Clinical trial results:
A Phase 2/3, Randomized, Parallel-group, Placebo-controlled, Double-Blind Study to Evaluate the Efficacy and Safety of CT-P59 in Combination with Standard of Care in Outpatients with Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) Infection

Summary

EudraCT number	2020-003369-20
Trial protocol	IE RO HU IT
Global end of trial date	20 October 2021

Results information

Result version number	v1 (current)
This version publication date	03 June 2022
First version publication date	03 June 2022

Trial information

Trial identification

Sponsor protocol code	CT-P59_3.2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04602000
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CELLTRION Inc.
Sponsor organisation address	23, Academy-ro, Yeonsu-gu, Incheon, Korea, Republic of, 22014
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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	14 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1
-To assess the clinically meaningful therapeutic efficacy of CT-P59 as determined by proportion of patients with clinical symptom requiring hospitalization, oxygen therapy, or experiencing mortality due to SARS-CoV-2 infection up to Day 28
-To assess the potential therapeutic efficacy of CT-P59 as determined by proportion of patients with negative conversion in nasopharyngeal swab specimen based on RT-qPCR at each visit up to Day 14
-To assess the potential therapeutic efficacy of CT-P59 as determined by time to negative conversion in nasopharyngeal swab specimen based on RT-qPCR up to Day 14
-To assess the potential therapeutic efficacy of CT-P59 as determined by time to clinical recovery up to Day 14
Part 2
- To demonstrate the clinically meaningful therapeutic efficacy of CT-P59 as determined by proportion of patients with clinical symptom requiring hospitalization, oxygen therapy, or experiencing mortality due to SARS-CoV-2 infection up to Day 28 in high-risk patients

Protection of trial subjects:

CT-P59 was diluted and administered intravenously over 90 minutes in Part 1 (60 minutes in Part 2) by a nurse or doctor. The rate of infusion would be slowed or interrupted if the patient developed any signs of infusion related reactions or other adverse reactions and appropriate treatment were initiated as necessary. Hypersensitivity was assessed by vital sign monitoring on the day of study drug administration at the time points: Prior to the beginning of study drug administration (within 30 minutes), 30 minutes (±15 minutes) and 60 minutes (±15 minutes) after the start of study drug administration, 15 minutes after the end of study drug administration (+15 minutes), 2 hours (±15 minutes) and 4 hours (±15 minutes) after the start of study drug administration. In addition, hypersensitivity was monitored by routine continuous clinical monitoring. In case of hypersensitivity, emergency medication and equipment (such as adrenaline, antihistamines, corticosteroids, and respiratory support including inhalational therapy,
oxygen, and artificial ventilation) were made available, and any types of ECG could be performed if a patient experienced cardiac symptoms. For patients who experienced or developed life-threatening treatment-related hypersensitivity reactions, study drug was stopped immediately.

Background therapy:

All enrolled patients were given optimal standard of care, which included rehydration therapy, antipyretics, or antitussives prescribed at the investigator's discretion. The routine use of antibiotics was not recommended, but antibiotics could be used if bacterial infections were present or suspected. The type of antibiotic would be selected based on the patient's clinical disease status and symptoms at the investigator's discretion.

Evidence for comparator:

Placebo contained the same ingredient as the CT-P59 formulation listed above, excluding SARS-CoV-2 receptor binding domain binding monoclonal antibody, in 16 mL water for injection. The pH of the placebo solution was 6.0.

Actual start date of recruitment	05 October 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 57
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Korea, Republic of: 52
Country: Number of subjects enrolled	North Macedonia: 56
Country: Number of subjects enrolled	Mexico: 138
Country: Number of subjects enrolled	Moldova, Republic of: 37
Country: Number of subjects enrolled	Peru: 20
Country: Number of subjects enrolled	Poland: 90
Country: Number of subjects enrolled	Romania: 902
Country: Number of subjects enrolled	Serbia: 47
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	Ukraine: 107
Country: Number of subjects enrolled	United States: 108
Worldwide total number of subjects	1642
EEA total number of subjects	1077

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)	1417
From 65 to 84 years	220
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

For Part 1, participants were screened from 23 study centers in 4 countries and were enrolled from 23 study centers in 4 countries.
For Part 2, participants were screened from 60 study centers in 14 countries and were enrolled from 58 study centers in 13 countries.

Pre-assignment

Screening details:

Main Selection Criteria:
- Adult male or female, aged 18 years or older
- Patients diagnosed with SARS-CoV-2 infection at Screening
- Patient with oxygen saturation >94% on room air and not requiring supplemental oxygen
- Patient whose onset of symptom is no more than 7 days

Period 1

Period 1 title	Part 1 + Part 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This study was double-blinded and the investigators, all designated study staff (with the exception of the unblinded study pharmacists or unblinded staff designated to prepare the study drug for infusion and predefined unblinded teams in the sponsor and CRO), and patients remained blinded until the generation of this final clinical study report.

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P59 40 mg/kg group (Part 1)

Arm description:

Each participant received CT-P59 (regdanvimab) 40 mg/kg by IV infusion on Day 1.

Arm type	Experimental
Investigational medicinal product name	CT-P59
Investigational medicinal product code	
Other name	regdanvimab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

- CT-P59 was supplied as a sterile, preservative-free solution of SARS-CoV-2 RBD binding monoclonal antibody in a 20 mL single-use vial for IV infusion. CT-P59 is a clear to opalescent, colorless to pale yellow solution for injection, with a pH of 6.0 and 960 mg of SARS-CoV-2 RBD binding monoclonal antibody in 16 mL for IV infusion.
- CT-P59 40 mg/kg was administered by single intravenous infusion over 90 minutes (±15 minutes) on Day 1.
- A 250 mL infusion solution of 0.9% weight/volume sodium chloride was used for the patient infusions. The bag was gently inverted to mix the solution in order to avoid foaming. Parenteral solutions were inspected visually for particulates and discoloration prior to administration, and administration was not performed if any particulates or discoloration were found. The detailed method for mixing the solution was described in the pharmacy manual.

Arm title	CT-P59 80 mg/kg group (Part 1)

Arm description:

Each participant received CT-P59 (regdanvimab) 80 mg/kg by IV infusion on Day 1.

Arm type	Experimental

Investigational medicinal product name	CT-P59
Investigational medicinal product code	
Other name	regdanvimab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

- CT-P59 was supplied as a sterile, preservative-free solution of SARS-CoV-2 RBD binding monoclonal antibody in a 20 mL single-use vial for IV infusion. CT-P59 is a clear to opalescent, colorless to pale yellow solution for injection, with a pH of 6.0 and 960 mg of SARS-CoV-2 RBD binding monoclonal antibody in 16 mL for IV infusion.
- CT-P59 80 mg/kg was administered by single intravenous infusion over 90 minutes (±15 minutes) on Day 1.
- A 250 mL infusion solution of 0.9% weight/volume sodium chloride was used for the patient infusions. The bag was gently inverted to mix the solution in order to avoid foaming. Parenteral solutions were inspected visually for particulates and discoloration prior to administration, and administration was not performed if any particulates or discoloration were found. The detailed method for mixing the solution was described in the pharmacy manual.

Arm title	Placebo group (Part 1)

Arm description:

Each participant received placebo, matching in volume of CT-P59 80 mg/kg, by IV infusion on Day 1.

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

Dosage and administration details:

- Placebo contained the same ingredient as the CT-P59 formulation listed above, excluding SARS-CoV-2 RBD binding monoclonal antibody, in 16 mL water for injection. The pH of the placebo solution was 6.0.
- Placebo matching in volume of CT-P59 80 mg/kg was administered by single intravenous infusion over 90 minutes (±15 minutes) on Day 1.
- A 250 mL infusion solution of 0.9% weight/volume sodium chloride was used for the patient infusions. The bag was gently inverted to mix the solution in order to avoid foaming. Parenteral solutions were inspected visually for particulates and discoloration prior to administration, and administration was not performed if any particulates or discoloration were found. The detailed method for mixing the solution was described in the pharmacy manual.

Arm title	CT-P59 40 mg/kg group (Part 2)

Arm description:

Each participant received CT-P59 (regdanvimab) 40 mg/kg by IV infusion on Day 1.

Arm type	Experimental
Investigational medicinal product name	CT-P59
Investigational medicinal product code	
Other name	regdanvimab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

- CT-P59 was supplied as a sterile, preservative-free solution of SARS-CoV-2 RBD binding monoclonal antibody in a 20 mL single-use vial for IV infusion. CT-P59 is a clear to opalescent, colorless to pale yellow solution for injection, with a pH of 6.0 and 960 mg of SARS-CoV-2 RBD binding monoclonal antibody in 16 mL for IV infusion.
- CT-P59 40 mg/kg was administered by single intravenous infusion over 60 minutes (±15 minutes) on Day 1.
- A 250 mL infusion solution of 0.9% weight/volume sodium chloride was used for the patient infusions. The bag was gently inverted to mix the solution in order to avoid foaming. Parenteral solutions were inspected visually for particulates and discoloration prior to administration, and administration was not performed if any particulates or discoloration were found. The detailed method for mixing the solution was described in the pharmacy manual.

Arm title	Placebo group (Part 2)

Arm description:

Each participant received placebo, matching in volume of CT-P59 40 mg/kg, by IV infusion on Day 1.

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

Dosage and administration details:

- Placebo contained the same ingredient as the CT-P59 formulation listed above, excluding SARS-CoV-2 RBD binding monoclonal antibody, in 16 mL water for injection. The pH of the placebo solution was 6.0.
- Placebo matching in volume of CT-P59 40 mg/kg was administered by single intravenous infusion over 60 minutes (±15 minutes) on Day 1.
- A 250 mL infusion solution of 0.9% weight/volume sodium chloride was used for the patient infusions. The bag was gently inverted to mix the solution in order to avoid foaming. Parenteral solutions were inspected visually for particulates and discoloration prior to administration, and administration was not performed if any particulates or discoloration were found. The detailed method for mixing the solution was described in the pharmacy manual.

Number of subjects in period 1	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)
Started	105	111	111
Completed	97	103	105
Not completed	8	8	6
Consent withdrawn by subject	3	6	3
Physician decision	1	-	-
Not entered into Follow-up period	-	-	1
other	4	2	2
Lost to follow-up	-	-	-

Number of subjects in period 1	CT-P59 40 mg/kg group (Part 2)	Placebo group (Part 2)
Started	656	659
Completed	618	608
Not completed	38	51
Consent withdrawn by subject	27	39
Physician decision	2	2
Not entered into Follow-up period	-	-
other	6	6
Lost to follow-up	3	4

Baseline characteristics

Reporting groups	
Reporting group title	CT-P59 40 mg/kg group (Part 1)
Reporting group description:	
Each participant received CT-P59 (regdanvimab) 40 mg/kg by IV infusion on Day 1.	
Reporting group title	CT-P59 80 mg/kg group (Part 1)
Reporting group description:	
Each participant received CT-P59 (regdanvimab) 80 mg/kg by IV infusion on Day 1.	
Reporting group title	Placebo group (Part 1)
Reporting group description:	
Each participant received placebo, matching in volume of CT-P59 80 mg/kg, by IV infusion on Day 1.	
Reporting group title	CT-P59 40 mg/kg group (Part 2)
Reporting group description:	
Each participant received CT-P59 (regdanvimab) 40 mg/kg by IV infusion on Day 1.	
Reporting group title	Placebo group (Part 2)
Reporting group description:	
Each participant received placebo, matching in volume of CT-P59 40 mg/kg, by IV infusion on Day 1.	

Reporting group values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)
Number of subjects	105	111	111
Age categorical Units: Subjects			
Adults (18-64 years)	90	90	93
Elderly (≥65 year)	15	21	18
Gender categorical Units: Subjects			
Female	46	52	63
Male	59	59	48

Reporting group values	CT-P59 40 mg/kg group (Part 2)	Placebo group (Part 2)	Total
Number of subjects	656	659	1642
Age categorical Units: Subjects			
Adults (18-64 years)	563	581	1417
Elderly (≥65 year)	93	78	225
Gender categorical Units: Subjects			
Female	309	332	802
Male	347	327	840

End points

End points reporting groups

Reporting group title	CT-P59 40 mg/kg group (Part 1)
Reporting group description:	
Each participant received CT-P59 (regdanvimab) 40 mg/kg by IV infusion on Day 1.	
Reporting group title	CT-P59 80 mg/kg group (Part 1)
Reporting group description:	
Each participant received CT-P59 (regdanvimab) 80 mg/kg by IV infusion on Day 1.	
Reporting group title	Placebo group (Part 1)
Reporting group description:	
Each participant received placebo, matching in volume of CT-P59 80 mg/kg, by IV infusion on Day 1.	
Reporting group title	CT-P59 40 mg/kg group (Part 2)
Reporting group description:	
Each participant received CT-P59 (regdanvimab) 40 mg/kg by IV infusion on Day 1.	
Reporting group title	Placebo group (Part 2)
Reporting group description:	
Each participant received placebo, matching in volume of CT-P59 40 mg/kg, by IV infusion on Day 1.	
Subject analysis set title	ITT Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT Set was defined as all patients randomly assigned to study drug. It is applied for both Part 1 and Part 2.	
Subject analysis set title	ITTI Set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The ITTI (Intent-to-treat Infected) Set was defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion (Day 1) result based on RT-qPCR and who received a complete or partial dose of the study drug. If the pre-infusion result at Day 1 was confirmed negative or missing and the Day 2 (or Day 3 for Part 2) result was confirmed positive, this patient was also considered as confirmed SARS-CoV-2 infection. It is applied for both Part 1 and Part 2.	
Subject analysis set title	ITT Set - High Risk (Part 2)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The ITT Set – High Risk was defined as all randomly assigned patients to study drug, who were at high-risk for progressing to severe COVID-19 and/or hospitalization and who met at least 1 of the high-risk criteria. The ITT Set – High Risk consisted of patients in ITT Set who met at least 1 of the high-risk criteria.	
Subject analysis set title	ITTI Set - High Risk (Part 2)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The ITTI Set - High Risk was defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion (Day 1) result based on RT-qPCR who received a complete or partial dose of the study drug, who were at high-risk for progressing to severe COVID-19 and/or hospitalization and who met at least 1 of the high-risk criteria. If the pre-infusion result at Day 1 was confirmed negative or missing and the Day 2 or Day 3 result was confirmed positive, this patient was also considered as confirmed SARS-CoV-2 infection.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Set was defined as all randomly assigned patients who received a complete or partial dose of study drug. It was applied for both Part 1 and Part 2.	
Subject analysis set title	PK Set (Part 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK Set was defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion (Day 1) result based on RT-qPCR and who had signed informed consent to participate in a PK sub-study, received a complete dose of study drug, and had at least 1 evaluable post-treatment PK result. If the pre-infusion result of RT-qPCR at Day 1 was confirmed negative or missing and the Day 2 result was confirmed positive, this patient was also considered as confirmed SARS-CoV-2 infection.

Primary: Proportion of Patients With Clinical Symptom Requiring Hospitalization, Oxygen Therapy, or Experiencing Mortality Due to SARS-CoV-2 Infection (Part 1)

End point title	Proportion of Patients With Clinical Symptom Requiring Hospitalization, Oxygen Therapy, or Experiencing Mortality Due to SARS-CoV-2 Infection (Part 1)[1][2]

End point description:

- ITTI Set (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion result [Day 1] of RT-qPCR and who received a complete or partial dose of the study drug; Patient who had confirmed negative or missing at Day 1 and positive at Day 2 was also included) was used for the analysis.
- This primary endpoint was to assess the clinically meaningful therapeutic efficacy of CT-P59 as determined by proportion of patients with clinical symptom requiring hospitalization, oxygen therapy, or experiencing mortality due to SARS-CoV-2 infection up to Day 28.

End point type	Primary

End point timeframe:

Up to Day 28

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: Statistical analyses of Part 2 primary endpoint was only specified since Part 1 of the study was exploratory.
[2] - 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: This endpoint was analyzed for Part 1 of the study. So, only arms in Part 1 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	103	103	
Units: Subjects	4	5	9	

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Patients With Negative Conversion in Nasopharyngeal Swab Specimen Based on RT-qPCR at Each Visit (Part 1)

End point title	Proportion of Patients With Negative Conversion in Nasopharyngeal Swab Specimen Based on RT-qPCR at Each Visit (Part 1)[3][4]

End point description:

- ITTI Set (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion result [Day 1] of RT-qPCR and who received a complete or partial dose of the study drug; Patient who had confirmed negative or missing at Day 1 and positive at Day 2 was also included) was used for the analysis.
- This supportive primary endpoint was to assess the potential therapeutic efficacy of CT-P59 as determined by proportion of negative conversion in nasopharyngeal swab specimen based on RT-qPCR up to Day 14.

End point type	Primary

End point timeframe:

Up to Day 14

Notes:

[3] - 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: Statistical analyses of Part 2 primary endpoint was only specified since Part 1 of the study was exploratory.
[4] - 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: This endpoint was analyzed for Part 1 of the study. So, only arms in Part 1 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	103	103	
Units: Subjects				
Day 2	0	1	0	
Day 3	4	4	3	
Day 4	2	6	4	
Day 5	7	3	2	
Day 6	5	5	4	
Day 7	8	12	7	
Day 10	19	18	19	
Day 14	23	19	23	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Negative Conversion in Nasopharyngeal Swab Specimen (Part 1)

End point title	Time to Negative Conversion in Nasopharyngeal Swab Specimen (Part 1)[5][6]

End point description:

- ITTI Set (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion result [Day 1] of RT-qPCR and who received a complete or partial dose of the study drug; Patient who had confirmed negative or missing at Day 1 and positive at Day 2 was also included) was used for the analysis.
- This supportive primary endpoint was to evaluate the therapeutic efficacy of CT-P59 as determined by time to negative conversion by RT-qPCR up to Day 14.

End point type	Primary

End point timeframe:

Up to Day 14

Notes:

[5] - 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: Statistical analyses of Part 2 primary endpoint was only specified since Part 1 of the study was exploratory.
[6] - 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: This endpoint was analyzed for Part 1 of the study. So, only arms in Part 1 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	101	103	103	
Units: Days				
median (confidence interval 95%)	12.75 (9.00 to 12.84)	11.89 (8.94 to 12.91)	12.94 (12.75 to 13.99)	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Clinical Recovery (Part 1)

End point title	Time to Clinical Recovery (Part 1)[7][8]

End point description:

- ITTI Set (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion result [Day 1] of RT-qPCR and who received a complete or partial dose of the study drug; Patient who had confirmed negative or missing at Day 1 and positive at Day 2 was also included; Patients who have absent for all symptoms or at least one missing at baseline are excluded.) was used for the analysis.
- This supportive primary endpoint was to assess the potential therapeutic efficacy of CT-P59 as determined by time to clinical recovery up to Day 14.

End point type	Primary

End point timeframe:

Up to Day 14

Notes:

[7] - 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: Statistical analyses of Part 2 primary endpoint was only specified since Part 1 of the study was exploratory.
[8] - 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: This endpoint was analyzed for Part 1 of the study. So, only arms in Part 1 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	92	98	
Units: Days				
median (confidence interval 95%)	7.18 (5.50 to 9.37)	7.30 (5.72 to 9.33)	8.80 (6.88 to 13.09)	

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of Patients With Clinical Symptom Requiring Hospitalization, Oxygen Therapy, or Experiencing Mortality Due to SARS-CoV-2 Infection up to Day

28 in High-risk Patients (Part 2)	
End point title	Proportion of Patients With Clinical Symptom Requiring Hospitalization, Oxygen Therapy, or Experiencing Mortality Due to SARS-CoV-2 Infection up to Day 28 in High-risk Patients (Part 2)[9]

End point description:

- ITT Set - High Risk (defined as all randomly assigned patients to the study drug, who were at high-risk for progressing to severe COVID-19 and/or hospitalization and who met at least 1 of the high-risk criteria) was used for the analysis.
- This primary endpoint was to demonstrate the clinically meaningful therapeutic efficacy of CT-P59 as determined by proportion of patients with clinical symptom requiring hospitalization, oxygen therapy, or experiencing mortality due to SARS-CoV-2 infection up to Day 28 in high-risk patients.

End point type	Primary

End point timeframe:

Up to Day 28

Notes:

[9] - 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: This endpoint was analyzed for Part 2 of the study. So, only arms in Part 2 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 2)	Placebo group (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	446	434		
Units: Subjects	14	48		

Statistical analyses

Statistical analysis title	Statistical analysis of primary endpoint (Part 2)

Statistical analysis description:

95% stratified Newcombe CI with CMH weights were presented.

Comparison groups	CT-P59 40 mg/kg group (Part 2) v Placebo group (Part 2)
Number of subjects included in analysis	880
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference % estimated using CMH weights
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	-4.5

Notes:

[10] - P-value was calculated using CMH test stratified by age (≥60 vs. <60 years), baseline comorbidities (Yes vs. No) and region (US vs. EU vs. Other).

Secondary: Proportion of Patients With Clinical Symptom Requiring Hospitalization, Oxygen Therapy, or Experiencing Mortality Due to SARS-CoV-2 Infection up to Day 28 in All Randomized Patients (Part 2)

End point title	Proportion of Patients With Clinical Symptom Requiring Hospitalization, Oxygen Therapy, or Experiencing Mortality Due to SARS-CoV-2 Infection up to Day 28 in All Randomized Patients (Part 2)[11]

End point description:

- 1st key seconday endpoint
- ITT Set (defined as all randomly assigned patients to the study drug) was used for the analysis.
- This key secondary endpoint was to demonstrate the clinically meaningful therapeutic efficacy of CT-P59 as determined by proportion of patients with clinical symptom requiring hospitalization, oxygen therapy, or experiencing mortality due to SARS-CoV-2 infection up to Day 28 in all randomized patients.

End point type	Secondary

End point timeframe:

Up to Day 28

Notes:

[11] - 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: This endpoint was analyzed for Part 2 of the study. So, only arms in Part 2 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 2)	Placebo group (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	656	659		
Units: Subjects	16	53		

Statistical analyses

Statistical analysis title	Statistical analysis of 1st key seconadry endpoint

Statistical analysis description:

- 95% stratified Newcombe CI with CMH weights were presented.
- The first key secondary endpoint was tested after the primary endpoint was statistically significant.

Comparison groups	CT-P59 40 mg/kg group (Part 2) v Placebo group (Part 2)
Number of subjects included in analysis	1315
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference % estimated using CMH weights
Point estimate	-5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	-3.3

Notes:

[12] - P-value was calculated using CMH test stratified by age (≥60 vs. <60 years), baseline comorbidities (Yes vs. No) and region (US vs. EU vs. Other).

Secondary: Time to Clinical Recovery up to Day 14 in High-risk Patients (Part 2)

End point title	Time to Clinical Recovery up to Day 14 in High-risk Patients (Part 2)[13]

End point description:

- 2nd key secondary endpoint
- ITT Set - High Risk (defined as all randomly assigned patients to the study drug, who were at high-risk for progressing to severe COVID-19 and/or
hospitalization and who met at least 1 of the high-risk criteria; Patient who reported at least 1 symptom at baseline was included) was used for the analysis.
- This key secondary endpoint was to assess the potential therapeutic efficacy of CT-P59 as determined by time to clinical recovery up to Day 14 in high-risk patients.
- The median time in Placebo group was not reached as less than 50% of patients achieved clinical recovery. Also, the number of patients achieved clinical recovery in Placebo group was not sufficient to calculate the upper CI. Both results should be recorded as Not Calculated (N.C.) but 14.0 was recorded instead of N.C. as alphabetical letters were not allowed to be recorded into the system.

End point type	Secondary

End point timeframe:

Up to Day 14

Notes:

[13] - 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: This endpoint was analyzed for Part 2 of the study. So, only arms in Part 2 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 2)	Placebo group (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	406		
Units: Days				
median (confidence interval 95%)	9.27 (8.27 to 11.05)	14.0 (12.35 to 14.0)		

Statistical analyses

Statistical analysis title	Statistical analysis of 2nd key seconadry endpoint

Statistical analysis description:

- The 2nd key seconadry endpoint was tested after the 1st key secondary endpoint was statistically significant.

Comparison groups	CT-P59 40 mg/kg group (Part 2) v Placebo group (Part 2)
Number of subjects included in analysis	835
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [14]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	1.9

Notes:

[14] - P-value was calculated using stratified log-rank test stratified by age (≥60 vs. <60 years), baseline comorbidities (Yes vs. No) and region (US vs. EU vs. Other).

Secondary: Time to Clinical Recovery up to Day 14 in All Randomized Patients (Part

2)

End point title	Time to Clinical Recovery up to Day 14 in All Randomized Patients (Part 2)[15]

End point description:

- 3rd key secondary endpoint
- ITT Set (defined as all randomly assigned patients to the study drug; Patient who reported at least 1 symptom at baseline was included) was used for the analysis.
- This key secondary endpoint was to assess the potential therapeutic efficacy of CT-P59 as determined by time to clinical recovery up to Day 14 in all randomized patients.
- The number of patients achieved clinical recovery in Placebo group was not sufficient to calculate the upper CI. The
result should be recorded as Not Calculated (N.C.) but 14.0 was recorded instead of N.C. as alphabetical letters were
not allowed to be recorded into the system.

End point type	Secondary

End point timeframe:

Up to Day 14

Notes:

[15] - 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: This endpoint was analyzed for Part 2 of the study. So, only arms in Part 2 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 2)	Placebo group (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	629	618		
Units: Days				
median (confidence interval 95%)	8.38 (7.91 to 9.33)	13.25 (11.94 to 14.0)		

Statistical analyses

Statistical analysis title	Statistical analysis of 3rd key secondary endpoint

Statistical analysis description:

- The 3rd key seconadry endpoint was tested after the 2nd key secondary endpoint was statistically significant.

Comparison groups	CT-P59 40 mg/kg group (Part 2) v Placebo group (Part 2)
Number of subjects included in analysis	1247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [16]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	1.73

Notes:

[16] - P-value was calculated using stratified log-rank test stratified by age (≥60 vs. <60 years), baseline comorbidities (Yes vs. No) and region (US vs. EU vs. Other).

Secondary: Time to Negative Conversion in Nasopharyngeal Swab Specimen Based on RT-qPCR (Part 1 and Part 2)

End point title	Time to Negative Conversion in Nasopharyngeal Swab Specimen Based on RT-qPCR (Part 1 and Part 2)

End point description:

- ITTI Set for Part 1 (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion result [Day 1] of RT-qPCR and who received a complete or partial dose of the study drug; Patient who had confirmed negative or missing at Day 1 and positive at Day 2 was also included) and ITT Set for Part 2 (defined as all randomly assigned patients to study drug; Patient who had positive result confirmed based on the negative threshold at baseline was included) were used for the analysis.
- This secondary endpont was to evaluate the additional efficacy of CT-P59.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)	CT-P59 40 mg/kg group (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	101	103	103	612
Units: Days				
median (confidence interval 95%)	12.75 (9.00 to 12.84)	11.89 (8.94 to 12.91)	12.94 (12.75 to 13.99)	11.90 (9.02 to 12.83)

End point values	Placebo group (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	618			
Units: Days				
median (confidence interval 95%)	13.15 (12.97 to 18.80)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Viral Serology for SARS-CoV-2 Antibody (Part 1 and Part 2)

End point title	Viral Serology for SARS-CoV-2 Antibody (Part 1 and Part 2)

End point description:

- The ITTI Set (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion (Day 1) result based on RT-qPCR and who received a complete or partial dose of the study drug; Patient who had confirmed negative or missing at Day 1 and positive at Day 2 (or Day 3 for Part 2) was also included) was used for the Part 1 and Part 2 analysis.
- This exploratory endpoint was to assess the serology of SARS-CoV-2 antibody (IgG and IgM).

End point type	Other pre-specified

End point timeframe:

Days 1, 7, 14, 28, and 56

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)	CT-P59 40 mg/kg group (Part 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	101	103	103	612
Units: Subjects				
IgG - Day 1	0	6	3	45
IgG - Day 7	27	32	32	354
IgG - Day 14	77	82	86	498
IgG - Day 28	84	94	91	535
IgG - Day 56	78	85	86	506
IgM - Day 1	2	6	4	53
IgM - Day 7	38	43	49	362
IgM - Day 14	78	82	87	467
IgM - Day 28	59	77	65	461
IgM - Day 56	39	54	51	407

End point values	Placebo group (Part 2)			
Subject group type	Reporting group			
Number of subjects analysed	618			
Units: Subjects				
IgG - Day 1	35			
IgG - Day 7	322			
IgG - Day 14	509			
IgG - Day 28	548			
IgG - Day 56	532			
IgM - Day 1	55			
IgM - Day 7	332			
IgM - Day 14	491			
IgM - Day 28	493			
IgM - Day 56	441			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area Under the Concentration-time Curve From Time Zero to Infinity (AUC0-inf) (Part 1)

End point title	Area Under the Concentration-time Curve From Time Zero to Infinity (AUC0-inf) (Part 1)[17]

End point description:

- PK Set (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion [Day 1] result based on RT-qPCR and who had signed informed consent to participate in a PK sub-study, received a complete dose of study drug, and had at least 1 evaluable post-treatment PK result; If the pre-infusion result at Day 1 was confirmed negative or missing and the Day 2 result was confirmed positive, this patient was also included) was used for the analysis.
- This exploratory endpoint was to assess the PK of CT-P59.

End point type	Other pre-specified

End point timeframe:

Throughout the study

Notes:

[17] - 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: This endpoint was analyzed for Part 1 of the study. So, only arms in Part 1 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: h*µg/mL				
arithmetic mean (standard deviation)	212460.507 (± 46724.5556)	426694.643 (± 121171.182)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Maximum Serum Concentration (Cmax) (Part 1)

End point title	Maximum Serum Concentration (Cmax) (Part 1)[18]

End point description:

- PK Set (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion [Day 1] result based on RT-qPCR and who had signed informed consent to participate in a PK sub-study, received a complete dose of study drug, and had at least 1 evaluable post-treatment PK result; If the pre-infusion result at Day 1 was confirmed negative or missing and the Day 2 result was confirmed positive, this patient was also included) was used for the analysis.
- This exploratory endpoint was to assess the PK of CT-P59.

End point type	Other pre-specified

End point timeframe:

Throughout the study

Notes:

[18] - 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: This endpoint was analyzed for Part 1 of the study. So, only arms in Part 1 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: µg/mL				
arithmetic mean (standard deviation)	1016.6 (± 268.97)	2007.6 (± 477.97)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Terminal Half-life (t1/2) (Part 1)

End point title	Terminal Half-life (t1/2) (Part 1)[19]

End point description:

- PK Set (defined as all randomly assigned patients with confirmed SARS-CoV-2 infection by pre-infusion [Day 1] result based on RT-qPCR and who had signed informed consent to participate in a PK sub-study, received a complete dose of study drug, and had at least 1 evaluable post-treatment PK result; If the pre-infusion result at Day 1 was confirmed negative or missing and the Day 2 result was confirmed positive, this patient was also included) was used for the analysis.
- This exploratory endoint was to assess the PK of CT-P59.

End point type	Other pre-specified

End point timeframe:

Throughout the study

Notes:

[19] - 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: This endpoint was analyzed for Part 1 of the study. So, only arms in Part 1 among baseline period arms were reported.

End point values	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	32		
Units: hour				
arithmetic mean (standard deviation)	403.916 (± 147.8450)	453.442 (± 107.5620)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs/AEs were reported by the investigator from the date patients signed the informed consent form until the last assessment date or End-of-Treatment (EOT) visit, regardless of the relationship to the study drug.

Adverse event reporting additional description:

The investigator was responsible for reporting all AEs that were observed or reported from signing of ICF to
EOT, regardless of their relationship to study drug or their clinical significance.
Cases of worsening of SARS-CoV-2 infection which were considered as unrelated to the study drug were not
reported as an (S)AE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	CT-P59 40 mg/kg group (Part 1)

Reporting group description:

Each participant received CT-P59 (regdanvimab) 40 mg/kg by IV infusion on Day 1.

Reporting group title	CT-P59 80 mg/kg group (Part 1)

Reporting group description:

Each participant received CT-P59 (regdanvimab) 80 mg/kg by IV infusion on Day 1.

Reporting group title	Placebo group (Part 1)

Reporting group description:

Each participant received placebo, matching in volume of CT-P59 80 mg/kg, by IV infusion on Day 1.

Reporting group title	CT-P59 40 mg/kg group (Part 2)

Reporting group description:

Each participant received CT-P59 (regdanvimab) 40 mg/kg by IV infusion on Day 1.

Reporting group title	Placebo group (Part 2)

Reporting group description:

Each participant received placebo, matching in volume of CT-P59 40 mg/kg, by IV infusion on Day 1.

Serious adverse events	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intraocular melanoma			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Appendicitis			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CT-P59 40 mg/kg group (Part 2)	Placebo group (Part 2)	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 652 (0.92%)	5 / 650 (0.77%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 652 (0.00%)	1 / 650 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular melanoma			
subjects affected / exposed	0 / 652 (0.00%)	1 / 650 (0.15%)	
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			
Infusion related reaction			
subjects affected / exposed	1 / 652 (0.15%)	0 / 650 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	1 / 652 (0.15%)	0 / 650 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 652 (0.15%)	0 / 650 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 652 (0.00%)	1 / 650 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 652 (0.00%)	1 / 650 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 652 (0.15%)	0 / 650 (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			
Appendicitis			
subjects affected / exposed	1 / 652 (0.15%)	0 / 650 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 652 (0.15%)	0 / 650 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	0 / 652 (0.00%)	1 / 650 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	CT-P59 40 mg/kg group (Part 1)	CT-P59 80 mg/kg group (Part 1)	Placebo group (Part 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 105 (18.10%)	18 / 110 (16.36%)	17 / 110 (15.45%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 105 (0.00%)	1 / 110 (0.91%)	1 / 110 (0.91%)
occurrences (all)	0	2	1
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 105 (4.76%)	2 / 110 (1.82%)	1 / 110 (0.91%)
occurrences (all)	5	2	1
C-reactive protein increased			
subjects affected / exposed	1 / 105 (0.95%)	0 / 110 (0.00%)	0 / 110 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 105 (0.00%)	1 / 110 (0.91%)	1 / 110 (0.91%)
occurrences (all)	0	1	2
Hepatic enzyme increased			
subjects affected / exposed	0 / 105 (0.00%)	2 / 110 (1.82%)	0 / 110 (0.00%)
occurrences (all)	0	2	0
Inflammatory marker increased			
subjects affected / exposed	0 / 105 (0.00%)	3 / 110 (2.73%)	2 / 110 (1.82%)
occurrences (all)	0	3	2
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 105 (0.95%)	1 / 110 (0.91%)	0 / 110 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 105 (0.00%)	0 / 110 (0.00%)	3 / 110 (2.73%)
occurrences (all)	0	0	4
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	3 / 105 (2.86%)	3 / 110 (2.73%)	0 / 110 (0.00%)
occurrences (all)	3	3	0
Thrombocytosis			
subjects affected / exposed	3 / 105 (2.86%)	1 / 110 (0.91%)	2 / 110 (1.82%)
occurrences (all)	3	1	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 105 (0.00%)	3 / 110 (2.73%)	1 / 110 (0.91%)
occurrences (all)	0	3	1
Infections and infestations			
Bacteriuria			
subjects affected / exposed	2 / 105 (1.90%)	2 / 110 (1.82%)	2 / 110 (1.82%)
occurrences (all)	2	2	2
Cystitis			
subjects affected / exposed	3 / 105 (2.86%)	2 / 110 (1.82%)	0 / 110 (0.00%)
occurrences (all)	3	2	0
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	4 / 105 (3.81%)	3 / 110 (2.73%)	2 / 110 (1.82%)
occurrences (all)	4	3	2
Hyperglycaemia			
subjects affected / exposed	2 / 105 (1.90%)	2 / 110 (1.82%)	3 / 110 (2.73%)
occurrences (all)	2	2	4
Hyperkalaemia			
subjects affected / exposed	1 / 105 (0.95%)	3 / 110 (2.73%)	2 / 110 (1.82%)
occurrences (all)	1	5	2
Hypertriglyceridaemia			
subjects affected / exposed	6 / 105 (5.71%)	0 / 110 (0.00%)	3 / 110 (2.73%)
occurrences (all)	7	0	5

Non-serious adverse events	CT-P59 40 mg/kg group (Part 2)	Placebo group (Part 2)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	119 / 652 (18.25%)	128 / 650 (19.69%)	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	19 / 652 (2.91%)	31 / 650 (4.77%)	
occurrences (all)	22	34	
Blood creatine phosphokinase increased			
subjects affected / exposed	14 / 652 (2.15%)	10 / 650 (1.54%)	
occurrences (all)	14	10	
C-reactive protein increased			
subjects affected / exposed	18 / 652 (2.76%)	10 / 650 (1.54%)	
occurrences (all)	18	10	
Gamma-glutamyltransferase increased			
subjects affected / exposed	8 / 652 (1.23%)	20 / 650 (3.08%)	
occurrences (all)	8	20	
Hepatic enzyme increased			
subjects affected / exposed	21 / 652 (3.22%)	15 / 650 (2.31%)	
occurrences (all)	21	16	
Inflammatory marker increased			
subjects affected / exposed	14 / 652 (2.15%)	17 / 650 (2.62%)	
occurrences (all)	14	18	
Vascular disorders			
Hypertension			
subjects affected / exposed	17 / 652 (2.61%)	14 / 650 (2.15%)	
occurrences (all)	22	15	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 652 (0.00%)	2 / 650 (0.31%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	6 / 652 (0.92%)	12 / 650 (1.85%)	
occurrences (all)	6	12	
Thrombocytosis			
subjects affected / exposed	11 / 652 (1.69%)	5 / 650 (0.77%)	
occurrences (all)	11	5	
Psychiatric disorders			

Insomnia			
subjects affected / exposed	0 / 652 (0.00%)	5 / 650 (0.77%)	
occurrences (all)	0	5	
Infections and infestations			
Bacteriuria			
subjects affected / exposed	3 / 652 (0.46%)	3 / 650 (0.46%)	
occurrences (all)	3	3	
Cystitis			
subjects affected / exposed	0 / 652 (0.00%)	1 / 650 (0.15%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	7 / 652 (1.07%)	9 / 650 (1.38%)	
occurrences (all)	7	9	
Hyperglycaemia			
subjects affected / exposed	12 / 652 (1.84%)	9 / 650 (1.38%)	
occurrences (all)	12	9	
Hyperkalaemia			
subjects affected / exposed	9 / 652 (1.38%)	6 / 650 (0.92%)	
occurrences (all)	10	7	
Hypertriglyceridaemia			
subjects affected / exposed	29 / 652 (4.45%)	33 / 650 (5.08%)	
occurrences (all)	35	40	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 September 2020	- The baseline severity categorization (mild to moderate) and key inclusion criteria (not requiring supplemental oxygen therapy) were added to various sub-sections of the protocol. To give further clarification about the study population, the definition of outpatient used in this study was added. - Based on the FDA recommendation, medically attended visit was deleted from the primary objectives of Part 1 and Part 2. - The word 'mild' was deleted from inclusion criterion #3 to match the definition of patient's condition categorized in both the FDA and WHO guidelines for COVID-19. The condition for enrolling pneumonia patients was added to follow the recommendation from MFDS. - Inclusion criterion #7 was updated to only include patients with a body weight of ≤99.9 kg in the study. - Exclusion criterion #1 was updated - Exclusion criterion #2 was updated to clarify the use of prohibited drugs for chronic HIV infection because the therapeutic effect on HIV patients has not yet been studied. Additional examples of prohibited medications or treatments were added. - Exclusion criterion #5 was updated to delete the BMI limitation of <18 kg/m2. The range of clinical laboratory results of abnormal liver function and renal impairment was extended, considering the characteristics of mild to moderate patients and the dosing regimen of the investigational product (single use). The criterion of uncontrolled hypertension was deleted because the definition of of uncontrolled DM and hypertension can vary by investigator and clinical findings. - The criterion for the possible enrollment of pregnant female participants in Part 2 was deleted. - Sample size calculation was updated to accommodate the deletion of medically attended visit from the primary endpoint, and further explanation for the assumption of sample size was added. - To take into account FDA's recommendation, the analysis set was updated from ITTI to ITT for primary efficacy analysis.
19 October 2020	- Amendments initially made in the protocol Version 3.0, including country specific A.0 which needed to be applied in all study centers were applied. - As per HPRA's recommendation, the review frequency of SAE listings was updated from monthly to biweekly, and an additional description was added to clearly state that an additional DSMB meeting can be called when needed.
16 December 2020	- The rationale for dose selection was updated as per the clinical updated data of Studies CT-P59 1.1 and 1.2. - To initiate Part 2, dose and infusion time was updated as 40 mg/kg over 60 minutes (± 15 minutes) - Schedule of viral shedding in Part 2 was updated as there were changes in frequency of the test. - Note of exclusion criteria #5b and #5c was added to reduce the time required for the tests and to efficiently operate the study. - How to assess the clinical recovery when a symptom was recorded as 'absent' at baseline was added for futher clarification. Consideirng the data from Part 1 which showed that the most of patients had received the study drug during the evening in Part 1, frequecny of writing patient diary and measuring body temperature were changed from twice a day to once a day. - Additional guideline for reporting AEs/SAEs, which any events related to aggravation of COVID were not to be capture as AEs/SAEs, was added. - Number of sampling time point for nasopharyngeal swab in Part 2 was reduced for the sake of patients. - Description of DSMB was separately stated by Parts. - As per the updated plan for the study, the number of CSRs were updated. - Other administrative changes were made

08 January 2021	- Amendments initially made in the protocol Version 4.1, including country specific A.1, which needed to be applied in all study centers were applied. - The rationale for dose selection was updated as per the clinical updated data of Study CT-59 3.2 Part 1. - Other administrative changes were made.
22 March 2021	- Primary objective was updated to demonstrate the efficacy of the product in high-risk patients. - Key secondary efficacy endpoints were newly added to assess the efficacy of the product in all randomized patients and high-risk patients. - Sample size of Part 2 was reassessed and updated to include the target number of high-risk patients. - Statistical method for the primary efficacy endpoint of Part 2 was updated to CMH test. - Statistical analysis for key secondary efficacy endpoints were newly added. - Statistical method the secondary efficacy endpoints of Part 2 was updated. - Supportive statistical power calculations for key secondary endpoints were added. - Definition of high-risk patients was newly added. Analysis sets for high-risk were defined. - To achieve the target number of high-risk patients, footnote of proceeding patient enrolment was added. - Number of participating countries and sites in Part 2 were updated - To encourage high-risk patients' enrolment, the exclusion criteria (#5a, #5b, #5c, #5d, #5e, #5f, and #5g) relevant to high-risk patients were deleted. - As monitoring purpose included those who were not in severe condition but needed to be monitored under hospital setting, monitoring purpose in a hospitalized setting was deleted to take into account FDA's comment. - Other administrative changes were made
30 April 2021	- Non-severe pneumonia was deleted from the high-risk criteria as per the recommendation from EMA. - Sample size calculation was updated based on the results from Part 1 of this study and reference data from other companies. - Statistical methods for primary and key secondary endpoints were updated as per the recommendation from FDA. - Amendments made in the protocol Version 6.0, including country specific H.1, were applied.

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.

None reported.

Notes: