ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/09/2014

ClinicalTrials.gov ID: NCT00545402

Study Identification

Unique Protocol ID:	ML21273
Brief Title:	A Study of CellCept (Mycophenolate Mofetil) in Combination Therapy in Liver Transplant Patients.
Official Title:	A Randomized, Open Label Study Comparing the Effect of CellCept With Therapeutic Drug Monitoring, Tacrolimus and a Corticosteroid-sparing Regimen Versus Fixed Dose CellCept, Tacrolimus and Corticosteroids Maintained up to 6 Months, on Acute Rejection and Safety in Liver Transplant Patients.
Secondary IDs:	

Study Status

Record Verification:	June 2014
Overall Status:	Completed
Study Start:	November 2007
Primary Completion:	July 2011 [Actual]
Study Completion:	July 2011 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 2007/37 Board Name: Ile-de-France IV Board Affiliation: Unknown Phone: +33142389288 Email: cpp.iledefrance4@orange.fr
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	France:Agence francaise de securite sanitaire des produits de sante (AFSSAPS)

Study Description

Brief Summary:	This 2 arm study will compare the efficacy and safety of two CellCept-containing treatment regimens in de novo liver transplant patients. Patients will be randomized into one of two groups, to receive either CellCept (at a starting dose of 3g/day po, adjusted according to exposure) standard dose tacrolimus and corticosteroids (10-15 mg/kg i.v. on day 0), or fixed dose CellCept 2g/day po, standard dose tacrolimus and corticosteroids (10-15mg/kg i.v. on day 0, then reducing from 20mg to 5mg over 6 months, and discontinuing after 6 months). The anticipated time on study treatment is 3-12 months, and the target sample size is 100-500 individuals.
Detailed Description:	

Conditions

Conditions:	Liver Transplantation
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 180 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: MMF, Adjusted Dose; Tacrolimus; Corticosteroids Participants received mycophenolate mofetil (MMF) 3 grams per day (g/d), orally (PO), twice per day (BID) with meals from Day 0 to Day 4; the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14, Months 1, 13, 6, 9, and 12. Participants also received tacrolimus adjusted to a target trough level of 8 to (-) 12 nanograms per milliliter (ng/mL) from Day 0 to Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received corticosteroids 10-15 milligrams per kilogram (mg/kg), intravenously (IV), pre-operation on Day 0.	Drug: Mycophenolate mofetil, adjusted dose 3 g/d PO BID during meals from Day 0 to Day 4, followed by dose adjustment based on AUC using the Bayesian method with limited sampling strategy on Days 5 and 14, Months 1, 13, 6, 9, and 12. Other Names: • CellCept Drug: Tacrolimus Target trough level of 8-2 ng/mL from Day 0 to Month 1, adjusted to a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12 Drug: Corticosteroids, IV 10-15 mg/kg IV pre-operation on Day 0 Other Names: • Solu-Medrol
Active Comparator: MMF, Standard Dose; Tacrolimus; Corticosteroids Participants received MMF 2 g/d, PO, BID with meals from Day 0 to Month 12. Participants also received tacrolimus adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received corticosteroids 10-15 mg/kg, IV, pre-operation on Day 0; followed by 20 mg/d, PO, 4 times per day (QDS) from Day 0 through Month 1; 15 mg/d, PO, 3 times per day (TID) from the end of Month 1 through Month 2; 10 mg/d, PO, BID from the end of Month 2 through Month 3; and 5 mg/d once per day from the end of Month 3 through Month 6.	Drug: Tacrolimus Target trough level of 8-2 ng/mL from Day 0 to Month 1, adjusted to a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12 Drug: Corticosteroids, IV 10-15 mg/kg IV pre-operation on Day 0 Other Names: • Solu-Medrol Drug: Mycophenolate mofetil, Standard dose 2 g/d PO BID during meals from Day 0 to Month 12 Other Names: • CellCept Drug: Corticosteroids, PO 20 mg/d QDS from Day 0 through Month 1; 15 mg/day, TID from the end of Month 1 through Month 2; 10 mg/d BID from the end of Month 2 through Month 3; and 5 mg/d once per day from the end of Month 3 through Month 6. Other Names: • Cortancyl

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, >=18 years of age;
- recipient of a first orthotopic liver transplant.

Exclusion Criteria:

- history of organ transplants;
- patient receiving a multi-organ transplant;
- calculated creatinine clearance <=30mL/min before transplant;
- leukocyte count < 2000/mm3 at randomization;
- history of cancer within past 5 years, except for successfully treated basal cell or squamous cell cancer, or in situ cervical cancer;
- pregnant or breast-feeding females, or females of childbearing age not using effective contraception.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: France
Clichy, France, 92118

Grenoble, France, 38043

Lyon, France, 69317

Creteil, France, 94010

Lille, France, 59037

Lyon cedex 3, France, 69437

Marseille, France, 13385

Paris, France, 75679

Rennes, France, 35033

Villejuif, France, 94804

Nice, France, 06202

Bordeaux, France, 33076

Toulouse, France, 31059

Besancon, France, 25030

Montpellier, France, 34295

Caen, France, 14033

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Adjusted Mycophenolate Mofetil (MMF)+Tacrolimus+Corticosteroid	Participants received MMF tablets or capsules, 3 grams per day (g/d), orally (PO), twice daily (BID) with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (area under the concentration-time curve [AUC]) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 nanograms per milliliter (ng/mL) from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an intravenous (IV) bolus of methylprednisolone 10-15 milligrams per kilogram (mg/kg) pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + Corticosteroid (CS)	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Overall Study

	Adjusted Mycophenolate Mofetil (MMF)+Tacrolimus+Corticosteroid	Fixed-Dose MMF + Tacrolimus + Corticosteroid (CS)
Started	90	90
Completed	56	61
Not Completed	34	29
Discontinuation of treatment	17	9
Use of unauthorized immunosuppressant	8	7
Death	5	7
Graft loss	2	4
Withdrawal by Subject	0	1
Protocol Violation	1	0
Reason not specified	1	1

Baseline Characteristics

Analysis Population Description

Intent to treat (ITT) population includes all randomized participants who received at least 1 dose of MMF.

Reporting Groups

	Description
Adjusted MMF + Tacrolimus + CS	Participants received MMF tablets or capsules, 3 g/d, PO, BID with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an IV bolus of methylprednisolone 10-15 mg/kg pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + CS	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Baseline Measures

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS	Total
Number of Participants	90	90	180
Age, Continuous [units: years] Mean (Standard Deviation)	53.4 (8.5)	55.1 (8.3)	54.2 (8.4)
Gender, Male/Female [units: participants]			
Female	16	19	35
Male	74	71	145

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Treated Biopsy Proven Acute Rejection (BPAR) According to Banff Criteria up to 12 Months Post-Transplant

Measure Description	Banff criteria required at least 2 of the 3 following features for a histopathological diagnosis of acute rejection: portal inflammation, bile duct inflammation, and venous endothelial inflammation. Each item was graded from 0 to 3 where 0 equals (=) mild, 2 = moderate, and 3 = severe. The sum of the 3 individual scores, from 0 to 9, corresponded to the Rejection Activity Index (RAI). If RAI = 0, 1, or 2, there was no evidence of rejection. If RAI = 3, there was borderline acute rejection. If RAI = 4 or 5, there was mild acute rejection. If RAI = 6 or 7, there was moderate acute rejection. If RAI = 8 or 9, there was severe acute rejection.
Time Frame	Days 0, 5, and 14, Month 1, 2, 3, 6, 9, and 12, 28 days after Month 12 or last dose of study treatment, and 6 and 12 months after the last dose of study treatment
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Adjusted MMF + Tacrolimus + CS	Participants received MMF tablets or capsules, 3 g/d, PO, BID with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an IV bolus of methylprednisolone 10-15 mg/kg pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + CS	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Measured Values

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
Number of Participants Analyzed	87	87
Percentage of Participants With Treated Biopsy Proven Acute Rejection (BPAR) According to Banff Criteria up to 12 Months Post-Transplant [units: percentage of participants]	8.0	8.2

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Graft Loss
Measure Description	Graft survival was defined as the time between the randomization date and the graft loss date. Participants were censored at the date of last follow up, the date of last contact or premature withdrawal, and date of death.
Time Frame	Days 0, 5, and 14, Month 1, 2, 3, 6, 9, and 12, 28 days after Month 12 or last dose of study treatment, and 6 and 12 months after the last dose of study treatment.
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Adjusted MMF + Tacrolimus + CS	Participants received MMF tablets or capsules, 3 g/d, PO, BID with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an IV bolus of methylprednisolone 10-15 mg/kg pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + CS	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Measured Values

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
Number of Participants Analyzed	90	90
Percentage of Participants With Graft Loss [units: percentage of participants]	2.2	5.6

Statistical Analysis 1 for Percentage of Participants With Graft Loss

Statistical Analysis Overview	Comparison Groups	Adjusted MMF + Tacrolimus + CS, Fixed-Dose MMF + Tacrolimus + CS
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2611
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Graft Survival
Measure Description	The median time, in months, between randomization and graft loss event. Participants were censored at the date of last follow up, the date of last contact or premature withdrawal, and date of death.
Time Frame	Days 0, 5, and 14, Month 1, 2, 3, 6, 9, and 12, 28 days after Month 12 or last dose of study treatment, and 6 and 12 months after the last dose of study treatment.
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Adjusted MMF + Tacrolimus + CS	Participants received MMF tablets or capsules, 3 g/d, PO, BID with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an IV bolus of methylprednisolone 10-15 mg/kg pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + CS	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Measured Values

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
Number of Participants Analyzed	90	90
Graft Survival [units: months] Median (Full Range)	12.9 (0.0 to 24.5)	12.9 (0.0 to 20.2)

4. Secondary Outcome Measure:

Measure Title	Overall Survival (OS) at Month 12 - Percentage of Participants With an Event
Measure Description	OS was defined as the time between the date of randomization and death up to Month 12. Participants were censored at the date of last follow up and the date of last contact or premature withdrawal.
Time Frame	Days 0, 5, and 14, Month 1, 2, 3, 6, 9, and 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Adjusted MMF + Tacrolimus + CS	Participants received MMF tablets or capsules, 3 g/d, PO, BID with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an IV bolus of methylprednisolone 10-15 mg/kg pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + CS	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Measured Values

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
Number of Participants Analyzed	90	90

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
Overall Survival (OS) at Month 12 - Percentage of Participants With an Event [units: percentage of participants]	8.9	11.1

Statistical Analysis 1 for Overall Survival (OS) at Month 12 - Percentage of Participants With an Event

Statistical Analysis Overview	Comparison Groups	Adjusted MMF + Tacrolimus + CS, Fixed-Dose MMF + Tacrolimus + CS
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7091
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Overall Survival at Month 12
Measure Description	The median time, in months, between randomization and OS event. Participants were censored at the date of last follow up and the date of last contact or premature withdrawal.
Time Frame	Days 0, 5, and 14, Month 1, 2, 3, 6, 9, and 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Adjusted MMF + Tacrolimus + CS	Participants received MMF tablets or capsules, 3 g/d, PO, BID with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an IV bolus of methylprednisolone 10-15 mg/kg pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + CS	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Measured Values

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
Number of Participants Analyzed	90	90
Overall Survival at Month 12 [units: months] Median (Full Range)	12.9 (0.0 to 24.5)	12.9 (0.1 to 20.2)

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants by Graft Histology at 12 Months Post-Transplant - Central Review
Measure Description	The percentage of participants with biopsies of grafts evaluated by central review and scored according to Banff criteria at Month 12 post-transplant.
Time Frame	Days 0, 5, and 14, Month 1, 2, 3, 6, 9, and 12
Safety Issue?	No

Analysis Population Description

ITT population; only participants with evaluable biopsies were included in the analysis.

Reporting Groups

	Description
Adjusted MMF + Tacrolimus + CS	Participants received MMF tablets or capsules, 3 g/d, PO, BID with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an IV bolus of methylprednisolone 10-15 mg/kg pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + CS	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Measured Values

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
Number of Participants Analyzed	42	35
Percentage of Participants by Graft Histology at 12 Months Post-Transplant - Central Review [units: percentage of participants]		
Normal liver	4.8	11.4
Minor lesions	4.8	17.1
Acute rejection	0.0	0.0
Chronic rejection	7.1	2.9
Chronic hepatitis	26.2	22.9
Vascular lesions	35.7	11.4
Pathology of biliary obstruction	4.8	5.7
Lobular hepatitis	4.8	2.9
Recurrence of initial autoimmune disease	0.0	0.0
Other	35.7	45.7

Reported Adverse Events

Time Frame	Adverse events were recorded from study start to 28 days after Month 12 or the last dose of study treatment.
Additional Description	All participants who were randomized and received at least one dose of MMF and/or corticosteroids were included in the safety analysis. Nonserious adverse events presented in this record include all adverse events reported during the study, not just nonserious events.

Reporting Groups

	Description
Adjusted MMF + Tacrolimus + CS	Participants received MMF tablets or capsules, 3 g/d, PO, BID with meals from Day 0 to Day 4; thereafter the dose was adjusted based on total exposure (AUC) using the Bayesian method with limited sampling strategy on Days 5 and 14 and Months 1, 3, 6, 9, and 12. Participants also received tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 through Month 1; the dose was adjusted to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12. Participants also received an IV bolus of methylprednisolone 10-15 mg/kg pre-operative on Day 0 per standard practice of the center.
Fixed-Dose MMF + Tacrolimus + CS	Participants received MMF capsules or tablets, 2 g/d, PO, BID with meals from Day 0 to Month 12; tacrolimus capsules, adjusted to a target trough level of 8-12 ng/mL from Day 0 to Month 1; the dose was reduced to reach a target trough level of 3-8 ng/mL from the end of Month 1 through Month 12; and IV bolus of prednisone, 10-15 mg/kg, pre-operative on Day 0 followed by prednisone tablets, 20 mg/d, PO, from Day 0 through Month 1; 15 mg/d, PO, from the end of Month 1 through Month 2; 10 mg/d, PO, from the end of Month 2 through Month 3; and 5 mg/d from the end of Month 3 through Month 6. Prednisone was discontinued from Month 7 through end of treatment.

Serious Adverse Events

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Total	70/91 (76.92%)	69/92 (75%)
Blood and lymphatic system disorders		
Agranulocytosis [A] *	2/91 (2.2%)	0/92 (0%)
Anaemia [A] *	0/91 (0%)	3/92 (3.26%)
Coagulopathy [A] *	0/91 (0%)	1/92 (1.09%)
Febrile neutropenia [A] *	2/91 (2.2%)	0/92 (0%)
Haemolytic anaemia [A] *	1/91 (1.1%)	0/92 (0%)
Leukopenia [A] *	2/91 (2.2%)	0/92 (0%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Neutropenia [A] *	1/91 (1.1%)	2/92 (2.17%)
Pancytopenia [A] *	2/91 (2.2%)	0/92 (0%)
Cardiac disorders		
Cardio-respiratory arrest [A] *	1/91 (1.1%)	0/92 (0%)
Cardiogenic shock [A] *	1/91 (1.1%)	0/92 (0%)
Myocardial infarction [A] *	0/91 (0%)	1/92 (1.09%)
Ventricular tachycardia [A] *	1/91 (1.1%)	1/92 (1.09%)
Congenital, familial and genetic disorders		
Hereditary neuropathic amyloidosis [A] *	0/91 (0%)	1/92 (1.09%)
Endocrine disorders		
Hyperparathyroidism [A] *	0/91 (0%)	1/92 (1.09%)
Gastrointestinal disorders		
Abdominal hernia [A] *	3/91 (3.3%)	0/92 (0%)
Abdominal pain upper [A] *	0/91 (0%)	2/92 (2.17%)
Abdominal wall haematoma [A] *	1/91 (1.1%)	0/92 (0%)
Ascites [A] *	2/91 (2.2%)	2/92 (2.17%)
Diarrhoea [A] *	6/91 (6.59%)	2/92 (2.17%)
Gastrointestinal disorder [A] *	0/91 (0%)	1/92 (1.09%)
Gastrointestinal necrosis [A] *	1/91 (1.1%)	0/92 (0%)
Inguinal hernia [A] *	2/91 (2.2%)	4/92 (4.35%)
Intestinal haemorrhage [A] *	1/91 (1.1%)	0/92 (0%)
Intra-abdominal haemorrhage [A] *	1/91 (1.1%)	0/92 (0%)
Pancreatitis [A] *	1/91 (1.1%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Pancreatitis acute [A] *	0/91 (0%)	1/92 (1.09%)
Peritoneal haemorrhage [A] *	1/91 (1.1%)	1/92 (1.09%)
Peritonitis [A] *	1/91 (1.1%)	2/92 (2.17%)
Small intestinal obstruction [A] *	1/91 (1.1%)	0/92 (0%)
Umbilical hernia [A] *	1/91 (1.1%)	1/92 (1.09%)
Volvulus of small bowel [A] *	0/91 (0%)	1/92 (1.09%)
Vomiting [A] *	2/91 (2.2%)	0/92 (0%)
General disorders		
Chest pain [A] *	1/91 (1.1%)	1/92 (1.09%)
General physical health deterioration [A] *	1/91 (1.1%)	2/92 (2.17%)
Hyperthermia [A] *	0/91 (0%)	1/92 (1.09%)
Inflammation [A] *	1/91 (1.1%)	0/92 (0%)
Malaise [A] *	1/91 (1.1%)	0/92 (0%)
Multi-organ failure [A] *	5/91 (5.49%)	3/92 (3.26%)
Pyrexia [A] *	0/91 (0%)	2/92 (2.17%)
Sudden death [A] *	0/91 (0%)	2/92 (2.17%)
Ulcer haemorrhage [A] *	1/91 (1.1%)	0/92 (0%)
Hepatobiliary disorders		
Bile duct necrosis [A] *	1/91 (1.1%)	0/92 (0%)
Bile duct stenosis [A] *	2/91 (2.2%)	4/92 (4.35%)
Biliary cyst [A] *	0/91 (0%)	1/92 (1.09%)
Biliary fistula [A] *	3/91 (3.3%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Biliary tract disorder [A] *	1/91 (1.1%)	0/92 (0%)
Cholangitis [A] *	2/91 (2.2%)	4/92 (4.35%)
Cholelithiasis [A] *	1/91 (1.1%)	0/92 (0%)
Cholestasis [A] *	0/91 (0%)	4/92 (4.35%)
Cytolytic hepatitis [A] *	0/91 (0%)	2/92 (2.17%)
Hepatic artery aneurysm [A] *	1/91 (1.1%)	0/92 (0%)
Hepatic artery stenosis [A] *	3/91 (3.3%)	2/92 (2.17%)
Hepatic artery thrombosis [A] *	1/91 (1.1%)	5/92 (5.43%)
Hepatic ischaemia [A] *	0/91 (0%)	1/92 (1.09%)
Hepatic vein stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Portal vein thrombosis [A] *	0/91 (0%)	1/92 (1.09%)
Immune system disorders		
Liver transplant rejection [A] *	0/91 (0%)	1/92 (1.09%)
Infections and infestations		
Appendicitis [A] *	0/91 (0%)	1/92 (1.09%)
Arthritis bacterial [A] *	1/91 (1.1%)	0/92 (0%)
Aspergillosis [A] *	1/91 (1.1%)	0/92 (0%)
Bacterial sepsis [A] *	1/91 (1.1%)	0/92 (0%)
Biliary sepsis [A] *	1/91 (1.1%)	1/92 (1.09%)
Candida sepsis [A] *	0/91 (0%)	2/92 (2.17%)
Cytomegalovirus colitis [A] *	0/91 (0%)	1/92 (1.09%)
Cytomegalovirus infection [A] *	1/91 (1.1%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Device related infection [A] *	1/91 (1.1%)	0/92 (0%)
Enterocolitis infectious [A] *	0/91 (0%)	1/92 (1.09%)
Hepatitis C [A] *	3/91 (3.3%)	7/92 (7.61%)
Hepatitis E [A] *	1/91 (1.1%)	0/92 (0%)
Herpes zoster [A] *	1/91 (1.1%)	0/92 (0%)
Infection [A] *	1/91 (1.1%)	0/92 (0%)
Liver abscess [A] *	0/91 (0%)	1/92 (1.09%)
Nocardiosis [A] *	0/91 (0%)	1/92 (1.09%)
Peritoneal infection [A] *	2/91 (2.2%)	1/92 (1.09%)
Pneumocystis jiroveci pneumonia [A] *	0/91 (0%)	1/92 (1.09%)
Pneumonia [A] *	0/91 (0%)	1/92 (1.09%)
Pneumonia cytomegaloviral [A] *	1/91 (1.1%)	0/92 (0%)
Sepsis [A] *	3/91 (3.3%)	4/92 (4.35%)
Septic shock [A] *	4/91 (4.4%)	1/92 (1.09%)
Systemic candida [A] *	1/91 (1.1%)	0/92 (0%)
Urinary tract infection [A] *	0/91 (0%)	1/92 (1.09%)
Viral diarrhoea [A] *	1/91 (1.1%)	0/92 (0%)
Injury, poisoning and procedural complications		
Anastomotic stenosis [A] *	0/91 (0%)	4/92 (4.35%)
Biliary anastomosis complication [A] *	5/91 (5.49%)	6/92 (6.52%)
Complications of transplant surgery [A] *	0/91 (0%)	1/92 (1.09%)
Complications of transplanted liver [A] *	1/91 (1.1%)	0/92 (0%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Endotracheal intubation complication [A] *	1/91 (1.1%)	0/92 (0%)
Femoral neck fracture [A] *	0/91 (0%)	1/92 (1.09%)
Graft dysfunction [A] *	1/91 (1.1%)	1/92 (1.09%)
Graft thrombosis [A] *	1/91 (1.1%)	0/92 (0%)
Overdose [A] *	0/91 (0%)	2/92 (2.17%)
Post procedural haemorrhage [A] *	0/91 (0%)	1/92 (1.09%)
Wound dehiscence [A] *	1/91 (1.1%)	1/92 (1.09%)
Wound evisceration [A] *	0/91 (0%)	1/92 (1.09%)
Wound secretion [A] *	0/91 (0%)	1/92 (1.09%)
Investigations		
Cytomegalovirus antibody positive [A] *	0/91 (0%)	1/92 (1.09%)
Liver function test abnormal [A] *	0/91 (0%)	3/92 (3.26%)
Oesophagogastroduodenoscopy [A] *	1/91 (1.1%)	0/92 (0%)
Metabolism and nutrition disorders		
Cell death [A] *	1/91 (1.1%)	0/92 (0%)
Diabetes mellitus [A] *	0/91 (0%)	3/92 (3.26%)
Diabetes mellitus inadequate control [A] *	2/91 (2.2%)	1/92 (1.09%)
Hyperkalaemia [A] *	1/91 (1.1%)	2/92 (2.17%)
Type 1 diabetes mellitus [A] *	0/91 (0%)	2/92 (2.17%)
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain [A] *	1/91 (1.1%)	0/92 (0%)
Osteoarthritis [A] *	0/91 (0%)	2/92 (2.17%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Hepatic neoplasm malignant [A] *	0/91 (0%)	1/92 (1.09%)
Lung neoplasm malignant [A] *	0/91 (0%)	1/92 (1.09%)
Metastases to bone [A] *	0/91 (0%)	1/92 (1.09%)
Metastases to spine [A] *	1/91 (1.1%)	0/92 (0%)
Prostate cancer [A] *	0/91 (0%)	1/92 (1.09%)
Thyroid neoplasm [A] *	1/91 (1.1%)	0/92 (0%)
Nervous system disorders		
Cerebral haemorrhage [A] *	0/91 (0%)	1/92 (1.09%)
Cerebral ischaemia [A] *	0/91 (0%)	1/92 (1.09%)
Cerebrovascular accident [A] *	1/91 (1.1%)	0/92 (0%)
Coma [A] *	0/91 (0%)	1/92 (1.09%)
Convulsion [A] *	1/91 (1.1%)	0/92 (0%)
Encephalopathy [A] *	1/91 (1.1%)	1/92 (1.09%)
Epilepsy [A] *	2/91 (2.2%)	0/92 (0%)
Febrile convulsion [A] *	1/91 (1.1%)	0/92 (0%)
Metabolic encephalopathy [A] *	1/91 (1.1%)	0/92 (0%)
Neuropathy peripheral [A] *	0/91 (0%)	1/92 (1.09%)
Toxic encephalopathy [A] *	1/91 (1.1%)	0/92 (0%)
Vocal cord paresis [A] *	0/91 (0%)	1/92 (1.09%)
Psychiatric disorders		
Confusional state [A] *	2/91 (2.2%)	2/92 (2.17%)
Delirium [A] *	0/91 (0%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Depression [A] *	0/91 (0%)	1/92 (1.09%)
Mental disorder [A] *	1/91 (1.1%)	1/92 (1.09%)
Renal and urinary disorders		
Renal failure [A] *	6/91 (6.59%)	6/92 (6.52%)
Renal failure acute [A] *	14/91 (15.38%)	5/92 (5.43%)
Ureteric stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Reproductive system and breast disorders		
Prostatitis [A] *	0/91 (0%)	1/92 (1.09%)
Testicular torsion [A] *	0/91 (0%)	1/92 (1.09%)
Respiratory, thoracic and mediastinal disorders		
Acute respiratory distress syndrome [A] *	2/91 (2.2%)	1/92 (1.09%)
Bronchopneumopathy [A] *	1/91 (1.1%)	0/92 (0%)
Hypoxia [A] *	1/91 (1.1%)	0/92 (0%)
Lung disorder [A] *	5/91 (5.49%)	4/92 (4.35%)
Pleural effusion [A] *	1/91 (1.1%)	3/92 (3.26%)
Pulmonary embolism [A] *	2/91 (2.2%)	1/92 (1.09%)
Pulmonary oedema [A] *	1/91 (1.1%)	0/92 (0%)
Respiratory failure [A] *	0/91 (0%)	1/92 (1.09%)
Surgical and medical procedures		
Biliary anastomosis [A] *	0/91 (0%)	1/92 (1.09%)
Biliary drainage [A] *	1/91 (1.1%)	0/92 (0%)
Catheter removal [A] *	0/91 (0%)	1/92 (1.09%)
Surgical vascular shunt [A] *	0/91 (0%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Vascular disorders		
Aneurysm [A] *	1/91 (1.1%)	0/92 (0%)
Angiopathy [A] *	1/91 (1.1%)	0/92 (0%)
Arterial haemorrhage [A] *	1/91 (1.1%)	1/92 (1.09%)
Arterial stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Arterial thrombosis limb [A] *	0/91 (0%)	1/92 (1.09%)
Haematoma [A] *	0/91 (0%)	1/92 (1.09%)
Haemodynamic instability [A] *	0/91 (0%)	1/92 (1.09%)
Jugular vein thrombosis [A] *	1/91 (1.1%)	0/92 (0%)
Shock haemorrhagic [A] *	2/91 (2.2%)	2/92 (2.17%)
Thrombosis [A] *	1/91 (1.1%)	0/92 (0%)
Vascular stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Venous thrombosis [A] *	1/91 (1.1%)	0/92 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.0)

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Total	91/91 (100%)	91/92 (98.91%)
Blood and lymphatic system disorders		
Agranulocytosis [A] *	2/91 (2.2%)	0/92 (0%)
Anaemia [A] *	45/91 (49.45%)	44/92 (47.83%)
Bone marrow failure [A] *	0/91 (0%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Coagulopathy [A] *	0/91 (0%)	1/92 (1.09%)
Deficiency anaemia [A] *	6/91 (6.59%)	3/92 (3.26%)
Disseminated intravascular coagulation [A] *	1/91 (1.1%)	1/92 (1.09%)
Febrile bone marrow aplasia [A] *	1/91 (1.1%)	0/92 (0%)
Febrile neutropenia [A] *	2/91 (2.2%)	0/92 (0%)
Haemolytic anaemia [A] *	1/91 (1.1%)	0/92 (0%)
Idiopathic thrombocytopenic purpura [A] *	0/91 (0%)	1/92 (1.09%)
Iron deficiency anaemia [A] *	0/91 (0%)	1/92 (1.09%)
Jaundice acholuric [A] *	1/91 (1.1%)	0/92 (0%)
Leukocytosis [A] *	1/91 (1.1%)	3/92 (3.26%)
Leukopenia [A] *	14/91 (15.38%)	2/92 (2.17%)
Lymphadenopathy [A] *	0/91 (0%)	1/92 (1.09%)
Lymphopenia [A] *	2/91 (2.2%)	1/92 (1.09%)
Neutropenia [A] *	13/91 (14.29%)	6/92 (6.52%)
Pancytopenia [A] *	11/91 (12.09%)	4/92 (4.35%)
Polycythaemia [A] *	0/91 (0%)	1/92 (1.09%)
Splenomegaly [A] *	0/91 (0%)	1/92 (1.09%)
Thrombocythaemia [A] *	1/91 (1.1%)	0/92 (0%)
Thrombocytopenia [A] *	16/91 (17.58%)	13/92 (14.13%)
Thrombotic microangiopathy [A] *	0/91 (0%)	1/92 (1.09%)
Cardiac disorders		
Acute coronary syndrome [A] *	2/91 (2.2%)	2/92 (2.17%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Arrhythmia [A] *	0/91 (0%)	3/92 (3.26%)
Arrhythmia supraventricular [A] *	0/91 (0%)	1/92 (1.09%)
Atrial fibrillation [A] *	3/91 (3.3%)	3/92 (3.26%)
Atrial flutter [A] *	1/91 (1.1%)	0/92 (0%)
Bradycardia [A] *	2/91 (2.2%)	1/92 (1.09%)
Cardiac failure [A] *	1/91 (1.1%)	0/92 (0%)
Cardio-respiratory arrest [A] *	1/91 (1.1%)	0/92 (0%)
Cardiogenic shock [A] *	1/91 (1.1%)	0/92 (0%)
Cardiomyopathy [A] *	1/91 (1.1%)	0/92 (0%)
Myocardial infarction [A] *	0/91 (0%)	1/92 (1.09%)
Palpitations [A] *	1/91 (1.1%)	0/92 (0%)
Pericardial disease [A] *	1/91 (1.1%)	0/92 (0%)
Pericardial effusion [A] *	1/91 (1.1%)	1/92 (1.09%)
Stress cardiomyopathy [A] *	0/91 (0%)	1/92 (1.09%)
Supraventricular tachycardia [A] *	1/91 (1.1%)	1/92 (1.09%)
Tachycardia [A] *	6/91 (6.59%)	1/92 (1.09%)
Ventricular extrasystoles [A] *	0/91 (0%)	1/92 (1.09%)
Ventricular tachycardia [A] *	1/91 (1.1%)	1/92 (1.09%)
Congenital, familial and genetic disorders		
Hereditary neuropathic amyloidosis [A] *	0/91 (0%)	1/92 (1.09%)
Hydrocele [A] *	1/91 (1.1%)	0/92 (0%)
Ear and labyrinth disorders		

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Ear haemorrhage [A] *	0/91 (0%)	1/92 (1.09%)
Ear pain [A] *	0/91 (0%)	1/92 (1.09%)
Endocrine disorders		
Hyperparathyroidism [A] *	0/91 (0%)	1/92 (1.09%)
Hyperthyroidism [A] *	1/91 (1.1%)	0/92 (0%)
Eye disorders		
Uveitis [A] *	0/91 (0%)	1/92 (1.09%)
Visual acuity reduced [A] *	1/91 (1.1%)	2/92 (2.17%)
Visual disturbance [A] *	1/91 (1.1%)	1/92 (1.09%)
Gastrointestinal disorders		
Abdominal hernia [A] *	3/91 (3.3%)	0/92 (0%)
Abdominal pain [A] *	12/91 (13.19%)	12/92 (13.04%)
Abdominal pain upper [A] *	2/91 (2.2%)	5/92 (5.43%)
Abdominal wall haematoma [A] *	1/91 (1.1%)	0/92 (0%)
Ascites [A] *	9/91 (9.89%)	11/92 (11.96%)
Coeliac artery stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Colitis [A] *	0/91 (0%)	1/92 (1.09%)
Constipation [A] *	8/91 (8.79%)	11/92 (11.96%)
Diarrhoea [A] *	31/91 (34.07%)	26/92 (28.26%)
Duodenal ulcer [A] *	1/91 (1.1%)	0/92 (0%)
Duodenal ulcer haemorrhage [A] *	1/91 (1.1%)	0/92 (0%)
Duodenitis [A] *	1/91 (1.1%)	0/92 (0%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Dyspepsia [A] *	2/91 (2.2%)	3/92 (3.26%)
Dysphagia [A] *	0/91 (0%)	2/92 (2.17%)
Gastric ulcer [A] *	1/91 (1.1%)	0/92 (0%)
Gastritis [A] *	1/91 (1.1%)	0/92 (0%)
Gastritis erosive [A] *	0/91 (0%)	1/92 (1.09%)
Gastrointestinal disorder [A] *	2/91 (2.2%)	7/92 (7.61%)
Gastrointestinal motility disorder [A] *	0/91 (0%)	1/92 (1.09%)
Gastrointestinal necrosis [A] *	1/91 (1.1%)	0/92 (0%)
Gastrointestinal pain [A] *	1/91 (1.1%)	0/92 (0%)
Gastrooesophageal reflux disease [A] *	0/91 (0%)	2/92 (2.17%)
Haematemesis [A] *	0/91 (0%)	1/92 (1.09%)
Haemorrhoids [A] *	0/91 (0%)	1/92 (1.09%)
Impaired gastric emptying [A] *	1/91 (1.1%)	1/92 (1.09%)
Inguinal hernia [A] *	2/91 (2.2%)	7/92 (7.61%)
Intestinal haemorrhage [A] *	1/91 (1.1%)	0/92 (0%)
Intestinal obstruction [A] *	1/91 (1.1%)	0/92 (0%)
Intra-abdominal haemorrhage [A] *	1/91 (1.1%)	1/92 (1.09%)
Melaena [A] *	0/91 (0%)	1/92 (1.09%)
Nausea [A] *	8/91 (8.79%)	8/92 (8.7%)
Oesophageal ulcer [A] *	1/91 (1.1%)	0/92 (0%)
Oesophagitis [A] *	1/91 (1.1%)	0/92 (0%)
Oesophagitis ulcerative [A] *	0/91 (0%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Pancreatitis [A] *	1/91 (1.1%)	1/92 (1.09%)
Pancreatitis acute [A] *	0/91 (0%)	2/92 (2.17%)
Peritoneal effusion [A] *	0/91 (0%)	1/92 (1.09%)
Peritoneal haemorrhage [A] *	1/91 (1.1%)	1/92 (1.09%)
Peritonitis [A] *	2/91 (2.2%)	2/92 (2.17%)
Pneumoperitoneum [A] *	1/91 (1.1%)	0/92 (0%)
Portal venous gas [A] *	1/91 (1.1%)	0/92 (0%)
Small bowel angioedema [A] *	0/91 (0%)	1/92 (1.09%)
Small intestinal obstruction [A] *	1/91 (1.1%)	0/92 (0%)
Stomatitis [A] *	1/91 (1.1%)	0/92 (0%)
Subileus [A] *	2/91 (2.2%)	0/92 (0%)
Toothache [A] *	1/91 (1.1%)	0/92 (0%)
Umbilical hernia [A] *	1/91 (1.1%)	1/92 (1.09%)
Volvulus of small bowel [A] *	0/91 (0%)	1/92 (1.09%)
Vomiting [A] *	10/91 (10.99%)	5/92 (5.43%)
General disorders		
Asthenia [A] *	2/91 (2.2%)	6/92 (6.52%)
Catheter site necrosis [A] *	0/91 (0%)	1/92 (1.09%)
Chest pain [A] *	2/91 (2.2%)	2/92 (2.17%)
Chills [A] *	0/91 (0%)	1/92 (1.09%)
Effusion [A] *	2/91 (2.2%)	0/92 (0%)
General physical health deterioration [A] *	1/91 (1.1%)	2/92 (2.17%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Generalised oedema [A] *	1/91 (1.1%)	0/92 (0%)
Hyperthermia [A] *	8/91 (8.79%)	5/92 (5.43%)
Hypothermia [A] *	1/91 (1.1%)	2/92 (2.17%)
Inflammation [A] *	2/91 (2.2%)	5/92 (5.43%)
Influenza like illness [A] *	1/91 (1.1%)	1/92 (1.09%)
Malaise [A] *	1/91 (1.1%)	0/92 (0%)
Multi-organ failure [A] *	5/91 (5.49%)	5/92 (5.43%)
Necrosis [A] *	1/91 (1.1%)	0/92 (0%)
Oedema [A] *	7/91 (7.69%)	5/92 (5.43%)
Oedema peripheral [A] *	10/91 (10.99%)	17/92 (18.48%)
Pain [A] *	12/91 (13.19%)	10/92 (10.87%)
Polyp [A] *	1/91 (1.1%)	0/92 (0%)
Pyrexia [A] *	11/91 (12.09%)	4/92 (4.35%)
Sudden death [A] *	0/91 (0%)	2/92 (2.17%)
Ulcer [A] *	1/91 (1.1%)	0/92 (0%)
Ulcer haemorrhage [A] *	1/91 (1.1%)	0/92 (0%)
Hepatobiliary disorders		
Bile duct necrosis [A] *	1/91 (1.1%)	0/92 (0%)
Bile duct stenosis [A] *	4/91 (4.4%)	4/92 (4.35%)
Biliary cyst [A] *	1/91 (1.1%)	1/92 (1.09%)
Biliary fistula [A] *	3/91 (3.3%)	3/92 (3.26%)
Biliary tract disorder [A] *	2/91 (2.2%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Biloma [A] *	2/91 (2.2%)	2/92 (2.17%)
Cholangitis [A] *	5/91 (5.49%)	6/92 (6.52%)
Cholelithiasis [A] *	1/91 (1.1%)	0/92 (0%)
Cholestasis [A] *	24/91 (26.37%)	19/92 (20.65%)
Cytolytic hepatitis [A] *	4/91 (4.4%)	3/92 (3.26%)
Hepatic artery aneurysm [A] *	1/91 (1.1%)	0/92 (0%)
Hepatic artery stenosis [A] *	4/91 (4.4%)	3/92 (3.26%)
Hepatic artery thrombosis [A] *	1/91 (1.1%)	7/92 (7.61%)
Hepatic cirrhosis [A] *	2/91 (2.2%)	0/92 (0%)
Hepatic failure [A] *	0/91 (0%)	2/92 (2.17%)
Hepatic function abnormal [A] *	1/91 (1.1%)	2/92 (2.17%)
Hepatic ischaemia [A] *	0/91 (0%)	1/92 (1.09%)
Hepatic vein stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Hepatitis cholestatic [A] *	1/91 (1.1%)	0/92 (0%)
Hepatorenal syndrome [A] *	1/91 (1.1%)	0/92 (0%)
Hyperbilirubinaemia [A] *	2/91 (2.2%)	0/92 (0%)
Jaundice [A] *	5/91 (5.49%)	2/92 (2.17%)
Portal vein thrombosis [A] *	5/91 (5.49%)	1/92 (1.09%)
Immune system disorders		
Drug hypersensitivity [A] *	1/91 (1.1%)	3/92 (3.26%)
Hypersensitivity [A] *	0/91 (0%)	1/92 (1.09%)
Liver transplant rejection [A] *	0/91 (0%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Transplant rejection [A] *	0/91 (0%)	1/92 (1.09%)
Infections and infestations		
Abdominal wall abscess [A] *	2/91 (2.2%)	2/92 (2.17%)
Abscess [A] *	1/91 (1.1%)	0/92 (0%)
Appendicitis [A] *	0/91 (0%)	1/92 (1.09%)
Arthritis bacterial [A] *	1/91 (1.1%)	1/92 (1.09%)
Ascites infection [A] *	2/91 (2.2%)	2/92 (2.17%)
Aspergillosis [A] *	1/91 (1.1%)	0/92 (0%)
Bacterial infection [A] *	1/91 (1.1%)	0/92 (0%)
Bacterial sepsis [A] *	1/91 (1.1%)	0/92 (0%)
Biliary sepsis [A] *	1/91 (1.1%)	1/92 (1.09%)
Bronchitis [A] *	2/91 (2.2%)	5/92 (5.43%)
Bronchopulmonary aspergillosis [A] *	1/91 (1.1%)	0/92 (0%)
Candida sepsis [A] *	0/91 (0%)	2/92 (2.17%)
Candidiasis [A] *	1/91 (1.1%)	0/92 (0%)
Catheter related infection [A] *	0/91 (0%)	2/92 (2.17%)
Cellulitis [A] *	1/91 (1.1%)	0/92 (0%)
Cholecystitis infective [A] *	0/91 (0%)	1/92 (1.09%)
Citrobacter infection [A] *	1/91 (1.1%)	0/92 (0%)
Clostridial infection [A] *	1/91 (1.1%)	1/92 (1.09%)
Clostridium difficile colitis [A] *	1/91 (1.1%)	0/92 (0%)
Cystitis [A] *	0/91 (0%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Cytomegalovirus colitis [A] *	0/91 (0%)	1/92 (1.09%)
Cytomegalovirus infection [A] *	7/91 (7.69%)	6/92 (6.52%)
Cytomegalovirus viraemia [A] *	0/91 (0%)	1/92 (1.09%)
Device related infection [A] *	1/91 (1.1%)	1/92 (1.09%)
Endocarditis [A] *	0/91 (0%)	1/92 (1.09%)
Enterobacter bacteraemia [A] *	0/91 (0%)	1/92 (1.09%)
Enterococcal infection [A] *	4/91 (4.4%)	0/92 (0%)
Enterocolitis infectious [A] *	0/91 (0%)	1/92 (1.09%)
Fungal infection [A] *	1/91 (1.1%)	1/92 (1.09%)
Furuncle [A] *	0/91 (0%)	1/92 (1.09%)
Gastroenteritis viral [A] *	1/91 (1.1%)	1/92 (1.09%)
Hepatitis C [A] *	7/91 (7.69%)	11/92 (11.96%)
Hepatitis E [A] *	1/91 (1.1%)	0/92 (0%)
Hepatobiliary infection [A] *	0/91 (0%)	1/92 (1.09%)
Herpes simplex [A] *	0/91 (0%)	1/92 (1.09%)
Herpes zoster [A] *	1/91 (1.1%)	1/92 (1.09%)
Infection [A] *	4/91 (4.4%)	1/92 (1.09%)
Influenza [A] *	1/91 (1.1%)	0/92 (0%)
Infusion site infection [A] *	1/91 (1.1%)	0/92 (0%)
Liver abscess [A] *	0/91 (0%)	1/92 (1.09%)
Lung infection [A] *	3/91 (3.3%)	1/92 (1.09%)
Nasopharyngitis [A] *	1/91 (1.1%)	2/92 (2.17%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Nocardiosis [A] *	0/91 (0%)	1/92 (1.09%)
Oesophageal candidiasis [A] *	1/91 (1.1%)	0/92 (0%)
Oral candidiasis [A] *	0/91 (0%)	3/92 (3.26%)
Oral fungal infection [A] *	1/91 (1.1%)	0/92 (0%)
Orchitis [A] *	0/91 (0%)	1/92 (1.09%)
Paronychia [A] *	1/91 (1.1%)	0/92 (0%)
Peritoneal infection [A] *	3/91 (3.3%)	1/92 (1.09%)
Pneumocystis jiroveci pneumonia [A] *	0/91 (0%)	1/92 (1.09%)
Pneumonia [A] *	0/91 (0%)	1/92 (1.09%)
Pneumonia cytomegaloviral [A] *	1/91 (1.1%)	0/92 (0%)
Postoperative wound infection [A] *	1/91 (1.1%)	1/92 (1.09%)
Pseudomonal sepsis [A] *	1/91 (1.1%)	0/92 (0%)
Puncture site infection [A] *	3/91 (3.3%)	2/92 (2.17%)
Rhinitis [A] *	0/91 (0%)	1/92 (1.09%)
Sepsis [A] *	9/91 (9.89%)	8/92 (8.7%)
Septic shock [A] *	4/91 (4.4%)	2/92 (2.17%)
Serratia infection [A] *	0/91 (0%)	1/92 (1.09%)
Skin infection [A] *	1/91 (1.1%)	0/92 (0%)
Staphylococcal bacteraemia [A] *	0/91 (0%)	1/92 (1.09%)
Staphylococcal infection [A] *	4/91 (4.4%)	6/92 (6.52%)
Staphylococcal sepsis [A] *	1/91 (1.1%)	2/92 (2.17%)
Streptococcal infection [A] *	1/91 (1.1%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Systemic candida [A] *	1/91 (1.1%)	0/92 (0%)
Tonsillitis [A] *	2/91 (2.2%)	1/92 (1.09%)
Urinary tract infection [A] *	13/91 (14.29%)	14/92 (15.22%)
Viral diarrhoea [A] *	1/91 (1.1%)	0/92 (0%)
Injury, poisoning and procedural complications		
Accidental overdose [A] *	3/91 (3.3%)	0/92 (0%)
Anastomotic stenosis [A] *	2/91 (2.2%)	4/92 (4.35%)
Biliary anastomosis complication [A] *	7/91 (7.69%)	6/92 (6.52%)
Complications of transplant surgery [A] *	0/91 (0%)	1/92 (1.09%)
Complications of transplanted liver [A] *	1/91 (1.1%)	0/92 (0%)
Endotracheal intubation complication [A] *	2/91 (2.2%)	0/92 (0%)
Eschar [A] *	3/91 (3.3%)	1/92 (1.09%)
Facial bones fracture [A] *	0/91 (0%)	1/92 (1.09%)
Fall [A] *	0/91 (0%)	1/92 (1.09%)
Femoral neck fracture [A] *	0/91 (0%)	1/92 (1.09%)
Foot fracture [A] *	1/91 (1.1%)	0/92 (0%)
Graft dysfunction [A] *	2/91 (2.2%)	1/92 (1.09%)
Graft thrombosis [A] *	1/91 (1.1%)	0/92 (0%)
Hepatic haematoma [A] *	1/91 (1.1%)	3/92 (3.26%)
Operative haemorrhage [A] *	1/91 (1.1%)	2/92 (2.17%)
Overdose [A] *	1/91 (1.1%)	6/92 (6.52%)
Poisoning [A] *	0/91 (0%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Post procedural haemorrhage [A] *	0/91 (0%)	1/92 (1.09%)
Procedural pain [A] *	4/91 (4.4%)	0/92 (0%)
Radiation leukopenia [A] *	1/91 (1.1%)	0/92 (0%)
Radiation oesophagitis [A] *	1/91 (1.1%)	0/92 (0%)
Rib fracture [A] *	0/91 (0%)	1/92 (1.09%)
Seroma [A] *	4/91 (4.4%)	5/92 (5.43%)
Spinal compression fracture [A] *	0/91 (0%)	1/92 (1.09%)
Surgical procedure repeated [A] *	1/91 (1.1%)	0/92 (0%)
Thoracic vertebral fracture [A] *	0/91 (0%)	1/92 (1.09%)
Tooth fracture [A] *	0/91 (0%)	1/92 (1.09%)
Wound [A] *	1/91 (1.1%)	0/92 (0%)
Wound dehiscence [A] *	3/91 (3.3%)	1/92 (1.09%)
Wound evisceration [A] *	0/91 (0%)	1/92 (1.09%)
Wound secretion [A] *	0/91 (0%)	1/92 (1.09%)
Investigations		
Aspiration tracheal [A] *	1/91 (1.1%)	0/92 (0%)
Band neutrophil percentage decreased [A] *	4/91 (4.4%)	5/92 (5.43%)
Blood bilirubin increased [A] *	2/91 (2.2%)	1/92 (1.09%)
Blood glucose [A] *	1/91 (1.1%)	0/92 (0%)
Blood urea increased [A] *	2/91 (2.2%)	1/92 (1.09%)
Cytomegalovirus antibody positive [A] *	0/91 (0%)	1/92 (1.09%)
Gamma-glutamyltransferase increased [A] *	3/91 (3.3%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Haematology test abnormal [A] *	0/91 (0%)	2/92 (2.17%)
Liver function test abnormal [A] *	1/91 (1.1%)	5/92 (5.43%)
Oesophagogastroduodenoscopy [A] *	1/91 (1.1%)	0/92 (0%)
Prothrombin level decreased [A] *	1/91 (1.1%)	0/92 (0%)
Red blood cell count decreased [A] *	3/91 (3.3%)	4/92 (4.35%)
Serum ferritin increased [A] *	0/91 (0%)	1/92 (1.09%)
Weight decreased [A] *	4/91 (4.4%)	5/92 (5.43%)
Weight increased [A] *	3/91 (3.3%)	2/92 (2.17%)
Metabolism and nutrition disorders		
Acidosis [A] *	1/91 (1.1%)	1/92 (1.09%)
Anorexia [A] *	2/91 (2.2%)	2/92 (2.17%)
Cachexia [A] *	1/91 (1.1%)	0/92 (0%)
Cell death [A] *	12/91 (13.19%)	8/92 (8.7%)
Decreased appetite [A] *	0/91 (0%)	1/92 (1.09%)
Dehydration [A] *	1/91 (1.1%)	0/92 (0%)
Diabetes mellitus [A] *	6/91 (6.59%)	19/92 (20.65%)
Diabetes mellitus inadequate control [A] *	5/91 (5.49%)	3/92 (3.26%)
Dyslipidaemia [A] *	1/91 (1.1%)	5/92 (5.43%)
Electrolyte imbalance [A] *	0/91 (0%)	2/92 (2.17%)
Fluid overload [A] *	0/91 (0%)	1/92 (1.09%)
Gout [A] *	1/91 (1.1%)	0/92 (0%)
Hypercalcaemia [A] *	2/91 (2.2%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Hypercholesterolaemia [A] *	0/91 (0%)	3/92 (3.26%)
Hyperglycaemia [A] *	11/91 (12.09%)	13/92 (14.13%)
Hyperkalaemia [A] *	15/91 (16.48%)	14/92 (15.22%)
Hypernatraemia [A] *	0/91 (0%)	1/92 (1.09%)
Hypertriglyceridaemia [A] *	0/91 (0%)	1/92 (1.09%)
Hypoalbuminaemia [A] *	1/91 (1.1%)	2/92 (2.17%)
Hypocalcaemia [A] *	1/91 (1.1%)	1/92 (1.09%)
Hypoglycaemia [A] *	0/91 (0%)	2/92 (2.17%)
Hypokalaemia [A] *	5/91 (5.49%)	8/92 (8.7%)
Hypomagnesaemia [A] *	2/91 (2.2%)	2/92 (2.17%)
Hyponatraemia [A] *	0/91 (0%)	1/92 (1.09%)
Hypovitaminosis [A] *	1/91 (1.1%)	0/92 (0%)
Iron deficiency [A] *	0/91 (0%)	2/92 (2.17%)
Lactic acidosis [A] *	1/91 (1.1%)	0/92 (0%)
Metabolic acidosis [A] *	1/91 (1.1%)	1/92 (1.09%)
Metabolic syndrome [A] *	1/91 (1.1%)	0/92 (0%)
Mineral deficiency [A] *	0/91 (0%)	1/92 (1.09%)
Phlebitis [A] *	0/91 (0%)	1/92 (1.09%)
Type 1 diabetes mellitus [A] *	1/91 (1.1%)	4/92 (4.35%)
Weight fluctuation [A] *	1/91 (1.1%)	1/92 (1.09%)
Musculoskeletal and connective tissue disorders		
Amyotrophy [A] *	1/91 (1.1%)	0/92 (0%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Arthralgia [A] *	1/91 (1.1%)	1/92 (1.09%)
Back pain [A] *	7/91 (7.69%)	7/92 (7.61%)
Bursitis [A] *	1/91 (1.1%)	0/92 (0%)
Hypercreatinaemia [A] *	1/91 (1.1%)	1/92 (1.09%)
Intervertebral disc protrusion [A] *	0/91 (0%)	1/92 (1.09%)
Muscle haemorrhage [A] *	0/91 (0%)	1/92 (1.09%)
Muscle spasms [A] *	5/91 (5.49%)	4/92 (4.35%)
Musculoskeletal chest pain [A] *	0/91 (0%)	1/92 (1.09%)
Musculoskeletal pain [A] *	1/91 (1.1%)	1/92 (1.09%)
Myalgia [A] *	0/91 (0%)	1/92 (1.09%)
Neck pain [A] *	0/91 (0%)	1/92 (1.09%)
Osteoarthritis [A] *	0/91 (0%)	3/92 (3.26%)
Osteopenia [A] *	3/91 (3.3%)	1/92 (1.09%)
Osteoporosis [A] *	1/91 (1.1%)	3/92 (3.26%)
Pain in extremity [A] *	3/91 (3.3%)	1/92 (1.09%)
Spinal osteoarthritis [A] *	0/91 (0%)	1/92 (1.09%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma [A] *	1/91 (1.1%)	0/92 (0%)
Hepatic neoplasm malignant [A] *	0/91 (0%)	1/92 (1.09%)
Lung neoplasm malignant [A] *	0/91 (0%)	1/92 (1.09%)
Metastases to bone [A] *	0/91 (0%)	1/92 (1.09%)
Metastases to spine [A] *	1/91 (1.1%)	0/92 (0%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Prostate cancer [A] *	0/91 (0%)	1/92 (1.09%)
Thyroid neoplasm [A] *	1/91 (1.1%)	0/92 (0%)
Nervous system disorders		
Altered state of consciousness [A] *	1/91 (1.1%)	0/92 (0%)
Amnesia [A] *	1/91 (1.1%)	1/92 (1.09%)
Aphonia [A] *	0/91 (0%)	1/92 (1.09%)
Carpal tunnel syndrome [A] *	1/91 (1.1%)	1/92 (1.09%)
Cerebral haemorrhage [A] *	0/91 (0%)	1/92 (1.09%)
Cerebral ischaemia [A] *	0/91 (0%)	1/92 (1.09%)
Cerebrovascular accident [A] *	1/91 (1.1%)	0/92 (0%)
Cognitive disorder [A] *	1/91 (1.1%)	0/92 (0%)
Coma [A] *	0/91 (0%)	1/92 (1.09%)
Convulsion [A] *	1/91 (1.1%)	4/92 (4.35%)
Depressed level of consciousness [A] *	0/91 (0%)	1/92 (1.09%)
Dizziness [A] *	1/91 (1.1%)	2/92 (2.17%)
Dysarthria [A] *	1/91 (1.1%)	2/92 (2.17%)
Encephalopathy [A] *	3/91 (3.3%)	1/92 (1.09%)
Epilepsy [A] *	2/91 (2.2%)	1/92 (1.09%)
Febrile convulsion [A] *	4/91 (4.4%)	1/92 (1.09%)
Headache [A] *	9/91 (9.89%)	10/92 (10.87%)
Hyperreflexia [A] *	0/91 (0%)	1/92 (1.09%)
Ischaemic stroke [A] *	1/91 (1.1%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Memory impairment [A] *	0/91 (0%)	1/92 (1.09%)
Metabolic encephalopathy [A] *	1/91 (1.1%)	0/92 (0%)
Neuropathy peripheral [A] *	0/91 (0%)	1/92 (1.09%)
Paraesthesia [A] *	1/91 (1.1%)	2/92 (2.17%)
Paresis [A] *	0/91 (0%)	1/92 (1.09%)
Polyneuropathy [A] *	1/91 (1.1%)	1/92 (1.09%)
Psychomotor skills impaired [A] *	1/91 (1.1%)	0/92 (0%)
Somnolence [A] *	0/91 (0%)	2/92 (2.17%)
Subarachnoid haemorrhage [A] *	0/91 (0%)	1/92 (1.09%)
Syncope vasovagal [A] *	3/91 (3.3%)	0/92 (0%)
Toxic encephalopathy [A] *	1/91 (1.1%)	0/92 (0%)
Tremor [A] *	8/91 (8.79%)	9/92 (9.78%)
Vocal cord paralysis [A] *	1/91 (1.1%)	0/92 (0%)
Vocal cord paresis [A] *	0/91 (0%)	1/92 (1.09%)
Psychiatric disorders		
Affective disorder [A] *	0/91 (0%)	1/92 (1.09%)
Agitation [A] *	8/91 (8.79%)	8/92 (8.7%)
Anxiety [A] *	4/91 (4.4%)	12/92 (13.04%)
Confusional state [A] *	11/91 (12.09%)	14/92 (15.22%)
Delirium [A] *	0/91 (0%)	2/92 (2.17%)
Depression [A] *	1/91 (1.1%)	6/92 (6.52%)
Hallucination [A] *	0/91 (0%)	1/92 (1.09%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Hallucination, visual [A] *	1/91 (1.1%)	0/92 (0%)
Insomnia [A] *	15/91 (16.48%)	10/92 (10.87%)
Mental disorder [A] *	1/91 (1.1%)	1/92 (1.09%)
Sleep disorder [A] *	0/91 (0%)	1/92 (1.09%)
Renal and urinary disorders		
Anuria [A] *	1/91 (1.1%)	1/92 (1.09%)
Dysuria [A] *	0/91 (0%)	2/92 (2.17%)
Micturition disorder [A] *	0/91 (0%)	1/92 (1.09%)
Oliguria [A] *	4/91 (4.4%)	5/92 (5.43%)
Polyuria [A] *	0/91 (0%)	1/92 (1.09%)
Renal colic [A] *	0/91 (0%)	1/92 (1.09%)
Renal failure [A] *	24/91 (26.37%)	23/92 (25%)
Renal failure acute [A] *	22/91 (24.18%)	16/92 (17.39%)
Renal impairment [A] *	6/91 (6.59%)	8/92 (8.7%)
Renal pain [A] *	0/91 (0%)	1/92 (1.09%)
Renal tubular disorder [A] *	1/91 (1.1%)	0/92 (0%)
Ureteric stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Urinary incontinence [A] *	0/91 (0%)	1/92 (1.09%)
Urinary retention [A] *	0/91 (0%)	1/92 (1.09%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia [A] *	0/91 (0%)	1/92 (1.09%)
Oedema genital [A] *	1/91 (1.1%)	0/92 (0%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Ovarian cyst [A] *	1/91 (1.1%)	0/92 (0%)
Prostatitis [A] *	0/91 (0%)	2/92 (2.17%)
Pruritus genital [A] *	0/91 (0%)	1/92 (1.09%)
Testicular torsion [A] *	0/91 (0%)	1/92 (1.09%)
Respiratory, thoracic and mediastinal disorders		
Acute pulmonary oedema [A] *	3/91 (3.3%)	0/92 (0%)
Acute respiratory distress syndrome [A] *	3/91 (3.3%)	1/92 (1.09%)
Atelectasis [A] *	2/91 (2.2%)	2/92 (2.17%)
Bronchial obstruction [A] *	1/91 (1.1%)	1/92 (1.09%)
Bronchopneumopathy [A] *	1/91 (1.1%)	1/92 (1.09%)
Cough [A] *	5/91 (5.49%)	1/92 (1.09%)
Dyspnoea [A] *	3/91 (3.3%)	3/92 (3.26%)
Dyspnoea exertional [A] *	0/91 (0%)	1/92 (1.09%)
Epistaxis [A] *	0/91 (0%)	1/92 (1.09%)
Hydropneumothorax [A] *	0/91 (0%)	1/92 (1.09%)
Hydrothorax [A] *	1/91 (1.1%)	0/92 (0%)
Hypoxia [A] *	3/91 (3.3%)	1/92 (1.09%)
Lung disorder [A] *	13/91 (14.29%)	9/92 (9.78%)
Pleural effusion [A] *	22/91 (24.18%)	25/92 (27.17%)
Pneumothorax [A] *	1/91 (1.1%)	0/92 (0%)
Pulmonary embolism [A] *	2/91 (2.2%)	1/92 (1.09%)
Pulmonary oedema [A] *	1/91 (1.1%)	0/92 (0%)

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Respiratory distress [A] *	1/91 (1.1%)	2/92 (2.17%)
Respiratory failure [A] *	1/91 (1.1%)	1/92 (1.09%)
Respiratory gas exchange disorder [A] *	1/91 (1.1%)	0/92 (0%)
Rhinorrhoea [A] *	1/91 (1.1%)	0/92 (0%)
Skin and subcutaneous tissue disorders		
Dermatitis exfoliative [A] *	0/91 (0%)	1/92 (1.09%)
Erythema [A] *	2/91 (2.2%)	1/92 (1.09%)
Pruritus [A] *	8/91 (8.79%)	3/92 (3.26%)
Rash [A] *	0/91 (0%)	1/92 (1.09%)
Scar pain [A] *	0/91 (0%)	1/92 (1.09%)
Skin lesion [A] *	0/91 (0%)	1/92 (1.09%)
Skin necrosis [A] *	1/91 (1.1%)	4/92 (4.35%)
Urticaria [A] *	0/91 (0%)	1/92 (1.09%)
Vascular purpura [A] *	1/91 (1.1%)	0/92 (0%)
Social circumstances		
Alcohol use [A] *	0/91 (0%)	1/92 (1.09%)
Surgical and medical procedures		
Biliary anastomosis [A] *	0/91 (0%)	1/92 (1.09%)
Biliary drainage [A] *	1/91 (1.1%)	0/92 (0%)
Catheter removal [A] *	0/91 (0%)	1/92 (1.09%)
Skin neoplasm excision [A] *	1/91 (1.1%)	0/92 (0%)
Surgical vascular shunt [A] *	0/91 (0%)	1/92 (1.09%)
Vascular disorders		

	Adjusted MMF + Tacrolimus + CS	Fixed-Dose MMF + Tacrolimus + CS
	Affected/At Risk (%)	Affected/At Risk (%)
Aneurysm [A] *	1/91 (1.1%)	0/92 (0%)
Angiopathy [A] *	1/91 (1.1%)	0/92 (0%)
Arterial haemorrhage [A] *	1/91 (1.1%)	1/92 (1.09%)
Arterial stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Arterial thrombosis limb [A] *	0/91 (0%)	1/92 (1.09%)
Haematoma [A] *	2/91 (2.2%)	2/92 (2.17%)
Haemodynamic instability [A] *	3/91 (3.3%)	7/92 (7.61%)
Haemorrhage [A] *	3/91 (3.3%)	4/92 (4.35%)
Hypertension [A] *	31/91 (34.07%)	31/92 (33.7%)
Hypotension [A] *	3/91 (3.3%)	3/92 (3.26%)
Hypovolaemic shock [A] *	0/91 (0%)	1/92 (1.09%)
Jugular vein thrombosis [A] *	1/91 (1.1%)	0/92 (0%)
Lymphoedema [A] *	1/91 (1.1%)	0/92 (0%)
Orthostatic hypotension [A] *	0/91 (0%)	1/92 (1.09%)
Shock haemorrhagic [A] *	2/91 (2.2%)	2/92 (2.17%)
Thrombophlebitis [A] *	0/91 (0%)	1/92 (1.09%)
Thrombosis [A] *	1/91 (1.1%)	0/92 (0%)
Vascular stenosis [A] *	0/91 (0%)	1/92 (1.09%)
Vein discolouration [A] *	1/91 (1.1%)	1/92 (1.09%)
Venous stasis [A] *	1/91 (1.1%)	0/92 (0%)
Venous thrombosis [A] *	7/91 (7.69%)	4/92 (4.35%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (11.0)

Limitations and Caveats

Nonserious adverse events presented in this record include all adverse events reported during the study, not just nonserious events.

More Information

Certain Agreements:

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

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

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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