



Clinical trial results:

A RANDOMIZED, OPEN-LABEL, MULTICENTER, CONTROLLED STUDY TO ASSESS SAFETY AND EFFICACY OF ELAD IN SUBJECTS WITH ALCOHOL-INDUCED LIVER DECOMPENSATION (AILD)

Summary

EudraCT number	2012-005563-27
Trial protocol	GB DE ES
Global end of trial date	07 May 2015

Results information

Result version number	v1 (current)
This version publication date	30 September 2016
First version publication date	30 September 2016

Trial information

Trial identification

Sponsor protocol code	VTI-208
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01471028
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vital Therapies, Inc.
Sponsor organisation address	15010 Avenue of Science, Suite 200, San Diego, United States, 92128
Public contact	Duane Nash, President, Vital Therapies, Inc., 001 858-673-6840, dnash@vitaltherapies.com
Scientific contact	Robert Ashley, Chief Technical Officer, Vital Therapies, Inc., 001 858-673-6840, rashley@vitaltherapies.com

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	31 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 May 2015
Global end of trial reached?	Yes
Global end of trial date	07 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate safety and efficacy of ELAD with respect to overall survival (OS) of subjects with a clinical diagnosis of alcohol-induced liver decompensation (AILD) up to at least Study Day 91, with follow-up Protocol VTI-208E providing additional survival data up to a maximum of 5 years that will be included, as available, through VTI-208 study termination (after the last surviving enrolled subject completes Study Day 91). This will be assessed using a Kaplan-Meier survival analysis of the ITT population utilizing a log-rank test.

Protection of trial subjects:

Continuous monitoring of the ELAD System by trained ELAD Specialists during ELAD treatment. Administration of diphenhydramine or equivalent immediately prior to initiation of ELAD treatment to prevent hypersensitivity reactions.

Background therapy:

The majority of subjects with AILD present with clinical characteristics of alcoholic hepatitis (AH). The Standard of Care (background therapy) for the secondary medical problems associated with AH was derived from the practice guidelines issued by the American Association for the Study of Liver Disease (AASLD) and the European Association for the Study of Liver (EASL). These guidelines were applied to both the ELAD-treated and Control subjects during this study.

Evidence for comparator:

VTI-208 was a randomized, multicenter, open-label, concurrent control study of subjects with AILD. Subjects meeting the eligibility requirements of the study received either standard of care treatment for AILD (as defined in the protocol) plus treatment with the ELAD System (ELAD group) or standard of care treatment for AILD alone (Control group).

Treatment options for patients with AILD are limited. The majority of subjects with AILD present with clinical characteristics of AH. Patients with severe AH (defined as a Maddrey Discriminant Function of ≥ 32) have a poor prognosis, with 90-day survival of around 50%. Regimens that have been used for the past 40 years, including corticosteroids, theophylline with corticosteroids, pentoxifylline, and infliximab, have had no significant effect on the long term survival of patients with AILD.

Of particular importance are the results of the UK NIHR-supported STOPAH study, a study in alcoholic hepatitis reporting out in 2015. Results from this study, which randomized 1103 subjects in 40 clinical sites in the UK, showed that the administration of steroids and pentoxifylline had no effect on survival at 90 days either alone or in combination.

While a sham control is a potential comparator, regulatory and ethical bodies have determined that the administration of a sham extracorporeal therapy without the possibility of benefit is unethical, and therefore could not be considered for study VTI-208. Consequently, the best available standard of care in accord with AASLD and EASL guidelines was recommended in the VTI-208 study protocol for all participants irrespective of treatment arm.

Actual start date of recruitment	20 March 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety, Ethical reason, Regulatory reason, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	United States: 176
Country: Number of subjects enrolled	Australia: 15
Worldwide total number of subjects	203
EEA total number of subjects	12

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)	198
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with clinical (protocol-guided) or biopsy-proven evidence of AILD who met study inclusion/exclusion criteria were eligible for participation in the study. Subjects were recruited from March 2013 through February 2015 in the United States, United Kingdom and Australia.

Pre-assignment

Screening details:

A total of 372 participants were screened, out of which 169 were screen failures, and 203 were randomized, of which 95 received ELAD treatment. Of the 203 subjects randomized, 193 had AH; 10 had non-AH AILD. Participants who successfully completed the initial 91-day treatment period were entered into a 5-year extension phase (VTI-208E) of the study.

Period 1

Period 1 title	VTI-208
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Investigative staff who carried out follow-up treatment visits were blinded to participant treatment assignment. Home visit staff who carried out weekly home visits for participants discharged from the hospital were also blinded to participant treatment assignment. Sponsor staff, with the exception of those involved in the monitoring of study safety, were blinded to treatment outcomes. The Data and Safety Monitoring Board was blinded to study outcomes.

Arms

Are arms mutually exclusive?	Yes
Arm title	ELAD Treatment

Arm description:

Participants randomized to the ELAD group received ELAD treatment plus protocol-directed Standard of Care treatment for a period of up to 5 days followed by Standard of Care treatment through Study Day 91.

Arm type	Experimental
Investigational medicinal product name	ELAD
Investigational medicinal product code	ELAD System
Other name	VTL C3A cells
Pharmaceutical forms	Living tissue equivalent
Routes of administration	Haemodialysis

Dosage and administration details:

Four cartridges, each containing approximately 110 grams of VTL C3A cells (approximately 440 grams total or approximately 20% to 30% of the native liver, a residual mass necessary for survival). ELAD treatment duration spans for up to 5 days. Continuous extracorporeal circulation by central venous catheter allowing plasma fraction interaction with VTL C3A cells incorporated in ELAD C3A cell cartridges.

Arm title	Control
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Arm description:

Participants randomized to the Control group received protocol-directed Standard of Care treatment in accord with AASLD and EASL guidelines for up to 91 days.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	ELAD Treatment	Control
Started	96	107
Completed Study VTI-208	56	63
Completed	56	63
Not completed	40	44
Adverse event, serious fatal	39	41
Consent withdrawn by subject	-	2
Lost to follow-up	1	1

Period 2

Period 2 title	VTI-208E
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	ELAD Treatment

Arm description:

Participants randomized to the ELAD group and who received ELAD treatment plus protocol-directed Standard of Care treatment for a period of up to 5 days during study VTI-208 were followed up for up to 5 years.

Arm type	Experimental
Investigational medicinal product name	ELAD
Investigational medicinal product code	ELAD System
Other name	VTL C3A cells
Pharmaceutical forms	Living tissue equivalent
Routes of administration	Haemodialysis

Dosage and administration details:

Four cartridges, each containing approximately 110 grams of VTL C3A cells (approximately 440 grams total or approximately 20% to 30% of the native liver, a residual mass necessary for survival). ELAD treatment duration spans for up to 5 days. Continuous extracorporeal circulation by central venous catheter allowing plasma fraction interaction with VTL C3A cells incorporated in ELAD C3A cell cartridges.

Arm title	Control
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Arm description:

Participants randomized to the Control group and who received protocol-directed Standard of Care during the VTI-208 study in accord with AASLD and EASL guidelines were followed up for up to 5 years.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	ELAD Treatment	Control
Started	56	63
Data Lock, 31 July 2015	56	63
Completed	48	51
Not completed	8	12
Adverse event, serious fatal	7	10
Consent withdrawn by subject	1	-
Lost to follow-up	-	2

Baseline characteristics

Reporting groups

Reporting group title	ELAD Treatment
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Reporting group description:

Participants randomized to the ELAD group received ELAD treatment plus protocol-directed Standard of Care treatment for a period of up to 5 days followed by Standard of Care treatment through Study Day 91.

Reporting group title	Control
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Reporting group description:

Participants randomized to the Control group received protocol-directed Standard of Care treatment in accord with AASLD and EASL guidelines for up to 91 days.

Reporting group values	ELAD Treatment	Control	Total
Number of subjects	96	107	203
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	94	104	198
From 65-84 years	2	3	5
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	46.5	44.8	
standard deviation	± 9.06	± 10.66	-
Gender categorical			
Units: Subjects			
Female	41	42	83
Male	55	65	120
Race			
Units: Subjects			
White	84	91	175
Black or African American	7	9	16
Asian	2	2	4
Native Hawaiian or Other Pacific Islander	0	0	0
American Indian or Alaskan Native	0	1	1
Other	3	4	7
Baseline MELD			
Baseline value of the Model for End Stage Liver Disease score.			
Units: MELD score			
arithmetic mean	27.6	27.1	
standard deviation	± 3.94	± 3.79	-

End points

End points reporting groups

Reporting group title	ELAD Treatment
Reporting group description: Participants randomized to the ELAD group received ELAD treatment plus protocol-directed Standard of Care treatment for a period of up to 5 days followed by Standard of Care treatment through Study Day 91.	
Reporting group title	Control
Reporting group description: Participants randomized to the Control group received protocol-directed Standard of Care treatment in accord with AASLD and EASL guidelines for up to 91 days.	
Reporting group title	ELAD Treatment
Reporting group description: Participants randomized to the ELAD group and who received ELAD treatment plus protocol-directed Standard of Care treatment for a period of up to 5 days during study VTI-208 were followed up for up to 5 years.	
Reporting group title	Control
Reporting group description: Participants randomized to the Control group and who received protocol-directed Standard of Care during the VTI-208 study in accord with AASLD and EASL guidelines were followed up for up to 5 years.	

Primary: Overall Survival

End point title	Overall Survival
End point description: The primary endpoint of the study was a comparison of overall survival between the ELAD-treated and Control groups defined by a Kaplan-Meier analysis of survival up to at least Study Day 91, with protocol VTI-208E providing additional survival data up to a maximum of 5 years, that was included as available at the time of database lock (31 July 2015).	
End point type	Primary
End point timeframe: Up to at least Study Day 91, with protocol VTI-208E providing additional survival data up to 5 years from randomization.	

End point values	ELAD Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	107		
Units: subjects				
Alive	48	51		
Dead	46	51		
Withdrew Consent	1	2		
Lost to Follow-Up	1	3		

Attachments (see zip file)	Summary - K-M Analysis of Overall Survival-ITT Pop/f14.2.1a-

Statistical analyses

Statistical analysis title	Kaplan-Meier Analysis of Overall Survival
Statistical analysis description:	
The primary endpoint was assessed using a Kaplan-Meier survival analysis of the Intent-to-treat (ITT) population utilizing a log-rank test.	
Comparison groups	ELAD Treatment v Control
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.027
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.689
upper limit	1.53

Secondary: Proportion of Survivors at Study Day 91

End point title	Proportion of Survivors at Study Day 91
End point description:	
Proportion of survivors at Study Day 91.	
End point type	Secondary
End point timeframe:	
Up to Study Day 91.	

End point values	ELAD Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	107		
Units: subjects				
Alive	57	66		
Dead	39	41		

Attachments (see zip file)	Proportion of Survivors at Study Day 91-ITT/t14.2.4.1a-t-
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Statistical analyses

Statistical analysis title	Proportion of Survivors at Study Day 91
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Statistical analysis description:

Proportion of Survivors at Study Day 91

Comparison groups	ELAD Treatment v Control
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Randomization through Study Day 91.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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Reporting groups

Reporting group title	ELAD Treatment
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Reporting group description:

Participants received ELAD treatment plus protocol-guided standard of care for a period of up to 5 days followed by standard of care through Study Day 91.

Reporting group title	Control
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Reporting group description:

Subjects randomized to the Control group received protocol-guided standard of care in accord with AASLD and EASL guidelines for up to 91 days.

Serious adverse events	ELAD Treatment	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	73 / 95 (76.84%)	75 / 108 (69.44%)	
number of deaths (all causes)	38	42	
number of deaths resulting from adverse events	2	0	
Vascular disorders			
Cerebellar haemorrhage			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	7 / 95 (7.37%)	6 / 108 (5.56%)	
occurrences causally related to treatment / all	3 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 2	
Haematochezia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypotension			
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	2 / 95 (2.11%)	4 / 108 (3.70%)	
occurrences causally related to treatment / all	1 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Shock			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Shock haemorrhagic			

subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothermia			

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	7 / 95 (7.37%)	10 / 108 (9.26%)	
occurrences causally related to treatment / all	1 / 7	0 / 10	
deaths causally related to treatment / all	1 / 5	0 / 9	
Pyrexia			
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	5 / 95 (5.26%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Bacterial test positive			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Hepatotoxicity			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac tamponade			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			

subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	8 / 95 (8.42%)	6 / 108 (5.56%)	
occurrences causally related to treatment / all	0 / 11	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 95 (8.42%)	6 / 108 (5.56%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	3 / 95 (3.16%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 95 (1.05%)	4 / 108 (3.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diarrhoea			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 95 (1.05%)	3 / 108 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 95 (1.05%)	3 / 108 (2.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatobiliary disorders			
Ascites			
subjects affected / exposed	6 / 95 (6.32%)	13 / 108 (12.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	13 / 95 (13.68%)	10 / 108 (9.26%)	
occurrences causally related to treatment / all	0 / 14	0 / 10	
deaths causally related to treatment / all	0 / 12	0 / 10	
Hepatitis alcoholic			
subjects affected / exposed	2 / 95 (2.11%)	4 / 108 (3.70%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 3	
Hepatorenal syndrome			
subjects affected / exposed	3 / 95 (3.16%)	9 / 108 (8.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 2	0 / 5	
Hyperammonaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cellulitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Emphysematous cystitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	4 / 95 (4.21%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Renal failure acute			
subjects affected / exposed	6 / 95 (6.32%)	12 / 108 (11.11%)	
occurrences causally related to treatment / all	1 / 6	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal impairment			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Peritonitis bacterial			
subjects affected / exposed	2 / 95 (2.11%)	3 / 108 (2.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial infection			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Device related sepsis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterial infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 95 (2.11%)	6 / 108 (5.56%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	4 / 95 (4.21%)	2 / 108 (1.85%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Urinary tract infection			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	2 / 95 (2.11%)	3 / 108 (2.78%)	
occurrences causally related to treatment / all	1 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Generalised oedema			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ELAD Treatment	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	95 / 95 (100.00%)	107 / 108 (99.07%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon adenoma			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Colonic polyp			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Abdominal compartment syndrome			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences (all)	2	0	
Aneurysm			

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Angiopathy		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Aortic aneurysm		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Aortic arteriosclerosis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Arteriosclerosis		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Arteriospasm coronary		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Cardiovascular deconditioning		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Contusion		
subjects affected / exposed	8 / 95 (8.42%)	6 / 108 (5.56%)
occurrences (all)	8	6
Coronary artery disease		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Cyanosis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Deep vein thrombosis		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	2	1
Dizziness postural		
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	2	1
Gastric haemorrhage		

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Gastric varices		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Gastrointestinal haemorrhage		
subjects affected / exposed	4 / 95 (4.21%)	4 / 108 (3.70%)
occurrences (all)	4	4
Gingival bleeding		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Haematochezia		
subjects affected / exposed	3 / 95 (3.16%)	4 / 108 (3.70%)
occurrences (all)	3	4
Haematoma		
subjects affected / exposed	6 / 95 (6.32%)	3 / 108 (2.78%)
occurrences (all)	6	3
Haemodynamic instability		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Haemoptysis		
subjects affected / exposed	3 / 95 (3.16%)	2 / 108 (1.85%)
occurrences (all)	3	2
Haemorrhage		
subjects affected / exposed	4 / 95 (4.21%)	0 / 108 (0.00%)
occurrences (all)	5	0
Haemorrhage intracranial		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Haemorrhage urinary tract		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Haemorrhoids		
subjects affected / exposed	5 / 95 (5.26%)	8 / 108 (7.41%)
occurrences (all)	5	8
Haemothorax		

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hypertension		
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)
occurrences (all)	1	2
Hypotension		
subjects affected / exposed	29 / 95 (30.53%)	18 / 108 (16.67%)
occurrences (all)	37	20
Hypovolaemic shock		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Melaena		
subjects affected / exposed	5 / 95 (5.26%)	3 / 108 (2.78%)
occurrences (all)	6	4
Mucosal haemorrhage		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Orthostatic hypotension		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Pallor		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Penile haemorrhage		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Peripheral artery aneurysm		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Petechiae		
subjects affected / exposed	4 / 95 (4.21%)	2 / 108 (1.85%)
occurrences (all)	5	2
Pharyngeal haemorrhage		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Portal hypertensive gastropathy		

subjects affected / exposed	3 / 95 (3.16%)	9 / 108 (8.33%)
occurrences (all)	3	9
Portal vein thrombosis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Presyncope		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Procedural haemorrhage		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Pulmonary alveolar haemorrhage		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Pulmonary congestion		
subjects affected / exposed	5 / 95 (5.26%)	0 / 108 (0.00%)
occurrences (all)	5	0
Pulmonary hypertension		
subjects affected / exposed	4 / 95 (4.21%)	0 / 108 (0.00%)
occurrences (all)	4	0
Purpura		
subjects affected / exposed	0 / 95 (0.00%)	3 / 108 (2.78%)
occurrences (all)	0	3
Retroperitoneal haemorrhage		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Scrotal haematoma		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Septic shock		
subjects affected / exposed	5 / 95 (5.26%)	1 / 108 (0.93%)
occurrences (all)	5	1
Shock		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Shock haemorrhagic		

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Spider naevus		
subjects affected / exposed	5 / 95 (5.26%)	5 / 108 (4.63%)
occurrences (all)	5	5
Splenic infarction		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Splenic varices		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Splenic vein thrombosis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	2
Syncope		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Systemic inflammatory response syndrome		
subjects affected / exposed	2 / 95 (2.11%)	3 / 108 (2.78%)
occurrences (all)	2	3
Telangiectasia		
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)
occurrences (all)	0	2
Upper gastrointestinal haemorrhage		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Urogenital haemorrhage		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Vaginal haemorrhage		
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)
occurrences (all)	3	1
Varices oesophageal		
subjects affected / exposed	3 / 95 (3.16%)	6 / 108 (5.56%)
occurrences (all)	3	6

Vascular anomaly subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	0 / 108 (0.00%) 0	
Vasodilatation subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Surgical and medical procedures			
Biliary drainage subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Bladder catheterisation subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Central venous catheterisation subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Extubation subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Intravenous catheter management subjects affected / exposed occurrences (all)	4 / 95 (4.21%) 4	0 / 108 (0.00%) 0	
Removal of foreign body from external ear subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Suture insertion subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Wound drainage subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
General disorders and administration site conditions			
Administration site pain subjects affected / exposed occurrences (all)	4 / 95 (4.21%) 4	0 / 108 (0.00%) 0	
Asthenia			

subjects affected / exposed	6 / 95 (6.32%)	12 / 108 (11.11%)
occurrences (all)	7	14
Catheter site haemorrhage		
subjects affected / exposed	9 / 95 (9.47%)	4 / 108 (3.70%)
occurrences (all)	10	4
Chest pain		
subjects affected / exposed	8 / 95 (8.42%)	5 / 108 (4.63%)
occurrences (all)	9	5
Cyst		
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)
occurrences (all)	0	2
Device component issue		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Device damage		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Device occlusion		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Effusion		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	2
Fatigue		
subjects affected / exposed	7 / 95 (7.37%)	6 / 108 (5.56%)
occurrences (all)	7	7
Feeling abnormal		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Gait disturbance		
subjects affected / exposed	1 / 95 (1.05%)	3 / 108 (2.78%)
occurrences (all)	1	3
Hyperthermia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hypothermia		

subjects affected / exposed	4 / 95 (4.21%)	1 / 108 (0.93%)
occurrences (all)	4	1
Inflammation		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Infusion site haemorrhage		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Local swelling		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Malaise		
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)
occurrences (all)	0	2
Medical device complication		
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	3	1
Mucosal dryness		
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)
occurrences (all)	1	2
Multi-organ failure		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Pain		
subjects affected / exposed	7 / 95 (7.37%)	9 / 108 (8.33%)
occurrences (all)	8	10
Puncture site haemorrhage		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Puncture site pain		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Pyrexia		
subjects affected / exposed	25 / 95 (26.32%)	10 / 108 (9.26%)
occurrences (all)	28	10
Secretion discharge		

subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Temperature intolerance subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Ulcer subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Oedema peripheral subjects affected / exposed occurrences (all)	32 / 95 (33.68%) 38	33 / 108 (30.56%) 41	
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Reproductive system and breast disorders Breast mass subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Cervical dysplasia subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Genital swelling subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Gynaecomastia subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1	
Menorrhagia subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Prostatic calcification subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Scrotal irritation			

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Scrotal oedema			
subjects affected / exposed	1 / 95 (1.05%)	4 / 108 (3.70%)	
occurrences (all)	2	4	
Scrotal pain			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Vaginal infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Vaginal lesion			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Acquired diaphragmatic eventration			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Acute respiratory distress syndrome			
subjects affected / exposed	4 / 95 (4.21%)	2 / 108 (1.85%)	
occurrences (all)	5	2	
Acute respiratory failure			
subjects affected / exposed	6 / 95 (6.32%)	2 / 108 (1.85%)	
occurrences (all)	6	2	
Asthma			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Atelectasis			
subjects affected / exposed	14 / 95 (14.74%)	6 / 108 (5.56%)	
occurrences (all)	15	6	
Bronchial disorder			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Bronchospasm			

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Cough		
subjects affected / exposed	6 / 95 (6.32%)	8 / 108 (7.41%)
occurrences (all)	6	8
Dry throat		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Dyspnoea		
subjects affected / exposed	21 / 95 (22.11%)	21 / 108 (19.44%)
occurrences (all)	25	26
Epistaxis		
subjects affected / exposed	10 / 95 (10.53%)	6 / 108 (5.56%)
occurrences (all)	11	6
Hepatic hydrothorax		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hiccups		
subjects affected / exposed	1 / 95 (1.05%)	3 / 108 (2.78%)
occurrences (all)	1	3
Hyperventilation		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hypopnoea		
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)
occurrences (all)	3	1
Hypoventilation		
subjects affected / exposed	4 / 95 (4.21%)	0 / 108 (0.00%)
occurrences (all)	4	0
Hypoxia		
subjects affected / exposed	6 / 95 (6.32%)	4 / 108 (3.70%)
occurrences (all)	6	4

Increased bronchial secretion subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	1 / 108 (0.93%) 1
Influenza subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Laryngitis bacterial subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Lower respiratory tract infection subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	0 / 108 (0.00%) 0
Lung consolidation subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0
Lung disorder subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0
Lung infiltration subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	2 / 108 (1.85%) 2
Lung neoplasm subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Nasal congestion subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1
Nasal dryness subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1

Obstructive airways disorder subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 95 (5.26%) 5	4 / 108 (3.70%) 4
Pharyngeal erythema subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1
Pleural effusion subjects affected / exposed occurrences (all)	12 / 95 (12.63%) 12	14 / 108 (12.96%) 14
Pleuritic pain subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Pneumonia aspiration subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	2 / 108 (1.85%) 2
Pneumothorax subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 4	1 / 108 (0.93%) 1
Productive cough subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	2 / 108 (1.85%) 2
Pulmonary mass subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0
Pulmonary oedema subjects affected / exposed occurrences (all)	7 / 95 (7.37%) 8	5 / 108 (4.63%) 5
Rales subjects affected / exposed occurrences (all)	8 / 95 (8.42%) 8	6 / 108 (5.56%) 6
Respiration abnormal subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0

Respiratory acidosis subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Respiratory alkalosis subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	1 / 108 (0.93%) 1	
Respiratory distress subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 3	0 / 108 (0.00%) 0	
respiratory failure subjects affected / exposed occurrences (all)	6 / 95 (6.32%) 6	4 / 108 (3.70%) 4	
Respiratory tract congestion subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Rhonchi subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1	
Sleep apnoea syndrome subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	2 / 108 (1.85%) 2	
Tachypnoea subjects affected / exposed occurrences (all)	7 / 95 (7.37%) 7	6 / 108 (5.56%) 7	
Vocal cord disorder subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Wheezing subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 3	4 / 108 (3.70%) 4	
Psychiatric disorders Adjustment disorder			

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Aggression		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Agitation		
subjects affected / exposed	16 / 95 (16.84%)	8 / 108 (7.41%)
occurrences (all)	17	8
Alcohol abuse		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Amnesia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	2	0
Anxiety		
subjects affected / exposed	21 / 95 (22.11%)	9 / 108 (8.33%)
occurrences (all)	22	10
Apraxia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Catatonia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Circadian rhythm sleep disorder		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Confusional state		
subjects affected / exposed	14 / 95 (14.74%)	3 / 108 (2.78%)
occurrences (all)	14	3
Delirium		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Delirium tremens		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Delusion		

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Depression		
subjects affected / exposed	7 / 95 (7.37%)	7 / 108 (6.48%)
occurrences (all)	7	7
Emotional distress		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Failure to thrive		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Hallucination		
subjects affected / exposed	3 / 95 (3.16%)	2 / 108 (1.85%)
occurrences (all)	3	2
Hallucination, auditory		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Hallucination, visual		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hypophagia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Irritability		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Irritable bowel syndrome		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Korsakoff's syndrome		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Memory impairment		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Mental status changes		

subjects affected / exposed occurrences (all)	4 / 95 (4.21%) 4	2 / 108 (1.85%) 2	
Panic attack subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Poor quality sleep subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Restlessness subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1	
Selective mutism subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Speech disorder subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Stupor subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	0 / 108 (0.00%) 0	
Suicidal ideation subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Drug abuse subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 2	
Investigations			
Acinetobacter test positive subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 3	0 / 108 (0.00%) 0	
Alanine aminotransferase increased			

subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	2	1
Alpha 1 foetoprotein increased		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	3
Ammonia abnormal		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Ammonia increased		
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)
occurrences (all)	3	1
Antibiotic resistant staphylococcus test positive		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Aspartate aminotransferase increased		
subjects affected / exposed	7 / 95 (7.37%)	0 / 108 (0.00%)
occurrences (all)	7	0
Aspiration bronchial		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Bacterial test positive		
subjects affected / exposed	5 / 95 (5.26%)	1 / 108 (0.93%)
occurrences (all)	5	1
Blood aldosterone decreased		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Blood amylase increased		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Blood bilirubin increased		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Blood cortisol decreased		

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Blood creatinine increased		
subjects affected / exposed	5 / 95 (5.26%)	4 / 108 (3.70%)
occurrences (all)	5	4
Blood fibrinogen decreased		
subjects affected / exposed	4 / 95 (4.21%)	0 / 108 (0.00%)
occurrences (all)	4	0
Blood glucose fluctuation		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Blood lactate dehydrogenase increased		
subjects affected / exposed	6 / 95 (6.32%)	1 / 108 (0.93%)
occurrences (all)	6	1
Blood lactic acid abnormal		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Blood lactic acid increased		
subjects affected / exposed	4 / 95 (4.21%)	1 / 108 (0.93%)
occurrences (all)	4	1
Blood magnesium decreased		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Blood phosphorus abnormal		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Blood phosphorus decreased		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Blood potassium abnormal		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Blood pressure decreased		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1

Blood pressure systolic decreased subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Blood urea increased subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Body surface area increased subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Body temperature decreased subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Body temperature increased subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Breath sounds abnormal subjects affected / exposed occurrences (all)	6 / 95 (6.32%) 6	4 / 108 (3.70%) 4	
Cardiac murmur subjects affected / exposed occurrences (all)	10 / 95 (10.53%) 10	8 / 108 (7.41%) 10	
Clostridium test positive subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	1 / 108 (0.93%) 1	
Computerised tomogram head subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Culture urine positive subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	2 / 108 (1.85%) 2	
Drug screen positive			

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Electrocardiogram QRS complex abnormal		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Electrocardiogram QT prolonged		
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)
occurrences (all)	1	2
Enterococcus test positive		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Full blood count abnormal		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Fungal test positive		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Gamma-glutamyltransferase increased		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Haematocrit decreased		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Haemoglobin decreased		
subjects affected / exposed	3 / 95 (3.16%)	2 / 108 (1.85%)
occurrences (all)	5	2
Intraocular pressure increased		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Laboratory test abnormal		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Liver function test abnormal		

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Low density lipoprotein increased		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Oxygen saturation decreased		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	2
Procalcitonin increased		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Pulmonary function test decreased		
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)
occurrences (all)	2	2
Respiratory rate increased		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Serum ferritin increased		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Sputum culture positive		
subjects affected / exposed	3 / 95 (3.16%)	0 / 108 (0.00%)
occurrences (all)	3	0
Total lung capacity decreased		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Urine colour abnormal		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Urine output decreased		
subjects affected / exposed	4 / 95 (4.21%)	0 / 108 (0.00%)
occurrences (all)	4	0
Volume blood decreased		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Weight decreased		

subjects affected / exposed occurrences (all)	5 / 95 (5.26%) 5	1 / 108 (0.93%) 1	
Injury, poisoning and procedural complications			
Catheter site discharge			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Catheter site haematoma			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Catheter site related reaction			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Colon injury			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Excoriation			
subjects affected / exposed	10 / 95 (10.53%)	5 / 108 (4.63%)	
occurrences (all)	10	6	
Fall			
subjects affected / exposed	8 / 95 (8.42%)	5 / 108 (4.63%)	
occurrences (all)	8	7	
Febrile nonhaemolytic transfusion reaction			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Feeding tube complication			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Incision site complication			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Incision site pain			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences (all)	1	1	
Injection site haematoma			

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Injection site haemorrhage			
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)	
occurrences (all)	2	1	
Rib fracture			
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)	
occurrences (all)	0	2	
Spinal column injury			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Transfusion reaction			
subjects affected / exposed	3 / 95 (3.16%)	0 / 108 (0.00%)	
occurrences (all)	3	0	
Vessel puncture site haematoma			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences (all)	2	0	
Wound			
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)	
occurrences (all)	2	2	
Wound complication			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Wound secretion			
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)	
occurrences (all)	3	1	
Alcohol poisoning			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Arteriovenous malformation			

subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	2 / 108 (1.85%) 2	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	5 / 95 (5.26%)	2 / 108 (1.85%)	
occurrences (all)	6	2	
Atrial flutter			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Bradycardia			
subjects affected / exposed	4 / 95 (4.21%)	4 / 108 (3.70%)	
occurrences (all)	4	7	
Cardiac arrest			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	2	0	
Cardiac failure			
subjects affected / exposed	1 / 95 (1.05%)	3 / 108 (2.78%)	
occurrences (all)	1	3	
Cardiac failure congestive			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Cardiomegaly			
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)	
occurrences (all)	2	1	
Chest discomfort			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Hyperdynamic left ventricle			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Left ventricular dysfunction			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	

Left ventricular hypertrophy subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Mitral valve incompetence subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 3	0 / 108 (0.00%) 0	
Palpitations subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Pulmonary valve incompetence subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Right atrial dilatation subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Sinus tachycardia subjects affected / exposed occurrences (all)	7 / 95 (7.37%) 7	1 / 108 (0.93%) 1	
Supraventricular tachycardia subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Tachycardia subjects affected / exposed occurrences (all)	17 / 95 (17.89%) 19	10 / 108 (9.26%) 10	
Tricuspid valve incompetence subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	0 / 108 (0.00%) 0	
Ventricular tachycardia subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	2 / 108 (1.85%) 2	
Nervous system disorders Asterixis subjects affected / exposed occurrences (all)	9 / 95 (9.47%) 9	16 / 108 (14.81%) 16	
Ataxia			

subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Balance disorder		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Cerebral atrophy		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Coma		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	2	1
Coma hepatic		
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	5	1
Complex regional pain syndrome		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Convulsion		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	3
Coordination abnormal		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Depressed level of consciousness		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Facial spasm		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Headache		
subjects affected / exposed	11 / 95 (11.58%)	7 / 108 (6.48%)
occurrences (all)	14	7
Hepatic encephalopathy		
subjects affected / exposed	36 / 95 (37.89%)	29 / 108 (26.85%)
occurrences (all)	45	30
Hereditary cerebral degeneration		

subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Hyperreflexia		
subjects affected / exposed	3 / 95 (3.16%)	2 / 108 (1.85%)
occurrences (all)	3	2
Hypoaesthesia		
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)
occurrences (all)	4	1
Hyporeflexia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hyporesponsive to stimuli		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Insomnia		
subjects affected / exposed	14 / 95 (14.74%)	15 / 108 (13.89%)
occurrences (all)	14	15
Lethargy		
subjects affected / exposed	4 / 95 (4.21%)	5 / 108 (4.63%)
occurrences (all)	4	5
Metabolic encephalopathy		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Mobility decreased		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Myoclonic epilepsy		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Myoclonus		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Neuralgia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Neuropathy peripheral		

subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences (all)	1	2	
Nystagmus			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences (all)	1	1	
Paraesthesia			
subjects affected / exposed	2 / 95 (2.11%)	3 / 108 (2.78%)	
occurrences (all)	2	3	
Pupils unequal			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Restless legs syndrome			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	4 / 95 (4.21%)	5 / 108 (4.63%)	
occurrences (all)	4	5	
Tension headache			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	14 / 95 (14.74%)	10 / 108 (9.26%)	
occurrences (all)	14	11	
Dizziness			
subjects affected / exposed	2 / 95 (2.11%)	12 / 108 (11.11%)	
occurrences (all)	3	15	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	42 / 95 (44.21%)	17 / 108 (15.74%)	
occurrences (all)	47	19	
Anaemia macrocytic			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences (all)	1	1	
Anisocytosis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	

Coagulopathy		
subjects affected / exposed	29 / 95 (30.53%)	13 / 108 (12.04%)
occurrences (all)	34	15
Disseminated intravascular coagulation		
subjects affected / exposed	7 / 95 (7.37%)	0 / 108 (0.00%)
occurrences (all)	7	0
Haemolysis		
subjects affected / exposed	3 / 95 (3.16%)	0 / 108 (0.00%)
occurrences (all)	3	0
Haemolytic anaemia		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Heparin-induced thrombocytopenia		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Hypochromasia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hypofibrinogenaemia		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Hypoprothrombinaemia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Leukaemoid reaction		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Leukocytosis		
subjects affected / exposed	13 / 95 (13.68%)	13 / 108 (12.04%)
occurrences (all)	16	13
Lymphadenopathy		
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)
occurrences (all)	3	1
Pancytopenia		

subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Splenomegaly subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 3	1 / 108 (0.93%) 1	
Thrombocytopenia subjects affected / exposed occurrences (all)	33 / 95 (34.74%) 36	12 / 108 (11.11%) 12	
White blood cell disorder subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Ear and labyrinth disorders Cerumen impaction subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Eye disorders Dry eye subjects affected / exposed occurrences (all)	4 / 95 (4.21%) 4	1 / 108 (0.93%) 1	
Eye discharge subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Eye swelling subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Keratitis subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Keratopathy subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Limbal swelling subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Scleral discolouration			

subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)	
occurrences (all)	0	2	
Scleral disorder			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Scleral oedema			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences (all)	3	0	
Ulcerative keratitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)	
occurrences (all)	3	1	
Abdominal distension			
subjects affected / exposed	16 / 95 (16.84%)	8 / 108 (7.41%)	
occurrences (all)	17	10	
Abdominal pain			
subjects affected / exposed	27 / 95 (28.42%)	22 / 108 (20.37%)	
occurrences (all)	37	29	
Abdominal tenderness			
subjects affected / exposed	2 / 95 (2.11%)	3 / 108 (2.78%)	
occurrences (all)	3	3	
Anastomotic ulcer			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Anorectal discomfort			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Bacterascites			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	

Breath odour		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Colitis		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	2
Constipation		
subjects affected / exposed	19 / 95 (20.00%)	10 / 108 (9.26%)
occurrences (all)	20	10
Diarrhoea		
subjects affected / exposed	19 / 95 (20.00%)	17 / 108 (15.74%)
occurrences (all)	20	19
Diverticulum gastric		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Diverticulum intestinal		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Dry mouth		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Duodenal ulcer		
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)
occurrences (all)	0	2
Duodenogastric reflux		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Dyspepsia		
subjects affected / exposed	6 / 95 (6.32%)	4 / 108 (3.70%)
occurrences (all)	6	4
Dysphagia		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	2
Faecal incontinence		
subjects affected / exposed	3 / 95 (3.16%)	3 / 108 (2.78%)
occurrences (all)	3	3

Faeces discoloured subjects affected / exposed occurrences (all)	4 / 95 (4.21%) 4	4 / 108 (3.70%) 4
Faeces pale subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	5 / 95 (5.26%) 5	2 / 108 (1.85%) 2
Frequent bowel movements subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0
Functional gastrointestinal disorder subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0
Gastric mucosal lesion subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Gastritis subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	3 / 108 (2.78%) 3
Gastritis erosive subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1
Gastrointestinal oedema subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0
Gastrointestinal sounds abnormal subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 3	2 / 108 (1.85%) 2
Glossitis subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0
Haematemesis subjects affected / exposed occurrences (all)	6 / 95 (6.32%) 6	4 / 108 (3.70%) 5

Hiatus hernia		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	2
Ileus		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	2
Impaired gastric emptying		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Inguinal hernia		
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)
occurrences (all)	1	2
Mouth haemorrhage		
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)
occurrences (all)	1	2
Mouth ulceration		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Nausea		
subjects affected / exposed	15 / 95 (15.79%)	23 / 108 (21.30%)
occurrences (all)	18	27
Odynophagia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Oesophageal ulcer		
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)
occurrences (all)	1	2
Oesophagitis		
subjects affected / exposed	0 / 95 (0.00%)	3 / 108 (2.78%)
occurrences (all)	0	3
Oral discharge		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Oral disorder		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1

Oral pain		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Pancreatitis		
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)
occurrences (all)	0	2
Peptic ulcer		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Peritoneal disorder		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Pneumatosis intestinalis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Pneumoperitoneum		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Proctalgia		
subjects affected / exposed	0 / 95 (0.00%)	4 / 108 (3.70%)
occurrences (all)	0	4
Rectal haemorrhage		
subjects affected / exposed	8 / 95 (8.42%)	4 / 108 (3.70%)
occurrences (all)	9	4
Rectal ulcer		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Retroperitoneal haematoma		
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)
occurrences (all)	2	0
Small intestinal obstruction		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Tongue coated		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1

Tongue disorder subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1	
Tooth disorder subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Toothache subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Umbilical hernia subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 3	3 / 108 (2.78%) 3	
Vomiting subjects affected / exposed occurrences (all)	14 / 95 (14.74%) 17	17 / 108 (15.74%) 21	
Oesophageal varices haemorrhage subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Hepatobiliary disorders Ascites subjects affected / exposed occurrences (all)	34 / 95 (35.79%) 37	30 / 108 (27.78%) 40	
Bile duct obstruction subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Biliary colic subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Caput medusae subjects affected / exposed occurrences (all)	2 / 95 (2.11%) 2	3 / 108 (2.78%) 3	
Cholecystitis subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Cholelithiasis			

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Cholestasis		
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)
occurrences (all)	0	2
Cirrhosis alcoholic		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Foetor hepaticus		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Gallbladder disorder		
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	2	1
Hepatic cirrhosis		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hepatic failure		
subjects affected / exposed	2 / 95 (2.11%)	3 / 108 (2.78%)
occurrences (all)	3	3
Hepatic fibrosis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Hepatitis alcoholic		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Hepatomegaly		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	2
Hepatorenal syndrome		
subjects affected / exposed	11 / 95 (11.58%)	11 / 108 (10.19%)
occurrences (all)	12	13
Hyperammonaemia		
subjects affected / exposed	3 / 95 (3.16%)	0 / 108 (0.00%)
occurrences (all)	3	0
Jaundice		

subjects affected / exposed	2 / 95 (2.11%)	4 / 108 (3.70%)	
occurrences (all)	2	4	
Ocular icterus			
subjects affected / exposed	1 / 95 (1.05%)	3 / 108 (2.78%)	
occurrences (all)	1	3	
Portal hypertension			
subjects affected / exposed	2 / 95 (2.11%)	4 / 108 (3.70%)	
occurrences (all)	2	4	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Anogenital warts			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Blister			
subjects affected / exposed	0 / 95 (0.00%)	3 / 108 (2.78%)	
occurrences (all)	0	3	
Cellulitis			
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)	
occurrences (all)	2	1	
Decubitus ulcer			
subjects affected / exposed	5 / 95 (5.26%)	0 / 108 (0.00%)	
occurrences (all)	5	0	
Dermatitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	2	0	
Dry skin			
subjects affected / exposed	0 / 95 (0.00%)	5 / 108 (4.63%)	
occurrences (all)	0	5	
Ecchymosis			
subjects affected / exposed	9 / 95 (9.47%)	6 / 108 (5.56%)	
occurrences (all)	9	9	
Erythema			
subjects affected / exposed	3 / 95 (3.16%)	3 / 108 (2.78%)	
occurrences (all)	3	4	

Eschar		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Face oedema		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Facial wasting		
subjects affected / exposed	1 / 95 (1.05%)	4 / 108 (3.70%)
occurrences (all)	1	4
Folliculitis		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Herpes simplex		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Hyperhidrosis		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Hyperkeratosis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Laceration		
subjects affected / exposed	4 / 95 (4.21%)	1 / 108 (0.93%)
occurrences (all)	4	1
Nail discolouration		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Night sweats		
subjects affected / exposed	1 / 95 (1.05%)	2 / 108 (1.85%)
occurrences (all)	1	2
Onychomycosis		
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)
occurrences (all)	0	2
Palmar erythema		
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)
occurrences (all)	3	1

Perianal erythema		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Pruritus		
subjects affected / exposed	19 / 95 (20.00%)	19 / 108 (17.59%)
occurrences (all)	20	20
Psoriasis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Rash		
subjects affected / exposed	7 / 95 (7.37%)	11 / 108 (10.19%)
occurrences (all)	7	12
Rash pustular		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Scab		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Scratch		
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	3	1
Skin disorder		
subjects affected / exposed	3 / 95 (3.16%)	0 / 108 (0.00%)
occurrences (all)	3	0
Skin erosion		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Skin exfoliation		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Skin irritation		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Skin lesion		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1

Skin ulcer			
subjects affected / exposed	5 / 95 (5.26%)	3 / 108 (2.78%)	
occurrences (all)	5	3	
Stasis dermatitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Swelling face			
subjects affected / exposed	3 / 95 (3.16%)	0 / 108 (0.00%)	
occurrences (all)	3	0	
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences (all)	1	1	
Anuria			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences (all)	2	0	
Azotaemia			
subjects affected / exposed	1 / 95 (1.05%)	3 / 108 (2.78%)	
occurrences (all)	1	3	
Costovertebral angle tenderness			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)	
occurrences (all)	2	1	
Haematuria			
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)	
occurrences (all)	2	1	
Hydronephrosis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)	
occurrences (all)	0	1	
Incontinence			

subjects affected / exposed	4 / 95 (4.21%)	0 / 108 (0.00%)
occurrences (all)	4	0
Micturition urgency		
subjects affected / exposed	0 / 95 (0.00%)	2 / 108 (1.85%)
occurrences (all)	0	2
Nephrolithiasis		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Nocturia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Oliguria		
subjects affected / exposed	6 / 95 (6.32%)	0 / 108 (0.00%)
occurrences (all)	6	0
Polyuria		
subjects affected / exposed	4 / 95 (4.21%)	2 / 108 (1.85%)
occurrences (all)	4	2
Pyelonephritis		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Renal disorder		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Renal failure		
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)
occurrences (all)	3	1
Renal failure acute		
subjects affected / exposed	22 / 95 (23.16%)	21 / 108 (19.44%)
occurrences (all)	23	25
Renal impairment		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Urethral pain		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Urinary incontinence		

subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)	
occurrences (all)	2	1	
Urinary retention			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences (all)	2	0	
Urinary tract pain			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 95 (7.37%)	3 / 108 (2.78%)	
occurrences (all)	7	3	
Back pain			
subjects affected / exposed	9 / 95 (9.47%)	13 / 108 (12.04%)	
occurrences (all)	12	16	
Chills			
subjects affected / exposed	4 / 95 (4.21%)	3 / 108 (2.78%)	
occurrences (all)	4	3	
Groin pain			
subjects affected / exposed	2 / 95 (2.11%)	0 / 108 (0.00%)	
occurrences (all)	2	0	
Joint range of motion decreased			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)	
occurrences (all)	1	0	
Muscle atrophy			
subjects affected / exposed	8 / 95 (8.42%)	6 / 108 (5.56%)	
occurrences (all)	8	6	
Muscle spasms			

subjects affected / exposed	5 / 95 (5.26%)	3 / 108 (2.78%)
occurrences (all)	5	3
Musculoskeletal discomfort		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Musculoskeletal pain		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Musculoskeletal stiffness		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Myalgia		
subjects affected / exposed	5 / 95 (5.26%)	0 / 108 (0.00%)
occurrences (all)	5	0
Myopathy		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Neck pain		
subjects affected / exposed	3 / 95 (3.16%)	2 / 108 (1.85%)
occurrences (all)	3	2
Osteoarthritis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Osteopenia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Pain in extremity		
subjects affected / exposed	7 / 95 (7.37%)	4 / 108 (3.70%)
occurrences (all)	7	5
Rotator cuff syndrome		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Sarcopenia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Spinal disorder		

subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Spinal osteoarthritis subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Muscular weakness subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	3 / 108 (2.78%) 3	
Flank pain subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1	
Infections and infestations			
Aspergillosis subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Bacteraemia subjects affected / exposed occurrences (all)	16 / 95 (16.84%) 18	7 / 108 (6.48%) 8	
Candidiasis subjects affected / exposed occurrences (all)	9 / 95 (9.47%) 10	3 / 108 (2.78%) 3	
Candiduria subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Clostridial infection subjects affected / exposed occurrences (all)	4 / 95 (4.21%) 4	6 / 108 (5.56%) 6	
Clostridium difficile colitis subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Device related infection subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1	
Diverticulitis subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1	

Endocarditis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Enterococcal infection		
subjects affected / exposed	2 / 95 (2.11%)	2 / 108 (1.85%)
occurrences (all)	2	2
Escherichia infection		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Fungaemia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Fungal infection		
subjects affected / exposed	3 / 95 (3.16%)	2 / 108 (1.85%)
occurrences (all)	3	2
Fungal skin infection		
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	2	1
Gastroenteritis		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Helicobacter infection		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Infection		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Lyme disease		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Oesophageal candidiasis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Oral candidiasis		
subjects affected / exposed	8 / 95 (8.42%)	6 / 108 (5.56%)
occurrences (all)	8	6

Oral herpes		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Paronychia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Peritonitis bacterial		
subjects affected / exposed	6 / 95 (6.32%)	4 / 108 (3.70%)
occurrences (all)	6	4
Pharyngitis streptococcal		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Pneumonia		
subjects affected / exposed	13 / 95 (13.68%)	10 / 108 (9.26%)
occurrences (all)	13	10
Propionibacterium infection		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Respiratory tract infection		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Sepsis		
subjects affected / exposed	7 / 95 (7.37%)	7 / 108 (6.48%)
occurrences (all)	7	8
Septic encephalopathy		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Staphylococcal infection		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Tinea infection		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Tooth abscess		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0	1 / 108 (0.93%) 1	
Urinary tract infection subjects affected / exposed occurrences (all)	14 / 95 (14.74%) 19	16 / 108 (14.81%) 19	
Viral infection subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Metabolism and nutrition disorders			
Acidosis subjects affected / exposed occurrences (all)	3 / 95 (3.16%) 4	2 / 108 (1.85%) 2	
Adrenal insufficiency subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	0 / 108 (0.00%) 0	
Cachexia subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	3 / 108 (2.78%) 3	
Decreased appetite subjects affected / exposed occurrences (all)	7 / 95 (7.37%) 7	7 / 108 (6.48%) 7	
Dehydration subjects affected / exposed occurrences (all)	6 / 95 (6.32%) 6	5 / 108 (4.63%) 6	
Electrolyte imbalance subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	1 / 108 (0.93%) 1	
Fluid overload subjects affected / exposed occurrences (all)	8 / 95 (8.42%) 8	4 / 108 (3.70%) 4	
Fluid retention subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1	3 / 108 (2.78%) 4	
Generalised oedema			

subjects affected / exposed	9 / 95 (9.47%)	4 / 108 (3.70%)
occurrences (all)	9	4
Goitre		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Hepatic steatosis		
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	2	1
Hyperbilirubinaemia		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Hypercalcaemia		
subjects affected / exposed	2 / 95 (2.11%)	1 / 108 (0.93%)
occurrences (all)	2	1
Hyperchloraemia		
subjects affected / exposed	3 / 95 (3.16%)	0 / 108 (0.00%)
occurrences (all)	3	0
Hyperglycaemia		
subjects affected / exposed	19 / 95 (20.00%)	10 / 108 (9.26%)
occurrences (all)	21	12
Hyperkalaemia		
subjects affected / exposed	8 / 95 (8.42%)	4 / 108 (3.70%)
occurrences (all)	8	6
Hypermagnesaemia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Hypernatraemia		
subjects affected / exposed	8 / 95 (8.42%)	5 / 108 (4.63%)
occurrences (all)	8	5
Hyperphosphataemia		
subjects affected / exposed	6 / 95 (6.32%)	3 / 108 (2.78%)
occurrences (all)	7	3
Hypervolaemia		
subjects affected / exposed	3 / 95 (3.16%)	1 / 108 (0.93%)
occurrences (all)	3	1
Hypoalbuminaemia		

subjects affected / exposed	4 / 95 (4.21%)	7 / 108 (6.48%)
occurrences (all)	4	7
Hypocalcaemia		
subjects affected / exposed	18 / 95 (18.95%)	3 / 108 (2.78%)
occurrences (all)	24	5
Hypochloraemia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Hypoglycaemia		
subjects affected / exposed	6 / 95 (6.32%)	4 / 108 (3.70%)
occurrences (all)	6	4
Hypokalaemia		
subjects affected / exposed	21 / 95 (22.11%)	29 / 108 (26.85%)
occurrences (all)	23	34
Hypomagnesaemia		
subjects affected / exposed	21 / 95 (22.11%)	14 / 108 (12.96%)
occurrences (all)	25	14
Hyponatraemia		
subjects affected / exposed	8 / 95 (8.42%)	15 / 108 (13.89%)
occurrences (all)	8	17
Hypophosphataemia		
subjects affected / exposed	23 / 95 (24.21%)	14 / 108 (12.96%)
occurrences (all)	23	14
Hypoproteinaemia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Hypothyroidism		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Hypovolaemia		
subjects affected / exposed	5 / 95 (5.26%)	5 / 108 (4.63%)
occurrences (all)	5	5
Lactic acidosis		
subjects affected / exposed	5 / 95 (5.26%)	2 / 108 (1.85%)
occurrences (all)	7	2
Lactose intolerance		

subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Localised oedema		
subjects affected / exposed	1 / 95 (1.05%)	1 / 108 (0.93%)
occurrences (all)	1	1
Malnutrition		
subjects affected / exposed	5 / 95 (5.26%)	5 / 108 (4.63%)
occurrences (all)	5	5
Metabolic acidosis		
subjects affected / exposed	16 / 95 (16.84%)	13 / 108 (12.04%)
occurrences (all)	16	14
Metabolic alkalosis		
subjects affected / exposed	1 / 95 (1.05%)	0 / 108 (0.00%)
occurrences (all)	1	0
Oedema		
subjects affected / exposed	9 / 95 (9.47%)	12 / 108 (11.11%)
occurrences (all)	9	15
Osteoporosis		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Vitamin D deficiency		
subjects affected / exposed	0 / 95 (0.00%)	1 / 108 (0.93%)
occurrences (all)	0	1
Zinc deficiency		
subjects affected / exposed	0 / 95 (0.00%)	4 / 108 (3.70%)
occurrences (all)	0	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2012	Amendment 1, Version 14.0 - All sites - The number of planned subjects was increased to 200 in order to increase the power to achieve the planned significance level of 0.05 while maintaining the same assumptions for the treatment effect.
27 November 2012	Amendment 2, Version 15.0 - All sites - The inclusion/exclusion criteria were updated to provide clarity to the definition of the patient population. The protocol was updated to be in accord with ISO 14155, the EU Device Directives, and pertinent US device regulations.
14 August 2013	Amendment 4, Version 17.0 - UK only - Standard of Care treatment guidelines for viral hepatitis were added. A quality of life questionnaire (EQ-5D-5L) was added. Procedures related to subjects lost to follow-up were defined.
30 September 2013	Amendment 3, Version 16.0 - All sites - This amendment was never initiated and no patients were consented or randomized under this protocol version.
25 October 2013	Amendment 5, Version 18.0 - UK only - Added instruction for sites to notify VTL immediately if any ultrafiltrate culture results were positive, and provided clarification that collection of AEs/SAEs should begin at randomization; not the signing of consent. There was also incorporation of pertinent ISO 14155 wording regarding IRB/EC notification of protocol deviations and amendments.
12 April 2014	Amendment 6 - Global - Global harmonization of the protocol to better assist investigators and clinical sites in the conduct of the trial, specifically related to: screening and enrollment, lab and imaging data collection and allowable windows for collection, physical exam and encephalopathy assessment, and follow-up evaluations. Significant changes in this protocol amendment included the following: -The statistical sections were updated to reflect the Statistical Analysis Plan; -Specific instructions for reporting of ultrafiltrate culture results were added; -The adverse event reporting sections were revised, and a Clinical Trial Pharmacovigilance Investigator Guide was added; and -A validated Quality of Life Questionnaire (EQ-5D-5L) was added for VTI-208 and VTI-208E.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

None

Notes: