Clinical trial results:
Phase 3, Randomized, Placebo Controlled, Double-blind, Multicenter, Stratified Study of CPI-006 Plus Standard of Care Versus Placebo Plus Standard of Care in Mild to Moderately Symptomatic Hospitalized Covid-19 Patients

Summary

EudraCT number	2020-005305-54
Trial protocol	DE
Global end of trial date	18 August 2021

Results information

Result version number	v1 (current)
This version publication date	01 October 2022
First version publication date	01 October 2022

Trial information

Trial identification

Sponsor protocol code	CPI-006-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04734873
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Corvus Pharmaceuticals, Inc.
Sponsor organisation address	863 Mitten Road, Burlingame, CA, United States, 94010
Public contact	Clinical Trial Information, Corvus Pharmaceuticals, Inc, clinicaltrials@corvuspharma.com
Scientific contact	Clinical Trial Information, Corvus Pharmaceuticals, Inc, clinicaltrials@corvuspharma.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	18 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 August 2021
Global end of trial reached?	Yes
Global end of trial date	18 August 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the proportion of participants alive and respiratory failure free during the 28 days after dosing with CPI-006 plus SOC versus placebo plus SOC in hospitalized participants with mild to moderately symptomatic Covid-19 infection

Protection of trial subjects:

The study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP), all applicable regulatory requirements, and the general ethical principles outlined in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 February 2021
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: 1
Country: Number of subjects enrolled	United States: 41
Worldwide total number of subjects	42
EEA total number of subjects	1

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)	38
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

46 participants were screened and 42 were randomized. Of the 42 participants randomized, only 40 received the treatment assigned at randomization (2 were randomized but withdrew consent prior to receiving study treatment).

Pre-assignment

Screening details:

46 participants were screened and 42 were randomized. Of the 42 participants randomized, only 40 received the treatment assigned at randomization (2 were randomized but withdrew consent prior to receiving study treatment).

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	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment A: CPI-006 2 mg/kg + SOC

Arm description:

IV CPI-006 2 mg/kg up to a maximum dose of 200 mg on Day 1 plus standard of care.

Arm type	Experimental
Investigational medicinal product name	CPI-006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV CPI-006 2 mg/kg up to a maximum dose of 200 mg on Day 1 plus standard of care

Arm title	Treatment B: CPI-006 1 mg/kg + SOC

Arm description:

IV CPI-006 1 mg/kg up to a maximum dose of 100 mg on Day 1 plus standard of care.

Arm type	Experimental
Investigational medicinal product name	CPI-006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV CPI-006 1 mg/kg up to a maximum dose of 100 mg on Day 1 plus standard of care

Arm title	Treatment C : Placebo + SOC

Arm description:

IV placebo on Day 1 plus standard of care.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV placebo on Day 1 plus standard of care

Number of subjects in period 1	Treatment A: CPI-006 2 mg/kg + SOC	Treatment B: CPI-006 1 mg/kg + SOC	Treatment C : Placebo + SOC
Started	16	14	12
Completed	14	11	9
Not completed	2	3	3
Lost to follow-up	1	3	2
Randomised but not dosed	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment A: CPI-006 2 mg/kg + SOC
Reporting group description:	
IV CPI-006 2 mg/kg up to a maximum dose of 200 mg on Day 1 plus standard of care.	
Reporting group title	Treatment B: CPI-006 1 mg/kg + SOC
Reporting group description:	
IV CPI-006 1 mg/kg up to a maximum dose of 100 mg on Day 1 plus standard of care.	
Reporting group title	Treatment C : Placebo + SOC
Reporting group description:	
IV placebo on Day 1 plus standard of care.	

Reporting group values	Treatment A: CPI-006 2 mg/kg + SOC	Treatment B: CPI-006 1 mg/kg + SOC	Treatment C : Placebo + SOC
Number of subjects	16	14	12
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)	13	13	12
From 65-84 years	3	1	0
85 years and over	0	0	0
Age continuous Units: years			
median	56.5	53.0	55.0
full range (min-max)	28 to 69	25 to 67	21 to 63
Gender categorical Units: Subjects			
Female	6	3	9
Male	10	11	3
Ethinicity Units: Subjects			
Hispanic or Latino	6	3	3
Not Hispanic or Latino	8	11	8
Unknown or Not Reported	2	0	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	2	2
White	13	11	9

More than one race	0	0	0
Unknown or Not Reported	1	0	0
Region of Enrollment Units: Subjects			
United States	16	13	12
Spain	0	1	0
8-point Ordinal Scale			
Scale Categories: 1= Not hospitalized, no limitations on activities; 2= Not hospitalized, limitation on activities and/or requiring home oxygen; 3= Hospitalized, not requiring supplemental oxygen- no longer requiring ongoing medical care; 4= Hospitalized, not requiring supplemental oxygen-requiring ongoing medical care (Covid-19 related or otherwise); 5= Hospitalized, requiring supplemental oxygen; 6= Hospitalized, on non-invasive ventilation or high flow oxygen devices; 7= Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation; 8= Death			
Units: Subjects			
Four	0	3	2
Five	7	10	7
Six	9	1	3

Reporting group values	Total		
Number of subjects	42		
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)	38		
From 65-84 years	4		
85 years and over	0		
Age continuous Units: years median full range (min-max)	--		
Gender categorical Units: Subjects			
Female	18		
Male	24		
Ethinicity Units: Subjects			
Hispanic or Latino	12		
Not Hispanic or Latino	27		
Unknown or Not Reported	3		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	2		

Native Hawaiian or Other Pacific Islander	0		
Black or African American	6		
White	33		
More than one race	0		
Unknown or Not Reported	1		
Region of Enrollment Units: Subjects			
United States	41		
Spain	1		
8-point Ordinal Scale			
Scale Categories: 1= Not hospitalized, no limitations on activities; 2= Not hospitalized, limitation on activities and/or requiring home oxygen; 3= Hospitalized, not requiring supplemental oxygen- no longer requiring ongoing medical care; 4= Hospitalized, not requiring supplemental oxygen-requiring ongoing medical care (Covid-19 related or otherwise); 5= Hospitalized, requiring supplemental oxygen; 6= Hospitalized, on non-invasive ventilation or high flow oxygen devices; 7= Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation; 8= Death			
Units: Subjects			
Four	5		
Five	24		
Six	13		

End points

End points reporting groups

Reporting group title	Treatment A: CPI-006 2 mg/kg + SOC
Reporting group description: IV CPI-006 2 mg/kg up to a maximum dose of 200 mg on Day 1 plus standard of care.	
Reporting group title	Treatment B: CPI-006 1 mg/kg + SOC
Reporting group description: IV CPI-006 1 mg/kg up to a maximum dose of 100 mg on Day 1 plus standard of care.	
Reporting group title	Treatment C : Placebo + SOC
Reporting group description: IV placebo on Day 1 plus standard of care.	

Primary: Proportion of Participants Alive and Respiratory Failure Free of CPI-006 Plus SOC Versus Placebo Plus SOC

End point title	Proportion of Participants Alive and Respiratory Failure Free of CPI-006 Plus SOC Versus Placebo Plus SOC[1]

End point description:

Proportion of participants who are alive and free from respiratory deterioration in each active arm compared to placebo arm as measured by the modified World Health Organization (WHO) 8-point Ordinal Scale for Clinical Improvement in which: 1=Not hospitalized, no limitations on activities; 2=Not hospitalized, limitation on activities and/or requiring home oxygen; 3=Hospitalized, not requiring supplemental oxygen -no longer requiring ongoing medical care; 4=Hospitalized, not requiring supplemental oxygen -requiring ongoing medical care (Covid-19 related or otherwise); 5=Hospitalized, requiring supplemental oxygen; 6=Hospitalized, on non-invasive ventilation or high flow oxygen devices; 7=Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation; 8=Death.

End point type	Primary

End point timeframe:

During the 28 days after dosing.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Primary endpoint consists of proportion of participants who are alive and free from respiratory deterioration in each active arm compared to placebo arm and such percentages cannot be populated in EudraCT.

End point values	Treatment A: CPI-006 2 mg/kg + SOC	Treatment B: CPI-006 1 mg/kg + SOC	Treatment C : Placebo + SOC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	11	
Units: Participants	14	12	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Recovery of CPI-006 Plus SOC Versus Placebo Plus SOC

End point title	Time to Recovery of CPI-006 Plus SOC Versus Placebo Plus

	SOC

End point description:

Time to recovery after dosing in each active arm compared to placebo arm as measured by the modified WHO 8-point Ordinal Scale for Clinical Improvement in which: 1=Not hospitalized, no limitations on activities; 2=Not hospitalized, limitation on activitiesand/or requiring home oxygen; 3=Hospitalized, not requiring supplemental oxygen -no longer requiring ongoing medical care; 4=Hospitalized, not requiring supplemental oxygen -requiring ongoing medical care (Covid-19 related or otherwise); 5=Hospitalized,requiring supplemental oxygen; 6=Hospitalized, on non-invasive ventilation or high flow oxygen devices; 7=Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation; 8=Death.

End point type	Secondary

End point timeframe:

During the 28 days after dosing.

End point values	Treatment A: CPI-006 2 mg/kg + SOC	Treatment B: CPI-006 1 mg/kg + SOC	Treatment C : Placebo + SOC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	10	
Units: Days				
median (confidence interval 95%)	6.0 (4.0 to 9.0)	4.5 (3.0 to 8.0)	7.0 (2.0 to 12.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Clinical Improvement of CPI-006 Plus SOC Versus Placebo Plus SOC

End point title	Time to Clinical Improvement of CPI-006 Plus SOC Versus Placebo Plus SOC

End point description:

Time to clinical improvement in each active arm compared to placebo arm as measured by the modified WHO 8-point Ordinal Scale for Clinical Improvement in which: 1=Not hospitalized, no limitations on activities; 2=Not hospitalized, limitation on activities and/or requiring home oxygen; 3=Hospitalized, not requiring supplemental oxygen -no longer requiring ongoing medical care; 4=Hospitalized, not requiring supplemental oxygen -requiring ongoing medical care (Covid-19 related or otherwise); 5=Hospitalized, requiring supplemental oxygen; 6=Hospitalized, on non-invasive ventilation or high flow oxygen devices; 7=Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation; 8=Death. Clinical improvement is defined as ≥ 2 points improvement in the 8-point ordinal scale.

End point type	Secondary

End point timeframe:

During the 28 days after dosing.

End point values	Treatment A: CPI-006 2 mg/kg + SOC	Treatment B: CPI-006 1 mg/kg + SOC	Treatment C : Placebo + SOC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	11	
Units: Days				
median (confidence interval 95%)	6.0 (4.0 to 9.0)	4.5 (3.0 to 8.0)	7.0 (2.0 to 12.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mortality Rate Due to Any Cause of CPI-006 Plus SOC Versus Placebo Plus SOC

End point title	Mortality Rate Due to Any Cause of CPI-006 Plus SOC Versus Placebo Plus SOC

End point description:

Proportion of participants who died in each active arm compared to placebo arm.

End point type	Secondary

End point timeframe:

During the 28 days after dosing.

End point values	Treatment A: CPI-006 2 mg/kg + SOC	Treatment B: CPI-006 1 mg/kg + SOC	Treatment C : Placebo + SOC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	14	11	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From initiation of study treatment through study Day 28 (4 weeks)	
Adverse event reporting additional description:	
The Safety Population includes all participants who received any amount of study treatment (CPI-006, placebo, or SOC).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Treatment A: CPI-006 2 mg/kg + SOC
Reporting group description:	
IV CPI-006 2 mg/kg up to a maximum dose of 200 mg on Day 1 plus standard of care.	
Reporting group title	Treatment B: CPI-006 1 mg/kg + SOC
Reporting group description:	
IV CPI-006 1 mg/kg up to a maximum dose of 100 mg on Day 1 plus standard of care.	
Reporting group title	Treatment C: Placebo + SOC
Reporting group description:	
IV placebo on Day 1 plus standard of care.	

Serious adverse events	Treatment A: CPI-006 2 mg/kg + SOC	Treatment B: CPI-006 1 mg/kg + SOC	Treatment C: Placebo + SOC
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	2 / 11 (18.18%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Substance-induced psychotic disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Treatment A: CPI-006 2 mg/kg + SOC	Treatment B: CPI-006 1 mg/kg + SOC	Treatment C: Placebo + SOC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 15 (33.33%)	2 / 14 (14.29%)	2 / 11 (18.18%)
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dyskinesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Myopia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Visual impairment			

subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Diverticulitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pneumonia escherichia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pneumonia klebsiella			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin candida			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 January 2021	Protocol version 002 (Amendment 1) main updates: - An additional study drug treatment arm for 1 mg/kg CPI-006 plus standard of care (SOC) was added to create a 3-arm study, increasing the total sample size to 1000 participants, and changing the randomization schedule - Primary Endpoint: proportion of patients alive and free of respiratory deterioration has been added and replaces prior primary endpoint of time to recovery during the 28 days after dosing (Section 3). The primary endpoint was updated to account for mortality in the efficacy evaluation of the study treatment.
23 March 2021	Protocol version 003 (Amendment 2) main changes: - Update of Supportive Secondary Endpoints and Key Secondary Endpoints - Clarification and update of inclusion criteria for increased flexibility of disease onset and duration

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated due to enrollment difficulties and, as a result, some of the originally planned efficacy analyses could not
be performed.

Notes: