



Clinical trial results:

Open-Label, Phase 2 Study to Evaluate the Efficacy and Safety of CUDC-907 in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma, Including Patients With MYC Alterations

Summary

EudraCT number	2014-004509-34
Trial protocol	DE NL ES HU FR
Global end of trial date	28 May 2019

Results information

Result version number	v1 (current)
This version publication date	02 June 2021
First version publication date	02 June 2021

Trial information

Trial identification

Sponsor protocol code	CUDC-907-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02674750
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Curis, Inc.
Sponsor organisation address	128 Spring St. Building C, Suite 500, Lexington, United States, 02421
Public contact	Reinhard von Roemeling, Curis, Inc., 617 503 6500,
Scientific contact	Reinhard von Roemeling, Curis, Inc., 617 503 6500,

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	28 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2019
Global end of trial reached?	Yes
Global end of trial date	28 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to evaluate the efficacy of CUDC-907 as measured by the objective response rate (ORR) in Group B participants with Relapsed/Refractory Diffuse Large B-Cell Lymphoma (RR DLBCL) with MYC-altered disease by IHC.

Protection of trial subjects:

The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with ICH, GCP guidelines, applicable regulatory requirements, and Curis policies. The Investigator ensured that this study was conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Patients of Research, as drafted by the U.S. National Commission for the Protection of Human Patients of Biomedical and Behavioral Research (18 April 1979) and codified in 45 Code of Federal Regulations (CFR) Part 46 and/or the ICH E6.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 July 2016
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	France: 4
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United States: 61
Worldwide total number of subjects	70
EEA total number of subjects	9

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)	40
From 65 to 84 years	29
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were recruited at 16 study centres in the United States, Spain and France.

Pre-assignment

Screening details:

A screening period of up to 28 days occurred before treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Group A
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Arm description:

Participants with MYC translocation+ and/or MYC gene copy number gain by fluorescence in-situ hybridization (FISH).

Arm type	Experimental
Investigational medicinal product name	CUDC-907
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received CUDC-907 in 21-day cycles.

Arm title	Group B
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Arm description:

Participants with MYC expression in $\geq 40\%$ of tumor cells by immunohistochemistry (IHC).

Arm type	Experimental
Investigational medicinal product name	CUDC-907
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received CUDC-907 in 21-day cycles.

Arm title	Group C
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Arm description:

Participants with MYC translocation by FISH, and MYC expression in $< 40\%$ of tumor cells, and no MYC gene copy number gain by FISH. Participants who did not meet the criteria for Groups A or B based on central laboratory testing and review were assigned to Group C.

Arm type	Experimental
Investigational medicinal product name	CUDC-907
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received CUDC-907 in 21-day cycles.

Number of subjects in period 1	Group A	Group B	Group C
Started	5	49	16
Completed	0	0	0
Not completed	5	49	16
Consent withdrawn by subject	-	1	1
Death	4	32	8
Other	-	4	-
Study Terminated by Sponsor	-	4	4
Progressive disease	1	7	3
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Group A
Reporting group description: Participants with MYC translocation+ and/or MYC gene copy number gain by fluorescence in-situ hybridization (FISH).	
Reporting group title	Group B
Reporting group description: Participants with MYC expression in $\geq 40\%$ of tumor cells by immunohistochemistry (IHC).	
Reporting group title	Group C
Reporting group description: Participants with MYC translocation by FISH, and MYC expression in $< 40\%$ of tumor cells, and no MYC gene copy number gain by FISH. Participants who did not meet the criteria for Groups A or B based on central laboratory testing and review were assigned to Group C.	

Reporting group values	Group A	Group B	Group C
Number of subjects	5	49	16
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 Units: years			
arithmetic mean	65.0	62.9	63.1
standard deviation	± 7.38	± 10.57	± 10.25
Gender categorical Units: Subjects			
Female	2	20	7
Male	3	29	9
Race Units: Subjects			
White	4	44	14
Black or African American	0	3	0
Asian	0	0	1
Other	1	1	1
Missing	0	1	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	4	1
Not Hispanic or Latino	3	44	14

Not Reported	1	0	0
Unknown	0	1	0
Missing	0	0	1

Reporting group values	Total		
Number of subjects	70		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	29		
Male	41		
Race			
Units: Subjects			
White	62		
Black or African American	3		
Asian	1		
Other	3		
Missing	1		
Ethnicity			
Units: Subjects			
Hispanic or Latino	6		
Not Hispanic or Latino	61		
Not Reported	1		
Unknown	1		
Missing	1		

End points

End points reporting groups

Reporting group title	Group A
Reporting group description: Participants with MYC translocation+ and/or MYC gene copy number gain by fluorescence in-situ hybridization (FISH).	
Reporting group title	Group B
Reporting group description: Participants with MYC expression in $\geq 40\%$ of tumor cells by immunohistochemistry (IHC).	
Reporting group title	Group C
Reporting group description: Participants with MYC translocation by FISH, and MYC expression in $< 40\%$ of tumor cells, and no MYC gene copy number gain by FISH. Participants who did not meet the criteria for Groups A or B based on central laboratory testing and review were assigned to Group C.	

Primary: Objective Response Rate (ORR) (Central Determination) in Group B Participants

End point title	Objective Response Rate (ORR) (Central Determination) in Group B Participants ^{[1][2]}
End point description:	
End point type	Primary
End point timeframe: Up to 2 years	
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: The primary endpoint was not analyzed since only data from local radiographic review were available for analysis. [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: Only Group B Analysis was planned for this endpoint.	

End point values	Group B			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[3]			
Units: Number of Participants				

Notes:

[3] - Analysis of ORR in Group B was not performed since central radiographic review was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: ORR (Local Determination) in Group B Participants

End point title	ORR (Local Determination) in Group B Participants ^[4]
End point description: Intent-to-Treat (ITT) Population.	

End point type	Secondary
End point timeframe:	
Up to 2 years	
Notes:	
[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: Only Group B Analysis was planned for this endpoint.	

End point values	Group B			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: Percentage of Participants				
number (confidence interval 95%)	14.3 (5.94 to 27.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in Group B Participants

End point title	Progression Free Survival (PFS) in Group B Participants ^[5]
End point description:	
Evaluable Population.	
End point type	Secondary
End point timeframe:	
Up to 2 years	
Notes:	
[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only Group B Analysis was planned for this endpoint.	

End point values	Group B			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Months				
median (confidence interval 95%)	2.7 (1.28 to 4.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS Status at 6 Months in Group B Participants

End point title	PFS Status at 6 Months in Group B Participants ^[6]
End point description:	
Evaluable Population.	
End point type	Secondary

End point timeframe:

6 months

Notes:

[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: Only Group B Analysis was planned for this endpoint.

End point values	Group B			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Number of Participants				
Event	18			
Censored	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in Group B Participants

End point title	Overall Survival (OS) in Group B Participants ^[7]
End point description:	
Evaluable Population.	
End point type	Secondary
End point timeframe:	
Up to 2 years	

Notes:

[7] - 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: Only Group B Analysis was planned for this endpoint.

End point values	Group B			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Months				
median (confidence interval 95%)	6.3 (3.75 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) (Local Determination) in Group B Participants

End point title	Disease Control Rate (DCR) (Local Determination) in Group B Participants ^[8]
End point description:	
Evaluable Population.	

End point type	Secondary
End point timeframe:	
Up to 2 years	
Notes:	
[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: Only Group B Analysis was planned for this endpoint.	

End point values	Group B			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Percentage of Participants				
number (confidence interval 95%)	46.4 (27.51 to 66.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) (Local Determination) in Group B Participants

End point title	Duration of Response (DOR) (Local Determination) in Group B Participants ^[9]
End point description:	
Evaluable Population.	
End point type	Secondary
End point timeframe:	
Up to 2 years	
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: Only Group B Analysis was planned for this endpoint.	

End point values	Group B			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Months				
median (confidence interval 95%)	2.8 (1.41 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: ORR in Group A and Group C Participants

End point title	ORR in Group A and Group C Participants ^[10]
End point description:	
ITT Population.	

End point type	Secondary
End point timeframe:	
Up to 2 years	
Notes:	
[10] - 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: Only Group A and Group C Analyses were planned for this endpoint.	

End point values	Group A	Group C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	16		
Units: Percentage of Participants				
number (confidence interval 95%)	0.0 (0.00 to 52.18)	6.3 (0.16 to 30.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced an Adverse Event (AE)

End point title	Number of Participants who Experienced an Adverse Event (AE)
End point description:	
Safety Population.	
End point type	Secondary
End point timeframe:	
Up to 2 years	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	47	16	
Units: Number of Participants	5	47	16	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a Serious Adverse Event (SAE)

End point title	Number of Participants who Experienced a Serious Adverse Event (SAE)
End point description:	
Safety Population.	
End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	47	16	
Units: Number of Participants	0	22	8	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 2 years

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Group A
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Reporting group description:

Participants with MYC translocation+ and/or MYC gene copy number gain by fluorescence in-situ hybridization (FISH).

Reporting group title	Group B
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Reporting group description:

Participants with MYC expression in $\geq 40\%$ of tumor cells by immunohistochemistry (IHC).

Reporting group title	Group C
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Reporting group description:

Participants with MYC translocation by FISH, and MYC expression in $< 40\%$ of tumor cells, and no MYC gene copy number gain by FISH. Participants who did not meet the criteria for Groups A or B based on central laboratory testing and review were assigned to Group C.

Serious adverse events	Group A	Group B	Group C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	22 / 47 (46.81%)	8 / 16 (50.00%)
number of deaths (all causes)	4	32	8
number of deaths resulting from adverse events	0	10	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 5 (0.00%)	6 / 47 (12.77%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 6	0 / 0
Lymphoma			
subjects affected / exposed	0 / 5 (0.00%)	3 / 47 (6.38%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device occlusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Tracheal obstruction			

subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Guillain-Barre syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	3 / 16 (18.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			

subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			

subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Citrobacter bacteraemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Group A	Group B	Group C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	47 / 47 (100.00%)	16 / 16 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	3 / 47 (6.38%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Hot flush			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	15 / 47 (31.91%)	8 / 16 (50.00%)
occurrences (all)	1	19	8
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	8 / 47 (17.02%)	4 / 16 (25.00%)
occurrences (all)	0	11	4
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	6 / 47 (12.77%)	2 / 16 (12.50%)
occurrences (all)	0	8	3
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	3 / 47 (6.38%)	1 / 16 (6.25%)
occurrences (all)	0	3	3
Chills			
subjects affected / exposed	1 / 5 (20.00%)	3 / 47 (6.38%)	0 / 16 (0.00%)
occurrences (all)	1	4	0
Mass			
subjects affected / exposed	1 / 5 (20.00%)	2 / 47 (4.26%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Oedema			
subjects affected / exposed	0 / 5 (0.00%)	3 / 47 (6.38%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Chest pain			

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 47 (0.00%) 0	0 / 16 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	9 / 47 (19.15%) 15	3 / 16 (18.75%) 3
Cough subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	9 / 47 (19.15%) 9	0 / 16 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	5 / 47 (10.64%) 5	1 / 16 (6.25%) 1
Dysphonia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	3 / 47 (6.38%) 3	0 / 16 (0.00%) 0
Productive cough subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 47 (2.13%) 1	0 / 16 (0.00%) 0
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Pneumonitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Sinus congestion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Upper-airway cough syndrome			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	4 / 47 (8.51%) 4	0 / 16 (0.00%) 0
Investigations White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	6 / 47 (12.77%) 20	4 / 16 (25.00%) 7
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	6 / 47 (12.77%) 18	3 / 16 (18.75%) 7
Weight decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	7 / 47 (14.89%) 10	1 / 16 (6.25%) 1
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	2 / 47 (4.26%) 2	3 / 16 (18.75%) 3
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	3 / 47 (6.38%) 4	1 / 16 (6.25%) 1
Brain natriuretic peptide increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	2 / 47 (4.26%) 3	1 / 16 (6.25%) 1
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 47 (2.13%) 1	1 / 16 (6.25%) 1
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1

Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	8 / 47 (17.02%)	3 / 16 (18.75%)
occurrences (all)	0	10	3
Headache			
subjects affected / exposed	0 / 5 (0.00%)	4 / 47 (8.51%)	2 / 16 (12.50%)
occurrences (all)	0	4	2
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	2 / 16 (12.50%)
occurrences (all)	0	3	2
Neuropathy peripheral			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	3 / 47 (6.38%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Ageusia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 47 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Parosmia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 5 (20.00%)	20 / 47 (42.55%)	7 / 16 (43.75%)
occurrences (all)	3	41	18
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	11 / 47 (23.40%)	6 / 16 (37.50%)
occurrences (all)	0	16	13
Neutropenia			
subjects affected / exposed	2 / 5 (40.00%)	8 / 47 (17.02%)	4 / 16 (25.00%)
occurrences (all)	2	14	6
Leukopenia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Iron deficiency anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 5 (80.00%)	35 / 47 (74.47%)	7 / 16 (43.75%)
occurrences (all)	6	82	29
Nausea			
subjects affected / exposed	2 / 5 (40.00%)	25 / 47 (53.19%)	6 / 16 (37.50%)
occurrences (all)	2	31	8
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	14 / 47 (29.79%)	5 / 16 (31.25%)
occurrences (all)	0	19	11
Constipation			
subjects affected / exposed	1 / 5 (20.00%)	11 / 47 (23.40%)	2 / 16 (12.50%)
occurrences (all)	1	13	2
Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)	5 / 47 (10.64%)	3 / 16 (18.75%)
occurrences (all)	1	7	4
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	3 / 16 (18.75%)
occurrences (all)	0	1	4
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Dysphagia			
subjects affected / exposed	0 / 5 (0.00%)	3 / 47 (6.38%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Haemorrhoids			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	1 / 16 (6.25%)
occurrences (all)	0	2	1

Impaired gastric emptying subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 2
Toothache subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	3 / 47 (6.38%) 4	0 / 16 (0.00%) 0
Alopecia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	2 / 47 (4.26%) 2	1 / 16 (6.25%) 1
Rash subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	2 / 47 (4.26%) 2	1 / 16 (6.25%) 1
Dry skin subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	3 / 47 (6.38%) 3	3 / 16 (18.75%) 4
Dysuria subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 47 (2.13%) 1	0 / 16 (0.00%) 0
Haematuria subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 47 (2.13%) 1	1 / 16 (6.25%) 1
Urinary tract pain			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 47 (0.00%) 0	1 / 16 (6.25%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	7 / 47 (14.89%)	2 / 16 (12.50%)
occurrences (all)	0	12	2
Pain in extremity			
subjects affected / exposed	1 / 5 (20.00%)	6 / 47 (12.77%)	1 / 16 (6.25%)
occurrences (all)	1	10	1
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	6 / 47 (12.77%)	0 / 16 (0.00%)
occurrences (all)	0	11	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	4 / 47 (8.51%)	1 / 16 (6.25%)
occurrences (all)	0	5	1
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Bone pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 47 (2.13%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	5 / 47 (10.64%)	0 / 16 (0.00%)
occurrences (all)	0	6	0
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Urinary tract infection			

subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	2 / 16 (12.50%)
occurrences (all)	0	1	2
Candida infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Clostridium difficile colitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 47 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	2 / 5 (40.00%)	12 / 47 (25.53%)	9 / 16 (56.25%)
occurrences (all)	2	18	17
Decreased appetite			
subjects affected / exposed	2 / 5 (40.00%)	15 / 47 (31.91%)	5 / 16 (31.25%)
occurrences (all)	2	16	5
Hypomagnesaemia			
subjects affected / exposed	1 / 5 (20.00%)	6 / 47 (12.77%)	5 / 16 (31.25%)
occurrences (all)	1	15	11
Hypophosphataemia			
subjects affected / exposed	1 / 5 (20.00%)	5 / 47 (10.64%)	1 / 16 (6.25%)
occurrences (all)	2	12	5
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 47 (2.13%)	4 / 16 (25.00%)
occurrences (all)	0	2	7
Hypocalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	4 / 47 (8.51%)	2 / 16 (12.50%)
occurrences (all)	0	10	3
Hyperuricaemia			
subjects affected / exposed	0 / 5 (0.00%)	4 / 47 (8.51%)	0 / 16 (0.00%)
occurrences (all)	0	5	0
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 47 (4.26%)	2 / 16 (12.50%)
occurrences (all)	0	2	2

Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	3 / 47 (6.38%)	0 / 16 (0.00%)
occurrences (all)	0	5	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 47 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2016	Primary and secondary endpoints, eligibility criteria, and analysis population for the primary endpoint were updated.
17 June 2016	Eligibility criteria was updated.
30 August 2016	Study design was changed from Simon Two-stage to single-arm to remove risk of holding study enrollment and to increase the number of subjects that may receive CUDC-907 alone.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported