Longitudinal Data Reviewer's Guide

A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults

Adaptive COVID-19 Treatment Trial ACTT-2

DMID Protocol: 20-0006

Version 3.0

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Table of Contents

1 Introduction

1.1 Purpose

This document provides context for the data contained in the ACTT-2 longitudinal dataset.

1.2 Acronyms

Acronym	Translation
ACTT	Adaptive COVID-19 Treatment Trial
ACTT-2	Adaptive COVID-19 Treatment Trial Stage 2
ADaM	Analysis Data Model
COVID-19	Coronavirus Disease 2019
IG	Implementation Guide

1.3 Study Data Standards and Dictionary Inventory

No dictionaries were used for the data included in the transfer. See Section 3.2.1 for the definitions of the Ordinal Scale Scores.

1.4 Source Data Used for Analysis Dataset Creation

The source data for the Longitudinal Data was ACTT-2 Clinical Study Report ADaM datasets.

2 Protocol Description

2.1 Protocol Number and Title

Protocol Number: 20-0006

Protocol Title: Adaptive COVID-19 (Coronavirus Disease 2019) Treatment Trial (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

Protocol Version: Version: 6.0

2.2 Treatment Variables

ARM

- Planned/Randomized Treatment

ACTARM

- Actual Treatment

2.3 Use of Visit Windowing, Unscheduled Visits, and Record Selection

Was windowing used in one or more analysis datasets?

Yes. For Day 15, Day 22, and Day 29, if the subject died within the visit window then an ordinal score of 8 was used for the visit regardless of whether a lower ordinal score was recorded at the actual visit. The visit windows for Day 15 was +/- 2 days, Day 22 was +/- 3 days and Day 29 was +/- 3 days.

Were unscheduled visits used in any analyses?

Unscheduled visits were rare in this study as subjects were in the hospital at the start of the study and had daily visits until discharged. There were no clinical ordinal scores collected at unscheduled visits.

When were ordinal scores assessed?

Subjects were assessed for ordinal score every day while hospitalized and on Day 15, Day 22, Day 29 after discharge. The ordinal score recorded is the worst score on the previous day of the visit date. Assessment date is the date the ordinal score occurred.

2.4 Subject Issues that Require Special Analysis Rules

There were no special analysis rules identified.

3 Analysis Dataset Descriptions

3.1 Overview

Do the analysis datasets support all protocol- and statistical analysis plan-specified objectives?

No. The longitudinal data set only contains a small subset of the protocol and statistical analysis plan objectives.

3.2 Analysis Datasets

Dataset **Dataset Label**	**Efficacy**	**Safety**	**Baseline or other subject characteristics**	**Primary Objective**	**Structure**
actt2_longitudinal_addarm Time-to-Event Dataset	X		X	X	One observation per subject per analysis visit

3.2.1 actt2_longitudinal_addvars_19OCT2021 – Longitudinal Analysis Data Set

actt2_longitudinal_addvars is an analysis dataset of the parameters for time to recovery, clinical ordinal score and mortality.

The table below provides a definition for each parameter.

Label	Variable	Definition
Unique Subject ID	USUBJID	Unique Subject Identifier
Randomized Treatment	ARM	Treatment Randomized to Receive
Actual Treatment	ACTARM	Treatment Received
Baseline Severity – Actual Ordinal Scale	BCSOSN	Baseline Ordinal Scale Score at Time or Randomization
Time to Death (days)[1]	D29DTHE0	Date of Death – Date of Randomization
Time to Death Censor Time Point (days) [1]	D29 DTHE1	Date of Last Visit – Date of Randomization
Time to Recovery (days) [1,2]	TTRECOV0	Date of Recovery – Date of Randomization
Time to Recovery Censor Time Point (days) [1]	TTRECOV1	Date of Last Visit – Date of Randomization
Ordinal Scale Score Assessment Day[1]	ADYC	Baseline=Last Observed Ordinal Score prior to Randomization ADYC="1" is ordinal score between Randomization and midnight on day of Randomization. ADYC="2", "3"… is Assessment Date – Randomization Date + 1
Ordinal Scale Score[2]	ORDSCOR	See table below. This column does not include any imputations for missing data, other than death. Death was carried forward for Assessment Days 15, 22 and 29, if the death occurred prior to the visit.
Ordinal Scale Score Day 15	OR15SCOR	If a subject was missing Day 15 ordinal score, then the following imputations were used: •Subject was randomized but had no ordinal score data available for any timepoint (pre- or post-randomization): OR15SCOR="7". • Subject died on or prior to study day 15: OR15SCOR = "8" • Subject was discharged from the hospital not due to death or transfer to hospice/another hospital and did not return for the Day 15 visit: OR15SCOR = "2" • Subject was discharged from the hospital due to transfer to hospice: OR15SCOR = "7". • Subject was discharged from the hospital due to transfer to another hospital: OR15SCOR = last observed ORDSCOR. • Subject was terminated from the study while hospitalized (termination not due to death) prior to Day 15 assessment: OR15SCOR = last observed ORDSCOR. • Subject was discharged and readmitted 2 or more days later to the hospital prior to Day 15 assessment and was still hospitalized at study day 15: OR15SCOR = "7".

Label	Variable	Definition
Age (years)	AGEC	Age at Time of Randomization. Note: Age is a character field as all subjects > 89 years of age are included with an age of >89 to help maintain data anonymity.
Sex	SEX	M=Male F=Female
Duration of Symptoms (days)	BDURSYMP	Subject Reported Duration of Symptoms at Time of Randomization
Comorbidities	COMORB1	Any Comorbidities Reported at Baseline Categorized as: • Any Comorbidities • No Comorbidities • Unknown The following Comorbidities are included: • Baseline Hypertension • Baseline Coronary Artery Disease • Baseline Congestive Heart Failure • Baseline Chronic Respiratory Disease • Baseline Chronic Oxygen Requirement • Baseline Chronic Liver Disease • Baseline Chronic Kidney Disease • Baseline Diabetes I • Baseline Diabetes II • Baseline Obesity • Baseline Cancer • Baseline Immune Deficiency • Baseline Asthma
Comorbidities	COMORB2	Number of Comorbidities Reported at Baseline Categorized as: • None • 1 Comorbidity • 2 or More Comorbidities The following comorbidities are included: • Baseline Hypertension • Baseline Coronary Artery Disease • Baseline Congestive Heart Failure • Baseline Chronic Respiratory Disease • Baseline Chronic Oxygen Requirement • Baseline Chronic Liver Disease • Baseline Chronic Kidney Disease • Baseline Diabetes I • Baseline Diabetes II • Baseline Obesity • Baseline Cancer • Baseline Immune Deficiency • Baseline Asthma • Baseline Cardiac Valvular Disease

Label	Variable	Definition
		• Baseline Coagulopathy • Current or Prior Deep Vein Thrombosis or Pulmonary Embolism
Race	RACE	Reported Race, including: • American Indian or Alaska Native • Asian • Native Hawaiian or Other Pacific Islander • Black or African American • White • Multiple • Unknown
Ethnicity	ETHNIC	Reported Ethnicity, including: • Not Hispanic or Latino • Hispanic or Latino • Not Reported • Unknown
BMI (kg/m2)	BMI	Defined as: Weight / (Height / 100)^2
Geographic Region 1	REGION1	• US Site • Non-US Site
Geographic Region 2	REGION2	• North America • Europe • Asia
Randomized Disease Severity Stratum (N)	STRATAR	Disease Severity used for Randomization: • Severe Disease • Moderate Disease
Actual Disease Severity Stratum (N)	STRATAV	Actual Disease Severity at the Time of Randomization: • Severe Disease • Moderate Disease
Baseline Hypertension Flag	HYPTFL	Y, N, or null; subject reported hypertension at time of screening
Baseline Coronary Artery Disease Flag	CADFL	Y, N, or null; subject reported coronary artery disease at time of screening
Baseline Congestive Heart Failure Flag	CHFFL	Y, N, or null; subject reported congestive heart failure at time of screening
Baseline Chronic Resp Disease Flag	CRDFL	Y, N, or null; subject reported chronic respiratory disease at time of screening
Baseline Chronic Oxygen Requirement Flag	CORQFL	Y, N, or null; subject reported chronic oxygen requirement at time of screening
Baseline Chronic Liver Disease Flag	CLDFL	Y, N, or null; subject reported chronic liver disease at time of screening
Baseline Chronic Kidney Disease Flag	CKDFL	Y, N, or null; subject reported chronic kidney disease at time of screening
Baseline Diabetes I Flag	DIAB1FL	Y, N, or null; subject reported Diabetes I at time of screening
Baseline Diabetes II Flag	DIAB2FL	Y, N, or null; subject reported Diabetes II at time of screening

Label	Variable	Definition
Baseline Obesity Flag	OBESIFL	Y, N, or null; subject reported obesity at time of screening
Baseline Cancer Flag	CANCFL	Y, N, or null; subject reported cancer at time of screening
Baseline Asthma Flag	ASTHMAFL	Y, N, or null; subject reported asthma at time of screening
Baseline Cardiac Valvular Disease Flag	CVDFL	Y, N, or null; subject reported cardiac valvular disease at time of screening
Baseline Coagulopathy Flag	COAGFL	Y, N, or null; subject reported coagulopathy at time of screening
Baseline Nicotine Consumption Flag	NICFL	Y, N, or null; subject reported nicotine consumption at time of screening
Baseline Risk Factor for DVT or PE Flag	RFDVTFL	Y, N, or null; subject reported risk factor for DVT or PE at time of screening
Current or Prior Major Surgery Flag	SURGFL	Y, N, or null; subject reported current or prior major surgery at time of screening
Current or Prior Prolong Immobility Flag	IMMOFL	Y, N, or null; subject reported current or prior prolong immobility at time of screening
Current or Prior DVT or PE Flag	CPDVTFL	Y, N, or null; subject reported current or prior DVT or PE at time of screening

[1]Time to death and time to recovery fields will be one day less than the Ordinal Scale Score Assessment Day. The Assessment Day is the Study Day while the time to death or recovery is the days from randomization. For example, subjects are randomized on Day 1 and if a subject died on Day 3, the time to death would be 2 days.
[2]Time to recovery does not align with the first observed ordinal score of a 1, 2 or 3 in many cases. This is due to subjects being discharged from the hospital and the site then collects the next ordinal scale score at their next visit on Days 15, 22 or 29. Since they are discharged, the subject meets the definition of a 1 or 2 ordinal scale score once discharged and their time to recovery is the time to discharge.

The table below provides the ordinal scale definitions.

Ordinal Scale	Ordinal Scale Score
Death	8
Hospitalized, on invasive mechanical ventilation or ECMO	7
Hospitalized, on non-invasive ventilation or high flow oxygen devices	6
Hospitalized, requiring supplemental oxygen	5
Hospitalized, not requiring supplemental oxygen, requiring ongoing medical care	4
Hospitalized, not requiring supplemental oxygen, no longer requires ongoing medical care	3
Not hospitalized, limitation on activities and/or requiring home oxygen	2
Not hospitalized, no limitation on activities	1