



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
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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)	EMA-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)
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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
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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)
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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)
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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)
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Subject analysis set type	Safety analysis
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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)
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Subject analysis set type	Safety analysis
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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)
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Subject analysis set type	Per protocol
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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)
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Subject analysis set type	Per protocol
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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)
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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)
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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)
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Subject analysis set type	Safety analysis
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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)
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Subject analysis set type	Safety analysis
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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)
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Subject analysis set type	Per protocol
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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)
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Subject analysis set type	Per protocol
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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].
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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
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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
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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
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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
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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
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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
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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
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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 participants	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)
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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
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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
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End point description:

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

End point type	Secondary
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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
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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
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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
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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
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End point timeframe:

Days 3, 7 \pm 1, 14 \pm 2, 21 \pm 2, 28 \pm 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 participants				
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
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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
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End point timeframe:

days 3, 7 \pm 1, 14 \pm 2, 21 \pm 2, 28 \pm 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 participants				
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)
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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
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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)		
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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
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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
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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
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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
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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
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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
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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:	
<p>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.</p> <p>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).</p>	
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
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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 (\geq 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 (\pm 0.0)	0.3 (\pm 2.6)		
Day 180	0.0 (\pm 0.0)	0.1 (\pm 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
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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
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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 Participants				
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)
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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 Participants				
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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

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

Reporting group title	Placebo + Standard of Care (SAF)
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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	
Embololic 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 occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Peripheral venous disease subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Phlebitis subjects affected / exposed occurrences (all)	2 / 200 (1.00%) 2	1 / 194 (0.52%) 1	
Splenic infarction subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Syncope subjects affected / exposed occurrences (all)	2 / 200 (1.00%) 2	2 / 194 (1.03%) 2	
Surgical and medical procedures Knee arthroplasty subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Mitral valve repair subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Renal stone removal subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Therapy cessation subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	2 / 200 (1.00%) 2	2 / 194 (1.03%) 3	
Chest discomfort subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	2 / 194 (1.03%) 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 occurrences (all)	2 / 200 (1.00%) 2	3 / 194 (1.55%) 3	
Sudden death subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Systemic inflammatory response syndrome subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Reproductive system and breast disorders			
Adenomyosis subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Balanoposthitis subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Pelvic haematoma subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Acute respiratory failure subjects affected / exposed occurrences (all)	6 / 200 (3.00%) 8	5 / 194 (2.58%) 6	
Aspiration subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Asthma subjects affected / exposed occurrences (all)	2 / 200 (1.00%) 2	2 / 194 (1.03%) 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 occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Respiration abnormal subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Respiratory failure subjects affected / exposed occurrences (all)	6 / 200 (3.00%) 6	9 / 194 (4.64%) 11	
Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Rhinitis atrophic subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Sinusitis subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Tachypnoea subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	1 / 194 (0.52%) 1	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 200 (1.00%) 2	2 / 194 (1.03%) 2	
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	4 / 200 (2.00%) 4	0 / 194 (0.00%) 0	
Confusional state subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Generalised anxiety disorder subjects affected / exposed occurrences (all)	2 / 200 (1.00%) 2	0 / 194 (0.00%) 0	
Insomnia			

subjects affected / exposed occurrences (all)	6 / 200 (3.00%) 6	2 / 194 (1.03%) 3	
Mania subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Mental status changes subjects affected / exposed occurrences (all)	2 / 200 (1.00%) 2	0 / 194 (0.00%) 0	
Post-traumatic stress disorder subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Restlessness subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Sleep disorder subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 2	2 / 194 (1.03%) 2	
Tobacco withdrawal symptoms subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	3 / 194 (1.55%) 3	
Amylase increased subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Anion gap increased subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	2 / 194 (1.03%) 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	
Cranio-cerebral 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 occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Tachycardia subjects affected / exposed occurrences (all)	4 / 200 (2.00%) 4	1 / 194 (0.52%) 1	
Ventricular dysfunction subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Ventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Ventricular tachycardia subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	2 / 194 (1.03%) 2	
Nervous system disorders			
Cerebrovascular accident subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Disturbance in attention subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 2	
Encephalopathy subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	7 / 200 (3.50%) 8	5 / 194 (2.58%) 5	
Hemiparesis subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 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	
Hypertransaminaemia			
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 occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Renal failure subjects affected / exposed occurrences (all)	3 / 200 (1.50%) 3	0 / 194 (0.00%) 0	
Renal impairment subjects affected / exposed occurrences (all)	2 / 200 (1.00%) 2	0 / 194 (0.00%) 0	
Urinary retention subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Endocrine disorders Adrenal haemorrhage subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Hyperthyroidism subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Hypothyroidism subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	0 / 194 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 200 (0.50%) 1	3 / 194 (1.55%) 3	
Back pain subjects affected / exposed occurrences (all)	3 / 200 (1.50%) 4	4 / 194 (2.06%) 4	
Haematoma muscle subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 1	
Joint stiffness subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	1 / 194 (0.52%) 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: