ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 04/08/2016

ClinicalTrials.gov ID: NCT01292226

Study Identification

Unique Protocol ID:	ML19835
Brief Title:	A Study of the Correlation Between Pharmacokinetic and Pharmacodynamic Parameters of CellCept (Mycophenolate Mofetil).
Official Title:	Relationships Between Pharmacokinetic and Pharmacodynamic Strategies for Assessment of the Risks for Acute Rejection and Side Effects of Mycophenolate Mofetil
Secondary IDs:	

Study Status

Record Verification:	April 2016
Overall Status:	Completed
Study Start:	December 2006
Primary Completion:	September 2008 [Actual]
Study Completion:	September 2008 [Actual]

Sponsor/Collaborators

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

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? No

	Delayed Posting?
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 03-07-2006 Board Name: Comitato Etico dell'Azienda Ospedaliera Universitaria S. Giovanni Battista di Torino Board Affiliation: A.O. UNIVERSITARIA S. GIOVANNI BATTISTA-MOLINETTE DI TORINO Phone: 0039-0116334171 Email: comitatoetico@molinette.piemonte.it
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Italy: Ministry of Health

Study Description

Brief Summary:	This study will evaluate the correlation between the pharmacokinetic and pharmacodynamic parameters of CellCept in patients undergoing primary kidney transplantation, in order to assess the impact on clinical outcome and the risks of acute rejection. All patients will receive oral CellCept, 1g twice daily, and pharmacokinetic and pharmacodynamic parameters will be measured at weeks 2, 4, 12 and 24. The anticipated time on study treatment is 24 weeks.
Detailed Description:	

Conditions

Conditions:	Kidney Transplantation
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	N/A
Endpoint Classification:	Pharmacokinetics/Dynamics Study

Enrollment: 45 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Mycophenolate Mofetil Monotherapy Participants received an initial dose of mycophenolate mofetil (MMF), 1 gram (g), orally (PO), twice per day (BID), within 5 days of transplant for 24 weeks. Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.	Drug: mycophenolate mofetil 1 g PO BID for 24 weeks Other Names: • CellCept Drug: antibody induction According to manufacturer recommendation Drug: Cyclosporine According to manufacturer recommendation Drug: corticosteroid According to manufacturer recommendation

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 65 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Adult patients, 18 to 65 years of age
- Patients undergoing primary kidney transplantation

Exclusion Criteria:

- Recipients of multiple organ transplants
- Prior therapy with CellCept
- Presence or history of malignancies, except for successfully treated basal or squamous cell carcinoma of the skin
- Active peptic ulcer or active serious digestive system disease that may affect the absorption of CellCept

Contacts/Locations

Study Officials: Clinical Trials
Study Chair
Hoffmann-La Roche

Locations: Italy
Brescia, Italy, 25123

Coppito, Italy, 67100

Verona, Italy, 37126

Roma, Italy, 00168

Napoli, Italy, 80131

Bari, Italy, 70124

Torino, Italy, 10126

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Mycophenolate Mofetil (MMF) Monotherapy	Participants received an initial dose of MMF 1 gram (g), orally (PO), twice per day (BID), started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Overall Study

	Mycophenolate Mofetil (MMF) Monotherapy
Started	45
Completed	32
Not Completed	13
Adverse Event	5
Death	1
Graft loss	1
Protocol Violation	3
Withdrawal by Subject	1
Not specified	2

Baseline Characteristics

Analysis Population Description
All enrolled participants.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Baseline Measures

	MMF Monotherapy
Number of Participants	45
Age, Continuous [units: years] Mean (Standard Deviation)	46.60 (9.92)
Gender, Male/Female [units: participants]	
Female	20
Male	25

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Acute Rejection
Measure Description	Diagnosis of acute rejection was suspected in any participant with an increase in serum creatinine greater than or equal to (≥) 25 percent (%). All suspected acute rejections were confirmed by biopsy. The start date of acute rejection was identified as the date of biopsy.
Time Frame	Day 1, Weeks 2, 4, 12, 24, and 28
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: all eligible participants who had at least baseline (BL) and 1 assessment of pharmacokinetics (PK) and pharmacodynamics (PD). Acute rejection was analyzed in any participant with an increase in serum creatinine of 25%.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Percentage of Participants With Acute Rejection [units: percentage of participants]	9.1

2. Primary Outcome Measure:

Measure Title	Time to Rejection
Measure Description	The mean time, in days, from the date of enrollment to date of biopsy confirming acute rejection.
Time Frame	Day 1, Weeks 2, 4, 12, 24, and 28
Safety Issue?	No

Analysis Population Description

ITT population; only participants with acute or biopsy-proven rejection were included in the analysis.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	6
Time to Rejection [units: days] Mean (Standard Deviation)	23.67 (21.44)

3. Primary Outcome Measure:

Measure Title	Percentage of Participants With Biopsy-Proven Acute Rejection (BPAR)
Measure Description	BPAR was defined according to 1997 Banff Criteria as a biopsy Banff grade of IA, IB, IIA, IIB, or III. Grade IA was defined as significant interstitial infiltration with greater than (>)25% of parenchyma affected, and foci of moderate tubulitis with >4 mononuclear cells per tubular cross section or group of 10 tubular cells. Grade IB was defined as significant interstitial infiltration with >25% parenchyma affected, and foci of severe tubulitis with >10% mononuclear cells per tubular cross section or group of 10 tubular cells. Grade IIA was defined as mild to moderate intimal arteritis. Grade IIB was defined as severe intimal arteritis comprising >25% of the luminal area. Grade III was defined as transmural arteritis and/or arterial fibrinoid changes and necrosis of medial smooth muscle cells.
Time Frame	Day 1, Weeks 2, 4, 12, 24, and 28
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Percentage of Participants With Biopsy-Proven Acute Rejection (BPAR) [units: percentage of participants]	4.5

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Graft Loss
Measure Description	An allograft was presumed to be lost if a participant started dialysis and was not able to subsequently be removed from dialysis.
Time Frame	Day 1, Weeks 2, 4, 12, 24, and 28
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Percentage of Participants With Graft Loss	2.3

	MMF Monotherapy
[units: percentage of participants]	

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Surviving
Measure Description	
Time Frame	Day 1, Weeks 2, 4, 12, 24, and 28
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Percentage of Participants Surviving [units: percentage of participants]	97.7

6. Secondary Outcome Measure:

Measure Title	Total Mycophenolate Acid (MPA) by Visit and Timepoint
Measure Description	Drug quantification of total MPA (micrograms per milliliter [mcg/mL]) in the plasma was measured at time (T) = 0 minutes (min), 40 mins, and 120 mins.
Time Frame	Weeks 2, 4, 12, 24, and 28 (Safety Follow-Up Visit), and any unscheduled visits
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	491
Total Mycophenolate Acid (MPA) by Visit and Timepoint [units: mcg/mL] Mean (Standard Deviation)	
T=0, Week 2 (n=41)	1.75 (1.49)
T=0, Week 4 (n=42)	1.87 (1.62)
T=0, Week 12 (n=35)	1.79 (1.04)
T=0, Week 24 (n=35)	1.90 (1.53)
T=0, safety follow-up (n=3)	1.16 (0.22)
T=0, unscheduled visit (n=7)	1.32 (0.67)
T=0, overall mean value (n=163)	1.79 (1.40)
T=40, Week 2 (n=43)	6.44 (4.37)
T=40, Week 4 (n=42)	6.96 (3.92)
T=40, Week 12 (n=35)	7.23 (4.27)
T=40, Week 24 (n=35)	6.47 (3.35)
T=40, safety follow-up (n=3)	5.71 (0.55)
T=40, unscheduled visit (n=7)	4.06 (1.05)
T=40, overall mean value (n=165)	6.63 (3.91)
T=120, Week 2 (n=41)	8.86 (7.30)

	MMF Monotherapy
T=120, Week 4 (n=42)	8.95 (6.33)
T=120, Week 12 (n=35)	8.57 (6.71)
T=120, safety follow-up (n=3)	4.91 (2.09)
T=120, Week 24 (n=35)	10.04 (6.91)
T=120, unscheduled visit (n=7)	7.03 (5.31)
T=120, overall mean value (n=163)	8.92 (6.68)

7. Secondary Outcome Measure:

Measure Title	Free MPA (mcg/mL) by Visit
Measure Description	Drug quantification of free MPA in the plasma was measured at T = 0, 40, and 120 mins.
Time Frame	Weeks 2, 4, 12, 24, safety follow-up (Week 28), and any unscheduled visits
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	482
Free MPA (mcg/mL) by Visit [units: mcg/mL] Mean (Standard Deviation)	
T=0, Week 2 (n=40)	0.03 (0.03)

	MMF Monotherapy
T=0, Week 4 (n=39)	0.04 (0.03)
T=0, Week 12 (n=33)	0.03 (0.02)
T=0, Week 24 (n=32)	0.03 (0.02)
T=0, safety follow-up (n=3)	0.01 (0.01)
T=0, unscheduled visit (n=7)	0.04 (0.03)
T=0, overall mean value (n=154)	0.03 (0.03)
T=40, Week 2 (n=41)	0.11 (0.09)
T=40, Week 4 (n=42)	0.11 (0.07)
T=40, Week 12 (n=35)	0.11 (0.06)
T=40, Week 24 (n=35)	0.38 (1.35)
T=40, safety follow-up (n=3)	0.06 (0.02)
T=40, unscheduled visit (n=7)	0.09 (0.07)
T=40, overall mean value (n=163)	0.17 (0.63)
T=120, Week 2 (n=43)	0.11 (0.07)
T=120, Week 4 (n=42)	0.11 (0.07)
T=120, Week 12 (n=35)	0.16 (0.36)
T=120, Week 24 (n=35)	0.10 (0.06)
T=120, safety follow-up (n=3)	0.10 (0.03)
T=120, unscheduled visit (n=7)	0.07 (0.03)
T=120, overall mean value (n=165)	0.12 (0.18)

8. Secondary Outcome Measure:

Measure Title	MPA Area Under the Concentration - Time Curve From Time 0 to 12 Hours (AUC0-12) (mcg/mL) by Visit
Measure Description	The AUC0-12 of MPA was estimated on the validated limited sampling strategy, AUC (milligrams multiplied by height over liter [mg.h/L]) = 7.182 + 4.607 multiplied by (*) concentration at 0 minutes (C0)+ 0.998 * the concentration at 40 minutes (C0.67) + 2.149 * the concentration at 120 minutes (C2).
Time Frame	Predose and 40 minutes and 2 hours postdose at Weeks 2, 4, 12, and 24, and at the Safety follow-up (Week 28)

Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
MPA Area Under the Concentration - Time Curve From Time 0 to 12 Hours (AUC0-12) (mcg/mL) by Visit [units: mcg*hr/mL] Mean (Standard Deviation)	
Week 2 (n=41)	38.3 (17.9)
Week 4 (n=42)	39.7 (17.4)
Week 12 (n=35)	39.7 (16.5)
Week 24 (n=35)	39.8 (17.0)
Follow-up (n=3)	29.7 (3.7)

9. Secondary Outcome Measure:

Measure Title	Inosine MonoPhosphate DeHydrogenase (IMPDH) Activity by Visit and Timepoint
Measure Description	IMPDH activity in peripheral blood mononuclear cells (PBMCs) was measured at 2 timepoints per visit, 0 and 120 minutes and presented in enzyme units. The unit of measure of enzyme activity is "U". One U is defined as the amount of the enzyme that produces a certain amount of enzymatic activity that is, the amount that catalyzes the conversion of 1 micro mole of substrate per minute under pre-specified conditions (temperature, pH).
Time Frame	BL and Weeks 2, 4, 12, and 24, and safety follow-up (Week 28) and any unscheduled visits
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	364
Inosine MonoPhosphate DeHydrogenase (IMPDH) Activity by Visit and Timepoint [units: enzyme units] Mean (Standard Deviation)	
T=0, BL (n=44)	5.01 (5.17)
T=0, Week 2 (n=42)	3.96 (3.58)
T=0, Week 4 (n=42)	3.89 (2.36)
T=0, Week 12 (n=35)	6.74 (11.79)
T=0, Week 24 (n=34)	9.58 (10.81)
T=0, safety follow-up (n=0)	0 (0)
T=0, unscheduled visit (n=7)	6.00 (6.12)
T=0, mean value (n=204)	5.65 (7.54)
T=120, BL (n=0)	0 (0)
T=120, Week 2 (n=42)	3.06 (3.42)
T=120, Week 4 (n=42)	3.10 (2.66)
T=120, Week 12 (n=35)	3.75 (5.02)
T=120, Week 24 (n=34)	6.39 (6.14)
T=120, safety follow-up (n=0)	0 (0)

	MMF Monotherapy
T=120, unscheduled visit (n=7)	3.89 (1.82)
T=120, mean value (n=160)	3.97 (4.46)

10. Secondary Outcome Measure:

Measure Title	IMPDH Expression I by Visit and Timepoint
Measure Description	IMPDH I gene expression was measured by real time polymerase chain reaction (QRT-PCR) based cytokine measurement of PBMCs at 2 timepoints per visit, 0 and 120 minutes and expressed as number of messenger ribonucleic acid (mRNA) copies per cell (copies/cell).
Time Frame	BL and Weeks 2, 4, 12, and 24, and safety follow-up (Week 28) and any unscheduled visits
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	369
IMPDH Expression I by Visit and Timepoint [units: number of mRNA copies/cell] Mean (Standard Deviation)	
T=0, BL (n=44)	2.32 (3.02)
T=0, Week 2 (n=41)	32.29 (188.29)
T=0, Week 4 (n=42)	3.16 (8.59)
T=0, Week 12 (n=34)	4.10 (15.09)

	MMF Monotherapy
T=0, Week 24 (n=34)	1.95 (2.94)
T=0, safety follow-up (n=3)	11803.48 (20432.48)
T=0, unscheduled visit (n=7)	4.00 (3.84)
T=0, mean value (n=205)	181.48 (2473.05)
T=120, BL (n=0)	0 (0)
T=120, Week 2 (n=43)	4146.17 (14891.57)
T=120, Week 4 (n=42)	1692.11 (6690.21)
T=120, Week 12 (n=35)	1556.06 (5856.17)
T=120, Week 24 (n=34)	3.02 (7.53)
T=120, safety follow-up (n=3)	107.30 (179.38)
T=120, unscheduled visit (n=7)	1038.52 (1781.89)
T=120, mean value (n=164)	1899.45 (8824.89)

11. Secondary Outcome Measure:

Measure Title	IMPDH Expression II by Visit and Timepoint
Measure Description	IMPDH II gene expression was measured by QRT-PCR based cytokine measurement of PBMCs at 2 timepoints per visit, 0 and 120 minutes and expressed as number of mRNA copies/cell.
Time Frame	BL and Weeks 2, 4, 12, and 24, and safety follow-up (Week 28) and any unscheduled visits
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	369
IMPDH Expression II by Visit and Timepoint [units: number of mRNA copies/cell] Mean (Standard Deviation)	
T=0, BL (n=44)	115.33 (19.81)
T=0, Week 2 (n=41)	113.43 (21.67)
T=0, Week 4 (n=42)	117.16 (30.72)
T=0, Week 12 (n=34)	112.43 (24.57)
T=0, Week 24 (n=34)	114.21 (19.79)
T=0, safety follow-up (n=3)	123.86 (37.61)
T=0, unscheduled visit (n=7)	116.57 (19.25)
T=0, mean value (n=205)	114.82 (23.54)
T=120, BL (n=0)	0 (0)
T=120, Week 2 (n=43)	304.64 (309.26)
T=120, Week 4 (n=42)	148.32 (206.39)
T=120, Week 12 (n=35)	143.11 (82.95)
T=120, Week 24 (n=34)	109.00 (22.81)
T=120, safety follow-up (n=3)	140.51 (42.37)
T=120, unscheduled visit (n=7)	167.19 (155.73)
T=120, mean value (n=164)	180.71 (208.68)

12. Secondary Outcome Measure:

Measure Title	Interleukin 8 (IL-8) Expression by Visit and Timepoint
Measure Description	IL-8 gene expression was measured by QRT-PCR based cytokine measurement of PBMCs at 2 timepoints per visit, 0 and 120 minutes and expressed as number of mRNA copies/cell.
Time Frame	BL and Weeks 2, 4, 12, and 24, and safety follow-up (Week 28) and any unscheduled visits

Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	369
Interleukin 8 (IL-8) Expression by Visit and Timepoint [units: number of mRNA copies/cell] Mean (Standard Deviation)	
T=0, BL (n=44)	4532.72 (11598.93)
T=0, Week 2 (n=41)	29960.41 (128979.24)
T=0, Week 4 (n=42)	54101.30 (262581.32)
T=0, Week 12 (n=34)	1829.87 (6411.17)
T=0, Week 24 (n=34)	10391.60 (42574.52)
T=0, safety follow-up (n=3)	1254.29 (1150.40)
T=0, unscheduled visit (n=7)	19148.94 (49991.25)
T=0, mean value (n=205)	20748.32 (1333817.10)
T=120, BL (n=0)	0.0 (0.0)
T=120, Week 2 (n=43)	1028.93 (4210.43)
T=120, Week 4 (n=42)	21227.11 (103517.73)
T=120, Week 12 (n=35)	12022.83 (63647.48)
T=120, Week 24 (n=34)	9418.65 (29084.00)
T=120, safety follow-up (n=3)	397887.30 (688477.81)

	MMF Monotherapy
T=120, unscheduled visit (n=7)	220.14 (457.26)
T=120, mean value (n=164)	17512.31 (110920.39)

13. Secondary Outcome Measure:

Measure Title	Tumor Necrosis Factor (TNF) Expression by Visit and Timepoint
Measure Description	TNF gene expression was measured by QRT-PCR based cytokine measurement of PBMCs at 2 timepoints per visit, 0 and 120 minutes and expressed as number of mRNA copies/cell.
Time Frame	BL and Weeks 2, 4, 12, and 24, and safety follow-up (Week 28) and any unscheduled visits
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	369
Tumor Necrosis Factor (TNF) Expression by Visit and Timepoint [units: number of mRNA copies/cell] Mean (Standard Deviation)	
T=0, BL (n=44)	4532.72 (11598.93)
T=0, Week 2 (n=41)	29960.41 (128979.24)
T=0, Week 4 (n=42)	54101.30 (262581.32)
T=0, Week 12 (n=34)	1829.87 (6411.17)

	MMF Monotherapy
T=0, Week 24 (n=34)	10391.60 (42574.52)
T=0, safety follow-up (n=3)	1254.29 (1150.40)
T=0, unscheduled visit (n=7)	19148.94 (49991.25)
T=0, mean value (n=205)	20748.32 (133817.10)
T=120, BL (n=0)	0 (0)
T=120, Week 2 (n=43)	1028.93 (4210.43)
T=120, Week 4 (n=42)	21227.11 (103517.73)
T=120, Week 12 (n=35)	12022.83 (63647.48)
T=120, Week 24 (n=34)	9418.65 (29084.00)
T=120, safety follow-up (n=3)	397887.30 (688477.81)
T=120, unscheduled visit (n=7)	220.14 (457.26)
T=120, mean value (n=164)	17512.31 (110920.39)

14. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Infection
Measure Description	Infections were graded according to the World Health Organization (WHO) worst grade observed.
Time Frame	BL and Weeks 2, 4, 12, 24, and 28 (Safety Follow-Up)
Safety Issue?	Yes

Analysis Population Description

Safety population: all enrolled participants

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	45
Percentage of Participants With Infection [units: percentage of participants]	
Acarodermatitis (mild)	2.22
Bronchitis (moderate)	2.22
Cytomegalovirus (CMV) infection (mild)	13.33
CMV infection (moderate)	8.89
CMV infection (severe)	4.44
CMV viraemia (mild)	2.22
Gastroenteritis proteus (severe)	2.22
Gastrointestinal infection (severe)	2.22
Legionella infection (life-threatening)	2.22
Oral herpes (mild)	2.22
Sepsis (life-threatening)	2.22
Tracheitis (mild)	2.22
Urethritis (mild)	2.22
Urinary tract infection (mild)	28.89
Urinary tract infection (moderate)	2.22

15. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Gastrointestinal Toxicities
Measure Description	Gastrointestinal adverse events (AEs) according to WHO worst grade observed.
Time Frame	BL and Weeks 2, 4, 12, 24, and 28 (Safety Follow-up Visit)
Safety Issue?	Yes

Analysis Population Description

Safety population

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	45
Percentage of Participants With Gastrointestinal Toxicities [units: percentage of participants]	
Abdominal pain (moderate)	2.22
Abdominal pain (severe)	2.22
Anal fissure (mild)	2.22
Diarrhoea (mild)	4.44
Diarrhoea (moderate)	2.22
Diarrhoea (severe)	2.22
Dyspepsia (mild)	2.22
Gastritis (moderate)	2.22
Gastritis erosive (moderate)	2.22
Gingival hyperplasia (mild)	2.22
Haemorrhoids (mild)	2.22
Intra-abdominal haematoma (mild)	2.22
Nausea (moderate)	2.22
Stomatitis (mild)	2.22
Vomiting (mild)	2.22
Vomiting (moderate)	4.44
Vomiting (severe)	4.44

16. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Hematologic Toxicity
Measure Description	Hematological toxicities graded according to WHO worst grade observed (Grade 1=mild, Grade 2=moderate).
Time Frame	BL and Weeks 2, 4, 12, 24, and 28 (Safety Follow-Up)
Safety Issue?	Yes

Analysis Population Description

Safety population

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	45
Percentage of Participants With Hematologic Toxicity [units: percentage of participants]	
Grade 1 hemoglobin decreased	13.33
Grade 1 leukocytes decreased	11.11
Grade 2 leukocytes decreased	8.89
Grade 1 granulocytes decreased	6.67
Grade 2 granulocytes decreased	6.67
Grade 1 platelets decreased	6.67
Grade 1 bilirubin increased	4.44
Grade 2 bilirubin increased	2.22
Grade 1 hypoglycemia	4.44
Grade 1 alkaline phosphatase increased	13.33

	MMF Monotherapy
Grade 2 alkaline phosphatase increased	2.22
Grade 1 aspartate aminotransferase increased	6.67
Grade 1 alanine aminotransferase increased	8.89
Grade 2 alanine aminotransferase increased	2.22
Grade 1 cholesterol increased	26.67
Grade 2 cholesterol increased	8.89
Grade 1 triglycerides increased	24.44
Grade 2 triglycerides increased	2.22
Grade 1 blood urea nitrogen increased	2.22
Grade 2 blood urea nitrogen increased	2.22

17. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between MPA Levels and IMPDH Activity
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	305
Spearman's Rank Correlation Coefficient Between MPA Levels and IMPDH Activity [units: correlation coefficient]	
Free MPA, T=0 (n=144)	0.063
Free MPA, T=120 (n=153)	0.028
Total MPA, T=0 (n=152)	0.034
Total MPA, T=120 (n=153)	-0.050

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between MPA Levels and IMPDH Activity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4505
	Comments	Free MPA, time 0 [trough]
	Method	ANOVA
	Comments	Analysis of variance (ANOVA)

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between MPA Levels and IMPDH Activity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7322
	Comments	Free MPA, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 3 for Spearman's Rank Correlation Coefficient Between MPA Levels and IMPDH Activity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6798
	Comments	Total MPA, time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 4 for Spearman's Rank Correlation Coefficient Between MPA Levels and IMPDH Activity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5410
	Comments	Total MPA, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

18. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between IMPDH I Expression and MPA Levels

Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	290
Spearman's Rank Correlation Coefficient Between IMPDH I Expression and MPA Levels [units: correlation coefficient]	
Free MPA, T=0 (n=141)	0.073
Free MPA, T=120 (n=143)	-0.024
Total MPA, T=0 (n=147)	0.037
Total MPA, T=120 (n=143)	-0.140

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between IMPDH I Expression and MPA Levels

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3892
	Comments	Free MPA, time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between IMPDH I Expression and MPA Levels

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6564
	Comments	Total MPA, time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 3 for Spearman's Rank Correlation Coefficient Between IMPDH I Expression and MPA Levels

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7772
	Comments	Free MPA, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 4 for Spearman's Rank Correlation Coefficient Between IMPDH I Expression and MPA Levels

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]

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

Statistical Test of Hypothesis	P-Value	0.0958
	Comments	Total MPA, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

19. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between IMPDH I Expression and Free Fraction
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	283
Spearman's Rank Correlation Coefficient Between IMPDH I Expression and Free Fraction [units: correlation coefficient]	
p Free fraction, T=0 (n=140)	0.047

	MMF Monotherapy
p Free fraction, T=120 (n=143)	0.080

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between IMPDH I Expression and Free Fraction

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5796
	Comments	Time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between IMPDH I Expression and Free Fraction

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3428
	Comments	Time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

20. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between IMPDH II Expression and MPA Levels
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.

Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	305
Spearman's Rank Correlation Coefficient Between IMPDH II Expression and MPA Levels [units: correlation coefficient]	
Free MPA, T=0 (n=145)	0.007
Free MPA, T=120 (n=153)	0.073
Total MPA, T=0 (n=152)	-0.001
Total MPA, T=120 (n=153)	0.084

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between IMPDH II Expression and MPA Levels

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9372
	Comments	Free MPA, time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between IMPDH II Expression and MPA Levels

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9904
	Comments	Total MPA, time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 3 for Spearman's Rank Correlation Coefficient Between IMPDH II Expression and MPA Levels

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3658
	Comments	Free MPA, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 4 for Spearman's Rank Correlation Coefficient Between IMPDH II Expression and MPA Levels

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]

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

Statistical Test of Hypothesis	P-Value	0.2987
	Comments	Total MPA, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

21. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between IMPDH II Expression and Free Fraction
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	297
Spearman's Rank Correlation Coefficient Between IMPDH II Expression and Free Fraction [units: correlation coefficient]	
p Free fraction, T=0 (n=144)	-0.027

	MMF Monotherapy
p Free fraction, T=120 (n=153)	0.015

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between IMPDH II Expression and Free Fraction

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7455
	Comments	time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between IMPDH II Expression and Free Fraction

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8504
	Comments	Time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

22. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between IMPDH Inhibition and Risk of Acute Rejection
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.

Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	353
Spearman's Rank Correlation Coefficient Between IMPDH Inhibition and Risk of Acute Rejection [units: correlation coefficient]	
IMPDH I expression, T=0 (n=189)	0.030
IMPDH I expression T=120 (n=145)	0.083
IMPDH II expression, T=0 (n=196)	-0.062
IMPDH II expression (T=120, n=155)	-0.010
MPDH Activity, T=0 (n=198)	-0.121
IMPDH Activity, T=120 (n=155)	-0.004

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between IMPDH Inhibition and Risk of Acute Rejection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6847
	Comments	IMPDH I, time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between IMPDH Inhibition and Risk of Acute Rejection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3184
	Comments	IMPDH I, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 3 for Spearman's Rank Correlation Coefficient Between IMPDH Inhibition and Risk of Acute Rejection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3862
	Comments	IMPDH II, time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 4 for Spearman's Rank Correlation Coefficient Between IMPDH Inhibition and Risk of Acute Rejection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]

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

Statistical Test of Hypothesis	P-Value	0.9040
	Comments	IMPDH II, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 5 for Spearman's Rank Correlation Coefficient Between IMPDH Inhibition and Risk of Acute Rejection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0907
	Comments	IMPDH activity, time 0 [trough]
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 6 for Spearman's Rank Correlation Coefficient Between IMPDH Inhibition and Risk of Acute Rejection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9630
	Comments	IMPDH activity, time 120 [2 hours after administration at Week 12]
	Method	ANOVA
	Comments	[Not specified]

23. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Infection
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples analyzed.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	351
Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Infection [units: correlation coefficient]	
IMPDH I expression (n=334)	0.045
IMPDH II expression (n=351)	0.047

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Infection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4130
	Comments	IMPDH I
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Infection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3823
	Comments	IMPDH II
	Method	ANOVA
	Comments	[Not specified]

24. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Hematologic Toxicity
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	351
Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Hematologic Toxicity [units: correlation coefficient]	
IMPDH I expression (n=334)	-0.116
IMPDH II expression (n=351)	-0.004

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Hematologic Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0316
	Comments	IMPDH I
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Hematologic Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9440
	Comments	IMPDH II

	Method	ANOVA
	Comments	[Not specified]

25. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Gastrointestinal Toxicity
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	351
Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Gastrointestinal Toxicity [units: correlation coefficient]	
IMPDH I expression (n=334)	0.082
IMPDH II expression (n=351)	0.030

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Gastrointestinal Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1328
	Comments	IMPDH I
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between IMPDH Expression and Risk of Gastrointestinal Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5760
	Comments	IMPDH II
	Method	ANOVA
	Comments	[Not specified]

26. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Infection
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	308
Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Infection [units: correlation coefficient]	
Free MPA (n=300)	-0.020
Total MPA (n=308)	0.063
AUC MPA (n=152)	0.030

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Infection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7332
	Comments	Free MPA
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Infection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2681
	Comments	Total MPA
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 3 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Infection

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7087
	Comments	AUC MPA
	Method	ANOVA
	Comments	[Not specified]

27. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Hematologic Toxicity
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	308
Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Hematologic Toxicity [units: correlation coefficient]	
Free MPA (n=300)	-0.004
Total MPA (n=308)	-0.037
AUC MPA (n=152)	-0.038

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Hematologic Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9432
	Comments	Free MPA
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Hematologic Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5177
	Comments	Total MPA
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 3 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Hematologic Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6398
	Comments	AUC MPA
	Method	ANOVA
	Comments	[Not specified]

28. Secondary Outcome Measure:

Measure Title	Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Gastrointestinal Toxicity
Measure Description	The Spearman's rank correlation coefficient was computed by ranking the data from 2 time points, 0 minutes and 120 minutes, and using the ranks in the Pearson product-moment correlation formula. In case of ties, the averaged ranks were used.
Time Frame	BL and Weeks 2, 4, 12, and 24
Safety Issue?	No

Analysis Population Description

ITT population; n=number of samples

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Measured Values

	MMF Monotherapy
Number of Participants Analyzed	44
Number of Samples Analyzed	308
Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Gastrointestinal Toxicity [units: correlation coefficient]	
Free MPA (n=300)	0.106
Total MPA (n=308)	0.142
AUC MPA (n=152)	0.187

Statistical Analysis 1 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Gastrointestinal Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0656
	Comments	Free MPA
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 2 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Gastrointestinal Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0131
	Comments	Total MPA
	Method	ANOVA
	Comments	[Not specified]

Statistical Analysis 3 for Spearman's Rank Correlation Coefficient Between MPA Levels and Risk of Gastrointestinal Toxicity

Statistical Analysis Overview	Comparison Groups	MMF Monotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0515
	Comments	AUC MPA
	Method	ANOVA
	Comments	[Not specified]

Reported Adverse Events

Time Frame	Adverse events (AEs) were recorded throughout treatment to the safety evaluation follow up 4 weeks after treatment discontinuation, for up to 28 weeks.
Additional Description	The safety assessment population included all eligible participants who received at least 1 dose of study treatment.

Reporting Groups

	Description
MMF Monotherapy	Participants received an initial dose of MMF 1 g, PO, BID, started within 5 days of transplant, for up to 24 weeks. MMF dose could be titrated to a maximum daily dose of 2 g (minimum daily dose was 1 g). Participants also received concurrent antibody induction, cyclosporine, and corticosteroids as needed according to center's practice.

Serious Adverse Events

	MMF Monotherapy
	Affected/At Risk (%)
Total	20/45 (44.44%)
Blood and lymphatic system disorders	
Leucopenia [A] *	1/45 (2.22%)
Lymphocele [A] *	15/45 (33.33%)
Gastrointestinal disorders	
Vomiting [A] *	1/45 (2.22%)
General disorders	
Edema of the left leg [A] *	1/45 (2.22%)
Infections and infestations	
CMV infection [A] *	3/45 (6.67%)
Gastrointestinal infection [A] *	1/45 (2.22%)
Infection due to Legionella and Pseudomonas [A] *	1/45 (2.22%)
Proteus mirabilis infection [A] *	1/45 (2.22%)
Sepsis [A] *	1/45 (2.22%)
Injury, poisoning and procedural complications	
Acute rejection [A] *	3/45 (6.67%)
Acute vascular and interstitial rejection [A] *	1/45 (2.22%)
Investigations	

	MMF Monotherapy
	Affected/At Risk (%)
Increase in creatinine [A] *	2/45 (4.44%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Carcinoma of the bladder [A] *	1/45 (2.22%)
Prostatic adenocarcinoma [A] *	1/45 (2.22%)
Renal and urinary disorders	
Acute renal failure [A] *	1/45 (2.22%)
Acute tubular necrosis [A] *	2/45 (4.44%)
Hydronephrosis [A] *	1/45 (2.22%)
Tubulitis [A] *	1/45 (2.22%)
Ureteral stenosis [A] *	1/45 (2.22%)
Urinary anastomotic leak [A] *	1/45 (2.22%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, WHO Guidelines

Other Adverse Events

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

	MMF Monotherapy
	Affected/At Risk (%)
Total	43/45 (95.56%)
Blood and lymphatic system disorders	
Acidosis [A] *	1/45 (2.22%)
Anaemia [A] *	10/45 (22.22%)
Antithrombin III deficiency [A] *	2/45 (4.44%)
Coagulopathy [A] *	1/45 (2.22%)
Iron deficiency anaemia [A] *	1/45 (2.22%)

	MMF Monotherapy
	Affected/At Risk (%)
Leukopenia [A] *	13/45 (28.89%)
Lymphocele [A] *	1/45 (2.22%)
Lymphocytopenia [A] *	1/45 (2.22%)
Thrombocytopenia [A] *	2/45 (4.44%)
Cardiac disorders	
Angina pectoris [A] *	1/45 (2.22%)
Erythema [A] *	1/45 (2.22%)
Tachycardia [A] *	1/45 (2.22%)
Gastrointestinal disorders	
Abdominal pain [A] *	2/45 (4.44%)
Anal fissure [A] *	1/45 (2.22%)
Diarrhoea [A] *	7/45 (15.56%)
Dyspepsia [A] *	1/45 (2.22%)
Gastritis [A] *	1/45 (2.22%)
Gastritis erosive [A] *	1/45 (2.22%)
Gingival hyperplasia [A] *	1/45 (2.22%)
Haemorrhoids [A] *	1/45 (2.22%)
Intra-abdominal haematoma [A] *	1/45 (2.22%)
Nausea [A] *	1/45 (2.22%)
Oral herpes [A] *	1/45 (2.22%)
Stomatitis [A] *	1/45 (2.22%)
Vomiting [A] *	5/45 (11.11%)

	MMF Monotherapy
	Affected/At Risk (%)
General disorders	
Asthenia [A] *	1/45 (2.22%)
Ear pain [A] *	1/45 (2.22%)
Hearing impaired [A] *	1/45 (2.22%)
Oedema peripheral [A] *	4/45 (8.89%)
Pharyngolaryngeal pain [A] *	1/45 (2.22%)
Pyrexia [A] *	12/45 (26.67%)
Hepatobiliary disorders	
Cholestasis [A] *	1/45 (2.22%)
Lipidosis [A] *	1/45 (2.22%)
Infections and infestations	
Catheter related infection [A] *	1/45 (2.22%)
Cytomegalovirus infection [A] *	9/45 (20%)
Cytomegalovirus viraemia [A] *	1/45 (2.22%)
Tracheitis [A] *	1/45 (2.22%)
Urethritis [A] *	1/45 (2.22%)
Urinary tract infection [A] *	22/45 (48.89%)
Injury, poisoning and procedural complications	
Post-procedural haemorrhage [A] *	1/45 (2.22%)
Investigations	
Alanine aminotransferase increased [A] *	1/45 (2.22%)
Blood bilirubin increased [A] *	1/45 (2.22%)
Blood cholesterol increased [A] *	3/45 (6.67%)

	MMF Monotherapy
	Affected/At Risk (%)
Blood creatinine increased [A] *	8/45 (17.78%)
White blood cell count decreased [A] *	2/45 (4.44%)
Metabolism and nutrition disorders	
Diabetes mellitus [A] *	1/45 (2.22%)
Hypercholesterolemia [A] *	4/45 (8.89%)
Hyperlipemia [A] *	3/45 (6.67%)
Hyperuricaemia [A] *	7/45 (15.56%)
Hypocalcaemia [A] *	2/45 (4.44%)
Hypokalaemia [A] *	8/45 (17.78%)
Iron deficiency [A] *	1/45 (2.22%)
Musculoskeletal and connective tissue disorders	
Arthralgia [A] *	1/45 (2.22%)
Myalgia [A] *	1/45 (2.22%)
Myopathy [A] *	1/45 (2.22%)
Rhabdomyolysis [A] *	1/45 (2.22%)
Nervous system disorders	
Headache [A] *	2/45 (4.44%)
Paraesthesia [A] *	1/45 (2.22%)
Psychiatric disorders	
Anxiety [A] *	1/45 (2.22%)
Insomnia [A] *	5/45 (11.11%)
Renal and urinary disorders	
Dysuria [A] *	1/45 (2.22%)

	MMF Monotherapy
	Affected/At Risk (%)
Glomerulosclerosis [A] *	1/45 (2.22%)
Haematuria [A] *	2/45 (4.44%)
Nocturia [A] *	1/45 (2.22%)
Perirenal haematoma [A] *	1/45 (2.22%)
Renal artery stenosis [A] *	1/45 (2.22%)
Renal colic [A] *	2/45 (4.44%)
Respiratory, thoracic and mediastinal disorders	
Bronchitis [A] *	1/45 (2.22%)
Cough [A] *	2/45 (4.44%)
Dyspnoea [A] *	1/45 (2.22%)
Skin and subcutaneous tissue disorders	
Acarodermatitis [A] *	1/45 (2.22%)
Pruritus [A] *	1/45 (2.22%)
Surgical and medical procedures	
Operative haemorrhage [A] *	1/45 (2.22%)
Wound haemorrhage [A] *	1/45 (2.22%)
Vascular disorders	
Arteriovenous fistula [A] *	1/45 (2.22%)
Arteriovenous fistula thrombosis [A] *	1/45 (2.22%)
Hypertension [A] *	6/45 (13.33%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, WHO Guidelines

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

All Principal Investigators ARE employed by the organization sponsoring the study.

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