Clinical trial results:
A Phase II, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Safety and Efficacy of MSTT1041A or UTTR1147A in Patients with Severe COVID-19 Pneumonia

Summary

EudraCT number	2020-002713-17
Trial protocol	ES
Global end of trial date	12 February 2021

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	GA42469

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04386616
WHO universal trial number (UTN)	-
Other trial identifiers	BARDA: OT number: HHSO100201800036C

Notes:

Sponsors

Sponsor organisation name	Genentech, Inc. c/o F. Hoffmann-La Roche Ltd.
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche Ltd., 41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche Ltd., 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 January 2021
Global end of trial reached?	Yes
Global end of trial date	12 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective for this study is to evaluate the efficacy of MSTT1041A compared with placebo and of UTTR1147A compared with placebo, in combination with standard of care, on the basis of the following endpoint: Time to recovery, defined as time to score of 1 or 2 on the 7-category ordinal scale (whichever occurs first).

Protection of trial subjects:

This study was conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the applicable laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 59
Country: Number of subjects enrolled	Mexico: 54
Country: Number of subjects enrolled	Spain: 44
Country: Number of subjects enrolled	United States: 239
Worldwide total number of subjects	396
EEA total number of subjects	44

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	276
From 65 to 84 years	116
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

410 patients were randomized, but 14 of those patients were not enrolled (i.e., did not participate in the study) and did not receive a dose of any study drug; they were therefore excluded from the analysis.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	All Placebo

Arm description:

Participants randomized to this arm received one intravenous (IV) infusion of either MSTT1041A-matched placebo or UTTR1147A-matched placebo on Day 1. A second IV infusion of either MSTT1041A-matched placebo or UTTR1147A-matched placebo (same placebo as the first infusion) was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to UTTR1147A)
Investigational medicinal product code	N/A
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received one intravenous (IV) infusion of UTTR1147A-matched Placebo on Day 1, delivered over 60 (+/-10) minutes. A second IV infusion of UTTR1147A-matched Placebo was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen.

Investigational medicinal product name	Placebo (matched to MSTT1014A)
Investigational medicinal product code	N/A
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received one intravenous (IV) infusion of MSTT1041A-matched Placebo on Day 1, delivered over 60 (+/-10) minutes. A second IV infusion of MSTT1041A-matched Placebo was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen.

Arm title	MSTT1041A

Arm description:

Participants randomized to this arm received one intravenous (IV) infusion of MSTT1041A 700 milligrams (mg) on Day 1. A second IV dose of MSTT1041A 350 mg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Arm type	Experimental

Investigational medicinal product name	MSTT1041A
Investigational medicinal product code	RO7187807/F01
Other name	Astegolimab
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received one intravenous (IV) infusion of MSTT1041A 700 milligrams (mg) on Day 1, delivered over 60 (+/-10) minutes. A second IV dose of MSTT1041A 350 mg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen.

Arm title	UTTR1147A

Arm description:

Participants randomized to this arm received one intravenous (IV) infusion of UTTR1147A 90 micrograms/kilogram body weight (µg/kg) on Day 1. A second IV dose of UTTR1147A 90 µg/kg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Arm type	Experimental
Investigational medicinal product name	UTTR1147A
Investigational medicinal product code	RO7021610/F01
Other name	Efmarodocokin alfa
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received one intravenous (IV) infusion of UTTR1147A 90 micrograms/kilogram body weight (µg/kg) on Day 1, delivered over 60 (+/-10) minutes. A second IV dose of UTTR1147A 90 µg/kg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Weight-based infusions of UTTR1147A have a maximum dose given based on 100 kg total body weight.

Number of subjects in period 1	All Placebo	MSTT1041A	UTTR1147A
Started	134	130	132
Received at Least 1 Dose of Study Drug	134	130	132
Completed 2 Doses of Study Drug, Day 15	31 [1]	27 [2]	25 [3]
Completed	104	95	104
Not completed	30	35	28
Consent withdrawn by subject	2	4	1
Adverse event, non-fatal	1	1	-
Death	22	22	21
Lost to follow-up	5	8	6

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Not all participants received a second dose of study treatment according to the protocol. Only those that remained hospitalized with a requirement for supplemental oxygen received a second dose.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Not all participants received a second dose of study treatment according to the protocol. Only those that remained hospitalized with a requirement for supplemental oxygen received a second

dose.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Not all participants received a second dose of study treatment according to the protocol. Only those that remained hospitalized with a requirement for supplemental oxygen received a second dose.

Baseline characteristics

Reporting groups	
Reporting group title	All Placebo
Reporting group description:	
Participants randomized to this arm received one intravenous (IV) infusion of either MSTT1041A-matched placebo or UTTR1147A-matched placebo on Day 1. A second IV infusion of either MSTT1041A-matched placebo or UTTR1147A-matched placebo (same placebo as the first infusion) was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.	
Reporting group title	MSTT1041A
Reporting group description:	
Participants randomized to this arm received one intravenous (IV) infusion of MSTT1041A 700 milligrams (mg) on Day 1. A second IV dose of MSTT1041A 350 mg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.	
Reporting group title	UTTR1147A
Reporting group description:	
Participants randomized to this arm received one intravenous (IV) infusion of UTTR1147A 90 micrograms/kilogram body weight (µg/kg) on Day 1. A second IV dose of UTTR1147A 90 µg/kg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.	

Reporting group values	All Placebo	MSTT1041A	UTTR1147A
Number of subjects	134	130	132
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	97	88	91
From 65-84 years	35	41	40
85 years and over	2	1	1
Age Continuous Units: Years			
arithmetic mean	56.0	57.3	57.8
standard deviation	± 13.5	± 13.4	± 12.6
Sex: Female, Male Units: Participants			
Female	45	56	52
Male	89	74	80
Ethnicity Units: Subjects			
Hispanic or Latino	77	72	70
Not Hispanic or Latino	53	53	58
Unknown or Not Reported	4	5	4
Race			

Units: Subjects			
American Indian or Alaska Native	2	4	0
Asian	6	4	5
Native Hawaiian or Other Pacific Islander	0	4	1
Black or African American	10	7	10
White	92	87	89
Unknown	24	24	27
Region of Enrollment			
Regional enrollment sites included the following countries: North America = Mexico and United States; South America = Brazil; and Western Europe = Spain. This was one of the two stratification factors at randomization.			
Units: Subjects			
North America	99	97	97
South America	19	20	20
Western Europe	16	13	15
Baseline Mechanical Ventilation Required (Yes/No)			
This was one of the two stratification factors at randomization.			
Units: Subjects			
Yes, Baseline Mechanical Ventilation	12	13	11
No Baseline Mechanical Ventilation	122	117	121
Clinical Status Score at Baseline			
The 7 categories of the clinical status ordinal scale are defined as follows: 1. Discharged (or "ready for discharge"); 2. Non-Intensive Care Unit (ICU) hospital ward (or "ready for hospital ward") not requiring supplemental oxygen; 3. Non-ICU hospital ward (or "ready for hospital ward") requiring supplemental oxygen; 4. ICU or non-ICU hospital ward, requiring non-invasive ventilation or high-flow oxygen; 5. ICU, requiring intubation and mechanical ventilation; 6. ICU, requiring ECMO or mechanical ventilation and additional organ support; 7. Death			
Units: Subjects			
Clinical Status Score of 1	0	0	0
Clinical Status Score of 2	3	4	1
Clinical Status Score of 3	47	49	57
Clinical Status Score of 4	71	64	63
Clinical Status Score of 5	10	8	8
Clinical Status Score of 6	3	4	2
Clinical Status Score of 7	0	0	0
Clinical Status Score Not Available	0	1	1

Reporting group values	Total		
Number of subjects	396		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	276		
From 65-84 years	116		
85 years and over	4		

Age Continuous Units: Years arithmetic mean standard deviation	- 		
Sex: Female, Male Units: Participants			
Female	153		
Male	243		
Ethnicity Units: Subjects			
Hispanic or Latino	219		
Not Hispanic or Latino	164		
Unknown or Not Reported	13		
Race Units: Subjects			
American Indian or Alaska Native	6		
Asian	15		
Native Hawaiian or Other Pacific Islander	5		
Black or African American	27		
White	268		
Unknown	75		
Region of Enrollment			
Regional enrollment sites included the following countries: North America = Mexico and United States; South America = Brazil; and Western Europe = Spain. This was one of the two stratification factors at randomization.			
Units: Subjects			
North America	293		
South America	59		
Western Europe	44		
Baseline Mechanical Ventilation Required (Yes/No)			
This was one of the two stratification factors at randomization.			
Units: Subjects			
Yes, Baseline Mechanical Ventilation	36		
No Baseline Mechanical Ventilation	360		
Clinical Status Score at Baseline			
The 7 categories of the clinical status ordinal scale are defined as follows: 1. Discharged (or "ready for discharge"); 2. Non-Intensive Care Unit (ICU) hospital ward (or "ready for hospital ward") not requiring supplemental oxygen; 3. Non-ICU hospital ward (or "ready for hospital ward") requiring supplemental oxygen; 4. ICU or non-ICU hospital ward, requiring non-invasive ventilation or high-flow oxygen; 5. ICU, requiring intubation and mechanical ventilation; 6. ICU, requiring ECMO or mechanical ventilation and additional organ support; 7. Death			
Units: Subjects			
Clinical Status Score of 1	0		
Clinical Status Score of 2	8		
Clinical Status Score of 3	153		
Clinical Status Score of 4	198		
Clinical Status Score of 5	26		
Clinical Status Score of 6	9		
Clinical Status Score of 7	0		
Clinical Status Score Not Available	2		

End points

End points reporting groups

Reporting group title	All Placebo

Reporting group description:

Participants randomized to this arm received one intravenous (IV) infusion of either MSTT1041A-matched placebo or UTTR1147A-matched placebo on Day 1. A second IV infusion of either MSTT1041A-matched placebo or UTTR1147A-matched placebo (same placebo as the first infusion) was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Reporting group title	MSTT1041A

Reporting group description:

Participants randomized to this arm received one intravenous (IV) infusion of MSTT1041A 700 milligrams (mg) on Day 1. A second IV dose of MSTT1041A 350 mg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Reporting group title	UTTR1147A

Reporting group description:

Participants randomized to this arm received one intravenous (IV) infusion of UTTR1147A 90 micrograms/kilogram body weight (µg/kg) on Day 1. A second IV dose of UTTR1147A 90 µg/kg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Subject analysis set title	MSTT1041A-Matched Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in this analysis group received treatment with MSTT1041A-matched placebo. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Subject analysis set title	UTTR1147A-Matched Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in this analysis group received treatment with UTTR1147A-matched placebo. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Subject analysis set title	UTTR1147A - PK Participants who Only Received First Dose
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All participants in this analysis group only received one intravenous (IV) infusion of UTTR1147A 90 micrograms/kilogram body weight (µg/kg) on Day 1. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Subject analysis set title	UTTR1147A - PK Participants who Received Both Doses
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All participants in this analysis group received one intravenous (IV) infusion of UTTR1147A 90 micrograms/kilogram body weight (µg/kg) on Day 1 and a second IV dose of UTTR1147A 90 µg/kg on Day 15 because they remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Subject analysis set title	UTTR1147A - All PK Participants, Days 1 to 15
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in this analysis group either received only the first dose or both doses of UTTR1147A. One intravenous (IV) infusion of UTTR1147A 90 micrograms/kilogram body weight (µg/kg) was given on Day 1, and a second IV dose of UTTR1147A 90 µg/kg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Subject analysis set title	MSTT1041A - PK Participants who Only Received First Dose
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All participants in this analysis group only received one intravenous (IV) infusion of MSTT1041A 700

milligrams (mg) on Day 1. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Subject analysis set title	MSTT1041A - PK Participants who Received Both Doses
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All participants in this analysis group received one intravenous (IV) infusion of MSTT1041A 700 milligrams (mg) on Day 1 and a second IV dose of MSTT1041A 350 mg was given on Day 15 because they remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Subject analysis set title	MSTT1041A - All PK Participants, Days 1 to 15
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in this analysis group either received only the first dose or both doses of MSTT1041A. One intravenous (IV) infusion of MSTT1041A 700 milligrams (mg) on Day 1, and a second IV dose of MSTT1041A 350 mg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.

Primary: Time to Recovery, Defined as the Time to a Clinical Status Score of 1 or 2 on the 7-Category Ordinal Scale (Whichever Occurs First) by Day 28

End point title	Time to Recovery, Defined as the Time to a Clinical Status Score of 1 or 2 on the 7-Category Ordinal Scale (Whichever Occurs First) by Day 28

End point description:

The time to recovery was defined as the time from baseline to a clinical status score of 1 or 2 on the 7-category ordinal scale (whichever occurs first); clinical status scores are defined as follows: 1. Discharged (or "ready for discharge" as evidenced by normal body temperature and respiratory rate, and stable oxygen saturation on ambient air or ≤2 Litres supplemental oxygen); 2. Non-Intensive Care Unit (ICU) hospital ward (or "ready for hospital ward") not requiring supplemental oxygen; 3. Non-ICU hospital ward (or "ready for hospital ward") requiring supplemental oxygen; 4. ICU or non-ICU hospital ward, requiring non-invasive ventilation or high-flow oxygen; 5. ICU, requiring intubation and mechanical ventilation; 6. ICU, requiring extracorporeal membrane oxygenation (ECMO) or mechanical ventilation and additional organ support (e.g., vasopressors, renal replacement therapy); 7. Death.

End point type	Primary

End point timeframe:

From Baseline up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Days				
median (confidence interval 95%)	10.0 (8.0 to 14.0)	11.0 (9.0 to 14.0)	10.0 (8.0 to 13.0)	

Statistical analyses

Statistical analysis title	Hazard Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A

Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9266 [1]
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.36

Notes:

[1] - p<0.05 threshold for statistical significance

Statistical analysis title	Hazard Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.357 [2]
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.54

Notes:

[2] - p<0.05 threshold for statistical significance

Statistical analysis title	Hazard Ratio (Stratified) - MSTT1014A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9812 [3]
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.36

Notes:

[3] - p<0.05 threshold for statistical significance

Statistical analysis title	Hazard Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5151 [4]
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.49

Notes:

[4] - p<0.05 threshold for statistical significance

Secondary: Time to Improvement of at Least 2 Categories Relative to Baseline on a 7-Category Ordinal Scale of Clinical Status by Day 28

End point title	Time to Improvement of at Least 2 Categories Relative to Baseline on a 7-Category Ordinal Scale of Clinical Status by Day 28

End point description:

The 7 categories of the clinical status ordinal scale are defined as follows: 1. Discharged (or "ready for discharge" as evidenced by normal body temperature and respiratory rate, and stable oxygen saturation on ambient air or ≤2 Litres supplemental oxygen); 2. Non-Intensive Care Unit (ICU) hospital ward (or "ready for hospital ward") not requiring supplemental oxygen; 3. Non-ICU hospital ward (or "ready for hospital ward") requiring supplemental oxygen; 4. ICU or non-ICU hospital ward, requiring non-invasive ventilation or high-flow oxygen; 5. ICU, requiring intubation and mechanical ventilation; 6. ICU, requiring ECMO or mechanical ventilation and additional organ support (e.g., vasopressors, renal replacement therapy); 7. Death

End point type	Secondary

End point timeframe:

From Baseline up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Days				
median (confidence interval 95%)	10.0 (8.0 to 14.0)	11.0 (9.0 to 13.0)	10.0 (8.0 to 12.0)	

Statistical analyses

Statistical analysis title	Hazard Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8373
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.39

Statistical analysis title	Hazard Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3396
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.55

Statistical analysis title	Hazard Ratio (Stratified) - MSTT1014A vs. Placebo
Statistical analysis description:	
The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.	
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8619
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.39

Statistical analysis title	Hazard Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4913
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.5

Secondary: Time to Hospital Discharge or "Ready for Discharge" by Day 28

End point title	Time to Hospital Discharge or "Ready for Discharge" by Day 28

End point description:

Hospital discharge is category number 1 out of the 7 categories of the clinical status ordinal scale, and it is defined as follows: 1. Discharged (or "ready for discharge" as evidenced by normal body temperature and respiratory rate, and stable oxygen saturation on ambient air or ≤2 Litres supplemental oxygen).

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Days				
median (confidence interval 95%)	10.0 (8.0 to 14.0)	11.0 (9.0 to 13.0)	10.0 (8.0 to 13.0)	

Statistical analyses

Statistical analysis title	Hazard Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4711
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.49

Statistical analysis title	Hazard Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3135
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.56

Statistical analysis title	Hazard Ratio (Stratified) - MSTT1014A vs. Placebo
Statistical analysis description:	
The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.	
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5735
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.48

Statistical analysis title	Hazard Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5973
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.46

Secondary: Duration of Supplemental Oxygen by Day 28

End point title	Duration of Supplemental Oxygen by Day 28

End point description:

Duration of supplemental oxygen was defined as the number of days during the 28-day treatment period when the participant is alive and receives "Supplemental Oxygen or other forms of ventilation", as recorded in the Vital Signs and Oxygen Saturation form. For each participant, the duration of multiple non-consecutive periods during which the participant received supplemental oxygen was summed. For any days prior to Day 28 where status of supplemental oxygen use was missing, the last known status was to be carried forward.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Days				
median (confidence interval 95%)	18.00 (13.00 to 27.00)	17.00 (11.00 to 27.00)	13.50 (10.00 to 21.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Alive and Free of Respiratory Failure by Day 28

End point title	Percentage of Participants Alive and Free of Respiratory Failure by Day 28
End point description:	
Respiratory failure was defined as requiring non-invasive ventilation, high-flow oxygen, mechanical ventilation, or extracorporeal membrane oxygenation [ECMO]).	
End point type	Secondary
End point timeframe:	
Up to 28 days	

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Percentage of participants				
number (confidence interval 95%)	38.1 (29.47 to 46.65)	39.2 (30.45 to 48.01)	40.2 (31.41 to 48.89)	

Statistical analyses

Statistical analysis title	Odds Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8451
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.72

Statistical analysis title	Odds Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7267
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.79

Statistical analysis title	Odds Ratio (Stratified) - MSTT1014A vs. Placebo
Statistical analysis description:	
The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.	
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8458
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.79

Statistical analysis title	Odds Ratio (Stratified) - UTTR1147A vs. Placebo
Statistical analysis description:	
The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.	
Comparison groups	All Placebo v UTTR1147A

Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7907
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.81

Secondary: Clinical Status Score at Day 14, Assessed Using a 7-Category Ordinal Scale

End point title	Clinical Status Score at Day 14, Assessed Using a 7-Category Ordinal Scale

End point description:

The clinical status scores of the 7 category ordinal scale are defined as follows: 1. Discharged (or "ready for discharge" as evidenced by normal body temperature and respiratory rate, and stable oxygen saturation on ambient air or ≤2 Litres supplemental oxygen); 2. Non-Intensive Care Unit (ICU) hospital ward (or "ready for hospital ward") not requiring supplemental oxygen; 3. Non-ICU hospital ward (or "ready for hospital ward") requiring supplemental oxygen; 4. ICU or non-ICU hospital ward, requiring non-invasive ventilation or high-flow oxygen; 5. ICU, requiring intubation and mechanical ventilation; 6. ICU, requiring ECMO or mechanical ventilation and additional organ support (e.g., vasopressors, renal replacement therapy); 7. Death

End point type	Secondary

End point timeframe:

Day 14

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Score on a scale				
median (inter-quartile range (Q1-Q3))	1.0 (1.0 to 4.0)	1.0 (1.0 to 3.0)	1.0 (1.0 to 4.0)	

Statistical analyses

Statistical analysis title	Odds Ratio - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A

Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5652
Method	Proportional Odds Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.89

Statistical analysis title	Odds Ratio - MSTT1014A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5475
Method	Proportional Odds Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.91

Secondary: Clinical Status Score at Day 28, Assessed Using a 7-Category Ordinal Scale

End point title	Clinical Status Score at Day 28, Assessed Using a 7-Category Ordinal Scale

End point description:

The clinical status scores of the 7 category ordinal scale are defined as follows: 1. Discharged (or "ready for discharge" as evidenced by normal body temperature and respiratory rate, and stable oxygen saturation on ambient air or ≤2 Litres supplemental oxygen); 2. Non-Intensive Care Unit (ICU) hospital ward (or "ready for hospital ward") not requiring supplemental oxygen; 3. Non-ICU hospital ward (or "ready for hospital ward") requiring supplemental oxygen; 4. ICU or non-ICU hospital ward, requiring non-invasive ventilation or high-flow oxygen; 5. ICU, requiring intubation and mechanical ventilation; 6. ICU, requiring ECMO or mechanical ventilation and additional organ support (e.g., vasopressors, renal replacement therapy); 7. Death

End point type	Secondary

End point timeframe:

Day 28

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Score on a scale				
median (inter-quartile range (Q1-Q3))	1.0 (1.0 to 4.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	

Statistical analyses

Statistical analysis title	Odds Ratio - MSTT1014A vs. Placebo
Statistical analysis description:	
The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.	
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3408
Method	Proportional Odds Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.29

Statistical analysis title	Odds Ratio - UTTR1147A vs. Placebo
Statistical analysis description:	
The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.	
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.332
Method	Proportional Odds Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	2.29

Secondary: Percentage of Participants Needing Invasive Mechanical Ventilation or Extracorporeal Membrane Oxygenation (ECMO) by Day 28

End point title	Percentage of Participants Needing Invasive Mechanical Ventilation or Extracorporeal Membrane Oxygenation (ECMO) by Day 28

End point description:

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Percentage of participants				
number (confidence interval 95%)	24.6 (16.96 to 32.29)	28.5 (20.32 to 36.60)	24.2 (16.55 to 31.93)	

Statistical analyses

Statistical analysis title	Difference in Event Rate - MSTT1041A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of participants
Point estimate	3.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.57
upper limit	15.24

Statistical analysis title	Difference in Event Rate - UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A

Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of participants
Point estimate	-0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.46
upper limit	10.7

Statistical analysis title	Odds Ratio (Unstratified) - MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4804
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.1

Statistical analysis title	Odds Ratio (Unstratified) - UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9418
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.71

Statistical analysis title	Odds Ratio (Stratified) - MSTT1014A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for

mechanical ventilation.

Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4988
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2.44

Statistical analysis title	Odds Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9043
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.96

Secondary: Number of Ventilator-Free Days by Day 28

End point title	Number of Ventilator-Free Days by Day 28

End point description:

The number of ventilator-free days was defined as the number of days during the 28-day treatment period when the participant is alive and without need for invasive mechanical ventilation. For any day during Day 1 and Day 28, if invasive mechanical ventilation or ECMO was recorded for any part of the day (>= 12 hours during mechanical invasive ventilation for patients with tracheostomy), the day was not to be counted as a ventilator-free day; otherwise, the day was to be counted. For any days prior to Day 28 where status of mechanical ventilator was missing, the last known status was to be carried forward. The total number of days was the sum of all ventilator-free days, regardless of whether the days occurred consecutively or in nonconsecutive intervals.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Days				
median (inter-quartile range (Q1-Q3))	28.0 (20.00 to 28.00)	28.0 (20.00 to 28.00)	28.0 (23.50 to 28.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an Intensive Care Unit (ICU) Stay by Day 28

End point title	Percentage of Participants with an Intensive Care Unit (ICU) Stay by Day 28

End point description:

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Percentage of participants				
number (confidence interval 95%)	58.2 (49.48 to 66.93)	54.6 (45.67 to 63.56)	46.2 (37.33 to 55.10)	

Statistical analyses

Statistical analysis title	Difference in Event Rate - MSTT1041A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of participants
Point estimate	-3.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.31
upper limit	9.12

Statistical analysis title	Difference in Event Rate - UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of participants
Point estimate	-12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.67
upper limit	0.67

Statistical analysis title	Odds Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.556
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.41

Statistical analysis title	Odds Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0502
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	0.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1

Statistical analysis title	Odds Ratio (Stratified) - MSTT1014A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7002
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.6

Statistical analysis title	Odds Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0448
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.99

Secondary: Duration of Intensive Care Unit (ICU) Stay by Day 28

End point title	Duration of Intensive Care Unit (ICU) Stay by Day 28

End point description:

Duration of ICU stay was calculated as the total number of hours (expressed in days) spent in ICU up to and inclusive of 28 days. ICU duration was derived from the ICU Stay Information Log using the difference between ICU discharge date/time and ICU admission date/time. If ICU admission occurred before randomization, the ICU duration was to be counted from the date of dosing. Partial admission and discharge date/time were to be imputed following a conservative approach. For each participant, durations of multiple ICU stays were to be summed.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Days				
median (confidence interval 95%)	3.10 (0.00 to 5.23)	2.62 (0.00 to 6.02)	0.00 (0.00 to 2.14)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Clinical Failure by Day 28, Defined as the Time to Death, Mechanical Ventilation, ICU Admission, or Withdrawal of Care (Whichever Occurs First)

End point title	Time to Clinical Failure by Day 28, Defined as the Time to Death, Mechanical Ventilation, ICU Admission, or Withdrawal of Care (Whichever Occurs First)

End point description:

The value '999999' indicates that the median and interquartile range limit(s) could not be estimated because an insufficient number of clinical failure events had occurred.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Days				
median (inter-quartile range (Q1-Q3))	999999 (13.0 to 999999)	999999 (9.0 to 999999)	999999 (999999 to 999999)	

Statistical analyses

Statistical analysis title	Hazard Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4456
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.88

Statistical analysis title	Hazard Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7213
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.48

Statistical analysis title	Hazard Ratio (Stratified) - MSTT1014A vs. Placebo
Statistical analysis description:	
The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.	
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3963
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.96

Statistical analysis title	Hazard Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9174
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.58

Secondary: Percentage of Participants who Died by Day 14

End point title	Percentage of Participants who Died by Day 14

End point description:

End point type	Secondary

End point timeframe:

Up to Day 14

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Percentage of participants				
number (confidence interval 95%)	6.0 (1.59 to 10.35)	8.5 (3.29 to 13.63)	8.3 (3.24 to 13.43)	

Statistical analyses

Statistical analysis title	Difference in Event Rate - MSTT1041A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Mortality Rates
Point estimate	2.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.51
upper limit	9.49

Statistical analysis title	Difference in Event Rate - UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Mortality Rates
Point estimate	2.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.58
upper limit	9.31

Statistical analysis title	Odds Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4336
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	3.74

Statistical analysis title	Odds Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A

Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4543
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	3.68

Statistical analysis title	Odds Ratio (Stratified) - MSTT1014A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.49
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	3.97

Statistical analysis title	Odds Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3595
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.58

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	4.28

Secondary: Percentage of Participants who Died by Day 28

End point title	Percentage of Participants who Died by Day 28
End point description:	

End point type	Secondary
End point timeframe:	
Up to Day 28	

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Percentage of participants				
number (confidence interval 95%)	11.2 (5.48 to 16.91)	14.6 (8.16 to 21.07)	12.9 (6.79 to 18.97)	

Statistical analyses

Statistical analysis title	Difference in Event Rate - MSTT1041A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Mortality Rates
Point estimate	3.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.42
upper limit	12.26

Statistical analysis title	Difference in Event Rate - UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A

Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Mortality Rates
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.89
upper limit	10.26

Statistical analysis title	Odds Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4067
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	2.8

Statistical analysis title	Odds Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6728
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	2.46

Statistical analysis title	Odds Ratio (Stratified) - MSTT1014A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for

mechanical ventilation.

Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5495
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	2.87

Statistical analysis title	Odds Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5551
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	2.71

Secondary: Time to Clinical Improvement, Defined as a National Early Warning Score 2 (NEWS2) Aggregate Score of ≤2 Maintained for 24 Hours

End point title	Time to Clinical Improvement, Defined as a National Early Warning Score 2 (NEWS2) Aggregate Score of ≤2 Maintained for 24 Hours

End point description:

The National Early Warning Score 2 (NEWS2) is a system for scoring the physiological measurements that are routinely recorded at the patient's bedside. Its purpose is to identify acutely ill patients. The NEWS2 scoring system measures 7 physiological parameters: respiration rate, peripheral capillary oxygen saturation, breathing air or supplementary oxygen, systolic blood pressure, pulse rate, level of consciousness or new-onset confusion, and body temperature. A score of 0, 1, 2, or 3 is allocated to each parameter (except for air or oxygen, with respective scores of 0 and 2). A higher score means the parameter is further from the normal range. The score is then aggregated, and a higher score indicates a worse clinical condition of the patient, thus indicating the need for a more urgent clinical response.

End point type	Secondary

End point timeframe: Up to 28 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Days				
median (confidence interval 95%)	5.5 (4.0 to 7.0)	6.0 (4.0 to 8.0)	6.0 (3.0 to 9.0)	

Statistical analyses

Statistical analysis title	Hazard Ratio (Unstratified)- MSTT1014A vs. Placebo
Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3831
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	2.4

Statistical analysis title	Hazard Ratio (Unstratified)- UTTR1147A vs. Placebo
Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5925
Method	Unstratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	2.15

Statistical analysis title	Hazard Ratio (Stratified) - MSTT1014A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v MSTT1041A
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7487
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.05

Statistical analysis title	Hazard Ratio (Stratified) - UTTR1147A vs. Placebo

Statistical analysis description:

The analysis was adjusted for the baseline characteristics of region of enrollment and need for mechanical ventilation.

Comparison groups	All Placebo v UTTR1147A
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6092
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	2.21

Secondary: Safety Summary of the Number of Participants with at Least One Adverse Event, with Severity Determined According to National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0)

End point title	Safety Summary of the Number of Participants with at Least One Adverse Event, with Severity Determined According to National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0)

End point description:

The terms “severe” and “serious” are not synonymous with respect to an adverse event (AE). Severity refers to the intensity of an AE (rated according to NCI-CTCAE v5.0 criteria or, if not listed, the following scale: Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, Grade 4 is life-threatening, and Grade 5 is death related to AE), whereas a serious AE (SAE) is a significant medical event (per standard criteria), such as a life-threatening or fatal AE or an AE that prolongs inpatient hospitalization. Severity and

seriousness were independently assessed by the investigator for each AE that was recorded. The investigator also assessed each AE for whether the event was considered to be related to the study drug.

End point type	Secondary

End point timeframe:

Up to 60 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Participants				
Any Adverse Event (AE)	87	85	95	
AE with Fatal Outcome	23	23	21	
Serious AE (SAE)	38	38	34	
SAE Leading to Withdrawal from Treatment	2	2	1	
SAE Leading to Dose Mod./Interruption	0	0	0	
Related SAE	0	2	3	
AE Leading to Withdrawal from Treatment	4	3	3	
AE Leading to Dose Mod./Interruption	0	0	0	
Related AE	15	12	25	
Related AE Leading to Withdrawal from Treatment	0	0	1	
Related AE Leading to Dose Mod./Interruption	0	0	0	
Grade 3-5 AE	43	46	41	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinical Laboratory Test Abnormalities by Highest NCI-CTCAE Grade Post-Baseline

End point title	Number of Participants with Clinical Laboratory Test Abnormalities by Highest NCI-CTCAE Grade Post-Baseline

End point description:

Clinical laboratory tests were performed over the course of the study and the grading of any abnormal values outside of the normal range (High or Low) was based on the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0 (NCI-CTCAE v5.0); the higher the grade, the greater the lab parameter deviates from the normal range. Not every abnormal laboratory value qualified as an adverse event, only if it met any of the following criteria: clinically significant (per investigator); accompanied by clinical symptoms; resulted in a change in study treatment; or required a change in concomitant therapy. Abs. = absolute count; SGPT/ALT = alanine aminotransferase; SGOT/AST = aspartate aminotransferase; INR = international normalized ratio; aPTT = activated partial thromboplastin time

End point type	Secondary

End point timeframe:

From Baseline up to 60 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Participants				
Albumin, Low - Any Grade (Gr.)(n=133,129,131)	103	105	118	
Albumin, Low - Gr. 1 (n=133,129,131)	32	36	40	
Albumin, Low - Gr. 2 (n=133,129,131)	56	58	66	
Albumin, Low - Gr. 3 (n=133,129,131)	15	11	12	
Alkaline Phosphatase, High -Any Gr.(n=133,130,132)	20	23	24	
Alkaline Phosphatase, High -Gr. 1 (n=133,130,132)	14	22	22	
Alkaline Phosphatase, High -Gr. 2 (n=133,130,132)	5	1	1	
Alkaline Phosphatase, High -Gr. 3 (n=133,130,132)	1	0	1	
SGPT/ALT, High - Any Gr. (n=132,129,132)	60	48	60	
SGPT/ALT, High - Gr. 1 (n=132,129,132)	48	37	47	
SGPT/ALT, High - Gr. 2 (n=132,129,132)	5	7	7	
SGPT/ALT, High - Gr. 3 (n=132,129,132)	5	3	5	
SGPT/ALT, High - Gr. 4 (n=132,129,132)	2	1	1	
SGOT/AST, High - Any Gr. (n=133,129,131)	47	38	44	
SGOT/AST, High - Gr. 1 (n=133,129,131)	40	30	36	
SGOT/AST, High - Gr. 2 (n=133,129,131)	4	5	4	
SGOT/AST, High - Gr. 3 (n=133,129,131)	0	2	2	
SGOT/AST, High - Gr. 4 (n=133,129,131)	3	1	2	
Calcium, Low - Any Gr. (n=133,130,132)	73	82	84	
Calcium, Low - Gr. 1 (n=133,130,132)	34	47	48	
Calcium, Low - Gr. 2 (n=133,130,132)	31	26	29	
Calcium, Low - Gr. 3 (n=133,130,132)	5	7	4	
Calcium, Low - Gr. 4 (n=133,130,132)	3	2	3	
Calcium, High - Any Gr. (n=133,130,132)	5	2	4	
Calcium, High - Gr. 1 (n=133,130,132)	5	2	4	
Creatinine, High - Any Gr. (n=133,130,132)	24	39	29	
Creatinine, High - Gr. 1 (n=133,130,132)	6	11	8	
Creatinine, High - Gr. 2 (n=133,130,132)	11	24	15	
Creatinine, High - Gr. 3 (n=133,130,132)	7	3	5	

Creatinine, High - Gr. 4 (n=133,130,132)	0	1	1	
Fibrinogen, Low - Any Gr. (n=125,122,130)	7	3	1	
Fibrinogen, Low - Gr. 1 (n=125,122,130)	1	1	0	
Fibrinogen, Low - Gr. 2 (n=125,122,130)	3	2	0	
Fibrinogen, Low - Gr. 3 (n=125,122,130)	2	0	0	
Fibrinogen, Low - Gr. 4 (n=125,122,130)	1	0	1	
Glucose, Low - Any Gr. (n=133,130,132)	8	11	12	
Glucose, Low - Gr. 1 (n=133,130,132)	6	6	9	
Glucose, Low - Gr. 2 (n=133,130,132)	1	5	0	
Glucose, Low - Gr. 3 (n=133,130,132)	1	0	2	
Glucose, Low - Gr. 4 (n=133,130,132)	0	0	1	
Hemoglobin, Low - Any Gr. (n=133,130,132)	77	72	78	
Hemoglobin, Low - Gr. 1 (n=133,130,132)	43	47	46	
Hemoglobin, Low - Gr. 2 (n=133,130,132)	17	17	21	
Hemoglobin, Low - Gr. 3 (n=133,130,132)	17	8	11	
Hemoglobin, High - Any Gr. (n=133,130,132)	9	7	5	
Hemoglobin, High - Gr. 1 (n=133,130,132)	9	6	5	
Hemoglobin, High - Gr. 3 (n=133,130,132)	0	1	0	
Lymphocytes, Abs, Low - Any Gr.(n=100,91,93)	61	45	48	
Lymphocytes, Abs, Low - Gr. 1 (n=100,91,93)	14	9	11	
Lymphocytes, Abs, Low - Gr. 2 (n=100,91,93)	23	17	23	
Lymphocytes, Abs, Low - Gr. 3 (n=100,91,93)	23	18	11	
Lymphocytes, Abs, Low - Gr. 4 (n=100,91,93)	1	1	3	
Lymphocytes, Abs, High - Any Gr. (n=100,91,93)	4	4	1	
Lymphocytes, Abs, High - Gr. 2 (n=100,91,93)	4	4	1	
Neutrophils, Total(Abs), Low -Any Gr.(n=100,91,93)	5	3	1	
Neutrophils, Total (Abs), Low -Gr. 1 (n=100,91,93)	4	3	0	
Neutrophils, Total (Abs), Low -Gr. 2 (n=100,91,93)	1	0	1	
Platelets, Low - Any Gr. (n=133,130,132)	17	17	12	
Platelets, Low - Gr. 1 (n=133,130,132)	14	15	9	
Platelets, Low - Gr. 2 (n=133,130,132)	2	0	2	
Platelets, Low - Gr. 3 (n=133,130,132)	1	1	0	
Platelets, Low - Gr. 4 (n=133,130,132)	0	1	1	
Potassium, Low - Any Gr. (n=133,130,132)	29	19	25	

Potassium, Low - Gr. 2 (n=133,130,132)	25	18	23	
Potassium, Low - Gr. 3 (n=133,130,132)	4	1	2	
Potassium, High - Any Gr. (n=133,130,132)	15	25	16	
Potassium, High - Gr. 1 (n=133,130,132)	7	19	12	
Potassium, High - Gr. 2 (n=133,130,132)	5	3	3	
Potassium, High - Gr. 3 (n=133,130,132)	2	3	1	
Potassium, High - Gr. 4 (n=133,130,132)	1	0	0	
INR, High - Any Gr. (n=126,125,130)	71	69	75	
INR, High - Gr. 1 (n=126,125,130)	60	61	67	
INR, High - Gr. 2 (n=126,125,130)	9	8	6	
INR, High - Gr. 3 (n=126,125,130)	2	0	2	
aPTT, High - Any Gr. (n=121,126,128)	47	42	42	
aPTT, High - Gr. 1 (n=121,126,128)	38	35	36	
aPTT, High - Gr. 2 (n=121,126,128)	6	5	3	
aPTT, High - Gr. 3 (n=121,126,128)	3	2	3	
Sodium, Low - Any Gr. (n=133,130,132)	67	58	58	
Sodium, Low - Gr. 1 (n=133,130,132)	60	50	51	
Sodium, Low - Gr. 2 (n=133,130,132)	6	6	7	
Sodium, Low - Gr. 3 (n=133,130,132)	1	1	0	
Sodium, Low - Gr. 4 (n=133,130,132)	0	1	0	
Sodium, High - Any Gr. (n=133,130,132)	17	16	23	
Sodium, High - Gr. 1 (n=133,130,132)	11	10	21	
Sodium, High - Gr. 2 (n=133,130,132)	5	5	1	
Sodium, High - Gr. 3 (n=133,130,132)	0	1	0	
Sodium, High - Gr. 4 (n=133,130,132)	1	0	1	
Bilirubin, High - Any Gr. (n=133,130,132)	16	14	11	
Bilirubin, High - Gr. 1 (n=133,130,132)	12	9	8	
Bilirubin, High - Gr. 2 (n=133,130,132)	2	5	2	
Bilirubin, High - Gr. 3 (n=133,130,132)	2	0	1	
Uric Acid, High - Any Gr. (n=114,112,114)	33	24	22	
Uric Acid, High - Gr. 3 (n=114,112,114)	33	24	22	
Total Leukocyte Count, Low -Any Gr.(n=133,130,132)	12	6	10	
Total Leukocyte Count, Low - Gr. 1 (n=133,130,132)	10	6	10	
Total Leukocyte Count, Low - Gr. 2 (n=133,130,132)	2	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Vital Sign Abnormalities at Anytime Post-

Baseline

End point title	Number of Participants with Vital Sign Abnormalities at Anytime Post-Baseline

End point description:

The number of participants with vital sign abnormalities outside of the normal upper (i.e., High) and lower limits (i.e., Low) were summarized for each parameter. The normal reference range used for each vital sign parameter was as follows: Diastolic Blood Pressure, 50-90 millimetres of mercury (mmHg); Oxygen Saturation, ≥94%; Pulse Rate, 60-100 beats per minute; Respiratory Rate, 8-20 breaths per minute; Systolic Blood Pressure, 90-140 mmHg; Temperature, 36.5-38 degrees Celsius (C). Not every vital sign abnormality qualified as an adverse event. A vital sign result was to be reported as an adverse event if it met any of the following criteria: was accompanied by clinical symptoms; resulted in a change in study treatment; resulted in a medical intervention or a change in concomitant therapy; or was clinically significant in the investigator's judgement.

End point type	Secondary

End point timeframe:

From Baseline up to 60 days

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	133	130	132	
Units: Participants				
Diastolic Blood Pressure - Low	23	23	21	
Diastolic Blood Pressure - High	39	43	39	
Oxygen Saturation - Low	112	107	105	
Pulse Rate - Low	66	66	61	
Pulse Rate - High	75	62	57	
Respiratory Rate - Low	1	0	2	
Respiratory Rate - High	108	104	103	
Systolic Blood Pressure - Low	20	11	17	
Systolic Blood Pressure - High	77	81	70	
Temperature - Low	116	113	113	
Temperature - High	13	10	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants by the Investigator's Interpretations of Electrocardiogram Recordings at Specified Timepoints

End point title	Number of Participants by the Investigator's Interpretations of Electrocardiogram Recordings at Specified Timepoints

End point description:

Electrocardiogram (ECG) recordings were to be performed after the participant had been resting in a supine position for at least 10 minutes if possible. The investigator's interpretation of the ECG (e.g., normal or abnormal) was recorded.

End point type	Secondary

End point timeframe:

Baseline, Days 14 and 28, Discharge Day (up to Day 28), and Study Completion Visit (up to Day 60)

End point values	All Placebo	MSTT1041A	UTTR1147A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	130	132	
Units: Participants				
Baseline - Abnormal ECG (n=132,126,130)	56	60	55	
Baseline - Normal ECG (n=132,126,130)	76	66	75	
Day 14 - Abnormal ECG (n=34,29,24)	20	13	14	
Day 14 - Normal ECG (n=34,29,24)	14	16	10	
Day 28 - Abnormal ECG (n=15,5,7)	12	3	4	
Day 28 - Normal ECG (n=15,5,7)	3	2	3	
Discharge Day - Abnormal ECG (n=64,75,76)	27	28	37	
Discharge Day - Normal ECG (n=64,75,76)	37	47	39	
Study Completion - Abnormal ECG (n=69,65,62)	13	18	21	
Study Completion - Normal ECG (n=69,65,62)	56	46	40	
Study Completion - Unable to Evaluate (n=69,65,62)	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Tested Positive for Anti-Drug Antibodies (ADAs) to MSTT1041A and UTTR1147A at Baseline and at Anytime Post-Baseline

End point title	Percentage of Participants who Tested Positive for Anti-Drug Antibodies (ADAs) to MSTT1041A and UTTR1147A at Baseline and at Anytime Post-Baseline[5]

End point description:

Serum samples were collected, and participants who received treatment with MSTT1041A or MSTT1041A-matched placebo were assessed for antidrug antibodies (ADAs) to MSTT1041A, while those who received UTTR1147A or UTTR1147A-matched placebo were assessed for ADAs to UTTR1147A. The percentage of ADA-positive participants at baseline (baseline prevalence) and after drug administration (postbaseline incidence; for experimental drugs only, not placebo) are summarized. When determining postbaseline incidence, participants were considered to be ADA positive if they were ADA negative or had missing data at baseline but developed an ADA response following study drug exposure (treatment-induced ADAs), or if they were ADA positive at baseline and the titer of one or more postbaseline samples was at least 0.60 titer unit greater than the titer of the baseline sample (treatment-enhanced ADAs). The value '999999' indicates that no results are available because 0 participants were analyzed.

End point type	Secondary

End point timeframe:

At Baseline (pre-dose on Day 1) and post-baseline (Days 15 and 28; and discharge day and study completion [up to 60 days])

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The percentage of participants who test positive for ADAs at Baseline is also presented here for those in the All Placebo Arm, but this arm is split into 2 subgroups according to the type of

placebo received (i.e., MSTT1041A-matched or UTTR1147A-matched).

End point values	MSTT1041A	UTTR1147A	MSTT1041A-Matched Placebo	UTTR1147A-Matched Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	130	132	59	59
Units: Percentage of participants				
number (not applicable)				
ADA Positive at Baseline (n=117,126,59,59)	2.6	1.6	3.4	1.7
ADA Positive Post-Baseline, Total (n=104,107,0,0)	2.9	0.9	999999	999999
Treatment-Induced ADA Positive (n=104,107,0,0)	1.9	0.9	999999	999999
Treatment-Enhanced ADA Positive (n=104,107,0,0)	1.0	0.0	999999	999999

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of UTTR1147A at Specified Timepoints

End point title	Serum Concentration of UTTR1147A at Specified Timepoints

End point description:

The Pharmacokinetics (PK) analysis population for UTTR1147A consisted of participants who received at least one dose of UTTR1147A and had at least one evaluable PK concentration data point. The PK analysis population is further divided into three groups: participants who only received the first dose, participants who received both doses, and all participants who received the first dose only or both doses (from Days 1 to 15). The value '999999' indicates that no results are available because 0 participants were analyzed at that timepoint. The value '99999' indicates that the standard deviation could not be calculated with data from 1 participant.

End point type	Secondary

End point timeframe:

For the first dose: at 0.5 hours post-dose on Day 1, on Days 2, 3, 7, and 15; and for the second dose: Days 15 (0.5 hours post-dose), 21, and 28

End point values	UTTR1147A - PK Participants who Only Received First Dose	UTTR1147A - PK Participants who Received Both Doses	UTTR1147A - All PK Participants, Days 1 to 15	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	105	25	130	
Units: nanograms per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
Day 1, 0.5 hours post-dose (n=98,24,122)	1260 (± 568)	1600 (± 1820)	1320 (± 952)	
Day 2 (n = 96, 23, 119)	707 (± 268)	674 (± 372)	700 (± 290)	
Day 3 (n = 84, 24, 108)	518 (± 221)	604 (± 222)	537 (± 223)	

Day 7 (n = 46, 24, 70)	258 (± 110)	259 (± 109)	258 (± 109)	
Day 15, pre-dose (n = 4, 25, 29)	42.3 (± 27.8)	88.1 (± 40.6)	81.8 (± 41.9)	
Day 15, 0.5 hours post-dose (n=0,25,0)	999999 (± 999999)	1410 (± 802)	999999 (± 999999)	
Day 21 (n = 1, 14, 0)	2.69 (± 99999)	297 (± 147)	999999 (± 999999)	
Day 28 (n = 3, 8, 0)	11.3 (± 8.89)	173 (± 78.4)	999999 (± 999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of MSTT1041A at Specified Timepoints

End point title	Serum Concentration of MSTT1041A at Specified Timepoints

End point description:

The Pharmacokinetics (PK) analysis population for MSTT1041A consisted of participants who received at least one dose of MSTT1041A and had at least one evaluable PK concentration data point. The PK analysis population is further divided into three groups: participants who only received the first dose, participants who received both doses, and all participants who received the first dose only or both doses (from Days 1 to 15). The value '999999' indicates that no results are available because 0 participants were analyzed at that timepoint.

End point type	Secondary

End point timeframe:

For the first dose: at 0.5 hours post-dose on Day 1, on Days 2, 3, 7, and 15; and for the second dose: Days 15 (0.5 hours post-dose), 21, and 28

End point values	MSTT1041A - PK Participants who Only Received First Dose	MSTT1041A - PK Participants who Received Both Doses	MSTT1041A - All PK Participants, Days 1 to 15	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	96	23	119	
Units: micrograms per millilitre (µg/mL)				
arithmetic mean (standard deviation)				
Day 1, 0.5 hours post-dose (n=90,22,112)	206 (± 71.1)	227 (± 66.7)	210 (± 70.4)	
Day 2 (n = 89, 23, 112)	175 (± 49.1)	178 (± 54.3)	176 (± 50.0)	
Day 3 (n = 81, 23, 104)	147 (± 40.1)	135 (± 41.0)	144 (± 40.4)	
Day 7 (n = 49, 23, 72)	88.6 (± 32.3)	83.9 (± 28.1)	87.1 (± 30.9)	
Day 15, pre-dose (n = 4, 22, 26)	32.2 (± 15.2)	33.8 (± 17.2)	33.5 (± 16.6)	
Day 15, 0.5 hours post-dose (n=0,21,0)	999999 (± 999999)	144 (± 48.0)	999999 (± 999999)	
Day 21 (n = 0, 9, 0)	999999 (± 999999)	45.4 (± 20.8)	999999 (± 999999)	
Day 28 (n = 0, 5, 0)	999999 (± 999999)	22.5 (± 9.17)	999999 (± 999999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Baseline until study completion/discontinuation (up to 60 days)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	All Placebo
Reporting group description:	
Participants randomized to this arm received one intravenous (IV) infusion of either MSTT1041A-matched placebo or UTTR1147A-matched placebo on Day 1. A second IV infusion of either MSTT1041A-matched placebo or UTTR1147A-matched placebo (same placebo as the first infusion) was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.	
Reporting group title	MSTT1041A
Reporting group description:	
Participants randomized to this arm received one intravenous (IV) infusion of MSTT1041A 700 milligrams (mg) on Day 1. A second IV dose of MSTT1041A 700 mg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.	
Reporting group title	UTTR1147A
Reporting group description:	
Participants randomized to this arm received one intravenous (IV) infusion of UTTR1147A 90 micrograms/kilogram body weight (µg/kg) on Day 1. A second IV dose of UTTR1147A 90 µg/kg was given on Day 15 if the participant remained hospitalized with a requirement for supplemental oxygen. Study treatment was given in combination with the standard of care for COVID-19 pneumonia.	

Serious adverse events	All Placebo	MSTT1041A	UTTR1147A
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 134 (28.36%)	38 / 130 (29.23%)	34 / 132 (25.76%)
number of deaths (all causes)	23	23	21
number of deaths resulting from adverse events	0	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Distributive shock			

subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 134 (1.49%)	2 / 130 (1.54%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Shock haemorrhagic			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Ill-defined disorder			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 134 (0.75%)	2 / 130 (1.54%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Respiratory, thoracic and mediastinal disorders			

Acute respiratory distress syndrome			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute respiratory failure			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	4 / 132 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Dyspnoea			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 134 (0.00%)	2 / 130 (1.54%)	3 / 132 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumomediastinum			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumothorax			
subjects affected / exposed	5 / 134 (3.73%)	2 / 130 (1.54%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary embolism			

subjects affected / exposed	3 / 134 (2.24%)	1 / 130 (0.77%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	5 / 134 (3.73%)	4 / 130 (3.08%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 5	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 2
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Oxygen saturation decreased			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 134 (0.00%)	2 / 130 (1.54%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	2 / 134 (1.49%)	3 / 130 (2.31%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 134 (0.75%)	1 / 130 (0.77%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Cardiac failure			
subjects affected / exposed	1 / 134 (0.75%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	5 / 134 (3.73%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 5	0 / 0	0 / 1

Left ventricular failure			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular dysfunction			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal incontinence			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			

subjects affected / exposed	1 / 134 (0.75%)	2 / 130 (1.54%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 134 (1.49%)	2 / 130 (1.54%)	3 / 132 (2.27%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haematuria			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	2 / 134 (1.49%)	0 / 130 (0.00%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal impairment			
subjects affected / exposed	2 / 134 (1.49%)	1 / 130 (0.77%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacillus bacteraemia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	2 / 134 (1.49%)	3 / 130 (2.31%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	5 / 134 (3.73%)	7 / 130 (5.38%)	5 / 132 (3.79%)
occurrences causally related to treatment / all	0 / 5	0 / 7	0 / 5
deaths causally related to treatment / all	0 / 5	0 / 7	0 / 5
Candida sepsis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Orchitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 134 (0.75%)	3 / 130 (2.31%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 3	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 134 (0.75%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pseudomonal			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	2 / 134 (1.49%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 130 (0.00%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	3 / 134 (2.24%)	3 / 130 (2.31%)	4 / 132 (3.03%)
occurrences causally related to treatment / all	0 / 3	0 / 3	1 / 4
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 2
Superinfection bacterial			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 130 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 130 (0.77%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	All Placebo	MSTT1041A	UTTR1147A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 134 (21.64%)	42 / 130 (32.31%)	40 / 132 (30.30%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 134 (2.99%)	8 / 130 (6.15%)	2 / 132 (1.52%)
occurrences (all)	4	8	2
Hypotension			

subjects affected / exposed	5 / 134 (3.73%)	7 / 130 (5.38%)	5 / 132 (3.79%)
occurrences (all)	6	8	6
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 134 (2.99%)	7 / 130 (5.38%)	4 / 132 (3.03%)
occurrences (all)	4	8	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 134 (4.48%)	9 / 130 (6.92%)	7 / 132 (5.30%)
occurrences (all)	6	9	8
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 134 (1.49%)	3 / 130 (2.31%)	7 / 132 (5.30%)
occurrences (all)	2	3	7
Constipation			
subjects affected / exposed	6 / 134 (4.48%)	10 / 130 (7.69%)	10 / 132 (7.58%)
occurrences (all)	6	10	10
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	5 / 134 (3.73%)	4 / 130 (3.08%)	9 / 132 (6.82%)
occurrences (all)	5	4	9
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 134 (0.75%)	5 / 130 (3.85%)	8 / 132 (6.06%)
occurrences (all)	1	5	8
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	8 / 134 (5.97%)	9 / 130 (6.92%)	8 / 132 (6.06%)
occurrences (all)	8	9	10

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2020	Protocol Version 2: The purpose of this update was to define the time to clinical failure for patients entering the study who were already in the ICU or on mechanical ventilation. A new secondary endpoint, "Proportion of patients alive and free of respiratory failure at Day 28", was added. The protocol was updated to indicate that the re-screening assessments were required at specified durations after the initial screen failure. The peripheral capillary oxygen saturation (SpO2) inclusion criterion was updated, and the protocol was updated to require that the specific form of ventilation required be recorded. The protocol was updated to clarify that all concomitant therapy for COVID-19 should be recorded on the appropriate electronic Case Report Form (eCRF), independently of the start date of such therapy, and to prohibit concomitant therapy with tumor necrosis factor (TNF) inhibitors, anti-IL-1 agents, and investigational agents other than for COVID-19. Details on laboratory abnormalities associated with RO7021610 were added; the protocol was updated to specify reporting of dermatological toxicity on the rash eCRF.MSTT1041A/UTTR1147A—Genentech, Inc. 4/Protocol GA42469, Version 2. Guidelines for managing patients who experienced infusion-related reactions (IRR) was added.
03 August 2020	Protocol Version 3: Amended to allow for use of a conventional troponin assay if a high-sensitivity immunoassay was not available locally. Incidence of ECMO was upgraded from an exploratory to a secondary efficacy endpoint, and duration of hypoxemia was removed from the list of secondary efficacy endpoints. Language was updated to clarify that a stratification factor, the enrollment cap, and certain statistical summaries and analyses would be based on invasive mechanical ventilation. Language was updated to clarify that discharge assessments were applicable to patients transferred to a different care facility upon discharge from the hospital. The inclusion criteria and description of laboratory tests were modified to accommodate sites at an altitude 5000 feet. Language regarding pregnancy testing was updated to account for the fact that either a urine or serum test may be performed and to clarify that women of childbearing potential must have a negative pregnancy test at screening. Exclusion criteria (EC) were modified to allow enrollment of patients with a troponin level equal to the ULN. EC were also modified to clarify that prolonged QT interval was based on QT interval corrected (Fridericia's formula) and to include guidance for patients with a ventricular pacemaker. Language was modified to clarify timing for recording vital signs, oxygen saturation, and NEWS2 specific assessments, and for assessing clinical status. Statistical analysis methods for the primary endpoint was modified to indicate that a non-parametric method that does not assume proportional odds (Van Elteren test) would be used if the proportional odds assumption is violated. Language was modified to clarify the timing of PK samples. The timing of the second dose of study drug was modified to allow for drug administration on Days 14, 16, or 17 for cases when the dose could not be given on Day 15, provided certain assessments were performed prior to administration.

16 September 2020	Protocol Version 4: The protocol was amended to change the primary endpoint and increase the sample size. Substantive changes to the protocol, along with a rationale for each change, are summarized below: The primary endpoint was changed to "Time to recovery, defined as time to score of 1 or 2 on the 7-category ordinal scale (whichever occurs first)". The previous primary endpoint, "Clinical status assessed using a 7-category ordinal scale at Day 28," was moved to the secondary efficacy endpoints. On the basis of published data from other clinical trials for COVID-19 pneumonia (Beigel et al. 2020; McCreary and Angus 2020), there appeared to be growing consensus that time to recovery reflected a clinically meaningful outcome measurement for the targeted patient population. Additionally, given the variable time course of COVID-19, a fixed time endpoint could miss recognition of clinical benefit and therefore may not be optimal (Dodd et al. 2020). The incidence of mechanical ventilation and extracorporeal membrane oxygenation was combined into a single secondary efficacy endpoint, as both represented a worsening of the clinical status and choice of management could vary between institutions. Clarifications were made to the reporting requirements for possible RO7021610-mediated dermatologic reactions. The sample size was increased from 300 patients to approximately 390 patients with severe COVID-19 pneumonia, which was anticipated provide approximately 80% power to detect a difference between treatment groups for the new primary endpoint, "time to recovery, defined as time to score of 1 or 2 on the 7-category ordinal scale (whichever occurs first)".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported