Clinical trial results:
A Multicenter, Adaptive, Randomised Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults - Version for European Union/United Kingdom Sites

Summary

EudraCT number	2020-001052-18
Trial protocol	DK GB DE GR ES
Global end of trial date	10 September 2020

Results information

Result version number	v1 (current)
This version publication date	01 April 2021
First version publication date	01 April 2021
Summary attachment (see zip file)	ACTT-1 final results (ACTT-1_final_results-paper_nejm_08Oct2020.pdf) ACTT-2 final results (ACTT-2_Publication_NEJM_11Dec2020.pdf)

Trial information

Trial identification

Sponsor protocol code	010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04280705
WHO universal trial number (UTN)	-
Other trial identifiers	DMID - NIH: 20-0006, Version no. 6.0

Notes:

Sponsors

Sponsor organisation name	US NIAID, Div. of Microbiology and Infectious Diseases (DMID) National Institute of Health (NIH)
Sponsor organisation address	5601 Fishers Lane, Bethesda, United States, MD 20892-9806
Public contact	Janice Arega, US NIAID, Div. of Microbiology and Infectious Diseases (DMID) National Institute of Health (NIH), +1 240292-0928, aregaj@niaid.nih.gov
Scientific contact	Janice Arega, US NIAID, Div. of Microbiology and Infectious Diseases (DMID) National Institute of Health (NIH), +1 240292-0928, aregaj@niaid.nih.gov
Sponsor organisation name	University of Minnesota
Sponsor organisation address	420 Johnston Hall, 101 Pleasant St. SE, Minneapolis, United States, 55455
Public contact	Eileen Denning, Coordinating Centers for Biometric Research, Div. of Biostatistics, School of Public Health, edenning@umn.edu
Scientific contact	James D. Neaton, Coordinating Centers for Biometric Research, Div. of Biostatistics, School of Public Health, neato001@umn.edu

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	09 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2020
Global end of trial reached?	Yes
Global end of trial date	10 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical efficacy, as assessed by time to recovery, of different investigational therapeutics for COVID-19 as compared to the control arm. In the first study of this platform trial reported here, remdesivir vs. placebo was studied.

Protection of trial subjects:

No additional measures beyond usual care of individuals hospitalised with COVID-19.

Background therapy:

none

Evidence for comparator: -

Actual start date of recruitment	23 March 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	Spain: 28
Country: Number of subjects enrolled	United Kingdom: 46
Country: Number of subjects enrolled	Denmark: 43
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Greece: 33
Country: Number of subjects enrolled	Japan: 15
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Singapore: 16

Country: Number of subjects enrolled	Korea, Republic of: 21
Country: Number of subjects enrolled	United States: 837
Worldwide total number of subjects	1062
EEA total number of subjects	117

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)	678
From 65 to 84 years	340
85 years and over	44

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from participating hospitals between 21 Feb 2020 and 20 Apr 2020

Pre-assignment

Screening details:

Hospitalized adults with COVID-19

Pre-assignment period milestones

Number of subjects started	1062
Number of subjects completed	1062

Period 1

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

Blinding implementation details:

Randomizer was given a treatment ID, which was sent to the pharmacy. The ID was decoded in the pharmacy. A saline placebo infusion was used. The infusion bag was covered with a colored sleeve to mask the slight different in color between the active product and placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Normal saline given at equal volume on the same schedule

Arm type	Placebo
Investigational medicinal product name	normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

A normal saline placebo will be given at an equal volume to the remdesivir infusion

Arm title	Remdesivir

Arm description:

200 mg of Remdesivir administered intravenously on Day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir while hospitalized for up to a 10 days total course.

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

Arm type	Experimental

Investigational medicinal product name	remdesivir
Investigational medicinal product code	
Other name	Veklury
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg of Remdesivir administered intravenously on Day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir while hospitalized for up to a 10 days total course

Number of subjects in period 1	Placebo	Remdesivir
Started	521	541
Received treatment	517	531
Completed	508	517
Not completed	13	24
Physician decision	1	-
Consent withdrawn by subject	7	9
Adverse event, non-fatal	-	4
Transferred to another hospital	1	1
Enrolled but not treated	4	10

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Normal saline given at equal volume on the same schedule	
Reporting group title	Remdesivir
Reporting group description:	
200 mg of Remdesivir administered intravenously on Day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir while hospitalized for up to a 10 days total course. Remdesivir: Drug Remdesivir is a single diastereomer monophosphoramidate prodrug designed for the intracellular delivery of a modified adenine nucleoside analog GS-441524. In addition to the active ingredient, the lyophilized formulation of Remdesivir contains the following inactive ingredients: water for injection, sulfobutylether beta-cyclodextrin sodium (SBECD), and hydrochloric acid and/or sodium hydroxide.	

Reporting group values	Placebo	Remdesivir	Total
Number of subjects	521	541	1062
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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	59.2	59.6	
standard deviation	± 15.4	± 14.6	-
Gender categorical Units: Subjects			
Female	189	189	378
Male	332	352	684

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Normal saline given at equal volume on the same schedule	
Reporting group title	Remdesivir
Reporting group description:	
200 mg of Remdesivir administered intravenously on Day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir while hospitalized for up to a 10 days total course. Remdesivir: Drug Remdesivir is a single diastereomer monophosphoramidate prodrug designed for the intracellular delivery of a modified adenine nucleoside analog GS-441524. In addition to the active ingredient, the lyophilized formulation of Remdesivir contains the following inactive ingredients: water for injection, sulfobutylether beta-cyclodextrin sodium (SBECD), and hydrochloric acid and/or sodium hydroxide.	

Primary: Time to recovery

End point title	Time to recovery
End point description:	
Day of recovery is defined as the first day on which the subject satisfies one of the following three categories from the ordinal scale: 1) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 2) Not hospitalized, limitation on activities and/or requiring home oxygen; 3) Not hospitalized, no limitations on activities.	
End point type	Primary
End point timeframe:	
Day 1-29 (entire trial period)	

End point values	Placebo	Remdesivir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	521	541		
Units: days				
median (confidence interval 95%)	15 (13 to 18)	10 (9 to 11)		

Statistical analyses

Statistical analysis title	Main analysis
Comparison groups	Placebo v Remdesivir
Number of subjects included in analysis	1062
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.29

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.49

Secondary: Mean change in ordinal scale

End point title	Mean change in ordinal scale

End point description:

The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 8) Death; 7) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 6) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 5) Hospitalized, requiring supplemental oxygen; 4) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 3) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 2) Not hospitalized, limitation on activities and/or requiring home oxygen; 1) Not hospitalized, no limitations on activities. A positive change indicates a worsening and a negative change is an improvement.

End point type	Secondary

End point timeframe:

Through Day 29. The ordinal scale was measured at Day 1, 3, 5, 8, 11, 15, 22, and 29

End point values	Placebo	Remdesivir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	518	533		
Units: units on a scale				
arithmetic mean (standard deviation)	-2.7 (± 2.3)	-2.3 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants at each clinical status using ordinal scale at Day 15

End point title	Percentage of participants at each clinical status using ordinal scale at Day 15

End point description:

The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 8) Death; 7) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 6) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 5) Hospitalized, requiring supplemental oxygen; 4) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 3) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 2) Not hospitalized, limitation on activities and/or requiring home oxygen; 1) Not hospitalized, no limitations on activities

End point type	Secondary

End point timeframe:

At Day 15

End point values	Placebo	Remdesivir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	521	541		
Units: percent				
number (confidence interval 95%)				
Death at or before study visit	11 (9 to 14)	6 (5 to 9)		
Hospitalized, on invasive mech. vent. or ECMO	22 (19 to 26)	15 (13 to 19)		
hospitalized, on non-invasive vent./high flow O2	4 (3 to 6)	4 (3 to 6)		
Hospitalized, requiring supplemental O2	11 (9 to 14)	10 (8 to 13)		
Hospitalized, not on O2, requiring ongoing care	6 (5 to 9)	7 (5 to 9)		
Hospitalized, not requiring O2, no longer req care	2 (1 to 3)	3 (2 to 4)		
Not hospitalized, limit on activities/req home O2	17 (14 to 21)	19 (16 to 22)		
Not hospitalized, no limitations on activities	22 (19 to 26)	29 (25 to 33)		
No clinical status score reported - Hospitalized	0 (0 to 1)	0 (0 to 1)		
No clinical status score reported - Discharged	2 (1 to 3)	2 (1 to 4)		
No clinical status score reported - Discontinued	3 (2 to 4)	5 (3 to 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mortality

End point title	Mortality

End point description:

The mortality rate was estimated as the percentage of participants who died by study Day 29.

End point type	Secondary

End point timeframe:

Entire trial (through day 29)

End point values	Placebo	Remdesivir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	521	541		
Units: perc				
number (confidence interval 95%)	15 (12 to 19)	11 (9 to 15)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Days 1-29 (entire trial)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	Placebo
Reporting group description: Normal saline given at equal volume on the same schedule	
Reporting group title	Remdesivir
Reporting group description: 200 mg of Remdesivir administered intravenously on Day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir while hospitalized for up to a 10 days total course. Remdesivir: Drug Remdesivir is a single diastereomer monophosphoramidate prodrug designed for the intracellular delivery of a modified adenine nucleoside analog GS-441524. In addition to the active ingredient, the lyophilized formulation of Remdesivir contains the following inactive ingredients: water for injection, sulfobutylether beta-cyclodextrin sodium (SBECD), and hydrochloric acid and/or sodium hydroxide.	

Serious adverse events	Placebo	Remdesivir	
Total subjects affected by serious adverse events			
subjects affected / exposed	163 / 516 (31.59%)	131 / 532 (24.62%)	
number of deaths (all causes)	77	59	
number of deaths resulting from adverse events			
Vascular disorders			
Hypotension			
subjects affected / exposed	7 / 516 (1.36%)	4 / 532 (0.75%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Shock			
subjects affected / exposed	4 / 516 (0.78%)	5 / 532 (0.94%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Deep vein thrombosis			
subjects affected / exposed	1 / 516 (0.19%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Embolism venous			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Endotracheal intubation			
subjects affected / exposed	9 / 516 (1.74%)	6 / 532 (1.13%)	
occurrences causally related to treatment / all	0 / 9	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ventilation			
subjects affected / exposed	3 / 516 (0.58%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	3 / 516 (0.58%)	5 / 532 (0.94%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 3	0 / 4	
Pyrexia			
subjects affected / exposed	2 / 516 (0.39%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Death			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	58 / 516 (11.24%)	35 / 532 (6.58%)	
occurrences causally related to treatment / all	0 / 59	0 / 36	
deaths causally related to treatment / all	0 / 28	0 / 20	
Acute respiratory failure			
subjects affected / exposed	14 / 516 (2.71%)	8 / 532 (1.50%)	
occurrences causally related to treatment / all	0 / 14	0 / 8	
deaths causally related to treatment / all	0 / 6	0 / 2	
Respiratory distress			
subjects affected / exposed	11 / 516 (2.13%)	6 / 532 (1.13%)	
occurrences causally related to treatment / all	0 / 11	0 / 6	
deaths causally related to treatment / all	0 / 4	0 / 2	
Acute respiratory distress syndrome			
subjects affected / exposed	5 / 516 (0.97%)	7 / 532 (1.32%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 5	0 / 4	
Pneumothorax			
subjects affected / exposed	5 / 516 (0.97%)	5 / 532 (0.94%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	4 / 516 (0.78%)	5 / 532 (0.94%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 4	0 / 0	

Hypoxia			
subjects affected / exposed	4 / 516 (0.78%)	4 / 532 (0.75%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonia aspiration			
subjects affected / exposed	2 / 516 (0.39%)	4 / 532 (0.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Dyspnoea			
subjects affected / exposed	1 / 516 (0.19%)	3 / 532 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	2 / 516 (0.39%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic respiratory failure			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemoptysis			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			

subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Glomerular filtration rate decreased			
subjects affected / exposed	2 / 516 (0.39%)	5 / 532 (0.94%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	2 / 516 (0.39%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			
subjects affected / exposed	1 / 516 (0.19%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Procedural pneumothorax			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	7 / 516 (1.36%)	10 / 532 (1.88%)	
occurrences causally related to treatment / all	0 / 7	0 / 10	
deaths causally related to treatment / all	0 / 4	0 / 7	
Atrial fibrillation			
subjects affected / exposed	1 / 516 (0.19%)	5 / 532 (0.94%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	3 / 516 (0.58%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Myocardial infarction			
subjects affected / exposed	4 / 516 (0.78%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	3 / 516 (0.58%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 516 (0.00%)	2 / 532 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 516 (0.19%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	1 / 516 (0.19%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	2 / 516 (0.39%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Palpitations			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ventricular fibrillation			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			

subjects affected / exposed	1 / 516 (0.19%)	3 / 532 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 516 (0.19%)	2 / 532 (0.38%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic transformation stroke			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			

subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intensive care unit acquired weakness			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal ischaemia			
subjects affected / exposed	0 / 516 (0.00%)	3 / 532 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Diarrhoea			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Duodenal perforation			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematemesis			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer haemorrhage			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Subcutaneous emphysema			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	12 / 516 (2.33%)	7 / 532 (1.32%)	
occurrences causally related to treatment / all	1 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	5 / 516 (0.97%)	2 / 532 (0.38%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	3 / 516 (0.58%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic shock			

subjects affected / exposed	15 / 516 (2.91%)	8 / 532 (1.50%)	
occurrences causally related to treatment / all	0 / 15	0 / 8	
deaths causally related to treatment / all	0 / 5	0 / 3	
COVID-19			
subjects affected / exposed	5 / 516 (0.97%)	2 / 532 (0.38%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Bacteraemia			
subjects affected / exposed	2 / 516 (0.39%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 516 (0.39%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Sepsis			
subjects affected / exposed	2 / 516 (0.39%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 516 (0.39%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter bacteraemia			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			

subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 516 (0.19%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypernatraemia			
subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	0 / 516 (0.00%)	1 / 532 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 516 (0.19%)	0 / 532 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Remdesivir	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	295 / 516 (57.17%)	276 / 532 (51.88%)	
Investigations			
Glomerular filtration rate decreased			
subjects affected / exposed	74 / 516 (14.34%)	55 / 532 (10.34%)	
occurrences (all)	81	59	
Haemoglobin decreased			
subjects affected / exposed	62 / 516 (12.02%)	48 / 532 (9.02%)	
occurrences (all)	69	51	
Lymphocyte count decreased			
subjects affected / exposed	54 / 516 (10.47%)	44 / 532 (8.27%)	
occurrences (all)	63	56	
Blood creatinine increased			
subjects affected / exposed	36 / 516 (6.98%)	31 / 532 (5.83%)	
occurrences (all)	41	33	
Blood glucose increased			
subjects affected / exposed	27 / 516 (5.23%)	39 / 532 (7.33%)	
occurrences (all)	31	45	
Aspartate aminotransferase increased			
subjects affected / exposed	33 / 516 (6.40%)	18 / 532 (3.38%)	
occurrences (all)	35	19	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	52 / 516 (10.08%)	42 / 532 (7.89%)	
occurrences (all)	58	52	
Lymphopenia			
subjects affected / exposed	30 / 516 (5.81%)	13 / 532 (2.44%)	
occurrences (all)	34	15	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	32 / 516 (6.20%)	38 / 532 (7.14%)	
occurrences (all)	37	52	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	34 / 516 (6.59%)	34 / 532 (6.39%)	
occurrences (all)	43	36	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2020	After remdesivir was shown to be effective in ACTT-1, this platform protocol was amended to ACTT-2, which compared baricitanib vs. placebo on a background of remdesivir as standard of care. The results of ACTT-2 are reported in an attachment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32445440