Clinical trial results:
A Multicenter, Open-label, Randomized, Two Arm Study to Investigate the Efficacy and Safety of a Therapy Avoiding Intraoperative Steroids in Combination With Basiliximab, Cyclosporine/Cyclosporine Microemulsion, and Steroids in Pediatric de Novo Liver Transplant Recipients

Summary

EudraCT number	2015-003528-29
Trial protocol	Outside EU/EEA
Global end of trial date	09 March 2009

Results information

Result version number	v1 (current)
This version publication date	19 December 2016
First version publication date	19 December 2016

Trial information

Trial identification

Sponsor protocol code	CCHI621ADE04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00149890
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals AG, +41 613241111,

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	09 March 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 March 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the effect of an immunosuppressive therapy administered with intraoperative versus without intraoperative steroids in combination with Simulect®, Sandimmun®/ Sandimmun® Optoral and steroids, as measured by the incidence of at least one biopsy proven acute rejection episode, graft loss, or death within the first three months post-transplantation in pediatric de novo liver transplant recipients.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2004
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 77
Worldwide total number of subjects	77
EEA total number of subjects	77

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)	45
Children (2-11 years)	23
Adolescents (12-17 years)	9
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

It was initially planned to include a total of 80 patients. A total of 77 patients were screened and treated with study medication .

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	With Intraoperative Steroids

Arm description:

Intraoperative steroids were administered during transplantation and Basiliximab was administered on Day 0 and 4 (10 mg if the body weight was <35 kg; 20 mg if body weight was ≥35 kg) in combination with cyclosporine/cyclosporine microemulsion and steroids. Basiliximab was administered as an intravenous bolus injection within 8 hours after reperfusion of the graft.

Arm type	Experimental
Investigational medicinal product name	Basiliximab
Investigational medicinal product code	
Other name	Simulect®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Basiliximab (10 mg) was supplied as a lyophilisate in vials with ampoules of sterile water for injection (5 mL) and had to be given of 10 mg (body weight <35 kg) or 20 mg (body weight ≥35 kg) strength.

Investigational medicinal product name	Cyclosporine/cyclosporine microemulsion
Investigational medicinal product code	
Other name	Sandimmun®/Sandimmun® Optoral
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Cyclosporine/cyclosporine microemulsion had to be started with 100 mg/m^2/day intravenous (i.v) (2x4h) for 7 days and was to be continued i.v. or orally from day 8 onwards as per center practice. During the 6 months treatment period Cyclosporine doses had to be adjusted according to Cyclosporine A (CsA)-trough levels.

Investigational medicinal product name	Steroid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous prednisolone (loading dose: 300 mg/m^2, maximum 500 mg) had to be administered intraoperatively only in treatment arm 1 (day 0). The first dose of steroids in treatment arm 2 (day 0) had to be administered within 8 hours after reperfusion of the graft. Beginning from day 1 to day 6 doses of 15 mg/m^2/day had to be given intravenously (i.v.) in both treatment arms. Then, the steroid doses (oral prednisone or its equivalent) were to be decreased from 10 mg/m^2/day orally (day 7-13),

to 7.5 mg/m²/day orally (day 14-30), to 4 mg/m^2/day orally (until end of month 2), to 2.5 mg/m^2/day orally (until end of month 3) and to 1 mg/m^2/day orally (until end of month 6).

Arm title	Without Intraoperative Steroids

Arm description:

No intraoperative steroids were administered during transplantation and Basiliximab was administered on Day 0 and 4 (10 mg if the body weight was <35 kg; 20 mg if body weight was ≥35 kg) in combination with cyclosporine/cyclosporine microemulsion and steroids. Basiliximab and the first dose of steroids had to be administered within 8 hours after reperfusion of the graft and basiliximab was given as an intravenous bolus injection.

Arm type	Active comparator
Investigational medicinal product name	Basiliximab
Investigational medicinal product code	
Other name	Simulect®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Basiliximab (10 mg) was supplied as a lyophilisate in vials with ampoules of sterile water for injection (5 mL) and had to be given of 10 mg (body weight <35 kg) or 20 mg (body weight ≥35 kg) strength.

Investigational medicinal product name	Cyclosporine/cyclosporine microemulsion
Investigational medicinal product code	
Other name	Sandimmun®/Sandimmun® Optoral
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Cyclosporine/cyclosporine microemulsion had to be started with 100 mg/m^2/day intravenous (i.v) (2x4h) for 7 days and was to be continued i.v. or orally from day 8 onwards as per center practice. During the 6 months treatment period Cyclosporine doses had to be adjusted according to Cyclosporine A (CsA)-trough levels.

Investigational medicinal product name	Steroid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous prednisolone (loading dose: 300 mg/m^2, maximum 500 mg) had to be administered intraoperatively only in treatment arm 1 (day 0). The first dose of steroids in treatment arm 2 (day 0) had to be administered within 8 hours after reperfusion of the graft. Beginning from day 1 to day 6 doses of 15 mg/m^2/day had to be given intravenously (i.v.) in both treatment arms. Then, the steroid doses (oral prednisone or its equivalent) were to be decreased from 10 mg/m^2/day orally (day 7-13), to 7.5 mg/m²/day orally (day 14-30), to 4 mg/m^2/day orally (until end of month 2), to 2.5 mg/m^2/day orally (until end of month 3) and to 1 mg/m^2/day orally (until end of month 6).

Number of subjects in period 1	With Intraoperative Steroids	Without Intraoperative Steroids
Started	39	38
Completed	26	20
Not completed	13	18
Protocol Violavtion	1	-
Graft loss	2	1
Adverse event, non-fatal	1	8
Lost to follow-up	1	-
Lack of efficacy	8	9

Baseline characteristics

Reporting groups

Reporting group title	With Intraoperative Steroids

Reporting group description:

Intraoperative steroids were administered during transplantation and Basiliximab was administered on Day 0 and 4 (10 mg if the body weight was <35 kg; 20 mg if body weight was ≥35 kg) in combination with cyclosporine/cyclosporine microemulsion and steroids. Basiliximab was administered as an intravenous bolus injection within 8 hours after reperfusion of the graft.

Reporting group title	Without Intraoperative Steroids

Reporting group description:

No intraoperative steroids were administered during transplantation and Basiliximab was administered on Day 0 and 4 (10 mg if the body weight was <35 kg; 20 mg if body weight was ≥35 kg) in combination with cyclosporine/cyclosporine microemulsion and steroids. Basiliximab and the first dose of steroids had to be administered within 8 hours after reperfusion of the graft and basiliximab was given as an intravenous bolus injection.

Reporting group values	With Intraoperative Steroids	Without Intraoperative Steroids	Total
Number of subjects	39	38	77
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	21	24	45
Children (2-11 years)	15	8	23
Adolescents (12-17 years)	3	6	9
Age continuous Units: years			
arithmetic mean	3.08	3.71	
standard deviation	± 4.09	± 5.36	-
Gender categorical Units: Subjects			
Female	21	19	40
Male	18	19	37

End points

End points reporting groups

Reporting group title	With Intraoperative Steroids

Reporting group description:

Intraoperative steroids were administered during transplantation and Basiliximab was administered on Day 0 and 4 (10 mg if the body weight was <35 kg; 20 mg if body weight was ≥35 kg) in combination with cyclosporine/cyclosporine microemulsion and steroids. Basiliximab was administered as an intravenous bolus injection within 8 hours after reperfusion of the graft.

Reporting group title	Without Intraoperative Steroids

Reporting group description:

No intraoperative steroids were administered during transplantation and Basiliximab was administered on Day 0 and 4 (10 mg if the body weight was <35 kg; 20 mg if body weight was ≥35 kg) in combination with cyclosporine/cyclosporine microemulsion and steroids. Basiliximab and the first dose of steroids had to be administered within 8 hours after reperfusion of the graft and basiliximab was given as an intravenous bolus injection.

Primary: Number of Participants With at Least One Biopsy Proven Acute Rejection (BPAR) Episode, Graft Loss or Death Within the First Three Months Post-transplantation

End point title	Number of Participants With at Least One Biopsy Proven Acute Rejection (BPAR) Episode, Graft Loss or Death Within the First Three Months Post-transplantation[1]

End point description:

Graft loss is defined as being listed for a re-transplantation. The analysis was based on the locally performed biopsy assessments. Generally, patients not experiencing a relevant event (i.e., acute rejection, graft loss or death) were censored with the last visit date.

End point type	Primary

End point timeframe:

3 months after treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis provided for Number of Participants With at Least One Biopsy Proven Acute Rejection (BPAR) Episode, Graft Loss or Death Within the First Three Months Post-transplantation
.

End point values	With Intraoperative Steroids	Without Intraoperative Steroids		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39[2]	38[3]		
Units: Participants				
number (not applicable)				
Stratum age < 2 years (N=21, 24)	8	15		
Stratum age 2-16 years (N=18, 14)	14	11		
Total (N= 39, 38)	22	26		

Notes:

[2] - safety/Intent to Treat (ITT) population

[3] - safety/Intent to Treat (ITT) population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Biopsy Proven Acute Rejection (BPAR) Episodes Within the First Three Months

End point title	Number of Participants With Biopsy Proven Acute Rejection (BPAR) Episodes Within the First Three Months

End point description:

At biopsy of transplanted tissue sample, acute rejection has an onset 2-60 days after transplantation, with interstitial vascular endothelial cell swelling, interstitial accumulation of lymphocytes, plasma cells, immunoblasts, macrophages, neutrophils; tubular separation with edema/necrosis of tubular epithelium; swelling and vacuolization of the endothelial cells, vascular edema, bleeding and inflammation. Clinical signs and symptoms include malaise, fever, and hypertension.

End point type	Secondary

End point timeframe:

3 months

End point values	With Intraoperative Steroids	Without Intraoperative Steroids		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39[4]	38[5]		
Units: Participants				
number (not applicable)	20	26		

Notes:

[4] - safety/Intent to Treat (ITT) population

[5] - safety/Intent to Treat (ITT) population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Steroid Resistant Rejection Episodes Within Three and Six Months

End point title	Number of Participants With Steroid Resistant Rejection Episodes Within Three and Six Months

End point description:

To evaluate the efficacy of a regimen with intraoperative versus without intraoperative steroids in combination with basiliximab, cyclosporine/cyclosporine microemulsion and steroids as measured by the incidence of steroid resistant rejection episodes within three and six months.

End point type	Secondary

End point timeframe:

3 and 6 months

End point values	With Intraoperative Steroids	Without Intraoperative Steroids		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39[6]	38[7]		
Units: Participants				
number (not applicable)				
Within 3 months post treatment	2	2		
Within 6 months post treatment	2	2		

Notes:

[6] - safety/Intent to Treat (ITT) population

[7] - safety/Intent to Treat (ITT) population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Death or Graft Loss Within Three and Six Months After Transplantation

End point title	Percentage of Participants Experiencing Death or Graft Loss Within Three and Six Months After Transplantation

End point description:

Graft loss is defined as being listed for a re-transplantation.

End point type	Secondary

End point timeframe:

3 months and 6 months

End point values	With Intraoperative Steroids	Without Intraoperative Steroids		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39[8]	38[9]		
Units: Percentage of participants				
number (not applicable)				
Death within 3 months post treatment	0	2.6		
Death within 6 months post treatment	0	2.6		
Graft Loss within 3 months post treatment	5.1	2.6		
Graft Loss within 6 months post treatment	5.1	5.3		

Notes:

[8] - safety/Intent to Treat (ITT) population

[9] - safety/Intent to Treat (ITT) population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Bacterial, Viral and Fungal Infections During Six Months

End point title	Number of Participants With Bacterial, Viral and Fungal Infections During Six Months

End point description:

To evaluate the safety of a regimen with intraoperative versus without intraoperative steroids in combination with basiliximab, cyclosporine/cyclosporine microemulsion and steroids as measured by the episodes of bacterial, viral and fungal infections during six months.

End point type	Secondary

End point timeframe:

6 months

End point values	With Intraoperative Steroids	Without Intraoperative Steroids		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39[10]	38[11]		
Units: Participants				
number (not applicable)				
Fungal	16	16		
Viral	15	14		
Bacterial	10	18		

Notes:

[10] - Safety Population

[11] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Onset of a First Biopsy Proven Acute Rejection

End point title	Time of Onset of a First Biopsy Proven Acute Rejection

End point description:

Biopsied Tissue shows rejection at onset 2-60 days after transplantation, with interstitial vascular endothelial cell swelling, interstitial accumulation of lymphocytes, plasma cells, immunoblasts, macrophages, neutrophils; tubular separation with edema/necrosis of tubular epithelium; swelling and vacuolization of the endothelial cells, vascular edema, bleeding and inflammation. Clinical signs and symptoms include malaise, fever and hypertension

End point type	Secondary

End point timeframe:

6 months

End point values	With Intraoperative Steroids	Without Intraoperative Steroids		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39[12]	38[13]		
Units: months				
median (confidence interval 95%)	1.93 (0.99 to 9.99)	0.75 (0.4 to 1.31)		

Notes:

[12] - safety/ITT population
0.99/9.99 = Upper bound of the Confidence Interval was not attained

[13] - safety/Intent to Treat (ITT) population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment Failure Within Three and Six Months

End point title	Percentage of Participants With Treatment Failure Within Three and Six Months

End point description:

To evaluate the proportion of patients with treatment failure treated with a therapy consisting of intraoperative versus without intraoperative steroids in combination with basiliximab, cyclosporine/cyclosporine microemulsion and steroids within three and six months.

End point type	Secondary

End point timeframe:

3 and 6 months

End point values	With Intraoperative Steroids	Without Intraoperative Steroids		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39[14]	38[15]		
Units: Percentage of participants				
number (confidence interval 95%)				
3 month: Age < 2 years (N= 21, 24)	0 (0 to 16.11)	4.17 (0.11 to 21.12)		
3 month: Age 2-16 years (N= 18, 14)	11.11 (1.38 to 34.71)	7.14 (0.18 to 33.87)		
3 Month: Total	5.13 (0.63 to 17.32)	5.26 (0.64 to 17.75)		
6 month: Age < 2 years (N= 21, 24)	0 (0 to 16.11)	4.17 (0.11 to 21.12)		
6 month: Age 2-16 years (N= 18, 14)	11.11 (1.38 to 34.71)	7.14 (0.18 to 33.87)		
6 Month: Total	5.13 (0.63 to 17.32)	5.26 (0.64 to 17.75)		

Notes:

[14] - Intention to treat population

[15] - Intention to treat population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	With intraoperative steroids
Reporting group description:	
With intraoperative steroids	
Reporting group title	Without intraoperative steroids
Reporting group description:	
Without intraoperative steroids	

Serious adverse events	With intraoperative steroids	Without intraoperative steroids	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 39 (46.15%)	23 / 38 (60.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Histiocytosis haematophagic			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Inferior vena caval occlusion			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haematoma			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reperfusion injury			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Device occlusion			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyrexia			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
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			
Atelectasis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchomalacia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chylothorax			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic rupture			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatopulmonary syndrome			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pleural effusion			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachypnoea			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal stenosis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Epstein-barr virus antibody positive			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immunosuppressant drug level decreased			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Transaminases increased			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial injury			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary anastomosis complication			
subjects affected / exposed	1 / 39 (2.56%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complications of transplanted liver			
subjects affected / exposed	3 / 39 (7.69%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft complication			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft loss			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatic haematoma			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic rupture			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak			
subjects affected / exposed	0 / 39 (0.00%)	5 / 38 (13.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiovascular insufficiency			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
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			
Bone marrow failure			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 39 (2.56%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (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	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Coeliac disease			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal fistula			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
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 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dilatation			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biloma			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	2 / 39 (5.13%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic hepatic failure			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemobilia			

subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic artery thrombosis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic necrosis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic vein thrombosis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein stenosis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (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	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			

subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	5 / 39 (12.82%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Enterococcal infection			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-barr viraemia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 39 (5.13%)	3 / 38 (7.89%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis astroviral			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 39 (2.56%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 39 (2.56%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 39 (2.56%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoproteinaemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 39 (2.56%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	With intraoperative steroids	Without intraoperative steroids	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 39 (100.00%)	38 / 38 (100.00%)	
Vascular disorders			
Hypertension			

subjects affected / exposed	29 / 39 (74.36%)	27 / 38 (71.05%)	
occurrences (all)	35	35	
Hypotension			
subjects affected / exposed	7 / 39 (17.95%)	8 / 38 (21.05%)	
occurrences (all)	7	12	
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
Vena cava thrombosis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Drug withdrawal syndrome			
subjects affected / exposed	7 / 39 (17.95%)	7 / 38 (18.42%)	
occurrences (all)	7	10	
Obstruction			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Oedema			
subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
Pain			
subjects affected / exposed	2 / 39 (5.13%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
Pyrexia			
subjects affected / exposed	19 / 39 (48.72%)	25 / 38 (65.79%)	
occurrences (all)	31	44	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	10 / 39 (25.64%)	12 / 38 (31.58%)	
occurrences (all)	12	14	
Chylothorax			

subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
Epistaxis			
subjects affected / exposed	2 / 39 (5.13%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
Obstructive airways disorder			
subjects affected / exposed	11 / 39 (28.21%)	14 / 38 (36.84%)	
occurrences (all)	11	16	
Pleural effusion			
subjects affected / exposed	18 / 39 (46.15%)	24 / 38 (63.16%)	
occurrences (all)	20	32	
Pneumothorax			
subjects affected / exposed	3 / 39 (7.69%)	4 / 38 (10.53%)	
occurrences (all)	4	4	
Respiratory failure			
subjects affected / exposed	2 / 39 (5.13%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Tachypnoea			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 39 (10.26%)	4 / 38 (10.53%)	
occurrences (all)	4	4	
Restlessness			
subjects affected / exposed	10 / 39 (25.64%)	14 / 38 (36.84%)	
occurrences (all)	10	15	
Investigations			
Antithrombin iii decreased			
subjects affected / exposed	16 / 39 (41.03%)	16 / 38 (42.11%)	
occurrences (all)	16	16	
Blood magnesium decreased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Blood urea increased			

subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
C-reactive protein increased			
subjects affected / exposed	3 / 39 (7.69%)	7 / 38 (18.42%)	
occurrences (all)	4	8	
Drug level decreased			
subjects affected / exposed	0 / 39 (0.00%)	3 / 38 (7.89%)	
occurrences (all)	0	3	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Immunoglobulins decreased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Platelet count decreased			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Red blood cell count decreased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Transaminases increased			
subjects affected / exposed	5 / 39 (12.82%)	3 / 38 (7.89%)	
occurrences (all)	5	3	
Injury, poisoning and procedural complications			
Complications of transplanted liver			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Hepatic haematoma			
subjects affected / exposed	2 / 39 (5.13%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Post procedural bile leak			
subjects affected / exposed	2 / 39 (5.13%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Procedural pain			

subjects affected / exposed	2 / 39 (5.13%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Bradycardia			
subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
Tachycardia			
subjects affected / exposed	3 / 39 (7.69%)	2 / 38 (5.26%)	
occurrences (all)	3	2	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	17 / 39 (43.59%)	17 / 38 (44.74%)	
occurrences (all)	26	24	
Coagulopathy			
subjects affected / exposed	2 / 39 (5.13%)	6 / 38 (15.79%)	
occurrences (all)	2	8	
Iron deficiency anaemia			
subjects affected / exposed	3 / 39 (7.69%)	1 / 38 (2.63%)	
occurrences (all)	3	1	
Leukocytosis			
subjects affected / exposed	2 / 39 (5.13%)	6 / 38 (15.79%)	
occurrences (all)	3	6	
Leukopenia			
subjects affected / exposed	1 / 39 (2.56%)	4 / 38 (10.53%)	
occurrences (all)	1	5	
Thrombocytopenia			
subjects affected / exposed	10 / 39 (25.64%)	11 / 38 (28.95%)	
occurrences (all)	12	14	
Thrombocytosis			

subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 39 (20.51%)	14 / 38 (36.84%)	
occurrences (all)	9	21	
Ascites			
subjects affected / exposed	12 / 39 (30.77%)	12 / 38 (31.58%)	
occurrences (all)	13	15	
Constipation			
subjects affected / exposed	15 / 39 (38.46%)	17 / 38 (44.74%)	
occurrences (all)	18	22	
Diarrhoea			
subjects affected / exposed	6 / 39 (15.38%)	3 / 38 (7.89%)	
occurrences (all)	7	3	
Flatulence			
subjects affected / exposed	20 / 39 (51.28%)	16 / 38 (42.11%)	
occurrences (all)	22	18	
Gingival hyperplasia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	6 / 39 (15.38%)	2 / 38 (5.26%)	
occurrences (all)	6	4	
Peritonitis			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Vomiting			
subjects affected / exposed	10 / 39 (25.64%)	15 / 38 (39.47%)	
occurrences (all)	14	22	
Hepatobiliary disorders			
Bile duct necrosis			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Bile duct obstruction			

subjects affected / exposed	2 / 39 (5.13%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Cholangitis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Cholestasis			
subjects affected / exposed	1 / 39 (2.56%)	7 / 38 (18.42%)	
occurrences (all)	1	8	
Hepatic ischaemia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Hyperbilirubinaemia			
subjects affected / exposed	2 / 39 (5.13%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Pneumobilia			
subjects affected / exposed	3 / 39 (7.69%)	1 / 38 (2.63%)	
occurrences (all)	3	1	
Portal vein stenosis			
subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
Skin and subcutaneous tissue disorders			
Hirsutism			
subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
Petechiae			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	3 / 39 (7.69%)	3 / 38 (7.89%)	
occurrences (all)	3	3	
Renal and urinary disorders			
Oliguria			
subjects affected / exposed	2 / 39 (5.13%)	5 / 38 (13.16%)	
occurrences (all)	3	6	
Renal failure			

subjects affected / exposed	3 / 39 (7.69%)	6 / 38 (15.79%)	
occurrences (all)	3	6	
Renal failure chronic			
subjects affected / exposed	2 / 39 (5.13%)	2 / 38 (5.26%)	
occurrences (all)	2	2	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Hypothyroidism			
subjects affected / exposed	3 / 39 (7.69%)	2 / 38 (5.26%)	
occurrences (all)	3	2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	3	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	2 / 39 (5.13%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
Adenovirus infection			
subjects affected / exposed	2 / 39 (5.13%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Bacterial infection			
subjects affected / exposed	1 / 39 (2.56%)	3 / 38 (7.89%)	
occurrences (all)	1	3	
Bronchitis			
subjects affected / exposed	3 / 39 (7.69%)	2 / 38 (5.26%)	
occurrences (all)	4	2	
Candidiasis			
subjects affected / exposed	7 / 39 (17.95%)	11 / 38 (28.95%)	
occurrences (all)	7	12	
Cytomegalovirus infection			
subjects affected / exposed	6 / 39 (15.38%)	6 / 38 (15.79%)	
occurrences (all)	6	6	
Enterococcal infection			

subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Epstein-barr virus infection			
subjects affected / exposed	7 / 39 (17.95%)	9 / 38 (23.68%)	
occurrences (all)	8	9	
Fungal infection			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Gastroenteritis			
subjects affected / exposed	4 / 39 (10.26%)	2 / 38 (5.26%)	
occurrences (all)	4	3	
Human herpesvirus 6 infection			
subjects affected / exposed	2 / 39 (5.13%)	4 / 38 (10.53%)	
occurrences (all)	2	4	
Infection			
subjects affected / exposed	4 / 39 (10.26%)	5 / 38 (13.16%)	
occurrences (all)	4	5	
Infectious disease carrier			
subjects affected / exposed	6 / 39 (15.38%)	4 / 38 (10.53%)	
occurrences (all)	6	4	
Oral herpes			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Pneumonia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Respiratory tract infection			
subjects affected / exposed	1 / 39 (2.56%)	4 / 38 (10.53%)	
occurrences (all)	1	5	
Rhinitis			
subjects affected / exposed	3 / 39 (7.69%)	3 / 38 (7.89%)	
occurrences (all)	3	3	
Sepsis			
subjects affected / exposed	3 / 39 (7.69%)	4 / 38 (10.53%)	
occurrences (all)	3	6	
Staphylococcal infection			

subjects affected / exposed	3 / 39 (7.69%)	2 / 38 (5.26%)	
occurrences (all)	3	2	
Wound infection			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	5 / 39 (12.82%)	6 / 38 (15.79%)	
occurrences (all)	5	11	
Hyperglycaemia			
subjects affected / exposed	8 / 39 (20.51%)	15 / 38 (39.47%)	
occurrences (all)	9	17	
Hyperkalaemia			
subjects affected / exposed	8 / 39 (20.51%)	8 / 38 (21.05%)	
occurrences (all)	13	11	
Hyperlipidaemia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Hyperphosphataemia			
subjects affected / exposed	3 / 39 (7.69%)	4 / 38 (10.53%)	
occurrences (all)	3	5	
Hypertriglyceridaemia			
subjects affected / exposed	2 / 39 (5.13%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Hypoalbuminaemia			
subjects affected / exposed	4 / 39 (10.26%)	4 / 38 (10.53%)	
occurrences (all)	5	6	
Hypocalcaemia			
subjects affected / exposed	8 / 39 (20.51%)	15 / 38 (39.47%)	
occurrences (all)	9	23	
Hypoglycaemia			
subjects affected / exposed	4 / 39 (10.26%)	2 / 38 (5.26%)	
occurrences (all)	5	3	
Hypokalaemia			
subjects affected / exposed	8 / 39 (20.51%)	13 / 38 (34.21%)	
occurrences (all)	10	20	

Hypomagnesaemia			
subjects affected / exposed	21 / 39 (53.85%)	15 / 38 (39.47%)	
occurrences (all)	25	19	
Hyponatraemia			
subjects affected / exposed	6 / 39 (15.38%)	6 / 38 (15.79%)	
occurrences (all)	6	7	
Hypophosphataemia			
subjects affected / exposed	5 / 39 (12.82%)	4 / 38 (10.53%)	
occurrences (all)	5	5	
Hypoproteinaemia			
subjects affected / exposed	10 / 39 (25.64%)	5 / 38 (13.16%)	
occurrences (all)	10	6	
Hypovolaemia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Metabolic acidosis			
subjects affected / exposed	1 / 39 (2.56%)	2 / 38 (5.26%)	
occurrences (all)	1	4	
Vitamin k deficiency			
subjects affected / exposed	3 / 39 (7.69%)	2 / 38 (5.26%)	
occurrences (all)	3	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported