Clinical trial results:
A 12-month, open-label, multicenter, randomized, safety, efficacy, pharmacokinetic (PK) and pharmacodynamic (PD) study of two regimens of anti-CD40 monoclonal antibody, CFZ533 vs. standard of care control, in adult de novo liver transplant recipients with a 12-month additional follow-up and a long-term extension (CONTRAIL I)

Summary

EudraCT number	2018-001836-24
Trial protocol	DE BE ES GB HU FR NL IT
Global end of trial date	20 April 2023

Results information

Result version number	v2 (current)
This version publication date	20 July 2024
First version publication date	04 April 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CCFZ533A2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03781414
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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	20 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 April 2023
Global end of trial reached?	Yes
Global end of trial date	20 April 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the rate of composite efficacy failure (Biopsy Proven Acute Rejection (BPAR), graft loss or death) with CFZ533 600 mg and 300 mg regimens compared to TAC Control at Month 12 post-transplantation. The primary objective would be demonstrated, if the composite efficacy failure rate difference between any of the two CFZ533 arms and the TAC arm is below to the pre-defined non-inferiority margin (0.15) with probability >80%. Hence, the primary endpoint was met for CFZ533 300 mg and was not met for CFZ533 600 mg.

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	07 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United States: 50
Worldwide total number of subjects	128
EEA total number of subjects	72

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	101
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were enrolled at 3 sites in Argentina, 1 in Belgium, 1 in Czech Republic, 4 in France, 4 in Germany, 1 in Hungary, 1 in Italy, 1 in The Netherlands, 4 in Spain and 9 in United States.

Pre-assignment

Screening details:

Patients were randomized at a ratio of 2:3:3 to TAC Control (Arm 1) or one of two maintenance regimens of CFZ533: 600 mg CFZ533 subcutaneous (SC) injections every 2 weeks (Arm 2) or 300 mg CFZ533 SC injections every 2 weeks (Arm 3) combined with MMF and CS.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)

Arm description:

Single loading dose of 30 mg/kg IV on Day 8 (with +/- 2 days window). The SC administration of 300 mg (1 injection of 2 mL CFZ533 at 150 mg/mL) every 2 weeks started on Day 29, in combination with MMF and CS up to EOS.

Arm type	Experimental
Investigational medicinal product name	CFZ533 300 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for infusion in pre-filled syringe, Solution for injection in pre-filled syringe, Solution for injection/infusion in pre-filled syringe
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Single loading dose of 30 mg/kg IV on Day 8 (with +/- 2 days window). The SC administration of 300 mg (1 injection of 2 mL CFZ533 at 150 mg/mL) every 2 weeks started on Day 29, in combination with Mycophenolate mofetil (MMF) + Corticosteroids (CS) up to EOS.

Arm title	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)

Arm description:

Loading doses of 30 mg/kg IV on Day 8 (with +/- 2 days window), and 15 mg/kg IV on Day 15. The subcutaneous (SC) administration of 600 mg (2 injections of 2 mL CFZ533 at 150 mg/mL) every 2 weeks started on Day 29, in combination with MMF and CS up to EOS.

Arm type	Experimental
Investigational medicinal product name	CFZ533 600 mg
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Solution for infusion in pre-filled syringe, Solution for injection in pre-filled syringe, Solution for injection/infusion in pre-filled syringe
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Loading doses of 30 mg/kg IV on Day 8 (with +/- 2 days window), and 15 mg/kg IV on Day 15. The SC administration of 600 mg (2 injections of 2 mL CFZ533 at 150 mg/mL) every 2 weeks started on Day 29, in combination with Mycophenolate mofetil (MMF) + Corticosteroids (CS) up to EOS.

Arm title	TAC Control (TAC + MMF)

Arm description:

Tacrolimus (TAC) + Mycophenolate mofetil (MMF) + Corticosteroids (CS) up to End of Study (EOS). Initial TAC target trough were between 5-15 ng/mL during the run-in period. From randomization onwards, the TAC levels were adjusted as per local label.

Arm type	Active comparator
Investigational medicinal product name	Tacrolimus (TAC) + Mycophenolate mofetil (MMF) + Corticosteroids (CS)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe, Solution for injection in pre-filled syringe, Solution for injection/infusion in pre-filled syringe, Tablet
Routes of administration	Intravenous use, Subcutaneous use, Oral use

Dosage and administration details:

Tacrolimus (TAC) + Mycophenolate mofetil (MMF) + Corticosteroids (CS) up to End of Study (EOS). Initial TAC target trough were between 5-15 ng/mL during the run-in period. From randomization onwards, the TAC levels were adjusted as per local label.

Number of subjects in period 1	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)	TAC Control (TAC + MMF)
Started	48	48	32
Safety Set (SAF)	48	47	32
Completed	0	0	0
Not completed	48	48	32
Adverse event, serious fatal	1	4	-
Physician decision	2	-	1
Consent withdrawn by subject	2	3	3
Adverse event, non-fatal	3	6	3
Study terminated by sponsor	39	34	25
Lost to follow-up	1	1	-

Baseline characteristics

Reporting groups	
Reporting group title	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)
Reporting group description:	
Single loading dose of 30 mg/kg IV on Day 8 (with +/- 2 days window). The SC administration of 300 mg (1 injection of 2 mL CFZ533 at 150 mg/mL) every 2 weeks started on Day 29, in combination with MMF and CS up to EOS.	
Reporting group title	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)
Reporting group description:	
Loading doses of 30 mg/kg IV on Day 8 (with +/- 2 days window), and 15 mg/kg IV on Day 15. The subcutaneous (SC) administration of 600 mg (2 injections of 2 mL CFZ533 at 150 mg/mL) every 2 weeks started on Day 29, in combination with MMF and CS up to EOS.	
Reporting group title	TAC Control (TAC + MMF)
Reporting group description:	
Tacrolimus (TAC) + Mycophenolate mofetil (MMF) + Corticosteroids (CS) up to End of Study (EOS). Initial TAC target trough were between 5-15 ng/mL during the run-in period. From randomization onwards, the TAC levels were adjusted as per local label.	

Reporting group values	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)	TAC Control (TAC + MMF)
Number of subjects	48	48	32
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	36	39	26
From 65-84 years	12	9	6
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	56.7	56.2	54.0
standard deviation	± 9.94	± 6.98	± 9.90
Sex: Female, Male			
Units: Participants			
Female	11	15	8
Male	37	33	24
Race/Ethnicity, Customized			
Units: Subjects			
White	45	46	29
Black or African American	3	2	2
Unknown	0	0	1

Reporting group values	Total		
Number of subjects	128		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	101		
From 65-84 years	27		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	34		
Male	94		
Race/Ethnicity, Customized Units: Subjects			
White	120		
Black or African American	7		
Unknown	1		

End points

End points reporting groups

Reporting group title	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)
Reporting group description:	
Single loading dose of 30 mg/kg IV on Day 8 (with +/- 2 days window). The SC administration of 300 mg (1 injection of 2 mL CFZ533 at 150 mg/mL) every 2 weeks started on Day 29, in combination with MMF and CS up to EOS.	
Reporting group title	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)
Reporting group description:	
Loading doses of 30 mg/kg IV on Day 8 (with +/- 2 days window), and 15 mg/kg IV on Day 15. The subcutaneous (SC) administration of 600 mg (2 injections of 2 mL CFZ533 at 150 mg/mL) every 2 weeks started on Day 29, in combination with MMF and CS up to EOS.	
Reporting group title	TAC Control (TAC + MMF)
Reporting group description:	
Tacrolimus (TAC) + Mycophenolate mofetil (MMF) + Corticosteroids (CS) up to End of Study (EOS). Initial TAC target trough were between 5-15 ng/mL during the run-in period. From randomization onwards, the TAC levels were adjusted as per local label.	

Primary: Percentage of patients with composite event (Biopsy Proven Acute Rejection (BPAR), Graft Loss or Death) over 12 months

End point title	Percentage of patients with composite event (Biopsy Proven Acute Rejection (BPAR), Graft Loss or Death) over 12 months
End point description:	
The occurrence of biopsy proven acute rejection (BPAR) was evaluated based on central pathologist evaluation. Graft loss and death was evaluated as per local evaluation.	
End point type	Primary
End point timeframe:	
Baseline to Month 12	

End point values	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)	TAC Control (TAC + MMF)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	32	
Units: Participants	8	12	3	

Statistical analyses

Statistical analysis title	Composite event (BPAR, Graft Loss or Death)
Comparison groups	CFZ533 600 mg regimen (CFZ533 600 mg + MMF) v TAC Control (TAC + MMF)

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Rate difference
Point estimate	0.1696
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0072
upper limit	0.3276

Statistical analysis title	Composite event (BPAR, Graft Loss or Death)
Comparison groups	CFZ533 300 mg regimen (CFZ533 300 mg + MMF) v TAC Control (TAC + MMF)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Rate difference
Point estimate	0.0759
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0729
upper limit	0.2165

Secondary: Mean change in estimated Glomerular Filtration Rate (eGFR) from randomization to Month 12

End point title	Mean change in estimated Glomerular Filtration Rate (eGFR) from randomization to Month 12

End point description:

Renal function as measured by estimated Glomerular Filtration Rate (eGFR) was evaluated using the MDRD formula: eGFR = 175 x (serum concentration of creatinine (SCr))-1.154 x (age)-0.203 x 0.742 [if female] x 1.212 [if Black].

End point type	Secondary

End point timeframe:

Baseline to Month 12

End point values	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)	TAC Control (TAC + MMF)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	32	
Units: mL/min/1.73 m^2				
arithmetic mean (full range (min-max))	2.05 (-60.4 to 71.5)	-9.31 (-55.8 to 28.7)	-14.74 (-104.0 to 20.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events

End point title	Number of Participants with Treatment Emergent Adverse Events

End point description:

The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs), Deaths due to AEs and TEAEs leading to discontinuation, through the monitoring of relevant clinical and laboratory safety parameters.

End point type	Secondary

End point timeframe:

Baseline up to 14 weeks after last dose of study medication (CFZ533 participants) and until 12 weeks for TAC participants, up to approx. 184 weeks.

End point values	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)	TAC Control (TAC + MMF)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	32	
Units: Participants				
TEAEs	48	44	32	
TESAEs	30	29	20	
Fatal TESAEs	1	4	0	
TEAEs leading to discontinuation	14	17	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with dose interruptions and permanent discontinuation of study treatment

End point title	Percentage of patients with dose interruptions and permanent discontinuation of study treatment

End point description:

The number and percentage of participants with dose changes (MMF and TAC), dose interruptions (only in cases of ascites drainage), and permanent discontinuation was summarized. In the CFZ533 arms, during the immediate peri and post-transplant period, TAC was given to provide immunological coverage but TAC needed to be completely weaned off by Day 22.

End point type	Secondary

End point timeframe:

Baseline to Month 24

End point values	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)	TAC Control (TAC + MMF)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	32	
Units: Participants				
CFZ533: Subjects with dose interrupted	8	5	999	
CFZ533: Subjects with permanent d/c of study tx	2	3	999	
TAC: Subjects with dose interrupted	3	3	6	
TAC: Subjects with permanent d/c of study tx	4	8	4	
MMF: Subjects with dose interrupted	18	23	15	
MMF: Subjects with permanent d/c of study tx	9	5	1	

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point description:

On-treatment deaths were reported from first dose of study treatment to 14 weeks after last dose of study medication (CFZ533 participants) and until 12 weeks for TAC participants, up to approx. 184 weeks.
Post-treatment deaths were collected in the post treatment period from 15 weeks after last dose of study medication (CFZ533 participants, Arms 2 & 3) and from 13 weeks for TAC participants (Arm 1), up to approx. 184 weeks. These are not considered Adverse Events.

End point type	Post-hoc

End point timeframe:

On-treatment deaths: Up to approximately 184 weeks. Post-treatment deaths: Up to approximately 184 weeks.

End point values	CFZ533 300 mg regimen (CFZ533 300 mg + MMF)	CFZ533 600 mg regimen (CFZ533 600 mg + MMF)	TAC Control (TAC + MMF)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	47	32	
Units: Participants				
On-treatment deaths	1	3	0	
Post-treatment deaths	0	1	0	
All deaths	1	4	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment adverse events and deaths were reported from first dose of study treatment to 14 weeks after last dose of study medication (CFZ533 participants) and until 12 weeks for TAC participants, up to approx. 184 weeks.

Adverse event reporting additional description:

Any sign or symptom that occurred during the conduct of the trial and safety follow-up. The safety analysis were done on the safety population, which included all randomized subjects who received at least one dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	CFZ533 300 mg + MMF

Reporting group description:

CFZ533 300 mg + MMF

Reporting group title	TAC + MMF

Reporting group description:

TAC + MMF

Reporting group title	CFZ533 600 mg + MMF

Reporting group description:

CFZ533 600 mg + MMF

Serious adverse events	CFZ533 300 mg + MMF	TAC + MMF	CFZ533 600 mg + MMF
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 48 (62.50%)	20 / 32 (62.50%)	29 / 47 (61.70%)
number of deaths (all causes)	1	0	3
number of deaths resulting from adverse events	0	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant peritoneal neoplasm			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangiocarcinoma			

subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Haematoma			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 48 (10.42%)	0 / 32 (0.00%)	5 / 47 (10.64%)
occurrences causally related to treatment / all	2 / 5	0 / 0	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1

Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Chest pain			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Transplant rejection			
subjects affected / exposed	4 / 48 (8.33%)	2 / 32 (6.25%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	3 / 4	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver transplant rejection			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Interstitial lung disease			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			

Device dislocation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	3 / 47 (6.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carbohydrate antigen 19-9 increased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anastomotic stenosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Biliary anastomosis complication			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	1 / 48 (2.08%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress fracture			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural bile leak			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver transplant failure			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			

subjects affected / exposed	1 / 48 (2.08%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft loss			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complications of transplanted liver			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripancreatic fluid collection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 48 (2.08%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular extrasystoles			

subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus arrhythmia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Lethargy			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 48 (2.08%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	2 / 48 (4.17%)	2 / 32 (6.25%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis noninfective			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	2 / 48 (4.17%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic hernia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland calculus			

subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia strangulated			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland enlargement			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic artery stenosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute			

subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biloma			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract disorder			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary ischaemia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			

subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hepatitis cholestatic			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic haematoma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic artery thrombosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic mass			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			

subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Petechiae			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal cyst ruptured			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	4 / 48 (8.33%)	2 / 32 (6.25%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	2 / 4	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus colitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus hepatitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	3 / 48 (6.25%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endophthalmitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal infection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			

subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	2 / 48 (4.17%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxoplasmosis			

subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 48 (4.17%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypervolaemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	CFZ533 300 mg + MMF	TAC + MMF	CFZ533 600 mg + MMF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 48 (93.75%)	30 / 32 (93.75%)	42 / 47 (89.36%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 48 (6.25%)	6 / 32 (18.75%)	3 / 47 (6.38%)
occurrences (all)	3	6	3
Hypotension			
subjects affected / exposed	3 / 48 (6.25%)	1 / 32 (3.13%)	2 / 47 (4.26%)
occurrences (all)	3	1	2
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	5 / 48 (10.42%)	5 / 32 (15.63%)	5 / 47 (10.64%)
occurrences (all)	7	6	5
Oedema peripheral			
subjects affected / exposed	12 / 48 (25.00%)	4 / 32 (12.50%)	6 / 47 (12.77%)
occurrences (all)	12	4	6
Peripheral swelling			
subjects affected / exposed	1 / 48 (2.08%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	1	2	1
Pyrexia			
subjects affected / exposed	7 / 48 (14.58%)	5 / 32 (15.63%)	8 / 47 (17.02%)
occurrences (all)	22	5	24
Asthenia			
subjects affected / exposed	2 / 48 (4.17%)	3 / 32 (9.38%)	2 / 47 (4.26%)
occurrences (all)	2	3	2
Immune system disorders			
Liver transplant rejection			
subjects affected / exposed	1 / 48 (2.08%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	1	2	1
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	5 / 48 (10.42%)	3 / 32 (9.38%)	2 / 47 (4.26%)
occurrences (all)	5	5	2
Dyspnoea			
subjects affected / exposed	4 / 48 (8.33%)	3 / 32 (9.38%)	5 / 47 (10.64%)
occurrences (all)	5	3	6
Cough			
subjects affected / exposed	7 / 48 (14.58%)	0 / 32 (0.00%)	5 / 47 (10.64%)
occurrences (all)	9	0	7
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 48 (12.50%)	3 / 32 (9.38%)	3 / 47 (6.38%)
occurrences (all)	6	3	3
Anxiety			
subjects affected / exposed	5 / 48 (10.42%)	2 / 32 (6.25%)	3 / 47 (6.38%)
occurrences (all)	5	2	3

Alcoholism			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	3 / 47 (6.38%)
occurrences (all)	2	0	4
Blood alkaline phosphatase increased			
subjects affected / exposed	6 / 48 (12.50%)	1 / 32 (3.13%)	6 / 47 (12.77%)
occurrences (all)	6	1	6
Blood creatinine increased			
subjects affected / exposed	1 / 48 (2.08%)	4 / 32 (12.50%)	0 / 47 (0.00%)
occurrences (all)	1	4	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 48 (8.33%)	1 / 32 (3.13%)	2 / 47 (4.26%)
occurrences (all)	4	1	3
Hepatic enzyme increased			
subjects affected / exposed	1 / 48 (2.08%)	2 / 32 (6.25%)	4 / 47 (8.51%)
occurrences (all)	1	3	4
Liver function test increased			
subjects affected / exposed	8 / 48 (16.67%)	2 / 32 (6.25%)	4 / 47 (8.51%)
occurrences (all)	11	2	6
Weight increased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Overdose			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	4 / 47 (8.51%)
occurrences (all)	2	0	4

Palpitations			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Nervous system disorders			
Syncope			
subjects affected / exposed	4 / 48 (8.33%)	0 / 32 (0.00%)	1 / 47 (2.13%)
occurrences (all)	4	0	1
Headache			
subjects affected / exposed	5 / 48 (10.42%)	7 / 32 (21.88%)	10 / 47 (21.28%)
occurrences (all)	6	8	11
Tremor			
subjects affected / exposed	5 / 48 (10.42%)	7 / 32 (21.88%)	6 / 47 (12.77%)
occurrences (all)	6	9	6
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	14 / 48 (29.17%)	4 / 32 (12.50%)	10 / 47 (21.28%)
occurrences (all)	18	4	12
Lymphopenia			
subjects affected / exposed	2 / 48 (4.17%)	1 / 32 (3.13%)	5 / 47 (10.64%)
occurrences (all)	2	1	5
Leukopenia			
subjects affected / exposed	17 / 48 (35.42%)	9 / 32 (28.13%)	16 / 47 (34.04%)
occurrences (all)	20	11	20
Anaemia			
subjects affected / exposed	4 / 48 (8.33%)	4 / 32 (12.50%)	5 / 47 (10.64%)
occurrences (all)	4	4	5
Thrombocytopenia			
subjects affected / exposed	0 / 48 (0.00%)	3 / 32 (9.38%)	3 / 47 (6.38%)
occurrences (all)	0	3	3
Eye disorders			
Vision blurred			
subjects affected / exposed	3 / 48 (6.25%)	0 / 32 (0.00%)	0 / 47 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	6 / 48 (12.50%)	3 / 32 (9.38%)	1 / 47 (2.13%)
occurrences (all)	7	3	2

Vomiting			
subjects affected / exposed	7 / 48 (14.58%)	4 / 32 (12.50%)	3 / 47 (6.38%)
occurrences (all)	11	5	3
Nausea			
subjects affected / exposed	8 / 48 (16.67%)	5 / 32 (15.63%)	4 / 47 (8.51%)
occurrences (all)	10	7	8
Intra-abdominal fluid collection			
subjects affected / exposed	1 / 48 (2.08%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	1	3	1
Diarrhoea			
subjects affected / exposed	12 / 48 (25.00%)	9 / 32 (28.13%)	8 / 47 (17.02%)
occurrences (all)	15	9	12
Constipation			
subjects affected / exposed	6 / 48 (12.50%)	4 / 32 (12.50%)	4 / 47 (8.51%)
occurrences (all)	7	4	4
Abdominal pain upper			
subjects affected / exposed	5 / 48 (10.42%)	1 / 32 (3.13%)	5 / 47 (10.64%)
occurrences (all)	5	2	5
Abdominal pain			
subjects affected / exposed	5 / 48 (10.42%)	8 / 32 (25.00%)	7 / 47 (14.89%)
occurrences (all)	6	10	7
Ascites			
subjects affected / exposed	8 / 48 (16.67%)	3 / 32 (9.38%)	2 / 47 (4.26%)
occurrences (all)	11	4	2
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	4 / 47 (8.51%)
occurrences (all)	3	0	4
Cholangitis			
subjects affected / exposed	1 / 48 (2.08%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	1	2	1
Portal vein stenosis			
subjects affected / exposed	1 / 48 (2.08%)	2 / 32 (6.25%)	0 / 47 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	2 / 48 (4.17%)	4 / 32 (12.50%)	2 / 47 (4.26%)
occurrences (all)	3	6	3
Night sweats			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
Actinic keratosis			
subjects affected / exposed	0 / 48 (0.00%)	3 / 32 (9.38%)	0 / 47 (0.00%)
occurrences (all)	0	3	0
Rash			
subjects affected / exposed	3 / 48 (6.25%)	1 / 32 (3.13%)	5 / 47 (10.64%)
occurrences (all)	3	1	5
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Proteinuria			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Haematuria			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Dysuria			
subjects affected / exposed	4 / 48 (8.33%)	1 / 32 (3.13%)	1 / 47 (2.13%)
occurrences (all)	4	1	1
Acute kidney injury			
subjects affected / exposed	2 / 48 (4.17%)	3 / 32 (9.38%)	0 / 47 (0.00%)
occurrences (all)	3	6	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 48 (4.17%)	2 / 32 (6.25%)	2 / 47 (4.26%)
occurrences (all)	2	2	2
Muscle spasms			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Flank pain			

subjects affected / exposed	0 / 48 (0.00%)	1 / 32 (3.13%)	3 / 47 (6.38%)
occurrences (all)	0	1	3
Back pain			
subjects affected / exposed	8 / 48 (16.67%)	4 / 32 (12.50%)	5 / 47 (10.64%)
occurrences (all)	8	4	5
Arthralgia			
subjects affected / exposed	9 / 48 (18.75%)	2 / 32 (6.25%)	6 / 47 (12.77%)
occurrences (all)	11	2	6
Infections and infestations			
COVID-19			
subjects affected / exposed	15 / 48 (31.25%)	8 / 32 (25.00%)	15 / 47 (31.91%)
occurrences (all)	15	10	16
Cellulitis			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Cystitis			
subjects affected / exposed	1 / 48 (2.08%)	3 / 32 (9.38%)	2 / 47 (4.26%)
occurrences (all)	2	3	2
Cytomegalovirus infection			
subjects affected / exposed	8 / 48 (16.67%)	4 / 32 (12.50%)	5 / 47 (10.64%)
occurrences (all)	8	4	8
Cytomegalovirus infection reactivation			
subjects affected / exposed	2 / 48 (4.17%)	2 / 32 (6.25%)	5 / 47 (10.64%)
occurrences (all)	7	5	8
Cytomegalovirus viraemia			
subjects affected / exposed	5 / 48 (10.42%)	2 / 32 (6.25%)	6 / 47 (12.77%)
occurrences (all)	10	2	7
Nasopharyngitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 32 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
Oral herpes			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Sinusitis			

subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 48 (2.08%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	1	2	1
Urinary tract infection			
subjects affected / exposed	4 / 48 (8.33%)	7 / 32 (21.88%)	4 / 47 (8.51%)
occurrences (all)	9	8	6
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 48 (0.00%)	2 / 32 (6.25%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Iron deficiency			
subjects affected / exposed	3 / 48 (6.25%)	1 / 32 (3.13%)	0 / 47 (0.00%)
occurrences (all)	3	1	0
Hypomagnesaemia			
subjects affected / exposed	1 / 48 (2.08%)	1 / 32 (3.13%)	3 / 47 (6.38%)
occurrences (all)	1	1	4
Hypokalaemia			
subjects affected / exposed	4 / 48 (8.33%)	1 / 32 (3.13%)	3 / 47 (6.38%)
occurrences (all)	4	1	3
Hypoglycaemia			
subjects affected / exposed	1 / 48 (2.08%)	3 / 32 (9.38%)	1 / 47 (2.13%)
occurrences (all)	1	5	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 32 (0.00%)	6 / 47 (12.77%)
occurrences (all)	0	0	8
Hyperkalaemia			
subjects affected / exposed	2 / 48 (4.17%)	4 / 32 (12.50%)	2 / 47 (4.26%)
occurrences (all)	2	5	2
Hyperglycaemia			
subjects affected / exposed	2 / 48 (4.17%)	2 / 32 (6.25%)	2 / 47 (4.26%)
occurrences (all)	2	2	2
Decreased appetite			
subjects affected / exposed	2 / 48 (4.17%)	0 / 32 (0.00%)	3 / 47 (6.38%)
occurrences (all)	2	0	3

Cell death subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 3	0 / 32 (0.00%) 0	0 / 47 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2019	Amendment 1 introduced optional liver biopsies to explore the effect of the study drugs on histology of the liver over time up to 12 months after transplant.
05 March 2020	Amendment 2 clarified that the stopping rule for biopsy proven acute rejection is based on moderate and severe events (Rejection Activity Index (RAI) >= 6) evaluated by a blinded central pathologist; introduced the change of the screening period from 6 months to 2 months; increased the visit window for the randomization visit at Day 8 from +/- 1 to +/- 2 days; and clarified inclusion/exclusion criteria.
20 August 2020	Amendment 3 introduced pre-filled syringes (PFS) to allow for self-administration after Month 12 visit, to offer more flexibility and improve adherence; and added three inclusion/exclusion criteria. The protocol amendment 3 also changed the LPLV date as at time of last EOS visit. However, per GCP the LPLV has to be at the end of the safety-FU period. For this reason, the LPLV date was changed to the end of safety-FU period.
05 March 2021	Amendment 4 allowed to increase the study duration by adding an extension period to collect long-term data in a controlled, clinical trial setting; clarified one exclusion criterion (history of coagulopathy); and added a new exclusion criterion (exclude donors with confirmed history of SARS-CoV-2 infection).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com for complete trial results.

Notes: