Clinical trial results:
A Phase Ib/IIa, Randomised, Double Blind, Parallel Group, Placebo Controlled, Multicentre Study to Assess the Safety and Efficacy of Expanded Cx611 Allogeneic Adipose-derived Stem Cells (eASCs) for the Intravenous Treatment of Adult Patients With Severe Community-acquired Bacterial Pneumonia and Admitted to the Intensive Care Unit

Summary

EudraCT number	2015-002994-39
Trial protocol	ES BE LT GB FR IT
Global end of trial date	07 July 2020

Results information

Result version number	v1
This version publication date	23 July 2021
First version publication date	23 July 2021

Trial information

Trial identification

Sponsor protocol code	Cx611-0204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03158727
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.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	07 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The Primary purpose of this study is to assess the safety profile of two allogeneic Cx611 80 milliliter (mL) infusions administered through a central line within 3 days (on Days 1 and 3) at a dose of 160 million cells each (320 million cells total) and also to monitor any adverse event and potential immunological host responses against the administered cells during 90 days of follow-up after the first infusion.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	Spain: 45
Country: Number of subjects enrolled	Lithuania: 1
Country: Number of subjects enrolled	France: 18
Worldwide total number of subjects	83
EEA total number of subjects	83

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	43
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 20 investigative sites in Belgium, France, Lithuania, and Spain from 30 Jan 2017 to 07 July 2020.

Pre-assignment

Screening details:

Adult subjects with severe community-acquired bacterial pneumonia (sCABP) and admitted to the intensive care unit (ICU) were enrolled in 1 of the 2 treatment groups to receive Cx611 or placebo on Days 1 and 3.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received standard of care (SoC) therapy followed by 80 mL central line infusions of placebo, intravenously, on Days 1 and 3.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received SoC therapy followed by 80 mL central line infusions of placebo, intravenously, on Days 1 and 3.

Arm title	Cx611 160 mL

Arm description:

Subjects received SoC therapy followed by two 80 mL central line infusions of Cx611, intravenously, on Days 1 and 3 at a fixed dose of 160 million eASCs (320 million cells total).

Arm type	Experimental
Investigational medicinal product name	Cx611
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received SoC therapy followed by two 80 mL central line infusions of Cx611, intravenously, on Days 1 and 3 at a fixed dose of 160 million eASCs (320 million cells total).

Number of subjects in period 1	Placebo	Cx611 160 mL
Started	41	42
Completed	25	23
Not completed	16	19
Adverse event, serious fatal	11	12
Consent withdrawn by subject	2	6
Visit 11 not done by mistake	-	1
Subject doesn't want go back to hospital for visit	2	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received standard of care (SoC) therapy followed by 80 mL central line infusions of placebo, intravenously, on Days 1 and 3.	
Reporting group title	Cx611 160 mL
Reporting group description:	
Subjects received SoC therapy followed by two 80 mL central line infusions of Cx611, intravenously, on Days 1 and 3 at a fixed dose of 160 million eASCs (320 million cells total).	

Reporting group values	Placebo	Cx611 160 mL	Total
Number of subjects	41	42	83
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	23	40
From 65-84 years	24	19	43
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	63.4	61.1	
standard deviation	± 10.43	± 11.24	-
Sex: Female, Male Units: subjects			
Female	15	14	29
Male	26	28	54
Race/Ethnicity, Customized Units: Subjects			
Caucasian	31	28	59
Asian/Oriental	1	0	1
Hispanic	1	1	2
Latino	2	1	3
Unknown	6	12	18
Region of Enrollment Units: Subjects			
Belgium	12	7	19
Spain	23	22	45
Lithuania	0	1	1
France	6	12	18

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received standard of care (SoC) therapy followed by 80 mL central line infusions of placebo, intravenously, on Days 1 and 3.	
Reporting group title	Cx611 160 mL
Reporting group description:	
Subjects received SoC therapy followed by two 80 mL central line infusions of Cx611, intravenously, on Days 1 and 3 at a fixed dose of 160 million eASCs (320 million cells total).	

Primary: Number of Subjects Reporting one or More Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects Reporting one or More Treatment-emergent Adverse Events (TEAEs)[1]
End point description:	
The safety population included all randomised subjects who received at least one dose of the study treatment.	
End point type	Primary
End point timeframe:	
Baseline up to Day 90	

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: No statistical analysis.

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	37	40		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adverse Events of Special Interest (AESI)

End point title	Number of Subjects With Adverse Events of Special Interest (AESI)[2]
End point description:	
AESIs are predefined adverse events (AEs) that required close monitoring and prompt reporting to the sponsor. Protocol-specific AEs considered as AESI for this study are thromboembolic events and hypersensitivity reactions such as anaphylaxis. The safety population included all randomised subjects who received at least one dose of the study treatment.	
End point type	Primary
End point timeframe:	
Baseline up to Day 90	

Notes:

[2] - 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: No statistical analysis.

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	9	7		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Hypersensitivity Reactions

End point title	Number of Subjects With Hypersensitivity Reactions[3]

End point description:

Hypersensitivity reactions included anaphylaxis (changes in systolic and diastolic blood pressure, core temperature, respiratory rate [non-ventilated subjects], heart rate), episodes of skin reactions and signs and symptoms of respiratory distress, which require therapeutic intervention including drugs and/or changes in mechanical ventilation setting. Number of subjects with hypersensitivity reactions were reported for this outcome measure. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Primary

End point timeframe:

Baseline up to Day 90

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: No statistical analysis.

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Markedly Abnormal Values of 12-lead Electrocardiogram (ECG) Parameters on Day 1

End point title	Number of Subjects With Markedly Abnormal Values of 12-lead Electrocardiogram (ECG) Parameters on Day 1[4]

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Primary

End point timeframe:

Day 1

Notes:

[4] - 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: No statistical analysis.

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	3	7		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Markedly Abnormal Values of 12-lead Electrocardiogram (ECG) Parameters on Day 3

End point title	Number of Subjects With Markedly Abnormal Values of 12-lead Electrocardiogram (ECG) Parameters on Day 3[5]

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Primary

End point timeframe:

Day 3

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: No statistical analysis.

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	5	4		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Markedly Abnormal Laboratory Values

End point title	Number of Subjects With Markedly Abnormal Laboratory

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Primary

End point timeframe:

Baseline up to Day 90

Notes:

[6] - 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: No statistical analysis.

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Anti-human Leukocyte Antigen Complex (Anti-HLA)/Donor Antibodies At Day 1, 14, and 90

End point title	Number of Subjects With Anti-human Leukocyte Antigen Complex (Anti-HLA)/Donor Antibodies At Day 1, 14, and 90[7]

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment. Here, "overall number of subjects analyzed" are those who were evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Day 1, 14, and 90

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: No statistical analysis.

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects				
Subjects with Anti-HLA/Donor Antibodies at Day 1	6	4		
Subjects with Anti-HLA/Donor Antibodies at Day 14	4	5		
Subjects with Anti-HLA/Donor Antibodies at Day 90	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Mechanical Ventilation and Vasopressors Treatment-free Days

End point title	Mechanical Ventilation and Vasopressors Treatment-free Days

End point description:

Subjects with sCABP suffer either a respiratory failure that requires invasive mechanical ventilation and/or a severe hypotension that requires vasopressors. Number of days when subjects were alive and free from mechanical ventilation and vasopressors were reported. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 28

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))	19.0 (0 to 27)	13.5 (0 to 25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Alive and Free of Both Mechanical Ventilation and Vasopressors at Day 29

End point title	Percentage of Subjects Alive and Free of Both Mechanical Ventilation and Vasopressors at Day 29

End point description:

Subjects with sCABP suffer either a respiratory failure that requires invasive mechanical ventilation and/or a severe hypotension that requires vasopressors. Percentage of subjects who were alive and free of both mechanical ventilation and vasopressors at Day 29 were reported. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: percentage of subjects				
number (not applicable)	78.0	64.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Alive and Free of Mechanical Ventilation at Day 29

End point title	Percentage of Subjects Alive and Free of Mechanical Ventilation at Day 29

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: percentage of subjects				
number (not applicable)	78.0	66.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Ventilator Free Days (VeFD)

End point title	Number of Ventilator Free Days (VeFD)

End point description:

VeFD are defined as one point for each day during the measurement period that subjects are both alive and free from mechanical ventilation. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 28

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))	19.0 (0 to 28)	14.0 (0 to 28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Alive and Free of Vasopressors at Day 29

End point title	Percentage of Subjects Alive and Free of Vasopressors at Day 29

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: percentage of subjects				
number (not applicable)	85.4	76.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Vasopressor Treatment-free Days (VaFD)

End point title	Number of Vasopressor Treatment-free Days (VaFD)

End point description:

VaFD over 28 days defined as one point for each day during the measurement period that subjects are both alive and free of vasopressors. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 28

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))	24.0 (0 to 28)	23.5 (0 to 28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to end of Invasive Mechanical Ventilation

End point title	Time to end of Invasive Mechanical Ventilation

End point description:

Time in days, from the start date of invasive mechanical ventilation to the first stop date of invasive mechanical ventilation (that is, first time the subject ends mechanical ventilation), or death. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	39		
Units: days				
median (full range (min-max))	7.7 (4.6 to 11.5)	8.3 (4.6 to 12.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to end of Invasive and/or Non-invasive Mechanical Ventilation

End point title	Time to end of Invasive and/or Non-invasive Mechanical Ventilation

End point description:

Time in days, from the start date of invasive or non-invasive mechanical ventilation to the first stop date of invasive or non-invasive mechanical ventilation (that is, first time the subject ends mechanical ventilation), or death. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	39		
Units: days				
median (full range (min-max))	6.3 (3.3 to 10.3)	4.7 (2.9 to 8.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to end of Vasopressors Treatment

End point title	Time to end of Vasopressors Treatment

End point description:

Time in days, from the start date of vasopressors treatment to the first stop date of vasopressors treatment (that is, first time the subject ends vasopressors treatment), or death. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	34		
Units: days				
median (full range (min-max))	2.1 (1.4 to 3.0)	2.0 (1.0 to 2.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With sCABP Clinical Response Visit at Days 8-10, 14, and 29

End point title	Number of Subjects With sCABP Clinical Response Visit at Days 8-10, 14, and 29

End point description:

Cure:complete resolution of pneumonia at BL,no new symptoms/complications attributable to pneumonia.Non-response-failure related/unrelated to pneumonia: persistence/progression of baseline signs/symptoms of pneumonia/BL radiographic abnormalities after at least 2 days of treatment/ordevelopment of new pulmonary/extra pulmonary findings consistent with active infection/development of new pulmonary infection/extrapulmonary infection requiring antimicrobial therapy/persistence/progression of baseline signs/symptoms of severe sepsis/development of new signs/symptoms of severe sepsis/death due to sepsis. Cumulative data is reported only for subjects who were assessed from Day 8-10.The safety population included all randomised subjects who received at least one dose of the study treatment.Here, "overall number of subjects analyzed" are those who were evaluable for this outcome measure.Here "number analyzed" are the subjects who were evaluable for this outcome measure at given time points.

End point type	Secondary

End point timeframe:

Days 8 to 10, 14, and 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects				
Days 8 to 10 (Cure)	18	21		
Days 8 to 10 (Failure not resulting in death)	8	6		

Days 8 to 10 (Indeterminate)	11	9		
Days 8 to 10 (Missing)	1	0		
Day 14 (Cure) (n=36, 33)	24	24		
Day 14 (Failure not resulting in death) (n=36, 33)	5	4		
Day 14 (Indeterminate) (n=36, 33)	6	4		
Day 14 (Missing) (n=36, 33)	1	1		
Day 29 (Cure) (n=32, 30)	30	26		
Day 29 (Failure not resulting in death) (n=32, 30)	1	1		
Day 29 (Indeterminate) (n=32, 30)	0	3		
Day 29 (Missing) (n=32, 30)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to sCABP Clinical Cure

End point title	Time to sCABP Clinical Cure

End point description:

Cure is defined as complete resolution of pneumonia signs and symptoms present at baseline, no new symptoms or complications attributable to the pneumonia. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))	13.0 (10.0 to 16.0)	9.5 (8.0 to 14.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Antibiotic Treatment

End point title	Duration of Antibiotic Treatment

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	38		
Units: days				
median (full range (min-max))	9.0 (2 to 29)	8.0 (1 to 29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pneumonia Recurrence or Reinfection After Clinical Cure

End point title	Percentage of Subjects With Pneumonia Recurrence or Reinfection After Clinical Cure

End point description:

Pneumonia recurrence is defined as a new acute clinical episode of pneumonia, after clinical cure of the episode that qualified the subject for the study, based on the presence of two relevant signs (fever, tachypnoea, leukocytosis, or hypoxemia) and radiographic findings of new pulmonary infiltrate/s or clinically significant worsening of previous ones. If a bacterial pathogen isolated in the recurrent episode is phenotypically different from the one isolated in the previous episode this will be considered as reinfection. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 90

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: percentage of subjects				
Day 14: Recurrence	2	0		
Day 14: Reinfection	3	2		
Day 29: Recurrence	0	1		
Day 29: Reinfection	0	0		
Day 90: Recurrence	0	0		
Day 90: Reinfection	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Recurrence or Reinfection of Pneumonia After Clinical Cure at sCABP Clinical Response Assessments

End point title	Time to Recurrence or Reinfection of Pneumonia After Clinical Cure at sCABP Clinical Response Assessments

End point description:

Pneumonia recurrence is defined as a new acute clinical episode of pneumonia, after clinical cure of the episode that qualified the subject for the study, based on the presence of two relevant signs (fever, tachypnoea, leukocytosis, or hypoxemia) and radiographic findings of new pulmonary infiltrates or clinically significant worsening of previous ones. If a bacterial pathogen isolated in the recurrent episode is phenotypically different from the one isolated in the previous episode this will be considered as reinfection. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 90

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))	100.0 (100.0 to 100.0)	96.2 (75.7 to 99.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: 28-day All-cause Mortality

End point title	28-day All-cause Mortality

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment. Data could not be estimated because more than 50% subjects were censored from the analysis and therefore we have added 99999 as space fillers.

End point type	Secondary

End point timeframe:

Day 28

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	99999	99999		

Statistical analyses

No statistical analyses for this end point

Secondary: 28-day sCABP-associated Mortality

End point title	28-day sCABP-associated Mortality

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment. Data could not be estimated because more than 50% subjects were censored from the analysis and therefore we have added 99999 as space fillers.

End point type	Secondary

End point timeframe:

Day 28

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	99999	99999		

Statistical analyses

No statistical analyses for this end point

Secondary: Survival at Baseline, Days 10, 20, 30, 40, 50, 60, 70, 80, and 90

End point title	Survival at Baseline, Days 10, 20, 30, 40, 50, 60, 70, 80, and 90

End point description:

Survival data for percentage of subjects at Baseline and at Days 10, 20, 30, 40, 50, 60, 70, 80, and 90 was assessed and reported. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

At Baseline, Days 10, 20, 30, 40, 50, 60, 70, 80, and 90

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: percentage of subjects				
number (confidence interval 95%)				
Baseline	100.0 (100.0 to 100.0)	100.0 (100.0 to 100.0)		
Day 10	95.1 (81.9 to 98.8)	88.1 (73.7 to 94.9)		
Day 20	87.5 (72.6 to 94.6)	80.7 (65.0 to 89.8)		
Day 30	85.0 (69.5 to 93.0)	80.7 (65.0 to 89.8)		
Day 40	77.0 (60.4 to 87.3)	80.7 (65.0 to 89.8)		
Day 50	77.0 (60.4 to 87.3)	75.3 (58.9 to 85.9)		
Day 60	77.0 (60.4 to 87.3)	75.3 (58.9 to 85.9)		
Day 70	77.0 (60.4 to 87.3)	75.3 (58.9 to 85.9)		
Day 80	77.0 (60.4 to 87.3)	75.3 (58.9 to 85.9)		
Day 90	77.0 (60.4 to 87.3)	71.5 (54.0 to 83.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Death (Overall Survival)

End point title	Time to Death (Overall Survival)

End point description:

Time from Baseline and at Days 10, 20, 30, 40, 50, 60, 70, 80, and until subject dies or up to Day 90 post-treatment was assessed and reported. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

At Baseline, Days 10, 20, 30, 40, 50, 60, 70, 80, and 90

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: percentage of subjects				
number (confidence interval 95%)				
Baseline	100.0 (100.0 to 100.0)	100.0 (100.0 to 100.0)		
Day 10	95.1 (81.9 to 98.9)	88.1 (73.7 to 94.9)		

Day 20	87.5 (72.6 to 94.6)	80.7 (65.0 to 89.8)		
Day 30	85.0 (69.5 to 93.0)	80.7 (65.0 to 89.8)		
Day 40	77.0 (60.4 to 87.3)	80.7 (65.0 to 89.8)		
Day 50	77.0 (60.4 to 87.3)	75.3 (58.9 to 85.9)		
Day 60	77.0 (60.4 to 87.3)	75.3 (58.9 to 85.9)		
Day 70	77.0 (60.4 to 87.3)	75.3 (58.9 to 85.9)		
Day 80	77.0 (60.4 to 87.3)	75.3 (58.9 to 85.9)		
Day 90	77.0 (60.4 to 87.3)	71.5 (54.0 to 83.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Discharge From Intensive Care Unit (ICU)

End point title	Time to Discharge From Intensive Care Unit (ICU)

End point description:

Time to discharge from ICU was defined, in days, as the time between informed consent date and the date of discharge from the ICU. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 90

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))	11.1 (7.1 to 14.9)	13.0 (7.2 to 16.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Discharge From Hospital

End point title	Time to Discharge From Hospital

End point description:

Time to discharge from hospital was defined, in days, as the time between informed consent date and the date of discharge from the hospital. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 90

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))	19.2 (14.4 to 30.0)	18.3 (13.2 to 25.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of Stay (LOS) in ICU and Hospital After Randomization

End point title	Length of Stay (LOS) in ICU and Hospital After Randomization

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 90

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))				
Length of stay in ICU	11.1 (1 to 54)	12.3 (0 to 121)		
Length of stay in Hospital	19.2 (1 to 70)	19.3 (1 to 186)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of ICU-free Days

End point title	Number of ICU-free Days

End point description:

ICU-free days will be defined as the number of days during which the subject was not in ICU, starting from the randomization date, to Day 29, or day of discontinuation. The safety population included all

randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: days				
median (full range (min-max))	14.0 (0 to 26)	5.5 (0 to 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Sepsis-related Organ Failure Assessment (SOFA) Score During Stay at ICU

End point title	Change From Baseline in Sepsis-related Organ Failure Assessment (SOFA) Score During Stay at ICU

End point description:

The SOFA score used to assess the incidence of organ dysfunction or failure in the ICU. The SOFA score ranges from with 0 to 4 points assigned for each of 6 organ dysfunctions: respiration, coagulation, liver, cardiovascular, central nervous system and renal. Higher scores indicates more severe organ failure. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	42		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	7.9 (± 2.39)	8.5 (± 3.01)		
Change at Day 29	-6.1 (± 3.30)	-5.7 (± 3.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Categorized Based on the Chest X-ray Assessments

Compared to Previous Chest X-ray Assessment

End point title	Number of Subjects Categorized Based on the Chest X-ray Assessments Compared to Previous Chest X-ray Assessment

End point description:

Number of subjects with chest X-ray assessment compared to the previous assessment were assessed and reported. Number of subjects are reported who showed Comparison of previous X-ray data is reported on the basis of improvement, remission, stabilization, and worsening when comparison of X-rays was performed to previous X-ray data. Cumulative data is reported only for subjects who were assessed from Day 8-10. The safety population included all randomised subjects who received at least one dose of the study treatment. Here, "overall number of subjects analyzed" are those who were evaluable for this outcome measure. Here, "number analyzed" are the subjects who were evaluable for the outcome measure at given time points.

End point type	Secondary

End point timeframe:

Days 1, 2, 3, 4, 5, 6, 7, 8-10, 14, 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	31		
Units: subjects				
Improvement at Day 1 (n=9,10)	0	0		
Remission at Day 1 (n=9,10)	0	0		
Stabilization at Day 1 (n=9,10)	7	6		
Worsening at Day 1 (n=9,10)	2	4		
Improvement at Day 2 (n=34, 31)	9	6		
Remission at Day 2 (n=34, 31)	0	0		
Stabilization at Day 2 (n=34, 31)	17	17		
Worsening at Day 2 (n=34, 31)	8	8		
Improvement at Day 3 (n=37, 30)	19	8		
Remission at Day 3 (n=37, 30)	0	1		
Stabilization at Day 3 (n=37, 30)	17	17		
Worsening at Day 3 (n=37, 30)	1	4		
Improvement at Day 4 (n=30, 31)	14	8		
Remission at Day 4 (n=30, 31)	1	3		
Stabilization at Day 4 (n=30, 31)	15	12		
Worsening at Day 4 (n=30, 31)	0	8		
Improvement at Day 5 (n=20, 24)	5	8		
Remission at Day 5 (n=20, 24)	2	2		
Stabilization at Day 5 (n=20, 24)	7	9		
Worsening at Day 5 (n=20, 24)	6	5		
Improvement at Day 6 (n=29, 26)	11	12		
Remission at Day 6 (n=29, 26)	1	2		
Stabilization at Day 6 (n=29, 26)	15	10		
Worsening at Day 6 (n=29, 26)	2	2		
Improvement at Day 7 (n=18, 22)	8	8		
Remission at Day 7 (n=18, 22)	0	0		
Stabilization at Day 7 (n=18, 22)	7	11		
Worsening at Day 7 (n=18, 22)	3	3		
Improvement at Days 8-10 (n=27, 22)	8	9		
Remission at Days 8-10 (n=27, 22)	3	3		

Stabilization at Days 8-10 (n=27, 22)	11	7		
Worsening at Days 8-10 (n=27, 22)	5	3		
Improvement at Day 14 (n=21, 15)	10	10		
Remission at Day 14 (n=21, 15)	1	1		
Stabilization at Day 14 (n=21, 15)	5	3		
Worsening at Day 14 (n=21, 15)	5	1		
Improvement at Day 29 (n=9, 14)	3	6		
Remission at Day 29 (n=9, 14)	3	2		
Stabilization at Day 29 (n=9, 14)	2	4		
Worsening at Day 29 (n=9, 14)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the Ratio of the Partial Pressure of Oxygen to the Fraction of Inspired Oxygen (PaO2/FiO2 Ratio)

End point title	Change in the Ratio of the Partial Pressure of Oxygen to the Fraction of Inspired Oxygen (PaO2/FiO2 Ratio)

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 7

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: P/F ratio				
arithmetic mean (standard deviation)				
Baseline	131.6 (± 55.14)	278.6 (± 981.67)		
Change at Day 7	74.6 (± 97.20)	78.4 (± 68.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Requiring Mechanical Ventilation or Non-invasive Ventilation Twelve Hours After the Second Investigational Medicinal Product (IMP) Infusion

End point title	Number of Subjects Requiring Mechanical Ventilation or Non-invasive Ventilation Twelve Hours After the Second Investigational Medicinal Product (IMP) Infusion

End point description:

The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Day 3: 0 to 12 hours post-IMP infusion

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects				
Count of Participants	31	37		

Statistical analyses

No statistical analyses for this end point

Secondary: Number Subjects Using Rescue Antibiotics

End point title	Number Subjects Using Rescue Antibiotics

End point description:

Any new intravenous antibiotic for CABP indication that is started after Day 1 and before Day 29 was considered a rescue antibiotic. The safety population included all randomised subjects who received at least one dose of the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Day 29

End point values	Placebo	Cx611 160 mL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	42		
Units: subjects	28	32		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events are adverse events that started from the signature of the informed consent (Baseline) up to Day 730

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the subject or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received SoC therapy followed by central line infusions of placebo-matching Cx611, intravenously, on Days 1 and 3.

Reporting group title	Cx611 160 mL

Reporting group description:

Subjects received SoC therapy followed by two 80 mL central line infusions of Cx611, intravenously, on Days 1 and 3 at a fixed dose of 160 million eASCs (320 million cells total).

Serious adverse events	Placebo	Cx611 160 mL	
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 41 (48.78%)	24 / 42 (57.14%)	
number of deaths (all causes)	12	13	
number of deaths resulting from adverse events			
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			

subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Coronary artery bypass			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve replacement			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fibrosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multiple organ dysfunction syndrome			
subjects affected / exposed	4 / 41 (9.76%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	

Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypercapnia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 41 (4.88%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory acidosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory distress			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	3 / 41 (7.32%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration bronchial			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular dissociation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 41 (2.44%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cardiac failure congestive			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiogenic shock			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebral artery embolism			

subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebrovascular accident			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intensive care unit acquired weakness			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Haemolysis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Subileus			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischaemic hepatitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 41 (0.00%)	3 / 42 (7.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (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			
Bronchopulmonary aspergillosis			

subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal bacteraemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (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	0 / 41 (0.00%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Toxic shock syndrome			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urosepsis			

subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Cx611 160 mL	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 41 (100.00%)	42 / 42 (100.00%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	5 / 41 (12.20%)	1 / 42 (2.38%)	
occurrences (all)	5	1	
Hypertension			
subjects affected / exposed	2 / 41 (4.88%)	6 / 42 (14.29%)	
occurrences (all)	2	6	
Hypotension			
subjects affected / exposed	1 / 41 (2.44%)	2 / 42 (4.76%)	
occurrences (all)	1	2	
Ischaemia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Phlebitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Venous thrombosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Device related thrombosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Generalised oedema			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Hyperthermia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hypothermia			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	
occurrences (all)	2	0	
Malaise			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 41 (2.44%)	3 / 42 (7.14%)	
occurrences (all)	1	3	
Puncture site haemorrhage			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)	2 / 42 (4.76%)	
occurrences (all)	1	2	
Reproductive system and breast disorders			
Penile oedema			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Acute pulmonary oedema				
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)		
occurrences (all)	0	1		
Acute respiratory distress syndrome				
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)		
occurrences (all)	0	1		
Atelectasis				
subjects affected / exposed	2 / 41 (4.88%)	3 / 42 (7.14%)		
occurrences (all)	2	3		
Bronchospasm				
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)		
occurrences (all)	1	1		
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)		
occurrences (all)	1	1		
Cough				
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)		
occurrences (all)	1	0		
Epistaxis				
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)		
occurrences (all)	1	0		
Haemothorax				
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)		
occurrences (all)	1	0		
Hypercapnia				
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)		
occurrences (all)	1	0		
Hypoxia				
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)		
occurrences (all)	1	1		
Pharyngeal haemorrhage				
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)		
occurrences (all)	0	1		
Pleural effusion				

subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Pleuritic pain			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Pneumothorax			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Pulmonary embolism			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Pulmonary oedema			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Respiratory acidosis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Respiratory disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Respiratory distress			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Stridor			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 41 (4.88%)	4 / 42 (9.52%)	
occurrences (all)	2	4	

Aggression			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	0 / 41 (0.00%)	4 / 42 (9.52%)	
occurrences (all)	0	4	
Confusional state			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Delirium			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hallucination, visual			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase increased			

subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Staphylococcus test positive			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Axillary nerve injury			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Endotracheal intubation complication			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Eschar			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	
occurrences (all)	2	0	
Fall			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	
occurrences (all)	0	2	
Toxicity to various agents			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Tracheal haemorrhage			

subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	3 / 41 (7.32%)	6 / 42 (14.29%)	
occurrences (all)	3	6	
Bradycardia			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	
occurrences (all)	2	0	
Bundle branch block left			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	
occurrences (all)	0	2	
Cardiac failure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Extrasystoles			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Mitral valve incompetence			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Pericardial effusion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Sinus tachycardia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Supraventricular extrasystoles			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Supraventricular tachycardia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	

Tachycardia			
subjects affected / exposed	1 / 41 (2.44%)	2 / 42 (4.76%)	
occurrences (all)	1	2	
Nervous system disorders			
Agitation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Akinesia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Cerebrovascular accident			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Essential tremor			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Facial paralysis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hepatic encephalopathy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Intensive care unit acquired weakness			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Memory impairment			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Paraparesis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Partial seizures			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Partial seizures with secondary generalisation			

subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 41 (21.95%)	8 / 42 (19.05%)	
occurrences (all)	9	8	
Anaemia macrocytic			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Coagulopathy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Heparin-induced thrombocytopenia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Lymphopenia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	1 / 41 (2.44%)	3 / 42 (7.14%)	
occurrences (all)	1	3	
Thrombocytosis			
subjects affected / exposed	2 / 41 (4.88%)	1 / 42 (2.38%)	
occurrences (all)	2	1	

Thymus disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 41 (0.00%)	4 / 42 (9.52%)	
occurrences (all)	0	4	
Ascites			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Colonic pseudo-obstruction			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	4 / 41 (9.76%)	5 / 42 (11.90%)	
occurrences (all)	4	5	
Diarrhoea			
subjects affected / exposed	4 / 41 (9.76%)	5 / 42 (11.90%)	
occurrences (all)	4	5	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Haematemesis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Impaired gastric emptying			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Loose tooth			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Mouth haemorrhage			

subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Odynophagia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Oesophagitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Pancreatitis acute			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Rectal haemorrhage			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Tooth loss			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 41 (0.00%)	5 / 42 (11.90%)	
occurrences (all)	0	5	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	1 / 41 (2.44%)	5 / 42 (11.90%)	
occurrences (all)	1	5	
Hepatic cirrhosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hepatic failure			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	

Hepatocellular injury			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	
occurrences (all)	2	0	
Hepatomegaly			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Hepatorenal syndrome			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hypertransaminasaemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Decubitus ulcer			
subjects affected / exposed	2 / 41 (4.88%)	2 / 42 (4.76%)	
occurrences (all)	2	2	
Erythema			
subjects affected / exposed	1 / 41 (2.44%)	3 / 42 (7.14%)	
occurrences (all)	1	3	
Intertrigo			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	1 / 41 (2.44%)	2 / 42 (4.76%)	
occurrences (all)	1	2	
Rash macular			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Skin lesion			

subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Skin maceration			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Skin reaction			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Subcutaneous emphysema			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 41 (4.88%)	1 / 42 (2.38%)	
occurrences (all)	2	1	
Chronic kidney disease			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Neurogenic bladder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Oliguria			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	

Renal failure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Renal impairment			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	
occurrences (all)	0	2	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hyperparathyroidism			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Primary hypothyroidism			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Myopathy			
subjects affected / exposed	1 / 41 (2.44%)	2 / 42 (4.76%)	
occurrences (all)	1	2	
Infections and infestations			
Citrobacter infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	

Empyema			
subjects affected / exposed	2 / 41 (4.88%)	1 / 42 (2.38%)	
occurrences (all)	2	1	
Fungal skin infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Genital candidiasis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Herpes virus infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Infectious pleural effusion			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Mediastinitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Pseudomonal sepsis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Pseudomonas infection			
subjects affected / exposed	2 / 41 (4.88%)	0 / 42 (0.00%)	
occurrences (all)	2	0	

Rhinitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Sepsis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Septic shock			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Serratia infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Skin candida			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Subcutaneous abscess			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Tracheitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 41 (0.00%)	2 / 42 (4.76%)	
occurrences (all)	0	2	
Urinary tract infection pseudomonal			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Cell death			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Feeding intolerance			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hyperammonaemia			

subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hyperamylasaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hypercholesterolaemia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Hyperglycaemia			
subjects affected / exposed	1 / 41 (2.44%)	4 / 42 (9.52%)	
occurrences (all)	1	4	
Hyperkalaemia			
subjects affected / exposed	4 / 41 (9.76%)	2 / 42 (4.76%)	
occurrences (all)	4	2	
Hyperlactacidaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hypernatraemia			
subjects affected / exposed	6 / 41 (14.63%)	1 / 42 (2.38%)	
occurrences (all)	6	1	
Hyperphosphataemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Hypervolaemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Hypocalcaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	0 / 41 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	3	
Hypokalaemia			

subjects affected / exposed	4 / 41 (9.76%)	5 / 42 (11.90%)	
occurrences (all)	4	5	
Hypomagnesaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	0 / 41 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	3	
Hypophosphataemia			
subjects affected / exposed	3 / 41 (7.32%)	2 / 42 (4.76%)	
occurrences (all)	3	2	
Malnutrition			
subjects affected / exposed	0 / 41 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Metabolic acidosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Metabolic alkalosis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 42 (2.38%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2016	Protocol Amendment 1: The primary purpose of this amendment is to update the study objectives to explore the long term safety assessment.
01 August 2017	Protocol Amendment 2: The primary purpose of this amendment is to update the clinical study protocol regarding the reformulation of the placebo.
28 May 2018	Protocol Amendment 3: The primary purpose of this amendment is to update the inclusion and exclusion criteria's.
19 December 2019	Protocol Amendment 5: The primary purpose of this amendment is to update the enrollment number, Schedule of Study Assessments and the Study Design.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
26 June 2017	Study enrolment was temporarily paused in 2017 in order for the study's placebo to be reformulated.	01 August 2017

Notes:

Limitations and caveats

None reported