Clinical trial results:
Randomized, double-blind, placebo-controlled, single-centre, phase IIa study in healthy volunteers to evaluate the efficacy and safety of CT-P27 in an influenza challenge model

Summary

EudraCT number	2013-004544-32
Trial protocol	GB
Global end of trial date	19 June 2014

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	CT-P27/2.1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Celltrion, Inc
Sponsor organisation address	Academy-ro, Incheon, Korea, Republic of,
Public contact	Head of Clinical Planning Department, Celltrion, Inc, +82 8505000, contact@celltrion.com
Scientific contact	Head of Clinical Planning Department, Celltrion, Inc, +82 8505000, contact@celltrion.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	13 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the reduction in AUC of virus load from the nasopharyngeal mucosa as measured by quantitative PCR, in the CT-P27 treatment groups compared to placebo, post Viral Challenge, and post virus shedding.

Protection of trial subjects:

Every effort was made to monitor the health of the volunteers to minimize the unforeseen and not anticipated risks.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 81
Worldwide total number of subjects	81
EEA total number of subjects	81

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)	81
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited in United Kingdom.

Pre-assignment

Screening details:

Study-specific screening (SSS) occurred from Day -56 to Day -3.
Assessments to determine subjects' eligibility to participate and baseline measurements were performed.
First screening visit was on 15 February 2014.

Period 1

Period 1 title	Study specific screening
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:

The Investigator and all other clinical and non-clinical staff were remain blinded to the treatment allocation, until after the database has been locked and approval for study unblinding has been given.

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P27 10mg/kg

Arm description:

Subjects received 10 mg/kg CT-P27

Arm type	Experimental
Investigational medicinal product name	CT-P27
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single-dose IV infusion over 1.5 hours.

Arm title	CT-P27 20mg/kg

Arm description:

Subjects received 20 mg/kg CT-P27

Arm type	Experimental
Investigational medicinal product name	CT-P27
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single-dose IV infusion over 1.5 hours.

Arm title	Placebo

Arm description:

Subjects received placebo

Arm type	Placebo

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

Dosage and administration details:

Single-dose IV infusion over 1.5 hours.

Number of subjects in period 1	CT-P27 10mg/kg	CT-P27 20mg/kg	Placebo
Started	27	27	27
Completed	27	27	27

Period 2

Period 2 title	Quarantine and Challenge
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The Investigator and all other clinical and non-clinical staff were remain blinded to the treatment allocation, until after the database has been locked and approval for study unblinding has been given.

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P27 10mg/kg

Arm description:

Subjects received 10 mg/kg CT-P27

Arm type	Experimental
Investigational medicinal product name	CT-P27
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single-dose IV infusion over 1.5 hours.

Arm title	CT-P27 20mg/kg

Arm description:

Subjects received 20 mg/kg CT-P27

Arm type	Experimental

Investigational medicinal product name	CT-P27
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single-dose IV infusion over 1.5 hours.

Arm title	Placebo

Arm description:

Subjects received placebo

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

Dosage and administration details:

Single-dose IV infusion over 1.5 hours.

Number of subjects in period 2	CT-P27 10mg/kg	CT-P27 20mg/kg	Placebo
Started	27	27	27
Completed	27	27	27

Period 3

Period 3 title	Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The Investigator and all other clinical and non-clinical staff were remain blinded to the treatment allocation, until after the database has been locked and approval for study unblinding has been given.

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P27 10mg/kg

Arm description:

Subjects received 10 mg/kg CT-P27

Arm type	Experimental

Investigational medicinal product name	CT-P27
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:
Single-dose IV infusion over 1.5 hours

Arm title	CT-P27 20mg/kg

Arm description:
Subjects received 20 mg/kg CT-P27

Arm type	Experimental
Investigational medicinal product name	CT-P27
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:
Single-dose IV infusion over 1.5 hours.

Arm title	Placebo

Arm description:
Subjects received placebo

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

Dosage and administration details:
Single-dose IV infusion over 1.5 hours.

Number of subjects in period 3	CT-P27 10mg/kg	CT-P27 20mg/kg	Placebo
Started	27	27	27
Completed	27	27	27

Baseline characteristics

Reporting groups	
Reporting group title	CT-P27 10mg/kg
Reporting group description:	
Subjects received 10 mg/kg CT-P27	
Reporting group title	CT-P27 20mg/kg
Reporting group description:	
Subjects received 20 mg/kg CT-P27	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo	

Reporting group values	CT-P27 10mg/kg	CT-P27 20mg/kg	Placebo
Number of subjects	27	27	27
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
ITT population			
Units: years			
median	24.0	25.0	25.0
full range (min-max)	20 to 39	19 to 41	18 to 42
Gender categorical			
Units: Subjects			
Female	10	10	12
Male	17	17	15

Reporting group values	Total		
Number of subjects	81		
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			
ITT population			
Units: years			
median			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	32		
Male	49		

Subject analysis sets

Subject analysis set title	Intention-to-treat Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-treat (ITT) was defined as all subjects randomised to IMP or placebo. The treatment group was defined as the treatment randomised rather than the treatment actually received. All subjects were included as long as they were randomised, even patients who did not receive a treatment. All baseline and demographic summaries were performed on the ITT population.

Subject analysis set title	Efficacy Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Efficacy population was defined as all ITT subjects receiving Challenge Virus and IMP or placebo, with subjects having at least one non-missing result among PCR, cell culture and/or seroconversion detection. All efficacy analyses were performed on the efficacy population unless otherwise specified.

Subject analysis set title	Infected Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Infected population was defined as all subjects in the Efficacy population providing at least 2 positive nasopharyngeal swabs within 24 h when tested using quantitative PCR assay.
The primary endpoint analysis was on the Infected population. All efficacy analyses were performed on the infected population

Subject analysis set title	Per-protocol Population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) population was defined as all subjects in the Efficacy population who had no major protocol deviations and who complete the quarantine period up to the final day of Quarantine. All efficacy analyses, unless otherwise stated, were performed on the PP population unless the PP population was the same as the efficacy population.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety population was defined as subjects who received a complete or partial dose of IMP or placebo, with subjects allocated to the treatment group associated with the treatment actually received. Unless otherwise indicated, all safety analyses were performed on the Safety population. Data for any subjects who were randomised but did not receive study drug were presented in subject listings only.

Subject analysis set title	Pharmacokinetic Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population included all subjects who had received at least one dose of CT-P27 with at least one evaluable PK parameter and without any major protocol deviation thought to interfere with the absorption, distribution, metabolism, and excretion of the compound to be measured.
The PK evaluation was performed on the PK Population.

Reporting group values	Intention-to-treat Population	Efficacy Population	Infected Population
Number of subjects	81	81	61
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
ITT population			
Units: years			
median	25.0		
full range (min-max)	18 to 42		
Gender categorical			
Units: Subjects			
Female	32		
Male	49		

Reporting group values	Per-protocol Population	Safety Population	Pharmacokinetic Population
Number of subjects	81	81	81
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
ITT population			
Units: years			
median			
full range (min-max)			
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	CT-P27 10mg/kg

Reporting group description:

Subjects received 10 mg/kg CT-P27

Reporting group title	CT-P27 20mg/kg

Reporting group description:

Subjects received 20 mg/kg CT-P27

Reporting group title	Placebo

Reporting group description:

Subjects received placebo

Reporting group title	CT-P27 10mg/kg

Reporting group description:

Subjects received 10 mg/kg CT-P27

Reporting group title	CT-P27 20mg/kg

Reporting group description:

Subjects received 20 mg/kg CT-P27

Reporting group title	Placebo

Reporting group description:

Subjects received placebo

Reporting group title	CT-P27 10mg/kg

Reporting group description:

Subjects received 10 mg/kg CT-P27

Reporting group title	CT-P27 20mg/kg

Reporting group description:

Subjects received 20 mg/kg CT-P27

Reporting group title	Placebo

Reporting group description:

Subjects received placebo

Subject analysis set title	Intention-to-treat Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-treat (ITT) was defined as all subjects randomised to IMP or placebo. The treatment group was defined as the treatment randomised rather than the treatment actually received. All subjects were included as long as they were randomised, even patients who did not receive a treatment. All baseline and demographic summaries were performed on the ITT population.

Subject analysis set title	Efficacy Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Efficacy population was defined as all ITT subjects receiving Challenge Virus and IMP or placebo, with subjects having at least one non-missing result among PCR, cell culture and/or seroconversion detection. All efficacy analyses were performed on the efficacy population unless otherwise specified.

Subject analysis set title	Infected Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The Infected population was defined as all subjects in the Efficacy population providing at least 2 positive nasopharyngeal swabs within 24 h when tested using quantitative PCR assay.
The primary endpoint analysis was on the Infected population. All efficacy analyses were performed on the infected population

Subject analysis set title	Per-protocol Population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) population was defined as all subjects in the Efficacy population who had no major protocol deviations and who complete the quarantine period up to the final day of Quarantine. All efficacy analyses, unless otherwise stated, were performed on the PP population unless the PP population was the same as the efficacy population.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety population was defined as subjects who received a complete or partial dose of IMP or placebo, with subjects allocated to the treatment group associated with the treatment actually received. Unless otherwise indicated, all safety analyses were performed on the Safety population. Data for any subjects who were randomised but did not receive study drug were presented in subject listings only.

Subject analysis set title	Pharmacokinetic Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The PK population included all subjects who had received at least one dose of CT-P27 with at least one evaluable PK parameter and without any major protocol deviation thought to interfere with the absorption, distribution, metabolism, and excretion of the compound to be measured.
The PK evaluation was performed on the PK Population.

Primary: AUC of Viral Load, as Measured by Quantitative PCR of Nasopharyngeal Swab, Post-viral Challenge to the Last Assessment Day in Quarantine

End point title	AUC of Viral Load, as Measured by Quantitative PCR of Nasopharyngeal Swab, Post-viral Challenge to the Last Assessment Day in Quarantine

End point description:

Viral load AUC (Day 1 to Day 9) by nasopharyngeal swab quantitative PCR

End point type	Primary

End point timeframe:

Day 1 to Day 9

End point values	CT-P27 10mg/kg	CT-P27 20mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	20	21	
Units: Days*Eq log10 TCID50/mL				
arithmetic mean (standard deviation)	6.474 (± 9.0090)	6.974 (± 9.0817)	11.639 (± 9.7982)	

Statistical analyses

Statistical analysis title	Wilcoxon Rank-Sum p-value (versus placebo)
Comparison groups	CT-P27 10mg/kg v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.059
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Wilcoxon Rank-Sum p-value (versus placebo)
Comparison groups	CT-P27 20mg/kg v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.121
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From screening to End of study visit	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0
Reporting groups	
Reporting group title	CT-P27 10mg/kg
Reporting group description: -	
Reporting group title	CT-P27 20mg/kg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	CT-P27 10mg/kg	CT-P27 20mg/kg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 27 (0.00%)	0 / 27 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	CT-P27 10mg/kg	CT-P27 20mg/kg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 27 (66.67%)	19 / 27 (70.37%)	19 / 27 (70.37%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 27 (7.41%)	3 / 27 (11.11%)	2 / 27 (7.41%)
occurrences (all)	2	3	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 27 (3.70%)	2 / 27 (7.41%)	0 / 27 (0.00%)
occurrences (all)	1	2	0
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 27 (0.00%)	7 / 27 (25.93%)	0 / 27 (0.00%)
occurrences (all)	0	7	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 27 (3.70%)	1 / 27 (3.70%)	2 / 27 (7.41%)
occurrences (all)	1	1	2
Neutrophil count decreased			
subjects affected / exposed	2 / 27 (7.41%)	1 / 27 (3.70%)	0 / 27 (0.00%)
occurrences (all)	2	1	0
Injury, poisoning and procedural complications			
Procedural haemorrhage			
subjects affected / exposed	2 / 27 (7.41%)	1 / 27 (3.70%)	0 / 27 (0.00%)
occurrences (all)	2	1	0
Foot fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 27 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Nervous system disorders			
headache			
subjects affected / exposed	7 / 27 (25.93%)	6 / 27 (22.22%)	4 / 27 (14.81%)
occurrences (all)	7	6	4
Dysgeusia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 27 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 27 (3.70%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Gastrointestinal disorders			
Aphthous stomatitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 27 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			

Rash subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	2 / 27 (7.41%) 2	2 / 27 (7.41%) 2
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	0 / 27 (0.00%) 0	1 / 27 (3.70%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported