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Trial record **2 of 2** for: CRAD001H2304

Previous Study | Return to List | Next Study

Efficacy and Safety of Concentration-controlled Everolimus to Eliminate or to Reduce Tacrolimus Compared to Tacrolimus in de Novo Liver Transplant Recipients (RAD)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00622869

First received: February 13, 2008
Last updated: May 17, 2013
Last verified: May 2013
History of Changes

Full Text View | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Results First Received: April 2, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Liver Transplantation
Interventions:	Drug: Tacrolimus (reduced tacrolimus) Drug: Tacrolimus (tacrolimus elimination) Drug: Tacrolimus (tacrolimus control) Drug: Everolimus (reduced tacrolimus) Drug: Everolimus (tacrolimus elimination) Drug: Corticosteroids

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Low dose tacrolimus (tacrolimus reduced) + everolimus + corticosteroids.
Tacrolimus Elimination	Low-dose tacrolimus (until Month 4, then tacrolimus eliminated) + everolimus + corticosteroids.
Tacrolimus Control Arm	Control dose tacrolimus + corticosteroids.

Participant Flow: Overall Study

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control Arm
STARTED	245	231	243
COMPLETED	202	174	204
NOT COMPLETED	43	57	39
Subject Withdrew Consent	13	17	11
Administrative Problems	11	17	13
Death	12	15	10
Lost to Follow-up	2	4	2
Graft Loss	5	3	2
Missing	0	1	1

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Low dose tacrolimus (tacrolimus reduced) + everolimus + corticosteroids.
Tacrolimus Elimination	Low-dose tacrolimus (until Month 4, then tacrolimus eliminated) + everolimus + corticosteroids.
Tacrolimus Control Arm	Control dose tacrolimus + corticosteroids.
Total	Total of all reporting groups

Baseline Measures

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control Arm	Total
Number of Participants [units: participants]	245	231	243	719
Age [units: years] Mean (Standard Deviation)	53.6 (9.2)	53.2 (10.8)	54.5 (8.7)	53.8 (9.6)
Gender [units: participants]				
Female	65	67	64	196
Male	180	164	179	523

Outcome Measures

Hide All Outcome Measures

1. Primary: Incidence Rate of Composite Efficacy Failure From Randomization to Month 12 [Time Frame: Randomization to Month 12]

Measure Type	Primary
Measure Title	Incidence Rate of Composite Efficacy Failure From Randomization to Month 12

Measure Description	Composite efficacy failure was defined as treated biopsy proven acute rejection (tBPAR), graft loss, or death. A BPAR was defined as an acute rejection confirmed by biopsy with a Rejection Activity Index (RAI) score ≥ 3. tBPAR was defined as a BPAR which was treated with anti-rejection therapy. The RAI is used to score liver biopsies with acute rejection and is composed of 3 categories (portal inflammation, bile duct inflammation damage, venous endothelial inflammation) each scored on a scale of 0 (absent) to 3 (severe) by a trained pathologist. The total RAI score = the sum of the scores of the 3 categories and ranges from 0 to 9, with a higher score indicating greater rejection. The graft was presumed to be lost on the day the patient was newly listed for a liver graft, they received a graft re-transplant, or they died. The incidence rates of composite efficacy failure were estimated with a Kaplan-Meier product-limit formula.
Time Frame	Randomization to Month 12
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat population: All randomized patients.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Low dose tacrolimus (tacrolimus reduced) + everolimus + corticosteroids.
Tacrolimus Elimination	Low-dose tacrolimus (until Month 4, then tacrolimus eliminated) + everolimus + corticosteroids.
Tacrolimus Control Arm	Control dose tacrolimus + corticosteroids.

Measured Values

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control Arm
Number of Participants Analyzed [units: participants]	**245**	**231**	**243**
Incidence Rate of Composite Efficacy Failure From Randomization to Month 12 [units: Percentage of participants]	**6.7**	**24.2**	**9.7**

No statistical analysis provided for Incidence Rate of Composite Efficacy Failure From Randomization to Month 12

2. Secondary: Incidence Rate of Composite Efficacy Failure From Randomization to Month 24 [Time Frame: Randomization to Month 24]

Measure Type	Secondary
Measure Title	Incidence Rate of Composite Efficacy Failure From Randomization to Month 24
Measure Description	Composite efficacy failure was defined as treated biopsy proven acute rejection (tBPAR), graft loss, or death. The incidence rates of composite efficacy failure were estimated with a Kaplan-Meier product-limit formula.
Time Frame	Randomization to Month 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat population: All randomized patients.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Low dose tacrolimus (tacrolimus reduced) + everolimus + corticosteroids.
Tacrolimus Elimination	Low-dose tacrolimus (until Month 4, then tacrolimus eliminated) + everolimus + corticosteroids.
Tacrolimus Control Arm	Control dose tacrolimus + corticosteroids.

Measured Values

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control Arm
Number of Participants Analyzed [units: participants]	**245**	**231**	**243**
Incidence Rate of Composite Efficacy Failure From Randomization to Month 24 [units: Percentage]	**10.3**	**26.0**	**12.5**

No statistical analysis provided for Incidence Rate of Composite Efficacy Failure From Randomization to Month 24

3. Secondary: Incidence Rate of Treated Biopsy Proven Acute Rejection (tBPAR) at Months 12 and 24 [Time Frame: Randomization to Month 24]

Measure Type	Secondary
Measure Title	Incidence Rate of Treated Biopsy Proven Acute Rejection (tBPAR) at Months 12 and 24
Measure Description	tBPAR was defined as an acute rejection confirmed by biopsy with a Rejection Activity Index (RAI) score ≥ 3, which was treated with anti-rejection therapy. Liver biopsies were collected for all cases of suspected acute rejection preferably within 24 hours, at the latest within 48 hours, whenever clinically possible. The RAI is used to score liver biopsies with acute rejection and is composed of 3 categories (portal inflammation, bile duct inflammation damage, venous endothelial inflammation) each scored on a scale of 0 (absent) to 3 (severe) by a trained pathologist. The total RAI score = the sum of the scores of the 3 categories and ranges from 0 to 9, with a higher score indicating greater rejection. The graft was presumed to be lost on the day the patient was newly listed for a liver graft, they received a graft re-transplant, or they died. The incidence rates of tBPAR were estimated with a Kaplan-Meier product-limit formula.
Time Frame	Randomization to Month 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat population: All randomized patients.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Low dose tacrolimus (tacrolimus reduced) + everolimus + corticosteroids.
Tacrolimus Elimination	Low-dose tacrolimus (until Month 4, then tacrolimus eliminated) + everolimus + corticosteroids.
Tacrolimus Control Arm	Control dose tacrolimus + corticosteroids.

Measured Values

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control Arm
Number of Participants Analyzed			

[units: participants]	**245**	**231**	**243**
Incidence Rate of Treated Biopsy Proven Acute Rejection (tBPAR) at Months 12 and 24 [units: Percentage]			
Month 12	**3.0**	**18.8**	**7.2**
Month 24	**4.8**	**19.9**	**7.7**

No statistical analysis provided for Incidence Rate of Treated Biopsy Proven Acute Rejection (tBPAR) at Months 12 and 24

4. Secondary: Change in Renal Function From Randomization to Months 12 and 24 [Time Frame: Randomization to Month 24]

Measure Type	Secondary
Measure Title	Change in Renal Function From Randomization to Months 12 and 24
Measure Description	Change in renal function was assessed by the estimated Glomerular Filtration Rate (eGFR) using the abbreviated (4 variables) Modification of Diet in Renal Disease (MDRD-4) formula which was developed by the MDRD Study Group and has been validated in patients with chronic kidney disease. The MDRD-4 formula used for the eGFR calculation is: eGFR (mL/min/1.73m^2) = 186.3*(C^-1.154)*(A^-0.203)*G*R, where C is the serum concentration of creatinine (mg/dL), A is age (years), G=0.742 when gender is female, otherwise G=1, R=1.21 when race is black, otherwise R=1. The changes in renal function were analyzed via analysis of covariance (ANCOVA) with treatment, pre-transplant hepatitis C virus status and randomization eGFR as covariates. Based on these ANCOVA analyses, the least-squares mean and standard errors of change were reported.
Time Frame	Randomization to Month 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat population: All randomized patients.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Low dose tacrolimus (tacrolimus reduced) + everolimus + corticosteroids.
Tacrolimus Elimination	Low-dose tacrolimus (until Month 4, then tacrolimus eliminated) + everolimus + corticosteroids.
Tacrolimus Control Arm	Control dose tacrolimus + corticosteroids.

Measured Values

	Everolimus + Reduced Tacrolimus	**Tacrolimus Elimination**	**Tacrolimus Control Arm**
Number of Participants Analyzed [units: participants]	**245**	**231**	**243**
Change in Renal Function From Randomization to Months 12 and 24 [units: mL/min/1.73m^2] Least Squares Mean (Standard Error)			
Month 12 (N=244, 231, 243)	**-2.23 (1.54)**	**-1.51 (1.58)**	**-10.73 (1.54)**
Month 24 (N=245, 231, 243)	**-7.94 (1.53)**	**-4.19 (1.58)**	**-14.60 (1.54)**

No statistical analysis provided for Change in Renal Function From Randomization to Months 12 and 24

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Adverse events (AE) were followed until resolution or judged permanent. Serious AEs occurring after transplantation, until 30 days after study medication (SM) discontinuation, or > 4 weeks after study discontinuation if related to SM were reported.
Additional Description	Safety population: All patients who received at least 1 dose of randomized study medication. Adverse events up to Month 24 were reported.

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Low dose tacrolimus (tacrolimus reduced) + everolimus + corticosteroids
Tacrolimus Elimination	Low dose tacrolimus (until Month 4, then tacrolimus eliminated) + everolimus + corticosteroids
Tacrolimus Control Arm	Control dose tacrolimus + corticosteroids

Serious Adverse Events

	Everolimus + Reduced Tacrolimus	Tacrolimus Elimination	Tacrolimus Control Arm
Total, serious adverse events			
# participants affected / at risk	**138/245 (56.33%)**	**152/229 (66.38%)**	**131/242 (54.13%)**
Blood and lymphatic system disorders			
Anaemia † 1			
# participants affected / at risk	**4/245 (1.63%)**	**4/229 (1.75%)**	**5/242 (2.07%)**
Anaemia megaloblastic † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Coagulopathy † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Febrile neutropenia † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Leukocytosis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Neutropenia † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Pancytopenia † 1			
# participants affected / at risk	**6/245 (2.45%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Thrombocytopenia † 1			
# participants affected / at risk	**3/245 (1.22%)**	**2/229 (0.87%)**	**1/242 (0.41%)**
Thrombotic thrombocytopenic purpura † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Cardiac disorders			
Acute coronary syndrome † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Acute myocardial infarction † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**2/242 (0.83%)**

Angina pectoris † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**3/242 (1.24%)**
Angina unstable † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Arteriosclerosis coronary artery † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Atrial fibrillation † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Atrioventricular block second degree † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Cardiac arrest † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Cardiac failure † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Cardiac failure congestive † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Cardio-respiratory arrest † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Congestive cardiomyopathy † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Coronary artery disease † 1			
# participants affected / at risk	**3/245 (1.22%)**	**0/229 (0.00%)**	**3/242 (1.24%)**
Myocardial infarction † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Myocardial ischaemia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Palpitations † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Pericarditis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Tachyarrhythmia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Congenital, familial and genetic disorders			
Hepato-lenticular degeneration † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hydrocele † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Ear and labyrinth disorders			
Acute vestibular syndrome † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Vertigo † 1			
# participants affected / at risk	**0/245 (0.00%)**	**2/229 (0.87%)**	**0/242 (0.00%)**
Eye disorders			
Glaucoma † 1			

# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Retinal detachment † 1			
# participants affected / at risk	2/245 (0.82%)	0/229 (0.00%)	0/242 (0.00%)
Gastrointestinal disorders			
Abdominal hernia † 1			
# participants affected / at risk	5/245 (2.04%)	11/229 (4.80%)	5/242 (2.07%)
Abdominal pain † 1			
# participants affected / at risk	5/245 (2.04%)	7/229 (3.06%)	3/242 (1.24%)
Abdominal pain lower † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Abdominal pain upper † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)
Abdominal tenderness † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Ascites † 1			
# participants affected / at risk	4/245 (1.63%)	3/229 (1.31%)	2/242 (0.83%)
Colitis † 1			
# participants affected / at risk	0/245 (0.00%)	3/229 (1.31%)	0/242 (0.00%)
Colitis ulcerative † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	1/242 (0.41%)
Colonic polyp † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Constipation † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Crohn's disease † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Diarrhoea † 1			
# participants affected / at risk	4/245 (1.63%)	11/229 (4.80%)	4/242 (1.65%)
Diverticulum intestinal † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Dry mouth † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Duodenal perforation † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Duodenal ulcer † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)
Duodenal ulcer haemorrhage † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Duodenogastric reflux † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Femoral hernia † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Gastric ulcer † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)

Gastritis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Gastrointestinal disorder † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Gastrointestinal haemorrhage † 1			
# participants affected / at risk	**1/245 (0.41%)**	**2/229 (0.87%)**	**0/242 (0.00%)**
Gastrointestinal inflammation † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Gastrointestinal obstruction † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Gingival erosion † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Haemorrhoidal haemorrhage † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Haemorrhoids † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Hernial eventration † 1			
# participants affected / at risk	**2/245 (0.82%)**	**2/229 (0.87%)**	**0/242 (0.00%)**
Impaired gastric emptying † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Inguinal hernia † 1			
# participants affected / at risk	**2/245 (0.82%)**	**1/229 (0.44%)**	**3/242 (1.24%)**
Inguinal hernia strangulated † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Intestinal ischaemia † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Intestinal obstruction † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Intestinal perforation † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Large intestinal ulcer † 1			
# participants affected / at risk	**0/245 (0.00%)**	**2/229 (0.87%)**	**0/242 (0.00%)**
Localised intraabdominal fluid collection † 1			
# participants affected / at risk	**2/245 (0.82%)**	**2/229 (0.87%)**	**2/242 (0.83%)**
Lower gastrointestinal haemorrhage † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Melaena † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Mesenteric vein thrombosis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Nausea † 1			
# participants affected / at risk	**1/245 (0.41%)**	**3/229 (1.31%)**	**0/242 (0.00%)**
Oesophagitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**

Pancreatic mass † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Pancreatitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Pancreatitis acute † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Peritoneal haemorrhage † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Rectal haemorrhage † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Spigelian hernia † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Tongue oedema † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Umbilical hernia † 1			
# participants affected / at risk	**3/245 (1.22%)**	**3/229 (1.31%)**	**2/242 (0.83%)**
Umbilical hernia, obstructive † 1			
# participants affected / at risk	**2/245 (0.82%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Upper gastrointestinal haemorrhage † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Varices oesophageal † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Vomiting † 1			
# participants affected / at risk	**1/245 (0.41%)**	**6/229 (2.62%)**	**0/242 (0.00%)**
General disorders			
Asthenia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**3/229 (1.31%)**	**0/242 (0.00%)**
Device dislocation † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Device occlusion † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Drug ineffective † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Feeling jittery † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
General physical health deterioration † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Generalised oedema † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hernia obstructive † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Impaired healing † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Malaise † 1			

# participants affected / at risk	1/245 (0.41%)	1/229 (0.44%)	1/242 (0.41%)
Medical device complication † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)
Multi-organ failure † 1			
# participants affected / at risk	5/245 (2.04%)	1/229 (0.44%)	4/242 (1.65%)
Oedema peripheral † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Pyrexia † 1			
# participants affected / at risk	14/245 (5.71%)	20/229 (8.73%)	7/242 (2.89%)
Sensation of foreign body † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Spinal pain † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Sudden death † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	1/242 (0.41%)
Systemic inflammatory response syndrome † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Hepatobiliary disorders			
Acute hepatic failure † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)
Bile duct obstruction † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	1/242 (0.41%)
Bile duct stenosis † 1			
# participants affected / at risk	3/245 (1.22%)	7/229 (3.06%)	6/242 (2.48%)
Bile duct stone † 1			
# participants affected / at risk	1/245 (0.41%)	3/229 (1.31%)	1/242 (0.41%)
Biliary cast syndrome † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	2/242 (0.83%)
Biliary cirrhosis † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Biliary cirrhosis primary † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Biliary dilatation † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Biliary ischaemia † 1			
# participants affected / at risk	2/245 (0.82%)	2/229 (0.87%)	3/242 (1.24%)
Biliary tract disorder † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Biloma † 1			
# participants affected / at risk	3/245 (1.22%)	1/229 (0.44%)	0/242 (0.00%)
Cholangitis † 1			
# participants affected / at risk	11/245 (4.49%)	11/229 (4.80%)	6/242 (2.48%)
Cholangitis acute † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)

Cholangitis chronic † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Cholelithiasis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**2/229 (0.87%)**	**1/242 (0.41%)**
Cholelithiasis obstructive † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Cholestasis † 1			
# participants affected / at risk	**6/245 (2.45%)**	**3/229 (1.31%)**	**5/242 (2.07%)**
Chronic hepatic failure † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Cytolytic hepatitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hepatic artery stenosis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**4/229 (1.75%)**	**2/242 (0.83%)**
Hepatic artery thrombosis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Hepatic failure † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hepatic function abnormal † 1			
# participants affected / at risk	**2/245 (0.82%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Hepatic lesion † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hepatic necrosis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hepatic steatosis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Hepatic vein occlusion † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hepatitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**2/229 (0.87%)**	**1/242 (0.41%)**
Hepatitis acute † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Hepatitis cholestatic † 1			
# participants affected / at risk	**2/245 (0.82%)**	**2/229 (0.87%)**	**1/242 (0.41%)**
Hepatobiliary disease † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Hepatorenal syndrome † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hepatotoxicity † 1			
# participants affected / at risk	**2/245 (0.82%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Jaundice † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Jaundice cholestatic † 1			
# participants affected / at risk	**2/245 (0.82%)**	**1/229 (0.44%)**	**1/242 (0.41%)**

Liver injury † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Portal hypertension † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Portal vein thrombosis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Sphincter of Oddi dysfunction † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Immune system disorders			
Drug hypersensitivity † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Liver transplant rejection † 1			
# participants affected / at risk	**4/245 (1.63%)**	**24/229 (10.48%)**	**9/242 (3.72%)**
Overlap syndrome † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Serum sickness † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Infections and infestations			
Abdominal abscess † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Abdominal sepsis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Abdominal wall abscess † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Abscess intestinal † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Acute sinusitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Anal abscess † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Appendicitis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Bacterial infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Bacterial sepsis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Biliary sepsis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Bronchitis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Bronchopneumonia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Bronchopulmonary aspergillosis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**

Cellulitis † 1			
# participants affected / at risk	**4/245 (1.63%)**	**0/229 (0.00%)**	**3/242 (1.24%)**
Cholangitis suppurative † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Clostridium difficile colitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Cytomegalovirus infection † 1			
# participants affected / at risk	**3/245 (1.22%)**	**2/229 (0.87%)**	**1/242 (0.41%)**
Device related infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Diarrhoea infectious † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Diverticulitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Enterobacter sepsis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Enterococcal bacteraemia † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Enterococcal infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Enterococcal sepsis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**2/242 (0.83%)**
Erysipelas † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Escherichia bacteraemia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Escherichia sepsis † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Febrile infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Gastroenteritis † 1			
# participants affected / at risk	**3/245 (1.22%)**	**5/229 (2.18%)**	**1/242 (0.41%)**
Gastroenteritis salmonella † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Gastrointestinal infection † 1			
# participants affected / at risk	**3/245 (1.22%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
H1N1 influenza † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Hepatitis B † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Hepatitis C † 1			
# participants affected / at risk	**10/245 (4.08%)**	**7/229 (3.06%)**	**7/242 (2.89%)**
Herpes virus infection † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**

Herpes zoster † 1			
# participants affected / at risk	**0/245 (0.00%)**	**2/229 (0.87%)**	**1/242 (0.41%)**
Herpes zoster oticus † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Histoplasmosis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Incision site infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Infected bites † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Infected cyst † 1			
# participants affected / at risk	**1/245 (0.41%)**	**2/229 (0.87%)**	**0/242 (0.00%)**
Infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Infectious peritonitis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Influenza † 1			
# participants affected / at risk	**0/245 (0.00%)**	**2/229 (0.87%)**	**0/242 (0.00%)**
Intervertebral discitis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Kidney infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Klebsiella infection † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Klebsiella sepsis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Laryngitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Liver abscess † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**2/242 (0.83%)**
Localised infection † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Lung abscess † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Lung infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**3/229 (1.31%)**	**1/242 (0.41%)**
Meningitis cryptococcal † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Neutropenic sepsis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Oral candidiasis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Osteomyelitis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**

Otitis externa † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Peritoneal abscess † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Peritonitis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Peritonitis bacterial † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Pharyngitis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Pneumocystis jiroveci pneumonia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Pneumonia † 1			
# participants affected / at risk	**6/245 (2.45%)**	**9/229 (3.93%)**	**4/242 (1.65%)**
Pneumonia fungal † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Pneumonia herpes viral † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Postoperative wound infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Pseudomembranous colitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Pseudomonal bacteraemia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Pseudomonal sepsis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Pyelonephritis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Respiratory tract infection † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Respiratory tract infection viral † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Sepsis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**2/242 (0.83%)**
Septic shock † 1			
# participants affected / at risk	**3/245 (1.22%)**	**3/229 (1.31%)**	**0/242 (0.00%)**
Sinusitis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Sinusitis aspergillus † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Skin infection † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Splenic abscess † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**

Staphylococcal sepsis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Streptococcal sepsis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Tooth abscess † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Upper respiratory tract infection † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Urinary tract infection † 1			
# participants affected / at risk	**2/245 (0.82%)**	**3/229 (1.31%)**	**2/242 (0.83%)**
Urosepsis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Wound abscess † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Wound infection † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Injury, poisoning and procedural complications			
Abdominal wound dehiscence † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Anastomotic stenosis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Biliary anastomosis complication † 1			
# participants affected / at risk	**3/245 (1.22%)**	**3/229 (1.31%)**	**6/242 (2.48%)**
Cervical vertebral fracture † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Chemical peritonitis † 1			
# participants affected / at risk	**2/245 (0.82%)**	**2/229 (0.87%)**	**1/242 (0.41%)**
Complications of transplanted heart † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Complications of transplanted liver † 1			
# participants affected / at risk	**1/245 (0.41%)**	**4/229 (1.75%)**	**0/242 (0.00%)**
Contusion † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Craniocerebral injury † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Fall † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Femoral neck fracture † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Foot fracture † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Foreign body † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Graft dysfunction † 1			

# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Graft loss † 1			
# participants affected / at risk	1/245 (0.41%)	2/229 (0.87%)	2/242 (0.83%)
Hepatic haematoma † 1			
# participants affected / at risk	1/245 (0.41%)	1/229 (0.44%)	1/242 (0.41%)
Hip fracture † 1			
# participants affected / at risk	2/245 (0.82%)	0/229 (0.00%)	0/242 (0.00%)
Humerus fracture † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	2/242 (0.83%)
Hypoinsulinaemia postoperative † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Incisional hernia † 1			
# participants affected / at risk	9/245 (3.67%)	7/229 (3.06%)	5/242 (2.07%)
Joint dislocation † 1			
# participants affected / at risk	2/245 (0.82%)	0/229 (0.00%)	0/242 (0.00%)
Liver graft loss † 1			
# participants affected / at risk	2/245 (0.82%)	0/229 (0.00%)	1/242 (0.41%)
Lumbar vertebral fracture † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Overdose † 1			
# participants affected / at risk	0/245 (0.00%)	2/229 (0.87%)	0/242 (0.00%)
Pelvic fracture † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Post procedural bile leak † 1			
# participants affected / at risk	2/245 (0.82%)	2/229 (0.87%)	1/242 (0.41%)
Post procedural complication † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Post procedural haemorrhage † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Post-traumatic pain † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Postoperative hernia † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Procedural pain † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	1/242 (0.41%)
Pubis fracture † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Radius fracture † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	1/242 (0.41%)
Rib fracture † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	2/242 (0.83%)
Road traffic accident † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Spinal compression fracture † 1			

# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Spinal fracture † 1			
# participants affected / at risk	1/245 (0.41%)	1/229 (0.44%)	0/242 (0.00%)
Splenic rupture † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Toxicity to various agents † 1			
# participants affected / at risk	2/245 (0.82%)	2/229 (0.87%)	0/242 (0.00%)
Vascular pseudoaneurysm † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Wound dehiscence † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Investigations			
Blood alkaline phosphatase increased † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Blood lactic acid increased † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
C-reactive protein increased † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Chest X-ray abnormal † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Gamma-glutamyltransferase increased † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Hepatic enzyme abnormal † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Hepatic enzyme increased † 1			
# participants affected / at risk	4/245 (1.63%)	4/229 (1.75%)	5/242 (2.07%)
Immunosuppressant drug level increased † 1			
# participants affected / at risk	1/245 (0.41%)	1/229 (0.44%)	0/242 (0.00%)
Liver function test abnormal † 1			
# participants affected / at risk	3/245 (1.22%)	4/229 (1.75%)	2/242 (0.83%)
Platelet count decreased † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Renal function test abnormal † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	1/242 (0.41%)
Transaminases increased † 1			
# participants affected / at risk	4/245 (1.63%)	1/229 (0.44%)	3/242 (1.24%)
Urine output decreased † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Metabolism and nutrition disorders			
Cachexia † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Decreased appetite † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)

Dehydration † 1			
# participants affected / at risk	**2/245 (0.82%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Diabetes mellitus † 1			
# participants affected / at risk	**2/245 (0.82%)**	**2/229 (0.87%)**	**2/242 (0.83%)**
Diabetes mellitus malnutrition-related † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Diabetic ketoacidosis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Fluid overload † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Gout † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Hyperglycaemia † 1			
# participants affected / at risk	**4/245 (1.63%)**	**1/229 (0.44%)**	**3/242 (1.24%)**
Hyperkalaemia † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**2/242 (0.83%)**
Hypoglycaemia † 1			
# participants affected / at risk	**3/245 (1.22%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Hypomagnesaemia † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Ketoacidosis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Malnutrition † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Obesity † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Type 2 diabetes mellitus † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Musculoskeletal and connective tissue disorders			
Arthralgia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Arthritis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Back pain † 1			
# participants affected / at risk	**0/245 (0.00%)**	**2/229 (0.87%)**	**0/242 (0.00%)**
Costochondritis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Intervertebral disc protrusion † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Joint swelling † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Musculoskeletal pain † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Osteoporosis † 1			

# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Pain in extremity † 1			
# participants affected / at risk	0/245 (0.00%)	2/229 (0.87%)	0/242 (0.00%)
Pathological fracture † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Rhabdomyolysis † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Tendonitis † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Benign duodenal neoplasm † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Benign pancreatic neoplasm † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Castleman's disease † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Colorectal cancer metastatic † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Endometrial cancer † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Gastric sarcoma † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Glioblastoma † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Hepatic cancer metastatic † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	1/242 (0.41%)
Hepatic neoplasm malignant † 1			
# participants affected / at risk	3/245 (1.22%)	1/229 (0.44%)	1/242 (0.41%)
Hepatic neoplasm malignant recurrent † 1			
# participants affected / at risk	0/245 (0.00%)	2/229 (0.87%)	1/242 (0.41%)
Histiocytosis haematophagic † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Kaposi's sarcoma † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	2/242 (0.83%)
Laryngeal cancer † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Lung neoplasm † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Lung neoplasm malignant † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Lymphoma † 1			

# participants affected / at risk	2/245 (0.82%)	1/229 (0.44%)	0/242 (0.00%)
Malignant melanoma † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Metastases to adrenals † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Metastases to bone † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Metastases to spine † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Metastatic malignant melanoma † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Metastatic neoplasm † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Oropharyngeal cancer stage unspecified † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Plasmacytoma † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Post transplant lymphoproliferative disorder † 1			
# participants affected / at risk	2/245 (0.82%)	1/229 (0.44%)	0/242 (0.00%)
Prostate cancer † 1			
# participants affected / at risk	2/245 (0.82%)	0/229 (0.00%)	0/242 (0.00%)
Rectal cancer † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Retroperitoneal cancer † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Squamous cell carcinoma † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)
Squamous cell carcinoma of skin † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	2/242 (0.83%)
Nervous system disorders			
Aphasia † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Cerebral haemorrhage † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Cerebral infarction † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Cerebrovascular accident † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)
Cluster headache † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Convulsion † 1			
# participants affected / at risk	1/245 (0.41%)	1/229 (0.44%)	1/242 (0.41%)
Critical illness polyneuropathy † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)

Dizziness † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Dyskinesia † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Encephalitis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Epilepsy † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Headache † 1			
# participants affected / at risk	**3/245 (1.22%)**	**0/229 (0.00%)**	**3/242 (1.24%)**
Ischaemic stroke † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Lethargy † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Migraine † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Monoparesis † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Post herpetic neuralgia † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Psychomotor hyperactivity † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Radiculitis brachial † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Transient ischaemic attack † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Tremor † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
VIIth nerve paralysis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Pregnancy † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Psychiatric disorders			
Adjustment disorder † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Agitation † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Alcoholism † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Anxiety † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**

Bipolar I disorder † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Confusional state † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Delirium † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Depression † 1			
# participants affected / at risk	**2/245 (0.82%)**	**2/229 (0.87%)**	**0/242 (0.00%)**
Drug abuse † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Hallucination, visual † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Insomnia † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Major depression † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Mental status changes † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Nervousness † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Psychotic disorder † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Suicide attempt † 1			
# participants affected / at risk	**1/245 (0.41%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Renal and urinary disorders			
Acute prerenal failure † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Calculus urinary † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Nephrolithiasis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Nephropathy † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**2/242 (0.83%)**
Nephropathy toxic † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**1/242 (0.41%)**
Nephrosclerosis † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Nephrotic syndrome † 1			
# participants affected / at risk	**1/245 (0.41%)**	**1/229 (0.44%)**	**0/242 (0.00%)**
Proteinuria † 1			
# participants affected / at risk	**2/245 (0.82%)**	**0/229 (0.00%)**	**0/242 (0.00%)**
Renal failure † 1			
# participants affected / at risk	**9/245 (3.67%)**	**4/229 (1.75%)**	**7/242 (2.89%)**
Renal failure acute † 1			

# participants affected / at risk	11/245 (4.49%)	3/229 (1.31%)	5/242 (2.07%)
Renal failure chronic † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Renal impairment † 1			
# participants affected / at risk	0/245 (0.00%)	3/229 (1.31%)	0/242 (0.00%)
Ureteric fistula † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Reproductive system and breast disorders			
Endometrial dysplasia † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease † 1			
# participants affected / at risk	1/245 (0.41%)	1/229 (0.44%)	0/242 (0.00%)
Cough † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Dyspnoea † 1			
# participants affected / at risk	4/245 (1.63%)	1/229 (0.44%)	1/242 (0.41%)
Dyspnoea exertional † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Haemothorax † 1			
# participants affected / at risk	0/245 (0.00%)	2/229 (0.87%)	2/242 (0.83%)
Hydropneumothorax † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Hydrothorax † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Hypoxia † 1			
# participants affected / at risk	0/245 (0.00%)	2/229 (0.87%)	0/242 (0.00%)
Interstitial lung disease † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	1/242 (0.41%)
Lung disorder † 1			
# participants affected / at risk	2/245 (0.82%)	1/229 (0.44%)	0/242 (0.00%)
Pleural effusion † 1			
# participants affected / at risk	3/245 (1.22%)	1/229 (0.44%)	3/242 (1.24%)
Pulmonary embolism † 1			
# participants affected / at risk	2/245 (0.82%)	2/229 (0.87%)	0/242 (0.00%)
Pulmonary fibrosis † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Pulmonary hypertension † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)
Pulmonary oedema † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Respiratory acidosis † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Respiratory failure † 1			

# participants affected / at risk	4/245 (1.63%)	0/229 (0.00%)	0/242 (0.00%)
Sinus disorder † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Skin and subcutaneous tissue disorders			
Actinic keratosis † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Alopecia † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Cholestatic pruritus † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Decubitus ulcer † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Erythema nodosum † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Pruritus † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Scar † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Skin ulcer † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Stevens-Johnson syndrome † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Surgical and medical procedures			
Colostomy closure † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)
Vascular disorders			
Aortic aneurysm † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Circulatory collapse † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Deep vein thrombosis † 1			
# participants affected / at risk	2/245 (0.82%)	1/229 (0.44%)	0/242 (0.00%)
Haematoma † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Hyperaemia † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	0/242 (0.00%)
Hypertension † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	3/242 (1.24%)
Hypertensive crisis † 1			
# participants affected / at risk	0/245 (0.00%)	0/229 (0.00%)	1/242 (0.41%)
Hypotension † 1			
# participants affected / at risk	1/245 (0.41%)	0/229 (0.00%)	1/242 (0.41%)
Hypovolaemic shock † 1			
# participants affected / at risk	0/245 (0.00%)	1/229 (0.44%)	0/242 (0.00%)

Lymphocele † 1			
# participants affected / at risk	**0/245 (0.00%)**	**0/229 (0.00%)**	**1/242 (0.41%)**
Peripheral arterial occlusive disease † 1			
# participants affected / at risk	**0/245 (0.00%)**	**1/229 (0.44%)**	**0/242 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 15.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Adverse events (AE) were followed until resolution or judged permanent. Serious AEs occurring after transplantation, until 30 days after study medication (SM) discontinuation, or > 4 weeks after study discontinuation if related to SM were reported.
Additional Description	Safety population: All patients who received at least 1 dose of randomized study medication. Adverse events up to Month 24 were reported.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Everolimus + Reduced Tacrolimus	Low dose tacrolimus (tacrolimus reduced) + everolimus + corticosteroids
Tacrolimus Elimination	Low dose tacrolimus (until Month 4, then tacrolimus eliminated) + everolimus + corticosteroids
Tacrolimus Control Arm	Control dose tacrolimus + corticosteroids

Other Adverse Events

	Everolimus + Reduced Tacrolimus	**Tacrolimus Elimination**	**Tacrolimus Control Arm**
Total, other (not including serious) adverse events			
# participants affected / at risk	**218/245 (88.98%)**	**194/229 (84.72%)**	**205/242 (84.71%)**
Blood and lymphatic system disorders			
Anaemia † 1			
# participants affected / at risk	**22/245 (8.98%)**	**26/229 (11.35%)**	**20/242 (8.26%)**
Leukopenia † 1			
# participants affected / at risk	**31/245 (12.65%)**	**23/229 (10.04%)**	**12/242 (4.96%)**
Thrombocytopenia † 1			
# participants affected / at risk	**16/245 (6.53%)**	**17/229 (7.42%)**	**5/242 (2.07%)**
Gastrointestinal disorders			
Abdominal pain † 1			
# participants affected / at risk	**35/245 (14.29%)**	**29/229 (12.66%)**	**28/242 (11.57%)**
Abdominal pain upper † 1			
# participants affected / at risk	**13/245 (5.31%)**	**10/229 (4.37%)**	**16/242 (6.61%)**
Constipation † 1			
# participants affected / at risk	**18/245 (7.35%)**	**16/229 (6.99%)**	**20/242 (8.26%)**

Diarrhoea † 1			
# participants affected / at risk	**56/245 (22.86%)**	**55/229 (24.02%)**	**58/242 (23.97%)**
Nausea † 1			
# participants affected / at risk	**36/245 (14.69%)**	**23/229 (10.04%)**	**33/242 (13.64%)**
Vomiting † 1			
# participants affected / at risk	**20/245 (8.16%)**	**17/229 (7.42%)**	**21/242 (8.68%)**
General disorders			
Fatigue † 1			
# participants affected / at risk	**27/245 (11.02%)**	**22/229 (9.61%)**	**28/242 (11.57%)**
Oedema peripheral † 1			
# participants affected / at risk	**49/245 (20.00%)**	**43/229 (18.78%)**	**31/242 (12.81%)**
Pyrexia † 1			
# participants affected / at risk	**37/245 (15.10%)**	**39/229 (17.03%)**	**23/242 (9.50%)**
Hepatobiliary disorders			
Cholestasis † 1			
# participants affected / at risk	**15/245 (6.12%)**	**7/229 (3.06%)**	**7/242 (2.89%)**
Infections and infestations			
Hepatitis C † 1			
# participants affected / at risk	**25/245 (10.20%)**	**17/229 (7.42%)**	**21/242 (8.68%)**
Nasopharyngitis † 1			
# participants affected / at risk	**24/245 (9.80%)**	**24/229 (10.48%)**	**26/242 (10.74%)**
Urinary tract infection † 1			
# participants affected / at risk	**21/245 (8.57%)**	**16/229 (6.99%)**	**11/242 (4.55%)**
Injury, poisoning and procedural complications			
Incisional hernia † 1			
# participants affected / at risk	**19/245 (7.76%)**	**9/229 (3.93%)**	**15/242 (6.20%)**
Investigations			
Blood creatinine increased † 1			
# participants affected / at risk	**5/245 (2.04%)**	**6/229 (2.62%)**	**18/242 (7.44%)**
Hepatic enzyme increased † 1			
# participants affected / at risk	**13/245 (5.31%)**	**19/229 (8.30%)**	**14/242 (5.79%)**
Liver function test abnormal † 1			
# participants affected / at risk	**16/245 (6.53%)**	**25/229 (10.92%)**	**23/242 (9.50%)**
Transaminases increased † 1			
# participants affected / at risk	**14/245 (5.71%)**	**9/229 (3.93%)**	**9/242 (3.72%)**
Metabolism and nutrition disorders			
Decreased appetite † 1			
# participants affected / at risk	**16/245 (6.53%)**	**6/229 (2.62%)**	**16/242 (6.61%)**
Diabetes mellitus † 1			
# participants affected / at risk	**17/245 (6.94%)**	**8/229 (3.49%)**	**12/242 (4.96%)**
Hypercholesterolaemia † 1			
# participants affected / at risk	**27/245 (11.02%)**	**21/229 (9.17%)**	**9/242 (3.72%)**
Hyperkalaemia † 1			
# participants affected / at risk	**12/245 (4.90%)**	**8/229 (3.49%)**	**24/242 (9.92%)**

Hyperlipidaemia † 1			
# participants affected / at risk	**21/245 (8.57%)**	**24/229 (10.48%)**	**5/242 (2.07%)**
Hypertriglyceridaemia † 1			
# participants affected / at risk	**20/245 (8.16%)**	**9/229 (3.93%)**	**4/242 (1.65%)**
Hypokalaemia † 1			
# participants affected / at risk	**13/245 (5.31%)**	**9/229 (3.93%)**	**9/242 (3.72%)**
Hypomagnesaemia † 1			
# participants affected / at risk	**19/245 (7.76%)**	**6/229 (2.62%)**	**17/242 (7.02%)**
Musculoskeletal and connective tissue disorders			
Arthralgia † 1			
# participants affected / at risk	**21/245 (8.57%)**	**12/229 (5.24%)**	**23/242 (9.50%)**
Back pain † 1			
# participants affected / at risk	**20/245 (8.16%)**	**13/229 (5.68%)**	**29/242 (11.98%)**
Muscle spasms † 1			
# participants affected / at risk	**14/245 (5.71%)**	**9/229 (3.93%)**	**23/242 (9.50%)**
Musculoskeletal pain † 1			
# participants affected / at risk	**5/245 (2.04%)**	**1/229 (0.44%)**	**15/242 (6.20%)**
Pain in extremity † 1			
# participants affected / at risk	**10/245 (4.08%)**	**14/229 (6.11%)**	**16/242 (6.61%)**
Nervous system disorders			
Headache † 1			
# participants affected / at risk	**51/245 (20.82%)**	**40/229 (17.47%)**	**53/242 (21.90%)**
Tremor † 1			
# participants affected / at risk	**23/245 (9.39%)**	**17/229 (7.42%)**	**36/242 (14.88%)**
Psychiatric disorders			
Depression † 1			
# participants affected / at risk	**16/245 (6.53%)**	**9/229 (3.93%)**	**14/242 (5.79%)**
Insomnia † 1			
# participants affected / at risk	**16/245 (6.53%)**	**18/229 (7.86%)**	**24/242 (9.92%)**
Renal and urinary disorders			
Renal failure † 1			
# participants affected / at risk	**18/245 (7.35%)**	**12/229 (5.24%)**	**22/242 (9.09%)**
Renal impairment † 1			
# participants affected / at risk	**8/245 (3.27%)**	**7/229 (3.06%)**	**16/242 (6.61%)**
Respiratory, thoracic and mediastinal disorders			
Cough † 1			
# participants affected / at risk	**21/245 (8.57%)**	**14/229 (6.11%)**	**20/242 (8.26%)**
Dyspnoea † 1			
# participants affected / at risk	**17/245 (6.94%)**	**5/229 (2.18%)**	**13/242 (5.37%)**
Oropharyngeal pain † 1			
# participants affected / at risk	**16/245 (6.53%)**	**6/229 (2.62%)**	**4/242 (1.65%)**
Pleural effusion † 1			
# participants affected / at risk	**13/245 (5.31%)**	**6/229 (2.62%)**	**11/242 (4.55%)**

Skin and subcutaneous tissue disorders			
Pruritus † 1			
# participants affected / at risk	**13/245 (5.31%)**	**11/229 (4.80%)**	**6/242 (2.48%)**
Pruritus generalised † 1			
# participants affected / at risk	**13/245 (5.31%)**	**14/229 (6.11%)**	**17/242 (7.02%)**
Vascular disorders			
Hypertension † 1			
# participants affected / at risk	**51/245 (20.82%)**	**35/229 (15.28%)**	**42/242 (17.36%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 15.0

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (ie, data from all sites) in the clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862 778-8300

No publications provided by Novartis

Publications automatically indexed to this study:

Fischer L, Saliba F, Kaiser GM, De Carlis L, Metselaar HJ, De Simone P, Duvoux C, Nevens F, Fung JJ, Dong G, Rauer B, Junge G; H2304 Study Group. Three-year Outcomes in De Novo Liver Transplant Patients Receiving Everolimus With Reduced Tacrolimus: Follow-Up Results From a Randomized, Multicenter Study. Transplantation. 2015 Jul;99(7):1455-62. doi: 10.1097/TP.0000000000000555.

Saliba F, De Simone P, Nevens F, De Carlis L, Metselaar HJ, Beckebaum S, Jonas S, Sudan D, Fischer L, Duvoux C, Chavin KD, Koneru B, Huang MA, Chapman WC, Foltys D, Dong G, Lopez PM, Fung J, Junge G; H2304 Study Group. Renal function at two years in liver transplant patients receiving everolimus: results of a randomized, multicenter study. Am J Transplant. 2013 Jul;13(7):1734-45. doi: 10.1111/ajt.12280. Epub 2013 May 28.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
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