ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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ClinicalTrials.gov ID: NCT01033864

Study Identification

Unique Protocol ID:	ML22641
Brief Title:	A Pharmacokinetic Study of CellCept (Mycophenolate Mofetil) Versus Mycophenolate Sodium in Kidney Transplant Patients
Official Title:	Comparison of Pharmocokinetics of Mycophenolate Mofetil and Enteric Coated Mycophenolate Sodium in Calcineurininhibitor-free Treated Patients After Renal Transplantation
Secondary IDs:	2009-012355-15

Study Status

Record Verification:	August 2015
Overall Status:	Completed
Study Start:	November 2009
Primary Completion:	June 2010 [Actual]
Study Completion:	June 2010 [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: 249/09 Board Name: Ethik-Kommission Board Affiliation: Johann-Wolfgang-Goethe-Universität, Fachbereich Medizin Phone: 0049 69 63 01-4597 Email: Ethikkommission@kgu.de
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Germany: Bundesinstitut für Arzneimittel und Medizinprodukte

Study Description

Brief Summary:	This open-label, 2-arm study will compare the pharmacokinetics of CellCept and mycophenolate sodium in kidney transplanted patients on a calcineurininhibitor-free mycophenolic acid-based therapy. On the study day patients will take their prescribed medication (either CellCept or mycophenolate sodium). Blood samples will be drawn directly before and at intervals up to 12 hours after intake of the study medication. Anticipated time on study treatment is 12 hours and target sample size is 24.
Detailed Description:	

Conditions

Conditions:	Kidney 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:	Non-Randomized
Endpoint Classification:	Pharmacokinetics Study
Enrollment:	23 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: MMF, Prednisone Participants received mycophenolate mofetil (MMF) orally (PO) at a dose of 1 gram per day (g/day) twice daily (BID), and prednisone, PO, up to 5 milligrams per day (mg/day) for at least 1 month.	Drug: MMF 1 g per day b.i.d. p.o. for at least 1 month Other Names: • CellCept • mycophenolate mofetil Drug: Prednisone 5 mg per day p.o.
Active Comparator: EC-MPS Participants received mycophenolate sodium (EC-MPS), PO, at a dose of 720 mg/day BID, and prednisone PO up to 5 mg/day for at least 1 month.	Drug: EC-MPS 720 mg b.i.d. p.o. for at least 1 month Other Names: • mycophenolate sodium Drug: Prednisone 5 mg per day p.o.

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
- kidney transplantation >/=6 months ago
- on mycophenolic acid-based, calcineurininhibitor-free therapy for >/=3 months, >/=1 month on stable dose
- co-therapy with 5mg prednisone for >/=1 month

Exclusion Criteria:

- active gastrointestinal ulcus
- severe diarrhea od gastrointestinal disease
- severe impairment of renal function
- current malignancy

• Lesch-Nyhan- or Kelley-Seegmiller-Syndrome

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Germany
Frankfurt Am Main, Germany, 60528

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Mycophenolate Mofetil (MMF)/ Prednisone	Participants were administered MMF tablets or capsules, orally (PO), at a dose prescribed by their physician and prednisone up to 5 milligrams (mg) PO on Day 1.
Enteric-coated Mycophenolate Sodium (EC-MPS)/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Overall Study

	Mycophenolate Mofetil (MMF)/Prednisone	Enteric-coated Mycophenolate Sodium (EC-MPS)/Prednisone
Started	12	11
Completed	12	11
Not Completed	0	0

Baseline Characteristics

Analysis Population Description

The pharmacokinetic (PK) population included all randomized participants.

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Baseline Measures

	MMF/Prednisone	EC-MPS/Prednisone	Total
Number of Participants	12	11	23
Age, Continuous [units: years] Mean (Standard Deviation)	61.5 (11.06)	58.0 (8.04)	59.8 (9.68)
Gender, Male/Female [units: participants]			
Female	5	4	9
Male	7	7	14

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Pre-dose Trough Concentration (C0)
Measure Description	The mean mycophenolic acid (MPA) concentration in plasma was determined (in milligrams per liter [mg/L]) from blood samples collected predose (immediately before receiving study treatment).
Time Frame	Day 1 predose
Safety Issue?	No

Analysis Population Description

Pharmacokinetic (PK) population: all participants who took study drug and for whom all defined blood samples at the planned sampling time points were available.

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11
Pre-dose Trough Concentration (C0) [units: mg/L] Mean (Standard Deviation)	2.387 (1.1327)	2.944 (2.2103)

Statistical Analysis 1 for Pre-dose Trough Concentration (C0)

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8055
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Dose-Normalized C0
Measure Description	Dose normalized C0 was determined (in mg/L) from blood samples collected predose. Both MMF and EC-MPS doses were normalized to a standard dose of 1 g MMF or 720 mg EC-MPS, respectively. The dose normalization was calculated as follows: For the MMF group: Dose normalized C0 equals (=) C0 divided by (/) (actual dose taken/1000) For the EC-MPS group: Dose normalized C0 = C0 / (actual dose taken/720)

Time Frame	Day 1 predose
Safety Issue?	No

Analysis Population Description
PK population

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11
Dose-Normalized C0 [units: mg/L] Mean (Standard Deviation)	2.962 (1.4439)	4.658 (3.1121)

Statistical Analysis 1 for Dose-Normalized C0

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2548
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

3. Primary Outcome Measure:

Measure Title	Minimum Plasma Concentration (Cmin)

Measure Description	The mean minimum MPA concentration in plasma was determined (in mg/L) from blood samples collected predose and postdose on Day 1.
Time Frame	Day 1 predose and postdose at 30 and 60 minutes and 2, 3, 4, 5, 6, 8 10 and 12 hours
Safety Issue?	No

Analysis Population Description

PK population

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11
Minimum Plasma Concentration (Cmin) [units: mg/L] Mean (Standard Deviation)	1.385 (0.6061)	1.620 (0.6632)

Statistical Analysis 1 for Minimum Plasma Concentration (Cmin)

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4417
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

4. Primary Outcome Measure:

Measure Title	Dose-Normalized Cmin
Measure Description	Dose-normalized Cmin was determined (in mg/L) from blood samples collected predose and postdose. Both MMF and EC-MPS doses were normalized to a standard dose of 1 g MMF or 720 mg EC-MPS, respectively. The dose normalization was calculated as follows: For the MMF group: Dose normalized Cmin = Cmin/ (actual dose taken/1000) For the EC-MPS group: Dose normalized Cmin = Cmin / (actual dose taken/720)
Time Frame	Day 1 predose and postdose at 30 and 60 minutes and 2, 3, 4, 5, 6, 8 10 and 12 hours
Safety Issue?	No

Analysis Population Description

PK population

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11
Dose-Normalized Cmin [units: mg/L] Mean (Standard Deviation)	1.702 (0.8018)	2.613 (1.0291)

Statistical Analysis 1 for Dose-Normalized Cmin

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0455
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

5. Primary Outcome Measure:

Measure Title	Maximum Plasma Concentration (Cmax)
Measure Description	The mean maximum MPA concentration in plasma was determined (in mg/L) in blood samples collected predose and postdose on Day 1.
Time Frame	Day 1 predose and postdose at 30 and 60 minutes and 2, 3, 4, 5, 6, 8 10 and 12 hours
Safety Issue?	No

Analysis Population Description
PK population

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11
Maximum Plasma Concentration (Cmax) [units: mg/L] Mean (Standard Deviation)	15.385 (5.2320)	17.827 (4.2898)

Statistical Analysis 1 for Maximum Plasma Concentration (Cmax)

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]

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

Statistical Test of Hypothesis	P-Value	0.2300
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

6. Primary Outcome Measure:

Measure Title	Dose-Normalized Cmax (mg/L)
Measure Description	Dose-normalized Cmax in plasma was determined (in mg/L) from blood samples collected predose and postdose on Day 1. Both MMF and EC-MPS doses were normalized to a standard dose of 1 g MMF or 720 mg EC-MPS, respectively. The dose normalization was calculated as follows: For the MMF group: Dose normalized Cmax = Cmax / (actual dose taken/1000) For the EC-MPS group: Dose normalized Cmax = Cmax / (actual dose taken/720)
Time Frame	Day 1 predose and postdose at 30 and 60 minutes and 2, 3, 4, 5, 6, 8 10 and 12 hours
Safety Issue?	No

Analysis Population Description
PK population

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11
Dose-Normalized Cmax (mg/L) [units: mg/L] Mean (Standard Deviation)	18.402 (5.4349)	29.996 (11.3229)

Statistical Analysis 1 for Dose-Normalized Cmax (mg/L)

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0106
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

7. Primary Outcome Measure:

Measure Title	MPA Area Under the Curve From 0 to 12 Hours (AUC0-12)
Measure Description	The mean MPA AUC0-12 in plasma was determined (in mg multiplied by hours, per Liter [mg*h/L]) from blood samples collected predose and postdose on Day 1.
Time Frame	Day 1 predose and postdose at 30 and 60 minutes and 2, 3, 4, 5, 6, 8 10 and 12 hours
Safety Issue?	No

Analysis Population Description

PK population

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11

	MMF/Prednisone	EC-MPS/Prednisone
MPA Area Under the Curve From 0 to 12 Hours (AUC0-12) [units: mg*h/L] Mean (Standard Deviation)	50.36348 (15.423230)	57.06682 (10.965285)

Statistical Analysis 1 for MPA Area Under the Curve From 0 to 12 Hours (AUC0-12)

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3401
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

8. Primary Outcome Measure:

Measure Title	Dose-Normalized MPA AUC0-12
Measure Description	Dose-normalized MPA AUC0-12 in plasma was determined (mg*h/L) from blood samples collected predose and postdose on Day 1. Both MMF and EC-MPS doses were normalized to a standard dose of 1 g MMF or 720 mg EC-MPS, respectively. The dose normalization was calculated as follows: For the MMF group: Dose normalized MPA AUC = MPA AUC / (actual dose taken/1000) For the EC-MPS group: Dose normalized MPA AUC = MPA AUC / (actual dose taken/720)
Time Frame	Day 1 predose and postdose at 30 and 60 minutes and 2, 3, 4, 5, 6, 8 10 and 12 hours
Safety Issue?	No

Analysis Population Description
PK population

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11
Dose-Normalized MPA AUC0-12 [units: mg*h/L] Mean (Standard Deviation)	61.53862 (21.003959)	94.65765 (29.307839)

Statistical Analysis 1 for Dose-Normalized MPA AUC0-12

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0074
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

9. Primary Outcome Measure:

Measure Title	Percentage of Participants By Time to Maximum Plasma Concentration (Tmax)
Measure Description	
Time Frame	Day 1 predose and postdose at 30 and 60 minutes and 2, 3, 4, 5, 6, 8 10 and 12 hours
Safety Issue?	No

Analysis Population Description
PK population

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone	EC-MPS/Prednisone
Number of Participants Analyzed	12	11
Percentage of Participants By Time to Maximum Plasma Concentration (Tmax) [units: percentage of participants]		
Tmax equals (=) 0.5333 hours (hrs)	16.7	0.0
Tmax=0.6000 hrs	16.7	0.0
Tmax=0.7333 hrs	16.7	0.0
Tmax=0.7667 hrs	8.3	0.0
Tmax=1.0667 hrs	8.3	9.1
Tmax=1.0833 hrs	16.7	0.0
Tmax=1.1167 hrs	8.3	0.0
Tmax=1.2167 hrs	8.3	0.0
Tmax=2.0167 hrs	0.0	9.1
Tmax=2.0833 hrs	0.0	18.2
Tmax=2.1000 hrs	0.0	9.1
Tmax=2.1167 hrs	0.0	27.3
Tmax=2.1667 hrs	0.0	9.1
Tmax=3.1167 hrs	0.0	9.1
Tmax=3.1833 hrs	0.0	9.1

Statistical Analysis 1 for Percentage of Participants By Time to Maximum Plasma Concentration (Tmax)

Statistical Analysis Overview	Comparison Groups	MMF/Prednisone, EC-MPS/Prednisone
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

10. Secondary Outcome Measure:

Measure Title	Regression Coefficients For Participants Receiving MMF
Measure Description	The estimated regression coefficients for participants who received MMF presented in milligrams per liter (mg/L).
Time Frame	Day 1 at 30 minutes and 1 and 2 hours postdose
Safety Issue?	No

Analysis Population Description

PK population. Only participants in the MMF/Prednisone group were assessed for this outcome measure, n=12.

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Measured Values

	MMF/Prednisone
Number of Participants Analyzed	12
Regression Coefficients For Participants Receiving MMF [units: mg/L]	
Intercept	2.17192

	MMF/Prednisone
Concentration at 30 minutes (C0.5)	0.74031
Concentration at 1 hour (C1)	1.89323
Concentration at 2 hours (C2)	2.85923

Reported Adverse Events

Time Frame	The observational period, approximately 13 hours.
Additional Description	All randomized participants were included in the safety analysis.

Reporting Groups

	Description
MMF/Prednisone	Participants were administered MMF tablets or capsules, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.
EC-MPS/Prednisone	Participants were administered EC-MPS tablets, PO, at a dose prescribed by their physician and prednisone up to 5 mg PO on Day 1.

Serious Adverse Events

	MMF/Prednisone	EC-MPS/Prednisone
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/12 (0%)	0/11 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	MMF/Prednisone	EC-MPS/Prednisone
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/12 (0%)	0/11 (0%)

Limitations and Caveats

[Not specified]

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.

Results Point of Contact:

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