Clinical trial results:
A Randomized, Open-label, Multicenter, Controlled, Pivotal Study to Assess Safety and Efficacy of ELAD® in Subjects with Alcohol-Induced Liver Decompensation (AILD).

Summary

EudraCT number	2015-004529-14
Trial protocol	ES DE IE AT
Global end of trial date	14 September 2018

Results information

Result version number	v1 (current)
This version publication date	13 January 2019
First version publication date	13 January 2019

Trial information

Trial identification

Sponsor protocol code	VTL-308

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02612428
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vital Therapies, Inc.
Sponsor organisation address	15010 Avenue of Science, San Diego, United States, 92128
Public contact	EVP & Chief Technical Officer, Robert A. Ashley, Vital Therapies, Inc., 001 520289 3236, rashley@vitaltherapies.com
Scientific contact	EVP & Chief Technical Officer, Robert A. Ashley, Vital Therapies, Inc., 001 520289 3236, 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	28 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 June 2018
Global end of trial reached?	Yes
Global end of trial date	14 September 2018
Was the trial ended prematurely?	Yes

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) through at least Study Day 91, with follow-up Protocol VTL-308E providing additional survival data up to a maximum of 5 years that will be included, as available, through VTL-308 study termination (after the last surviving enrolled subject completes Study Day 91). The primary objective will be assessed using a Kaplan-Meier survival analysis of the Intent-to-Treat (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:

VTL-308 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 VTL-308. Consequently, the best available standard of care in accord with AASLD and EASL guidelines was recommended in the VTL-308 study protocol for all participants irrespective of treatment arm.

Actual start date of recruitment	16 May 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, 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	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	United States: 109
Worldwide total number of subjects	151
EEA total number of subjects	42

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)	151
From 65 to 84 years	0
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 May 2016 through March 2018 in the United States, United Kingdom and Australia.

Pre-assignment

Screening details:

A total of 179 participants were screened, out of which 28 were failures , and 151 were randomized, of which 76 received ELAD treatment. Participants who successfully completed the initial 91-day treatment period were entered into a 5-year extension phase (VTL-308E) of the study.

Period 1

Period 1 title	VTL-308
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

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	78	73
Completed	64	56
Not completed	14	17
Adverse event, serious fatal	14	16
Consent withdrawn by subject	-	1

Period 2

Period 2 title	VTL-308E
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 VTL-308 were followed up for up to 5 years.

Arm type	Experimental
Investigational medicinal product name	ELAD
Investigational medicinal product code	ELAD System
Other name	
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

Arm description:

Participants randomized to the Control group and who received protocol-directed Standard of Care during the VTL-308 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	64	56
Completed	53	49
Not completed	11	7
Adverse event, serious fatal	9	7
Lost to follow-up	2	-

Baseline characteristics

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 values	ELAD Treatment	Control	Total
Number of subjects	78	73	151
Age categorical Units: Subjects			
Between 18 and 35 years old	23	22	45
Between 36 and 50 years old	55	51	106
Age continuous Units: years			
arithmetic mean	39.1	39.5	
standard deviation	± 6.26	± 7.20	-
Gender categorical Units: Subjects			
Female	31	29	60
Male	47	44	91
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	1	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	2	7
White	70	67	137
More Than One Race	1	1	2
Unknown or Not Reported	0	2	2
Region of Enrollment Units: Subjects			
Austria	0	2	2
United States	57	52	109
Ireland	1	0	1
United Kingdom	11	11	22
Germany	4	5	9
Spain	5	3	8
Baseline MELD Score			
Measure Description: A higher baseline Model for End-stage Liver Disease (MELD) score value represents a worse outcome. The total Min/Max in all subjects in this study was 19/29. There were 42 subjects in the ELAD group and 52 subjects in the Control group that had baseline MELD scores greater than or equal to the median cutoff (≥25.0), while the remaining subjects had scores less than the median cutoff (<25).			

Units: MELD Score			
arithmetic mean	24.8	25.6	
standard deviation	± 2.37	± 2.35	-

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 VTL-308 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 VTL-308 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 VTL-308E providing additional survival data up to a maximum of 5 years, that was included as available at the time of database lock (28 August 2018).	
End point type	Primary
End point timeframe:	
Up to at last Study Day 91, with protocol VTL-308E 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	78	73		
Units: Number of Subjects				
Alive	51	49		
Dead	23	22		
Lost to follow-up	4	2		

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	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.913
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.509
upper limit	1.64

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	78	73		
Units: Number of Subjects				
Alive	63	57		
Dead	15	16		

Statistical analyses

Statistical analysis title	Proportion of Survivors at Study Day 91
Statistical analysis description:	
Proportion of Survivors at Study Day 91.	
Comparison groups	ELAD Treatment v Control

Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Chi-squared

Secondary: Proportion of Subjects with Early Change in Bilirubin Level Cutoff of 20% at Study Day 7

End point title	Proportion of Subjects with Early Change in Bilirubin Level Cutoff of 20% at Study Day 7

End point description:

Proportion of Subjects with ECBL 20 Up to Study Day 7.

End point type	Secondary

End point timeframe:

Up to Study Day 7.

End point values	ELAD Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	73		
Units: Number of Subjects				
Number of Subjects with ECBL <20%	40	49		
Number of Subjects with ECBL ≥20%	38	24		

Statistical analyses

Statistical analysis title	Proportion of Subjects with ECBL20 at Study Day 7
Comparison groups	ELAD Treatment v Control
Number of subjects included in analysis	151
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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	ELAD Treatment
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
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	47 / 76 (61.84%)	42 / 75 (56.00%)	
number of deaths (all causes)	14	17	
number of deaths resulting from adverse events	14	17	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 76 (1.32%)	3 / 75 (4.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			

subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Oesophageal variceal ligation			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site haematoma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (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 / 76 (9.21%)	13 / 75 (17.33%)	
occurrences causally related to treatment / all	0 / 7	0 / 13	
deaths causally related to treatment / all	0 / 6	0 / 12	
Oedema peripheral			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Systemic inflammatory response syndrome			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactoid reaction			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	3 / 76 (3.95%)	4 / 75 (5.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic hydrothorax			

subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory arrest			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol abuse			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
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	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Head injury			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pulseless electrical activity			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Demyelination			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	2 / 76 (2.63%)	7 / 75 (9.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Subarachnoid haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 76 (5.26%)	3 / 75 (4.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrile Neutropenia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 76 (3.95%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholic pancreatitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 76 (1.32%)	4 / 75 (5.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	6 / 76 (7.89%)	7 / 75 (9.33%)	
occurrences causally related to treatment / all	1 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	

Haematemesis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (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 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneocutaneous fistula			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Alcoholic liver disease			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	6 / 76 (7.89%)	5 / 75 (6.67%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 3	
Hepatic function abnormal			

subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis alcoholic			
subjects affected / exposed	3 / 76 (3.95%)	4 / 75 (5.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Hepatorenal failure			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatorenal syndrome			
subjects affected / exposed	7 / 76 (9.21%)	5 / 75 (6.67%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	7 / 76 (9.21%)	6 / 75 (8.00%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Renal failure			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			

subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (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			
Bacteraemia			
subjects affected / exposed	3 / 76 (3.95%)	3 / 75 (4.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 76 (5.26%)	5 / 75 (6.67%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sepsis syndrome			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (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	4 / 76 (5.26%)	4 / 75 (5.33%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ELAD Treatment	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 76 (100.00%)	74 / 75 (98.67%)	
Vascular disorders			
Aortic disorder			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	

Deep vein thrombosis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Distributive shock			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Haematoma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Hypotension			
subjects affected / exposed	21 / 76 (27.63%)	9 / 75 (12.00%)	
occurrences (all)	24	10	
Hypovolaemic shock			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Orthostatic hypotension			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Peripheral artery aneurysm			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Phlebitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Shock haemorrhagic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Splenorenal shunt			

subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Abasia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Adverse drug reaction			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Application site dysaesthesia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	3	1	
Catheter site haemorrhage			
subjects affected / exposed	4 / 76 (5.26%)	3 / 75 (4.00%)	
occurrences (all)	4	5	
Catheter site pain			
subjects affected / exposed	3 / 76 (3.95%)	4 / 75 (5.33%)	
occurrences (all)	4	4	
Catheter site pruritus			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Chills			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Fatigue			
subjects affected / exposed	3 / 76 (3.95%)	4 / 75 (5.33%)	
occurrences (all)	3	4	
Gait disturbance			

subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Generalised oedema			
subjects affected / exposed	6 / 76 (7.89%)	7 / 75 (9.33%)	
occurrences (all)	6	7	
Hypothermia			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Localised oedema			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Medical device complication			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Medical device site haemorrhage			
subjects affected / exposed	14 / 76 (18.42%)	0 / 75 (0.00%)	
occurrences (all)	15	0	
Medical device site pain			
subjects affected / exposed	11 / 76 (14.47%)	0 / 75 (0.00%)	
occurrences (all)	11	0	
Mucosal inflammation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Multi-organ failure			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Oedema			
subjects affected / exposed	4 / 76 (5.26%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Oedema peripheral			

subjects affected / exposed	20 / 76 (26.32%)	14 / 75 (18.67%)	
occurrences (all)	24	19	
Pain			
subjects affected / exposed	5 / 76 (6.58%)	2 / 75 (2.67%)	
occurrences (all)	5	3	
Pneumatosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	19 / 76 (25.00%)	16 / 75 (21.33%)	
occurrences (all)	21	17	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Temperature intolerance			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Thrombosis in device			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Erectile dysfunction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Genital rash			

subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Gynaecomastia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Nipple pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Scrotal oedema			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Scrotal pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Vaginal discharge			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Vaginal haemorrhage			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Vulvovaginal pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Acquired diaphragmatic eventration			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Acute respiratory failure			
subjects affected / exposed	4 / 76 (5.26%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Aspiration			

subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Atelectasis			
subjects affected / exposed	10 / 76 (13.16%)	4 / 75 (5.33%)	
occurrences (all)	11	4	
Bronchial hyperreactivity			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Bronchospasm			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	10 / 76 (13.16%)	12 / 75 (16.00%)	
occurrences (all)	12	12	
Dysphonia			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Dyspnoea			
subjects affected / exposed	16 / 76 (21.05%)	8 / 75 (10.67%)	
occurrences (all)	17	8	
Epistaxis			
subjects affected / exposed	8 / 76 (10.53%)	5 / 75 (6.67%)	
occurrences (all)	9	5	
Haemoptysis			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Hepatic hydrothorax			
subjects affected / exposed	14 / 76 (18.42%)	13 / 75 (17.33%)	
occurrences (all)	15	15	
Hypoventilation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Hypoxia			
subjects affected / exposed	6 / 76 (7.89%)	5 / 75 (6.67%)	
occurrences (all)	6	5	
Lung consolidation			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Lung infiltration			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Nasal dryness			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 76 (1.32%)	3 / 75 (4.00%)	
occurrences (all)	1	3	
Pharyngeal erythema			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Pneumonia aspiration			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Pneumothorax			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	3	
Productive cough			
subjects affected / exposed	0 / 76 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	3	
Pulmonary hypertension			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Pulmonary mass			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Pulmonary oedema			
subjects affected / exposed	11 / 76 (14.47%)	4 / 75 (5.33%)	
occurrences (all)	11	4	
Rales			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	3	
Respiratory acidosis			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Respiratory distress			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Respiratory failure			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Rhinalgia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Stridor			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Tachypnoea			
subjects affected / exposed	3 / 76 (3.95%)	5 / 75 (6.67%)	
occurrences (all)	3	5	
Tracheal fistula			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Upper respiratory tract congestion			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Acute stress disorder			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	

Adjustment disorder with depressed mood				
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)		
occurrences (all)	2	0		
Agitation				
subjects affected / exposed	7 / 76 (9.21%)	7 / 75 (9.33%)		
occurrences (all)	7	7		
Alcohol withdrawal syndrome				
subjects affected / exposed	3 / 76 (3.95%)	0 / 75 (0.00%)		
occurrences (all)	3	0		
Anxiety				
subjects affected / exposed	8 / 76 (10.53%)	4 / 75 (5.33%)		
occurrences (all)	8	4		
Confusional state				
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)		
occurrences (all)	1	2		
Delirium				
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)		
occurrences (all)	2	1		
Depressed mood				
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)		
occurrences (all)	1	0		
Depression				
subjects affected / exposed	3 / 76 (3.95%)	2 / 75 (2.67%)		
occurrences (all)	3	2		
Disorientation				
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)		
occurrences (all)	2	0		
Hallucination				
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)		
occurrences (all)	0	1		
Hallucination, visual				
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)		
occurrences (all)	1	0		
Insomnia				

subjects affected / exposed	13 / 76 (17.11%)	9 / 75 (12.00%)	
occurrences (all)	13	9	
Nervousness			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Panic attack			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Sleep disorder			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	3 / 76 (3.95%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Blood magnesium decreased			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Breath sounds abnormal			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Cardiac murmur			
subjects affected / exposed	3 / 76 (3.95%)	6 / 75 (8.00%)	
occurrences (all)	3	6	
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Influenza B virus test positive			

subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Intra-abdominal pressure increased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Ultrasound abdomen abnormal			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Weight increased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Anal injury			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	7 / 76 (9.21%)	2 / 75 (2.67%)	
occurrences (all)	8	2	
Corrosive gastritis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Craniocerebral injury			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Endotracheal intubation complication			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Excoriation			
subjects affected / exposed	6 / 76 (7.89%)	2 / 75 (2.67%)	
occurrences (all)	6	2	
Fall			

subjects affected / exposed	4 / 76 (5.26%)	1 / 75 (1.33%)	
occurrences (all)	6	1	
Head injury			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Joint injury			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Laceration			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Limb injury			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Lip injury			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Muscle strain			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Post procedural discomfort			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Post procedural haemorrhage			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Procedural complication			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Procedural pain			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Scratch			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Scrotal haematoma			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
skin abrasion			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Skin wound			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Suture related complication			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Tooth injury			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Transfusion reaction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
VIIth nerve injury			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Vascular pseudoaneurysm			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Wound			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Atrial tachycardia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	

Bradycardia			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Cardiac failure congestive			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Cardiomegaly			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Cardiovascular disorder			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Defect conduction intraventricular			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Dilatation ventricular			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Heart valve incompetence			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Left atrial dilatation			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Left ventricular dysfunction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Myocardial infarctionfarction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Right atrial dilatation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	

Tachycardia			
subjects affected / exposed	9 / 76 (11.84%)	8 / 75 (10.67%)	
occurrences (all)	9	8	
Tricuspid valve incompetence			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Nervous system disorders			
Asterixis			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Central nervous system lesion			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Cerebral atrophy			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Disturbance in attention			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	8 / 76 (10.53%)	3 / 75 (4.00%)	
occurrences (all)	8	3	
Dysarthria			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	9 / 76 (11.84%)	2 / 75 (2.67%)	
occurrences (all)	10	2	
Hemiparesis			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Hepatic encephalopathy			
subjects affected / exposed	27 / 76 (35.53%)	22 / 75 (29.33%)	
occurrences (all)	28	25	
Hypoaesthesia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Loss of consciousness			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Metabolic encephalopathy			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Neuropathy peripheral			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Nystagmus			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Peroneal nerve palsy			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Polyneuropathy			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Quadriparesis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Seizure			

subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	3	2	
Speech disorder			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	4 / 76 (5.26%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Blood and lymphatic system disorders			
Abdominal lymphadenopathy			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Acquired dysfibrinogenaemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Anaemia			
subjects affected / exposed	37 / 76 (48.68%)	18 / 75 (24.00%)	
occurrences (all)	42	19	
Coagulopathy			
subjects affected / exposed	14 / 76 (18.42%)	10 / 75 (13.33%)	
occurrences (all)	15	10	
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Hypofibrinogenaemia			
subjects affected / exposed	5 / 76 (6.58%)	1 / 75 (1.33%)	
occurrences (all)	6	1	
Leukocytosis			
subjects affected / exposed	13 / 76 (17.11%)	15 / 75 (20.00%)	
occurrences (all)	13	16	
Lymphadenopathy			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Neutropenia			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Neutrophilia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	17 / 76 (22.37%)	8 / 75 (10.67%)	
occurrences (all)	18	8	
Ear and labyrinth disorders			
Middle ear effusion			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 76 (3.95%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Vision blurred			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Vitreous floaters			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 76 (2.63%)	3 / 75 (4.00%)	
occurrences (all)	2	3	
Abdominal pain			
subjects affected / exposed	16 / 76 (21.05%)	15 / 75 (20.00%)	
occurrences (all)	21	18	
Anal fissure			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Anorectal discomfort			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Anorectal varices			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Ascites			
subjects affected / exposed	14 / 76 (18.42%)	22 / 75 (29.33%)	
occurrences (all)	14	22	
Colitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	5 / 76 (6.58%)	6 / 75 (8.00%)	
occurrences (all)	5	7	
Diarrhoea			
subjects affected / exposed	26 / 76 (34.21%)	19 / 75 (25.33%)	
occurrences (all)	29	19	
Diverticulum			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Dry mouth			
subjects affected / exposed	3 / 76 (3.95%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Duodenal ulcer			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Duodenitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	2 / 76 (2.63%)	3 / 75 (4.00%)	
occurrences (all)	2	3	
Faecal incontinence			

subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Gastric antral vascular ectasia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Gastric haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Gastric mucosal lesion			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Gastric ulcer			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Gastric varices			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	1 / 76 (1.32%)	3 / 75 (4.00%)	
occurrences (all)	1	3	
Gastritis erosive			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal haemorrhage			
subjects affected / exposed	11 / 76 (14.47%)	10 / 75 (13.33%)	
occurrences (all)	12	10	
Gastrointestinal mucosa hyperaemia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 76 (5.26%)	0 / 75 (0.00%)	
occurrences (all)	4	0	
Gingival pain			

subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Haematemesis			
subjects affected / exposed	1 / 76 (1.32%)	3 / 75 (4.00%)	
occurrences (all)	1	3	
Haemorrhoids			
subjects affected / exposed	6 / 76 (7.89%)	2 / 75 (2.67%)	
occurrences (all)	6	2	
Hiatus hernia			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Ileus			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Ileus paralytic			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Inguinal hernia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Large intestine polyp			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Lip dry			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Mesenteric haematoma			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	19 / 76 (25.00%)	13 / 75 (17.33%)	
occurrences (all)	20	14	
Oesophageal ulcer			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Oesophagitis			

subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)		
occurrences (all)	2	1		
Oesophagitis ulcerative				
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)		
occurrences (all)	0	1		
Painful defaecation				
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)		
occurrences (all)	1	0		
Pancreatitis				
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)		
occurrences (all)	1	1		
Pancreatolithiasis				
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)		
occurrences (all)	0	1		
Peridontal disease				
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)		
occurrences (all)	0	1		
Peritoneal haemorrhage				
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)		
occurrences (all)	1	0		
Peritoneocutaneous fistula				
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)		
occurrences (all)	1	1		
Portal hypertensive gastropathypathy				
subjects affected / exposed	8 / 76 (10.53%)	8 / 75 (10.67%)		
occurrences (all)	8	8		
Proctalgia				
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)		
occurrences (all)	1	1		
Rectal fissure				
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)		
occurrences (all)	0	1		
Rectal haemorrhage				
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)		
occurrences (all)	2	1		

Retroperitoneal haematoma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Small intestinal obstruction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Toothache			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Umbilical hernia			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Varices oesophageal			
subjects affected / exposed	7 / 76 (9.21%)	9 / 75 (12.00%)	
occurrences (all)	7	11	
Vomiting			
subjects affected / exposed	16 / 76 (21.05%)	7 / 75 (9.33%)	
occurrences (all)	17	10	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Cholestasis			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Gallbladder polyp			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Hepatic cirrhosis			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Hepatorenal syndrome			

subjects affected / exposed	3 / 76 (3.95%)	6 / 75 (8.00%)	
occurrences (all)	3	6	
Hypertransaminasaemia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Jaundice			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Portal hypertension			
subjects affected / exposed	3 / 76 (3.95%)	0 / 75 (0.00%)	
occurrences (all)	3	0	
Portal vein thrombosis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Blister			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Decubitus ulcer			
subjects affected / exposed	3 / 76 (3.95%)	7 / 75 (9.33%)	
occurrences (all)	4	7	
Dermatitis bullous			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	4 / 76 (5.26%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Ecchymosis			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	3	1	
Erythema			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	

Facial wasting			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Ingrowing nail			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Leukoplakia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Palmar erythema			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Petechiae			
subjects affected / exposed	3 / 76 (3.95%)	1 / 75 (1.33%)	
occurrences (all)	3	1	
Pruritus			
subjects affected / exposed	16 / 76 (21.05%)	18 / 75 (24.00%)	
occurrences (all)	19	18	
Rash			
subjects affected / exposed	6 / 76 (7.89%)	2 / 75 (2.67%)	
occurrences (all)	6	2	
Rash maculo-papular			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Rash morbilliform			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Rash papular			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Skin discolouration			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	

Skin irritation			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Spider naevus			
subjects affected / exposed	0 / 76 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	3	
Telangiectasia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	13 / 76 (17.11%)	17 / 75 (22.67%)	
occurrences (all)	14	21	
Anuria			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Chromaturia			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Dysuria			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Nephropathy toxic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Oliguria			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	7 / 76 (9.21%)	4 / 75 (5.33%)	
occurrences (all)	7	4	
Renal impairment			

subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Renal salt-wasting syndrome			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Urethral prolapse			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	0 / 76 (0.00%)	5 / 75 (6.67%)	
occurrences (all)	0	5	
Urinary retention			
subjects affected / exposed	0 / 76 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	3	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Hypothyroidism			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 76 (3.95%)	2 / 75 (2.67%)	
occurrences (all)	3	2	
Back pain			
subjects affected / exposed	4 / 76 (5.26%)	4 / 75 (5.33%)	
occurrences (all)	4	4	
Exostosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Flank pain			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Joint stiffness			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	3 / 76 (3.95%)	2 / 75 (2.67%)	
occurrences (all)	3	2	
Muscular weakness			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal stiffness			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	7 / 76 (9.21%)	3 / 75 (4.00%)	
occurrences (all)	8	3	
Sarcopenia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	11 / 76 (14.47%)	8 / 75 (10.67%)	
occurrences (all)	11	8	
Bacterial vaginosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	

Bronchitis			
subjects affected / exposed	1 / 76 (1.32%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Candida infection			
subjects affected / exposed	4 / 76 (5.26%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Catheter site infection			
subjects affected / exposed	0 / 76 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Cellulitis			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	3	2	
Clostridium difficile colitis			
subjects affected / exposed	2 / 76 (2.63%)	4 / 75 (5.33%)	
occurrences (all)	2	4	
Cystitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Device related infection			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Device related sepsis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Endocarditis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Enterococcal infection			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Fungal skin infection			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	

H1N1 influenza			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Oesophageal candidiasis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	2 / 76 (2.63%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Oral herpes			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Peritonitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Peritonitis bacterial			
subjects affected / exposed	6 / 76 (7.89%)	4 / 75 (5.33%)	
occurrences (all)	6	4	
Pneumonia			
subjects affected / exposed	8 / 76 (10.53%)	7 / 75 (9.33%)	
occurrences (all)	8	8	
Pyelonephritis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	

Pyuria			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Sepsis			
subjects affected / exposed	4 / 76 (5.26%)	4 / 75 (5.33%)	
occurrences (all)	4	4	
Septic shock			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Tinea cruris			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	14 / 76 (18.42%)	10 / 75 (13.33%)	
occurrences (all)	15	11	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Decreased appetitete			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Dehydration			
subjects affected / exposed	4 / 76 (5.26%)	2 / 75 (2.67%)	
occurrences (all)	4	2	
Diabetes mellitus			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Fluid overload			
subjects affected / exposed	4 / 76 (5.26%)	5 / 75 (6.67%)	
occurrences (all)	4	5	
Gout			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Hyperammonaemia			
subjects affected / exposed	5 / 76 (6.58%)	6 / 75 (8.00%)	
occurrences (all)	5	6	
Hypercalcaemia			
subjects affected / exposed	2 / 76 (2.63%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Hyperglycaemia			
subjects affected / exposed	13 / 76 (17.11%)	7 / 75 (9.33%)	
occurrences (all)	15	7	
Hyperkalaemia			
subjects affected / exposed	9 / 76 (11.84%)	5 / 75 (6.67%)	
occurrences (all)	9	5	
Hypermagnesaemia			
subjects affected / exposed	1 / 76 (1.32%)	1 / 75 (1.33%)	
occurrences (all)	1	1	
Hypernatraemia			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Hyperphosphataemia			
subjects affected / exposed	2 / 76 (2.63%)	4 / 75 (5.33%)	
occurrences (all)	2	4	
Hypoalbuminaemia			
subjects affected / exposed	3 / 76 (3.95%)	3 / 75 (4.00%)	
occurrences (all)	3	4	
Hypocalcaemia			
subjects affected / exposed	4 / 76 (5.26%)	2 / 75 (2.67%)	
occurrences (all)	4	2	
Hypoglycaemia			

subjects affected / exposed	4 / 76 (5.26%)	4 / 75 (5.33%)	
occurrences (all)	5	4	
Hypokalaemia			
subjects affected / exposed	9 / 76 (11.84%)	12 / 75 (16.00%)	
occurrences (all)	11	12	
Hypomagnesaemia			
subjects affected / exposed	12 / 76 (15.79%)	8 / 75 (10.67%)	
occurrences (all)	12	8	
Hyponatraemia			
subjects affected / exposed	10 / 76 (13.16%)	6 / 75 (8.00%)	
occurrences (all)	11	7	
Hypophosphataemia			
subjects affected / exposed	18 / 76 (23.68%)	11 / 75 (14.67%)	
occurrences (all)	21	11	
Hypovolaemia			
subjects affected / exposed	4 / 76 (5.26%)	2 / 75 (2.67%)	
occurrences (all)	4	2	
Lactic acidosis			
subjects affected / exposed	4 / 76 (5.26%)	5 / 75 (6.67%)	
occurrences (all)	4	5	
Malnutrition			
subjects affected / exposed	2 / 76 (2.63%)	3 / 75 (4.00%)	
occurrences (all)	2	3	
Metabolic acidosis			
subjects affected / exposed	10 / 76 (13.16%)	3 / 75 (4.00%)	
occurrences (all)	12	4	
Obesity			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Refeeding syndrome			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Vitamin A deficiency			

subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	2 / 76 (2.63%)	1 / 75 (1.33%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2015	The VTL-308 protocol includes the following revisions: • Revision of the primary analysis population to the Intent-to-Treat (ITT) population, not the Modified Intent-to-Treat (mITT) population • Clarification on steroid administration as part of standard of care • Revision of the study design to include a minimum number of events prior to analysis of the data, consistent with the event driven primary endpoint • Removal of the Coagulopathy and Thrombocytopenia Overview from Appendix E of the protocol, as it is not relevant to the conduct of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 September 2018	Although there was a numerical improvement in survival in the ELAD-treated group between three months and one year following randomization, the VTL-308 study failed to meet the primary endpoint of a significant improvement in overall survival through at least 91 days assessed using the Kaplan Meier statistical method. The secondary endpoint of proportion of survivors at study day 91 also showed no statistically significant difference between the groups. Due to these results, Vital Therapies, Inc. has ceased any further development of the ELAD System and closed all ongoing long term follow up studies.	-

Notes:

Limitations and caveats

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

None.

Notes: