Clinical trial results:
A pragmatic adaptive randomized controlled Phase II/III multicenter study of IFX-1 in patients with severe COVID-19 pneumonia - "PANAMO"

Summary

EudraCT number	2020-001335-28
Trial protocol	NL DE BE FR
Global end of trial date	01 December 2021

Results information

Result version number	v1 (current)
This version publication date	17 February 2023
First version publication date	17 February 2023

Trial information

Trial identification

Sponsor protocol code	IFX-1-P2.9

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04333420
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	InflaRx GmbH
Sponsor organisation address	Winzerlaer Strasse 2, Jena, Germany, 07745
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Scientific contact	Clinical Research and Development, InflaRX GmbH, +49 (0)3641-508 150, Niels.Riedemann@inflarx.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2021
Global end of trial reached?	Yes
Global end of trial date	01 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Phase II was to explore the effect of vilobelimab on COVID-19 related severe pneumonia (hypothesis generating).

The primary objective of Phase III was to demonstrate the efficacy of vilobelimab to improve survival outcomes of invasively mechanically ventilated COVID-19 pneumonia patients.

Protection of trial subjects:

Phase II: An Independent Safety Monitoring Board (ISMB) was constituted to support safety surveillance in both treatment arms throughout the phase II part of the study. The committee included 2 intensive care specialists not involved as Investigator in this study and an independent statistician. The ISMB monitored the safety of all patients regularly, after 10, 20, and 30 patients had completed their treatment in part II. At each review, the ISMB was able to recommend on continuing or ending the study. All available safety data were provided to the ISMB before each meeting. After completion of Phase II (30 patients), the ISMB assessed the totality of available data of all patients and recommended on proceeding to Phase III.
In Phase III, the ISMB from Phase II continued as an Independent (Clinical Trial) Data Monitoring Committee (IDMC). The IDMC met every 3 months throughout Phase III of the study to further assess safety. In addition, the IDMC performed an unblinded assessment of the data of the interim analysis and made recommendations on whether to continue the study or not according to the predefined early stop criterion. All available data were provided to the IDMC before each meeting. Details were described in a separate IDMC Charter.

Background therapy:

Standard of Care according to locally adopted treatment guidelines.

Evidence for comparator:

Standard of Care

Actual start date of recruitment	31 March 2020
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	Netherlands: 169
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Mexico: 37
Country: Number of subjects enrolled	Peru: 15
Country: Number of subjects enrolled	Brazil: 74
Country: Number of subjects enrolled	Russian Federation: 23

Country: Number of subjects enrolled	South Africa: 10
Worldwide total number of subjects	399
EEA total number of subjects	240

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)	279
From 65 to 84 years	120
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients at the study site matching the inclusion and exclusion criteria have been recruited. Study patients were considered enrolled into the study after signing of the informed consent form (by patient or his/her legal representatives), or after deferred consent procedure, whichever came first.

Pre-assignment

Screening details:

Screening failures are defined as patients who do not meet the criteria for participation in this study and thus, were either not randomized/assigned to IMP or randomized in error and did not receive study drug.
Re-screening was possible in Phase II but not applicable in Phase III.

Period 1

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

Blinding implementation details:

Phase II of the study was open-label and randomized, while Phase III was double-blind, placebo-controlled, and randomized.

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase II: IFX-1 + BSC

Arm description:

Patients were randomized 1:1 to IFX-1 plus Best Supportive Care (BSC) (15 patients). The treatment period was planned to comprise up to 4 weeks with a maximum of 7 intravenous doses of IFX-1 over a period of 29 days or until ICU discharge.

Arm type	Experimental
Investigational medicinal product name	IFX-1
Investigational medicinal product code	IFX-1
Other name	vilobelimab
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients in the Phase II IFX-1 + BSC arm were to be treated with a maximum of 7 intravenous (IV) doses of IFX-1 800 mg over a period of 29 days. The first 5 treatments at Days 1, 2, 4, 8, and 15 were to be administered to all patients randomized into the IFX-1 + BSC arm. Treatment at Day 22 was only to be administered in the event that a patient had not been extubated and discharged from ICU. In case a patient's clinical situation worsened after Day 8, although an initial clinical benefit was observed, one additional administration of 800 mg IFX-1 between Days 11 and 13 could have been given at Investigator's discretion. IFX-1 was administered as a 30-min infusion (-5/+10 min).

Investigational medicinal product name	Best supportive care
Investigational medicinal product code	BSC
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

BSC in the participating centers consisted of intensive care therapy according to current guidelines, evidence, and best practice, including but not limited to lung protective ventilation, thrombosis prophylaxis, renal replacement therapy, when indicated, and access to advanced therapies including extracorporeal membrane oxygenation. Use of antimalarials (e.g., chloroquine) was allowed during the study; however, active concomitant treatment with other immunomodulatory drugs was not allowed.

Arm title	Phase II: Best Supportive Care (BSC)

Arm description:

Patients were randomized 1:1 to the Phase II BSC arm (15 patients). The treatment period was planned to comprise up to 4 weeks over a period of 29 days or until ICU discharge.

Arm type	No IMP
Investigational medicinal product name	Best supportive care
Investigational medicinal product code	BSC
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

BSC in the participating centers consisted of intensive care therapy according to current guidelines, evidence, and best practice, including but not limited to lung protective ventilation, thrombosis prophylaxis, renal replacement therapy, when indicated, and access to advanced therapies including extracorporeal membrane oxygenation. Use of antimalarials (e.g., chloroquine) was allowed during the study; however, active concomitant treatment with other immunomodulatory drugs was not allowed.

Arm title	Phase III: IFX-1 + SOC

Arm description:

In the first stage of Phase III, about 90 patients were to be randomized into the IFX-1 + Standard of Care (SOC) arm using a 1:1 allocation ratio. Based on the results of the Phase III interim analysis, up to an additional 90 patients were to be randomized into the IFX-1+SOC arm in the second stage, using the same allocation ratio.

Arm type	Experimental
Investigational medicinal product name	IFX-1
Investigational medicinal product code	IFX-1
Other name	vilobelimab
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Phase III: Patients were treated with a maximum of six intravenous (iv) doses of IFX-1 800 mg administered as a 30-60-minute iv infusion. The six treatments were at Days 1, 2, 4, 8, 15, and 22 as long as the patient was still hospitalized, even if discharged from ICU.

Investigational medicinal product name	Standard of care
Investigational medicinal product code	SOC
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

All patients received SOC for the treatment of COVID-19, which included venous thromboembolism prophylaxis with anticoagulants at a minimum. Other international or country-specific recommended treatments for COVID-19 per the locally adopted treatment recommendations (including but not limited to corticosteroids, remdesivir, and other locally adopted SOC) were allowed as concomitant medications. SOC treatment was given at the Investigator’s discretion and could start and stop at any time.

Arm title	Phase III: Placebo + SOC

Arm description:

In the first stage of Phase III, about 90 patients were to be randomized into the Placebo+SOC arm using a 1:1 allocation ratio. Based on the results of the Phase III interim analysis, up to an additional 90 patients were to be randomized into the Placebo+SOC arm in the second stage, using the same allocation ratio.

Arm type	Placebo
Investigational medicinal product name	Standard of care
Investigational medicinal product code	SOC
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

All patients received standard of care (SOC) for the treatment of COVID-19, which included venous thromboembolism prophylaxis with anticoagulants at a minimum. Other international or country-specific recommended treatments for COVID-19 per the locally adopted treatment recommendations (including but not limited to corticosteroids, remdesivir, and other locally adopted SOC) were allowed as concomitant medications. SOC treatment was given at the Investigator's discretion and could start and stop at any time.

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

Dosage and administration details:

Patients received a maximum of six intravenous (iv) doses of Placebo administered as a 30-60-minute iv infusion. The six administrations were at Days 1, 2, 4, 8, 15, and 22 as long as the patient was still hospitalized, even if discharged from ICU.

Number of subjects in period 1	Phase II: IFX-1 + BSC	Phase II: Best Supportive Care (BSC)	Phase III: IFX-1 + SOC
Started	15	15	178
Completed	13	11	103
Not completed	2	4	75
Adverse event, serious fatal	2	4	62
Randomized in error	-	-	1
Consent withdrawn by subject	-	-	1
Transfer to another hospital	-	-	2
Withdrawal by legal representative/relative	-	-	5
Other	-	-	-
Lost to follow-up	-	-	4

Number of subjects in period 1	Phase III: Placebo + SOC
Started	191
Completed	93
Not completed	98
Adverse event, serious fatal	87
Randomized in error	-
Consent withdrawn by subject	2
Transfer to another hospital	4
Withdrawal by legal representative/relative	3
Other	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Phase II: IFX-1 + BSC
Reporting group description:	
Patients were randomized 1:1 to IFX-1 plus Best Supportive Care (BSC) (15 patients). The treatment period was planned to comprise up to 4 weeks with a maximum of 7 intravenous doses of IFX-1 over a period of 29 days or until ICU discharge.	
Reporting group title	Phase II: Best Supportive Care (BSC)
Reporting group description:	
Patients were randomized 1:1 to the Phase II BSC arm (15 patients). The treatment period was planned to comprise up to 4 weeks over a period of 29 days or until ICU discharge.	
Reporting group title	Phase III: IFX-1 + SOC
Reporting group description:	
In the first stage of Phase III, about 90 patients were to be randomized into the IFX-1 + Standard of Care (SOC) arm using a 1:1 allocation ratio. Based on the results of the Phase III interim analysis, up to an additional 90 patients were to be randomized into the IFX-1+SOC arm in the second stage, using the same allocation ratio.	
Reporting group title	Phase III: Placebo + SOC
Reporting group description:	
In the first stage of Phase III, about 90 patients were to be randomized into the Placebo+SOC arm using a 1:1 allocation ratio. Based on the results of the Phase III interim analysis, up to an additional 90 patients were to be randomized into the Placebo+SOC arm in the second stage, using the same allocation ratio.	

Reporting group values	Phase II: IFX-1 + BSC	Phase II: Best Supportive Care (BSC)	Phase III: IFX-1 + SOC
Number of subjects	15	15	178
Age categorical Units: Subjects			
Adults (18-64 years)	13	9	124
From 65-84 years	2	6	54
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	57.5	62.8	56.7
standard deviation	± 8.6	± 8.1	± 13.2
Gender categorical Units: Subjects			
Female	4	4	52
Male	11	11	126

Reporting group values	Phase III: Placebo + SOC	Total	
Number of subjects	191	399	
Age categorical Units: Subjects			
Adults (18-64 years)	133	279	
From 65-84 years	58	120	
85 years and over	0	0	

Age continuous Units: years arithmetic mean standard deviation	 55.9 ± 14.5	 -	
Gender categorical Units: Subjects			
Female Male	64 127	124 275	

Subject analysis sets

Subject analysis set title	FAS (Phase II)
Subject analysis set type	Full analysis

Subject analysis set description:

All randomized patients were included in the Full Analysis Set (FAS) according to the intention-to-treat principle, irrespective of their protocol adherence and continued participation in the study. Patients were analyzed according to their randomized treatment arm.

Subject analysis set title	SAF (Phase III)
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety analyses were based on all patients who received at least one infusion of IMP; patients were analyzed according to the treatment they actually received. The actual treatment group of each patient was VILO if they received any VILO infusion at any timepoint, and Placebo if they received only Placebo infusions at all timepoints.

Subject analysis set title	FAS (Phase III)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The primary efficacy analyses was performed based on all randomized patients according to the intention-to-treat principle, except for patients who were randomized in error (reason for early termination documented as “Randomized by mistake” in the eCRF) and did not receive IMP.

Reporting group values	FAS (Phase II)	SAF (Phase III)	FAS (Phase III)
Number of subjects	30	364	368
Age categorical Units: Subjects			
Adults (18-64 years)	22	253	257
From 65-84 years	8	111	111
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	60.2	56.3	56.3
standard deviation	± 8.7	± 14.0	± 13.9
Gender categorical Units: Subjects			
Female	8	116	116
Male	22	248	252

End points

End points reporting groups

Reporting group title	Phase II: IFX-1 + BSC

Reporting group description:

Patients were randomized 1:1 to IFX-1 plus Best Supportive Care (BSC) (15 patients). The treatment period was planned to comprise up to 4 weeks with a maximum of 7 intravenous doses of IFX-1 over a period of 29 days or until ICU discharge.

Reporting group title	Phase II: Best Supportive Care (BSC)

Reporting group description:

Patients were randomized 1:1 to the Phase II BSC arm (15 patients). The treatment period was planned to comprise up to 4 weeks over a period of 29 days or until ICU discharge.

Reporting group title	Phase III: IFX-1 + SOC

Reporting group description:

In the first stage of Phase III, about 90 patients were to be randomized into the IFX-1 + Standard of Care (SOC) arm using a 1:1 allocation ratio. Based on the results of the Phase III interim analysis, up to an additional 90 patients were to be randomized into the IFX-1+SOC arm in the second stage, using the same allocation ratio.

Reporting group title	Phase III: Placebo + SOC

Reporting group description:

In the first stage of Phase III, about 90 patients were to be randomized into the Placebo+SOC arm using a 1:1 allocation ratio. Based on the results of the Phase III interim analysis, up to an additional 90 patients were to be randomized into the Placebo+SOC arm in the second stage, using the same allocation ratio.

Subject analysis set title	FAS (Phase II)
Subject analysis set type	Full analysis

Subject analysis set description:

All randomized patients were included in the Full Analysis Set (FAS) according to the intention-to-treat principle, irrespective of their protocol adherence and continued participation in the study. Patients were analyzed according to their randomized treatment arm.

Subject analysis set title	SAF (Phase III)
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety analyses were based on all patients who received at least one infusion of IMP; patients were analyzed according to the treatment they actually received. The actual treatment group of each patient was VILO if they received any VILO infusion at any timepoint, and Placebo if they received only Placebo infusions at all timepoints.

Subject analysis set title	FAS (Phase III)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The primary efficacy analyses was performed based on all randomized patients according to the intention-to-treat principle, except for patients who were randomized in error (reason for early termination documented as “Randomized by mistake” in the eCRF) and did not receive IMP.

Primary: Phase II - Relative change (%) from baseline in Oxygenation Index

End point title	Phase II - Relative change (%) from baseline in Oxygenation Index[1]

End point description:

The primary endpoint of the Phase II part of the study was the relative change (%) from baseline (Day 1 prior to study drug administration at ± 1h of randomization) in Oxygenation Index (PaO2 / FiO2) in supine position at Day 5. Reported is the least square (LS) mean (95% confidence interval) for the relative change from baseline per arm for the FAS from a linear repeated measures model adjusting for covariates baseline Oxygenation Index, time point, sex, age, and intubation status.

End point type	Primary

End point timeframe:

Baseline until Day 5

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Relative change (%) from baseline in Oxygenation Index was the primary endpoint for the Phase II part of the trial. The other two arms belong to the Phase III part of the trial which has a different primary endpoint.

End point values	Phase II: IFX-1 + BSC	Phase II: Best Supportive Care (BSC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	15		
Units: Percentage				
number (confidence interval 95%)	15.5 (-11.4 to 42.4)	31.9 (6.0 to 57.9)		

Statistical analyses

Statistical analysis title	LS-means difference for relative change in OI
Comparison groups	Phase II: Best Supportive Care (BSC) v Phase II: IFX-1 + BSC
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.3677
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-16.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.2
upper limit	20.3
Variability estimate	Standard error of the mean
Dispersion value	17.91

Notes:

[2] - The relative change (%) from baseline in oxygenation index (OI) is analyzed and compared between arms IFX-1 + BSC and BSC by LS means difference with 95% CI and p-value from a linear repeated measures model.

Primary: Phase III - 28-day all-cause mortality (FAS)

End point title	Phase III - 28-day all-cause mortality (FAS)[3]

End point description:

The primary efficacy endpoint was 28-day all-cause mortality, i.e. the proportion of patients deceased until Day 28.

End point type	Primary

End point timeframe:

28 days

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 28-day all-cause mortality was the primary endpoint for the Phase III part of the trial. The other two arms belong to the Phase II part of the trial which has a different primary endpoint.

End point values	Phase III: IFX-1 + SOC	Phase III: Placebo + SOC	FAS (Phase III)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	177[4]	191[5]	368[6]	
Units: patients	54	77	131	

Notes:

[4] - The 177 analysed patients include 54 deceased pats + 8 pats with unknown survival status at Day 28

[5] - The 191 analysed patients include 77 deceased pats + 9 pats with unknown survival status at Day 28

[6] - The 368 analysed patients include 131 deceased pats + 17 pats with unknown survival status at Day 28

Statistical analyses

Statistical analysis title	Cox proportional hazards model by site

Statistical analysis description:

Cox proportional hazards regression model of 28-day all-cause mortality with explanatory variables treatment group and age as well as a stratification by site.

Comparison groups	Phase III: Placebo + SOC v Phase III: IFX-1 + SOC
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0941 [7]
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.728
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.502
upper limit	1.056
Variability estimate	Standard error of the mean
Dispersion value	0.18948

Notes:

[7] - 61 of 368 subjects from sites with no events (no deaths) or from single patient sites with death factually did not contribute to the analysis outcome.

Statistical analysis title	Cox prop. hazards model w/o stratification by site

Statistical analysis description:

Cox proportional hazards regression model of 28-day all-cause mortality with explanatory variables treatment group and age without stratification by site.

Comparison groups	Phase III: IFX-1 + SOC v Phase III: Placebo + SOC
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.0266
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.674
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.476
upper limit	0.955

Notes:
[8] - Original protocol-defined analysis method.

Statistical analysis title	Cox regression using Frailty model
Statistical analysis description:	
Age-adjusted Cox regression with random effect for site (“frailty” model).	
Comparison groups	Phase III: Placebo + SOC v Phase III: IFX-1 + SOC
Number of subjects included in analysis	368
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0181
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.648
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.453
upper limit	0.929

Statistical analysis title	Cox regression with stratification by country
Comparison groups	Phase III: Placebo + SOC v Phase III: IFX-1 + SOC
Number of subjects included in analysis	368
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0067
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.613
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.873

Statistical analysis title	Logistic regression (multiple imputation)
Statistical analysis description:	
Logistic regression: Missing values were imputed by multiple imputation. This analysis was performed on the all randomized patient set including the one patient who was randomized in error and excluded from the FAS. For this analyses the number of subjects analyzed is 369.	
Comparison groups	Phase III: IFX-1 + SOC v Phase III: Placebo + SOC

Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.0293
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	-11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.8
upper limit	-1.2

Notes:

[9] - Sensitivity analysis

Statistical analysis title	Log-rank test
Comparison groups	Phase III: IFX-1 + SOC v Phase III: Placebo + SOC
Number of subjects included in analysis	368
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0407
Method	Logrank

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs, serious and non-serious, were to be collected, documented, and reported from signing the informed consent onwards until the EOT visit / 30 days following the last IFX-1 administration.

Adverse event reporting additional description:

Adverse events for Phase II, Arm IFX-1 + BSC and Arm BSC, are reported for FAS.
Adverse events for Phase III, Arm IFX-1 + SOC and Arm Placebo + SOC, are reported for SAF.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	IFX-1 + BSC

Reporting group description:

Phase II: Patients were to be treated with a maximum of 7 intravenous (IV) doses of IFX-1 800 mg over a period of 29 days. The first 5 treatments at Days 1, 2, 4, 8, and 15 were to be administered to all patients randomized into this arm. Treatment at Day 22 was only administered in the event that a patient had not been extubated and discharged from intensive care unit (ICU). In case a patient's clinical situation worsened after Day 8, although an initial clinical benefit was observed, one additional administration of 800 mg IFX-1 between Days 11 and 13 could be given at Investigator's discretion.

Reporting group title	Best Supportive Care (BSC)

Reporting group description:

Phase II: Patients in the control group received BSC only.

Reporting group title	IFX-1 + SOC

Reporting group description:

Phase III: Patients were treated with a maximum of 6 intravenous (IV) doses of IFX-1 800 mg + SOC at Days 1, 2, 4, 8, 15, and
22, as long as the patient was still hospitalized (even if discharged from the intensive care unit [ICU]). IFX-1 treatment was to be ceased if signs of unacceptable toxicity or intolerability occurred.

Reporting group title	Placebo + SOC

Reporting group description:

Phase III: Patients were treated with a maximum of six IV doses of Placebo + SOC at Days 1, 2, 4, 8, 15, and 22, as long as the patient was still hospitalized (even if discharged from the ICU).

Serious adverse events	IFX-1 + BSC	Best Supportive Care (BSC)	IFX-1 + SOC
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 15 (60.00%)	7 / 15 (46.67%)	103 / 175 (58.86%)
number of deaths (all causes)	2	4	62
number of deaths resulting from adverse events	2	4	62
Vascular disorders			
Peripheral artery thrombosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Shock haemorrhagic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 175 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Distributive shock			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Deep vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Circulatory collapse			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive shock			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Shock			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 15 (0.00%)	4 / 15 (26.67%)	16 / 175 (9.14%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 4	0 / 16
Hyperthermia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fibrosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 15 (13.33%)	6 / 15 (40.00%)	10 / 175 (5.71%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	20 / 175 (11.43%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 23
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 11

Hypoxia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	5 / 175 (2.86%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2
Dyspnoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Laryngeal oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumomediastinum			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 175 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Aspiration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory distress			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anoxia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchopleural fistula			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercapnia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung opacity			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinal shift			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary necrosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sputum retention			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device leakage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
End-tidal CO2 increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oxygen saturation decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcus test positive			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchoalveolar lavage abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus test positive			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex test positive			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood culture positive			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glutamate dehydrogenase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella test positive			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sputum culture positive			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Endotracheal intubation complication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	5 / 175 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardio-respiratory arrest			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute myocardial infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bradycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac perforation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular extrasystoles			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic cerebral infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stroke in evolution			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heparin-induced thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic infarction			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary hypersecretion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal necrosis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis necrotising			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute hepatic failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic hepatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis sclerosing			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	16 / 175 (9.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	3 / 175 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oliguria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscle haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	3 / 15 (20.00%)	21 / 175 (12.00%)
occurrences causally related to treatment / all	1 / 1	0 / 3	4 / 29
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Device related sepsis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonas infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sepsis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	5 / 175 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Staphylococcal infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	6 / 175 (3.43%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	24 / 175 (13.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 29
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 11
Pulmonary sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	14 / 175 (8.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 21
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 5
Klebsiella infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	10 / 175 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchopulmonary aspergillosis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	6 / 175 (3.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	6 / 175 (3.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acinetobacter infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia acinetobacter			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	5 / 175 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia pseudomonal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 175 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	5 / 175 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urosepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	3 / 175 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Aspergillus infection			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tracheobronchitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related bacteraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia escherichia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenotrophomonas infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acinetobacter sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Citrobacter infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nosocomial infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia bacterial			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia serratia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection bacterial			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis bacterial			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cholangitis infective			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corynebacterium sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter tracheobronchitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex reactivation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella bacteraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Morganella infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia haemophilus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Providencia infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Severe acute respiratory syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Staphylococcal bacteraemia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenotrophomonas sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic candida			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection pseudomonal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acid-base balance disorder mixed			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemic hyperosmolar nonketotic syndrome			

subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo + SOC		
Total subjects affected by serious adverse events			
subjects affected / exposed	120 / 189 (63.49%)		
number of deaths (all causes)	87		
number of deaths resulting from adverse events	85		
Vascular disorders			
Peripheral artery thrombosis			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Distributive shock			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Deep vein thrombosis			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jugular vein thrombosis			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis			

subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Circulatory collapse				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive shock				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shock				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General disorders and administration site conditions				
Multiple organ dysfunction syndrome				
subjects affected / exposed	21 / 189 (11.11%)			
occurrences causally related to treatment / all	0 / 21			
deaths causally related to treatment / all	0 / 20			
Hyperthermia				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fibrosis				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medical device site haemorrhage				

subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
subjects affected / exposed	12 / 189 (6.35%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	24 / 189 (12.70%)			
occurrences causally related to treatment / all	0 / 25			
deaths causally related to treatment / all	0 / 20			
Hypoxia				
subjects affected / exposed	3 / 189 (1.59%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 3			
Dyspnoea				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	6 / 189 (3.17%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 1			
Acute respiratory distress syndrome				
subjects affected / exposed	3 / 189 (1.59%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 3			
Laryngeal oedema				

subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumomediastinum				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspiration				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anoxia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchial obstruction				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopleural fistula				

subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemothorax				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercapnia				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung opacity				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mediastinal shift				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Organising pneumonia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary fibrosis				

subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary hypertension				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary infarction				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary necrosis				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sputum retention				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Delirium				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Agitation				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device leakage				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device dislocation				

subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
End-tidal CO2 increased			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oxygen saturation decreased			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcus test positive			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchoalveolar lavage abnormal			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspergillus test positive			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes simplex test positive			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood culture positive			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Glutamate dehydrogenase increased			

subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme abnormal				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella test positive				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sputum culture positive				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Endotracheal intubation complication				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural complication				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				

subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	2 / 189 (1.06%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Cardio-respiratory arrest			
subjects affected / exposed	4 / 189 (2.12%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 2		
Acute myocardial infarction			
subjects affected / exposed	3 / 189 (1.59%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Bradycardia			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiogenic shock			
subjects affected / exposed	2 / 189 (1.06%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Ventricular tachycardia			
subjects affected / exposed	2 / 189 (1.06%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			

subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure acute			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac perforation			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiomyopathy			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiopulmonary failure			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			

subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular arrhythmia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ventricular extrasystoles				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular fibrillation				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Epilepsy				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic cerebral infarction				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	4 / 189 (2.12%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				

subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Autonomic nervous system imbalance				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic cerebral infarction				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stroke in evolution				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Toxic encephalopathy				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Heparin-induced thrombocytopenia			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Splenic infarction			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Salivary hypersecretion			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			

subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal haemorrhagic				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer haemorrhage				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal necrosis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mouth haemorrhage				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis necrotising				

subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Liver injury				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Acute hepatic failure				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hepatic failure				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Ischaemic hepatitis				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cholangitis sclerosing				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				

subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic infarction				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Subcutaneous emphysema				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	29 / 189 (15.34%)			
occurrences causally related to treatment / all	0 / 30			
deaths causally related to treatment / all	0 / 3			
Renal failure				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anuria				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oliguria				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue				

disorders				
Muscle haemorrhage				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	16 / 189 (8.47%)			
occurrences causally related to treatment / all	0 / 18			
deaths causally related to treatment / all	0 / 4			
Device related sepsis				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudomonas infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	5 / 189 (2.65%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
Urinary tract infection				
subjects affected / exposed	3 / 189 (1.59%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Vascular device infection				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Septic shock			
subjects affected / exposed	30 / 189 (15.87%)		
occurrences causally related to treatment / all	0 / 34		
deaths causally related to treatment / all	0 / 20		
Pulmonary sepsis			
subjects affected / exposed	11 / 189 (5.82%)		
occurrences causally related to treatment / all	1 / 14		
deaths causally related to treatment / all	0 / 5		
Klebsiella infection			
subjects affected / exposed	9 / 189 (4.76%)		
occurrences causally related to treatment / all	3 / 9		
deaths causally related to treatment / all	0 / 1		
Pneumonia staphylococcal			
subjects affected / exposed	3 / 189 (1.59%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary aspergillosis			
subjects affected / exposed	6 / 189 (3.17%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Pneumonia klebsiella			
subjects affected / exposed	4 / 189 (2.12%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Acinetobacter infection			
subjects affected / exposed	4 / 189 (2.12%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 1		
Pneumonia acinetobacter			
subjects affected / exposed	3 / 189 (1.59%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia pseudomonal			

subjects affected / exposed	3 / 189 (1.59%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterococcal sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Urosepsis				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Aspergillus infection				
subjects affected / exposed	3 / 189 (1.59%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Tracheobronchitis				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Device related bacteraemia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterococcal infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes simplex pneumonia				

subjects affected / exposed	3 / 189 (1.59%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	1 / 1			
Pneumonia escherichia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pseudomonal sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stenotrophomonas infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection enterococcal				
subjects affected / exposed	3 / 189 (1.59%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Acinetobacter sepsis				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Citrobacter infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterobacter pneumonia				

subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterococcal bacteraemia				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nosocomial infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				

subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia cytomegaloviral				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia serratia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Superinfection bacterial				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tracheobronchitis bacterial				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Candida sepsis				

subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis infective				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Corynebacterium sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Empyema				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterobacter infection				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterobacter sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterobacter tracheobronchitis				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epstein-Barr virus infection				

subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes simplex reactivation				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infectious pleural effusion				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella bacteraemia				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver abscess				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Morganella infection				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonia haemophilus				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia streptococcal				

subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Providencia infection				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudomonal bacteraemia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Severe acute respiratory syndrome				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal bacteraemia				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stenotrophomonas sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Streptococcal sepsis				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Systemic candida				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection pseudomonal				

subjects affected / exposed	0 / 189 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	2 / 189 (1.06%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Acid-base balance disorder mixed			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acidosis			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypovolaemia			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	IFX-1 + BSC	Best Supportive Care (BSC)	IFX-1 + SOC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 15 (93.33%)	14 / 15 (93.33%)	147 / 175 (84.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 175 (0.57%)
occurrences (all)	0	1	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 15 (20.00%)	3 / 15 (20.00%)	10 / 175 (5.71%)
occurrences (all)	3	3	10
Hypertension			
subjects affected / exposed	2 / 15 (13.33%)	2 / 15 (13.33%)	16 / 175 (9.14%)
occurrences (all)	2	2	17
Phlebitis			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	4 / 175 (2.29%)
occurrences (all)	2	1	4
Thrombophlebitis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences (all)	2	0	2
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	7 / 175 (4.00%)
occurrences (all)	1	0	8
Jugular vein thrombosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences (all)	1	0	2
Shock			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Systolic hypertension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 15 (0.00%)	4 / 15 (26.67%)	10 / 175 (5.71%)
occurrences (all)	0	4	19
Pyrexia			
subjects affected / exposed	3 / 15 (20.00%)	1 / 15 (6.67%)	15 / 175 (8.57%)
occurrences (all)	4	1	18
Chest discomfort			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	2 / 175 (1.14%)
occurrences (all)	0	1	2
Hypothermia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Infusion site discolouration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Infusion site extravasation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Infusion site vesicles			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Medical device site haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	3 / 15 (20.00%)	1 / 15 (6.67%)	9 / 175 (5.14%)
occurrences (all)	3	1	9
Respiratory failure			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	2 / 175 (1.14%)
occurrences (all)	1	2	2
Hypoxia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	3 / 175 (1.71%)
occurrences (all)	1	1	4
Bradypnoea			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Hypoventilation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	2	0	0
Pneumothorax			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	10 / 175 (5.71%)
occurrences (all)	0	1	10
Sleep apnoea syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Delirium			
subjects affected / exposed	3 / 15 (20.00%)	4 / 15 (26.67%)	13 / 175 (7.43%)
occurrences (all)	4	4	14
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 175 (0.57%)
occurrences (all)	0	1	1
Hallucination			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Nightmare			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Panic attack			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	9 / 175 (5.14%)
occurrences (all)	0	0	9
Intensive care unit delirium			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	9 / 175 (5.14%)
occurrences (all)	0	0	9
Product issues			
Device leakage			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 15 (6.67%)	3 / 15 (20.00%)	9 / 175 (5.14%)
occurrences (all)	1	3	9
Blood bicarbonate increased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	1	1	0
Blood potassium decreased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	1	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	1	1	0
Fluid balance positive			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	0 / 175 (0.00%)
occurrences (all)	0	2	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Blood culture positive			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences (all)	1	0	2
Blood fibrinogen increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Blood urea increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Computerised tomogram abnormal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0

Culture negative			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Culture urine			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Cytomegalovirus test positive			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Enterococcus test positive			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Eosinophil count increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Fibrin D dimer increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Liver function test abnormal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	3 / 175 (1.71%)
occurrences (all)	1	0	3
Oxygen saturation decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences (all)	1	0	2
Platelet count increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Protein urine present			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Sputum culture positive			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences (all)	1	0	4
Staphylococcus test positive			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	5 / 175 (2.86%)
occurrences (all)	1	0	5
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	3 / 175 (1.71%)
occurrences (all)	1	0	3
Infusion related reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Post procedural haematoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	6 / 175 (3.43%)
occurrences (all)	1	2	6
Atrial fibrillation			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	12 / 175 (6.86%)
occurrences (all)	1	1	12
Atrioventricular block second degree			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Bradycardia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	2 / 175 (1.14%)
occurrences (all)	0	1	2
Cardiac failure			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Defect conduction intraventricular			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	5 / 175 (2.86%)
occurrences (all)	1	0	9
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Hemiparesis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Intensive care unit acquired weakness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences (all)	1	0	3
Metabolic encephalopathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Peripheral nerve lesion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	2 / 15 (13.33%)	2 / 15 (13.33%)	14 / 175 (8.00%)
occurrences (all)	2	2	18
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	1	1	0
Eye irritation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Miosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Pupils unequal			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Impaired gastric emptying			
subjects affected / exposed	4 / 15 (26.67%)	7 / 15 (46.67%)	4 / 175 (2.29%)
occurrences (all)	4	7	4
Constipation			
subjects affected / exposed	2 / 15 (13.33%)	4 / 15 (26.67%)	6 / 175 (3.43%)
occurrences (all)	2	4	6
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	5 / 175 (2.86%)
occurrences (all)	1	1	5
Dysphagia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Frequent bowel movements			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Gastric haemorrhage			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Ileus			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	2 / 175 (1.14%)
occurrences (all)	0	1	2
Ileus paralytic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 175 (0.57%)
occurrences (all)	0	1	1
Rectal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	2 / 175 (1.14%)
occurrences (all)	0	1	2
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	6 / 175 (3.43%)
occurrences (all)	0	1	9
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	4 / 15 (26.67%)	6 / 15 (40.00%)	4 / 175 (2.29%)
occurrences (all)	5	6	4
Actinic keratosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Angioedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	2	0	0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 15 (13.33%)	3 / 15 (20.00%)	20 / 175 (11.43%)
occurrences (all)	2	3	21
Oliguria			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	2	0	0
Glycosuria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	21 / 175 (12.00%)
occurrences (all)	1	2	26
Aspergillus infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	4 / 175 (2.29%)
occurrences (all)	1	0	4
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 175 (0.57%)
occurrences (all)	0	1	1
Enterococcal infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	8 / 175 (4.57%)
occurrences (all)	1	0	9

Fungal infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Staphylococcal infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	5 / 175 (2.86%)
occurrences (all)	1	0	7
Vascular device infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	7 / 175 (4.00%)
occurrences (all)	0	0	8
Herpes simplex			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	11 / 175 (6.29%)
occurrences (all)	0	0	11
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	4 / 15 (26.67%)	5 / 15 (33.33%)	11 / 175 (6.29%)
occurrences (all)	4	5	12
Hypophosphataemia			
subjects affected / exposed	4 / 15 (26.67%)	5 / 15 (33.33%)	2 / 175 (1.14%)
occurrences (all)	5	6	2
Hypokalaemia			
subjects affected / exposed	4 / 15 (26.67%)	4 / 15 (26.67%)	7 / 175 (4.00%)
occurrences (all)	4	4	9
Hyperglycaemia			
subjects affected / exposed	4 / 15 (26.67%)	3 / 15 (20.00%)	6 / 175 (3.43%)
occurrences (all)	4	3	7
Hypercalcaemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	2 / 175 (1.14%)
occurrences (all)	1	1	2
Hyperkalaemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	3 / 175 (1.71%)
occurrences (all)	1	1	3
Hyponatraemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	2 / 175 (1.14%)
occurrences (all)	2	0	2
Fluid overload			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Hyperchloraemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	1 / 175 (0.57%)
occurrences (all)	0	1	1
Hypermagnesaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 175 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Metabolic alkalosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 175 (0.57%)
occurrences (all)	1	0	1
Refeeding syndrome			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	0 / 175 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo + SOC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	152 / 189 (80.42%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	8 / 189 (4.23%)		
occurrences (all)	8		
Hypertension			
subjects affected / exposed	13 / 189 (6.88%)		
occurrences (all)	13		
Phlebitis			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Thrombophlebitis			

subjects affected / exposed	2 / 189 (1.06%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	5 / 189 (2.65%)		
occurrences (all)	9		
Jugular vein thrombosis			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Shock			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Systolic hypertension			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	9 / 189 (4.76%)		
occurrences (all)	21		
Pyrexia			
subjects affected / exposed	16 / 189 (8.47%)		
occurrences (all)	30		
Chest discomfort			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Face oedema			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Hypothermia			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Infusion site discolouration			

subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Infusion site extravasation			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Infusion site vesicles			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Medical device site haemorrhage			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	5 / 189 (2.65%)		
occurrences (all)	5		
Respiratory failure			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Hypoxia			
subjects affected / exposed	3 / 189 (1.59%)		
occurrences (all)	3		
Bradypnoea			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Hypoventilation			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Pneumothorax			
subjects affected / exposed	5 / 189 (2.65%)		
occurrences (all)	6		
Sleep apnoea syndrome			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			

Delirium			
subjects affected / exposed	13 / 189 (6.88%)		
occurrences (all)	13		
Anxiety			
subjects affected / exposed	4 / 189 (2.12%)		
occurrences (all)	4		
Hallucination			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Nightmare			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Panic attack			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Restlessness			
subjects affected / exposed	9 / 189 (4.76%)		
occurrences (all)	9		
Intensive care unit delirium			
subjects affected / exposed	7 / 189 (3.70%)		
occurrences (all)	7		
Product issues			
Device leakage			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	6 / 189 (3.17%)		
occurrences (all)	6		
Blood bicarbonate increased			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Blood potassium decreased			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			

subjects affected / exposed	1 / 189 (0.53%)			
occurrences (all)	1			
Fluid balance positive				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences (all)	1			
Blood alkaline phosphatase increased				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences (all)	1			
Blood culture positive				
subjects affected / exposed	4 / 189 (2.12%)			
occurrences (all)	4			
Blood fibrinogen increased				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences (all)	0			
Blood phosphorus decreased				
subjects affected / exposed	2 / 189 (1.06%)			
occurrences (all)	2			
Blood urea increased				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences (all)	0			
Computerised tomogram abnormal				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences (all)	0			
Culture negative				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences (all)	0			
Culture urine				
subjects affected / exposed	1 / 189 (0.53%)			
occurrences (all)	1			
Cytomegalovirus test positive				
subjects affected / exposed	0 / 189 (0.00%)			
occurrences (all)	0			
Enterococcus test positive				
subjects affected / exposed	3 / 189 (1.59%)			
occurrences (all)	4			
Eosinophil count increased				

subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Fibrin D dimer increased			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Liver function test abnormal			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Oxygen saturation decreased			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Platelet count increased			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Protein urine present			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Sputum culture positive			
subjects affected / exposed	3 / 189 (1.59%)		
occurrences (all)	4		
Staphylococcus test positive			
subjects affected / exposed	8 / 189 (4.23%)		
occurrences (all)	11		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Infusion related reaction			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Limb injury			

subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Post procedural haematoma subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Cardiac disorders Supraventricular tachycardia subjects affected / exposed occurrences (all)	1 / 189 (0.53%) 1		
Atrial fibrillation subjects affected / exposed occurrences (all)	19 / 189 (10.05%) 19		
Atrioventricular block second degree subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Bradycardia subjects affected / exposed occurrences (all)	2 / 189 (1.06%) 2		
Cardiac failure subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Defect conduction intraventricular subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Sinus tachycardia subjects affected / exposed occurrences (all)	4 / 189 (2.12%) 11		
Tachycardia subjects affected / exposed occurrences (all)	2 / 189 (1.06%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Hemiparesis			

subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Intensive care unit acquired weakness			
subjects affected / exposed	6 / 189 (3.17%)		
occurrences (all)	6		
Metabolic encephalopathy			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Peripheral nerve lesion			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	17 / 189 (8.99%)		
occurrences (all)	18		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Eye irritation			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Miosis			

subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Pupils unequal			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Impaired gastric emptying			
subjects affected / exposed	3 / 189 (1.59%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	3 / 189 (1.59%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	3 / 189 (1.59%)		
occurrences (all)	3		
Dysphagia			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Frequent bowel movements			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Gastric haemorrhage			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Ileus			
subjects affected / exposed	2 / 189 (1.06%)		
occurrences (all)	2		
Ileus paralytic			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		

Rectal haemorrhage subjects affected / exposed occurrences (all)	1 / 189 (0.53%) 1		
Vomiting subjects affected / exposed occurrences (all)	5 / 189 (2.65%) 6		
Skin and subcutaneous tissue disorders			
Decubitus ulcer subjects affected / exposed occurrences (all)	5 / 189 (2.65%) 7		
Actinic keratosis subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Alopecia subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Angioedema subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	13 / 189 (6.88%) 13		
Oliguria subjects affected / exposed occurrences (all)	1 / 189 (0.53%) 1		
Glycosuria subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Urinary retention subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	11 / 189 (5.82%)		
occurrences (all)	15		
Aspergillus infection			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	0 / 189 (0.00%)		
occurrences (all)	0		
Enterococcal infection			
subjects affected / exposed	7 / 189 (3.70%)		
occurrences (all)	7		
Fungal infection			
subjects affected / exposed	1 / 189 (0.53%)		
occurrences (all)	1		
Staphylococcal infection			
subjects affected / exposed	11 / 189 (5.82%)		
occurrences (all)	13		
Vascular device infection			
subjects affected / exposed	11 / 189 (5.82%)		
occurrences (all)	12		
Herpes simplex			
subjects affected / exposed	5 / 189 (2.65%)		
occurrences (all)	5		
Metabolism and nutrition disorders			

Hypernatraemia subjects affected / exposed occurrences (all)	13 / 189 (6.88%) 15			
Hypophosphataemia subjects affected / exposed occurrences (all)	8 / 189 (4.23%) 8			
Hypokalaemia subjects affected / exposed occurrences (all)	8 / 189 (4.23%) 12			
Hyperglycaemia subjects affected / exposed occurrences (all)	10 / 189 (5.29%) 19			
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0			
Hyperkalaemia subjects affected / exposed occurrences (all)	4 / 189 (2.12%) 4			
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0			
Fluid overload subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0			
Hyperchloraemia subjects affected / exposed occurrences (all)	1 / 189 (0.53%) 2			
Hypermagnesaemia subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0			
Hypomagnesaemia subjects affected / exposed occurrences (all)	2 / 189 (1.06%) 2			
Metabolic alkalosis subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0			

Refeeding syndrome subjects affected / exposed occurrences (all)	0 / 189 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 July 2020	Amendment 1 was issued after completion of Phase II part. Changes to Phase III included added information on study design, endpoints, conduct, treatment administration, and statistical methods.
17 December 2020	Amendment 2 included the accounting for drop-outs/replacement patients and corresponding adaptations of the overall patient number and statistical analysis sets, specific timing of intubation in relation to the first IMP administration (inclusion and exclusion criteria), specifications regarding the diverse consenting options in an ICU setting, modifications of the Schedule of Assessments including timing of assessments and the follow-up visit, emergency unblinding, and clarifications on AE reporting.
12 May 2021	Amendment 3 was issued to eliminate statistical concerns of regulatory authorities about the early stop for efficacy at the interim analysis and to clarify the final analysis, including removal of the statistical 'stop for efficacy' criterion for the interim analysis, adaptation of the power calculation, clarification of the randomization of additional patients, upgrade of the '60-day mortality' endpoint to the first secondary endpoint, adaptation of the order of the secondary endpoints, and addition of an exploratory endpoint, and an increase of the number of sites from 45 to 60 sites to improve the ability to enroll the study in a timely manner.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported