Clinical trial results:
Reparixin 1200 mg three times a day as add-on therapy to standard of care to limit disease progression in hospitalised adult patients with COVID-19 and other community-acquired pneumonia. A multinational, multicentre, randomised, double blinded, placebo-controlled, parallel-group phase III trial.

Summary

EudraCT number	2021-006951-32
Trial protocol	AT IT DE
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	05 December 2025
First version publication date	05 December 2025

Trial information

Trial identification

Sponsor protocol code	REP0321

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05254990
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dompé farmaceutici S.p.A.
Sponsor organisation address	Via Santa Lucia, 6, Milan, Italy, 20122
Public contact	Clinical Trial Manager, Dompé farmaceutici S.p.A. , +39 02 583831, clinicaltrials@dompe.com
Scientific contact	Clinical Trial Manager, Dompé farmaceutici S.p.A. , +39 02 583831, clinicaltrials@dompe.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001693-PIP03-21
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	Interim
Date of interim/final analysis	27 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 July 2024
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective:
To compare the efficacy of reparixin vs. placebo in the proportion of patients dead or requiring IMV (or ECMO) by Day 28.

Key secondary objectives:
Compare the efficacy of reparixin vs placebo in:
- all-cause mortality at day 180.
- proportion of patients alive and discharged at day 28
- ventilatory-free days at day 28.
- proportion of patients with IMV (or ECMO) by day 28.
- length of primary hospital stay.

Other efficacy objectives
Compare the efficacy of reparixin vs placebo on several disease severity/progression measures including recovery, ventilatory free days and mortality.

Safety objectives:
Evaluate safety and tolerability of oral reparixin vs placebo in the specific clinical setting.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonisation (ICH) guideline E6: Good Clinical Practice (GCP) (including the respect of patient confidentiality according to E6 [R2] Principle 2.11), FDA 21 CFR 312.120, and other applicable local regulations. Documents were retained per ICH GCP, including the archiving of essential documents.

Background therapy:

All the patients received the Standard of Care (SoC) based on their clinical need, including COVID-19 and CAP medications, as per local standard therapy at the trial site and in line with international guidelines.

Evidence for comparator: -

Actual start date of recruitment	27 April 2022
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	Austria: 35
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 90
Country: Number of subjects enrolled	Argentina: 57
Country: Number of subjects enrolled	United States: 159
Country: Number of subjects enrolled	Australia: 5

Country: Number of subjects enrolled	Türkiye: 40
Worldwide total number of subjects	394
EEA total number of subjects	133

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)	163
From 65 to 84 years	207
85 years and over	24

Subject disposition

Recruitment

Recruitment details:

Of the 414 patients enrolled, 409 (98.8%) were randomised 1:1 to receive investigational products (oral reparixin [N = 205] or matched placebo [N = 204], three times a day (TID), for up to 21 days. Randomisation was stratified according to disease severity and site. 394 (reparixin [N = 201] or placebo [N = 193]) received at least one dose of IMP.

Pre-assignment

Screening details:

A total of 444 participants were screened and 414 were enrolled.

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, Carer

Blinding implementation details:

The appearance, including packaging and labelling, of the investigational product tablets (reparixin and placebo) were identical in appearance such that the actual treatment could not be identified.

The investigational product identity remained unknown to participants, site staff, CRO and Dompé personnel until after the study was completed and the database was unblinded (5 February 2025).

Arms

Are arms mutually exclusive?	Yes
Arm title	Reparixin + Standard of Care (FAS)

Arm description:

This represents the treatment group. Reparixin was administered orally, as add-on therapy to Standard of care, at the dose of 1200 mg (2 x 600 mg tablets) TID (6 tablets daily) for up to 21 days. The three daily doses were administered maintaining an interval between doses of about 8 hours.

Arm type	Experimental
Investigational medicinal product name	Reparixin
Investigational medicinal product code	
Other name	Repertaxin L-lysine salt
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Reparixin 600 mg tablets, administered orally at the dose of 1200 mg TID (2 tablets TID) as add-on therapy to standard of care up to 21 days. IMP was taken with a glass of water (about 250 mL) and a light meal or snack, as it was preferable that reparixin was taken with food. However, If the patient was unwilling or unable to administer oral tablets, investigator could decide a nasogastric tube as an alternative route.

Arm title	Placebo + Standard of Care (FAS)

Arm description:

Matched placebo was administered orally three times a day (TID) as add-on therapy to standard of care up to 21 days.

Arm type	Experimental

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	matched placebo
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally three times a day (TID) as add-on therapy to standard of care up to 21 days. Placebo was taken with a glass of water (about 250 mL) and a light meal or snack, as it was preferable that placebo was taken with food. However, If the patient was unwilling or unable to administer oral tablets, investigator could decide a nasogastric tube as an alternative route.

Number of subjects in period 1	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)
Started	201	193
Completed	90	96
Not completed	111	97
Consent withdrawn by subject	14	7
Physician decision	1	3
Adverse event, non-fatal	1	1
Other	2	-
Death	16	18
Other reasons	-	3
Lost to follow-up	24	22
Sponsor decision	53	43

Baseline characteristics

Reporting groups

Reporting group title	Reparixin + Standard of Care (FAS)

Reporting group description:

This represents the treatment group. Reparixin was administered orally, as add-on therapy to Standard of care, at the dose of 1200 mg (2 x 600 mg tablets) TID (6 tablets daily) for up to 21 days. The three daily doses were administered maintaining an interval between doses of about 8 hours.

Reporting group title	Placebo + Standard of Care (FAS)

Reporting group description:

Matched placebo was administered orally three times a day (TID) as add-on therapy to standard of care up to 21 days.

Reporting group values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)	Total
Number of subjects	201	193	394
Age categorical Units: Subjects			
Adults (18-64 years)	84	79	163
From 65-84 years	105	102	207
85 years and over	12	12	24
Age continuous Units: years			
arithmetic mean	64.3	65.9	
standard deviation	± 15.7	± 14.9	-
Gender categorical Units: Subjects			
Female	97	76	173
Male	104	117	221

Subject analysis sets

Subject analysis set title	Reparixin + Standard of Care (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who received at least one dose of the investigational product. The SAF set was analyzed according to the actual treatment received. The SAF population was used to present results on safety data.

Subject analysis set title	Placebo + Standard of Care (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who received at least one dose of the investigational product. The SAF set was analyzed according to the actual treatment received. The SAF population was used to present results on safety data.

Subject analysis set title	Reparixin + Standard of Care (PP)
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population comprised all patients in the FAS population who did not have any major protocol deviations.

Subject analysis set title	Placebo + Standard of Care (PP)

Subject analysis set type	Per protocol

Subject analysis set description:

The PP population comprised all patients in the FAS population who did not have any major protocol deviations.

Reporting group values	Reparixin + Standard of Care (SAF)	Placebo + Standard of Care (SAF)	Reparixin + Standard of Care (PP)
Number of subjects	201	193	139
Age categorical Units: Subjects			
Adults (18-64 years)	84	79	
From 65-84 years	105	102	
85 years and over	12	12	
Age continuous Units: years			
arithmetic mean	64.3	65.9	
standard deviation	± 15.7	± 14.9	±
Gender categorical Units: Subjects			
Female	97	76	
Male	104	117	

Reporting group values	Placebo + Standard of Care (PP)		
Number of subjects	133		
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean			
standard deviation	±		
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Reparixin + Standard of Care (FAS)

Reporting group description:

This represents the treatment group. Reparixin was administered orally, as add-on therapy to Standard of care, at the dose of 1200 mg (2 x 600 mg tablets) TID (6 tablets daily) for up to 21 days. The three daily doses were administered maintaining an interval between doses of about 8 hours.

Reporting group title	Placebo + Standard of Care (FAS)

Reporting group description:

Matched placebo was administered orally three times a day (TID) as add-on therapy to standard of care up to 21 days.

Subject analysis set title	Reparixin + Standard of Care (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who received at least one dose of the investigational product. The SAF set was analyzed according to the actual treatment received. The SAF population was used to present results on safety data.

Subject analysis set title	Placebo + Standard of Care (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who received at least one dose of the investigational product. The SAF set was analyzed according to the actual treatment received. The SAF population was used to present results on safety data.

Subject analysis set title	Reparixin + Standard of Care (PP)
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population comprised all patients in the FAS population who did not have any major protocol deviations.

Subject analysis set title	Placebo + Standard of Care (PP)
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population comprised all patients in the FAS population who did not have any major protocol deviations.

Primary: Proportion of Patients Dead or Requiring Invasive Mechanical Ventilation (IMV) or Extracorporeal Membrane Oxygenation (ECMO) by Day 28 [NIAID-OS 7].

End point title	Proportion of Patients Dead or Requiring Invasive Mechanical Ventilation (IMV) or Extracorporeal Membrane Oxygenation (ECMO) by Day 28 [NIAID-OS 7].

End point description:

The primary endpoint was based on NIAID-OS ordinal scale (National Institute of Allergy and Infectious Disease) with score OS 7 indicating patients "hospitalized, on invasive mechanical ventilation or ECMO". The scores on this scale of Disease severity range from OS 1 (best outcome) to OS 8 (worst outcome). NIAID-OS (National Institute of Allergy and Infectious Disease Ordinal Scale) SCORE Descriptor: OS 1 Not hospitalized, no limitations on activities, OS 2 Not hospitalized, limitation on activities and/or requiring home O2, OS 3 Hospitalized no supplemental O2 – no longer requires ongoing medical care, OS 4 Hospitalized, no supplemental O2 – requiring ongoing medical care, OS 5 Hospitalized, requiring supplemental O2, OS 6 Hospitalized, on non-invasive ventilation or high-flow oxygen devices, OS 7 Hospitalized, on invasive mechanical ventilation or ECMO, OS 8 Death.

End point type	Primary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	152		
Units: Count of Participants	7	12		

Statistical analyses

Statistical analysis title	Reparixin + SoC vs Placebo + SoC
Statistical analysis description: Day 28	
Comparison groups	Reparixin + Standard of Care (FAS) v Placebo + Standard of Care (FAS)
Number of subjects included in analysis	312
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.144 [1]
Method	Regression, Logistic

Notes:

[1] - Multivariate analysis using a logistic regression model, adjusted for fixed covariates and with multiple imputation (MI) for missing data.

Secondary: All-cause Mortality by Day 180

End point title	All-cause Mortality by Day 180
End point description: Key secondary endpoint. All-cause mortality is a measurement of the total number of deaths from any cause within a specific population over a defined period. It is a broad metric used in medical research and public health to assess overall population health, identify risk factors for premature death, and evaluate the effectiveness of interventions. Of 394 participants in the FAS, 212 had available data for the endpoint of all-cause mortality at day 180. The number of participants (in the form of unadjusted proportion) who met the endpoint is reported.	
End point type	Secondary
End point timeframe: Day 180	

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	108		
Units: Count of Participants	16	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients Alive and Discharged From the Hospital by Day 28

End point title	Proportion of Patients Alive and Discharged From the Hospital by Day 28

End point description:

Key secondary endpoint. The number of participants alive or discharged, expressed in the form of unadjusted proportion, who met the endpoint at the final analysis at day 28 is provided.

End point type	Secondary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	171		
Units: Count of Participants	170	159		

Statistical analyses

No statistical analyses for this end point

Secondary: Ventilatory-free Days (VFD) by Day 28

End point title	Ventilatory-free Days (VFD) by Day 28

End point description:

Key secondary endpoint. Number of days from Day 0 to Day 28 when the patient was alive and free of invasive ventilation is reported. In case of multiple periods of Invasive Mechanical Ventilation (IMV) during the first 28 days, the total duration of ventilation considered all periods of ventilation during the index admission. Patients who died within 28 days or who still were on invasive ventilation after 28 days were scored 0 VFDs.

End point type	Secondary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	171		
Units: number of days				
arithmetic mean (standard deviation)	27.4 (± 4.2)	26.5 (± 6.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients With IMV (or ECMO) by Day 28

End point title	Proportion of Patients With IMV (or ECMO) by Day 28

End point description:

Key secondary endpoint. The number of participants, expressed in the form of unadjusted proportion, who met the endpoint at the final analysis is reported.

End point type	Secondary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	150		
Units: Count of partecipants	6	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of Primary Hospital Stay (in Days)

End point title	Length of Primary Hospital Stay (in Days)

End point description:

Key secondary endpoint. The duration of primary hospital stay, expressed in days, are reported. This parameter is Included in the set of final evaluation, which comprises: no. of days of hospitalisation, etiologic agents (if identified), ICU admission and total days in ICU, occurrence, and duration of IMV and/or ECMO, if any.

End point type	Secondary

End point timeframe:

Throughout the trial till day 180 or end of trial

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	184		
Units: days of hospital stay				
arithmetic mean (standard deviation)	8.7 (± 6.3)	8.7 (± 7.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Failure by Day 3 and Day 7

End point title	Clinical Failure by Day 3 and Day 7

End point description:

Clinical failure was defined as the occurrence of IMV/ECMO or vasopressor, or death. IMV= invasive mechanical ventilation. ECMO=extracorporeal membrane oxygenation.

End point type	Secondary

End point timeframe:

day 3 and day 7

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195[2]	186[3]		
Units: Count of Participants				
by day 3	2	7		
by day 7	5	9		

Notes:

[2] - Please note that the number of subjects analyzed in set 1 - day 7 was 184

[3] - Please note that the number of subjects analyzed in set 2 - day 7 was 177

Statistical analyses

No statistical analyses for this end point

Secondary: 28-day ICU-free Days

End point title	28-day ICU-free Days

End point description:

ICU-free days = days of hospitalization out of the Intensive Care Unit. The ICU-free days at Day 28 were analyzed according to MI approach and ANOVA model. Death within Day 28 was handled as an unfavorable event and ICU-free days were set at 0. An additional analysis without imputing death as unfavorable event was performed but not reported on this platform.

End point type	Secondary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	171		
Units: Days				
arithmetic mean (standard deviation)	26.3 (± 5.0)	25.7 (± 6.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Days Free of IMV or ECMO (Number of Days With NIAID-OS 1-6) by Day 28

End point title	Days Free of IMV or ECMO (Number of Days With NIAID-OS 1-6) by Day 28

End point description:

These parameters are expressed as number of days with NIAID-OS score not equal to 7 or 8, where NIAID-OS is the National Institute of Allergy and Infectious Disease Ordinal Scale; a scale ranging from 1 to 8, where the lower the score, the better the outcome. The IMV/ECMO-free days at Day 28 were analyzed according to MI approach and ANOVA model. Death due to progression of the respiratory disease within Day 28 was handled as an unfavorable event and IMV/ECMO-free days at Day 28 was set at 0. An additional analysis without imputing death due to progression of the respiratory disease as unfavorable event was performed but not reported here.

End point type	Secondary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	169		
Units: Days				
arithmetic mean (standard deviation)	27.4 (± 4.2)	26.8 (± 5.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Antibiotic Therapy (Days) by Day 28

End point title	Duration of Antibiotic Therapy (Days) by Day 28

End point description:

A descriptive summary of duration of antibiotic therapy (days) at day 28 for the FAS is reported.

End point type	Secondary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	163		
Units: Days				
arithmetic mean (standard deviation)	9.6 (± 8.3)	9.2 (± 8.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Hospital Free Days

End point title	Hospital Free Days

End point description:

Results for hospital-free days at day 28 in the FAS are presented through an unadjusted descriptive summary.

End point type	Secondary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	171		
Units: Days				
arithmetic mean (standard deviation)	18.3 (± 6.7)	18.2 (± 7.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients Recovered

End point title	Proportion of Patients Recovered

End point description:

Results for the proportion of participants recovered at fixed timepoints in the FAS are presented. Recovering was defined as a downward shift from screening of ≤2 points on the NIAID-OS or live discharge from hospital. Unadjusted proportion is reported.

End point type	Secondary

End point timeframe:

Days 3, 7±1, 14±2, 21±2, 28 ±2 or at hospital discharge

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184[4]	178[5]		
Units: Count of partecipants				
Day 3	11	15		
Day 7	40	49		
Day 14	138	135		
Day 21	31	24		
Day 28	151	139		
at hospital discharge	146	145		

Notes:

[4] - Day 7 n=129
Day 14 n=165
Day 21 n=40
Day 28 n= 159
Hospital discharge n=183
[5] - Day 7 n=128
Day 14 n=159
Day 21 n=38
Day 28 n= 154
Hospital discharge n=177

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Patients Worsening

End point title	Proportion of Patients Worsening

End point description:

Results for the proportion of participants worsening at fixed timepoints in the FAS are presented. Worsening was expressed as upward shift from screening of at least >1 point of the NIAID-OS or if patient died before X Visit Day. An unadjusted proportion is reported.

End point type	Secondary

End point timeframe:

days 3, 7±1, 14±2, 21±2, 28 ±2 or at hospital discharge

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184[6]	178[7]		
Units: Count of partecipants				
Day 3	6	10		
Day 7	4	6		
Day 14	2	6		
Day 21	3	7		
Day 28	5	10		
At hospital discharge	5	4		

Notes:

[6] - Day 7 n=129
Day 14 n=165
Day 21 n=40
Day 28 n= 159
Hospital discharge n=183
[7] - Day 7 n=128
Day 14 n=159
Day 21 n=38
Day 28 n= 154
Hospital discharge n=177

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Arterial Partial Pressure of Oxygen (PaO2)

End point title	Change From Baseline in the Arterial Partial Pressure of Oxygen (PaO2)

End point description:

Descriptive statistics for the change from baseline in arterial partial pressure of oxygen (PaO2) at fixed timepoints are reported.

End point type	Secondary

End point timeframe:

days 3, 7±1, 14±2, 21±2, 28 ±2 or to hospital discharge

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180[8]	178[9]		
Units: mmHg				
arithmetic mean (standard deviation)				
To day 3	15.80 (± 27.96)	9.08 (± 22.18)		
To day 7	15.44 (± 29.50)	11.10 (± 27.94)		
To day 14	20.09 (± 30.42)	18.28 (± 20.62)		
To day 21	8.63 (± 37.04)	21.88 (± 26.43)		
To day 28	23.65 (± 30.02)	25.98 (± 21.54)		

To hospital discharge	25.45 (± 17.57)	24.52 (± 6.20)		

Notes:

[8] - Day 7 n=124
Day 14 n=108
Day 21 n=27
Day 28 n= 82
Hospital discharge n=3
[9] - Day 7 n=126
Day 14 n=98
Day 21 n=18
Day 28 n= 75
Hospital discharge n=2

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pulse Oximetry (SpO2)

End point title	Change From Baseline in Pulse Oximetry (SpO2)

End point description:

Descriptive statistics for the change from baseline in pulse oximetry, measured as peripheral arterial oxygen saturation (SpO2), at fixed timepoints are reported

End point type	Secondary

End point timeframe:

Days 3, 7±1, 14±2, 21±2, 28 ±2 or to hospital discharge

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180[10]	177[11]		
Units: percent of oxygen saturation				
arithmetic mean (standard deviation)				
To day 3	3.86 (± 5.90)	2.79 (± 6.48)		
To day 7	4.37 (± 6.53)	2.45 (± 7.79)		
To day 14	5.41 (± 5.87)	4.09 (± 7.05)		
To day 21	4.32 (± 6.62)	3.12 (± 4.55)		
To day 28	5.95 (± 5.42)	5.46 (± 7.19)		
To hospital discharge	4.53 (± 2.20)	9.25 (± 0.35)		

Notes:

[10] - Day 7 n=123
Day 14 n=107
Day 21 n=27
Day 28 n= 82
Hospital discharge n=3
[11] - Day 7 n=124
Day 14 n=98
Day 21 n=18
Day 28 n= 75
Hospital discharge n=2

Statistical analyses

No statistical analyses for this end point

Secondary: All-cause Mortality

End point title	All-cause Mortality

End point description:

Results for all-cause mortality rates in the FAS are reported, at day 28, day 60 (Table 14.2.4.13.2), and day 90 (Table 14.2.4.13.3). Analysis was based on logistic regression model with Multiple Imputation using retrieve dropouts with proportion of patients died up to Day 28 as dependent variable, treatment, disease severity at baseline (NIAID-OS <=5 vs. NIAID-OS 6), age class (<65, >= 65 years), sex and presence of concomitant disease at baseline as qualitative independent variables.

End point type	Secondary

End point timeframe:

Days 28, 60 and 90

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201[12]	193		
Units: % participants				
arithmetic mean (full range (min-max))				
Day 28	2.608 (0.00 to 5.219)	5.701 (1.612 to 9.790)		
Day 60	6.990 (2.326 to 11.653)	11.310 (4.956 to 17.664)		
Day 90	7.898 (2.890 to 12.906)	11.910 (5.448 to 18.371)		

Notes:

[12] - Day 28: the negative value for the lower limit of the 95% CI is not displayed, and was entered as 0.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of IMV and/or ECMO by Days 90 and 180

End point title	Duration of IMV and/or ECMO by Days 90 and 180

End point description:

The summary of IMV/ECMO duration by day 90 and day 180 for the FAS is presented.
The duration of IMV/ECMO use by day 90 was calculated as the total number of days between day 1 and the last available assessment day (≥ day 83) during which the participant was either receiving IMV/ECMO or had a NIAID-OS score of 7. Participants with less than 83 days of follow-up were considered non-evaluable for this endpoint. Similarly, the duration of IMV/ECMO by day 180 was calculated using the same methodology.

End point type	Secondary

End point timeframe:

Days 90 and 180

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152[13]	146[14]		
Units: Count of Participants				
Day 90	30	29		
Day 180	34	37		

Notes:

[13] - The number of Subjects analysed on Day 180 was 103

[14] - The number of Subjects analysed on Day 180 was 106

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Discharge or to a NEWS (National Early Warning Score) of ≤ 2 (for 24 Hours), Whichever Occurs First

End point title	Time to Discharge or to a NEWS (National Early Warning Score) of ≤ 2 (for 24 Hours), Whichever Occurs First

End point description:

The median time to discharge or to a NEWS (National Early Warning Score) of ≤ 2 (for 24 hours), whichever occurs first, was expressed using a "time to event" approach, and measured in days. NIAID-OS, National Early Warning Score (NEWS), was evaluated daily until day 28 (or hospital discharge). In a scored system standardising the assessment of acute-illness severity in the NHS, NEWS includes Blood Pressure (BP), Heart Rate (HR), Respiratory Rate (RR), body temperature, level of consciousness (A, V, P, U), peripheral arterial oxygen saturation (SpO2) and supplemental oxygen.

Time to discharge or to a NEWS of <= 2 (for 24 hours) = Min(Date of discharge, Date of NEWS of <= 2 (for 24 hours)) – Day 1 date + 1.
Date of NEWS of <= 2 (for 24 hours): Given two consecutive days with NEWS of <= 2, the date of the first assessment has been considered.

End point type	Secondary

End point timeframe:

Day 28

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	193		
Units: days				
number (confidence interval 95%)				
Day 28	5 (4.0 to 6.0)	5 (5.0 to 6.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Quality of Life Using EuroQol-5-dimensions-5 Levels (EQ-5D-5L) Questionnaire From Hospital Discharge to Day 90 and Day 180

End point title	Change in Quality of Life Using EuroQol-5-dimensions-5 Levels (EQ-5D-5L) Questionnaire From Hospital Discharge to Day 90 and Day 180

End point description:

The EQ-5D-5L asks patients to indicate whether they have no, slight, moderate, severe, extreme problems on each of 5 dimensions of health: mobility; self-care; usual activities; pain/discomfort; anxiety/depression.The count of patients of each level (1 - no problems, 2 - slight problems, 3 - moderate problems, 4 - severe problems, 5 - extreme problems) for each of the 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) were reported.
The higher the score for each dimension (range 1-5), the worse the outcome. EQ-5D-5L total score is a summary number that describes the patient's health state in its entirety. It ranges from 0 to 100 where the endpoints are labelled 'The best health you can imagine' (VAS = 100) and 'The worst health you can imagine' (VAS = 0).

End point type	Secondary

End point timeframe:

90±7 and 180±14 days

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120[15]	108[16]		
Units: Count of Participants				
Mobility - Day 90 - no problem	61	54		
Mobility - Day 90 - slight problems	41	29		
Mobility - Day 90 - moderate problems	10	16		
Mobility - Day 90 - severe problems	5	5		
Mobility - Day 90 - extreme problems	3	4		
Mobility - Day 180 - no problem	31	45		
Mobility - Day 180 - slight problems	26	20		
Mobility - Day 180 - moderate problems	9	10		
Mobility - Day 180 - severe problems	2	3		
Mobility - Day 180 - extreme problems	3	3		
Self-care - Day 90 - no problem	83	73		
Self-care - Day 90 - slight problems	21	20		
Self-care - Day 90 - moderate problems	9	6		
Self-care - Day 90 - severe problems	4	5		
Self-care - Day 90 - extreme problems	3	4		
Self-care - Day 180 - no problem	46	57		
Self-care - Day 180 - slight problems	15	14		
Self-care - Day 180 - moderate problems	7	4		
Self-care - Day 180 - severe problems	2	4		
Self-care - Day 180 - extreme problems	1	2		
Usual activities - Day 90 - no problem	52	50		
Usual activities - Day 90 - slight problems	36	33		
Usual activities - Day 90 - moderate problems	20	14		
Usual activities - Day 90 - severe problems	7	5		
Usual activities - Day 90 - extreme problems	5	5		
Usual activities - Day 180 - no problem	31	38		

Usual activities - Day 180 - slight problems	17	24		
Usual activities - Day 180 - moderate problems	15	11		
Usual activities - Day 180 - severe problems	5	4		
Usual activities - Day 180 - extreme problems	3	3		
Pain/discomfort - Day 90 - no problem	66	58		
Pain/discomfort - Day 90 - slight problems	33	38		
Pain/discomfort - Day 90 - moderate problems	16	11		
Pain/discomfort - Day 90 - severe problems	3	1		
Pain/discomfort - Day 90 - extreme problems	1	0		
Pain/discomfort - Day 180 - no problem	36	45		
Pain/discomfort - Day 180 - slight problems	21	25		
Pain/discomfort - Day 180 - moderate problems	9	11		
Pain/discomfort - Day 180 - severe problems	4	0		
Pain/discomfort - Day 180 - extreme problems	0	0		
Anxiety/Depression - Day 90 - no problem	62	69		
Anxiety/Depression - Day 90 - slight problems	33	32		
Anxiety/Depression - Day 90 - moderate problems	21	6		
Anxiety/Depression - Day 90 - severe problems	2	1		
Anxiety/Depression - Day 90 - extreme problems	2	0		
Anxiety/Depression - Day 180 - no problem	38	51		
Anxiety/Depression - Day 180 - slight problems	20	24		
Anxiety/Depression - Day 180 - moderate problems	11	4		
Anxiety/Depression - Day 180 - severe problems	1	1		
Anxiety/Depression - Day 180 - extreme problems	1	1		

Notes:

[15] - Mobility-Self-care-Usual activities-Anxiety/Dep. Day 180 n=71, Pain/disc. Day 90 n=119 Day 180 n=70

[16] - Mobility-Self-care-Pain/disc.-Anxiety/Dep. Day 180 n=81, Usual act. Day 90 n=107, Day 180 n=80

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of IMV and/or ECMO by Days 90 and 180

End point title	Duration of IMV and/or ECMO by Days 90 and 180

End point description:

The summary of IMV/ECMO duration by day 90 and day 180 for the FAS is presented.

The duration of IMV/ECMO use by day 90 was calculated as the total number of days between day 1 and the last available assessment day (≥ day 83) during which the participant was either receiving IMV/ECMO or had a NIAID-OS score of 7. Participants with less than 83 days of follow-up were considered non-evaluable for this endpoint. Similarly, the duration of IMV/ECMO by day 180 was calculated using the same methodology.

End point type	Secondary

End point timeframe:

Days 90 and 180

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	193		
Units: Days				
arithmetic mean (standard deviation)				
Day 90	0.0 (± 0.0)	0.3 (± 2.6)		
Day 180	0.0 (± 0.0)	0.1 (± 0.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants Requiring ICU Admission by Days 90 and 180

End point title	Proportion of Participants Requiring ICU Admission by Days 90 and 180

End point description:

Unadjusted proportion of ICU admission is reported as number and percentage of participants requiring ICU admission by day 90 and day 180.

End point type	Secondary

End point timeframe:

Days 90 and 180

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157[17]	145[18]		
Units: Count of Participants				
Day 90	25	20		
Day 180	26	20		

Notes:

[17] - The number of subjects analysed on Day 180 was 106

[18] - The number of subjects analysed on Day 180 was 100

Statistical analyses

No statistical analyses for this end point

Secondary: ICU Length of Stay by Days 90 and 180

End point title	ICU Length of Stay by Days 90 and 180
End point description:	
Results for the Intensive Care Unit length of stay (days) by day 90 and day 180 in the FAS are reported.	
End point type	Secondary
End point timeframe:	
Days 90 and 180	

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147[19]	140[20]		
Units: Days				
arithmetic mean (standard deviation)				
Day 90	0.9 (± 2.5)	1.0 (± 3.9)		
Day 180	0.7 (± 2.4)	0.8 (± 2.2)		

Notes:

[19] - The number of subjects analysed on Day 180 was 89

[20] - The number of subjects analysed on Day 180 was 91

Statistical analyses

No statistical analyses for this end point

Secondary: Hospital Length of Stay by Days 90 and 180

End point title	Hospital Length of Stay by Days 90 and 180
End point description:	
Results for hospital length of stay (days) by days 90 and 180 in the FAS are reported.	
End point type	Secondary
End point timeframe:	
Days 90 and 180	

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147[21]	140[22]		
Units: Days				
arithmetic mean (standard deviation)				
Day 90	9.8 (± 8.4)	9.9 (± 10.0)		
Day 180	12.0 (± 12.7)	10.5 (± 8.5)		

Notes:

[21] - The number of subjects analysed on Day 180 was 89

[22] - The number of subjects analysed on Day 180 was 91

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of Infections by Days 90 and 180

End point title	Occurrence of Infections by Days 90 and 180

End point description:

Occurrence of infections was expressed as the unadjusted proportion of participants with at least one infection by days 90 and 180 in the FAS.

End point type	Secondary

End point timeframe:

Days 90 and 180

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154[23]	145[24]		
Units: Count of Partecipants				
Day 90	21	19		
Day 180	23	19		

Notes:

[23] - The number of subjects analysed on Day 180 was 101

[24] - The number of subjects analysed on Day 180 was 103

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With at Least One Treatment-emergent Adverse Event (TEAE)

End point title	Number of Patients With at Least One Treatment-emergent Adverse Event (TEAE)

End point description:

A TEAE is defined as any adverse event reported in the study having a possible, probable, or highly probable relationship to investigational product. A serious AE is defined as any untoward medical occurrence that at any dose:
• results in death.
• is life-threatening (i.e. the patient was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe),
• requires inpatient hospitalization or prolongation of existing hospitalization,
• results in persistent or significant disability/incapacity,
• is a congenital anomaly/birth defect
• is a medically significant or important medical condition, i.e. an important medical event that based upon appropriate medical judgment, may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed above.

End point type	Secondary

End point timeframe:

Throughout the study till Day 180 or end of trial

End point values	Reparixin + Standard of Care (SAF)	Placebo + Standard of Care (SAF)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	200	194		
Units: Count of Partecipants				
with at least one TEAE	129	127		
with at least one serious TEAE	46	56		
with at least one non-Serious TEAE	115	106		
with at least one severe TEAE	32	33		
with TEAE leading to discontinuation of IMP	23	24		
with TEAE leading to discontinuation of study	1	1		
with TEAE Leading to Death	16	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes From Baseline in Inspired Oxygen (FiO2) Levels

End point title	Changes From Baseline in Inspired Oxygen (FiO2) Levels

End point description:

FiO2 is a parameter of lung function representing the fraction of oxygen in the inspired air, ranging from 0.21 (room air) to 1.00 (100% oxygen). The endpoint assesses the change from baseline in FiO2 levels at predefined timepoints during the study.

End point type	Secondary

End point timeframe:

days 3, 7±1, 14±2, 21±2, 28 ±2 or to hospital discharge

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167[25]	171[26]		
Units: Fraction (0.21 -1.00)				
arithmetic mean (standard deviation)				
To day 3	-0.010 (± 0.144)	-0.038 (± 0.140)		
To day 7±1	-0.061 (± 0.151)	-0.072 (± 0.169)		
To day 14±2	-0.071 (± 0.135)	-0.071 (± 0.180)		

To day 21±2	-0.061 (± 0.131)	-0.082 (± 0.111)		
To day 28 ±2	-0.078 (± 0.119)	-0.086 (± 0.097)		
Hospital discharge	-0.055 (± 0.078)	0.000 (± 0.000)		

Notes:

[25] - Day 7 n=116
Day 14 n=102
Day 21 n=27
Day 28 n=75
Hospital discharge n=2

[26] - Day 7 n=123
Day 14 n=93
Day 21 n=18
Day 28 n=71
Hospital discharge n=1

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PaO2/FiO2 Ratio

End point title	Change From Baseline in PaO2/FiO2 Ratio

End point description:

The PaO2/FiO2 ratio is a parameter of lung function that reflects the efficiency of oxygen transfer from the lungs to the blood. It is calculated as the ratio between the arterial partial pressure of oxygen (PaO2, measured in mmHg) and the fraction of inspired oxygen (FiO2, expressed as a fraction ranging from 0.21 to 1.00).
This endpoint assesses the change from baseline in the PaO2/FiO2 ratio at predefined timepoints during the study.

End point type	Secondary

End point timeframe:

days 3, 7±1, 14±2, 21±2, 28 ±2 or to hospital discharge

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167[27]	171[28]		
Units: mmHg				
arithmetic mean (standard deviation)				
To day 3	66.51 (± 115.49)	54.52 (± 97.65)		
To day 7±1	105.38 (± 122.94)	109.57 (± 138.44)		
To day 14±1	148.84 (± 128.09)	146.72 (± 129.19)		
To day 21±1	101.87 (± 134.94)	180.14 (± 164.18)		
To day 28±1	177.58 (± 133.95)	192.55 (± 116.18)		
Hospital discharge	172.34 (± 196.54)	137.62 (± 0.00)		

Notes:

[27] - Day 7 n=116
Day 14 n=102
Day 21 n=27
Day 28 n=75
Hospital discharge n=2

[28] - Day 7 n=123
Day 14 n=93
Day 21 n=18
Day 28 n=71
Hospital discharge n=1

Statistical analyses

No statistical analyses for this end point

Secondary: Changes From Baseline in SpO2/FiO2 Ratio

End point title	Changes From Baseline in SpO2/FiO2 Ratio

End point description:

The SpO2/FiO2 ratio is a noninvasive indicator of lung function and oxygenation efficiency, calculated as the ratio between peripheral oxygen saturation (SpO2, expressed as a percentage) and the fraction of inspired oxygen (FiO2, expressed as a fraction ranging from 0.21 to 1.00). This endpoint assesses the change from baseline in the SpO2/FiO2 ratio at predefined timepoints during the study.

End point type	Secondary

End point timeframe:

days 3, 7±1, 14±2, 21±2, 28 ±2

End point values	Reparixin + Standard of Care (FAS)	Placebo + Standard of Care (FAS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165[29]	169[30]		
Units: ratio (SpO2 [%] / FiO2 [fraction])				
arithmetic mean (standard deviation)				
To day 3	19.63 (± 103.39)	38.01 (± 104.26)		
To day 7±1	67.42 (± 108.71)	81.50 (± 131.69)		
To day14±1	98.30 (± 97.90)	96.20 (± 122.21)		
To day 21±1	74.69 (± 107.88)	101.45 (± 94.49)		
To day 28±1	109.34 (± 93.37)	118.75 (± 82.93)		

Notes:

[29] - Day 7 n=114
Day 14 n=100
Day 21 n=26
Day 28 n=74

[30] - Day 7 n=120
Day 14 n=92
Day 21 n=17
Day 28 n=70

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study, during the treatment period (up to 21 days) and during the follow-up period (till day 180 or EoT) considered together as an "overall period".

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Reparixin + Standard of Care (SAF)
Reporting group description: -	
Reporting group title	Placebo + Standard of Care (SAF)

Reporting group description: -

Serious adverse events	Reparixin + Standard of Care (SAF)	Placebo + Standard of Care (SAF)	
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 200 (23.00%)	56 / 194 (28.87%)	
number of deaths (all causes)	16	18	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign lung neoplasm			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematological malignancy			

subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung neoplasm malignant			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Therapy cessation			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (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			
Chest pain			
subjects affected / exposed	2 / 200 (1.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	3 / 200 (1.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Sudden death			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Reproductive system and breast disorders			
Pelvic haematoma			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (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	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			

subjects affected / exposed	6 / 200 (3.00%)	4 / 194 (2.06%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 3	0 / 3	
Aspiration			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthma			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	8 / 200 (4.00%)	5 / 194 (2.58%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 200 (0.00%)	4 / 194 (2.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercapnia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (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	1 / 200 (0.50%)	2 / 194 (1.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung infiltration			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	10 / 200 (5.00%)	11 / 194 (5.67%)	
occurrences causally related to treatment / all	0 / 11	0 / 11	
deaths causally related to treatment / all	0 / 2	0 / 1	
Pneumonia aspiration			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary cavitation			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	6 / 200 (3.00%)	9 / 194 (4.64%)	
occurrences causally related to treatment / all	0 / 6	0 / 10	
deaths causally related to treatment / all	0 / 4	0 / 6	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mania			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Alcohol poisoning			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ankle fracture			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative respiratory failure			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			

subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiorenal syndrome			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic left ventricular failure			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cor pulmonale			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular dysfunction			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular hypokinesia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status migrainosus			

subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 200 (0.00%)	3 / 194 (1.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
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			
Diabetic foot			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
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 kidney injury			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Haematoma muscle			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteomyelitis			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
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 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (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			

Diabetic ketoacidosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Reparixin + Standard of Care (SAF)	Placebo + Standard of Care (SAF)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	115 / 200 (57.50%)	56 / 194 (28.87%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Benign lung neoplasm			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Breast cancer			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Glioblastoma			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Haematological malignancy			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Lipoma			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Lung neoplasm malignant			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Melanocytic naevus			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Squamous cell carcinoma of lung			

subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	2	
Arteriosclerosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Carotid artery occlusion			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Carotid artery stenosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Cerebrovascular accident			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Embolic stroke			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Haemorrhage			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Haemorrhoids thrombosed			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	10 / 200 (5.00%)	7 / 194 (3.61%)	
occurrences (all)	10	7	
Hypertensive urgency			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	11 / 200 (5.50%)	4 / 194 (2.06%)	
occurrences (all)	11	4	

Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Peripheral venous disease			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Phlebitis			
subjects affected / exposed	2 / 200 (1.00%)	1 / 194 (0.52%)	
occurrences (all)	2	1	
Splenic infarction			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	2 / 200 (1.00%)	2 / 194 (1.03%)	
occurrences (all)	2	2	
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Mitral valve repair			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Renal stone removal			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Therapy cessation			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 200 (1.00%)	2 / 194 (1.03%)	
occurrences (all)	2	3	
Chest discomfort			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	
Chest pain			

subjects affected / exposed	5 / 200 (2.50%)	5 / 194 (2.58%)		
occurrences (all)	5	5		
Death				
subjects affected / exposed	3 / 200 (1.50%)	0 / 194 (0.00%)		
occurrences (all)	3	0		
Drug withdrawal syndrome				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Fatigue				
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)		
occurrences (all)	1	1		
Inflammation				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Influenza like illness				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Infusion site swelling				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Malaise				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Oedema				
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)		
occurrences (all)	1	1		
Oedema peripheral				
subjects affected / exposed	2 / 200 (1.00%)	1 / 194 (0.52%)		
occurrences (all)	2	1		
Pain				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Pyrexia				

subjects affected / exposed	2 / 200 (1.00%)	3 / 194 (1.55%)	
occurrences (all)	2	3	
Sudden death			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Balanoposthitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Pelvic haematoma			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Acute respiratory failure			
subjects affected / exposed	6 / 200 (3.00%)	5 / 194 (2.58%)	
occurrences (all)	8	6	
Aspiration			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Asthma			
subjects affected / exposed	2 / 200 (1.00%)	2 / 194 (1.03%)	
occurrences (all)	2	3	
Atelectasis			

subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Bronchiectasis				
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)		
occurrences (all)	4	1		
Bronchospasm				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
COVID-19				
subjects affected / exposed	2 / 200 (1.00%)	2 / 194 (1.03%)		
occurrences (all)	2	3		
Chronic obstructive pulmonary disease				
subjects affected / exposed	10 / 200 (5.00%)	6 / 194 (3.09%)		
occurrences (all)	10	6		
Cough				
subjects affected / exposed	5 / 200 (2.50%)	2 / 194 (1.03%)		
occurrences (all)	5	2		
Dysphonia				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Dyspnoea				
subjects affected / exposed	3 / 200 (1.50%)	7 / 194 (3.61%)		
occurrences (all)	3	7		
Dyspnoea exertional				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Emphysema				
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)		
occurrences (all)	1	1		
Epistaxis				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Haemoptysis				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		

Haemothorax			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Hypercapnia			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Hypocapnia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Hypoxia			
subjects affected / exposed	3 / 200 (1.50%)	5 / 194 (2.58%)	
occurrences (all)	3	5	
Infectious pleural effusion			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	3 / 200 (1.50%)	0 / 194 (0.00%)	
occurrences (all)	3	0	
Lung abscess			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Lung consolidation			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Lung infiltration			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	2 / 200 (1.00%)	4 / 194 (2.06%)	
occurrences (all)	2	4	

Pleurisy			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	11 / 200 (5.50%)	14 / 194 (7.22%)	
occurrences (all)	13	14	
Pneumonia aspiration			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Pneumonia streptococcal			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Pneumonia viral			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Pneumothorax			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Pulmonary cavitation			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Pulmonary embolism			
subjects affected / exposed	3 / 200 (1.50%)	3 / 194 (1.55%)	
occurrences (all)	3	3	
Pulmonary hypertension			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Pulmonary mass			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Pulmonary oedema			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	

Pulmonary pneumatocele			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Respiration abnormal			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Respiratory failure			
subjects affected / exposed	6 / 200 (3.00%)	9 / 194 (4.64%)	
occurrences (all)	6	11	
Respiratory tract infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Rhinitis atrophic			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Tachypnoea			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	2 / 200 (1.00%)	2 / 194 (1.03%)	
occurrences (all)	2	2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 200 (2.00%)	0 / 194 (0.00%)	
occurrences (all)	4	0	
Confusional state			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Generalised anxiety disorder			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Insomnia			

subjects affected / exposed	6 / 200 (3.00%)	2 / 194 (1.03%)	
occurrences (all)	6	3	
Mania			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Mental status changes			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Post-traumatic stress disorder			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)	
occurrences (all)	2	2	
Tobacco withdrawal symptoms			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 200 (0.00%)	3 / 194 (1.55%)	
occurrences (all)	0	3	
Amylase increased			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Anion gap increased			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	
Blood albumin decreased			

subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Blood creatinine increase				
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)		
occurrences (all)	1	2		
Blood ketone body				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 200 (0.00%)	3 / 194 (1.55%)		
occurrences (all)	0	3		
Blood pressure systolic abnormal				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Blood pressure systolic increased				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Electrocardiogram T wave inversion				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Electrocardiogram abnormal				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Eosinophil count increased				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Fibrin D dimer increased				
subjects affected / exposed	4 / 200 (2.00%)	3 / 194 (1.55%)		
occurrences (all)	4	3		
Glomerular filtration rate decreased				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Haematocrit decreased				
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)		
occurrences (all)	1	1		

Haematocrit increased				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Haemoglobin decreased				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Hepatic enzyme increased				
subjects affected / exposed	6 / 200 (3.00%)	4 / 194 (2.06%)		
occurrences (all)	6	4		
Liver function test increased				
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)		
occurrences (all)	1	2		
Lymphocyte count decreased				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
N-terminal prohormone brain natriuretic peptide increased				
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)		
occurrences (all)	0	2		
Neutrophil count increased				
subjects affected / exposed	0 / 200 (0.00%)	3 / 194 (1.55%)		
occurrences (all)	0	3		
PaO2/FiO2 ratio				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Platelet count increased				
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)		
occurrences (all)	1	2		
Procalcitonin increased				
subjects affected / exposed	2 / 200 (1.00%)	2 / 194 (1.03%)		
occurrences (all)	2	2		
Red blood cell count decreased				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Red blood cell count increased				

subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Serum ferritin increased			
subjects affected / exposed	2 / 200 (1.00%)	3 / 194 (1.55%)	
occurrences (all)	2	3	
Transaminases increased			
subjects affected / exposed	2 / 200 (1.00%)	6 / 194 (3.09%)	
occurrences (all)	2	6	
Troponin T			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Venous pressure jugular			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
White blood cell count decreased			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	2 / 200 (1.00%)	1 / 194 (0.52%)	
occurrences (all)	2	1	
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Ankle fracture			
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)	
occurrences (all)	1	2	
Craniocerebral injury			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Face injury			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Fall			

subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	2	1	
Fibula fracture			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Humerus fracture			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Penis injury			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Postoperative respiratory failure			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Product administration error			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Rib fracture			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Traumatic haematoma			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Wrist fracture			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	

Aortic valve stenosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Atrial flutter			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Bradycardia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Bundle branch block left			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Cardiac arrest			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Cardiac failure			
subjects affected / exposed	2 / 200 (1.00%)	4 / 194 (2.06%)	
occurrences (all)	2	4	
Cardiac failure acute			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Cardiac failure congestive			
subjects affected / exposed	3 / 200 (1.50%)	0 / 194 (0.00%)	
occurrences (all)	3	0	
Cardiogenic shock			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Cardiorenal syndrome			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Chronic left ventricular failure			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	

Cor pulmonale				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Coronary artery disease				
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)		
occurrences (all)	1	1		
Extrasystoles				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Left ventricular hypertrophy				
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)		
occurrences (all)	1	1		
Long QT syndrome				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Myocardial ischaemia				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Myocarditis				
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)		
occurrences (all)	0	2		
Palpitations				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Pericardial effusion				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Sinus node dysfunction				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		
Sinus tachycardia				
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)		
occurrences (all)	1	0		
Supraventricular extrasystoles				
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)		
occurrences (all)	0	1		

Supraventricular tachycardia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	4 / 200 (2.00%)	1 / 194 (0.52%)	
occurrences (all)	4	1	
Ventricular dysfunction			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Ventricular tachycardia			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Disturbance in attention			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	2	
Encephalopathy			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	7 / 200 (3.50%)	5 / 194 (2.58%)	
occurrences (all)	8	5	
Hemiparesis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Migraine			

subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Myoclonus			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Neuralgia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Status migrainosus			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Toxic encephalopathy			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Tremor			
subjects affected / exposed	2 / 200 (1.00%)	2 / 194 (1.03%)	
occurrences (all)	2	2	
Delirium			
subjects affected / exposed	3 / 200 (1.50%)	1 / 194 (0.52%)	
occurrences (all)	3	2	
Depression			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 200 (1.00%)	5 / 194 (2.58%)	
occurrences (all)	3	5	
Atrial fibrillation			
subjects affected / exposed	6 / 200 (3.00%)	3 / 194 (1.55%)	
occurrences (all)	6	3	
Hypochromic anaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	

Leukocytosis			
subjects affected / exposed	3 / 200 (1.50%)	4 / 194 (2.06%)	
occurrences (all)	4	4	
Leukopenia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Lymphopenia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Pancytopenia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Thrombocytosis			
subjects affected / exposed	4 / 200 (2.00%)	1 / 194 (0.52%)	
occurrences (all)	4	1	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	2	
Ear discomfort			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Middle ear effusion			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Vertigo positional			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Eye disorders			

Blindness			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Cataract			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Visual impairment			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	
Abdominal pain lower			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	3 / 200 (1.50%)	2 / 194 (1.03%)	
occurrences (all)	3	2	
Aphthous ulcer			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Chapped lips			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 200 (1.00%)	8 / 194 (4.12%)	
occurrences (all)	2	8	
Diarrhoea			

subjects affected / exposed	15 / 200 (7.50%)	11 / 194 (5.67%)	
occurrences (all)	16	12	
Diverticulum			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	
Dry mouth			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Duodenitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)	
occurrences (all)	1	2	
Gastritis erosive			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Glossodynia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Haematemesis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Haemorrhoidal haemorrhage			

subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Ileus			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Large intestine polyp			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	11 / 200 (5.50%)	8 / 194 (4.12%)	
occurrences (all)	11	8	
Oesophageal motility disorder			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Oral pain			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Ulcerative duodenitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	6 / 200 (3.00%)	7 / 194 (3.61%)	
occurrences (all)	6	8	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	

Hepatic lesion			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Hepatic pain			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Hepatic steatosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Hypertransaminasaemia			
subjects affected / exposed	1 / 200 (0.50%)	3 / 194 (1.55%)	
occurrences (all)	1	3	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Diabetic foot			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Drug eruption			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Dyshidrotic eczema			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Ecchymosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Erythema			

subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	2	
Ingrowing nail			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Nail hypertrophy			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	4 / 200 (2.00%)	2 / 194 (1.03%)	
occurrences (all)	4	2	
Rash papular			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Skin lesion			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	9 / 200 (4.50%)	1 / 194 (0.52%)	
occurrences (all)	10	1	
Bladder pain			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Hydronephrosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	

Renal colic			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	3 / 200 (1.50%)	0 / 194 (0.00%)	
occurrences (all)	3	0	
Renal impairment			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Urinary retention			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Adrenal haemorrhage			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Hyperthyroidism			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 200 (0.50%)	3 / 194 (1.55%)	
occurrences (all)	1	3	
Back pain			
subjects affected / exposed	3 / 200 (1.50%)	4 / 194 (2.06%)	
occurrences (all)	4	4	
Haematoma muscle			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Joint stiffness			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Joint swelling			

subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Osteoarthritis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Osteochondrosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	
Spinal osteoarthritis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	2	
Spinal pain			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Vertebral foraminal stenosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	2	
Infections and infestations			
Aspergilloma			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	

Aspergillus infection			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Bacteraemia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Candida infection			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Cellulitis			
subjects affected / exposed	4 / 200 (2.00%)	0 / 194 (0.00%)	
occurrences (all)	4	0	
Clostridium difficile infection			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Dengue fever			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Herpes simplex			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Infectious pleural effusion			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Lice infestation			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	

Meningitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Metapneumovirus infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Oesophageal candidiasis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	3 / 200 (1.50%)	1 / 194 (0.52%)	
occurrences (all)	3	1	
Oral herpes			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Oropharyngitis fungal			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Osteomyelitis			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Pneumococcal bacteraemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Pyelonephritis			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	
Pyuria			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Renal abscess			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	

Respiratory tract infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Sepsis			
subjects affected / exposed	3 / 200 (1.50%)	1 / 194 (0.52%)	
occurrences (all)	3	1	
Septic shock			
subjects affected / exposed	0 / 200 (0.00%)	2 / 194 (1.03%)	
occurrences (all)	0	2	
Tinea pedis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	4 / 200 (2.00%)	6 / 194 (3.09%)	
occurrences (all)	4	6	
Urosepsis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Vulvovaginitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Diabetes mellitus			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Diabetic neuropathy			

subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Electrolyte imbalance			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Folate deficiency			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Hyperferritinaemia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	1 / 200 (0.50%)	7 / 194 (3.61%)	
occurrences (all)	1	8	
Hyperkalaemia			
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)	
occurrences (all)	1	2	
Hyperlipidaemia			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Hypoalbuminaemia			
subjects affected / exposed	1 / 200 (0.50%)	2 / 194 (1.03%)	
occurrences (all)	1	2	
Hypocalcaemia			
subjects affected / exposed	1 / 200 (0.50%)	3 / 194 (1.55%)	
occurrences (all)	1	3	
Hypokalaemia			
subjects affected / exposed	15 / 200 (7.50%)	14 / 194 (7.22%)	
occurrences (all)	15	14	
Hypomagnesaemia			
subjects affected / exposed	2 / 200 (1.00%)	0 / 194 (0.00%)	
occurrences (all)	2	0	
Hyponatraemia			
subjects affected / exposed	2 / 200 (1.00%)	2 / 194 (1.03%)	
occurrences (all)	2	2	
Hypophagia			

subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	2 / 200 (1.00%)	1 / 194 (0.52%)	
occurrences (all)	2	1	
Hypoproteinaemia			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Hypouricaemia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	
Iron deficiency			
subjects affected / exposed	1 / 200 (0.50%)	1 / 194 (0.52%)	
occurrences (all)	1	1	
Magnesium deficiency			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Malnutrition			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Metabolic acidosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Metabolic alkalosis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 194 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 June 2022	Amendment 1 has been issued to extend the study population to all cases of community-acquired infectious pneumonia, to increase the sample size in order to allow detection of smaller differences between groups, to prolong the follow-up period from 60 to 180 days, to modify the selection criteria to include CAP patients, to revise and reorder the study endpoints to better reflect clinically meaningful outcomes for CAP, and to update the statistical methods to align with the new population, outcomes, and sample size, including a redefinition of the interim analysis to adopt a more conservative approach to early termination for efficacy. Additionally, the contact details on data management & statistics and pharmacovigilance have been updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The interim analysis of the first 250 patients met the pre-specified futility criteria for the primary efficacy endpoint. Following the DMC's recommendation, Dompé terminated the study early for futility, with no safety concerns identified.

Notes: