment Group: Restricted Mean Survival Time Analysis – mITT Population, Actual Baseline Ordinal Score 5 or 6

Study Day	Treatment Group	Actual Baseline Ordinal Score	n	Restricted Mean Mortality Time (Days)		Difference	
				Estimate	95% CI	Estimate	95% CI
Day 15	Baricitinib + PBO + RDV (N=X)	5	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)		x	x.x	x.x, x.x		
	Baricitinib + PBO + RDV (N=X)	6	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)		x	x.x	x.x, x.x		
	Baricitinib + PBO + RDV (N=X)	Baseline Clinical Status 5 or 6	x	x.x	x.x, x.x	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)		x	x.x	x.x, x.x		
Repeat for Day 29							

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 Baricitinib + PBO + RDV and PBO + Dexamethasone + RDV.

Table 76: Subjects Experiencing Grade 3 or 4 AEs and SAEs through Day 29 by Treatment Group and Actual Baseline Ordinal Score – As Treated Population

Safety Event Outcome	Baricitinib + PBO + RDV			PBO + Dexamethasone + RDV		
	n	%	95% CI	n	%	95% CI
Baseline Ordinal Score 5 (N = X)						
Grade 3 or 4 AE	x	x	x.x, x.x	x	x	x.x, x.x
SAE	x	x	x.x, x.x	x	x	x.x, x.x
Baseline Ordinal Score 6 (N = X)						
Grade 3 or 4 AE	x	x	x.x, x.x	x	x	x.x, x.x
SAE	x	x	x.x, x.x	x	x	x.x, x.x
Baseline Ordinal Score 5 or 6 (N = X)						
Grade 3 or 4 AE	x	x	x.x, x.x	x	x	x.x, x.x
SAE	x	x	x.x, x.x	x	x	x.x, x.x
Any Baseline Ordinal Score[a] (N = X)						
Grade 3 or 4 AE	x	x	x.x, x.x	x	x	x.x, x.x
SAE	x	x	x.x, x.x	x	x	x.x, x.x

N = Number of subjects in the As Treated Population and specified actual baseline ordinal score stratum.
n = Number of subjects in a given treatment group who experienced the specified safety event outcome.
95% CI calculated using C-P/Blaker method.
[a] [X] additional subjects are included in the 'Any Baseline Ordinal Score' row that were enrolled with a baseline ordinal score of 4. [Include as applicable]

Table 77: Analysis of Time to Death, SAEs, or Grade 3 or 4 AEs by Treatment Group – As Treated Population

Actual Baseline Ordinal Score	Treatment Group	n	HR	
			Estimate	95% CI
Baseline Ordinal Score 5 (N=X)	Baricitinib + PBO + RDV (N=X)	X	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)	X		
Baseline Ordinal Score 6 (N=X)	Baricitinib + PBO + RDV (N=X)	X	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)	X		
Baseline Ordinal Score 5 or 6 (N=X)	Baricitinib + PBO + RDV (N=X)	X	x.xx	x.xx, x.xx
	PBO + Dexamethasone + RDV (N=X)	X		

N= Number of subjects in the As Treated Population and specified actual baseline ordinal score stratum.
n = Number of subjects who died or experienced SAEs or Grade 3 or 4 AEs.
HR is the ratio of the hazard of Death/SAE/AE of Grade 3 or 4 in each treatment group estimated from the Cox model. The ratio is Baricitinib + PBO + RDV to PBO + Dexamethasone + RDV.
HRs for the 'Baseline Ordinal Score 5 or 6' are the hazard ratios from the stratified Cox Model.
P-value calculated using the Log-rank test

Table 78: Culture Results by Treatment Group and Infection AE Severity – As Treated Population

Anatomical Location	Pathogen	Baricitinib + PBO + RDV (N=X)									PBO + Dexamethasone + RDV (N=X)								
		Severe			Life-Threatening			Death			Severe			Life-Threatening			Death		
		n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Any Location	Any Pathogen	x	x	x	x	x	X	x	x	x	x	x	x	x	x	x	x	x	x
Location 1	Any Pathogen	x	x	x	x	x	X	x	x	x	x	x	x	x	x	x	x	x	x
	Pathogen 1	x	x	x	x	x	X	x	x	x	x	x	x	x	x	x	x	x	x
	Pathogen 2	x	x	x	x	x	X	x	x	x	x	x	x	x	x	x	x	x	x
Location 2	Any Pathogen	x	x	x	x	x	X	x	x	x	x	x	x	x	x	x	x	x	x
	Pathogen 1	x	x	x	x	x	X	x	x	x	x	x	x	x	x	x	x	x	x
	Pathogen 2	x	x	x	x	x	X	x	x	x	x	x	x	x	x	x	x	x	x

Note: Percents may not add to 100 because participants may have infections with multiple pathogens.
N=Number of participants randomized to Treatment group.
n=Number of participants with infection.

Table 79: New Infections by Treatment Group – As Treated Population, Actual Baseline Ordinal Score 5

Preferred Term	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)			Risk Difference	
	n	%	Events	n	%	Events	%	95% CI
Any New Infection	x	x	x	x	x	x	x.x	x.x, x.x
PT 1	x	x	x	x	x	x	x.x	x.x, x.x
PT 2	x	x	x	x	x	x	x.x	x.x, x.x
Etc.	x	x	x	x	x	x	x.x	x.x, x.x

N = Number of subjects in the As Treated Population.
n = Number of subjects reporting event.
Events = Total frequency of events reported.
New infections were identified by the site.

Tables with similar format:

Table 80: Opportunistic New Infections by Treatment Group – As Treated Population, Actual Baseline Ordinal Score 5

Table 81: New Infections by Treatment Group – As Treated Population, Actual Baseline Ordinal Score 6

Table 82: Opportunistic New Infections by Treatment Group – As Treated Population, Actual Baseline Ordinal Score 6

Table 83: New Infections by Treatment Group – As Treated Population, Actual Baseline Ordinal Score 5 or 6

Table 84: Opportunistic New Infections by Treatment Group – As Treated Population, Actual Baseline Ordinal Score 5 or 6

Table 85: New Infections by Treatment Group by Dexamethasone Prior to Enrollment – As Treated Population, Actual Baseline Ordinal Score 5 or 6

Table 86: Opportunistic New Infections by Treatment Group by Dexamethasone Prior to Enrollment – As Treated Population, Actual Baseline Ordinal Score 5 or 6

Programming Notes for Table 80, Table 82, Table 84, and Table 86:

Opportunistic infections will be identified by a Standardized MedDRA Query among the new infections identified by the site.

Table 87: VTEs by Treatment Group – As Treated Population, Actual Baseline Ordinal Score 5 or 6

Preferred Term	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)			Risk Difference	
	n	%	Events	n	%	Events	%	95% CI
Any VTE	**x**	**x**	**x**	**x**	**x**	**x**	**x.x**	**x.x, x.x**
PT 1	x	x	x	x	x	x	x.x	x.x, x.x
PT 2	x	x	x	x	x	x	x.x	x.x, x.x
Etc.	x	x	x	x	x	x	x.x	x.x, x.x

N = Number of subjects in the As Treated Population.
n = Number of subjects reporting event.
Events = Total frequency of events reported.
New infections were identified by the site.

Programming note: superficial venous thrombosis is not included as a VTE.

Table 88: Abnormal Laboratory Results of Grade 3 or 4 by Parameter, Maximum Severity, Time Point, and Treatment Group – As Treated Population, Actual Baseline Ordinal Score of 5 or 6

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

Programming Note: Vitamin D, D-dimer and CRP results are not included in this table. Include all lab parameters that are being graded in this table.

Table 89: Treatment-Emergent Laboratory Abnormalities - As Treated Population, Actual Baseline Ordinal Score of 5 or 6

Laboratory Parameter	Maximum Post Baseline Grade	Baricitinib + PBO + RDV (N=X)			PBO + Dexamethasone + RDV (N=X)		
		N	n	%	N	n	%
Any Parameter	1	x	x	x	x	x	x
	2	x	x	X	x	x	x
	3	x	x	X	x	x	x
	4	x	x	X	x	x	x
	Any Grade	x	x	X	x	x	x
Continue for all graded parameters							

N = number of subjects in the As Treated Population with any post-baseline data available for the specified Lab Parameter.
n = number of subjects in the As Treated Population with treatment emergent abnormalities for the specified Lab Parameter.
A treatment emergent laboratory abnormality is defined as a post-baseline abnormal value with a severity grade greater than at baseline.

Table 90: Summary Statistics of Laboratory Results by Parameter, Study Visit Day, and Treatment Group – As Treated Population, Actual Baseline Ordinal Score 5 or 6

Laboratory Parameter	Study Visit Day	Treatment Group	Absolute					Change from Baseline				
			N	Mean	95% CI	Median	Min, Max	N	Mean	95% CI	Median	Min, Max
Parameter 1	Baseline	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	---	---	---	---	---
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	---	---	---	---	---
	Day 3	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 5	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 8	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 11	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 15	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
	Day 29	Baricitinib + PBO + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
		PBO + Dexamethasone + RDV	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x	x	xx.x	xx.x, xx.x	xx.x	xx.x, xx.x
Continue for all parameters…Table												
N = Number of subjects in the As Treated Population with laboratory data available for the parameter at the specified study visit.												

Programming Note: Include all lab parameters in this table except d-dimer and CRP which are in table.

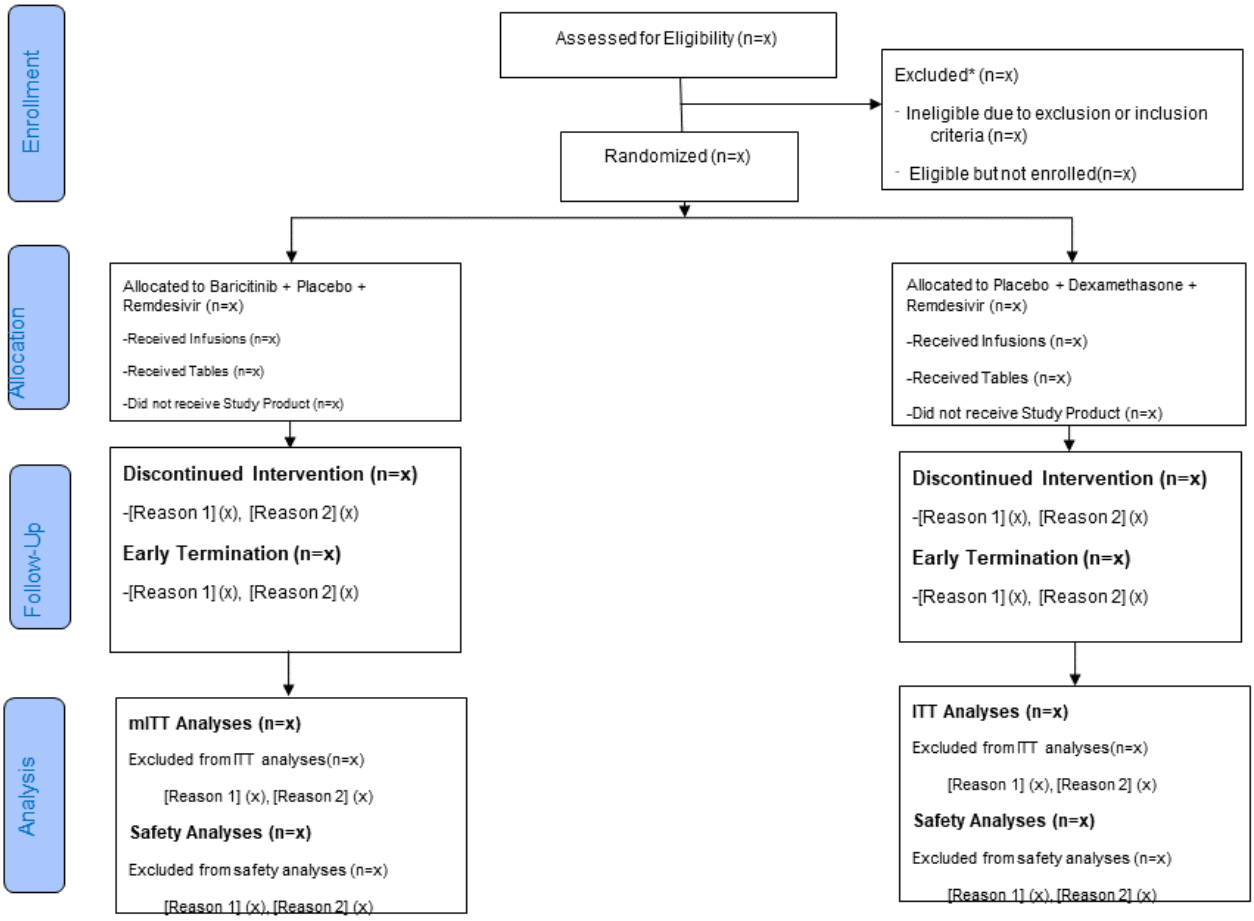
APPENDIX 2. FIGURE MOCK-UPS

General Programming Notes for figures:

- Treatment group labeling will be the following:
  - Baricitinib + PBO + RDV
  - PBO + Dexamethasone + RDV
- If the treatment group labels need to be abbreviated to improve fit, the following abbreviations will be used:
  - B + R
  - D + R
- Use the same color for a treatment on the different graphs (SAS standard colors):
  - Baricitinib + PBO + RDV = Blue
  - PBO + Dexamethasone + RDV = Red
- For severity graphs (SAS standard colors):
  - Mild = yellow
  - Moderate = orange
  - Severe = red
  - Life-threatening = brown
  - Death = black

LIST OF FIGURES

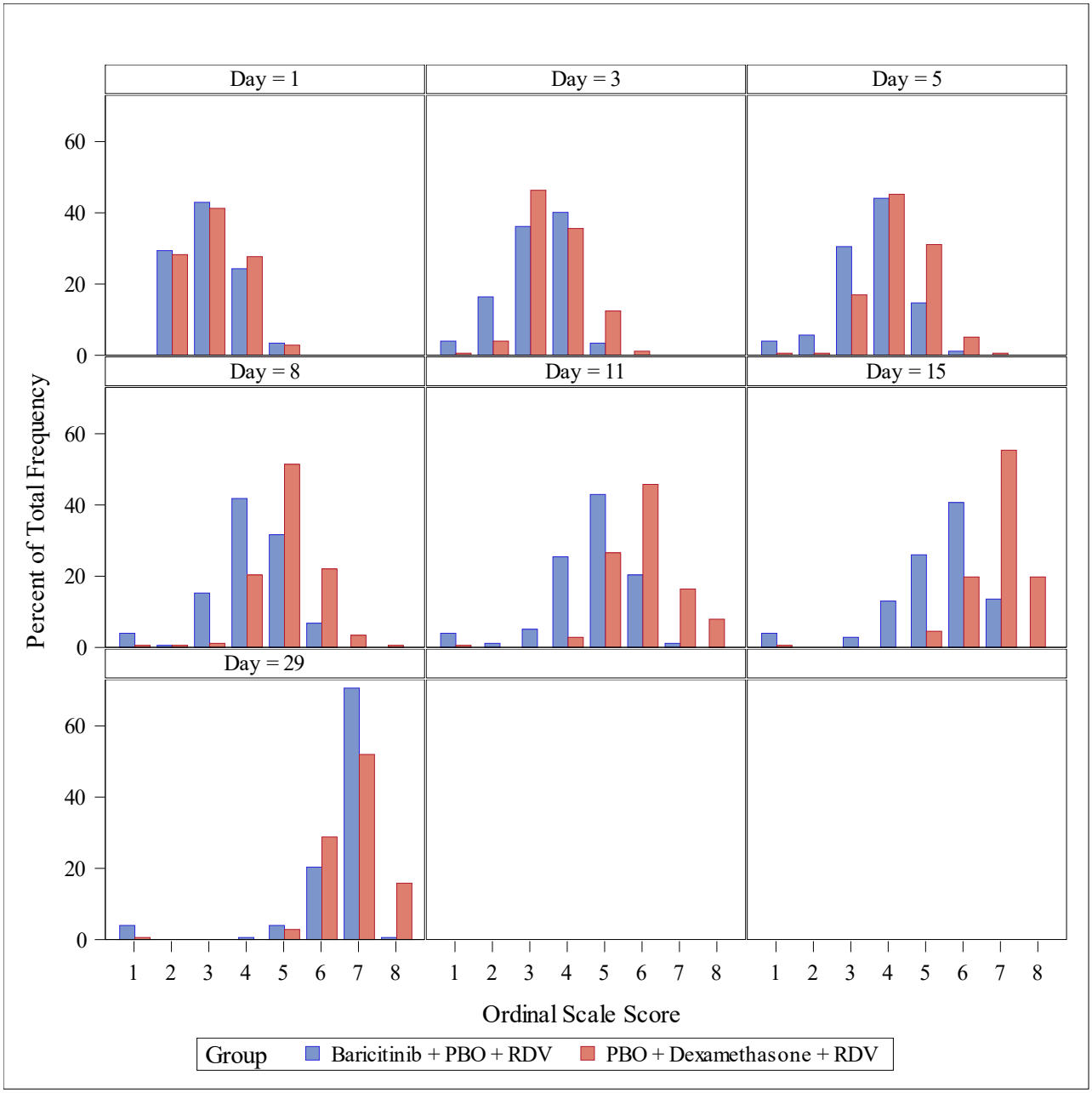
Figure 2: CONSORT Flow Diagram



Programming Note:

Diagram will collapse across baseline ordinal score strata. Content of individual boxes may be altered from the shell.

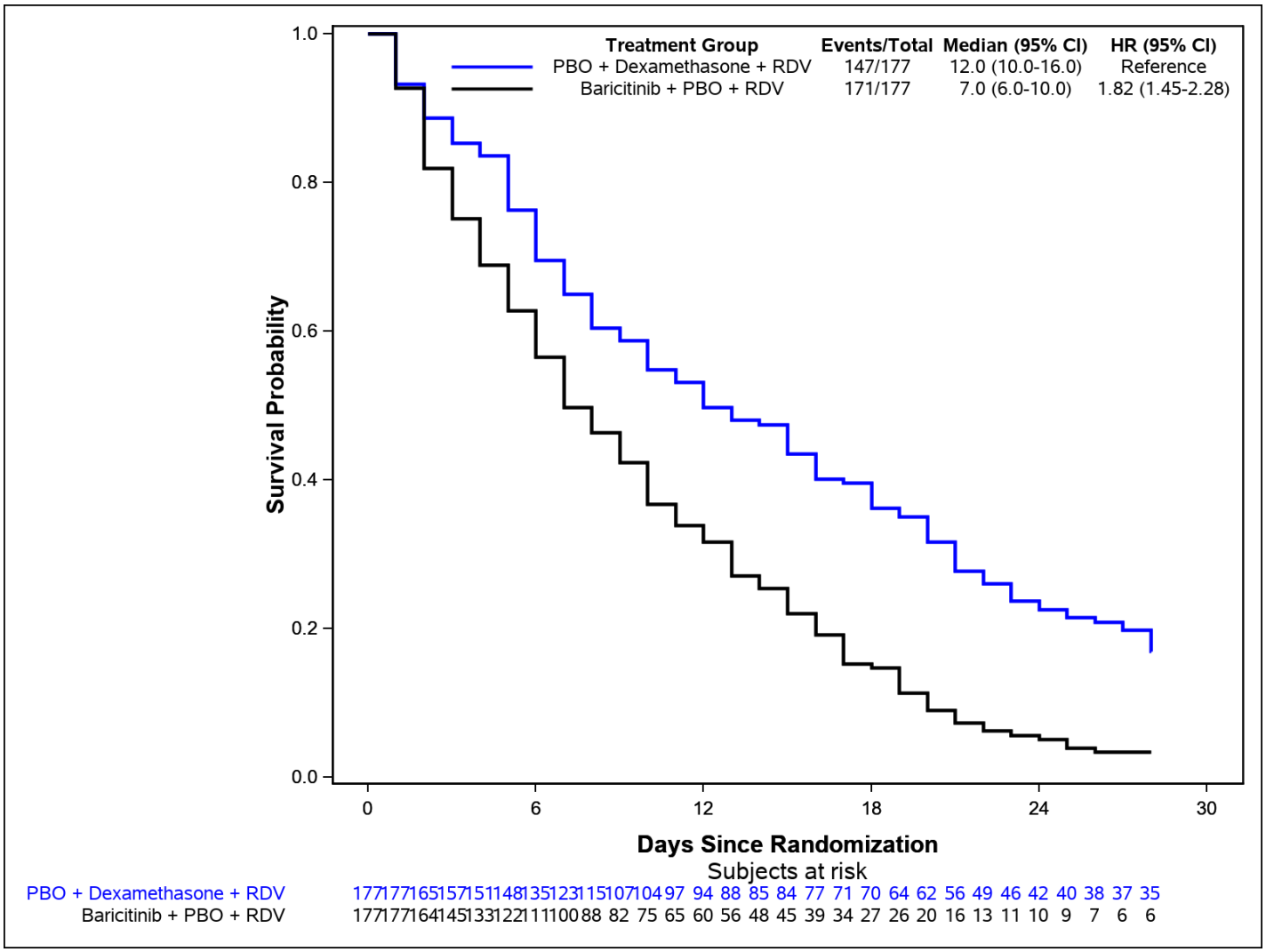
Figure 3: Number of Subjects that Early Terminated from the Study by Study Day and Hospitalization Status for Last Ordinal Score Collected, Actual Baseline Ordinal Score – mITT Population



Programming Notes:

The shell above is a generic shell. For the panels, the rows will be, going top to bottom, “All Subjects”, “Baricitinib + PBO + RDV” and “PBO + Dexamethasone + RDV”. The columns will be, going left to right, “Ordinal Score 5”, and “Ordinal Score 6”. Within each panel, the x-axis will be labeled “Study Day of Last Ordinal Score” and will have a tick at each Study Day. The blue bars will be “Hospitalized” and the red bars will be “Not Hospitalized”.

Figure 4: Kaplan-Meier Curve of Mechanical Ventilation Free Survival through Day 29 by Treatment Group – mITT Population

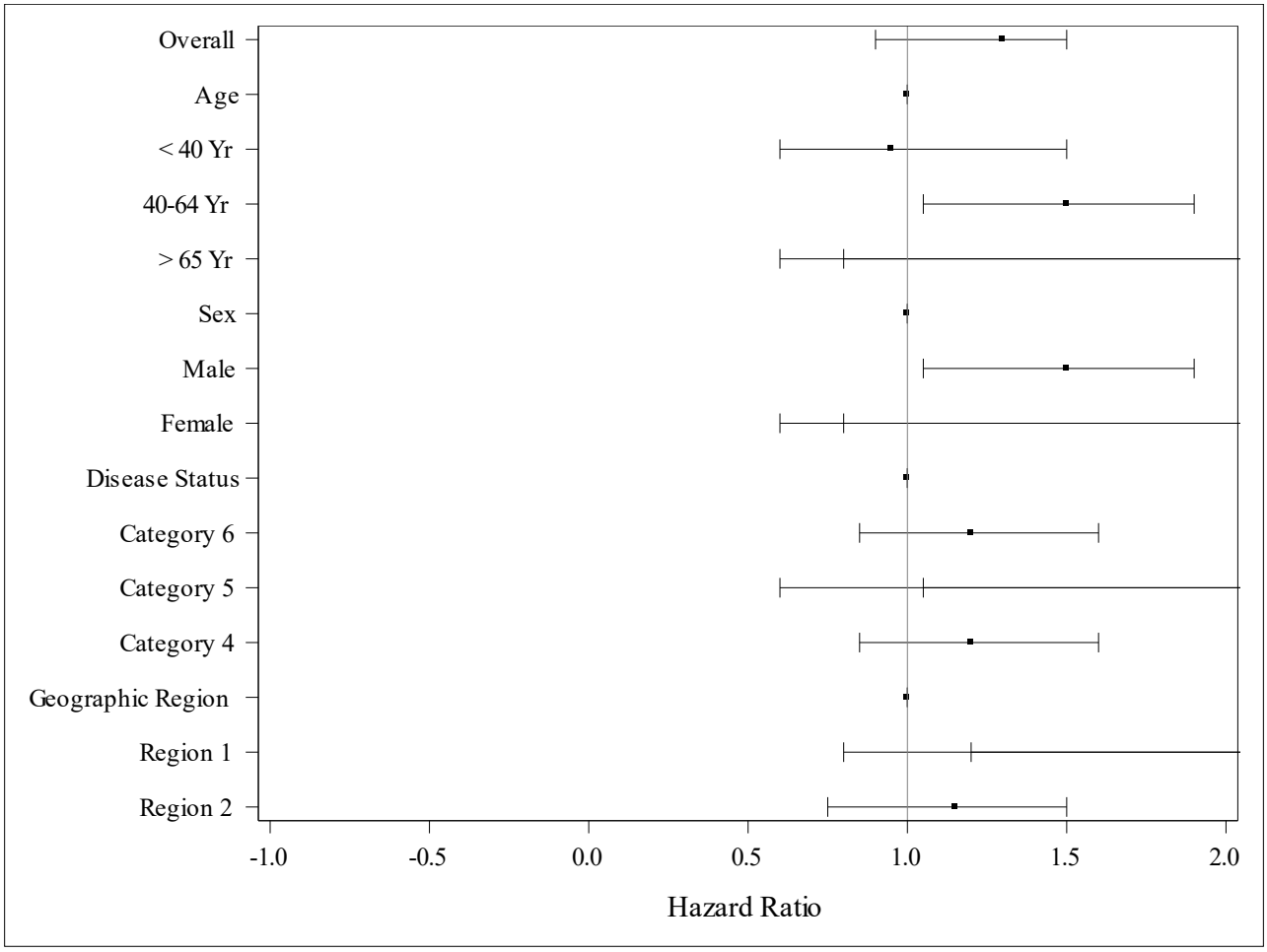


Programing Note:

Include p-value from stratified Chi-Square test as in Klein (2007).

Figures with similar format:

Figure 8: Forest Plot of Hazard Ratios of Mechanical Ventilation Free Survival by Subgroup - mITT Population



Figures with similar format:

Figure 9: Forest Plot of Hazard Ratios of Mechanical Ventilation Free Survival by Subgroup - mITT Population, Actual Baseline Clinical Status of 5

Figure 10: Forest Plot of Hazard Ratios of Mechanical Ventilation Free Survival by Subgroup - mITT Population, Actual Baseline Clinical Status of 6

Figure 11: Forest Plot of Hazard Ratios of Mechanical Ventilation Free Survival by Comorbidity - mITT Population

Figure 12: Forest Plot of Hazard Ratios of Mechanical Ventilation Free Survival: Leave One Site Out Sensitivity Analysis - mITT Population

Figure 13: Study Visit Day 15 Clinical Status Score by Baseline Ordinal Score and Treatment Group – mITT Population

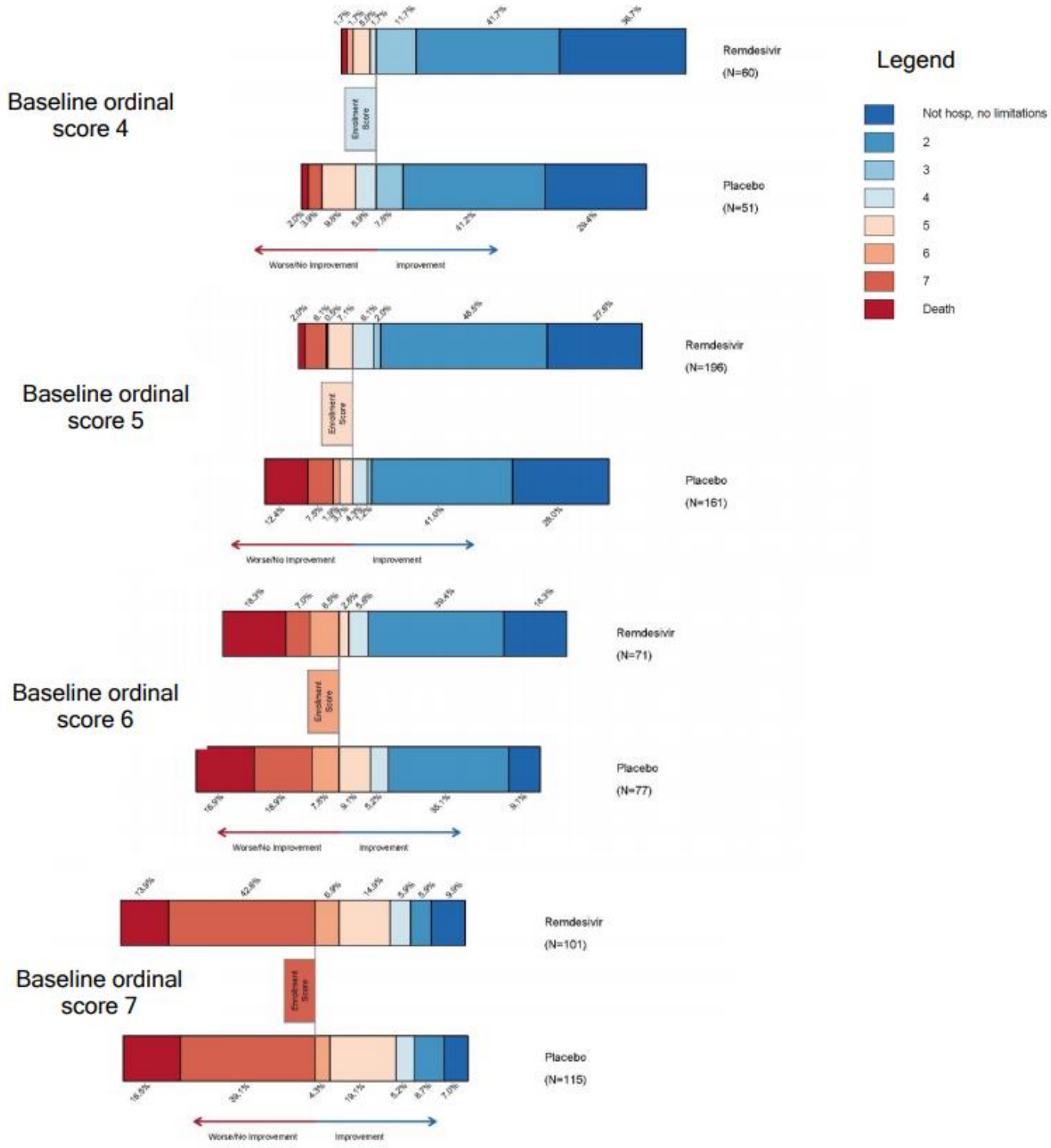


Figure 14: Kaplan-Meier Curves of Time to Improvement by at Least One Category of Clinical Status Score by Treatment Group – mITT Population, Actual Baseline Ordinal Score 5 or 6

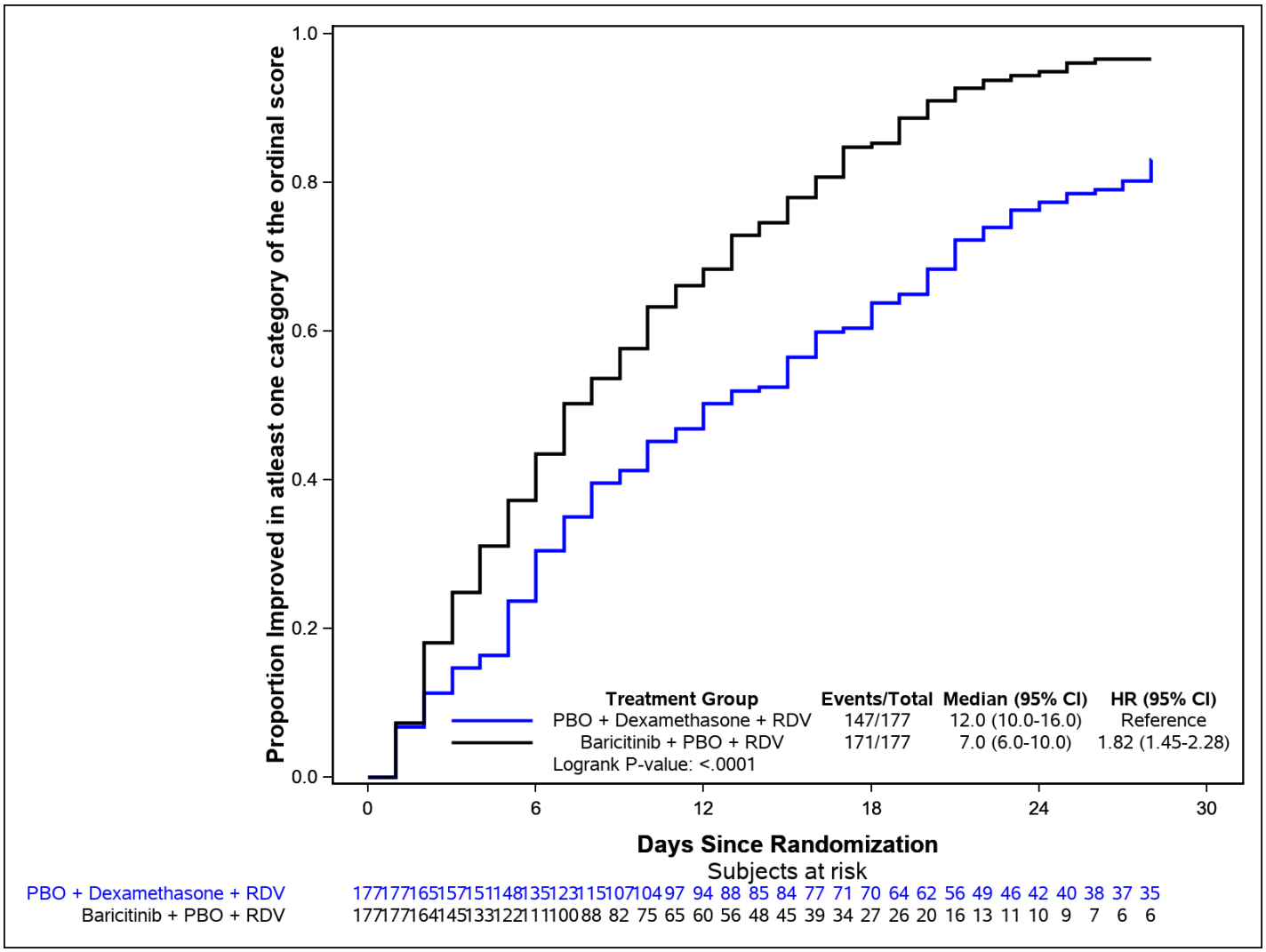
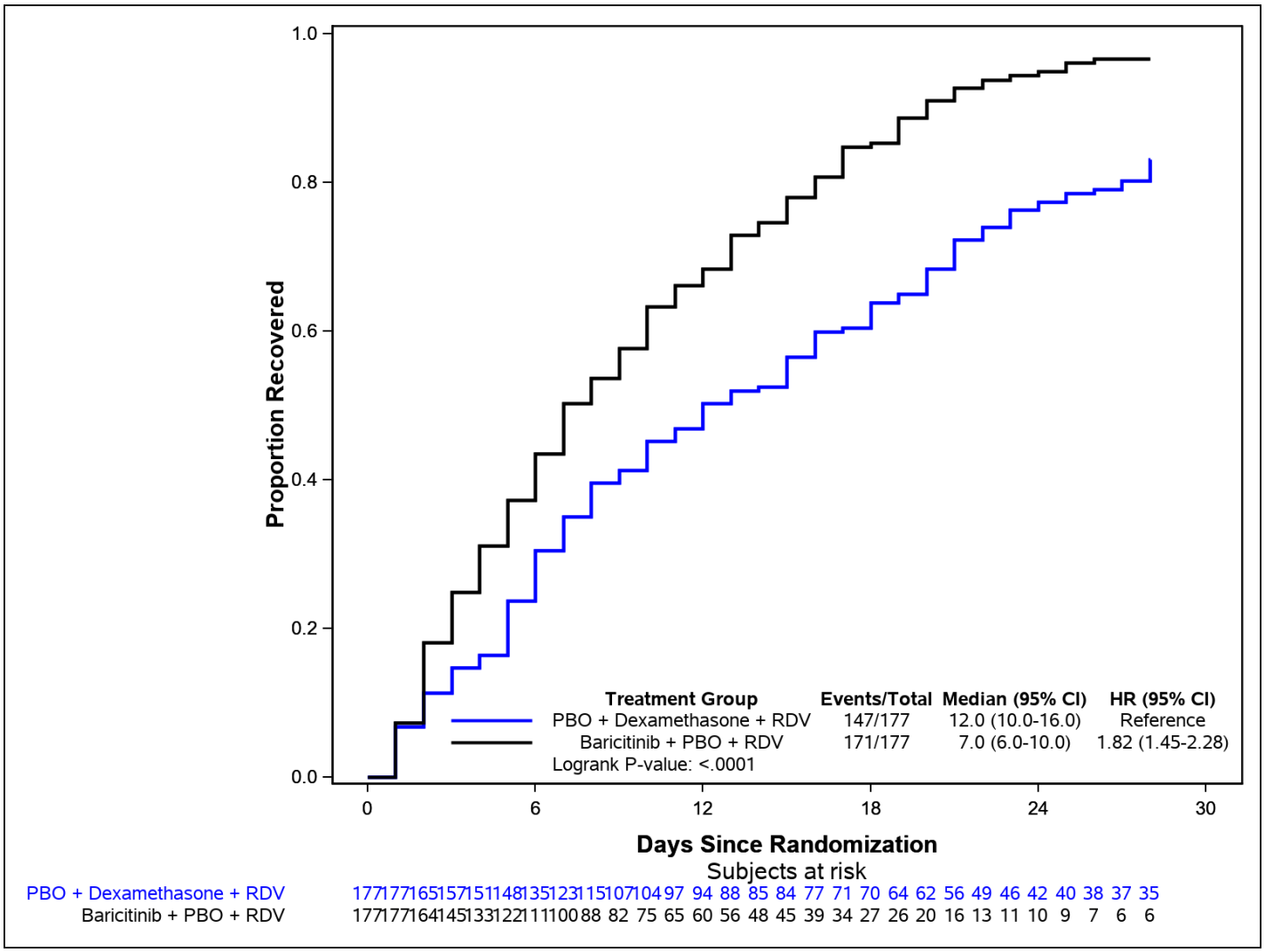


Figure 15: Kaplan-Meier Curves of Time to Recovery by Day 29 by Treatment Group – mITT Population



Programming Note:

For Subjects at risk counts, only display Days 1, 3, 5, 8, 11, 15, 22, 29.

Figures with similar format:

Figure 16: Kaplan-Meier Curve of Time to Recovery by Day 29 by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5

Figure 17: Kaplan-Meier Curve of Time to Recovery by Day 29 by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 6

Figure 18: Forest Plot of Hazard Ratios of Time to Recovery by Day 29 by Subgroup - mITT Population

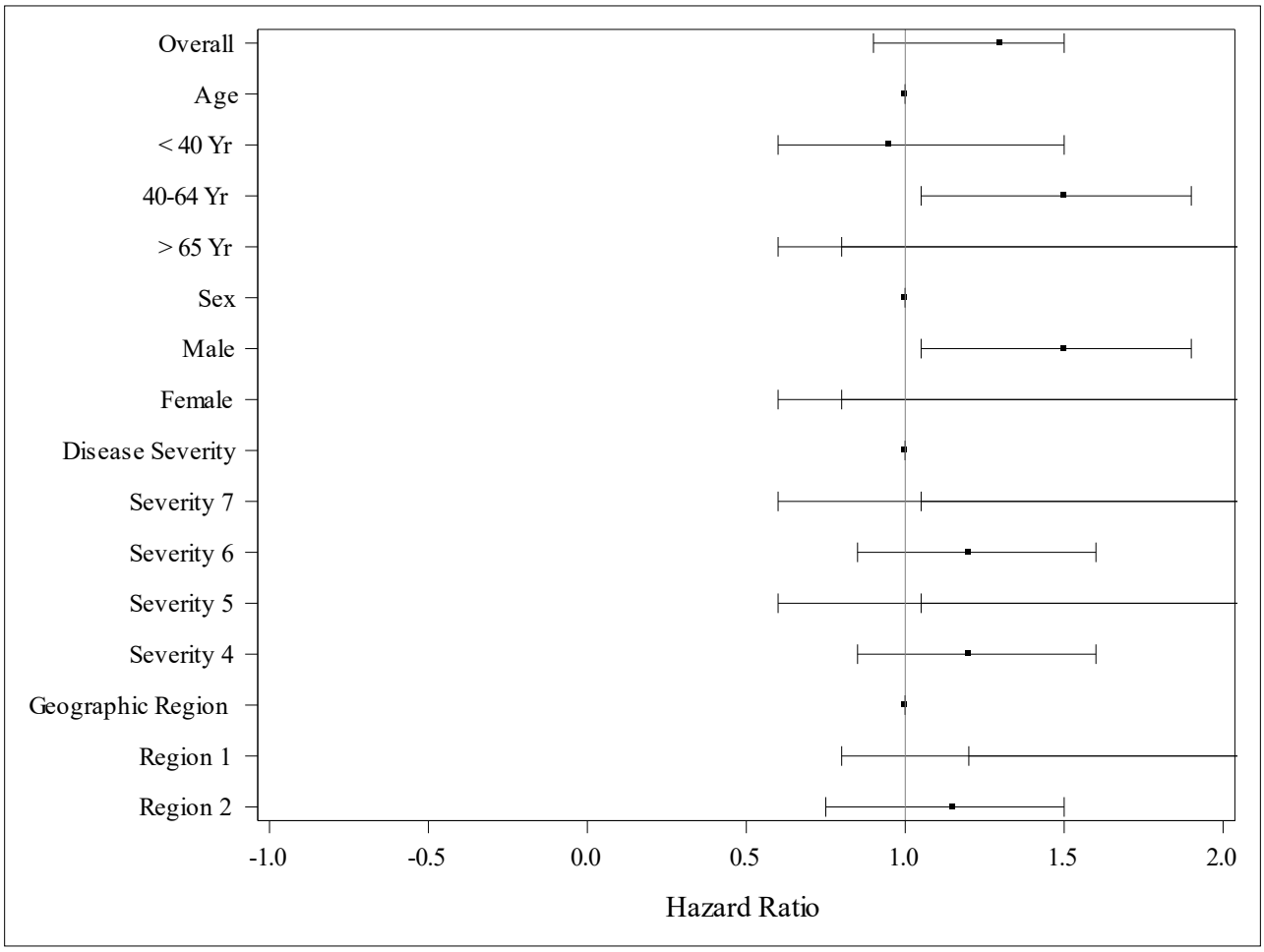
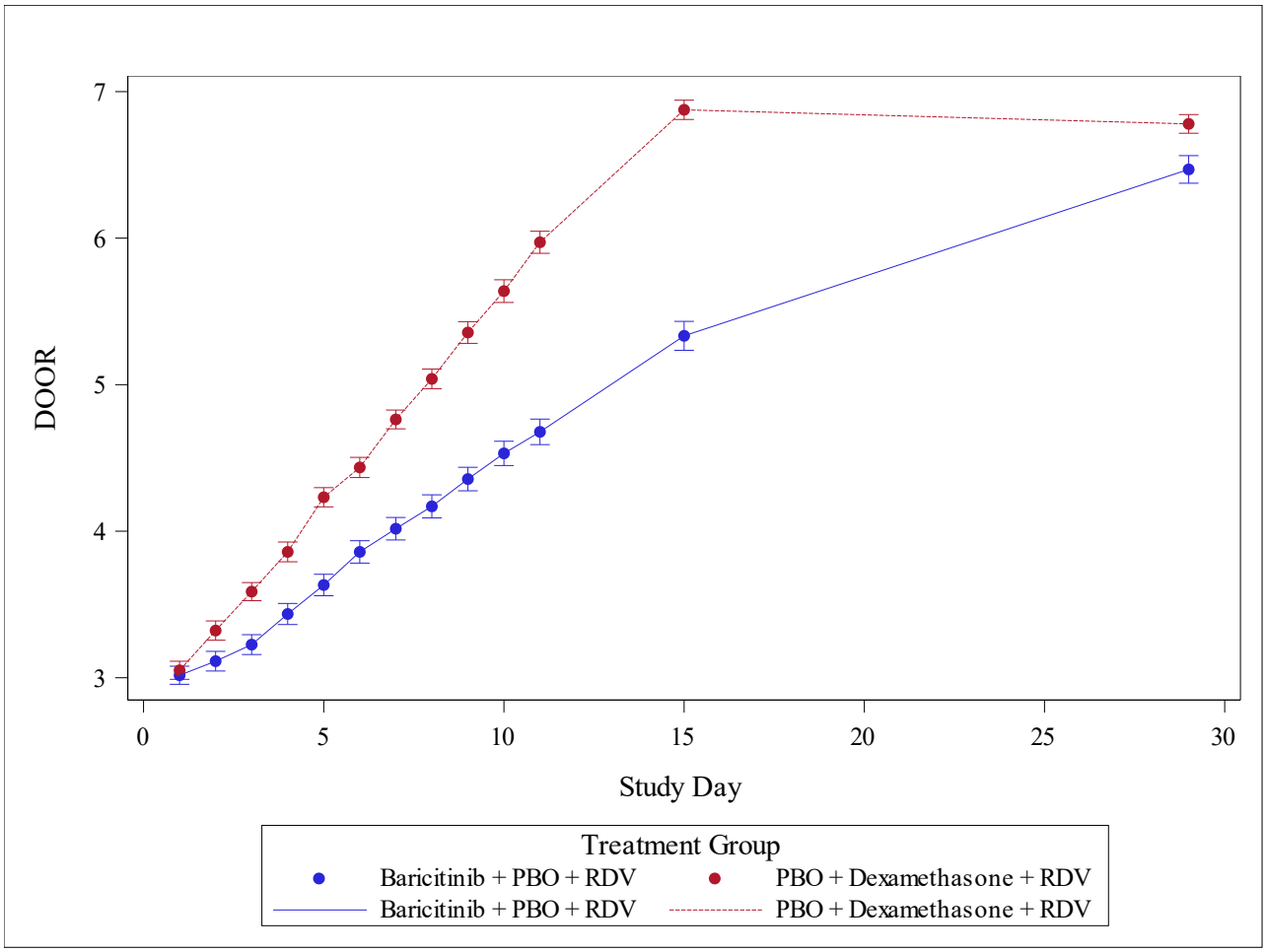


Figure with similar format:

Figure 19: Forest Plot of Hazard Ratios of Time to Recovery by Day 29 by Comorbidity - mITT Population

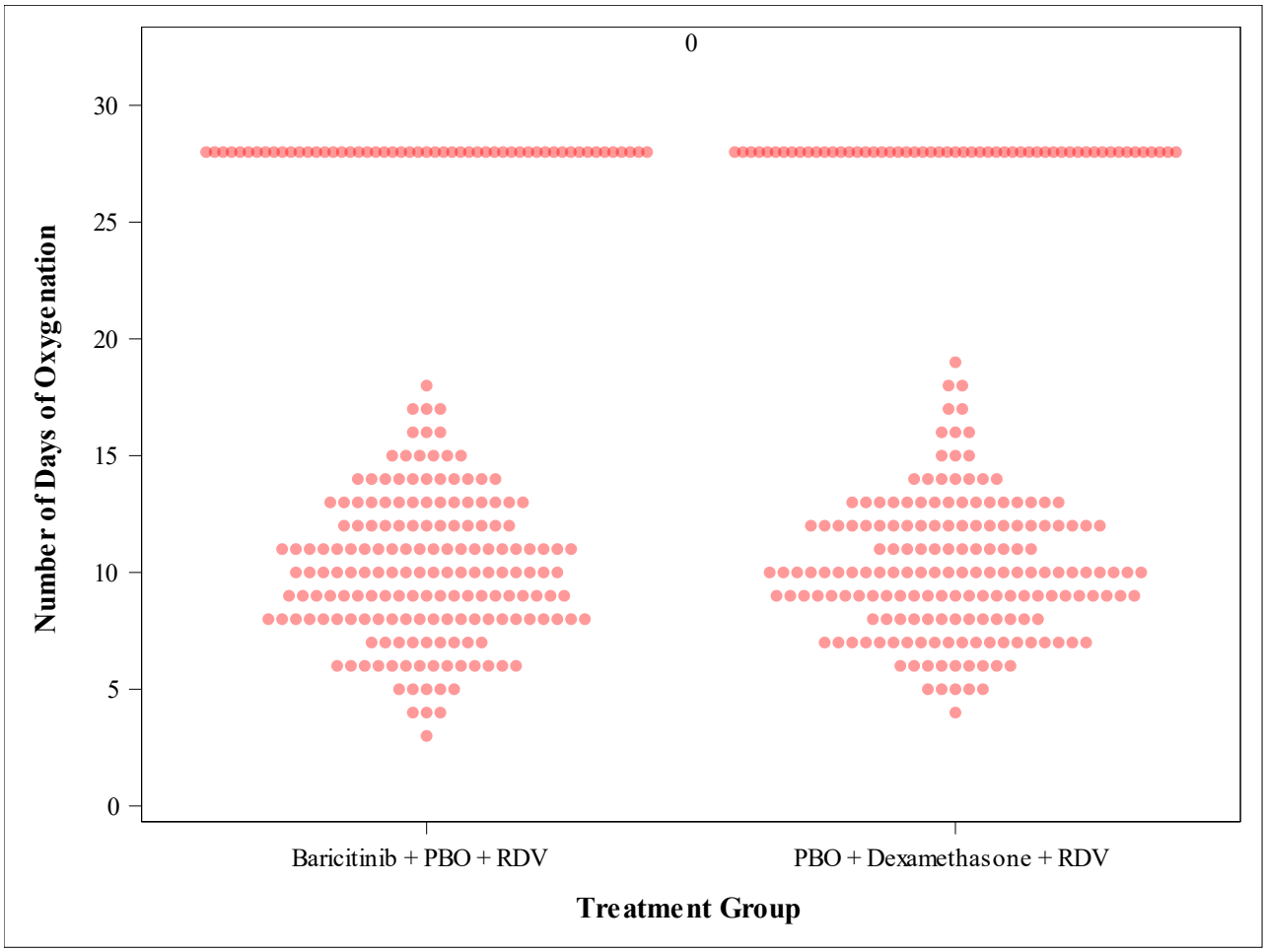
Figure 20: Mean DOOR by Day and Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5 or 6



Programming Note:

Bars reflect the CIs. No Day 0 will be available.

Figure 21: Bee Swarm Plot of Oxygen Days by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5 or 6



Programming Note:

Use the format used for ACTT-1 which incorporated summary statistics.

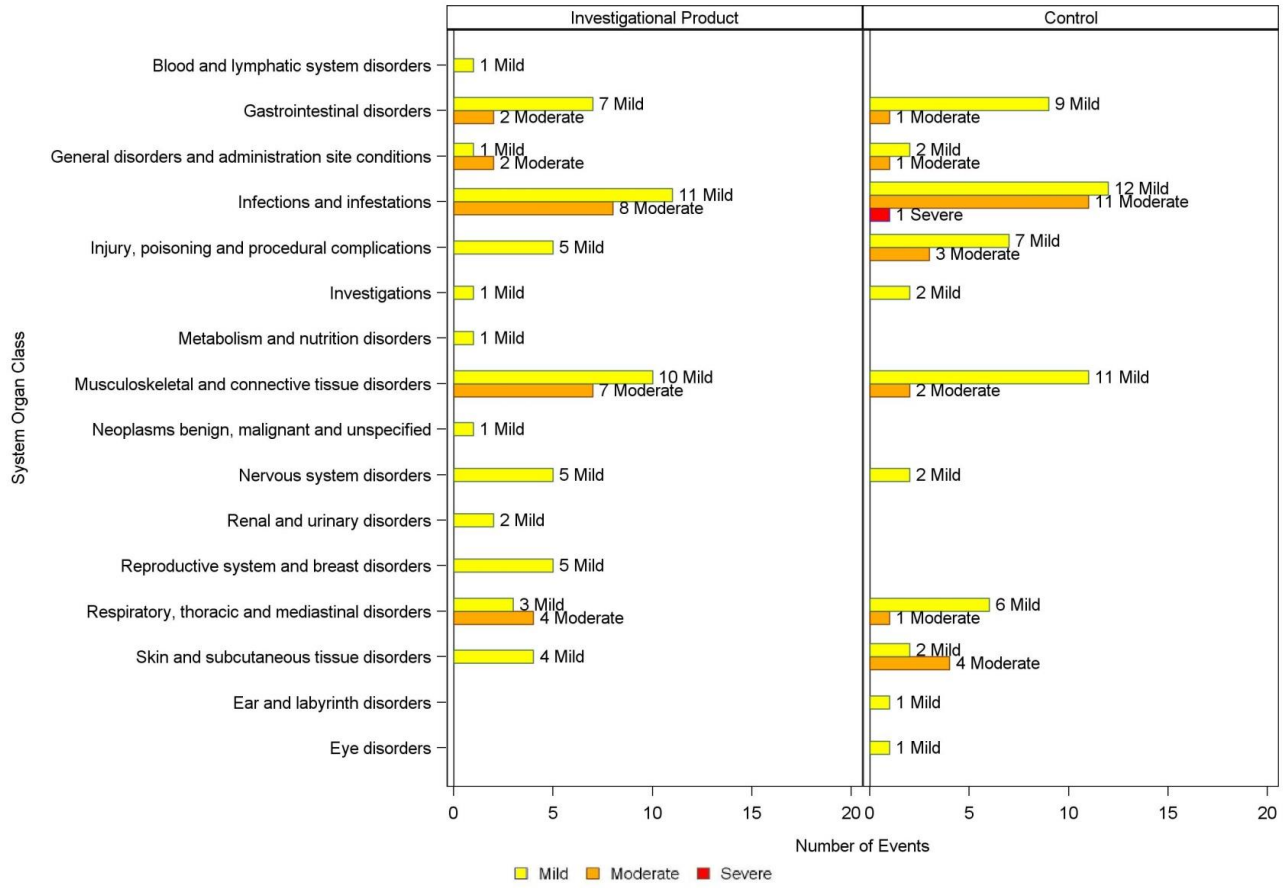
Figures with similar format:

Figure 22: Bee Swarm Plot of Non-Invasive Ventilation/High-Flow Oxygen Days by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5 or 6

Figure 23: Bee Swarm Plot of Invasive Mechanical Ventilation/ECMO Days by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5 or 6

Figure 24: Bee Swarm Plot of Hospitalization Days by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5 or 6

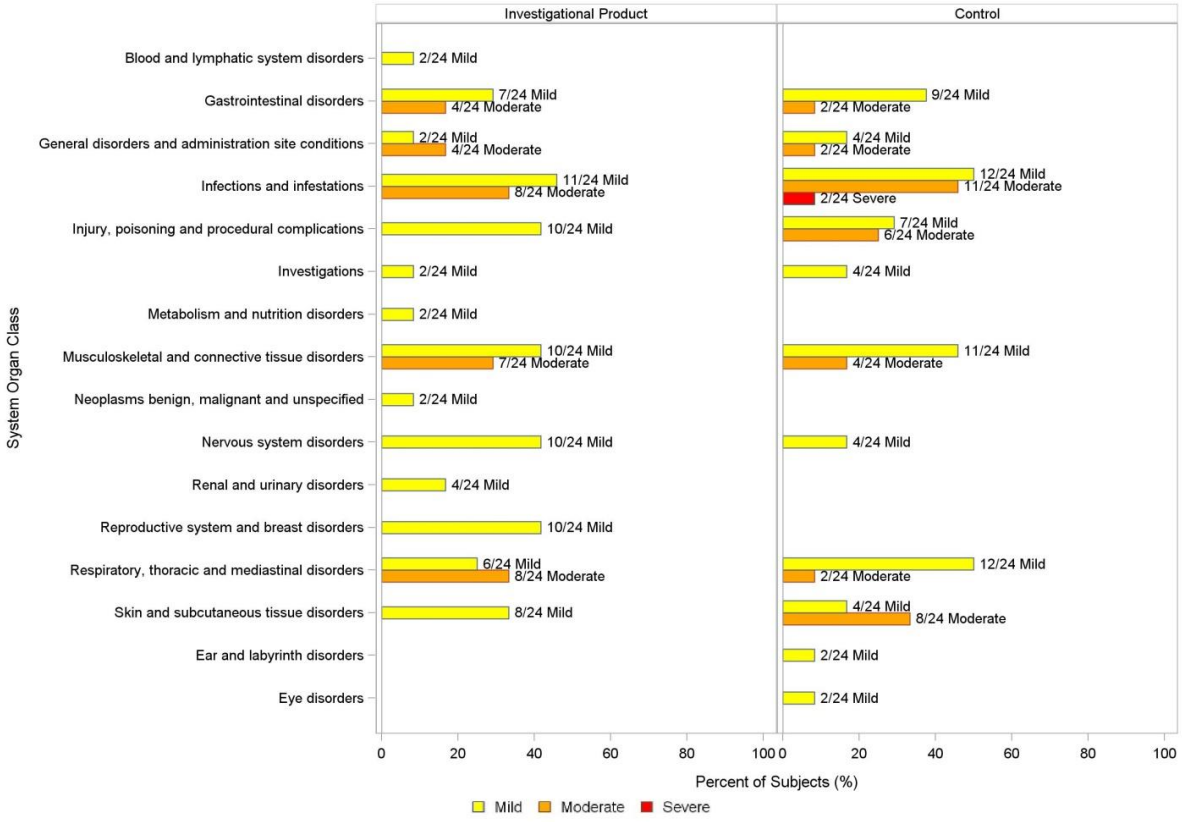
Figure 25: Frequency of Non-Serious Related Adverse Events by MedDRA System Organ Class, Severity, and Treatment Group - As Treated Population, Actual Baseline Ordinal Score



Programming Note:

Two separate sub-figures will be generated for each actual baseline ordinal score.

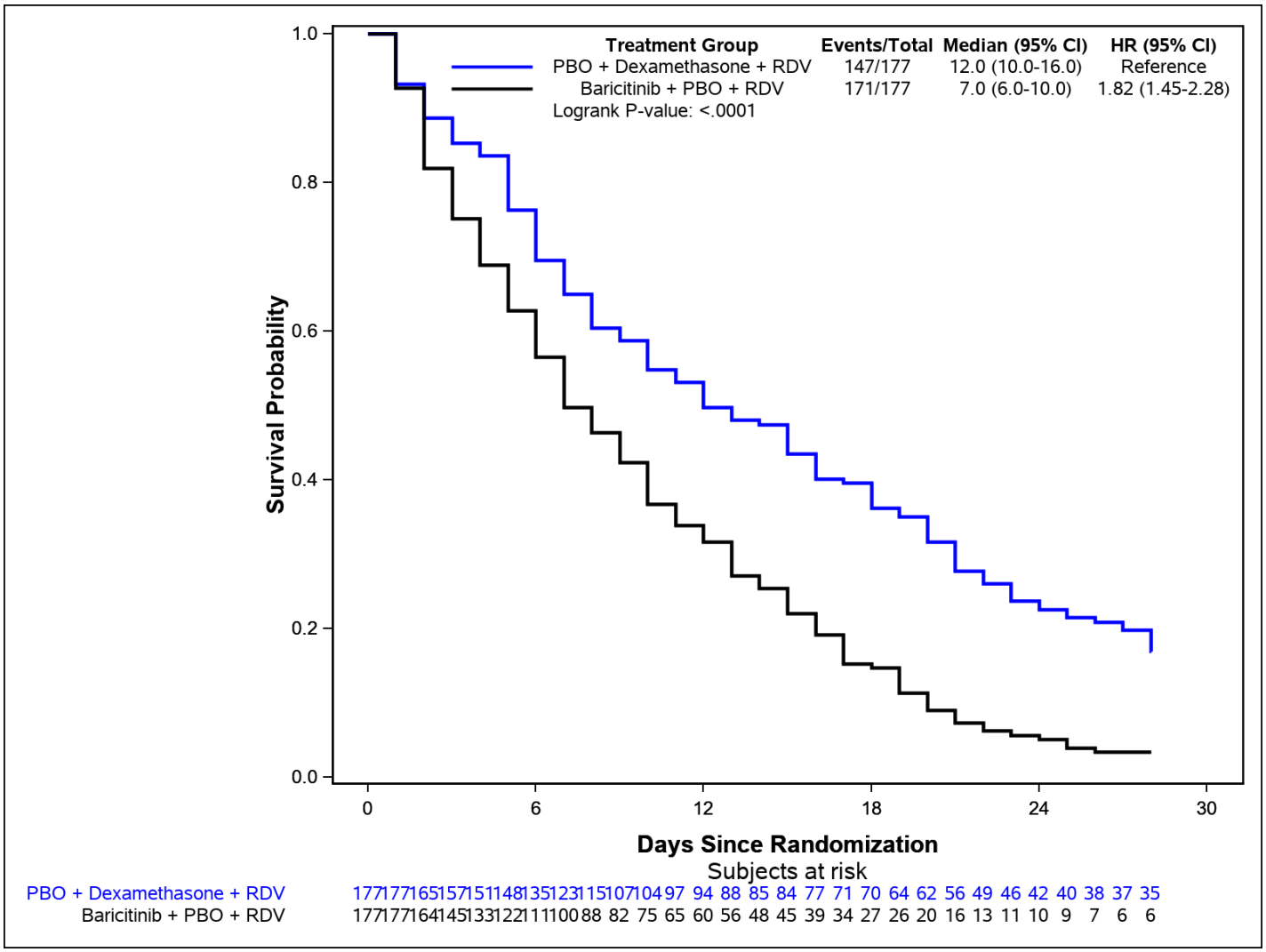
Figure 26: Incidence of Non-Serious Related Adverse Events by MedDRA System Organ Class, Severity, and Treatment Group - As Treated Population, Actual Baseline Ordinal Score



Programming Note:

Two separate sub-figures will be generated for each actual baseline ordinal score. Add footnote that Relationship is defined as related to any study product (remdesivir, baricitinib/placebo, dexamethasone/placebo).

Figure 27: Kaplan-Meier Curve of Time to Death through Day 29 by Treatment Group – mITT Population



Figures with similar format:

Figure 28: Kaplan-Meier Curve of Time to Death through Day 29 by Treatment Group – As Treated Population

Figure 29: Kaplan-Meier Curve of Time to Death through Day 29 by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5

Figure 30: Kaplan-Meier Curve of Time to Death through Day 29 by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 6

Figure 31: Kaplan-Meier Curve of Time to Death or Progression to Clinical Status 6, 7, or 8 through Day 29 by Treatment Group – mITT Population, Actual Baseline Ordinal Score of 5

Figure 32: Kaplan-Meier Curve of Time to Death or Progression to Clinical Status 6, 7, or 8 through Day 29 by Treatment Group – As Treated Population, Actual Baseline Ordinal Score of 5

Figure 33: Kaplan-Meier Curve of Time to Death, SAE, or Grade 3 or 4 AE through Day 29 by Treatment Group – As Treated Population

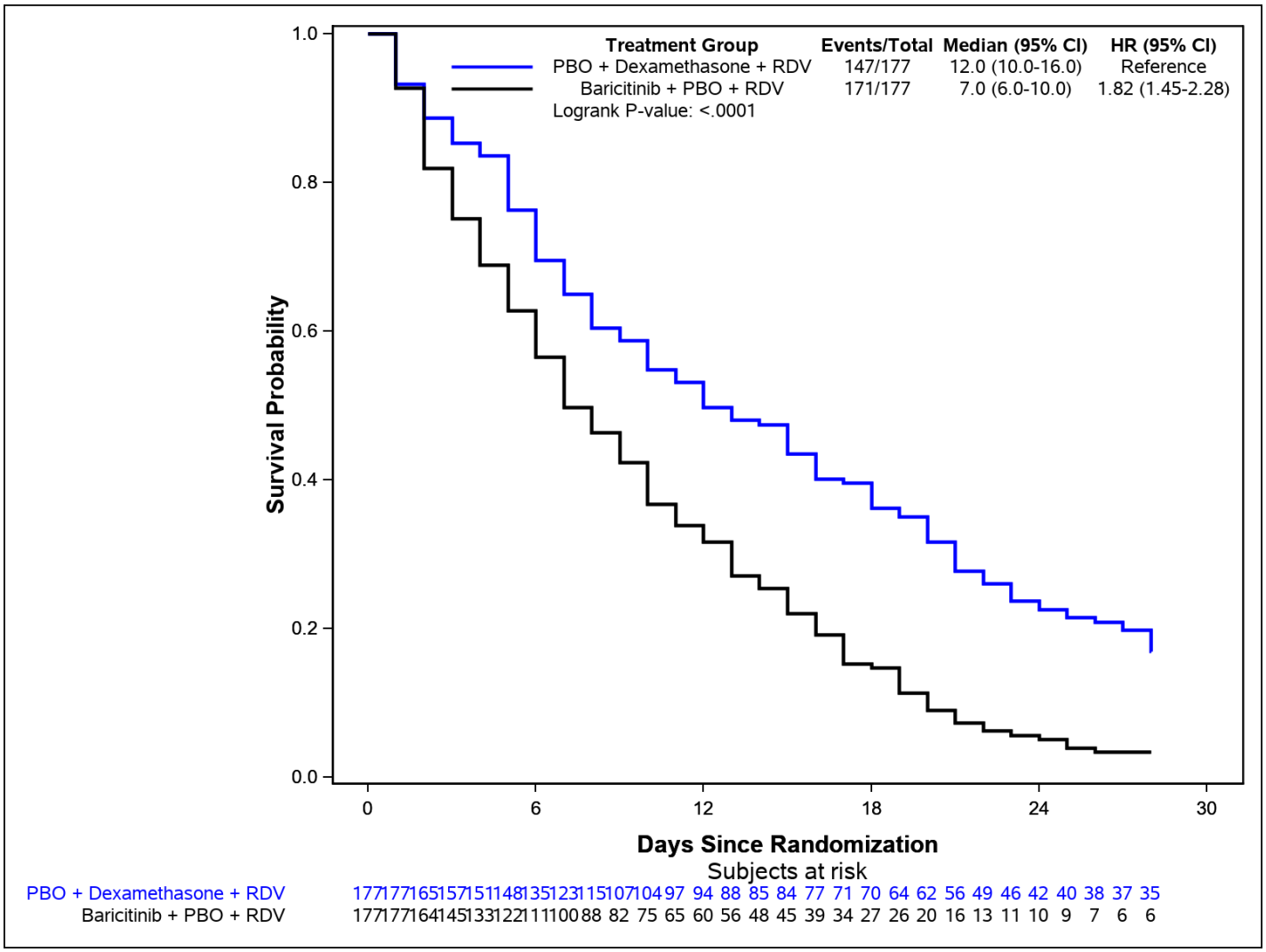
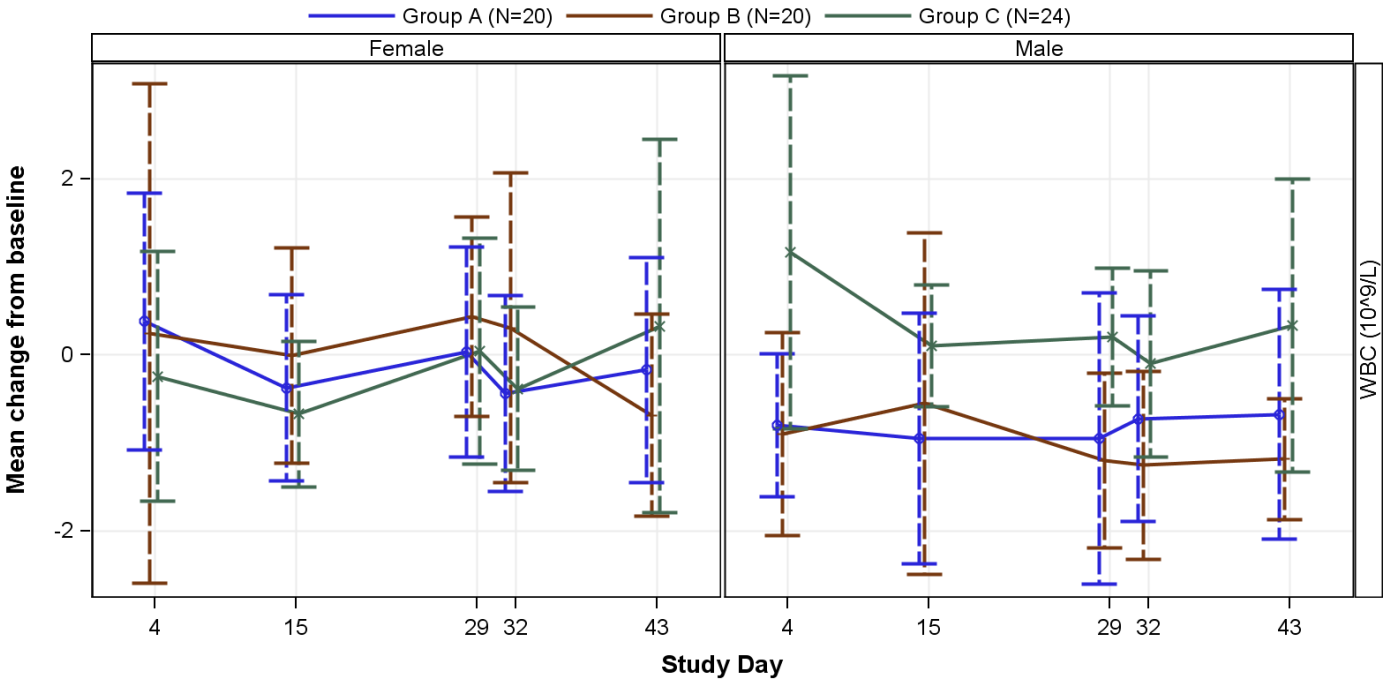


Figure 34: [Parameter X] Results by Scheduled Visits: Change from Baseline by Treatment Group – As Treated Population



Programming Note:

The shell provided is a generic figure. The Groups within a panel will be treatment groups and the panels will be actual baseline ordinal score (5 or 6). The points will be the median change from baseline and the bars will represent the Q1 and Q3 quartiles of the change from baseline at each time point. Panels for each laboratory parameter will be generated.

APPENDIX 3. LISTINGS MOCK-UPS

TABLE OF LISTINGS

Listing 1: Exclusions from the As Treated Population

Planned Treatment Group	Actual Baseline Ordinal Score	Subject ID
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	XXXXX

Programming Notes:

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

Listing 2: Subjects Who Early Terminated or Discontinued Treatment

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Category	Treatment Discontinued	Reason for Early Termination or Treatment Discontinuation	Study Day
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	XXXXX	Early Termination/Treatment Discontinuation	NA/Infusions/Tablets	Xxxxxx	xxxx

Programming Notes:

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 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?	Comments
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4	Xxxxx	xx	xxx	Major/Minor	xxx	x	xxxx	Yes/No	Yes/No	Yes/No	xxxx

Programming Notes:

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	Comments
xxxx	xxxx	xxxx	xxxx	Major/Minor	xxxx	Yes/No	Yes/No	xxxx	Xxxxx

Programming Notes:

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: Individual Efficacy Response Data: Ordinal Score Data

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Study Visit Day of Assessment	Actual Study Day of Assessment	Ordinal Score	Ordinal Status
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4	xxxxx	xx	xx	xx	xxxxx

Programming Notes:

Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e. 6, then 5 then 4), USUBJID, Study Day. Ordinal status should match the wording of the scale definitions in Section 4.3.

Listing 6: Individual Efficacy Response Data: DOOR

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Study Visit Day of Assessment	Actual Study Day of Assessment	DOOR	Ordinal Score	SAE/Death	Severe AE
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	xxxxx	xx	xx	1/2/3/4/5/6/7	xxxxx	Yes/No	Yes/No

Programming Notes:

Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e. 6, then 5 then 4), USUBJID, Study Visit Day. SAE/Death and Severe AE are No until a subject experiences an event, and Yes for every study visit day thereafter.

Listing 7: Demographic Data

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Geographic Region	Sex	Age at Randomization (years)	Ethnicity	Race	Duration of Symptoms prior to Randomization (Days)	Weight (Kg)	Height (Cm)	BMI
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	xxxxx	xxx	xxx	Xx	xxx	xxx	xxx	xx	Xx	Xxx

Programming Notes:

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

Listing 8: Pre-Existing and Concurrent Medical Conditions

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	History of DVT or PE	Major Surgery, Significant Trauma, Long Hospitalization within one month of screening	Prolonged Immobility within one month of screening	Medical History Number	Medical History Term	MedDRA System Organ Class	MedDRA Preferred Term
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	Xxx001	Yes/No/Unknown	Yes/No/Unknown	Yes/No/Unknown	01	xxxxx	Xxxx	xxxx
						02	xxxxx	Xxxx	xxxx

Programming Note:

Sort Order = Treatment Group, Actual Baseline Ordinal Score (descending order, i.e. 6, then 5 then 4), USUBJID, MH Number. Each subject will have one row per medical condition reported on the Medical History CRF. If the subject reported "no" they do not have that pre-existing condition, the condition is not present in the line listing. If there is not enough space to fit all columns within the eCTD specified margins, then Actual Treatment Group, Actual Baseline Ordinal Score, and Subject ID can be displayed in a header row as in the AE listings.

Listing 9: Concomitant Medications

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Medication Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	xxx	xx	xxxx	x	x	xxxx	Yes/No	Yes/No	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

Listing 10: Corticosteroid 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)
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	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)
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	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: Compliance Data

Dose Type	Dose Number	Dose Administered?	Number of Tablets Received	Dose Stopped or Slowed?	Reason Dose Missed, Stopped or Slowed	Did the Reason Result in Permanent Discontinuation?
Actual Treatment Group: , Actual Baseline Ordinal Score: , Subject ID: , Study Day of Discharge: , Study Day of Death:						
Remdesivir/IV Push/Tablets	1	Yes/No	1 / 2 / NA	Yes/No/NA	Reason / NA	Yes /No/NA
	2	Yes/No	1 / 2 / NA	Yes/No/NA	Reason / NA	Yes /No/NA
…	…			…	…	

Programming Notes:

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

Listing 13: Listing of Non-Serious Adverse Events

Adverse Event	Study Day	Duration (Days)	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Unanticipated Problem	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Actual Treatment Group: Actual Baseline Ordinal Score: , Subject ID: , AE Number:											
xxx	xx	x	xxx	Not Related/Related to each of Remdesivir, Baricitinib, Dexamethasone, or Placebo	xxxx	Yes/No	For each of Remdesivir, Baricitinib, Dexamethasone, or Placebo	Yes/No	xxxx	xxxx	xxxx
Comments: xxxx											

Programming Note:

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.

Listing 14: Listing of Related Adverse Events

Adverse Event	Study Day	Duration (Days)	Severity	Unanticipated Problem	Study Treatment	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Actual Treatment Group: Actual Baseline Ordinal Score: , Subject ID: , AE Number:										
xxx	xx	x	xxx	Yes/No	Dexamethasone/Baricitinib/ Remdesivir	xxx	Yes/No	xxxx	xxxx	xxxx
Comments: xxx										

Programming Note:

Sort order will be Treatment Group, Actual Baseline Ordinal Score (descending order, i.e. 6, then 5 then 4), Study Treatment, USUBJID, Study Day. List the study treatment the event is associated to, or more than one if multiple.

Listing 15: Listing of Non-Fatal Serious Adverse Events

Adverse Event	Study Day	Duration (Days)	No. of Days Post First Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Unanticipated Problem	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Actual Treatment Group: , Actual Baseline Ordinal Score: , Subject ID: , AE Number:													
xxxx	x	x	x	xxxxx	xxx	Not Related/Related to each of Remdesivir, Baricitinib, Dexamethasone, or Placebo	xxxx	Yes/No	For each of Remdesivir, Baricitinib, Dexamethasone, or Placebo	Yes/No	xxxxx	xxxxx	xxxxx
Comments: xxxx													

Programming Note:

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

Listing 16: Listing of Culture Results

Study Day	Anatomical Location	Pathogen 1	Pathogen 2	Pathogen 3	Pathogen 4	Associated with AE Number	Secondary AE Number
Actual Treatment Group: , Actual Baseline Ordinal Score: , Subject ID: ,							
xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Programming Note:

Sort order will be Treatment Group, Actual Baseline Ordinal Score, USUBJID, Study Day.

Listing 17: Listing of Deaths

Adverse Event	Study Day	Duration (Days)	No. of Days Post First Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Unanticipated Problem	Action Taken with Study Treatment	Subject Discontinued Due to AE	MedDRA System Organ Class	MedDRA Preferred Term
Actual Treatment Group: , Actual Baseline Ordinal Score: , Subject ID: , AE Number:												
xxxx	x	x	x	xxxxx	xxx	Not Related/Related to each of Remdesivir, Baricitinib, Dexamethasone, or Placebo	xxxx	Yes/No	For each of Remdesivir, Baricitinib, Dexamethasone, or Placebo	Yes/No	xxxxx	xxxxx
Comments: xxxx												

Programming Note:

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

Listing 18: Pregnancy Reports – Maternal Information

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

Listing 19: Pregnancy Reports – Gravida and Para

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

Listing 20: Pregnancy Reports – Live Birth Outcomes

Actual Treatment Group	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?
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV													
Congenital Anomalies are included in the Adverse Event listing.													

Listing 21: Pregnancy Reports – Still Birth Outcomes

Actual Treatment Group	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?
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV												

Listing 22: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Actual Treatment Group	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
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV							

Listing 23: Clinical Laboratory Results

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Planned Study Day	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Toxicity Grade)	Change from Baseline	Reference Range Low	Reference Range High
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	Category 7/6/5/4/3	xxx	xx	xx	Xx	x	xxx (xxx)	xxx (xxxx)	xxx	xxxx	xxxx

Programming Note:

Sort order will be Treatment Group, Actual 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.

Listing 24: Vital Signs

Study Visit Day	Actual Study Day	Respiratory Rate		O_2 Saturation		Any Supplemental O_2		Temperature		Systolic BP		Heart Rate		Level of Consciousness		Total NEW Score
		bpm	Score	%	Score	Yes/No	Score	°C	Score	mmHg	Score	bpm	Score	A/V/P/U	Score	
Actual Treatment Group: , Baseline Ordinal Score: , Subject ID:																
xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Listing 25: Physical Exam Findings

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Planned Study Day	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4	xxx	xx	xx	xxxx	xxxxxx	Yes/No/NA

Programming Note:

For respiratory findings denoted as 'Yes' on the Physical Exam CRF, denote the Body System as "Respiratory Finding' and denote the Abnormal Finding as the symptom name; e.g. if Wheezing is reported, the Abnormal Finding will be 'Wheezing'. The Reported as an AE cell will be denoted as 'NA' for respiratory findings. Each reported respiratory finding will appear in its own row. If the finding was not reported as an AE as recorded on the CRF or the site did not report whether the finding was reported as an AE, the cell will display 'No'.

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

Listing 26: Subjects Who Received the Incorrect Treatment

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Randomized Treatment Group	Number of Infusions Received	Number of Doses Received	Number of Incorrect Doses Received
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4	xxx	Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	x	x	x

Programming Note:

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

Listing 27: Subjects Randomized to the Incorrect Clinical Status Stratum

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Randomized Stratum
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	xxx	7/6/5/4/3

Programming Note:

Sort order will be Treatment Group, Actual Baseline Ordinal Score (descending order, i.e. 6, then 5 then 4), USUBJID. If subjects were randomized and not dosed "Not Treated" will be used for the actual treatment category.

Listing 28: Subjects Receiving Supplemental Oxygen Post Discharge

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Discharge Study Day	Oxygen Type	Is the Oxygen New Use?	Study Day Supplemental Oxygen Initiated	Study Day Supplemental Oxygen Stopped
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4/3	xxx	XXX	XXXX	Yes/No	XXX	XXX

Programming Note:

Sort order will be Treatment Group, Actual Baseline Ordinal Score (descending order, i.e. 6, then 5 then 4), USUBJID. If subjects were randomized and not dosed "Not Treated" will be used for the actual treatment category.

Listing 29: Subjects Readmitted

Subject ID	Actual Treatment Group	Actual Baseline Ordinal Score	Original Discharge Study Day	Study Day Readmitted	Reason for Readmission	Readmission Discharge Day
xxx	Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4	XXX	XXX	XXX	XXXX

Programming Note:

Sort order will be Treatment Group, Actual Baseline Ordinal Score (descending order, i.e. 6, then 5 then 4), USUBJID. If subjects were randomized and not dosed "Not Treated" will be used for the actual treatment category.

Listing 30: Listing of Day 60 Results

Actual Treatment Group	Actual Baseline Ordinal Score	Subject ID	Did the Visit Occur?	Study Day	Since the Day 29 / Last Study Contact				Any New Infections?	If New Infection, Type of Infection	Other New Diagnoses[a]	Ordinal Score
					Was the Subject Seen by a Healthcare Provider?	Was the Subject Re-admitted to the Hospital?	Was it Due to Worsening or Exacerbation of a Pre-existing Condition?	If Yes, Specify Associated Pre-Existing Condition				
Baricitinib + PBO + RDV/ PBO + Dexamethasone + RDV	7/6/5/4	xxx	Yes/No	XX	Yes/No	Yes/No	Yes/No/NA	Condition/NA	Yes/No			

[a]Other new diagnoses are based on a targeted list of diagnoses (chronic respiratory disease, pulmonary emboli, deep venous thrombosis, cardiac arrhythmia, myocardial infarction, stroke, major depression, anxiety, post-traumatic stress disorder) as well as an 'Other' option for site staff to specify other diagnoses.

Programming note: Combine all new diagnoses with a ";" separating multiple terms. Sort order will be Treatment Group, Actual Baseline Ordinal Score (descending order, i.e. 6, then 5 then 4), USUBJID. If subjects were randomized and not dosed "Not Treated" will be used for the actual treatment category.