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Trial record **1 of 1** for: CERL080AES08

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Multicenter, Randomized, Open-label Study to Assess Whether Treatment With Mycophenolate Sodium (MPS) Allows Higher Dose Optimization Versus Mycophenolate Mofetil (MMF) Leading to a Dose Reduction of Tacrolimus. Maximiza Study. (MAXIMIZA)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT01056822

First received: January 25, 2010
Last updated: December 2, 2014
Last verified: December 2014
History of Changes

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Results First Received: April 10, 2014

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Prophilaxis of Acute Rejection in Patients Receiving a Renal Allograft
Interventions:	Drug: 1 Drug: 2

Participant Flow

Hide Participant Flow

Recruitment Details

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

Pre-Assignment Details

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

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Participant Flow: Overall Study

	Mycophenolate Sodium (MPS)	Mycophenolate Mofetil (MMF)
STARTED	47	42
Intention-to-treat (ITT) Population: YES	43	38
Intention-to-treat (ITT) Population: NO	4	4
Per-protocol (PP) Population: YES	29	25
Per-protocol (PP) Population: NO	18	17
Safety (SAF) Population: YES	46	40
Safety (SAF) Population: NO	1	2
COMPLETED	39	35
NOT COMPLETED	8	7
Adverse Event	0	1
Protocol Violation	6	5
Withdrawal by Subject	1	1
Lost to Follow-up	1	0

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The intention-to-treat (ITT) population consisted of all randomised patients who gave signed informed consent and received at least one dose of the study medicinal product and have at least one baseline visit and one post-baseline visit (containing data to allow the primary endpoint to be calculated) Standard Deviation

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).
Total	Total of all reporting groups

Baseline Measures

	Mycophenolate Sodium (MPS)	Mycophenolate Mofetil (MMF)	Total
Number of Participants [units: participants]	43	38	81
Age [units: years] Mean (Standard Deviation)	52.88 (9.99)	48.50 (12.86)	50.83 (11.56)

Gender [units: participants]			
Female	15	13	28
Male	28	25	53
Race/Ethnicity, Customized [units: participants]			
Caucasian	39	36	75
Black	0	0	0
Asian	0	0	0
Other	4	2	6

Outcome Measures

Hide All Outcome Measures

1. Primary: Number of Participants Achieving at Least Two Mycophenolic Acid (MPA) Dose Steps Higher and Reducing Tacrolimus Dose at the End of the Study [Time Frame: at 12 months from baseline]

Measure Type	Primary
Measure Title	Number of Participants Achieving at Least Two Mycophenolic Acid (MPA) Dose Steps Higher and Reducing Tacrolimus Dose at the End of the Study
Measure Description	No text entered.
Time Frame	at 12 months from baseline
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus).

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	Mycophenolate Mofetil (MMF)
Number of Participants Analyzed [units: participants]	43	38

Number of Participants Achieving at Least Two Mycophenolic Acid (MPA) Dose Steps Higher and Reducing Tacrolimus Dose at the End of the Study [units: number of participants]		
# of participants with ≥2 MPA dose steps higher	0	0
# of participants with <2 MPA dose steps higher	43	38

No statistical analysis provided for Number of Participants Achieving at Least Two Mycophenolic Acid (MPA) Dose Steps Higher and Reducing Tacrolimus Dose at the End of the Study

2. Primary: Number of Participants That Achieved One Dose Step Higher With Mycophenolic Acid (MPA) or Mycophenolate Mofetil (MMF), According to the Treatment Group Assigned at the End of the Study (Final Visit) Compared to Baseline Dose [Time Frame: at 12 months from baseline]

Measure Type	Primary
Measure Title	Number of Participants That Achieved One Dose Step Higher With Mycophenolic Acid (MPA) or Mycophenolate Mofetil (MMF), According to the Treatment Group Assigned at the End of the Study (Final Visit) Compared to Baseline Dose
Measure Description	No text entered.
Time Frame	at 12 months from baseline
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus).

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**43**	**38**
Number of Participants That Achieved One Dose Step Higher With Mycophenolic Acid (MPA) or Mycophenolate Mofetil (MMF), According to the Treatment Group Assigned at the End of the Study (Final Visit) Compared to Baseline Dose [units: study participants]		
# of participants with ≥ 1 MPA dose steps higher	**37**	**30**
# of participants with < 1 MPA dose steps higher	**6**	**8**

No statistical analysis provided for Number of Participants That Achieved One Dose Step Higher With Mycophenolic Acid (MPA) or Mycophenolate Mofetil (MMF), According to the Treatment Group Assigned at the End of the Study (Final Visit) Compared to Baseline Dose

3. Primary: Participants With Reduction in Tacrolimus or Tacrolimus Extended Release Levels at the End of the Study (Final Visit) Compared to Baseline Dose. [Time Frame: at 12 months from baseline]

Measure Type	Primary
Measure Title	Participants With Reduction in Tacrolimus or Tacrolimus Extended Release Levels at the End of the Study (Final Visit) Compared to Baseline Dose.
Measure Description	No text entered.
Time Frame	at 12 months from baseline
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus).

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**43**	**38**
Participants With Reduction in Tacrolimus or Tacrolimus Extended Release Levels at the End of the Study (Final Visit) Compared to Baseline Dose. [units: Participants]		
Reduction in tacrolimus or tacrolimus ER levels	**27**	**18**
No reduction in tacrolimus or tacrolimus ER levels	**16**	**20**

No statistical analysis provided for Participants With Reduction in Tacrolimus or Tacrolimus Extended Release Levels at the End of the Study (Final Visit) Compared to Baseline Dose.

4. Primary: Mean Mycophenolic Acid (MPA) Doses at the End of the Study (Final Visit) Compared to Baseline Dose. [Time Frame: at 12 months from baseline]

Measure Type	Primary
Measure Title	Mean Mycophenolic Acid (MPA) Doses at the End of the Study (Final Visit) Compared to Baseline Dose.
Measure Description	No text entered.
Time Frame	at 12 months from baseline
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per protocol (PP) population included all subjects from the ITT population who received medication throughout the study and did not have major protocol deviations and who participated in the study for a minimum of 210 days +/- 15 days

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**29**	**25**
Mean Mycophenolic Acid (MPA) Doses at the End of the Study (Final Visit) Compared to Baseline Dose. [units: mg/day] Mean (Standard Deviation)	**1173.10 (278.94)**	**1195.20 (297.95)**

No statistical analysis provided for Mean Mycophenolic Acid (MPA) Doses at the End of the Study (Final Visit) Compared to Baseline Dose.

5. Secondary: Change in Renal Function Measured Using Cockcroft-Gault Creatinine Clearance (CrCl) [Time Frame: Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)]

Measure Type	Secondary
Measure Title	Change in Renal Function Measured Using Cockcroft-Gault Creatinine Clearance (CrCl)
Measure Description	No text entered.
Time Frame	Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)
Safety Issue	No

Population Description

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

Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus).

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	Mycophenolate Mofetil (MMF)
Number of Participants Analyzed [units: participants]	**43**	**38**
Number of participants Analyzed [units: participants]	**43**	**38**
Change in Renal Function Measured Using Cockcroft-Gault Creatinine Clearance (CrCl) [units: ml/min] Mean (Standard Deviation)		
Baseline (n=42,38)	**83.01 (26.51)**	**83.44 (29.10)**
Visit 1 (n=41,37)	**81.55 (26.88)**	**83.04 (27.06)**
Visit 2 (n=41,34)	**81.59 (26.60)**	**82.88 (24.70)**
Visit 3 (n=37,35)	**84.91 (24.20)**	**80.25 (23.25)**
Visit 4 (n=39,33)	**86.58 (26.82)**	**81.83 (24.89)**
Visit 5 (n=36,33)	**88.08 (26.40)**	**88.28 (29.17)**

No statistical analysis provided for Change in Renal Function Measured Using Cockcroft-Gault Creatinine Clearance (CrCl)

6. Secondary: Glomerular Filtration Rate (GFR) Using Abbreviated MDRD [Time Frame: Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)]

Measure Type	Secondary
Measure Title	Glomerular Filtration Rate (GFR) Using Abbreviated MDRD
Measure Description	Calculated GFR (MDRD formula): GFR [mL/min/1.73m2] = 186.3*(C-1.154)*(A-0.203)*G*R where C is the serum concentration of creatinine [mg/dL], A is age [years], G=0.742 when gender is female, otherwise G=1, R=1.21 when race is black, otherwise R=1
Time Frame	Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)
Safety Issue	No

Population Description

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

Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus).

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	Mycophenolate Mofetil (MMF)
Number of Participants Analyzed [units: participants]	**43**	**38**
Glomerular Filtration Rate (GFR) Using Abbreviated MDRD [units: mL/min/1.73m^2] Mean (Standard Deviation)		
Baseline visit (n=43, 38)	**64.83 (17.59)**	**61.08 (13.94)**
Visit 1 (n=42, 38; missings not included)	**62.68 (17.68)**	**59.78 (12.32)**
Visit 2 (n=41, 35; missings not included)	**62.71 (17.02)**	**60.84 (13.35)**
Visit 3 (n=40, 35; missings not included)	**67.74 (18.28)**	**59.32 (13.71)**
Visit 4 (n=42, 36; missings not included)	**67.21 (20.19)**	**61.20 (15.78)**
Visit 5 (n=38, 35; missings not included)	**70.24 (19.23)**	**68.11 (19.84)**

No statistical analysis provided for Glomerular Filtration Rate (GFR) Using Abbreviated MDRD

7. Secondary: Gastrointestinal Symptom Rating Scale (GSRS) Item Score [Time Frame: Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)]

Measure Type	Secondary
Measure Title	Gastrointestinal Symptom Rating Scale (GSRS) Item Score
Measure Description	The GSRS is a 15-item instrument design to assess the symptoms associated to gastrointestinal disorders. It has 5 subscales (reflux, diarrhoea, constipation, abdominal pain and indigestion) with scores rating from 1 to 7 (with a higher score representing more gastrointestinal symptoms)
Time Frame	Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus). Missings not included

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	Mycophenolate Mofetil (MMF)
Number of Participants Analyzed [units: participants]	**43**	**38**
Number of scores on a scale Analyzed [units: scores on a scale]	**43**	**38**
Gastrointestinal Symptom Rating Scale (GSRS) Item Score [units: scores on a scale] Mean (Standard Deviation)		
Baseline Visit, Upper Abdomen Pain(n=42,37)	**1.64 (1.08)**	**1.70 (1.02)**
Baseline Visit, Heartburn (n=42,37)	**1.29 (0.92)**	**1.54 (1.41)**
Baseline visit, Acid reflux (n=42,37)	**1.40 (0.77)**	**1.41 (0.98)**
Baseline visit, Hunger pains (n=43,37)	**2.30 (1.52)**	**1.92 (1.21)**
Baseline visit, Nausea (n=43,37)	**1.30 (0.99)**	**1.35 (0.95)**
Baseline visit, Rumbling in stomach (n=43,37)	**1.93 (1.12)**	**1.92 (1.36)**
Baseline visit, Bloated (n=43,37)	**1.77 (1.27)**	**2.27 (1.71)**
Baseline visit, Burping (n=43,37)	**1.91 (1.21)**	**2.00 (1.39)**
Baseline visit, Passing gas/Flatus (n=43,37)	**2.19 (1.38)**	**2.38 (1.48)**
Baseline visit, Constipation (n=42,37)	**1.71 (1.15)**	**1.62 (1.36)**
Baseline visit, Diorrhoea (n=42,37)	**1.45 (1.09)**	**1.51 (1.17)**
Baseline visit, Loose stool (n=42,37)	**1.69 (1.16)**	**1.84 (1.38)**
Baseline visit, Hard stool (n=42,37)	**1.52 (1.04)**	**1.65 (1.16)**
Baseline visit, Fecal incontinence (n=42,37)	**1.67 (1.18)**	**2.03 (1.69)**
Baseline, Incomplete bowel emptying (n=42,37)	**1.57 (0.99)**	**1.97 (1.36)**
Visit 2, Upper Abdomen Pain (n=40,34)	**1.43 (0.75)**	**1.74 (1.16)**
Visit 2, Heartburn (n=40,35)	**1.43 (1.06)**	**1.37 (0.73)**
Visit 2, Acid reflux (n=40,35)	**1.30 (0.76)**	**1.57 (0.95)**
Visit 2, Hunger pains (n=39,34)	**2.33 (1.77)**	**2.15 (1.33)**
Visit 2, Nausea (n=39,34)	**1.23 (0.67)**	**1.29 (0.76)**
Visit 2, Rumbling in stomach (n=39,34)	**1.85 (1.06)**	**1.85 (1.16)**
Visit 2, Bloated (n=40,35)	**1.73 (1.09)**	**2.09 (1.48)**
Visit 2, Burping (n=40,35)	**1.80 (1.11)**	**2.00 (1.55)**
Visit 2, Passing gas/Flatus (n=40,35)	**2.35 (1.42)**	**2.34 (1.49)**

Visit 2, Constipation (n=40,33)	1.58 (1.13)	1.52 (0.97)
Visit 2, Diorrhoea (n=40,33)	1.38 (0.84)	1.82 (1.42)
Visit 2, Loose stool (n=40,32)	1.73 (1.04)	1.91 (1.20)
Visit 2, Hard stool (n=39,35)	1.51 (1.12)	1.46 (0.82)
Visit 2, Fecal incontinence (n=39,34)	1.69 (1.30)	2.12 (1.51)
Visit 2, Incomplete bowel emptying (n=39,35)	1.67 (0.96)	1.69 (1.13)
Visit 4, Upper Abdomen Pain (n=41,34)	1.66 (1.26)	2.00 (1.30)
Visit 4, Heartburn (n=41,34)	1.59 (1.24)	1.74 (1.19)
Visit 4, Acid reflux (n=41,34)	1.46 (1.12)	1.56 (0.99)
Visit 4, Hunger pains (n=41,34)	2.00 (1.60)	2.26 (1.29)
Visit 4, Nausea (n=41,34)	1.37 (0.80)	1.59 (1.18)
Visit 4, Rumbling in stomach (n=41,34)	2.02 (1.09)	1.91 (1.22)
Visit 4, Bloated (n=41,34)	1.68 (1.04)	2.15 (1.58)
Visit 4, Burping (n=41,34)	2.02 (1.41)	2.21 (1.47)
Visit 4, Passing gas/Flatus (n=41,34)	2.46 (1.21)	2.44 (1.48)
Visit 4, Constipation (n=41,34)	1.41 (0.74)	1.85 (1.42)
Visit 4, Diorrhoea ((n=41,34)	1.59 (1.26)	1.88 (1.09)
Visit 4, Loose stool (n=41,34)	2.00 (1.50)	1.94 (1.13)
Visit 4, Hard stool (n=40,34)	1.53 (0.88)	1.85 (1.26)
Visit 4, Fecal incontinence (n=40,34)	1.68 (1.29)	2.12 (1.43)
Visit 4, Incomplete bowel emptying(n=40,34)	1.68 (0.92)	1.88 (1.25)
Visit 5, Upper Abdomen Pain (n=36,34)	1.72 (1.19)	1.85 (1.28)
Visit 5, Heartburn (n=36,34)	1.47 (0.94)	1.56 (1.08)
Visit 5, Acid reflux (n=36,34)	1.25 (0.60)	1.71 (1.14)
Visit 5, Hunger pains (n=36,34)	1.94 (1.49)	2.12 (2.03)
Visit 5, Nausea (n=36,34)	1.28 (0.70)	1.38 (0.92)
Visit 5, Rumbling in stomach (n=36,34)	2.03 (1.13)	2.00 (1.41)
Visit 5, Bloated (n=36,34)	1.69 (1.12)	2.12 (1.53)
Visit 5, Burping (n=36,34)	1.75 (1.18)	2.00 (1.50)
Visit 5, Passing gas/Flatus (n=36,34)	2.33 (1.31)	2.41 (1.60)
Visit 5, Constipation (n=36,34)	1.47 (0.91)	1.68 (1.01)
Visit 5, Diorrhoea (n=36,34)	1.42 (1.02)	1.71 (0.91)
Visit 5, Loose stool (n=36,34)	1.83 (1.23)	1.74 (0.96)
Visit 5, Hard stool (n=36,34)	1.36 (0.72)	1.79 (1.12)
Visit 5, Fecal incontinence (n=36,34)	1.86 (1.33)	2.32 (1.70)
Visit 5, Incomplete bowel emptying (n=36,34)	1.69 (1.04)	1.85 (1.18)

No statistical analysis provided for Gastrointestinal Symptom Rating Scale (GSRS) Item Score

8. Secondary: Gastrointestinal Symptom Rating Scale (GSRS) Subscale Score [Time Frame: Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)]

Measure Type	Secondary
Measure Title	Gastrointestinal Symptom Rating Scale (GSRS) Subscale Score
Measure Description	The GSRS is a 15-item instrument design to assess the symptoms associated to gastrointestinal disorders. It has 5 subscales (reflux, diarrhoea, constipation, abdominal pain and indigestion) with scores rating from 1 to 7 (with a higher score representing more gastrointestinal symptoms)
Time Frame	Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus). Missings not included

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**43**	**38**
Number of scores on a scale Analyzed [units: scores on a scale]	**43**	**38**
Gastrointestinal Symptom Rating Scale (GSRS) Subscale Score [units: scores on a scale] Mean (Standard Deviation)		
Baseline visit, Indigestion (n=43,37)	**1.95 (0.89)**	**2.14 (1.29)**
Baseline visit, Diorrhoea (n=41,37)	**1.58 (0.93)**	**1.79 (1.26)**
Baseline visit, Constipation (n=41,37)	**1.59 (0.91)**	**1.75 (1.12)**
Visit 2, Reflux (n=40,35)	**1.36 (0.81)**	**1.47 (0.74)**
Visit 2, Abdominal pain (n=39,33)	**1.67 (0.71)**	**1.71 (0.88)**
Visit 2, Indigestion (n=39,34)	**1.92 (0.87)**	**1.96 (1.08)**
Visit 2, Diorrhoea (n=39,32)	**1.59 (0.94)**	**1.94 (1.19)**
Visit 2, Constpation (n=39,33)	**1.59 (0.88)**	**1.56 (0.86)**
Visit 4, Reflux (n=41,34)	**1.52 (1.15)**	**1.65 (1.04)**
Visit 4, Abdominal pain (n=41,34)	**1.67 (0.83)**	**1.95 (1.12)**
Visit 4, Indigestion (n=41,34)	**2.05 (0.97)**	**2.18 (1.27)**
Visit 4, Diorrhoea (n=40,34)	**1.72 (1.23)**	**1.98 (1.08)**
Visit 4, Constipation(n=40,34)	**1.54 (0.68)**	**1.86 (1.12)**

Visit 5, Reflux (n=36,34)	**1.36 (0.69)**	**1.63 (1.06)**
Visit 5, Abdominal pain (n=36,34)	**1.65 (0.66)**	**1.78 (1.03)**
Visit 5, Indigestion (n=36,34)	**1.95 (0.95)**	**2.13 (1.28)**
Visit 5, Diorrhoea (n=36,34)	**1.70 (1.02)**	**1.92 (1.04)**
Visit 5, Constipation (n=36,34)	**1.51 (0.65)**	**1.77 (0.89)**

No statistical analysis provided for Gastrointestinal Symptom Rating Scale (GSRS) Subscale Score

9. Secondary: Health-related Quality of Life (HRQoL): Impact of Gastrointestinal Symptoms on Quality Of Life (SIGIT)-QoL Questionnaire. Total Score. [Time Frame: Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)]

Measure Type	Secondary
Measure Title	Health-related Quality of Life (HRQoL): Impact of Gastrointestinal Symptoms on Quality Of Life (SIGIT)-QoL Questionnaire. Total Score.
Measure Description	The SIGIT-QoL scale is a 17 items instrument, the score of each item ranges from 0 (always) to 4 (never). The scale score is obtained by adding the scores of the 17 items. Therefore, the total score ranges from 0 to 68 points. Higher score means, less impairment of Health Related QoL of the patient and vice versa, the lower the score, the greater severity of symptoms and worse perceived by the patient
Time Frame	Visit 1 (30 days +/-4), visit 2 (90 days +/- 15), visit 3 (150 days +/- 15), visit 4 (210 days +/- 15), visit 5 (365 days +/- 15)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus). Missings not included

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**43**	**38**
Number of scores on a scale Analyzed [units: scores on a scale]	**43**	**38**
Health-related Quality of Life (HRQoL): Impact of Gastrointestinal Symptoms on Quality Of Life (SIGIT)-QoL Questionnaire. Total Score.		

[units: scores on a scale] Mean (Standard Deviation)		
Baseline visit (n=41,37)	79.20 (6.86)	76.00 (9.55)
Visit 2 (n=38,32)	78.79 (6.20)	76.34 (10.12)
Visit 4 (n=40,34)	77.88 (6.64)	74.53 (10.24)
Visit 5, Diorrhoea (n=36,34)	78.53 (5.06)	76.41 (8.36)

No statistical analysis provided for Health-related Quality of Life (HRQoL): Impact of Gastrointestinal Symptoms on Quality Of Life (SIGIT)-QoL Questionnaire. Total Score.

10. Secondary: Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The GSRS is a 15-item instrument design to assess the symptoms associated to gastrointestinal disorders. It has 5 subscales (reflux, diarrhoea, constipation, abdominal pain and indigestion) with scores rating from 1 to 7 (with a higher score representing more gastrointestinal symptoms)
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms		

(SNPs) in the UGT1A9 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the UGT1A9 gene (n=3, 3)	1.67 (10.50)	0.00 (1.73)
No SNP present in the UGT1A9 gene (n=18, 25)	-0.72 (6.52)	1.52 (5.86)

No statistical analysis provided for Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population

11. Secondary: Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The GSRS is a 15-item instrument design to assess the symptoms associated to gastrointestinal disorders. It has 5 subscales (reflux, diarrhoea, constipation, abdominal pain and indigestion) with scores rating from 1 to 7 (with a higher score representing more gastrointestinal symptoms)
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population		

[units: scores on a scale] Mean (Standard Deviation)		
SNP present in the UGT1A9 gene (n=4, 3)	6.25 (12.39)	0.67 (2.31)
No SNP present in the UGT1A9 gene (n=19, 25)	1.42 (9.06)	2.96 (10.33)

No statistical analysis provided for Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population

12. Secondary: Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The GSRS is a 15-item instrument design to assess the symptoms associated to gastrointestinal disorders. It has 5 subscales (reflux, diarrhoea, constipation, abdominal pain and indigestion) with scores rating from 1 to 7 (with a higher score representing more gastrointestinal symptoms)
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus). Missing not included

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed **[units: participants]**	**24**	**31**
Number of scores on a scale Analyzed **[units: scores on a scale]**	**24**	**31**
Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population **[units: scores on a scale]** **Mean (Standard Deviation)**		

SNP present in the UGT1A9 gene (n=3,3)	**8.00 (13.86)**	**4.00 (4.00)**
No SNP present in the UGT1A9 gene (n=20, 23)	**1.10 (9.26)**	**-0.48 (9.55)**

No statistical analysis provided for Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the UGT1A9 Gene for the ITT Population

13. Secondary: Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The GSRS is a 15-item instrument design to assess the symptoms associated to gastrointestinal disorders. It has 5 subscales (reflux, diarrhoea, constipation, abdominal pain and indigestion) with scores rating from 1 to 7 (with a higher score representing more gastrointestinal symptoms)
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the MRP2 gene (n=9, 14)	**1.78 (6.65)**	**0.79 (5.91)**
No SNP present in the MRP2 gene (n=12, 14)	**-2.00 (6.94)**	**1.93 (5.36)**

No statistical analysis provided for Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population

14. Secondary: Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The GSRS is a 15-item instrument design to assess the symptoms associated to gastrointestinal disorders. It has 5 subscales (reflux, diarrhoea, constipation, abdominal pain and indigestion) with scores rating from 1 to 7 (with a higher score representing more gastrointestinal symptoms)
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the MRP2 gene (n=9, 14)	**5.67 (11.48)**	**3.71 (6.23)**
No SNP present in the MRP2 gene (n=14, 14)	**0.07 (7.79)**	**1.71 (12.57)**

No statistical analysis provided for Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 4 Stratified on the

Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population

15. Secondary: Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The GSRS is a 15-item instrument design to assess the symptoms associated to gastrointestinal disorders. It has 5 subscales (reflux, diarrhoea, constipation, abdominal pain and indigestion) with scores rating from 1 to 7 (with a higher score representing more gastrointestinal symptoms)
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the MRP2 gene (n=9, 14)	**3.67 (10.17)**	**1.92 (9.40)**
No SNP present in the MRP2 gene (n=14, 14)	**0.93 (9.88)**	**-1.57 (8.94)**

No statistical analysis provided for Change in Gastrointestinal Symptom Rating Scale (GSRS) Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of Single-nucleotide Polymorphisms (SNPs) in the MRP2 Gene for the ITT Population

16. Secondary: Change in SIGIT-QoL Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in SIGIT-QoL Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The SIGIT-QoL scale is a 17 items instrument, the score of each item ranges from 0 (always) to 4 (never). The scale score is obtained by adding the scores of the 17 items. Therefore, the total score ranges from 0 to 68 points. Higher score means, less impairment of Health Related QoL of the patient and vice versa, the lower the score, the greater severity of symptoms and worse perceived by the patient
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in SIGIT-QoL Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the UGT1A9 gene (n=4, 3)	**-5.50 (6.45)**	**0.33 (0.58)**
No SNP present in the MRP2 gene (n=18, 28)	**-0.44 (2.81)**	**-0.46 (5.35)**

No statistical analysis provided for Change in SIGIT-QoL Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population

17. Secondary: Change in SIGIT-QoL Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in SIGIT-QoL Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The SIGIT-QoL scale is a 17 items instrument, the score of each item ranges from 0 (always) to 4 (never). The scale score is obtained by adding the scores of the 17 items. Therefore, the total score ranges from 0 to 68 points. Higher score means, less impairment of Health Related QoL of the patient and vice versa, the lower the score, the greater severity of symptoms and worse perceived by the patient
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in SIGIT-QoL Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the UGT1A9 gene (n=4, 3)	**-5.75 (7.41)**	**-1.67 (2.52)**
No SNP present in the UGT1A9 gene (n=19, 27)	**-2.00 (7.14)**	**-2.63 (8.54)**

No statistical analysis provided for Change in SIGIT-QoL Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population

18. Secondary: Change in SIGIT-QoL Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in SIGIT-QoL Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The SIGIT-QoL scale is a 17 items instrument, the score of each item ranges from 0 (always) to 4 (never). The scale score is obtained by adding the scores of the 17 items. Therefore, the total score ranges from 0 to 68 points. Higher score means, less impairment of Health Related QoL of the patient and vice versa, the lower the score, the greater severity of symptoms and worse perceived by the patient
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in SIGIT-QoL Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the UGT1A9 gene (n=3, 3)	**-1.33 (8.39)**	**-3.67 (6.35)**
No SNP present in the UGT1A9 gene (n=20, 26)	**-0.55 (5.45)**	**-0.65 (7.03)**

No statistical analysis provided for Change in SIGIT-QoL Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of SNP in the UGT1A9 Gene for the ITT Population

19. Secondary: Change in SIGIT-QoL Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in SIGIT-QoL Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population

Measure Description	Sub-study primary endpoint. SIGIT-QoL scale is a 17 items instrument, the score of each item ranges from 0 (always) to 4 (never). The scale score is obtained by adding the scores of the 17 items. Therefore, the total score ranges from 0 to 68 points. Higher score means, less impairment of Health Related QoL of the patient and vice versa, the lower the score, the greater severity of symptoms and worse perceived by the patient
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus)

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in SIGIT-QoL Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the MRP2 gene (n=9,16)	**-0.89 (3.79)**	**0.56 (4.65)**
No SNP present in the MRP2 gene (n=13, 15)	**-1.69 (4.33)**	**-1.40 (5.49)**

No statistical analysis provided for Change in SIGIT-QoL Score From Baseline to Visit 2 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population

20. Secondary: Change in SIGIT-QoL Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in SIGIT-QoL Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The SIGIT-QoL scale is a 17 items instrument, the score of each item ranges from 0 (always) to 4 (never). The scale score is obtained by adding the scores of the 17 items. Therefore, the total score

	ranges from 0 to 68 points. Higher score means, less impairment of Health Related QoL of the patient and vice versa, the lower the score, the greater severity of symptoms and worse perceived by the patient
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus). Missings not included

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in SIGIT-QoL Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the MRP2 gene (n=9,15)	**-2.67 (7.78)**	**-1.73 (5.40)**
No SNP present in the MRP2 gene (n=14, 15)	**-2.64 (7.04)**	**-3.33 (10.29)**

No statistical analysis provided for Change in SIGIT-QoL Score From Baseline to Visit 4 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population

21. Secondary: Change in SIGIT-QoL Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Change in SIGIT-QoL Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population
Measure Description	Sub-study primary endpoint. The SIGIT-QoL scale is a 17 items instrument, the score of each item ranges from 0 (always) to 4 (never). The scale score is obtained by adding the scores of the 17 items. Therefore, the total score ranges from 0 to 68 points. Higher score means, less impairment of Health Related QoL of the patient and vice versa, the lower the score, the greater severity of symptoms and worse perceived by the patient
Time Frame	at 12 months from baseline

Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention-to-treat (ITT) population included all randomised patients who gave signed informed consent and received at least one dose of study medicinal product and had at least one baseline visit and one post-baseline visit (containing data to allow primary endpoint to be calculated, i.e. dose of MPA or MMF and Tacrolimus). Missing not included

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Sodium (MPS)	**Mycophenolate Mofetil (MMF)**
Number of Participants Analyzed [units: participants]	**24**	**31**
Number of scores on a scale Analyzed [units: scores on a scale]	**24**	**31**
Change in SIGIT-QoL Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population [units: scores on a scale] Mean (Standard Deviation)		
SNP present in the MRP2 gene (n=9,14)	**-1.11 (6.86)**	**-0.50 (7.85)**
No SNP present in the MRP2 gene (n=14, 15)	**-0.36 (5.02)**	**-1.40 (6.17)**

No statistical analysis provided for Change in SIGIT-QoL Score From Baseline to Visit 5 Stratified on the Basis of the Presence or Absence of SNP in the MRP2 Gene for the ITT Population

22. Secondary: Duration of Exposure to the Study Medicinal Product, Mycophenolate Sodium Descriptive Statistics. Safety Population Per Treatment Group [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Duration of Exposure to the Study Medicinal Product, Mycophenolate Sodium Descriptive Statistics. Safety Population Per Treatment Group
Measure Description	Exposure to study drug (MPS). Data presented only for safety population on the study treatment arm (not applicable for MMF arm)
Time Frame	at 12 months from baseline
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The safety population included all randomised patients who gave signed informed consent and received at least one dose of the study medicinal product.

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).

Measured Values

	Mycophenolate Sodium (MPS)
Number of Participants Analyzed [units: participants]	**46**
Number of participants Analyzed [units: participants]	**46**
Duration of Exposure to the Study Medicinal Product, Mycophenolate Sodium Descriptive Statistics. Safety Population Per Treatment Group [units: days] Mean (Standard Deviation)	**201.91 (49.00)**

No statistical analysis provided for Duration of Exposure to the Study Medicinal Product, Mycophenolate Sodium Descriptive Statistics. Safety Population Per Treatment Group

23. Secondary: Dose of the Study Medicinal Product Mycophenolate Sodium (MPS) [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Dose of the Study Medicinal Product Mycophenolate Sodium (MPS)
Measure Description	Safety population per visit and per treatment group
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The safety population included all randomised patients who gave signed informed consent and received at least one dose of the study medicinal product.

Reporting Groups

	Description
Mycophenolate Sodium (MPS)	Participants continued their treatment with MPS according to normal clinical practice, with the dose of MPS increasing at each visit (visit 1 to visit 3) by 250 mg every 12 h and the dose of tacrolimus or tacrolimus extended release (ER) reducing by 25% (to a minimum level of 4 ng/ml).1 The purpose of dosage adjustments was to establish and maintain the patient on the maximum tolerated dose of MPS (up to a maximum of 1 g every 12 h).

Measured Values

	Mycophenolate Sodium (MPS)

Number of Participants Analyzed [units: participants]	**46**
Number of patient doses Analyzed [units: patient doses]	**46**
Dose of the Study Medicinal Product Mycophenolate Sodium (MPS) [units: mg] Mean (Standard Deviation)	
Baseline visit (n=46)	**579.13 (165.03)**
Visit 1 (n=43)	**856.28 (181.65)**
Visit 2 (n=41)	**1080.00 (238.12)**
Visit 3 (n=40)	**1228.50 (263.81)**

No statistical analysis provided for Dose of the Study Medicinal Product Mycophenolate Sodium (MPS)

24. Secondary: Dose of the Study Medicinal Product Mycophenolate Mofetil (MMF) [Time Frame: at 12 months from baseline]

Measure Type	Secondary
Measure Title	Dose of the Study Medicinal Product Mycophenolate Mofetil (MMF)
Measure Description	Safety population per visit and per treatment group (missings not included)
Time Frame	at 12 months from baseline
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The safety population included all randomised patients who gave signed informed consent and received at least one dose of the study medicinal product.

Reporting Groups

	Description
Mycophenolate Mofetil (MMF)	Participants were converted to an equimolar dose of Mycophenolate mofetil at baseline visit. Dose of Mycophenolate mofetil was increased at each visit (visits 1 to visit 3) by 180 mg every 12 hours and the tacrolimus or tacrolimus extended release 6 dose was reduced by 25% (to a minimum level of 4 ng/ml). 1 Dosage adjustments allowed the patient to be established and maintained on the maximum tolerated dose of Mycophenolate mofetil (up to a maximum of 720 mg every 12 hours).

Measured Values

	Mycophenolate Mofetil (MMF)
Number of Participants Analyzed [units: participants]	**40**
Number of patient doses Analyzed [units: patient doses]	**40**
Dose of the Study Medicinal Product Mycophenolate Mofetil (MMF) [units: mg] Mean (Standard Deviation)	
Baseline visit (n=40)	**806.25 (222.80)**
Visit 1 (n=38)	**1250.00 (278.75)**
Visit 2 (n=35)	**1578.57 (382.39)**
Visit 3 (n=35)	**1757.14 (381.01)**

No statistical analysis provided for Dose of the Study Medicinal Product Mycophenolate Mofetil (MMF)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Micofenolato Sodium	Micofenolato sodium
Micofenolato Mofetilo	Micofenolato mofetilo

Serious Adverse Events

	Micofenolato Sodium	Micofenolato Mofetilo
Total, serious adverse events		
# participants affected / at risk	**2/46 (4.35%)**	**4/40 (10.00%)**
Cardiac disorders		
Acute coronary syndrome † 1		
# participants affected / at risk	**0/46 (0.00%)**	**1/40 (2.50%)**
Gastrointestinal disorders		
Diarrhoea † 1		
# participants affected / at risk	**1/46 (2.17%)**	**0/40 (0.00%)**
Infections and infestations		
Escherichia urinary tract infection † 1		
# participants affected / at risk	**1/46 (2.17%)**	**0/40 (0.00%)**
Graft infection † 1		
# participants affected / at risk	**0/46 (0.00%)**	**1/40 (2.50%)**
Human polyomavirus infection † 1		
# participants affected / at risk	**0/46 (0.00%)**	**1/40 (2.50%)**
Urinary tract infection † 1		
# participants affected / at risk	**0/46 (0.00%)**	**1/40 (2.50%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Renal cell carcinoma † 1		
# participants affected / at risk	**0/46 (0.00%)**	**1/40 (2.50%)**

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

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Micofenolato Sodium	Micofenolato sodium
Micofenolato Mofetilo	Micofenolato mofetilo

Other Adverse Events

	Micofenolato Sodium	Micofenolato Mofetilo
Total, other (not including serious) adverse events		
# participants affected / at risk	**13/46 (28.26%)**	**10/40 (25.00%)**
Gastrointestinal disorders		
Abdominal discomfort †1		
# participants affected / at risk	**1/46 (2.17%)**	**2/40 (5.00%)**
Diarrhoea †1		
# participants affected / at risk	**3/46 (6.52%)**	**3/40 (7.50%)**
Dyspepsia †1		
# participants affected / at risk	**3/46 (6.52%)**	**0/40 (0.00%)**
General disorders		
Fatigue †1		
# participants affected / at risk	**1/46 (2.17%)**	**2/40 (5.00%)**
Infections and infestations		
Urinary tract infection †1		
# participants affected / at risk	**5/46 (10.87%)**	**1/40 (2.50%)**
Investigations		
Blood creatinine increased †1		
# participants affected / at risk	**1/46 (2.17%)**	**2/40 (5.00%)**
Nervous system disorders		
Headache †1		
# participants affected / at risk	**0/46 (0.00%)**	**2/40 (5.00%)**

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

Limitations and Caveats

Hide Limitations and Caveats

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

More Information

Hide More Information

Certain Agreements:

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

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

The agreement is:

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

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

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

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

Results Point of Contact:

Name/Title: Novartis
Organization: Pharmaceuticals
phone: +1 (862) 778-8300

No publications provided

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