



Clinical trial results:

Evaluation of Acute Rejection Rates in de novo Renal Transplant Recipients Following Thymoglobulin Induction, CNI-free, Nulojix (belatacept) -based Immunosuppression

Summary

EudraCT number	2013-002090-21
Trial protocol	DE AT
Global end of trial date	05 February 2019

Results information

Result version number	v1 (current)
This version publication date	16 September 2021
First version publication date	16 September 2021

Trial information

Trial identification

Sponsor protocol code	IM103-177
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb International Corporation, Eu Study Start-Up Unit, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the incidence of clinically-suspected and biopsy proven acute rejection (CSBPAP) at 6 months post-transplant in de novo renal allograft recipients treated with thymoglobulin induction, rapid corticosteroid withdrawal, and maintenance belatacept in combination with EVL, or maintenance TAC in combination with MMF.

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 Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 11
Country: Number of subjects enrolled	United States: 56
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	68
EEA total number of subjects	1

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)	0
Adults (18-64 years)	59

From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

58 participants randomized and treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Treatment A
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Arm description:

BELA + EVL

Arm type	Experimental
Investigational medicinal product name	Belatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

250mg IV

Investigational medicinal product name	Everolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable/dispersible tablet
Routes of administration	Buccal use

Dosage and administration details:

0.25mg and 0.75mg

Investigational medicinal product name	Thymoglobulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.5 mg/kg IV

Arm title	Treatment B
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Arm description:

TAC + MMF

Arm type	Experimental
Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable/dispersible tablet
Routes of administration	Buccal use

Dosage and administration details:	
0.5mg and 1.0mg tablet	
Investigational medicinal product name	Thymoglobulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
1.5 mg/kg IV	
Investigational medicinal product name	Mycophenolate Mofetil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Chewable/dispersible tablet
Routes of administration	Buccal use
Dosage and administration details:	
0.5g to 2.0g	

Number of subjects in period 1^[1]	Treatment A	Treatment B
Started	26	32
Completed	23	26
Not completed	3	6
Withdrew Consent	1	1
Adverse event, non-fatal	2	2
Discontinued Study Treatment	-	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Treatment Error resulted in participant flow error

Baseline characteristics

Reporting groups

Reporting group title	Treatment A
Reporting group description: BELA + EVL	
Reporting group title	Treatment B
Reporting group description: TAC + MMF	

Reporting group values	Treatment A	Treatment B	Total
Number of subjects	26	32	58
Age Categorical Units: Participants			
< 65	22	28	50
≥ 65	4	4	8
Age Continuous Units: Years			
arithmetic mean	51.7	50.8	
standard deviation	± 12.8	± 10.9	-
Sex: Female, Male Units: Participants			
Female	5	9	14
Male	21	23	44
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	3	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	6	9
White	23	21	44
More than one race	0	0	0
Unknown or Not Reported	0	2	2

End points

End points reporting groups

Reporting group title	Treatment A
Reporting group description: BELA + EVL	
Reporting group title	Treatment B
Reporting group description: TAC + MMF	
Subject analysis set title	As Treated treatment A
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Due to treatment error, one participant from treatment A was treated in Treatment B	
Subject analysis set title	As Treated Treatment B
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Due to treatment error, one participant from treatment A was treated in Treatment B	

Primary: Percentage of Clinically-suspected biopsy-proven acute rejection (CSBPAP) at 6 Months

End point title	Percentage of Clinically-suspected biopsy-proven acute rejection (CSBPAP) at 6 Months ^[1]
End point description: Number of Participants with Clinically-suspected biopsy-proven acute rejection (CSBPAP) at 6 Months	
End point type	Primary
End point timeframe: 6 Months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This Endpoint does not have a statistical analysis

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: Percentage of participants				
number (confidence interval 95%)	7.7 (0.9 to 25.1)	9.4 (2.0 to 25.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Clinically-suspected biopsy-proven acute rejection (CSBPAP).

End point title	Time to Clinically-suspected biopsy-proven acute rejection (CSBPAP).
End point description: Time to Clinically suspected biopsy proven acute rejection	

Here 9999 means NA

End point type	Secondary
End point timeframe:	
Up to 24 Months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Months				
arithmetic mean (full range (min-max))	9999 (-9999 to 9999)	9999 (-9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment differences in Therapeutic Modalities

End point title	Treatment differences in Therapeutic Modalities
End point description:	
Treatment Received for Biopsy Proven Acute Rejection (Banff Grade IA or Higher), or Humoral (Antibody Mediated) Rejection Treatment regimen: Categorical analysis of CSBPAR episodes by treatment received.	
End point type	Secondary
End point timeframe:	
at 6, 12 and 24 Months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: Percentage of participants with CSBPARs				
number (not applicable)				
Corticosteroids (6 months)	7.7	9.4		
Lymphocyte depleting agent (6 months)	0	6.3		
Plasmapheresis (6 months)	0	0		
IVIg (6 months)	0	3.1		
Rituximab (6 months)	0	0		
Corticosteroids (12 months)	15.4	12.5		
Lymphocyte depleting agent (12 months)	3.8	6.3		
Plasmapheresis (12 months)	0	0		
IVIg (12 months)	0	3.1		
Rituximab (12 months)	0	0		
Corticosteroids (24 months)	19.2	12.5		

Lymphocyte depleting agent (24 months)	3.8	6.3		
Plasmapheresis (24 months)	0	0		
IVIG (24 months)	0	3.1		
Rituximab (24 months)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who survive with a functioning graft

End point title	Number of Participants who survive with a functioning graft
End point description:	
Number of all participants who survive with a functioning graft at 6, 12 and 24 months post transplant	
End point type	Secondary
End point timeframe:	
At 6, 12 and 24 months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: Participants				
At 6 Months	25	31		
At 12 Months	25	31		
At 24 Months	25	31		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants deaths post transplant

End point title	Number of Participants deaths post transplant
End point description:	
Number of participant deaths at 6, 12 and 24 months post transplant	
End point type	Secondary
End point timeframe:	
up to 24 months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: Participants				
At 6 Months	0	0		
At 12 Months	0	0		
At 24 Months	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who experience graft loss post transplant

End point title	Number of Participants who experience graft loss post transplant
End point description:	
Number of all participants who experience graft loss at 6, 12 and 24 months post transplant	
End point type	Secondary
End point timeframe:	
At 6, 12 and 24 months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: Participants				
At 6 Months	1	1		
At 12 Months	1	1		
At 24 Months	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Event: Graft Loss and death

End point title	Time to Event: Graft Loss and death
End point description:	
The Number of days to participant Graft Loss and death for any reason	
End point type	Secondary
End point timeframe:	
Up to 728 Days	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: Days				
Graft Loss	107	2		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute calculated Glomerular Filtration Rate (cGFR): Mean

End point title	Absolute calculated Glomerular Filtration Rate (cGFR): Mean
End point description:	
Absolute (mean and median) cGFR values at 3, 6, 12 and 24 months post-transplant, as determined from the 4-variable Modification of Diet in Renal Disease (MDRD) formula	
End point type	Secondary
End point timeframe:	
Up 24 Months post-transplant	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mL/min/1.73 m ²				
arithmetic mean (confidence interval 95%)				
At 3 Months	69.2 (60.2 to 78.3)	62.2 (55.3 to 69.1)		
At 6 Months	66.0 (55.8 to 76.2)	63.9 (56.2 to 71.5)		
At 12 Months	66.2 (56.9 to 75.4)	62.0 (53.4 to 70.6)		
At 24 Months	71.8 (62.5 to 81.0)	68.7 (59.2 to 78.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median calculated Glomerular Filtration Rate (cGFR)

End point title	Median calculated Glomerular Filtration Rate (cGFR)
End point description:	
Median cGFR values at 3, 6, 12 and 24 months post-transplant, as determined from the 4-variable Modification of Diet in Renal Disease (MDRD) formula	
End point type	Secondary

End point timeframe:

Up 24 Months post-transplant

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mL/min/1.73 m ²				
median (full range (min-max))				
At 3 Months	64.0 (52.0 to 80.0)	62.0 (55.0 to 79.0)		
At 6 Months	64.0 (56.0 to 79.0)	67.0 (55.0 to 75.0)		
At 12 Months	66.0 (58.0 to 77.0)	62.5 (47.5 to 74.0)		
At 24 Months	73.5 (59.5 to 84.5)	68.0 (56.0 to 82.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Month 3 in cGFR

End point title	Mean Change from Month 3 in cGFR
End point description:	The mean change from Month 3 cGFR at 3, 6, 12 and 24 months post-transplant
End point type	Secondary
End point timeframe:	Up 24 Months post-transplant

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mL/min/1.73 m ²				
arithmetic mean (confidence interval 95%)				
At 3 Months	0 (0 to 0)	0 (0 to 0)		
At 6 Months	-3.2 (-10.9 to 4.5)	2.8 (-0.2 to 5.8)		
At 12 Months	-3.1 (-12.6 to 6.5)	1.4 (-3.3 to 6.0)		
At 24 Months	1.8 (-8.6 to 12.3)	6.7 (1.6 to 11.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Urine Protein Creatinine Ratio (UPr/Cr)

End point title	Urine Protein Creatinine Ratio (UPr/Cr)
End point description: Urine protein to creatinine ratio (UPr/Cr) at 3, 6, 12 and 24 months post-transplant.	
End point type	Secondary
End point timeframe: Up 24 Months post-transplant	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mg Protein/mg Creatinine				
arithmetic mean (confidence interval 95%)				
At 3 Months	0.3146 (0.1985 to 0.4307)	0.1412 (0.1097 to 0.1726)		
At 6 Months	0.3896 (0.2326 to 0.5466)	0.1461 (0.1203 to 0.1720)		
At 12 Months	0.2835 (0.1648 to 0.4021)	0.1849 (0.1041 to 0.2658)		
At 24 Months	0.3940 (0.2199 to 0.5680)	0.1685 (0.1174 to 0.2195)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Donor Specific Anti-HLA Antibodies (DSA)

End point title	Percentage of Participants with Donor Specific Anti-HLA Antibodies (DSA)
End point description: Percentage of participants with, and titers of pre-existing (pre-transplant) DSA on Day 1 (pre-transplant, pre-dose), and at Months 12 and 24 posttransplant	
End point type	Secondary
End point timeframe: Up to 24 Months	

End point values	Treatment A	Treatment B	As Treated treatment A	As Treated Treatment B
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0 ^[2]	0 ^[3]	25	33
Units: Percentage of Participants				
number (not applicable)				
Baseline Class 1 DSA			10	0
Baseline Class 2 DSA			0	0
Baseline Both Class 1 and 2 DSA			0	0
12 Month Class 1 DSA			8	0
12 Month Class 2 DSA			0	3.03
12 Month Both Class 1 and 2 DSA			0	0
24 Month Class 1 DSA			8	3.03
24 Month Class 2 DSA			0	3.03
24 Month Both Class 1 and 2 DSA			0	0

Notes:

[2] - This is for the ITT population

[3] - This is for the ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with De Novo Donor Specific Anti-HLA Antibodies (DSA)

End point title	Percentage of Participants with De Novo Donor Specific Anti-HLA Antibodies (DSA)
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End point description:

Characterization of any de novo DSA detected by IgM and IgG subclasses, and by the presence or absence of complement fixing properties.

End point type	Secondary
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End point timeframe:

Up to 24 Months

End point values	Treatment A	Treatment B	As Treated treatment A	As Treated Treatment B
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0 ^[4]	0 ^[5]	25	33
Units: Percentage				
number (not applicable)				
Baseline Class 1 DSA			10	0
Baseline Class 2 DSA			0	0
Baseline Both Class 1 and 2 DSA			0	0
De Novo 12 Month Class 1 DSA			0	0
De Novo 12 Month Class 2 DSA			0	0
De Novo 12 Month Both Class 1 and 2 DSA			0	0
De Novo 24 Month Class 1 DSA			0	3.03
De Novo 24 Month Class 2 DSA			0	0
De Novo 24 Month Both Class 1 and 2 DSA			0	0

Notes:

[4] - This is for the ITT population

[5] - This is for the ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Adverse Events (AEs)

End point title	Percentage of participants with Adverse Events (AEs)
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End point description:

Percentage of participants with AEs up to 24 months post-transplant

End point type	Secondary
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End point timeframe:

Up to 24 months Post-Transplant

End point values	Treatment A	Treatment B	As Treated treatment A	As Treated Treatment B
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0 ^[6]	0 ^[7]	25	33
Units: Percentage of participants with AEs				
number (not applicable)			100.0	97.0

Notes:

[6] - This is for the As treated population

[7] - This is for the As treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Serious Adverse Events (SAEs)

End point title	Percentage of participants with Serious Adverse Events (SAEs)
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End point description:

Percentage of participants with SAEs up to 24 months post-transplant

End point type	Secondary
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End point timeframe:

Up to 24 months Post-Transplant

End point values	Treatment A	Treatment B	As Treated treatment A	As Treated Treatment B
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0 ^[8]	0 ^[9]	25	33
Units: Percentage of participants with SAEs				
number (not applicable)			52.0	60.6

Notes:

[8] - This is for the As treated population

[9] - This is for the As treated population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Events of Special Interest (ESIs)

End point title	Percentage of Participants with Events of Special Interest (ESIs)
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End point description:

Percentage of participants which have one of the following events of special interest: Serious Infections Post-Transplant Lymphoproliferative Disorder (PTLD) Progressive multifocal leukoencephalopathy (PML) Malignancies (Other than PTLD) including non-melanoma skin carcinomas (Malignancies) Tuberculosis Infections Central Nervous System (CNS) Infections Viral Infections Infusion Related reactions within 24 hours since belatacept infusion

End point type	Secondary
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End point timeframe:

Up to 24 Months

End point values	Treatment A	Treatment B	As Treated treatment A	As Treated Treatment B
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0 ^[10]	0 ^[11]	25	33
Units: Percentage of participants with ESIs				
number (not applicable)				
Serious Infections			16.0	15.2
PTLD			4.0	3.0
PML			0	0
Malignancies			4.0	3.0
TB			0	0
CNS Infections			0	0
Viral Infections			0	0
Infusion Related Reactions			1.0	0

Notes:

[10] - This is for the ITT population

[11] - This is for the ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean and Mean change from baseline in blood glucose

End point title	Mean and Mean change from baseline in blood glucose
End point description:	
Mean fasting blood glucose levels, and mean changes from baseline values at Months 6, 12 and 24 months post- transplant	
End point type	Secondary
End point timeframe:	
Up to 24 months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
Mean Value at 6 months	107.2 (86.6 to 127.8)	107.2 (93.8 to 120.7)		
Change from baseline at 6 months	4.9 (-5.8 to 15.7)	4.8 (-17.6 to 27.2)		
Mean Value at 12 months	101.1 (85.3 to 117.0)	127.5 (99.2 to 155.8)		
Change from baseline at 12 months	-1.3 (-24.7 to 22.1)	20.6 (0.4 to 40.8)		
Mean Value at 24 months	127.5 (93.7 to 161.4)	111.8 (87.1 to 136.5)		
Change from baseline at 24 months	22.3 (-15.7 to 60.3)	15.0 (-3.2 to 33.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean and Mean change from baseline in whole blood HbA1c

End point title	Mean and Mean change from baseline in whole blood HbA1c
End point description:	
Mean whole blood HbA1C concentrations, and mean changes from baseline values at Months 6, 12 and 24 months post-transplant.	
End point type	Secondary
End point timeframe:	
Up to 24 months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
Mean Value at 6 months	6.11 (5.47 to 6.75)	6.13 (5.44 to 6.82)		
Change from baseline at 6 months	0.34 (0.06 to 0.62)	0.48 (0.04 to 0.91)		
Mean Value at 12 months	6.18 (5.42 to 6.93)	6.21 (5.50 to 6.92)		
Change from baseline at 12 months	0.47 (-0.00 to 0.95)	0.32 (-0.17 to 0.81)		
Mean Value at 24 months	6.24 (5.27 to 7.20)	6.29 (5.38 to 7.20)		
Change from baseline at 24 months	0.66 (-0.05 to 1.37)	0.41 (-0.13 to 0.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with New onset diabetes after transplant

End point title	Percentage of participants with New onset diabetes after transplant
End point description:	
Percentage of participants with New Onset Diabetes After Transplantation (NODAT) at 6, 12, and 24 months post-transplant.	
End point type	Secondary
End point timeframe:	
up to 24 months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: Percentage of participants				
number (confidence interval 95%)				
Up to 6 Months	11.5 (2.4 to 30.2)	6.3 (0.8 to 20.8)		
Up to 12 Months	11.5 (2.4 to 30.2)	6.3 (0.8 to 20.8)		
Up to 24 Months	15.4 (4.4 to 34.9)	12.5 (3.5 to 29.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values of Blood Pressure: Mean

End point title	Absolute Values of Blood Pressure: Mean
End point description: Absolute (mean and median) values for SBP and DBP at 3, 6, 12 and 24 months posttransplant;	
End point type	Secondary
End point timeframe: Up to 24 Months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mmHg				
arithmetic mean (confidence interval 95%)				
Diastolic Month 3	78.7 (74.2 to 83.2)	77.7 (74.0 to 81.3)		
Systolic Month 3	134.2 (126.9 to 141.6)	131.0 (124.9 to 137.0)		
Diastolic Month 6	77.4 (73.6 to 81.3)	79.4 (76.0 to 82.9)		
Systolic Month 6	128.1 (121.8 to 134.5)	133.0 (127.2 to 138.8)		
Diastolic Month 12	78.7 (74.6 to 82.9)	80.1 (76.4 to 83.8)		
Systolic Month 12	131.0 (125.6 to 136.4)	131.0 (123.4 to 138.7)		
Diastolic Month 24	78.1 (74.2 to 81.9)	78.5 (74.3 to 82.8)		
Systolic Month 24	130.9 (125.2 to 136.5)	131.7 (125.2 to 138.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values of Blood Pressure: Median

End point title	Absolute Values of Blood Pressure: Median
End point description: Absolute (mean and median) values for SBP and DBP at 3, 6, 12 and 24 months posttransplant;	
End point type	Secondary
End point timeframe: Up to 24 Months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mmHg				
median (full range (min-max))				
Diastolic Month 3	78.5 (70.0 to 88.0)	80.0 (70.0 to 84.0)		
Systolic Month 3	135.5 (127.0 to 144.0)	131.0 (122.0 to 138.0)		
Diastolic Month 6	75.5 (70.5 to 83.0)	80.0 (71.0 to 85.5)		
Systolic Month 6	127.0 (114.5 to 136.5)	131.0 (124.0 to 142.5)		
Diastolic Month 12	77.0 (71.5 to 86.0)	81.0 (72.0 to 88.0)		
Systolic Month 12	130.0 (119.0 to 142.0)	126.0 (115.0 to 146.0)		
Diastolic Month 24	78.0 (71.0 to 86.0)	79.0 (69.5 to 85.0)		
Systolic Month 24	130.0 (122.0 to 142.0)	130.0 (121.5 to 139.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean changes from baseline values for Blood Pressure

End point title	Mean changes from baseline values for Blood Pressure
End point description:	Mean changes from baseline values for SBP and DBP at 6, 12 and 24 months post-transplant
End point type	Secondary
End point timeframe:	Up to 24 Months

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mmHg				
arithmetic mean (confidence interval 95%)				
Diastolic Month 6	1.0 (-4.7 to 6.7)	4.8 (-1.2 to 10.8)		
Systolic Month 6	-4.0 (-13.9 to 5.9)	-0.7 (-10.0 to 8.7)		
Diastolic Month 12	2.3 (-4.0 to 8.6)	5.4 (-1.0 to 11.7)		
Systolic Month 12	-1.1 (-9.6 to 7.4)	-3.2 (-14.7 to 8.3)		
Diastolic Month 24	0.9 (-5.5 to 7.3)	2.1 (-3.9 to 8.1)		

Systolic Month 24	-2.3 (-12.2 to 7.6)	-4.2 (-14.4 to 6.0)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values of Fasting Lipid Values: Mean

End point title	Absolute Values of Fasting Lipid Values: Mean
End point description: Absolute (mean and median) values at 3, 6, 12 and 24 months post-transplant for the following: Serum total cholesterol (TC) Serum high density lipoprotein (HDL) cholesterol Serum low density lipoprotein (LDL) cholesterol Serum triglycerides (TG)	
End point type	Secondary
End point timeframe: Up to 24 Months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
TC Month 3	181.2 (157.8 to 204.7)	174.4 (154.8 to 194.1)		
TC Month 6	197.7 (177.9 to 217.4)	175 (158.8 to 191.6)		
TC Month 12	189.0 (171.7 to 206.3)	169.9 (153.8 to 186.0)		
TC Month 24	193.2 (172.1 to 214.2)	168.2 (152.9 to 183.4)		
HDL Month 3	50.6 (43.5 to 57.6)	50.4 (43.9 to 56.9)		
HDL Month 6	46.4 (41.3 to 51.5)	53.9 (45.9 to 61.8)		
HDL Month 12	49.4 (44.0 to 54.8)	49.6 (42.5 to 56.6)		
HDL Month 24	50.1 (44.7 to 55.5)	51.3 (43.0 to 59.6)		
LDL Month 3	96.9 (77.9 to 115.9)	96.5 (80.3 to 112.6)		
LDL Month 6	115.2 (98.1 to 132.3)	93.7 (79.2 to 108.2)		
LDL Month 12	107.5 (92.8 to 122.2)	88.0 (74.3 to 101.8)		
LDL Month 24	97.9 (81.6 to 114.2)	91.5 (75.4 to 107.6)		
TG Month 3	171.6 (118.1 to 225.0)	137.8 (106.6 to 168.9)		

TG Month 6	180.0 (140.2 to 219.7)	138.3 (108.0 to 168.5)		
TG Month 12	162.4 (132.2 to 192.6)	161.3 (126.4 to 196.1)		
TG Month 24	263.4 (131.2 to 395.5)	145.0 (99.8 to 190.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values of Fasting Lipid Values: Median

End point title	Absolute Values of Fasting Lipid Values: Median
End point description:	
Absolute (mean and median) values at 3, 6, 12 and 24 months post-transplant for the following: Serum total cholesterol (TC) Serum high density lipoprotein (HDL) cholesterol Serum low density lipoprotein (LDL) cholesterol Serum triglycerides (TG)	
End point type	Secondary
End point timeframe:	
Up to 24 Months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mg/dL				
median (full range (min-max))				
TC Month 3	167.0 (160.0 to 213.0)	173.0 (146.0 to 197.0)		
TC Month 6	187.0 (170.5 to 226.5)	178.0 (146.0 to 199.0)		
TC Month 12	184.0 (166.0 to 213.0)	171.5 (146.5 to 193.5)		
TC Month 24	193.0 (166.0 to 206.0)	166.0 (137.0 to 201.0)		
HDL Month 3	45.0 (39.0 to 62.0)	49.0 (38.0 to 63.0)		
HDL Month 6	45.5 (39.0 to 51.0)	49.0 (37.0 to 68.0)		
HDL Month 12	50.0 (40.0 to 58.0)	47.0 (37.0 to 61.0)		
HDL Month 24	49.0 (43.0 to 58.0)	49.0 (35.0 to 71.0)		
LDL Month 3	89.0 (74.0 to 127.0)	95.0 (75.0 to 116.0)		
LDL Month 6	99.5 (85.5 to 143.0)	100.0 (66.0 to 115.0)		
LDL Month 12	104.0 (85.0 to 128.0)	91.5 (65.0 to 109.0)		
LDL Month 24	103.5 (74.0 to 121.0)	86.0 (70.0 to 119.0)		
TG Month 3	147.0 (107.0 to 195.0)	128.0 (81.0 to 174.0)		

TG Month 6	157.5 (113.5 to 245.5)	126.0 (85.0 to 194.0)		
TG Month 12	154.0 (100.0 to 230.0)	130.0 (106.0 to 202.0)		
TG Month 24	159.0 (137.0 to 284.0)	114.0 (80.0 to 174.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean changes from baseline values of Lipid values

End point title	Mean changes from baseline values of Lipid values
End point description:	
Mean changes from baseline values in the following: Serum total cholesterol (TC) Serum high density lipoprotein (HDL) cholesterol Serum low density lipoprotein (LDL) cholesterol Serum triglycerides (TG)	
End point type	Secondary
End point timeframe:	
at months 12 and 24	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
TC Month 12	25.7 (3.5 to 47.9)	-2.8 (-41.5 to 35.8)		
TC Month 24	26.6 (4.0 to 49.1)	10.0 (-9.9 to 29.9)		
HDL Month 12	5.4 (-0.3 to 11.0)	1.9 (-3.7 to 7.5)		
HDL Month 24	6.2 (0.7 to 11.6)	4.8 (-2.2 to 11.9)		
LDL Month 12	25.7 (7.9 to 43.4)	10.8 (-10.8 to 32.4)		
LDL Month 24	17.4 (0.0 to 34.7)	15.7 (-4.4 to 35.7)		
TG Month 12	3.3 (-26.0 to 32.5)	-86.1 (-288.9 to 116.7)		
TG Month 24	106.8 (-32.6 to 246.2)	-13.6 (-73.8 to 46.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically-suspected biopsy-proven acute rejection (CSBPAP) at 6, 12

and 24 Months

End point title	Clinically-suspected biopsy-proven acute rejection (CSBPAP) at 6, 12 and 24 Months
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End point description:

Clinically-suspected biopsy-proven acute rejection (CSBPAP) at 6, 12 and 24 Months Change in the incidence of CSBPAP at 6, 12 and 24 months post transplant, in the belatacept + EVL(Treatment A) as compared to TAC + MMF (Treatment B).

End point type	Secondary
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End point timeframe:

Up to 24 Months

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: Percentage of CSBPAP				
number (confidence interval 95%)				
CSBPAP at 6 Months	7.7 (0.9 to 25.1)	9.4 (2.0 to 25.0)		
CSBPAP at 12 months	11.5 (2.4 to 30.2)	12.5 (3.5 to 29.0)		
CSBPAP at 24 Months	15.4 (4.4 to 34.9)	12.5 (3.5 to 29.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis of CSBAR at 6 months
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Statistical analysis description:

Change in Incidence of Treatment A as compared to Treatment B at 6 Months

Comparison groups	Treatment A v Treatment B
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Number of subjects included in analysis	58
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Analysis specification	Pre-specified
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Analysis type	
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Parameter estimate	Incidence of Change
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Point estimate	-1.7
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-18.9
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upper limit	16.7
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Statistical analysis title	Statistical Analysis of CSBAR at 12 months
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Statistical analysis description:

Change in Incidence of Treatment A as compared to Treatment B at 12 Months

Comparison groups	Treatment A v Treatment B
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Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Incidence of Change
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.2
upper limit	18.9

Statistical analysis title	Statistical Analysis of CSBAR at 24 months
Statistical analysis description:	
Change in Incidence of Treatment A as compared to Treatment B at 24 Months	
Comparison groups	Treatment A v Treatment B
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Incidence of Change
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.1
upper limit	23.9

Secondary: Percentage of participants with BANFF Grade by severity grades. BANFF Type (Grade) for Acute/Active Rejection	
End point title	Percentage of participants with BANFF Grade by severity grades. BANFF Type (Grade) for Acute/Active Rejection
End point description:	
Treatment differences in the severity grades to treat all episodes of CSBPAP at 6, 12, and 24 months post-transplant. Type 1A - Cases with significant interstitial infiltration (>25% of parenchyma affected) and foci of moderate tubulitis (>4 mononuclear cells/Tubular cross section or group of 10 Tubular cell). Type 1B - Cases with significant interstitial infiltration (>25% of parenchyma affected) and foci of moderate tubulitis (>10 mononuclear cells/Tubular cross section or group of 10 Tubular cell).Type 2A - Cases with mild to moderate intimal arteritis.Type 2B - Cases with severe intimal arteritis comprising >25% of the luminal area. Type 3 - Cases with "transmural" arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells (v3 with accompanying lymphocytic inflammation)	
End point type	Secondary
End point timeframe:	
At 6, 12 and 24 Months	

End point values	Treatment A	Treatment B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	32		
Units: Percentage of Participants				
number (not applicable)				
6 Months: Mild Acute (1A)	3.8	0		
6 Months: Mild Acute (1B)	0	3.1		
6 Months: Moderate Acute (2A)	7.7	6.3		
6 Months: Moderate Acute (2B)	0	0		
6 Months: Severe Acute	0	0		
12 Months: Mild Acute (1A)	7.7	3.1		
12 Months: Mild Acute (1B)	0	3.1		
12 Months: Moderate Acute (2A)	7.7	6.3		
12 Months: Moderate Acute (2B)	0	0		
12 Months: Severe Acute	0	0		
24 Months: Mild Acute (1A)	11.5	3.1		
24 Months: Mild Acute (1B)	0	3.1		
24 Months: Moderate Acute (2A)	7.7	6.3		
24 Months: Moderate Acute (2B)	0	0		
24 Months: Severe Acute	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with laboratory test abnormalities (LTAs)

End point title	Percentage of participants with laboratory test abnormalities (LTAs)
End point description:	Percentage of participants with laboratory tests with marked laboratory abnormalities
End point type	Secondary
End point timeframe:	At 24 Months

End point values	Treatment A	Treatment B	As Treated treatment A	As Treated Treatment B
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0 ^[12]	0 ^[13]	25	33
Units: Percentage of participants				
number (not applicable)				
Hemoglobin (Low)			12.0	6.1
Leukocytes (low)			0	3.0
Lymphocyte (Absolute) (low)			84.0	69.7
Neutrophils (Absolute) (low)			0	3.0
Aspartate Aminotransferase (High)			4.0	0
Creatinine (High)			16.0	3.0
Inorganic Phosphorus (low)			24.0	12.1

Potassium (high)			4.0	0
Sodium (low)			4.0	0
Albumin (low)			0	3.0
Glucose (high)			8.0	12.1
Triglycerides (high)			12.0	0
Uric Acid (high)			8.0	0

Notes:

[12] - This is for the As Treated Population

[13] - This is for the As Treated population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs collected were reported between first dose upto 56 days after last dose of study treatment.

Adverse event reporting additional description:

Because 1 participant with BPAR had been randomized to the BELA+EVL group, but had then mistakenly been treated with TAC+MMF beginning on Day 1 and continuing through the entire 2-year study period, analysis was also performed using the modified ITT (as-treated) population, in which the participant was analyzed as having received TAC+MMF.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	Thymoglobulin + Tacrolimus + Mycophenolate Mofetil
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Reporting group description:

Subjects were administered thymoglobulin 1.5 mg/kg intravenously (IV) on day 1 (Day of transplant) and daily thereafter (or less frequently, as tolerated) for a total cumulative dose between 3.0 and 5.5 mg/kg plus Tacrolimus total initial dose of 0.1 mg/kg/day orally in 2 divided doses and adjusted thereafter on the basis of therapeutic drug monitoring, to target pre-dose blood concentrations of 4-11 ng/mL. plus Mycophenolate Mofetil 0.5-2.0 gram (g) per day (0.25 to 1.0 g bid) and up to 3.0 g per day administered orally or IV until the remainder of the study (24 months).

Reporting group title	Thymoglobulin + Belatacept + Everolimus
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Reporting group description:

Subjects were administered thymoglobulin 1.5 milligram (mg)/kg intravenously (IV) on day 1 (Day of transplant) and daily thereafter (or less frequently, as tolerated) for a total cumulative dose between 3.0 and 5.5 mg/kg plus Belatacept 10 mg/kg IV on days (1, 5, 14, 29, 43, 57, 71, 84), 5 mg/kg IV every 4 Weeks plus Everolimus 3.0 mg/day (1.5 mg bid) orally starting on Day 3, Dosing was adjusted to keep pre-dose levels at 6 to 10 nanogram (ng)/mL for the initial 3 months post-transplantation and at 4 to 8 ng/mL after 3 months until the remainder of the study (24 months).

Serious adverse events	Thymoglobulin + Tacrolimus + Mycophenolate Mofetil	Thymoglobulin + Belatacept + Everolimus	
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 33 (60.61%)	13 / 25 (52.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post transplant lymphoproliferative disorder			

subjects affected / exposed	1 / 33 (3.03%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Dry gangrene			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Renal transplant failure			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	3 / 33 (9.09%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			

subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arteriospasm coronary			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 33 (3.03%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Central nervous system vasculitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar ataxia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 33 (3.03%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutropenia			
subjects affected / exposed	4 / 33 (12.12%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal fluid collection			

subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haematoma			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bladder stenosis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perinephric collection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (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	1 / 33 (3.03%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral necrosis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis acute			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal graft infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 33 (0.00%)	3 / 25 (12.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Thymoglobulin + Tacrolimus + Mycophenolate Mofetil	Thymoglobulin + Belatacept + Everolimus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 33 (90.91%)	25 / 25 (100.00%)	
Vascular disorders			
Hypotension			

subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Hypertension			
subjects affected / exposed	8 / 33 (24.24%)	6 / 25 (24.00%)	
occurrences (all)	8	6	
Orthostatic hypotension			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	3	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	3 / 33 (9.09%)	4 / 25 (16.00%)	
occurrences (all)	3	7	
Oedema peripheral			
subjects affected / exposed	5 / 33 (15.15%)	5 / 25 (20.00%)	
occurrences (all)	6	7	
Pyrexia			
subjects affected / exposed	3 / 33 (9.09%)	2 / 25 (8.00%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 33 (6.06%)	2 / 25 (8.00%)	
occurrences (all)	3	3	
Dyspnoea			
subjects affected / exposed	2 / 33 (6.06%)	2 / 25 (8.00%)	
occurrences (all)	2	4	
Epistaxis			
subjects affected / exposed	0 / 33 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Nasal congestion			
subjects affected / exposed	2 / 33 (6.06%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	5 / 33 (15.15%) 5	1 / 25 (4.00%) 1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 33 (15.15%)	3 / 25 (12.00%)	
occurrences (all)	5	3	
Anxiety			
subjects affected / exposed	1 / 33 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Blood bicarbonate decreased			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Blood creatinine increased			
subjects affected / exposed	2 / 33 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Donor specific antibody present			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	3	
Hepatic enzyme increased			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	3	
Lymphocyte count decreased			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
White blood cell count decreased			
subjects affected / exposed	0 / 33 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Injury, poisoning and procedural complications			
Complications of transplanted kidney			
subjects affected / exposed	1 / 33 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Fall			

subjects affected / exposed	2 / 33 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Graft complication			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Incision site pain			
subjects affected / exposed	3 / 33 (9.09%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Procedural pain			
subjects affected / exposed	4 / 33 (12.12%)	4 / 25 (16.00%)	
occurrences (all)	4	4	
Limb injury			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Wound			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 33 (3.03%)	4 / 25 (16.00%)	
occurrences (all)	1	4	
Palpitations			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Tachycardia			
subjects affected / exposed	2 / 33 (6.06%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 33 (12.12%)	2 / 25 (8.00%)	
occurrences (all)	4	3	
Paraesthesia			
subjects affected / exposed	3 / 33 (9.09%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Hypoaesthesia			

subjects affected / exposed	3 / 33 (9.09%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Headache			
subjects affected / exposed	7 / 33 (21.21%)	5 / 25 (20.00%)	
occurrences (all)	7	6	
Tremor			
subjects affected / exposed	6 / 33 (18.18%)	0 / 25 (0.00%)	
occurrences (all)	6	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 33 (15.15%)	4 / 25 (16.00%)	
occurrences (all)	6	5	
Leukocytosis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Leukopenia			
subjects affected / exposed	7 / 33 (21.21%)	8 / 25 (32.00%)	
occurrences (all)	9	9	
Neutropenia			
subjects affected / exposed	2 / 33 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Thrombocytopenia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	4 / 33 (12.12%)	0 / 25 (0.00%)	
occurrences (all)	5	0	
Abdominal pain			
subjects affected / exposed	3 / 33 (9.09%)	2 / 25 (8.00%)	
occurrences (all)	3	2	
Abdominal pain lower			
subjects affected / exposed	2 / 33 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	4	1	
Abdominal pain upper			

subjects affected / exposed	1 / 33 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Aphthous ulcer			
subjects affected / exposed	2 / 33 (6.06%)	4 / 25 (16.00%)	
occurrences (all)	2	8	
Constipation			
subjects affected / exposed	10 / 33 (30.30%)	5 / 25 (20.00%)	
occurrences (all)	12	6	
Diarrhoea			
subjects affected / exposed	10 / 33 (30.30%)	4 / 25 (16.00%)	
occurrences (all)	14	4	
Dyspepsia			
subjects affected / exposed	4 / 33 (12.12%)	0 / 25 (0.00%)	
occurrences (all)	5	0	
Flatulence			
subjects affected / exposed	2 / 33 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 33 (15.15%)	0 / 25 (0.00%)	
occurrences (all)	6	0	
Mouth ulceration			
subjects affected / exposed	0 / 33 (0.00%)	10 / 25 (40.00%)	
occurrences (all)	0	18	
Nausea			
subjects affected / exposed	13 / 33 (39.39%)	5 / 25 (20.00%)	
occurrences (all)	19	5	
Vomiting			
subjects affected / exposed	7 / 33 (21.21%)	5 / 25 (20.00%)	
occurrences (all)	12	5	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	

Renal and urinary disorders			
Dysuria			
subjects affected / exposed	4 / 33 (12.12%)	3 / 25 (12.00%)	
occurrences (all)	4	3	
Haematuria			
subjects affected / exposed	5 / 33 (15.15%)	1 / 25 (4.00%)	
occurrences (all)	6	1	
Perinephric collection			
subjects affected / exposed	4 / 33 (12.12%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Renal tubular necrosis			
subjects affected / exposed	3 / 33 (9.09%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Renal impairment			
subjects affected / exposed	2 / 33 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Proteinuria			
subjects affected / exposed	2 / 33 (6.06%)	4 / 25 (16.00%)	
occurrences (all)	2	5	
Urinary retention			
subjects affected / exposed	2 / 33 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 33 (3.03%)	6 / 25 (24.00%)	
occurrences (all)	1	6	
Back pain			
subjects affected / exposed	2 / 33 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Flank pain			
subjects affected / exposed	0 / 33 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Muscle spasms			

subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3	0 / 25 (0.00%) 0	
Pain in extremity subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	1 / 25 (4.00%) 1	
Infections and infestations			
BK virus infection subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3	4 / 25 (16.00%) 4	
Body tinea subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	2 / 25 (8.00%) 2	
Bronchitis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	2 / 25 (8.00%) 2	
Cytomegalovirus viraemia subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 3	0 / 25 (0.00%) 0	
Fungal infection subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	2 / 25 (8.00%) 2	
Influenza subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3	1 / 25 (4.00%) 1	
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	1 / 25 (4.00%) 1	
Onychomycosis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	2 / 25 (8.00%) 2	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 4	2 / 25 (8.00%) 2	
Tooth infection subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 25 (0.00%) 0	

Urinary tract infection subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 11	5 / 25 (20.00%) 7	
Metabolism and nutrition disorders			
Dehydration subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	2 / 25 (8.00%) 2	
Diabetes mellitus subjects affected / exposed occurrences (all)	5 / 33 (15.15%) 5	2 / 25 (8.00%) 2	
Fluid overload subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	3 / 25 (12.00%) 5	
Hyperglycaemia subjects affected / exposed occurrences (all)	5 / 33 (15.15%) 6	3 / 25 (12.00%) 3	
Hyperkalaemia subjects affected / exposed occurrences (all)	11 / 33 (33.33%) 12	1 / 25 (4.00%) 1	
Hypocalcaemia subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3	2 / 25 (8.00%) 2	
Hypoglycaemia subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 3	0 / 25 (0.00%) 0	
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3	7 / 25 (28.00%) 10	
Hyponatraemia subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 25 (0.00%) 0	
Hypomagnesaemia subjects affected / exposed occurrences (all)	8 / 33 (24.24%) 9	2 / 25 (8.00%) 5	
Hypophosphataemia			

subjects affected / exposed	8 / 33 (24.24%)	9 / 25 (36.00%)	
occurrences (all)	8	12	
Metabolic acidosis			
subjects affected / exposed	3 / 33 (9.09%)	4 / 25 (16.00%)	
occurrences (all)	4	4	
Vitamin D deficiency			
subjects affected / exposed	2 / 33 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2013	Modifications were made to the WOCBP definition, including FSH requirements and HRT washout period to align with BMS standards. Exclusion criteria were updated to remove annual mammogram, WOCBP criteria that do not apply. Updates to The Time & Events Table include removal of the Annual Mammogram to allow Investigators to use standard of care practices, the addition of a Neurological Exam and clarifications to align the table with the protocol text and with BMS belatacept program clinical studies. Protocol was updated with Neurological Exam requirements, modification of the clinical criteria and monitoring of PTLD. Modifications were made to the Events of Special Interest. Inclusion of Data Monitoring Committee. Minor edits and clarifications.
23 December 2014	Modification of the study design, including the addition of an accepted standard of care active comparator treatment group and a change in the immunosuppressive medications paradigm. Updates to the research hypothesis and study objectives. Revisions to eligibility criteria. Addition of text for pregnancy precautions and U.S. reporting requirements from the CellCept Risk Evaluation and Mitigation Strategy. Clarification of the timing of randomization in relation to transplant surgery and initial dose of study drugs, and the temporal sequence of study drug dosing. Updates to the Time & Events Table including the addition of collection of safety and biomarker specimens; and clarifications to align the tables with the protocol text and other studies within belatacept clinical study program. Update the requirements for evaluation of renal biopsy specimens to include assessments for acute antibody-mediated and as T-cell mediated rejection. Updates to the primary and secondary endpoints and statistical section to support the revised study design and to eliminate the allowance of crossover subjects. Minor edits and clarifications, including section numbering
25 August 2015	Modification of the study design to remove an experimental treatment group: Thymoglobulin + belatacept + mycophenolate mofetil with rapid corticosteroid withdrawal, from the study design to eliminate a potentially higher risk of acute rejection. Updates to the randomization ratio, sample size per treatment group and sample size statistical determinations. Syntactical edits and clarifications to support the revised study design.
19 January 2016	Clarification of antiviral prophylaxis requirement. Updates treatment and rescreening of living donor patients with a positive IGRA at screening. Revise protocol with recent administrative changes.
11 November 2016	Decrease number of sites and subjects. Statistical Sample Size Considerations updated. Clarification that all grades of acute rejection, will be included in analyses of the primary and relevant secondary endpoints.
14 August 2017	Clarify timing of collection of belatacept and comparator blood levels for clinically suspected AR, PML or PTLD. Update Procedural Outline Tables 5.1-2 and 5.1-3 to allow for collection of a blood sample for determination of the belatacept or comparator blood level at the time of any clinically suspected episode of acute rejection, PML or PTLD. Provide guidance regarding the evaluation and acceptable range for oral immunosuppressive treatment compliance. The type of T-cell responses to be tested for in cases of clinically suspected PTLD or PML was clarified as being "anti-viral", rather than specifically "anti-EBV" in nature. Made modifications to secondary and exploratory endpoints to align the analyses of acute rejection with the statistical analysis plan, and corrected minor formatting and typographical errors throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

One participant with BPAR had been randomized to the BELA+EVL group, but had then mistakenly been treated with TAC+MMF beginning on Day 1 and continuing through the entire 2-year study period. Due to this, therefore inaccurate data is not presented.

Notes: