Clinical trial results:
Double-blind, randomized, parallel, placebo-controlled pilot clinical trial, nested in a prospective cohort observational study, for the evaluation of the efficacy and safetyof two doses of WJ-MSC in patients with acute respiratory distress syndrome secondary to infection by COVID-19

Summary

EudraCT number	2020-001505-22
Trial protocol	ES
Global end of trial date	20 December 2022

Results information

Result version number	v1 (current)
This version publication date	12 July 2023
First version publication date	12 July 2023
Summary attachment (see zip file)	COVIDMES Summary (CSR Summary ENG.pdf)

Trial information

Trial identification

Sponsor protocol code	BST-COVID-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Banc de Sang i Teixits
Sponsor organisation address	Passeig Taulat, 116, Barcelona, Spain, 08005
Public contact	Banc de Sang i Teixits, Banc de Sang i Teixits, 34 935573500 (6707), rucoll@bst.cat
Scientific contact	Banc de Sang i Teixits, Banc de Sang i Teixits, 34 935573500 (6707), rucoll@bst.cat

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	20 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2022
Global end of trial reached?	Yes
Global end of trial date	20 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

All-cause mortality at day 28

Protection of trial subjects:

Depending on the patient's condition, obtaining consent was follows:

- In conscious hospitalized patients, oral consent was obtained in the presence of a family witness (via telephone) or, if unavailable, an impartial witness (unrelated to the research team).
-In unconscious hospitalized patients, informed consent was obtained via telephone from a family member.
The following document should be completed and signed in both circumstances: "CONFIRMATION OF ORAL INFORMED CONSENT FOR COVID-19 EMERGENCY". This document served as proof that oral consent had been obtained. It was acceptable for the Principal Investigator or a research team member to explain the study remotely (via telephone, or video conference) in the presence of an impartial witness. Additionally, it had to be documented in the patient's medical record that temporary oral consent had been obtained. When circumstances permit, patients had to sign the written consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 July 2020
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	Spain: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	17
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients admitted to the Intensive Care Unit and affected with SARS-CoV-2 (positive PCR)

Pre-assignment

Screening details:

SARS-CoV-2 (positive PCR)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	WJ-MSC

Arm description:

Patients assigned to Wharton-Jelly mesenchymal stromal cells on D1 and D3

Arm type	Experimental
Investigational medicinal product name	WJ-MSC
Investigational medicinal product code	
Other name	XCEl-UMC-BETA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1E6cells/Kg administered endovenously

Arm title	Placebo

Arm description:

Patients assigned to placebo

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

Dosage and administration details:

Placebo for endovenous administration

Number of subjects in period 1	WJ-MSC	Placebo
Started	14	11
Completed	14	11

Baseline characteristics

Reporting groups	
Reporting group title	WJ-MSC
Reporting group description:	
Patients assigned to Wharton-Jelly mesenchymal stromal cells on D1 and D3	
Reporting group title	Placebo
Reporting group description:	
Patients assigned to placebo	

Reporting group values	WJ-MSC	Placebo	Total
Number of subjects	14	11	25
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)	14	11	25
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	59.93	57.55	
standard deviation	± 8.54	± 11.35	-
Gender categorical Units: Subjects			
Female	5	3	8
Male	9	8	17

Subject analysis sets	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis

Subject analysis set description:

Randomized population that has received at least one treatment dose and has the primary endpoint in the baseline evaluation and an evaluation after treatment. This set will be used in efficacy analysis for intention-to-treat (ITT) analysis.

Reporting group values	Full analysis		
Number of subjects	25		
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)	25		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±		
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	WJ-MSC
Reporting group description:	
Patients assigned to Wharton-Jelly mesenchymal stromal cells on D1 and D3	
Reporting group title	Placebo
Reporting group description:	
Patients assigned to placebo	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description:	
Randomized population that has received at least one treatment dose and has the primary endpoint in the baseline evaluation and an evaluation after treatment. This set will be used in efficacy analysis for intention-to-treat (ITT) analysis.	

Primary: Mortality

End point title	Mortality
End point description:	
End point type	Primary
End point timeframe:	
28days	

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	11		
Units: n	0	2		

Statistical analyses

Statistical analysis title	Mortality at day 28
Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1833
Method	Fisher exact

Secondary: Need of mechanical ventilation

End point title	Need of mechanical ventilation

End point description:	
Patients requiring invasive mechanical ventilation from the start of treatment to day +28, by treatment group	
End point type	Secondary
End point timeframe:	
28 days	

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	11		
Units: n	10	5		

Statistical analyses

Statistical analysis title	Mechanical ventilation
Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2406
Method	Fisher exact

Secondary: Duration of mechanical ventilation	
End point title	Duration of mechanical ventilation
End point description:	
Average number of days on mechanical ventilation, per treatment group	
End point type	Secondary
End point timeframe:	
28 days	

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	11		
Units: days	10	5		

Statistical analyses

Statistical analysis title	Days on mechanical ventilation
Statistical analysis description: Average number of days on mechanical ventilation	
Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0842
Method	Fisher exact

Secondary: Days free of mechanical ventilation

End point title	Days free of mechanical ventilation
End point description: Days after treatment in which the patient remained alive and free of invasive mechanical ventilation, until day +28, by treatment group	
End point type	Secondary
End point timeframe: 28 days	

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	11		
Units: days	10	5		

Statistical analyses

Statistical analysis title	Days free of mechanical ventilation
Statistical analysis description: Days after treatment in which the patient remained alive and free of invasive mechanical ventilation, until day +28, by treatment group	
Comparison groups	Placebo v WJ-MSC
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.42
Method	Fisher exact

Secondary: Evaluation of the SOFA index

End point title	Evaluation of the SOFA index
End point description:	

End point type	Secondary
End point timeframe:	
Day 28	

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: units				
arithmetic mean (standard deviation)	-1.57 (± 3.05)	-2.57 (± 1.51)		

Statistical analyses

Statistical analysis title	SOFA index
Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8893
Method	ANOVA

Secondary: Assessment of the APACHE II score

End point title	Assessment of the APACHE II score
End point description:	

End point type	Secondary
End point timeframe:	
Day 28	

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: score				
arithmetic mean (standard deviation)	-2.29 (± 5.41)	-5.29 (± 4.50)		

Statistical analyses

Statistical analysis title	APACHE II score
Comparison groups	WJ-MSC v Placebo

Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3552
Method	ANOVA

Secondary: Immune response (leukocyte count)

End point title	Immune response (leukocyte count)

End point description:

Variation in the leukocyte count after the start of treatment with respect to the baseline value, by treatment group

End point type	Secondary

End point timeframe:

Day 28

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: x109/L				
arithmetic mean (standard deviation)	-2.11 (± 5.24)	-2.48 (± 2.49)		

Statistical analyses

Statistical analysis title	Immune response (leukocyte)
Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5908
Method	ANOVA

Secondary: Immune response (neutrophil count)

End point title	Immune response (neutrophil count)

End point description:

End point type	Secondary

End point timeframe:

Day 28

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: x109/L				
arithmetic mean (standard deviation)	-3.18 (± 4.69)	-3.99 (± 2.86)		

Statistical analyses

Statistical analysis title	Immune response (neutrophil count)

Statistical analysis description:

Variation in the neutrophil count on day 28 post-initiation of treatment with respect to the baseline value, by treatment group

Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6127
Method	ANOVA

Secondary: Immune response (percentage of neutrophils)

End point title	Immune response (percentage of neutrophils)

End point description:

End point type	Secondary

End point timeframe:

Day 28

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	9		
Units: %				
arithmetic mean (standard deviation)	-20.75 (± 10.55)	-22.41 (± 12.98)		

Statistical analyses

Statistical analysis title	Immune response (percentage of neutrophils)
Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4035
Method	ANOVA

Secondary: Marker of disease progression Ferritin

End point title	Marker of disease progression Ferritin

End point description:

End point type	Secondary

End point timeframe:

Day 28

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	5		
Units: ng/mL				
arithmetic mean (standard deviation)	-1531.34 (± 2181.85)	-1461.06 (± 750.97)		

Statistical analyses

Statistical analysis title	• Markers of disease progression Ferritin

Statistical analysis description:

Variation in the value of Ferritin on day 28 after the start of treatment with respect to the baseline value, by treatment group

Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0
Method	ANOVA

Secondary: Marker of disease progression LDH

End point title	Marker of disease progression LDH

End point description:

End point type	Secondary

End point timeframe:

Day 28

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	6		
Units: U/L				
arithmetic mean (standard deviation)	-198.95 (± 170.00)	-242.60 (± 98.02)		

Statistical analyses

Statistical analysis title	Marker of disease progression LDH

Statistical analysis description:

Variation in the LDH value on day 28 after the start of treatment with respect to the baseline value, by treatment group

Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4875
Method	ANOVA

Secondary: Marker of disease progression RT-PCR

End point title	Marker of disease progression RT-PCR

End point description:

End point type	Secondary

End point timeframe:

Day 28

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	9		
Units: mg/dL				
arithmetic mean (standard deviation)	-19.58 (± 27.52)	-35.15 (± 36.94)		

Statistical analyses

Statistical analysis title	Marker of disease progression RT-PCR

Statistical analysis description:

Variation in the RT-PCR value on day 28 after the start of treatment with respect to the baseline value, by treatment group

Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.614
Method	ANOVA

Secondary: Marker of disease progression D-dimer

End point title	Marker of disease progression D-dimer

End point description:

End point type	Secondary

End point timeframe:

Day 28

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	7		
Units: ug/L				
arithmetic mean (standard deviation)	517.10 (± 1697.57)	306.29 (± 1248.83)		

Statistical analyses

Statistical analysis title	Marker of disease progression D-dimer

Statistical analysis description:

Variation in the D-dimer value on day 28 after the start of treatment with respect to the baseline value, by treatment group

Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8554
Method	ANOVA

Secondary: Marker of disease progression procalcitonin

End point title	Marker of disease progression procalcitonin

End point description:

End point type	Secondary

End point timeframe:

Day 28

End point values	WJ-MSC	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: ng/mL				
arithmetic mean (standard deviation)	-1.99 (± 5.19)	-0.37 (± 0.92)		

Statistical analyses

Statistical analysis title	Marker of disease progression Procalcitonin

Statistical analysis description:

Variation in the value of procalcitonin on day 28 after the start of treatment with respect to the baseline value, by treatment group

Comparison groups	WJ-MSC v Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.494
Method	ANOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the signature of the informed consent to the last visit	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	WJ-MSC
Reporting group description: -	

Serious adverse events	Placebo	WJ-MSC	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	4 / 14 (28.57%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	3 / 14 (21.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute renal failure			

subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo	WJ-MSC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 11 (45.45%)	8 / 14 (57.14%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Hypertension			

subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	2	
Hypoxia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Pneumothorax			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Pneumomediastinum			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	1 / 11 (9.09%)	2 / 14 (14.29%)	
occurrences (all)	1	2	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 11 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	2	
Delirium			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Investigations			
Fibrin D dimer increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	

Liver function test increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	4 / 14 (28.57%)	
occurrences (all)	0	4	
Systolic dysfunction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Intensive care unit acquired weakness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	2	
Anaemia macrocytic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Constipation			

subjects affected / exposed	1 / 11 (9.09%)	2 / 14 (14.29%)	
occurrences (all)	1	2	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Skin toxicity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Decubitus ulcer			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Renal and urinary disorders			
acute renal failure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Infections and infestations			
Aspergillus infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Pseudomonas bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Urinary tract infection			

subjects affected / exposed	1 / 11 (9.09%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Enterococcal infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Bacteraemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Medical device site infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Tracheobronchitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Tracheobronchitis bacterial			
subjects affected / exposed	1 / 11 (9.09%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Skin infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	

Hypernatraemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	2	
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2020	New centers and prolongation of recruitment period

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 June 2021	Due to difficulties to recruit patients, it was decided to close the study	-

Notes:

Limitations and caveats

None reported