Clinical trial results:
An Open Label Comparative Study of De Novo Renal Allograft Recipients Receiving CSA + MMF + Corticosteroids Versus CSA + Rapamune + Corticosteroids With Further CSA Elimination In The Rapamune Arm With The Introduction of MMF

Summary

EudraCT number	2014-004102-15
Trial protocol	Outside EU/EEA
Global end of trial date	26 March 2008

Results information

Result version number	v1 (current)
This version publication date	13 June 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	0468H-102012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01601821
WHO universal trial number (UTN)	-
Other trial identifiers	Alias identifier: B1741220

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer ClinicalTrials.gov Call Center, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer ClinicalTrials.gov Call Center, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 October 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 March 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the safety and efficacy of cyclosporine (CsA) + mycophenolate mofetil (MMF) + corticosteroids (Cs) to CsA + Rapamune + Cs with CsA elimination in the Rapamune arm with the introduction of MMF in de novo renal allograft recipients.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 April 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Iran, Islamic Republic of: 245
Worldwide total number of subjects	245
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	9
Adults (18-64 years)	228

From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 245 subjects were enrolled in the study from Iran and study started on 3- Apr-2006 and completed on 26-Mar-2008.

Period 1

Period 1 title	Overall Study (Overall period) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	CsA+Rapamune+CS

Arm description:

Month 0-3: rapamune 6 milligram (mg) tablet orally once as a loading dose within 48 hours of transplantation, followed by rapamune 2 mg tablet orally once daily as a maintenance dose to achieve a target trough level of 8-15 nanogram per milliliter (ng/mL) in combination with CsA tablets orally to achieve a trough level of 150-250 ng/mL. Month 4-6: CsA was withdrawn abruptly, MMF tablet orally at a dose of 1-1.5 grams per day (g/day) and rapamune dose adjusted to achieve a target trough level of 10-15 ng/mL. Month 7-12: rapamune dose adjusted to achieve a target trough level of 8-12 ng/mL, MMF tablet orally at a dose of 1-1.5 g/day. Subjects also received CS tablets orally as per local practice with a minimum daily dose of 5 mg over 12 months.

Arm type	Active comparator
Investigational medicinal product name	CsA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CsA tablets were administered orally to achieve a trough level of 150-250 ng/mL. In month 4-6 CsA was withdrawn abruptly.

Investigational medicinal product name	CS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CS tablets were administered orally as per local practice with a minimum daily dose of 5 mg over 12 months.

Investigational medicinal product name	Rapamune
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rapamune 6 mg tablet was administered orally once as a loading dose within 48 hours of transplantation, followed by rapamune 2 mg tablet orally once daily as a maintenance dose.

Arm title	CsA+MMF+CS

Arm description:

Month 0-5: CsA tablets orally to achieve a trough level of 150-300 ng/mL. Month 6-12: CsA tablets orally to achieve a trough level of 100-200 ng/mL. Subjects also received MMF tablet orally at a dose of 2 g/day and CS tablets orally as per local practice with a minimum daily dose of 5 mg over 12 months.

Arm type	Active comparator
Investigational medicinal product name	CsA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CsA tablets were administered orally to achieve a trough level of 150-250 ng/mL. In month 4-6 CsA was withdrawn abruptly.

Investigational medicinal product name	CS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CS tablets were administered orally as per local practice with a minimum daily dose of 5 mg over 12 months.

Investigational medicinal product name	MMF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MMF tablet was administered orally at a dose of 2 g/day.

Number of subjects in period 1	CsA+Rapamune+CS	CsA+MMF+CS
Started	125	120
Completed	96	91
Not completed	29	29
Adverse event, serious fatal	2	5
Consent withdrawn by subject	1	-
Graft Loss	6	6
Unspecified	5	1
Lost to follow-up	6	14
Study Events	7	1
Protocol deviation	2	2

Baseline characteristics

Reporting groups	
Reporting group title	CsA+Rapamune+CS
Reporting group description:	
Month 0-3: rapamune 6 milligram (mg) tablet orally once as a loading dose within 48 hours of transplantation, followed by rapamune 2 mg tablet orally once daily as a maintenance dose to achieve a target trough level of 8-15 nanogram per milliliter (ng/mL) in combination with CsA tablets orally to achieve a trough level of 150-250 ng/mL. Month 4-6: CsA was withdrawn abruptly, MMF tablet orally at a dose of 1-1.5 grams per day (g/day) and rapamune dose adjusted to achieve a target trough level of 10-15 ng/mL. Month 7-12: rapamune dose adjusted to achieve a target trough level of 8-12 ng/mL, MMF tablet orally at a dose of 1-1.5 g/day. Subjects also received CS tablets orally as per local practice with a minimum daily dose of 5 mg over 12 months.	
Reporting group title	CsA+MMF+CS
Reporting group description:	
Month 0-5: CsA tablets orally to achieve a trough level of 150-300 ng/mL. Month 6-12: CsA tablets orally to achieve a trough level of 100-200 ng/mL. Subjects also received MMF tablet orally at a dose of 2 g/day and CS tablets orally as per local practice with a minimum daily dose of 5 mg over 12 months.	

Reporting group values	CsA+Rapamune+CS	CsA+MMF+CS	Total
Number of subjects	125	120	245
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	38.2	41.6	
standard deviation	± 13.4	± 15.1	-
Gender, Male/Female Units: subjects			
Female	47	45	92
Male	78	75	153

End points

End points reporting groups

Reporting group title	CsA+Rapamune+CS

Reporting group description:

Month 0-3: rapamune 6 milligram (mg) tablet orally once as a loading dose within 48 hours of transplantation, followed by rapamune 2 mg tablet orally once daily as a maintenance dose to achieve a target trough level of 8-15 nanogram per milliliter (ng/mL) in combination with CsA tablets orally to achieve a trough level of 150-250 ng/mL. Month 4-6: CsA was withdrawn abruptly, MMF tablet orally at a dose of 1-1.5 grams per day (g/day) and rapamune dose adjusted to achieve a target trough level of 10-15 ng/mL. Month 7-12: rapamune dose adjusted to achieve a target trough level of 8-12 ng/mL, MMF tablet orally at a dose of 1-1.5 g/day. Subjects also received CS tablets orally as per local practice with a minimum daily dose of 5 mg over 12 months.

Reporting group title	CsA+MMF+CS

Reporting group description:

Month 0-5: CsA tablets orally to achieve a trough level of 150-300 ng/mL. Month 6-12: CsA tablets orally to achieve a trough level of 100-200 ng/mL. Subjects also received MMF tablet orally at a dose of 2 g/day and CS tablets orally as per local practice with a minimum daily dose of 5 mg over 12 months.

Primary: Incidence of Efficacy Failure

End point title	Incidence of Efficacy Failure

End point description:

Efficacy failure was defined as first occurrence of either biopsy confirmed acute rejection, graft loss or death within 12 months of post-transplantation. Percentage of subjects with efficacy failure was reported.

End point type	Primary

End point timeframe:

Baseline up to Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105[1]	104[2]		
Units: percentage of subjects				
number (not applicable)	11.4	13.5		

Notes:

[1] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

[2] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Analysis for incidence of efficacy failure

Statistical analysis description:

Chi-square test was used to test superiority of arm CsA+Rapamune+CS versus arm CsA+MMF+CS.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS

Number of subjects included in analysis	209
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.341
Method	Chi-squared
Parameter estimate	Percent Difference
Point estimate	-2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.5
upper limit	1.5

Secondary: Serum Creatinine Level

End point title	Serum Creatinine Level

End point description:

Serum creatinine is an indicator of kidney function. Creatinine is a substance formed from the metabolism of creatine, commonly found in blood, urine and muscle tissue. It is removed from the blood by the kidneys and excreted in urine. An increased level of creatinine in the blood indicates decreased kidney function. Normal adult blood levels of creatinine are 0.5 to 1.1 milligram per deciliter (mg/dL) for females and 0.6 to 1.2 mg/dL for males; however, the normal values are age-dependent as elderly patients typically have smaller muscle mass.

End point type	Secondary

End point timeframe:

Month 3, 6, 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102[3]	94[4]		
Units: mg/dL				
arithmetic mean (standard deviation)				
Month 3 (n=102, 94)	1.4 (± 0.4)	1.4 (± 0.4)		
Month 6 (n=101, 92)	1.2 (± 0.3)	1.3 (± 0.4)		
Month 12 (n=98, 91)	1.2 (± 0.3)	1.3 (± 0.3)		

Notes:

[3] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.
[4] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Serum Creatinine Level Month: 3

Statistical analysis description:

One-way analysis of variance (ANOVA) was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS

Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [5]
Method	ANOVA

Notes:

[5] - Statistical testing was based on 5% significance level.

Statistical analysis title	Serum Creatinine Level Month: 6

Statistical analysis description:

One-way ANOVA was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.381 [6]
Method	ANOVA

Notes:

[6] - Statistical testing was based on 5% significance level.

Statistical analysis title	Serum Creatinine Level Month: 12

Statistical analysis description:

One-way ANOVA was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.096 [7]
Method	ANOVA

Notes:

[7] - Statistical testing was based on 5% significance level.

Secondary: Creatinine Clearance

End point title	Creatinine Clearance

End point description:

Creatinine clearance (CCr) is a measure of kidney function. CCr is the volume of blood plasma that is cleared of creatinine by the kidneys per unit time. Normal values for healthy, young males are in the range of 100-135 millimeters per minute (mL/min) and for females, 90-125 mL/min. Creatinine clearance decreases with age. A low creatinine clearance rate indicates poor kidney function.

End point type	Secondary

End point timeframe:

Month 3, 6, 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102[8]	94[9]		
Units: mL/min				
arithmetic mean (standard deviation)				
Month 3 (n=102, 94)	64 (± 19.9)	63.9 (± 16)		
Month 6 (n=101, 92)	72.8 (± 19.3)	71.6 (± 18.3)		
Month 12 (n=98, 91)	76.4 (± 22.7)	74 (± 28.6)		

Notes:

[8] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.
[9] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Creatinine Clearance Month:3
Statistical analysis description:	
One-way ANOVA was used to test the difference.	
Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.979 [10]
Method	ANOVA

Notes:

[10] - Statistical testing was based on 5% significance level.

Statistical analysis title	Creatinine Clearance Month:12
Statistical analysis description:	
One-way ANOVA was used to test the difference.	
Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.518 [11]
Method	ANOVA

Notes:

[11] - Statistical testing was based on 5% significance level.

Statistical analysis title	Creatinine Clearance Month:6
Statistical analysis description:	
One-way ANOVA was used to test the difference.	
Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.66 [12]
Method	ANOVA

Notes:

[12] - Statistical testing was based on 5% significance level.

Secondary: Glomerular Filtration Rate (GFR) by Nankivell Method

End point title	Glomerular Filtration Rate (GFR) by Nankivell Method

End point description:

GFR is an index of kidney function. GFR describes the flow rate of filtered fluid through the kidney. GFR was calculated using the Nankivell formula. GFR by Nankivell equation= (6.7 per serum creatinine) plus (0.25*body weight) minus (0.5*serum urea) minus (100 per height square) plus (35 for male or 25 for female). A normal GFR is greater than (>)90 mL/min per 1.73 m^2 [mL/min/1.73 m^2], although children and older people usually have a lower GFR. Lower values indicated poor kidney function. A GFR less than (<)15 mL/min/1.73 m^2 indicated kidney failure.

End point type	Secondary

End point timeframe:

Month 3, 6, 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	94		
Units: mL/min/1.73 m^2				
arithmetic mean (standard deviation)				
Month 3 (n=102, 94)	59.5 (± 20.4)	58.8 (± 15.2)		
Month 6 (n=101, 92)	65.2 (± 16)	64.3 (± 19.5)		
Month 12 (n=98, 91)	67.4 (± 17.5)	67.5 (± 46.5)		

Statistical analyses

Statistical analysis title	GFR by Nankivell Method Month:3

Statistical analysis description:

One-way ANOVA was used to test the difference.

Comparison groups	CsA+Rapamune+CS v CsA+MMF+CS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.786 [13]
Method	ANOVA

Notes:

[13] - Statistical testing was based on 5% significance level.

Statistical analysis title	GFR by Nankivell Method Month:6

Statistical analysis description:

One-way ANOVA was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS

Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.738 [14]
Method	ANOVA

Notes:

[14] - Statistical testing was based on 5% significance level.

Statistical analysis title	GFR by Nankivell Method Month:12

Statistical analysis description:

One-way ANOVA was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.977 [15]
Method	ANOVA

Notes:

[15] - Statistical testing was based on 5% significance level.

Secondary: Incidence of Biopsy-Confirmed Acute Rejection

End point title	Incidence of Biopsy-Confirmed Acute Rejection

End point description:

Diagnosis of acute rejection was made via kidney biopsy using Banff criteria. Percentage of subjects with biopsy-confirmed acute rejection was reported.

End point type	Secondary

End point timeframe:

Baseline up to Month 6

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100[16]	95[17]		
Units: percentage of subjects				
number (not applicable)	4	3.2		

Notes:

[16] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

[17] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Incidence of Biopsy-Confirmed Acute Rejection

Statistical analysis description:

Fisher’s exact test was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS

Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.999 [18]
Method	Fisher exact

Notes:

[18] - Statistical testing was based on 5% significance level.

Secondary: Histologic Grade of First Acute Rejection

End point title	Histologic Grade of First Acute Rejection

End point description:

Diagnosis of acute rejection was made via kidney biopsy. Categorization of biopsies with suspected acute rejection was based on histological findings using updated 1997 Banff criteria. Grade 1A: cases with significant interstitial infiltration (>25% of parenchyma affected) and foci of moderate tubulitis (5-10 cells/tubular cross section), Grade 1B: with severe tubulitis (>10 cells/tubular cross section), Grade 2A: mild-moderate intimal arteritis, Grade 2B: severe intimal arteritis and Grade 3: transmural arterits and/or fibrinoid necrosis. Data is reported as percentage of subjects.

End point type	Secondary

End point timeframe:

Baseline up to Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[19]	3[20]		
Units: percentage of subjects				
number (not applicable)				
1A	100	66.7		
1B	0	33.3		

Notes:

[19] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

[20] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Survived

End point title	Percentage of Subjects Who Survived

End point description:

Survival defined as subjects living with or without a functioning graft.

End point type	Secondary

End point timeframe:

Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[21]	96[22]		
Units: percentage of subjects				
number (not applicable)	98	94.8		

Notes:

[21] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.
[22] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Analysis of premature elimination

Statistical analysis description:

Fisher’s exact test was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.276 [23]
Method	Fisher exact

Notes:

[23] - Statistical testing was based on 5% significance level.

Secondary: Percentage of Subjects With Graft Survival

End point title	Percentage of Subjects With Graft Survival

End point description:

Graft survival defined as those subjects who did not experience graft loss. Graft loss defined as physical loss (nephrectomy), functional loss (necessitating maintenance dialysis for >8 weeks), retransplant or death during the first 12 months after randomization.

End point type	Secondary

End point timeframe:

Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102[24]	97[25]		
Units: percentage of subjects				
number (not applicable)	94.1	93.8		

Notes:

[24] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.
[25] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Analysis of Graft Survival

Statistical analysis description:	
Fisher’s exact test was used to test the difference.	
Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.999 [26]
Method	Fisher exact

Notes:

[26] - Statistical testing was based on 5% significance level.

Secondary: Incidence of Presumptive or Documented Infection

End point title	Incidence of Presumptive or Documented Infection

End point description:

Presumptive or documented infection during the 12 months after transplantation; was confirmed by culture, biopsy, or serology and reported. Percentage of subjects with presumptive or documented infection was reported.

End point type	Secondary

End point timeframe:

Baseline up to Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[27]	118[28]		
Units: percentage of subjects				
number (not applicable)	20.3	18.6		

Notes:

[27] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

[28] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Incidence of Presumptive or Documented Infection
Statistical analysis description:	
Chi-square test was used to test the difference.	
Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.868 [29]
Method	Chi-squared

Notes:

[29] - Statistical testing was based on 5% significance level.

Secondary: Incidence of Histologically Confirmed Lymphoproliferative Disease

End point title	Incidence of Histologically Confirmed Lymphoproliferative Disease

End point description:

Lymphoproliferative disorder represents an abnormal proliferation of B cells in response to either primary or reactivated infection with Epstein-Barr virus. Percentage of subjects with histologically confirmed lymphoproliferative disease was reported.

End point type	Secondary

End point timeframe:

Baseline up to Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97[30]	91[31]		
Units: percentage of subjects				
number (not applicable)	1	0		

Notes:

[30] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.
[31] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Analysis of efficacy failure

Statistical analysis description:

Fisher’s exact test was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.999 [32]
Method	Fisher exact

Notes:

[32] - Statistical testing was based on 5% significance level.

Secondary: Percentage of Subjects with Efficacy Failure or Premature Elimination

End point title	Percentage of Subjects with Efficacy Failure or Premature Elimination

End point description:

Efficacy failure was defined as the first occurrence of acute rejection, graft loss, or death. Premature elimination was defined as elimination from the study for any other reason.

End point type	Secondary

End point timeframe:

Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[33]	118[34]		
Units: percentage of subjects				
number (not applicable)	22	22.9		

Notes:

[33] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.
[34] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Analysis of efficacy failure

Statistical analysis description:

Chi-square test was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.985 [35]
Method	Chi-squared

Notes:

[35] - Statistical testing was based on 5% significance level.

Secondary: Incidence of Anemia

End point title	Incidence of Anemia

End point description:

Diagnostic criterion for anemia was based on the laboratory results; in men: hemoglobin (Hb) <14 gram per deciliter (g/dL), hematocrit (Hct) <42%, or red blood cells (RBCs) <4.5 million/liter (million/L); for women: Hb <12 g/dL, Hct <37%, or RBC < 4 million/L. Percentage of subjects with anaemia was reported.

End point type	Secondary

End point timeframe:

Baseline up to Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123[36]	118[37]		
Units: percentage of subjects				
number (not applicable)	94.3	98.3		

Notes:

[36] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.
[37] - N=(number of subjects analyzed)signifies those subjects who were evaluable for this outcome measure.

Statistical analyses

Statistical analysis title	Analysis for Incidence of Anemia

Statistical analysis description:

Fisher’s exact test was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.172 [38]
Method	Fisher exact

Notes:

[38] - Statistical testing was based on 5% significance level.

Secondary: Number of Subjects Who Discontinued

End point title	Number of Subjects Who Discontinued

End point description:

Number of subjects who discontinued the study treatment due to any reason is reported.

End point type	Secondary

End point timeframe:

Month 12

End point values	CsA+Rapamune+CS	CsA+MMF+CS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	120		
Units: subjects				
number (not applicable)	29	29		

Statistical analyses

Statistical analysis title	Analysis of Subjects Who Discontinued

Statistical analysis description:

Chi-square test was used to test the difference.

Comparison groups	CsA+MMF+CS v CsA+Rapamune+CS
Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.978 [39]
Method	Chi-squared

Notes:

[39] - Statistical testing was based on 5% significance level.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events are reported from time of first dose of study treatment up to 9999 days after last dose of study treatment .

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	CsA+RAPAMUNE+CS

Reporting group description:

Enter Description here

Reporting group title	CsA+MMF+CS

Reporting group description:

Enter Description here

Serious adverse events	CsA+RAPAMUNE+CS	CsA+MMF+CS	
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 125 (44.80%)	44 / 120 (36.67%)	
number of deaths (all causes)	2	5	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial thrombosis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			

subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Transplant rejection			
subjects affected / exposed	13 / 125 (10.40%)	10 / 120 (8.33%)	
occurrences causally related to treatment / all	8 / 13	5 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			

subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	17 / 125 (13.60%)	5 / 120 (4.17%)	
occurrences causally related to treatment / all	12 / 17	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood urea increased			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus test positive			
subjects affected / exposed	1 / 125 (0.80%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipids increased			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Postoperative wound complication			
subjects affected / exposed	0 / 125 (0.00%)	2 / 120 (1.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney rupture			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	1 / 125 (0.80%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	8 / 125 (6.40%)	4 / 120 (3.33%)	
occurrences causally related to treatment / all	3 / 8	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myocardial infarction			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Diabetic neuropathy			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorder			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 125 (0.00%)	3 / 120 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Blood and lymphatic system disorders			
Aplasia pure red cell			
subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	4 / 125 (3.20%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic uraemic syndrome			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	4 / 125 (3.20%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute abdomen			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphthous stomatitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth ulceration			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal artery thrombosis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperoxaluria			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ureteral necrosis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	3 / 125 (2.40%)	3 / 120 (2.50%)	
occurrences causally related to treatment / all	2 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric stenosis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	1 / 125 (0.80%)	7 / 120 (5.83%)	
occurrences causally related to treatment / all	0 / 1	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus urinary tract infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diabetic foot infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	4 / 125 (3.20%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 125 (1.60%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 125 (0.80%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	2 / 125 (1.60%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 125 (0.80%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 125 (0.80%)	2 / 120 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	7 / 125 (5.60%)	3 / 120 (2.50%)	
occurrences causally related to treatment / all	1 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	2 / 125 (1.60%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection bacterial			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	1 / 125 (0.80%)	2 / 120 (1.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 125 (0.00%)	2 / 120 (1.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 125 (0.80%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	CsA+RAPAMUNE+CS	CsA+MMF+CS	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 125 (53.60%)	44 / 120 (36.67%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences (all)	0	1	
Lymphocele			
subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Impaired healing			

subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Transplant rejection			
subjects affected / exposed	2 / 125 (1.60%)	1 / 120 (0.83%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Pulmonary oedema			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 125 (5.60%)	4 / 120 (3.33%)	
occurrences (all)	7	4	
Blood cholesterol increased			
subjects affected / exposed	11 / 125 (8.80%)	3 / 120 (2.50%)	
occurrences (all)	11	3	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 125 (0.80%)	1 / 120 (0.83%)	
occurrences (all)	1	1	
Blood glucose increased			
subjects affected / exposed	6 / 125 (4.80%)	5 / 120 (4.17%)	
occurrences (all)	6	5	

Blood creatinine increased			
subjects affected / exposed	4 / 125 (3.20%)	6 / 120 (5.00%)	
occurrences (all)	4	6	
Blood triglycerides increased			
subjects affected / exposed	15 / 125 (12.00%)	5 / 120 (4.17%)	
occurrences (all)	15	5	
Cytomegalovirus test positive			
subjects affected / exposed	2 / 125 (1.60%)	4 / 120 (3.33%)	
occurrences (all)	2	4	
Drug level increased			
subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences (all)	2	0	
Haemoglobin decreased			
subjects affected / exposed	6 / 125 (4.80%)	6 / 120 (5.00%)	
occurrences (all)	6	6	
Immunosuppressant drug level increased			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences (all)	0	1	
Lipids increased			
subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences (all)	2	0	
Liver function test abnormal			
subjects affected / exposed	21 / 125 (16.80%)	8 / 120 (6.67%)	
occurrences (all)	21	8	
Platelet count decreased			
subjects affected / exposed	1 / 125 (0.80%)	1 / 120 (0.83%)	
occurrences (all)	1	1	
White blood cell count decreased			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Postoperative wound complication			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Seroma			

subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences (all)	2	0	
Wrist fracture			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Wound dehiscence			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Toxicity to various agents			
subjects affected / exposed	3 / 125 (2.40%)	1 / 120 (0.83%)	
occurrences (all)	3	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 125 (0.00%)	2 / 120 (1.67%)	
occurrences (all)	0	2	
Leukopenia			
subjects affected / exposed	5 / 125 (4.00%)	3 / 120 (2.50%)	
occurrences (all)	5	3	
Thrombocytopenia			
subjects affected / exposed	7 / 125 (5.60%)	0 / 120 (0.00%)	
occurrences (all)	7	0	
Thrombocytopenic purpura			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Aphthous stomatitis			
subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Oral disorder			

subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences (all)	2	0	
Pancreatitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Renal tubular necrosis			
subjects affected / exposed	3 / 125 (2.40%)	2 / 120 (1.67%)	
occurrences (all)	3	2	
Renal vein thrombosis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	2 / 125 (1.60%)	0 / 120 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Candida infection			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 125 (0.00%)	3 / 120 (2.50%)	
occurrences (all)	0	3	

Fungal infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences (all)	0	1	
Herpes simplex			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 125 (0.80%)	1 / 120 (0.83%)	
occurrences (all)	1	1	
Oral candidiasis			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	
Oral infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 120 (0.83%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	4 / 125 (3.20%)	5 / 120 (4.17%)	
occurrences (all)	4	5	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 125 (0.00%)	3 / 120 (2.50%)	
occurrences (all)	0	3	
Hyperglycaemia			
subjects affected / exposed	0 / 125 (0.00%)	2 / 120 (1.67%)	
occurrences (all)	0	2	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 125 (0.80%)	0 / 120 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported