Clinical trial results:
A phase II randomized, placebo-controlled, double-blind, dose controlled trial in patients suffering from early, newly developing abdominal or pulmonary derived septic organ dysfunction to evaluate safety, pharmacokinetics, pharmacodynamics and to estimate efficacy of the new humanized monoclonal i.v. administered antibody IFX-1

Summary

EudraCT number	2013-001037-40
Trial protocol	DE
Global end of trial date	03 December 2015

Results information

Result version number	v1 (current)
This version publication date	28 June 2021
First version publication date	28 June 2021

Trial information

Trial identification

Sponsor protocol code	IFX-1-P2.1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	InflaRx GmbH
Sponsor organisation address	Winzerlaer Str.2, Jena, Germany, 07745
Public contact	Trial Coordination, ZKS Leipzig - KKS, 49 3419716154, SCIENS@zks.uni-leipzig.de
Scientific contact	Trial Coordination, ZKS Leipzig - KKS, 49 3419716154, SCIENS@zks.uni-leipzig.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	23 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 December 2015
Global end of trial reached?	Yes
Global end of trial date	03 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to characterize the safety and tolerability of three dose regimens of IFX-1 and also to perform an assessment of the pharmacokinetics and pharmacodynamics of IFX-1.

Protection of trial subjects:

This study was carried out in accordance with the ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) Good Clinical Practice guidelines, the Declaration of Helsinki (Version of 1996), and standard operating procedures for clinical research and development at InflaRx GmbH and the Clinical Research Organizations involved.
Before admitting a subject into this study the subject had to provide written consent to participate in the study. The investigator was responsible to obtain informed consent in accordance with local laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2014
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	Germany: 72
Worldwide total number of subjects	72
EEA total number of subjects	72

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)	30
From 65 to 84 years	36

85 years and over	6

Subject disposition

Recruitment

Recruitment details:

The study included male or female patients of 18 years or older with occurrence of at least 2 criteria of a systemic inflammatory response syndrome and a suspected or confirmed abdominal or pulmonary infection. Between 25 April 2014 and 3 December 2015, 72 subjects were screened in 17 centers in Germany.

Pre-assignment

Screening details:

Of 2783 pre-screened patients, 72 patients were screened for eligibility before participating in the active treatment phase of the study. Subjects were not to be entered to the trial treatment if any of the eligibility criteria were violated. All of the 72 enrolled patients were randomized and treated.

Period 1

Period 1 title	Overall period (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:

All study participants were blinded with respect to IFX-1 and placebo. Standard measures were taken for the investigational medical product to ensure adequate blinding (e.g., same container/closure system, storage conditions, color, and foaming property).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Combined

Arm description:

Intravenous administration of placebo in any of the three cohorts corresponding to the Verum Cohorts 1, 2 and 3. The ratio between IFX-1 and placebo within one dose cohort was 2:1.
One patient completed the study at Day 28 after first treatment but stayed in hospital and had a serious fatal adverse event 4 weeks after study completion.

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

Dosage and administration details:

The placebo is a phosphat buffered saline solution with polysorbate 80. Administration was following the same treatment schedule as IFX-1:
Cohort 1: 2 x 2 mg/kg body weight (b.w.) on 0 h and 12 h
Cohort 2: 2 x 4 mg/kg b.w. on 0 h and 24 h
Cohort 3: 3 x 4 mg/kg b.w. on 0 h, 24 h, and 72 h
For patients wighing more than 100 kg the dose calculation was based on 100 kg b.w.

Arm title	Verum Cohort 1

Arm description:

Intravenous administration of IFX-1 according to the following schedule: 2 x 2 mg/kg body weight (b.w.) on 0 h and 12 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Arm type	Experimental

Investigational medicinal product name	IFX-1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The amount of study drug for a single infusion was based on the body weight (b.w.) of the subject (mg/kg) and the treatment arm:
Cohort 1: 2 x 2 mg/kg body weight (b.w.) on 0 h and 12 h
Cohort 2: 2 x 4 mg/kg b.w. on 0 h and 24 h
Cohort 3: 3 x 4 mg/kg b.w. on 0 h, 24 h, and 72 h
For patients wighing more than 100 kg the dose calculation was based on 100 kg b.w..

The volume of the administered IMP was calculated according to the following formula: Volume of IMP (in mL) = dose group (in mg/kg) x body weight (in kg) / 10 mg/mL. Afterwards the volume of IMP was filled up with sterile NaCl 0.9% solution used for injection to a total volume of 50 mL into a 50 mL infusion pump syringe. IFX-1 was supplied in 10 mL glass vials in strength of 10 mg/mL and is a monoclonal IgG4 anti-human C5a immunoglobulin.

Arm title	Verum Cohort 2

Arm description:

Intravenous administration of IFX-1 according to the following schedule: 2 x 4 mg/kg body weight (b.w.) on 0 h and 24 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Arm type	Experimental
Investigational medicinal product name	IFX-1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The amount of study drug for a single infusion was based on the body weight (b.w.) of the subject (mg/kg) and the treatment arm:
Cohort 1: 2 x 2 mg/kg body weight (b.w.) on 0 h and 12 h
Cohort 2: 2 x 4 mg/kg b.w. on 0 h and 24 h
Cohort 3: 3 x 4 mg/kg b.w. on 0 h, 24 h, and 72 h
For patients wighing more than 100 kg the dose calculation was based on 100 kg b.w..

The volume of the administered IMP was calculated according to the following formula: Volume of IMP (in mL) = dose group (in mg/kg) x body weight (in kg) / 10 mg/mL. Afterwards the volume of IMP was filled up with sterile NaCl 0.9% solution used for injection to a total volume of 50 mL into a 50 mL infusion pump syringe. IFX-1 was supplied in 10 mL glass vials in strength of 10 mg/mL and is a monoclonal IgG4 anti-human C5a immunoglobulin.

Arm title	Verum Cohort 3

Arm description:

Intravenous administration of IFX-1 according to the following schedule: 3 x 4 mg/kg body weight (b.w.) on 0 h, 24 h and 72 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Arm type	Experimental
Investigational medicinal product name	IFX-1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The amount of study drug for a single infusion was based on the body weight (b.w.) of the subject (mg/kg) and the treatment arm:
Cohort 1: 2 x 2 mg/kg body weight (b.w.) on 0 h and 12 h
Cohort 2: 2 x 4 mg/kg b.w. on 0 h and 24 h
Cohort 3: 3 x 4 mg/kg b.w. on 0 h, 24 h, and 72 h
For patients wighing more than 100 kg the dose calculation was based on 100 kg b.w..

The volume of the administered IMP was calculated according to the following formula: Volume of IMP (in mL) = dose group (in mg/kg) x body weight (in kg) / 10 mg/mL. Afterwards the volume of IMP was filled up with sterile NaCl 0.9% solution used for injection to a total volume of 50 mL into a 50 mL infusion pump syringe. IFX-1 was supplied in 10 mL glass vials in strength of 10 mg/mL and is a monoclonal IgG4 anti-human C5a immunoglobulin.

Number of subjects in period 1	Placebo Combined	Verum Cohort 1	Verum Cohort 2
Started	24	16	16
Completed	20	10	13
Not completed	4	6	3
Adverse event, serious fatal	3	6	3
Refusal of informed consent	1	-	-

Number of subjects in period 1	Verum Cohort 3
Started	16
Completed	14
Not completed	2
Adverse event, serious fatal	2
Refusal of informed consent	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo Combined
Reporting group description:	
Intravenous administration of placebo in any of the three cohorts corresponding to the Verum Cohorts 1, 2 and 3. The ratio between IFX-1 and placebo within one dose cohort was 2:1. One patient completed the study at Day 28 after first treatment but stayed in hospital and had a serious fatal adverse event 4 weeks after study completion.	
Reporting group title	Verum Cohort 1
Reporting group description:	
Intravenous administration of IFX-1 according to the following schedule: 2 x 2 mg/kg body weight (b.w.) on 0 h and 12 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.	
Reporting group title	Verum Cohort 2
Reporting group description:	
Intravenous administration of IFX-1 according to the following schedule: 2 x 4 mg/kg body weight (b.w.) on 0 h and 24 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.	
Reporting group title	Verum Cohort 3
Reporting group description:	
Intravenous administration of IFX-1 according to the following schedule: 3 x 4 mg/kg body weight (b.w.) on 0 h, 24 h and 72 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.	

Reporting group values	Placebo Combined	Verum Cohort 1	Verum Cohort 2
Number of subjects	24	16	16
Age categorical Units: Subjects			
Adults (18-64 years)	12	7	7
From 65-84 years	10	8	6
85 years and over	2	1	3
Gender categorical Units: Subjects			
Female	8	6	7
Male	16	10	9

Reporting group values	Verum Cohort 3	Total	
Number of subjects	16	72	
Age categorical Units: Subjects			
Adults (18-64 years)	4	30	
From 65-84 years	12	36	
85 years and over	0	6	
Gender categorical Units: Subjects			
Female	5	26	
Male	11	46	

End points

End points reporting groups

Reporting group title	Placebo Combined

Reporting group description:

Intravenous administration of placebo in any of the three cohorts corresponding to the Verum Cohorts 1, 2 and 3. The ratio between IFX-1 and placebo within one dose cohort was 2:1.
One patient completed the study at Day 28 after first treatment but stayed in hospital and had a serious fatal adverse event 4 weeks after study completion.

Reporting group title	Verum Cohort 1

Reporting group description:

Intravenous administration of IFX-1 according to the following schedule: 2 x 2 mg/kg body weight (b.w.) on 0 h and 12 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Reporting group title	Verum Cohort 2

Reporting group description:

Intravenous administration of IFX-1 according to the following schedule: 2 x 4 mg/kg body weight (b.w.) on 0 h and 24 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Reporting group title	Verum Cohort 3

Reporting group description:

Intravenous administration of IFX-1 according to the following schedule: 3 x 4 mg/kg body weight (b.w.) on 0 h, 24 h and 72 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Primary: IFX-1 plasma concentration

End point title	IFX-1 plasma concentration[1][2]

End point description:

Plasma concentration of IFX-1 at each time point.
Full Analysis Set (FAS): all subjects who were randomized and who received at least one dose of IFX-1.
Pharmacokinetic-Population (PK-PP): Only patients who were considered "meaningful evaluable" regarding their pharmacokinetics/pharmacodynamics laboratory measurements during the data review meeting are presented in this record. The number of subjects analysed varied between time points.

According to specifications made during the data review meeting, values below level of quantification were set to 0, if applicable.
For some time points, IFX-1 plasma concentration was not measured for all cohorts. Not applicable values are presented as "99999" or "-99999".

End point type	Primary

End point timeframe:

At 0 hours (h) and 2h, 6h, 12h, 14h (only verum cohort 1), 24h, 26h (only verum cohorts 2 and 3), 48h, 72h, 74h (only verum cohort 3), Day 5, Day 8, Day 13, Day 28 after first infusion of IFX-1 and at hospital discharge

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were defined and performed.

[2] - 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: IFX-1 plasma concentration was not presented for the Placebo Combined arm, as patients in this arm did not receive IFX-1 infusions.

End point values	Verum Cohort 1	Verum Cohort 2	Verum Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13[3]	12[4]	13[5]	
Units: µg/ml				
geometric mean (confidence interval 95%)				
0 h	99999 (99999 to 99999)	99999 (99999 to 99999)	0.067 (-99999 to 99999)	
2 h	33.215 (28.825 to 38.273)	77.623 (64.689 to 93.142)	68.361 (58.776 to 79.508)	
6 h	26.766 (22.964 to 31.198)	61.634 (54.205 to 70.081)	60.067 (51.825 to 69.620)	
12 h	19.351 (16.135 to 23.208)	50.039 (42.114 to 59.457)	44.251 (37.898 to 51.668)	
14 h	47.713 (40.187 to 56.648)	99999 (99999 to 99999)	99999 (99999 to 99999)	
24 h	33.347 (27.983 to 39.740)	33.369 (27.375 to 40.675)	30.146 (25.014 to 36.332)	
26 h	99999 (99999 to 99999)	102.133 (86.577 to 120.484)	88.844 (77.471 to 101.887)	
48 h	16.035 (12.444 to 20.663)	61.932 (52.028 to 73.721)	52.273 (41.223 to 66.285)	
72 h	8.064 (5.366 to 12.117)	37.737 (30.285 to 47.023)	35.764 (26.823 to 47.685)	
74 h	99999 (99999 to 99999)	99999 (99999 to 99999)	97.405 (85.671 to 110.748)	
Day 5	2.848 (1.911 to 4.244)	16.131 (11.981 to 21.719)	41.906 (32.324 to 54.329)	
Day 8	0.715 (0.507 to 1.008)	3.951 (2.675 to 5.834)	14.051 (9.993 to 19.758)	
Day 13	0.191 (0.092 to 0.399)	1.080 (0.436 to 2.675)	3.069 (1.835 to 5.132)	
Day 28	99999 (99999 to 99999)	0.230 (0.118 to 0.450)	0.452 (0.298 to 0.686)	
Hospital discharge	0.249 (0.033 to 1.889)	0.767 (0.129 to 4.548)	14.676 (-99999 to 99999)	

Notes:

[3] - FAS, PK-PP

[4] - FAS, PK-PP

[5] - FAS, PK-PP

Statistical analyses

No statistical analyses for this end point

Primary: Cmax

End point title	Cmax[6][7]

End point description:

Maximum observed IFX-1 plasma concentration (Cmax) by treatment (FAS, PK-PP).

End point type	Primary

End point timeframe:

At 0 hours (h) and 2h, 6h, 12h, 14h (only cohort 1), 24h, 26h (only cohorts 2 and 3), 48h, 72h, 74h (only cohort 3), Day 5, Day 8, Day 13, Day 28 after first infusion of IFX-1 and at hospital discharge

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were defined and performed.

[7] - 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: Cmax was not presented for the Placebo Combined arm, as patients in this arm did not receive IFX-1 infusions.

End point values	Verum Cohort 1	Verum Cohort 2	Verum Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13[8]	12[9]	13[10]	
Units: µg/mL				
geometric mean (confidence interval 95%)	47.71 (40.19 to 56.65)	103.25 (87.08 to 122.42)	103.63 (92.22 to 116.46)	

Notes:

[8] - FAS, PK-PP

[9] - FAS, PK-PP

[10] - FAS, PK-PP

Statistical analyses

No statistical analyses for this end point

Primary: Cthrough

End point title	Cthrough[11][12]

End point description:

IFX-1 plasma concentration measured directly before infusion (Cthrough) by treatment and infusion (FAS, PK-PP). The number of subjects analysed varied between infusions.
Not applicable values are presented as "99999" or "-99999".

End point type	Primary

End point timeframe:

Directly before infusions: for Cohort 1 at 0h and 12h, for Cohort 2 at 0h and 24h, and for Cohort 3 at 0h, 14h and 72h.

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were defined and performed.

[12] - 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: Cthrough was not presented for the Placebo Combined arm, as patients in this arm did not receive IFX-1 infusions.

End point values	Verum Cohort 1	Verum Cohort 2	Verum Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13[13]	12[14]	13[15]	
Units: µg/mL				
geometric mean (confidence interval 95%)				
First infusion	99999 (99999 to 99999)	99999 (99999 to 99999)	0.067 (-99999 to 99999)	
Second infusion	19.351 (16.135 to 23.208)	33.369 (27.375 to 40.675)	30.146 (25.014 to 36.332)	
Third infusion	99999 (99999 to 99999)	99999 (99999 to 99999)	35.764 (26.823 to 47.685)	

Notes:

[13] - FAS, PK-PP

[14] - FAS, PK-PP

[15] - FAS, PK-PP

Statistical analyses

No statistical analyses for this end point

Primary: AUC

End point title	AUC[16][17]

End point description:

Area under the curve (AUC) of IFX-1 plasma concentration (FAS, PK-PP)

End point type	Primary

End point timeframe:

At 0 hours (h) and 2h, 6h, 12h, 14h (only verum cohort 1), 24h, 26h (only verum cohorts 2 and 3), 48h, 72h, 74h (only verum cohort 3), Day 5, Day 8, Day 13, Day 28 after first infusion of IFX-1 and at hospital discharge

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were defined and performed.

[17] - 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: AUC for IFX-1 plasma concentration was not calculated for the Placebo Combined arm, as patients in this arm did not receive IFX-1 infusions.

End point values	Verum Cohort 1	Verum Cohort 2	Verum Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13[18]	12[19]	13[20]	
Units: h*µg/mL				
geometric mean (confidence interval 95%)	2101.4 (1690.2 to 2612.7)	6345.7 (5320.6 to 7568.2)	10799.6 (9232.8 to 12632.3)	

Notes:

[18] - FAS, PK-PP

[19] - FAS, PK-PP

[20] - FAS, PK-PP

Statistical analyses

No statistical analyses for this end point

Primary: C5a concentration

End point title	C5a concentration[21]

End point description:

Plasma concentration of free, detectable C5a at each time point (FAS).

The number of subjects analysed varied between time points.
Not applicable values are presented as "99999" or "-99999".

End point type	Primary

End point timeframe:

At 0 hours (h) and 2h, 6h, 12h, 24h, 72h, Day 5, Day 8, Day 13, Day 28 after first infusion of IFX-1 or placebo and at hospital discharge

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Performed statistical analyses were solely related to data exploration/description.

End point values	Placebo Combined	Verum Cohort 1	Verum Cohort 2	Verum Cohort 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24[22]	16[23]	16[24]	16[25]
Units: ng/mL				
geometric mean (confidence interval 95%)				
0 h	26.5 (21.0 to 33.5)	35.0 (27.4 to 44.7)	40.3 (28.4 to 57.2)	28.4 (19.6 to 41.2)
2 h	24.4 (20.2 to 29.5)	5.1 (4.5 to 5.7)	3.7 (3.1 to 4.4)	4.0 (3.5 to 4.6)
6 h	26.0 (21.0 to 32.2)	7.9 (7.0 to 8.8)	5.0 (4.2 to 5.9)	5.6 (4.8 to 6.7)
12 h	24.5 (19.6 to 30.6)	9.9 (8.4 to 11.6)	5.7 (4.7 to 6.9)	6.3 (5.4 to 7.4)
24 h	26.5 (21.4 to 32.9)	8.1 (6.8 to 9.7)	7.6 (6.0 to 9.7)	7.4 (6.2 to 8.7)
72 h	26.6 (21.7 to 32.6)	20.6 (15.4 to 27.5)	7.3 (5.9 to 9.1)	6.9 (5.8 to 8.2)
Day 5	27.3 (22.9 to 32.6)	36.0 (24.5 to 52.9)	12.4 (9.6 to 16.0)	6.8 (5.6 to 8.2)
Day 8	29.2 (23.9 to 35.6)	40.0 (27.0 to 59.1)	35.9 (19.8 to 65.3)	13.2 (10.6 to 16.4)
Day 13	32.9 (24.8 to 43.5)	40.2 (25.7 to 62.9)	40.2 (24.1 to 67.1)	22.7 (15.8 to 32.6)
Day 28	32.2 (23.2 to 44.5)	42.1 (15.7 to 112)	56.6 (22.6 to 142)	36.3 (20.7 to 63.9)
Hospital discharge	24.8 (19.8 to 31.2)	36.7 (18.7 to 72.0)	20.7 (1.7 to 248)	19.7 (-99999 to 99999)

Notes:

[22] - FAS

[23] - FAS

[24] - FAS

[25] - FAS

Statistical analyses

No statistical analyses for this end point

Primary: Relative change of C5a level

End point title	Relative change of C5a level[26]

End point description:

Relative change of C5a level compared to baseline by time point (FAS).
The number of subjects analysed varied between time points.

End point type	Primary

End point timeframe:

At 2 hours (h), 6h, 12h, 24h, 72h, Day 5, Day 8, Day 13, Day 28 after first infusion of IFX-1 or placebo and at hospital discharge

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were defined and performed.

End point values	Placebo Combined	Verum Cohort 1	Verum Cohort 2	Verum Cohort 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24[27]	16[28]	16[29]	16[30]
Units: Percentage				
median (inter-quartile range (Q1-Q3))				
2 h	-7.9 (-18 to 4)	-83.9 (-90 to -79)	-90.7 (-94 to -86)	-88.6 (-92 to -73)
6 h	-3.3 (-9 to 3)	-73.8 (-83 to -70)	-87.6 (-91 to -81)	-81.6 (-89 to -69)
12 h	-6.3 (-14 to 5)	-70.0 (-81 to -58)	-84.5 (-90 to -79)	-76.5 (-88 to -66)
24 h	-1.5 (-16 to 14)	-77.4 (-85 to -61)	-78.9 (-87 to -73)	-72.1 (-85 to -64)
72 h	-5.3 (-16 to 6)	-39.9 (-54 to -18)	-78.8 (-86 to -71)	-74.2 (-86 to -64)
Day 5	-6.8 (-11 to 18)	14.0 (-13 to 40)	-67.1 (-78 to -58)	-73.4 (-86 to -57)
Day 8	8.2 (-10 to 37)	21.4 (-11 to 38)	-16.3 (-53 to 33)	-56.7 (-74 to -15)
Day 13	10.8 (3 to 56)	1.5 (-24 to 42)	-9.3 (-37 to -1)	-5.0 (-33 to 30)
Day 28	24.0 (9 to 52)	39.7 (-20 to 107)	-18.3 (-36 to -11)	20.8 (6 to 40)
Hospital discharge	36.3 (8 to 46)	13.8 (-19 to 36)	-23.5 (-52 to 69)	-76.1 (-76.1 to -76.1)

Notes:

[27] - FAS

[28] - FAS

[29] - FAS

[30] - FAS

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dosing at Day 0 (0h) until Day 28 or hospital discharge, if prior to Day 28. In some cases of prolonged hospital stay after study completion but before database lock, occurrences of adverse events were also reported.

Adverse event reporting additional description:

Safety Analysis Set: All subjects who were randomized and who received any amount of IFX-1 or placebo.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Placebo Combined

Reporting group description:

Intravenous administration of placebo in any of the three cohorts corresponding to the Verum Cohorts 1, 2 and 3. The ratio between IFX-1 and placebo within one dose cohort was 2:1. One patient completed the study at Day 28 after first treatment but stayed in hospital and had a serious fatal adverse event 4 weeks after study completion.

Reporting group title	Verum Cohort 1

Reporting group description:

Intravenous administration of IFX-1 according to the following schedule: 2 x 2 mg/kg body weight (b.w.) on 0 h and 12 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Reporting group title	Verum Cohort 2

Reporting group description:

Intravenous administration of IFX-1 according to the following schedule: 2 x 4 mg/kg body weight (b.w.) on 0 h and 24 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Reporting group title	Verum Cohort 3

Reporting group description:

Intravenous administration of IFX-1 according to the following schedule: 3 x 4 mg/kg body weight (b.w.) on 0 h, 24 h and 72 h. For subjects weighing more than 100 kg the dose calculation was based on 100 kg b.w.

Serious adverse events	Placebo Combined	Verum Cohort 1	Verum Cohort 2
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 24 (54.17%)	10 / 16 (62.50%)	6 / 16 (37.50%)
number of deaths (all causes)	4	6	3
number of deaths resulting from adverse events	4	6	3
Vascular disorders			
Hypotension	Additional description: Hypotension		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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

Hypovolaemic shock	Additional description: Hypovolaemic shock		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Peripheral ischaemia	Additional description: Peripheral ischaemia		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Shock haemorrhagic	Additional description: Shock haemorrhagic		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
General disorders and administration site conditions			
Impaired healing	Additional description: Impaired healing		
subjects affected / exposed	2 / 24 (8.33%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Multi-organ failure	Additional description: Multi-organ failure		
subjects affected / exposed	2 / 24 (8.33%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism	Additional description: Pulmonary embolism		

subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	4 / 24 (16.67%)	2 / 16 (12.50%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Sopor	Additional description: Sopor		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Investigations			
Inflammatory marker increased	Additional description: Inflammatory marker increased		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Injury, poisoning and procedural complications			
Anastomotic leak	Additional description: Anastomotic leak		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal anastomotic leak	Additional description: Gastrointestinal anastomotic leak		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Hepatic rupture	Additional description: Hepatic rupture		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Post procedural haemorrhage	Additional description: Post procedural haemorrhage		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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

Suture related complication	Additional description: Suture related complication		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (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
Vena cava injury	Additional description: Vena cava injury		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Cardiomyopathy	Additional description: Cardiomyopathy		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (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
Tachyarrhythmia	Additional description: Tachyarrhythmia		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Nervous system disorders			
Cerebellar infarction	Additional description: Cerebellar infarction		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Critical illness polyneuropathy	Additional description: Critical illness polyneuropathy		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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

Eye disorders			
Diplopia	Additional description: Diplopia		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
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 disorders			
Gastric perforation	Additional description: Gastric perforation		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Gastrointestinal fistula	Additional description: Gastrointestinal fistula		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Intestinal ischaemia	Additional description: Intestinal ischaemia		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Intestinal perforation	Additional description: Intestinal perforation		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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	Additional description: Intra-abdominal haemorrhage		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Large intestine perforation	Additional description: Large intestine perforation		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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

Pancreatitis necrotising	Additional description: Pancreatitis necrotising		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Small intestinal perforation	Additional description: Small intestinal perforation		
subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Upper gastrointestinal haemorrhage	Additional description: Upper gastrointestinal haemorrhage		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (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			
Acute hepatic failure	Additional description: Acute hepatic failure		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hepatic haematoma	Additional description: Hepatic haematoma		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 24 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infections and infestations			
Abdominal infection	Additional description: Abdominal infection		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Abdominal wall abscess	Additional description: Abdominal wall abscess		

subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Appendicitis	Additional description: Appendicitis		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cholecystitis infective	Additional description: Cholecystitis infective		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (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
Endocarditis	Additional description: Endocarditis		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Gastroenteritis clostridial	Additional description: Gastroenteritis clostridial		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Infection	Additional description: Infection		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Peritonitis	Additional description: Peritonitis		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	2 / 24 (8.33%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Sepsis	Additional description: Sepsis		

subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Septic shock	Additional description: Septic shock		
subjects affected / exposed	4 / 24 (16.67%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Metabolism and nutrition disorders			
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	0 / 24 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Hypervolaemia	Additional description: Hypervolaemia		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (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
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lactic acidosis	Additional description: Lactic acidosis		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Serious adverse events	Verum Cohort 3		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Vascular disorders			
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hypovolaemic shock	Additional description: Hypovolaemic shock		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia	Additional description: Peripheral ischaemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic	Additional description: Shock haemorrhagic		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Impaired healing	Additional description: Impaired healing		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multi-organ failure	Additional description: Multi-organ failure		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism	Additional description: Pulmonary embolism		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Sopor	Additional description: Sopor		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Inflammatory marker increased	Additional description: Inflammatory marker increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Anastomotic leak	Additional description: Anastomotic leak		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal anastomotic leak	Additional description: Gastrointestinal anastomotic leak		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic rupture	Additional description: Hepatic rupture		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage	Additional description: Post procedural haemorrhage		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Suture related complication	Additional description: Suture related complication		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vena cava injury	Additional description: Vena cava injury		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiomyopathy	Additional description: Cardiomyopathy		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Tachyarrhythmia	Additional description: Tachyarrhythmia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebellar infarction	Additional description: Cerebellar infarction		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Critical illness polyneuropathy	Additional description: Critical illness polyneuropathy		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Eye disorders			
Diplopia	Additional description: Diplopia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Gastric perforation	Additional description: Gastric perforation		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal fistula	Additional description: Gastrointestinal fistula		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal ischaemia	Additional description: Intestinal ischaemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation	Additional description: Intestinal perforation		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intra-abdominal haemorrhage	Additional description: Intra-abdominal haemorrhage		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation	Additional description: Large intestine perforation		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pancreatitis necrotising	Additional description: Pancreatitis necrotising		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal perforation	Additional description: Small intestinal perforation		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage	Additional description: Upper gastrointestinal haemorrhage		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Acute hepatic failure	Additional description: Acute hepatic failure		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic haematoma	Additional description: Hepatic haematoma		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal infection	Additional description: Abdominal infection		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal wall abscess	Additional description: Abdominal wall abscess		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis	Additional description: Appendicitis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis infective	Additional description: Cholecystitis infective		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocarditis	Additional description: Endocarditis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis clostridial	Additional description: Gastroenteritis clostridial		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection	Additional description: Infection		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritonitis	Additional description: Peritonitis		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis	Additional description: Sepsis		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock	Additional description: Septic shock		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypervolaemia	Additional description: Hypervolaemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lactic acidosis	Additional description: Lactic acidosis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo Combined	Verum Cohort 1	Verum Cohort 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 24 (83.33%)	13 / 16 (81.25%)	10 / 16 (62.50%)
Vascular disorders			
Haemorrhage	Additional description: Haemorrhage		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypertension	Additional description: Hypertension		

subjects affected / exposed	2 / 24 (8.33%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Jugular vein thrombosis	Additional description: Jugular vein thrombosis		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Poor peripheral circulation	Additional description: Poor peripheral circulation		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Endotracheal intubation	Additional description: Endotracheal intubation		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Catheter site hypersensitivity	Additional description: Catheter site hypersensitivity		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Generalised oedema	Additional description: Generalised oedema		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hyperpyrexia	Additional description: Hyperpyrexia		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hyperthermia	Additional description: Hyperthermia		
subjects affected / exposed	2 / 24 (8.33%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Impaired healing	Additional description: Impaired healing		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Injection site haematoma	Additional description: Injection site haematoma		

subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Malaise	Additional description: Malaise		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Oedema	Additional description: Oedema		
subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	3 / 24 (12.50%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome	Additional description: Acute respiratory distress syndrome		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bronchial obstruction	Additional description: Bronchial obstruction		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cough	Additional description: Cough		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypercapnia	Additional description: Hypercapnia		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypoventilation	Additional description: Hypoventilation		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pleural effusion	Additional description: Pleural effusion		

subjects affected / exposed	1 / 24 (4.17%)	2 / 16 (12.50%)	2 / 16 (12.50%)
occurrences (all)	1	2	2
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pulmonary oedema	Additional description: Pulmonary oedema		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Respiration abnormal	Additional description: Respiration abnormal		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Agitation	Additional description: Agitation		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Delirium	Additional description: Delirium		
subjects affected / exposed	4 / 24 (16.67%)	2 / 16 (12.50%)	2 / 16 (12.50%)
occurrences (all)	4	2	2
Depression	Additional description: Depression		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Restlessness	Additional description: Restlessness		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Sopor	Additional description: Sopor		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Investigations			
Activated partial thromboplastin time prolonged	Additional description: Activated partial thromboplastin time prolonged		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased	Additional description: Blood bilirubin increased		

subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased	Additional description: Blood lactate dehydrogenase increased		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Body temperature decreased	Additional description: Body temperature decreased		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Body temperature increased	Additional description: Body temperature increased		
subjects affected / exposed	1 / 24 (4.17%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	1	3	0
Glutamate dehydrogenase increased	Additional description: Glutamate dehydrogenase increased		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Haematocrit decreased	Additional description: Haematocrit decreased		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	6 / 24 (25.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	8	3	1
Hepatic enzyme increased	Additional description: Hepatic enzyme increased		
subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Lipase increased	Additional description: Lipase increased		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Myocardial necrosis marker increased	Additional description: Myocardial necrosis marker increased		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Myoglobin blood increased	Additional description: Myoglobin blood increased		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oxygen saturation decreased	Additional description: Oxygen saturation decreased		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
PaO2/FIO2 ratio decreased	Additional description: PaO2/FIO2 ratio decreased		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	3 / 24 (12.50%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	3	0	0
Platelet count increased	Additional description: Platelet count increased		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	0 / 24 (0.00%)	2 / 16 (12.50%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Injury, poisoning and procedural complications			
Endotracheal intubation complication	Additional description: Endotracheal intubation complication		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Post procedural bile leak	Additional description: Post procedural bile leak		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Post procedural complication	Additional description: Post procedural complication		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Post procedural haemorrhage	Additional description: Post procedural haemorrhage		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Psychosis postoperative	Additional description: Psychosis postoperative		

subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Seroma	Additional description: Seroma		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Shunt thrombosis	Additional description: Shunt thrombosis		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Wound secretion	Additional description: Wound secretion		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Arrhythmia	Additional description: Arrhythmia		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	3 / 24 (12.50%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	4	1	1
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bradycardia	Additional description: Bradycardia		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	3
Myocardial ischaemia	Additional description: Myocardial ischaemia		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles	Additional description: Supraventricular extrasystoles		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Supraventricular tachycardia	Additional description: Supraventricular tachycardia		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Tachyarrhythmia	Additional description: Tachyarrhythmia		
subjects affected / exposed	5 / 24 (20.83%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	6	2	0
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Nervous system disorders			
Critical illness polyneuropathy	Additional description: Critical illness polyneuropathy		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention	Additional description: Disturbance in attention		
subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Epilepsy	Additional description: Epilepsy		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Headache	Additional description: Headache		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypertonia	Additional description: Hypertonia		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy	Additional description: Polyneuropathy		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Seizure	Additional description: Seizure		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	3 / 24 (12.50%)	2 / 16 (12.50%)	6 / 16 (37.50%)
occurrences (all)	3	2	7
Coagulopathy	Additional description: Coagulopathy		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Haemorrhagic anaemia	Additional description: Haemorrhagic anaemia		

subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	3 / 24 (12.50%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	3	2	0
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	1 / 24 (4.17%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Thrombocytosis	Additional description: Thrombocytosis		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Ascites	Additional description: Ascites		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Duodenal ulcer	Additional description: Duodenal ulcer		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastritis	Additional description: Gastritis		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal motility disorder	Additional description: Gastrointestinal motility disorder		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Impaired gastric emptying	Additional description: Impaired gastric emptying		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Intra-abdominal haematoma	Additional description: Intra-abdominal haematoma		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nausea	Additional description: Nausea		
subjects affected / exposed	2 / 24 (8.33%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	2	2	0
Oesophageal haemorrhage	Additional description: Oesophageal haemorrhage		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage	Additional description: Rectal haemorrhage		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Small intestinal perforation	Additional description: Small intestinal perforation		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Vomiting	Additional description: Vomiting		
subjects affected / exposed	2 / 24 (8.33%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Hepatobiliary disorders			
Cholestasis	Additional description: Cholestasis		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gallbladder perforation	Additional description: Gallbladder perforation		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hepatic failure	Additional description: Hepatic failure		

subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatocellular injury	Additional description: Hepatocellular injury		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Perforation bile duct	Additional description: Perforation bile duct		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Lividity	Additional description: Lividity		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Penile ulceration	Additional description: Penile ulceration		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Rash	Additional description: Rash		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Renal impairment	Additional description: Renal impairment		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism	Additional description: Hypothyroidism		
subjects affected / exposed	2 / 24 (8.33%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Infections and infestations			
Abdominal abscess	Additional description: Abdominal abscess		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Clostridium difficile colitis	Additional description: Clostridium difficile colitis		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Cystitis	Additional description: Cystitis		

subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Device related infection	Additional description: Device related infection		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Fungal infection	Additional description: Fungal infection		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Otitis media	Additional description: Otitis media		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Peritonitis	Additional description: Peritonitis		
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	2 / 24 (8.33%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	3 / 24 (12.50%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	3	1	0
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	2 / 24 (8.33%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	2	5	0
Hypernatraemia	Additional description: Hypernatraemia		
subjects affected / exposed	4 / 24 (16.67%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	4	2	1
Hyperuricaemia	Additional description: Hyperuricaemia		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	2 / 24 (8.33%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1

Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Hypoglycaemia	Additional description: Hypoglycaemia		
subjects affected / exposed	1 / 24 (4.17%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	3 / 24 (12.50%)	1 / 16 (6.25%)	2 / 16 (12.50%)
occurrences (all)	3	1	2
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Metabolic acidosis	Additional description: Metabolic acidosis		
subjects affected / exposed	0 / 24 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Verum Cohort 3		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 16 (87.50%)		
Vascular disorders			
Haemorrhage	Additional description: Haemorrhage		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypertension	Additional description: Hypertension		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Jugular vein thrombosis	Additional description: Jugular vein thrombosis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Poor peripheral circulation	Additional description: Poor peripheral circulation		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Endotracheal intubation	Additional description: Endotracheal intubation		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Catheter site hypersensitivity	Additional description: Catheter site hypersensitivity		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Generalised oedema	Additional description: Generalised oedema		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hyperpyrexia	Additional description: Hyperpyrexia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hyperthermia	Additional description: Hyperthermia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Impaired healing	Additional description: Impaired healing		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Injection site haematoma	Additional description: Injection site haematoma		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Malaise	Additional description: Malaise		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oedema	Additional description: Oedema		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oedema peripheral	Additional description: Oedema peripheral		

subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome	Additional description: Acute respiratory distress syndrome		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Bronchial obstruction	Additional description: Bronchial obstruction		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cough	Additional description: Cough		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypercapnia	Additional description: Hypercapnia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypoventilation	Additional description: Hypoventilation		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pulmonary oedema	Additional description: Pulmonary oedema		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Respiration abnormal	Additional description: Respiration abnormal		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Agitation	Additional description: Agitation		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Delirium	Additional description: Delirium		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Depression	Additional description: Depression		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Restlessness	Additional description: Restlessness		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Sopor	Additional description: Sopor		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Investigations			
Activated partial thromboplastin time prolonged	Additional description: Activated partial thromboplastin time prolonged		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased	Additional description: Blood lactate dehydrogenase increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood potassium decreased	Additional description: Blood potassium decreased		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Body temperature decreased	Additional description: Body temperature decreased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Body temperature increased	Additional description: Body temperature increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Glutamate dehydrogenase increased	Additional description: Glutamate dehydrogenase increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Haematocrit decreased	Additional description: Haematocrit decreased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hepatic enzyme increased	Additional description: Hepatic enzyme increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Lipase increased	Additional description: Lipase increased		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Myocardial necrosis marker increased	Additional description: Myocardial necrosis marker increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Myoglobin blood increased	Additional description: Myoglobin blood increased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oxygen saturation decreased	Additional description: Oxygen saturation decreased		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		

PaO2/FIO2 ratio decreased	Additional description: PaO2/FIO2 ratio decreased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Platelet count increased	Additional description: Platelet count increased		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Endotracheal intubation complication	Additional description: Endotracheal intubation complication		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Post procedural bile leak	Additional description: Post procedural bile leak		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Post procedural complication	Additional description: Post procedural complication		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Post procedural haemorrhage	Additional description: Post procedural haemorrhage		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Psychosis postoperative	Additional description: Psychosis postoperative		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Seroma	Additional description: Seroma		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Shunt thrombosis	Additional description: Shunt thrombosis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Wound secretion	Additional description: Wound secretion		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Arrhythmia	Additional description: Arrhythmia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Bradycardia	Additional description: Bradycardia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Myocardial ischaemia	Additional description: Myocardial ischaemia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Supraventricular extrasystoles	Additional description: Supraventricular extrasystoles		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Supraventricular tachycardia	Additional description: Supraventricular tachycardia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tachyarrhythmia	Additional description: Tachyarrhythmia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Critical illness polyneuropathy	Additional description: Critical illness polyneuropathy		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Disturbance in attention	Additional description: Disturbance in attention		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Epilepsy	Additional description: Epilepsy		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Headache	Additional description: Headache		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypertonia	Additional description: Hypertonia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Polyneuropathy	Additional description: Polyneuropathy		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Seizure	Additional description: Seizure		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Coagulopathy	Additional description: Coagulopathy		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Haemorrhagic anaemia	Additional description: Haemorrhagic anaemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Thrombocytosis	Additional description: Thrombocytosis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ascites	Additional description: Ascites		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Constipation	Additional description: Constipation		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Duodenal ulcer	Additional description: Duodenal ulcer		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gastritis	Additional description: Gastritis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gastrointestinal motility disorder	Additional description: Gastrointestinal motility disorder		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Impaired gastric emptying	Additional description: Impaired gastric emptying		

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Intra-abdominal haematoma	Additional description: Intra-abdominal haematoma		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nausea	Additional description: Nausea		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Oesophageal haemorrhage	Additional description: Oesophageal haemorrhage		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rectal haemorrhage	Additional description: Rectal haemorrhage		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Small intestinal perforation	Additional description: Small intestinal perforation		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Cholestasis	Additional description: Cholestasis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Gallbladder perforation	Additional description: Gallbladder perforation		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hepatic failure	Additional description: Hepatic failure		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hepatocellular injury	Additional description: Hepatocellular injury		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Perforation bile duct	Additional description: Perforation bile duct		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

Skin and subcutaneous tissue disorders			
Lividity	Additional description: Lividity		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Penile ulceration	Additional description: Penile ulceration		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rash	Additional description: Rash		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Renal impairment	Additional description: Renal impairment		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism	Additional description: Hypothyroidism		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Abdominal abscess	Additional description: Abdominal abscess		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Clostridium difficile colitis	Additional description: Clostridium difficile colitis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cystitis	Additional description: Cystitis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Device related infection	Additional description: Device related infection		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Fungal infection	Additional description: Fungal infection		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

Otitis media	Additional description: Otitis media		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Peritonitis	Additional description: Peritonitis		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypernatraemia	Additional description: Hypernatraemia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hyperuricaemia	Additional description: Hyperuricaemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypoglycaemia	Additional description: Hypoglycaemia		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypokalaemia	Additional description: Hypokalaemia		

subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Metabolic acidosis	Additional description: Metabolic acidosis		
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported