Clinical trial results:
A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of BMS-188667 (Abatacept) or Placebo on a Background of Mycophenolate Mofetil (MMF) and Corticosteroids in Subjects with Active Class III or IV Lupus Nephritis

Summary

EudraCT number	2012-000714-11
Trial protocol	IT CZ ES RO Outside EU/EEA
Global end of trial date	30 May 2018

Results information

Result version number	v1 (current)
This version publication date	22 June 2019
First version publication date	22 June 2019

Trial information

Trial identification

Sponsor protocol code	IM101-291

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01714817
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, 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 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the proportion of subjects with Complete Renal Response (CRR) of lupus glomerulonephritis at Day 365 following 1 year treatment with abatacept or placebo administered on a background of MMF and corticosteroids

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	21 February 2013
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: 50
Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	Brazil: 82
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Chile: 19
Country: Number of subjects enrolled	China: 90
Country: Number of subjects enrolled	Colombia: 66
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Hong Kong: 6
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Japan: 56
Country: Number of subjects enrolled	Korea, Republic of: 16
Country: Number of subjects enrolled	Mexico: 87
Country: Number of subjects enrolled	Peru: 56
Country: Number of subjects enrolled	Romania: 10
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Taiwan: 35
Country: Number of subjects enrolled	United States: 73

Worldwide total number of subjects	695
EEA total number of subjects	36

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)	2
Adults (18-64 years)	689
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

695 participants were enrolled; 406 randomized; 405 received treatment (1 received ACE inhibition and was not treated). 289 participants were screen failures; 233 were due to no longer meeting study criteria; 19 withdrew consent; 4 due to Adverse Events; 1 due to death; 1 due to poor/non-compliance; 1 was lost to follow up; and 30 were other.

Period 1

Period 1 title	Year 1 Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Abatacept IV

Arm description:

Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	BMS-188667
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks

Arm title	Placebo IV

Arm description:

Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo matching with BMS-188667
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks

Number of subjects in period 1[1]	Abatacept IV	Placebo IV
Started	202	203
Completed	155	161
Not completed	47	42
Adverse event, serious fatal	1	1
Consent withdrawn by subject	6	7
Adverse event, non-fatal	20	17
Hypersensitivity to the medication	-	1
Pregnancy	2	-
Need of use of Prohibited Medications	1	-
Participant no longer meets criteria	6	2
Lost to follow-up	-	2
Poor / non-compliance	-	1
Change in Concomitant Medication	-	1
Lack of efficacy	11	9
Antiproteinuric changed/dose increased	-	1

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: 695 participants enrolled, 406 were randomized to abatacept (203) and placebo arms (203). All but 1 randomized participant received at least 1 dose of double-blind study drug in the treatment period. A participant assigned to the abatacept group was not treated as the participant required initiation of ACE therapy.

Period 2

Period 2 title	Year 2 Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Abatacept IV

Arm description:

Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	BMS-188667
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g

tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks

Arm title	Placebo IV

Arm description:

Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo matching with BMS-188667
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks

Number of subjects in period 2	Abatacept IV	Placebo IV
Started	155	161
Completed	129	123
Not completed	26	38
Participant request to stop treatment	4	4
Administrative reason by Sponsor	4	3
Participant withdrew consent	1	5
Adverse event, non-fatal	7	6
Participant went to US stopped treatment	-	1
Pregnancy	1	1
Given cyclophosphamide, corticosteroids	-	1
Participant no longer meets criteria	1	4
Lost to follow-up	2	-
Lack of efficacy	4	12
Completed Year 1, did not enter Year 2	2	1

Period 3

Period 3 title	Long-Term Extension (LTE) Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Abatacept IV

Arm description:

Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	BMS-188667
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks

Arm title	Placebo IV

Arm description:

Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo matching with BMS-188667
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks

Number of subjects in period 3	Abatacept IV	Placebo IV
Started	129	123
Completed	62	53
Not completed	67	70
Administrative reason by Sponsor	27	21
Disease progression	1	4
Participant request to stop treatment	1	1
Participant withdrew consent	1	1

Completed Year 2, did not enter LTE	33	38
Absence of renal response	-	1
Participant no longer meets criteria	1	-
Not effective	-	1
Adverse Event unrelated to study drug	1	-
Study drug toxicity	1	-
Pregnancy	1	-
Investigator decision, study termination	-	1
Lost to follow-up	-	1
Study was terminated	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Abatacept IV
Reporting group description:	
Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks	
Reporting group title	Placebo IV
Reporting group description:	
Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks	

Reporting group values	Abatacept IV	Placebo IV	Total
Number of subjects	202	203	405
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	1	0	1
Adults (18-64 years)	200	202	402
From 65-84 years	1	1	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	33.1	33.2	
standard deviation	± 10.75	± 10.48	-
Gender, Male/Female Units: Subjects			
Female	182	178	360
Male	20	25	45
Race/Ethnicity, Customized Units: Subjects			
Asian	71	74	145
African American	15	15	30
Caucasian	85	71	156
Other	31	43	74

End points

End points reporting groups

Reporting group title	Abatacept IV
Reporting group description:	
Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks	

Reporting group title	Placebo IV
Reporting group description:	
Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks	

Reporting group title	Abatacept IV
Reporting group description:	
Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks	

Reporting group title	Placebo IV
Reporting group description:	
Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks	

Reporting group title	Abatacept IV
Reporting group description:	
Abatacept 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks	

Reporting group title	Placebo IV
Reporting group description:	
Placebo matching with Abatacept injection by intravenous on Days 1,15, 29, and 57, followed by every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 Weeks	

Primary: Percentage of participants in Complete Renal Response (CR) of lupus glomerulonephritis at Day 365 of the double-blind period

End point title	Percentage of participants in Complete Renal Response (CR) of lupus glomerulonephritis at Day 365 of the double-blind period
End point description:	
Number of participants achieving CR was divided by the total number of participants in that arm and expressed as a percentage. CR defined as: eGFR is normal or no <85% of the baseline; eGFR based on mean creatinine value from day 358 and 365. Proteinuria: UPCR<0.5 mg/mg. Urine sediment: No cellular casts. Corticosteroid dose: Daily dose must be no >10 mg prednisone or equiv. for at least 28 days prior to assessment. Participants with >10mg/day prednisone or equivalent for non-renal disease within 28 days prior to day 365 will be imputed as having achieved CR if the following are true: Met all criteria for CR at day 337 and all criteria for CR except corticosteroid dose at day 365; Investigator confirms increase in steroid dose is not related to renal disease. Adjusted odds ratio is estimated from logistic regression model which includes treatment group, baseline ACEi/ARBs use (Yes/No), race (Asian/ Black/Caucasian/Other) and baseline UPCR as a continuous variable.	
End point type	Primary
End point timeframe:	
Day 365	

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	203		
Units: Percentage				
number (not applicable)				
Percentage of participants in CR	35.1	33.5		

Statistical analyses

Statistical analysis title	Percentage of participants in CR at Day 365
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7264
Method	Stratified logistic regression
Parameter estimate	Odds ratio (OR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7077
upper limit	1.6421

Secondary: Percentage of nephrotic participants in Complete Renal Response of lupus glomerulonephritis at Day 365 of the double-blind period

End point title	Percentage of nephrotic participants in Complete Renal Response of lupus glomerulonephritis at Day 365 of the double-blind period

End point description:

Number of participants achieving CR was divided by total participants in that arm, expressed as a percentage. CR is defined the following criteria: eGFR is normal or no <85% of the baseline value; eGFR is based on mean creatinine value from day 358 and 365. Proteinuria: UPCR<0.5 mg/mg. Urine sediment: No cellular casts. Corticosteroid dose: Daily dose must be no >10 mg prednisone or equivalent for at least 28 days prior. Subjects with >10mg/day prednisone or equivalent for non-renal disease within 28 days prior to day 365 will be imputed as CR if the following are true: Met all criteria for CR at day 337 and all criteria for CR except corticosteroid dose at day 365; Investigator confirms increase in steroid dose is not related to renal disease. Adjusted odds ratio is estimated from logistic regression model which includes treatment group, baseline ACEi/ARBs use, race and baseline UPCR as a continuous variable.

End point type	Secondary

End point timeframe:

Day 365

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	88		
Units: Percentage				
number (not applicable)				
Percentage of nephrotic participants in CR	27	29.5		

Statistical analyses

Statistical analysis title	Percentage nephrotic participants in CR at Day 365
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4148
upper limit	1.5956

Secondary: Adjusted Mean Change from Baseline in Urine protein/creatinine ratio (UPCR) at Day 365 of the double-blind period in nephrotic participants

End point title	Adjusted Mean Change from Baseline in Urine protein/creatinine ratio (UPCR) at Day 365 of the double-blind period in nephrotic participants

End point description:

Adjusted Mean Change from Baseline in UPCR at Day 365 of the double-blind period in nephrotic participants

End point type	Secondary

End point timeframe:

Baseline and Day 365

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	68		
Units: UPCR (mg/mg)				
arithmetic mean (standard error)				
Adjusted Mean Change from Baseline in UPCR	-5.01 (± 0.33)	-4.84 (± 0.35)		

Statistical analyses

Statistical analysis title	Adjusted mean change UPCR at Day 365 (nephrotic)
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.571
Method	Mixed models analysis
Parameter estimate	Adjusted mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.42

Secondary: Adjusted Mean Change from Baseline in UPCR at Day 365 of the double-blind period in overall population

End point title	Adjusted Mean Change from Baseline in UPCR at Day 365 of the double-blind period in overall population
End point description:	
Adjusted Mean Change from Baseline in Urine protein/creatinine ratio (UPCR) at Day 365 of the double-blind period in the overall population	
End point type	Secondary
End point timeframe:	
Day 1 and Day 365	

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	163		
Units: UPCR (mg/mg)				
arithmetic mean (standard error)				
Adj. Mean Change from Baseline in UPCR	-2.99 (± 0.17)	-2.90 (± 0.16)		

Statistical analyses

Statistical analysis title	Adjusted mean change from baseline UPCR at Day 365
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	320
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.561
Method	Mixed models analysis
Parameter estimate	Adjusted mean difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.22

Secondary: Adjusted mean change from baseline in disease activity as measured by BILAG 2004 over time during Year 1 of the double-blind period

End point title	Adjusted mean change from baseline in disease activity as measured by BILAG 2004 over time during Year 1 of the double-blind period

End point description:

Adjusted mean change from baseline in British Isles Lupus Assessment Group (BILAG) score over time during Year 1 of the double-blind period based on a repeated measure mixed model and presented at each visit in the first 12-month of the double-blind period. BILAG index measures disease activity in different organs/systems separately. BILAG score is calculated for each of 9 systems depending on the clinical features present and whether they are new (4 points), worse (3 points), the same (2 points), improving (1 point) or not present (0 points) in the last 4 weeks compared with previously. BILAG "A" represents the presence of serious features of lupus. BILAG "B" represents more moderate features of the disease. BILAG "C" includes only mild symptomatic features. BILAG "D" represents prior activity with no current symptoms due to active lupus. BILAG "E" represents an organ that has never been involved. Overall BILAG score ranges from 0-108, with higher scores reflecting a worse outcome.

End point type	Secondary

End point timeframe:

at Day 365

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	161		
Units: Number				
arithmetic mean (confidence interval 95%)				
Adj mean change from baseline in disease activity	-8.22 (-9.29 to -7.16)	-7.60 (-8.66 to -6.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any Adverse Events (AEs) during Year 1 of the double-blind period

End point title	Number of participants with any Adverse Events (AEs) during Year 1 of the double-blind period

End point description:

All AEs were coded and grouped into preferred terms (PT) by system organ class (SOC), using the Medical Dictionary for Regulatory Activities (MedDRA, version 21.0). Investigators determined the intensity of each AE as mild, moderate, severe, or very severe and assessed the relationship to study drug.

End point type	Secondary

End point timeframe:

From Day 1 up to 56 days post last dose in Year 1 of the double-blind period

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	203		
Units: Participants				
Participants with Adverse Events	188	194		
Participants with Serious Adverse Events	49	39		
Participants with infection Adverse Events	150	147		
Participants with malignancies	2	1		
Participants with autoimmune events	10	9		
Participants with peri-infusional Adverse Events	7	9		
Participants with acute infusional Adverse Events	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ranked outcome of Complete Renal

Response, Partial Renal Response (PR), and No Renal Response (NR) during the double-blind period

End point title	Percentage of participants with ranked outcome of Complete Renal Response, Partial Renal Response (PR), and No Renal Response (NR) during the double-blind period

End point description:

Complete Renal Response or Complete Response (CR): defined as meeting ALL of the following criteria: eGFR normal OR no less than 85% of the baseline value; UPCR < 0.5; Urine sediment: No cellular casts; Daily corticosteroid dose must be no greater than 10 mg prednisone or equivalent for at least 28 days prior to assessment. Partial Renal Response or Partial Response (PR): defined as meeting ALL of the following criteria: Participant does not meet criteria for CR; eGFR no less than 85% of the lesser of the values at screening or randomization (Day 1); UPCR < 0.5 OR 50% reduced from baseline and < 1 if baseline value was < 3, OR 50% reduced from baseline and < 3 if baseline value was greater than or equal to 3; Urine sediment: no cellular casts; daily corticosteroid dose no greater than 10 mg/day prednisone or prednisone equivalent for at least 28 days prior to assessment. No Renal Response or No Response (NR): defined as not meeting criteria for CR or PR or withdrawn

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[1]	203[2]		
Units: Percentage				
number (not applicable)				
CR - Day 365	35.1	33.5		
PR - Day 365	20.8	21.7		
NR - Day 365	44.1	44.8		
CR - Day 729	99999	99999		
PR - Day 729	99999	99999		
NR - Day 729	99999	99999		

Notes:

[1] - Study terminated, efficacy not met

[2] - Study terminated, efficacy not met

Statistical analyses

Statistical analysis title	Percentage participants ranked outcome of CR PR NR
Statistical analysis description: CR - Day 365	
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Estimate of Difference
Point estimate	1.651
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.595828
upper limit	10.897784

Statistical analysis title	Percentage participants ranked outcome of CR PR NR
Statistical analysis description: PR - Day 365	
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Estimate of Difference
Point estimate	-0.8828
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.848056
upper limit	7.082461

Statistical analysis title	Percentage participants ranked outcome of CR PR NR
Statistical analysis description: NR - Day 365	
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Estimate of Difference
Point estimate	-0.7682
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.446714
upper limit	8.910353

Secondary: Median time to Complete Renal Response during the double-blind period in all participants

End point title	Median time to Complete Renal Response during the double-blind period in all participants

End point description:

The estimate of median time to Complete Renal Response is based on Kaplan-Meier analysis. Complete renal response (CR): defined as meeting ALL of the following criteria: eGFR normal OR no less than 85% of the baseline value; Urine protein/creatinine ratio (UPCR) < 0.5; Urine sediment: No cellular casts; Daily corticosteroid dose must be no greater than 10 mg prednisone or equivalent for at least 28 days prior to assessment.

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[3]	203[4]		
Units: Days				
median (confidence interval 95%)				
Day 365	280.0 (198.0 to 365.0)	309.0 (280.0 to 365.0)		
Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[3] - Study terminated, efficacy not met

[4] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to Complete Renal Response during the double-blind period in nephrotic participants

End point title	Median time to Complete Renal Response during the double-blind period in nephrotic participants

End point description:

The estimate of median time to Complete Renal Response in nephrotic participants is based on Kaplan-Meier analysis. Complete renal response (CR): defined as meeting ALL of the following criteria: eGFR normal OR no less than 85% of the baseline value; Urine protein/creatinine ratio (UPCR) < 0.5; Urine sediment: No cellular casts; Daily corticosteroid dose must be no greater than 10 mg prednisone or equivalent for at least 28 days prior to assessment.

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[5]	203[6]		
Units: Days				
median (confidence interval 95%)				
Day 365	366.0 (337.0 to 99999)	368.0 (311.0 to 368.0)		
Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[5] - Study terminated, efficacy not met

[6] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to Partial Renal Response during the double-blind period in all participants

End point title	Median time to Partial Renal Response during the double-blind period in all participants

End point description:

The estimate of median time to Partial Response (PR) is based on Kaplan-Meier analysis. Partial renal response (PR): defined as meeting ALL of the following criteria: Participant does not meet criteria for CR; eGFR no less than 85% of the lesser of the values at screening or randomization (Day 1); UPCR < 0.5 OR 50% reduced from baseline and < 1 if baseline value was < 3, OR 50% reduced from baseline and < 3 if baseline value was 3; Urine sediment: no cellular casts; daily corticosteroid dose no greater than 10 mg/day prednisone or prednisone equivalent for at least 28 days prior to assessment

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[7]	203[8]		
Units: Days				
median (confidence interval 95%)				
Day 365	226.0 (198.0 to 313.0)	253.0 (198.0 to 358.0)		
Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[7] - Study terminated, efficacy not met

[8] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to Partial Renal Response during the double-blind period in nephrotic participants

End point title	Median time to Partial Renal Response during the double-blind period in nephrotic participants

End point description:

The estimate of median time to Partial Response (PR) in nephrotic participants is based on Kaplan-Meier analysis. Partial renal response (PR): defined as meeting ALL of the following criteria: Participant does not meet criteria for CR; eGFR no less than 85% of the lesser of the values at screening or randomization (Day 1); UPCR < 0.5 OR 50% reduced from baseline and < 1 if baseline value was < 3, OR 50% reduced from baseline and < 3 if baseline value was 3; Urine sediment: no cellular casts; daily corticosteroid dose no greater than 10 mg/day prednisone or prednisone equivalent for at least 28 days prior to assessment

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[9]	203[10]		
Units: Days				
median (confidence interval 95%)				
Day 365	225.0 (196.0 to 311.0)	196.0 (170.0 to 225.0)		
Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[9] - Study terminated, efficacy not met

[10] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Adjusted mean change from baseline in UPCR over time

End point title	Adjusted mean change from baseline in UPCR over time

End point description:

A repeated measure mixed model that included the baseline UPCR value, randomization stratification factors, time, and time by treatment interaction as fixed effects and subject as a random effect was used.

End point type	Secondary

End point timeframe:

Day 365; Day 729, includes data up to July 1st 2017 when double-blind therapy ended

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	163		
Units: UPCR (mg/mg)				
arithmetic mean (standard error)				
Day 365	-2.95 (± 0.17)	-2.68 (± 0.17)		
Day 729	-3.13 (± 0.18)	-2.72 (± 0.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Percent Change from Baseline in UPCR over Time

End point title	Median Percent Change from Baseline in UPCR over Time

End point description:

A repeated measure mixed model that included the baseline UPCR value, randomization stratification factors, time, and time by treatment interaction as fixed effects and subject as a random effect was used. % Change from Baseline = (post baseline - baseline value) / baseline value x 100

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[11]	203[12]		
Units: Percent				
median (inter-quartile range (Q1-Q3))				
Day 365	-83.77 (-92.42 to -64.18)	-84.12 (-94.03 to -59.98)		
Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[11] - Study terminated, efficacy not met

[12] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Adjusted mean change from baseline in eGFR over time

End point title	Adjusted mean change from baseline in eGFR over time

End point description:

Estimated glomerular filtration rate(eGFR), will be calculated by the CKD-EPI formula shown below.50 eGFR is expressed as mL/min per 1.73m2. For the purpose of this study lower limit of normal eGFR is defined as 90mL/min per 1.73m2 eGFR = 141 X min (Scr/k, 1)α X max (Scr/k, 1)-1.209 X 0.993Age X (1.018 [if female]) X (1.159 [if black]) Where Scr is serum creatinine (mg/dL), k is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/k or 1, and max indicates the maximum of Scr/k or 1, age in years.

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[13]	203[14]		
Units: mL/min per 1.73m2				
arithmetic mean (confidence interval 95%)				
Day 365	6.85 (3.47 to 10.23)	5.85 (2.51 to 9.20)		
Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[13] - Study terminated, efficacy not met

[14] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to First Sustained Change to No Response During the Double-blind Period

End point title	Median Time to First Sustained Change to No Response During the Double-blind Period

End point description:

Sustained response defined as response present at 2 consecutive visits approximately 4 weeks apart. No renal response (NR): defined as not meeting criteria for CR or PR or withdrawn The estimate of median time is based on Kaplan-Meier analysis

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[15]	203[16]		
Units: Days				
median (confidence interval 95%)				
Day 365	99999 (392.0 to 99999)	99999 (99999 to 99999)		
Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[15] - Study terminated, efficacy not met

[16] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with sustained change from higher level of response to no response during the double-blind period

End point title	Number of participants with sustained change from higher level of response to no response during the double-blind period

End point description:

Sustained change to no response is defined as going from CR (or PR) to NR and remaining in NR for at least 2 consecutive visits; visits should be approximately 4 weeks apart. This analysis will be based on time from response CR (or PR) to the first visit in which the no response (NR) was achieved and sustained to the next visit.

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[17]	203[18]		
Units: Participants				
Day 365	5	3		
Day 729	99999	99999		

Notes:
[17] - Study terminated, efficacy not met
[18] - Study terminated, efficacy not met

Statistical analyses

Statistical analysis title	Sustained change from higher level response to NR
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3251
upper limit	6.2849

Secondary: Adjusted mean change from baseline and from Day 365 in disease activity as measured by BILAG 2004 over time during the double-blind period

End point title	Adjusted mean change from baseline and from Day 365 in disease activity as measured by BILAG 2004 over time during the double-blind period

End point description:

BILAG index measures and reports disease activity in different organs/systems separately. The BILAG score is calculated for each of nine systems depending on the clinical features present and whether they are new (4 points), worse (3 points), the same (2 points), improving (1 point) or not present (0 points) in the last 4 weeks compared with previously. A BILAG "A" represents the presence of one or more serious features of lupus. A BILAG "B" represents more moderate features of the disease. A BILAG "C" includes only mild symptomatic features. A BILAG "D" represents only prior activity with no current symptoms due to active lupus. A BILAG "E" represents an organ that has never been involved.

End point type	Secondary

End point timeframe:

at Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[19]	203[20]		
Units: Number				
arithmetic mean (standard error)				
from baseline (Day 1)	99999 (± 99999)	99999 (± 99999)		
from Day 365	99999 (± 99999)	99999 (± 99999)		

Notes:

[19] - Study terminated, efficacy not met

[20] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Cmin (ug/mL): Trough level serum concentration of abatacept prior to the administration of the IV infusion

End point title	Cmin (ug/mL): Trough level serum concentration of abatacept prior to the administration of the IV infusion

End point description:

Trough level serum concentration of abatacept prior to the administration of the IV infusion on Days 1 to 365

End point type	Secondary

End point timeframe:

Days 1 to 365

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	0[21]		
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Day 15	69.97 (± 91.4)	()		
Day 29	90.46 (± 56.8)	()		
Day 57	36.43 (± 84.4)	()		
Day 85	34.46 (± 55.4)	()		
Day 113	16.42 (± 69.2)	()		
Day 169	13.98 (± 64.5)	()		
Day 281	14.44 (± 54.7)	()		
Day 337	14.99 (± 73.6)	()		
Day 365	13.62 (± 51.7)	()		

Notes:

[21] - Data reported for Abatacept only

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax: Maximum observed serum concentration following participants receiving active abatacept IV

End point title	Cmax: Maximum observed serum concentration following participants receiving active abatacept IV

End point description:

Cmax: Maximum observed serum concentration following participants receiving active abatacept IV

End point type	Secondary

End point timeframe:

at 1 hour post Day 1 dose and 30 minutes post Day 337 dose

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	0[22]		
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Day 1	527.43 (± 59.6)	()		
Day 337	203.51 (± 30.6)	()		

Notes:

[22] - Data reported for Abatacept only

Statistical analyses

No statistical analyses for this end point

Secondary: AUC (TAU): Area under the serum concentration time curve over a dosing interval

End point title	AUC (TAU): Area under the serum concentration time curve over a dosing interval

End point description:

AUC (TAU): Area under the serum concentration time curve over a dosing interval between Days 337 to 365.

End point type	Secondary

End point timeframe:

Days 337 to 365

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	0[23]		
Units: ug*h/mL				
geometric mean (geometric coefficient of variation)				
AUC (TAU)	36480.24 (± 29.2)	()		

Notes:

[23] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Summary statistics for systolic blood pressure

End point title	Summary statistics for systolic blood pressure

End point description:

Summary statistics for systolic blood pressure

End point type	Secondary

End point timeframe:

Day 1 to Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[24]	203[25]		
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1, end of observation	122.0 (± 15.48)	122.6 (± 15.31)		
Day 365, end of observation	112.3 (± 18.45)	115.0 (± 7.07)		
Day 729	99999 (± 99999)	99999 (± 99999)		

Notes:

[24] - Study terminated, efficacy not met

[25] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Summary statistics for diastolic blood pressure

End point title	Summary statistics for diastolic blood pressure

End point description:

Summary statistics for diastolic blood pressure

End point type	Secondary

End point timeframe:

Day 1 to Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[26]	203[27]		
Units: mmHg				
arithmetic mean (standard deviation)				
Day 1, end of observation	76.5 (± 11.49)	77.0 (± 11.19)		
Day 365, end of observation	73.5 (± 10.75)	77.5 (± 10.61)		
Day 729	99999 (± 99999)	99999 (± 99999)		

Notes:
[26] - Study terminated, efficacy not met
[27] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Summary statistics for Heart Rate

End point title	Summary statistics for Heart Rate

End point description:
Summary statistics for Heart Rate

End point type	Secondary

End point timeframe:
Day 1 to Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[28]	203[29]		
Units: beats per minute				
arithmetic mean (standard deviation)				
Day 1, end of observation	80.6 (± 10.91)	81.4 (± 10.64)		
Day 365, end of observation	78.5 (± 9.57)	70.0 (± 14.14)		
Day 729	99999 (± 99999)	99999 (± 99999)		

Notes:
[28] - Study terminated, efficacy not met
[29] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Laboratory Analytes During the Double-blind Period

End point title	Mean Change from Baseline in Laboratory Analytes During the Double-blind Period

End point description:
Laboratory assessments were analyzed centrally, with the exception of pregnancy testing. Blood draws and urine collections were performed at visits specified in the protocol. Change from Baseline = Post-baseline - Baseline value.

End point type	Secondary

End point timeframe:
Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	160		
Units: SI units				
arithmetic mean (standard error)				
ALANINE AMINOTRANSFERASE (ALT) (U/L)	-2.2 (± 1.318)	-3.4 (± 1.521)		
ALBUMIN (G/L)	9.2 (± 0.580)	8.1 (± 0.604)		
ALKALINE PHOSPHATASE (ALP) (U/L)	8.2 (± 1.884)	11.7 (± 2.291)		
ASPARTATE AMINOTRANSFERASE (AST) (U/L)	0.3 (± 1.020)	0.3 (± 0.826)		
BILIRUBIN, TOTAL (UMOL/L)	1.77 (± 0.3509)	1.00 (± 0.2476)		
BLOOD UREA NITROGEN (MMOL/L)	-2.31 (± 0.3447)	-2.25 (± 0.2950)		
CALCIUM, TOTAL (MMOL/L)	0.097 (± 0.01434)	0.108 (± 0.01539)		
CHLORIDE, SERUM (MMOL/L)	-1.1 (± 0.307)	-0.5 (± 0.362)		
CREATININE (UMOL/L)	-5.6 (± 1.869)	-6.2 (± 2.314)		
EOSINOPHILS (ABSOLUTE) (X10*9 C/L)	0.034 (± 0.01119)	0.010 (± 0.01403)		
G-GLUTAMYL TRANSFERASE (GGT) (U/L)	-5.3 (± 2.914)	-4.1 (± 3.676)		
GLUCOSE, SERUM (MMOL/L)	-0.23 (± 0.1350)	-0.58 (± 0.1946)		
HEMATOCRIT (VOL)	0.0328 (± 0.004494)	0.0325 (± 0.005387)		
HEMOGLOBIN (G/L)	8.8 (± 1.414)	9.0 (± 1.758)		
LYMPHOCYTES (ABSOLUTE) (X10*9 C/L)	0.141 (± 0.07806)	-0.149 (± 0.07595)		
MONOCYTES (ABSOLUTE) (X10*9 C/L)	-0.018 (± 0.01735)	-0.050 (± 0.02143)		
NEUTROPHILS (ABSOLUTE) (X10*9 C/L)	-2.259 (± 0.26617)	-2.289 (± 0.33697)		
PHOSPHORUS, INORGANIC (MMOL/L)	-0.077 (± 0.02539)	-0.037 (± 0.02261)		
PLATELET COUNT (X10*9 C/L)	-4.9 (± 6.092)	-9.1 (± 7.581)		
POTASSIUM, SERUM (MMOL/L)	-0.02 (± 0.0403)	-0.10 (± 0.0541)		
PROTEIN, TOTAL (G/L)	9.9 (± 0.871)	10.1 (± 0.845)		
SODIUM, SERUM (MMOL/L)	-0.2 (± 0.263)	-0.5 (± 0.287)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Hematology laboratory abnormalities during Year 1 of the Double Blind period

End point title	Number of participants with Marked Hematology laboratory abnormalities during Year 1 of the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value HEMOGLOBIN g/L 4.0 HB >3 G/DL DECREASE FROM PRE RX HEMATOCRIT vol 6.3 HCT <0.75X PRE RX ERYTHROCYTES x10*12 c/L 5.2 RBC <0.75X PRE RX PLATELET COUNT x10*9 c/L 5.0 PLAT <0.67X LLN OR >1.5X ULN, OR IF PRE RX<LLN THEN USE 0.5X PRE RX AND <100,000/MM3 LEUKOCYTES x10*9 c/L 6.2 WBC <0.

75X LLN OR >1.25X ULN, OR IF PRE RX<LLN THEN USE <0.8X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.2X PRE RX OR <LLN EOSINOPHILS (ABSOLUTE) x10*9 c/L 8.3 EOSA IF VALUE > .750 X10*3 c/uL BASOPHILS (ABSOLUTE) x10*9 c/L 8.3 BASOA IF VALUE > 400/MM3 MONOCYTES (ABSOLUTE) x10*9 c/L 8.3 MONOA IF VALUE > 2000/MM3 LYMPHOCYTES (ABSOLUTE) x10*9 c/L 8.3 LYMPA IF VALUE < .750 X10*3 c/uL OR IF VALUE > 7.50 X10*3 c/uL N = the number of participants with at least 1 on treatment lab result for each analyte

End point type	Secondary

End point timeframe:

Day 1 to Day 365; includes data up to 56 days post last dose in year 1 of double-blind period or first dose date in the year 2 of double-blind period, whichever is earlier

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[30]	203[31]		
Units: participants				
HEMOGLOBIN, low	6	10		
HEMOGLOBIN, high	99999	99999		
HEMATOCRIT, low	12	12		
HEMATOCRIT, high	99999	99999		
ERYTHROCYTES, low	7	10		
ERYTHROCYTES, high	99999	99999		
PLATELET COUNT, low	4	3		
PLATELET COUNT, high	0	0		
LEUKOCYTES, low	35	21		
LEUKOCYTES, high	29	25		
EOSINOPHILS (ABSOLUTE), low	99999	99999		
EOSINOPHILS (ABSOLUTE), high	2	6		
BASOPHILS (ABSOLUTE), low	99999	99999		
BASOPHILS (ABSOLUTE), high	1	1		
MONOCYTES (ABSOLUTE), low	99999	99999		
MONOCYTES (ABSOLUTE), high	0	1		
LYMPHOCYTES (ABSOLUTE), low	81	104		
LYMPHOCYTES (ABSOLUTE), high	1	2		

Notes:

[30] - Study terminated, efficacy not met

[31] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Liver and Kidney Function Laboratory Abnormalities during Year 1 of the Double Blind period

End point title	Number of participants with Marked Liver and Kidney Function Laboratory Abnormalities during Year 1 of the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value ALKALINE PHOSPHATASE (ALP) U/L 5.0 ALP >2X ULN, OR IF PRE RX>ULN THEN USE >3X PRE RX ASPARTATE AMINOTRANSFERASE (AST) U/L 5.0 AST >3X ULN, OR IF PRE RX>ULN THEN USE >4X PRE RX ALANINE AMINOTRANSFERASE (ALT) U/L 5.0 ALT >3X ULN, OR IF PRE RX>ULN THEN USE >4X PRE RX G-GLUTAMYL TRANSFERASE (GGT) U/L 5.0 GGT >2X ULN, OR IF PRE RX>ULN THEN USE >3X PRE RX BILIRUBIN, TOTAL umol/L 5.1 TBILI >2X ULN, OR IF PRE RX>ULN THEN USE >4X PRE RX BILIRUBIN,

DIRECT umol/L 5.1 DBILI >1.5X ULN, OR IF PRE RX>ULN THEN USE >2X PRE RX BLOOD UREA NITROGEN mmol/L 5.1 BUN >2X PRE RX CREATININE umol/L 5.0 CREAT >1.5X PRE RX N = the number of participants with at least 1 on treatment lab result for each analyte

End point type	Secondary

End point timeframe:

Day 1 to Day 365; includes data up to 56 days post last dose in year 1 of double-blind period or first dose date in the year 2 of double-blind period, whichever is earlier

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[32]	203[33]		
Units: participants				
ALKALINE PHOSPHATASE (ALP), low	99999	99999		
ALKALINE PHOSPHATASE (ALP), high	1	1		
ASPARTATE AMINOTRANSFERASE (AST), low	99999	99999		
ASPARTATE AMINOTRANSFERASE (AST), high	5	0		
ALANINE AMINOTRANSFERASE (ALT), low	99999	99999		
ALANINE AMINOTRANSFERASE (ALT), high	8	2		
G-GLUTAMYL TRANSFERASE (GGT), low	99999	99999		
G-GLUTAMYL TRANSFERASE (GGT), high	17	15		
BILIRUBIN, TOTAL, low	99999	99999		
BILIRUBIN, TOTAL, high	0	0		
BILIRUBIN, DIRECT, low	99999	99999		
BILIRUBIN, DIRECT, high	0	0		
BLOOD UREA NITROGEN, low	99999	99999		
BLOOD UREA NITROGEN, high	20	12		
CREATININE, low	99999	99999		
CREATININE, high	24	20		

Notes:

[32] - Study terminated, efficacy not met

[33] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Electrolyte Laboratory Abnormalities during Year 1 of the Double Blind period

End point title	Number of participants with Marked Electrolyte Laboratory Abnormalities during Year 1 of the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value SODIUM, SERUM mmol/L 4.0 NA <0.95X LLN OR >1.05X ULN, OR IF PRE RX<LLN THEN USE <0.95X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.05X PRE RX OR <LLN POTASSIUM, SERUM mmol/L 4.1 K <0.9X LLN OR >1.1X ULN, OR IF PRE RX<LLN THEN USE <0.9X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.1X PRE RX OR <LLN CHLORIDE, SERUM mmol/L 5.0 CL <0.9X LLN OR >1.1X ULN, OR IF PRE RX<LLN THEN USE <0.9X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.1X PRE RX OR <LLN N = the number of participants with at least 1 on treatment lab result for each analyte

End point type	Secondary

End point timeframe:

Day 1 to Day 365; includes data up to 56 days post last dose in year 1 of double-blind period or first dose date in the year 2 of double-blind period, whichever is earlier

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	203		
Units: participants				
SODIUM, SERUM, low	1	1		
SODIUM, SERUM, high	2	2		
POTASSIUM, SERUM, low	3	5		
POTASSIUM, SERUM, high	7	7		
CHLORIDE, SERUM, low	0	1		
CHLORIDE, SERUM, high	0	0		
CALCIUM, TOTAL, low	1	1		
CALCIUM, TOTAL, high	2	0		
PHOSPHORUS, INORGANIC, low	9	7		
PHOSPHORUS, INORGANIC, high	13	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Urinalysis Laboratory Abnormalities during Year 1 of the Double Blind period

End point title	Number of participants with Marked Urinalysis Laboratory Abnormalities during Year 1 of the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value PROTEIN, URINE Unknown UPRO IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4 GLUCOSE, URINE N/A UGLU IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4 BLOOD, URINE N/A UBLD IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4 RBC, URINE hpf 5.0 URBC IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4 WBC, URINE hpf 5.0 UWBC IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4

End point type	Secondary

End point timeframe:

Day 1 to Day 365; includes data up to 56 days post last dose in year 1 of double-blind period or first dose date in the year 2 of double-blind period, whichever is earlier

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[34]	203[35]		
Units: participants				
PROTEIN, URINE, low	99999	99999		
PROTEIN, URINE, high	0	0		
GLUCOSE, URINE, low	99999	99999		
GLUCOSE, URINE, high	0	0		
BLOOD, URINE, low	99999	99999		
BLOOD, URINE, high	0	0		
Red blood cells (RBC), URINE, low	99999	99999		
Red blood cells (RBC), URINE, high	93	103		
White blood cells (WBC), URINE, low	99999	99999		
White blood cells (WBC), URINE, high	91	98		

Notes:

[34] - Study terminated, efficacy not met

[35] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with other Marked Chemistry Laboratory Abnormalities during Year 1 of the Double Blind period

End point title	Number of participants with other Marked Chemistry Laboratory Abnormalities during Year 1 of the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value CALCIUM, TOTAL mmol/L 5.2 CA <0.8X LLN OR >1.2X ULN, OR IF PRE RX<LLN THEN USE <0.75X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.25X PRE RX OR <LLN PHOSPHORUS, INORGANIC mmol/L 5.2 PHOS <0.75X LLN OR >1.25X ULN, OR IF PRE RX<LLN THEN USE <0.67X PRE RX OR >ULN GLUCOSE, SERUM mmol/L 4.1 GLUC <65 mg/dL, OR >220 mg/dL PROTEIN, TOTAL g/L 5.0 TPRO <0.9X LLN OR >1.1X ULN, OR IF PRE RX<LLN THEN USE 0.9X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE 1.1X PRE RX OR <LLN ALBUMIN g/L 3.0 ALB <0.9X LLN, OR IF PRE RX<LLN THEN USE <0.75X PRE RX CHOLESTEROL, TOTAL (TC) mmol/L 5.2 CHOL >2X PRE R N = the number of participants with at least 1 on treatment lab result for each analyte

End point type	Secondary

End point timeframe:

Day 1 to Day 365; includes data up to 56 days post last dose in year 1 of double-blind period or first dose date in the year 2 of double-blind period, whichever is earlier

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[36]	203[37]		
Units: participants				
GLUCOSE, SERUM, low	33	29		
GLUCOSE, SERUM, high	10	5		
PROTEIN, TOTAL, low	44	26		
PROTEIN, TOTAL, high	0	1		
ALBUMIN, low	10	11		
ALBUMIN, high	99999	99999		

Notes:

[36] - Study terminated, efficacy not met

[37] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any Adverse Events (AEs) during Year 2 of the double-blind period and long-term extension

End point title	Number of participants with any Adverse Events (AEs) during Year 2 of the double-blind period and long-term extension

End point description:

All AEs were coded and grouped into preferred terms (PT) by system organ class (SOC), using the Medical Dictionary for Regulatory Activities (MedDRA, version 21.0). Investigators determined the intensity of each AE as mild, moderate, severe, or very severe and assessed the relationship to study drug.

End point type	Secondary

End point timeframe:

From the first dose in Year 2 of the double-blind period up to 56 days post last dose

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	160		
Units: Participants				
Participants with Adverse Events	127	137		
Participants with Serious Adverse Events	15	25		
Participants with infection Adverse Events	100	107		
Participants with malignancies	0	1		
Participants with autoimmune events	7	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in treatment failure over time during the double-blind period

End point title	Percentage of participants in treatment failure over time during the double-blind period

End point description:

Lupus treatment failure is defined as any of the following: Death, unless due to physical trauma or violence; Renal Flare; sustained doubling of creatinine from baseline (greater of Screening or Study Day 1 value); initiation of rescue therapy for treatment of active lupus nephritis after Study Week 20. Overall treatment failure is defined as lupus treatment failure plus discontinuation of study drug for any reason except death due to physical trauma or violence, pregnancy or administrative decision by Sponsor.

End point type	Secondary

End point timeframe:
Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[38]	203[39]		
Units: Percentage				
number (confidence interval 95%)				
Lupus treatment failure (LTF) - Day 365	3.5 (0.943 to 5.988)	4.4 (1.602 to 7.265)		
Overall treatment failure (OTF) - Day 365	4.5 (1.610 to 7.301)	4.9 (1.949 to 7.903)		
LTF - Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		
OTF - Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:
[38] - Study terminated, efficacy not met
[39] - Study terminated, efficacy not met

Statistical analyses

Statistical analysis title	Percentage participants in treatment failure
Statistical analysis description: Lupus treatment failure - Day 365	
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Estimate of Difference
Point estimate	-0.9682
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.760178
upper limit	2.823876

Statistical analysis title	Percentage participants in treatment failure
Statistical analysis description: Overall treatment failure - Day 365	
Comparison groups	Abatacept IV v Placebo IV
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Estimate of Difference
Point estimate	-0.4707

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.588691
upper limit	3.647365

Secondary: Median Time to First Treatment Failure and Overall Treatment Failure During the Double-blind Period

End point title	Median Time to First Treatment Failure and Overall Treatment Failure During the Double-blind Period

End point description:

First treatment failure (or Lupus treatment failure) is defined as any of the following: Death, unless due to physical trauma or violence; Renal Flare; sustained doubling of creatinine from baseline (greater of Screening or Study Day 1 value); initiation of rescue therapy for treatment of active lupus nephritis after Study Week 20. Overall treatment failure is defined as lupus treatment failure plus discontinuation of study drug for any reason except death due to physical trauma or violence, pregnancy or administrative decision by Sponsor. The hazard ratio is estimated using the Cox proportional hazards model which includes treatment group, stratification variables (baseline ACEis/ARBs use, RACE) and baseline UPCR. The estimate of median time is based on Kaplan-Meier analysis

End point type	Secondary

End point timeframe:

Day 365, Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[40]	203[41]		
Units: Days				
median (confidence interval 95%)				
First treatment failure (FTF) - Day 365	99999 (99999 to 99999)	99999 (99999 to 99999)		
Overall treatment failure (OTF) - Day 365	99999 (99999 to 99999)	99999 (99999 to 99999)		
FTF - Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		
OTF - Day 729	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[40] - Study terminated, efficacy not met

[41] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of nephrotic participants in Complete Renal Response of lupus glomerulonephritis at Day 729 of the double-blind period

End point title	Percentage of nephrotic participants in Complete Renal Response of lupus glomerulonephritis at Day 729 of the double-blind period

End point description:

Number of participants achieving CR was divided by total participants in that arm, expressed as a

percentage. CR is defined the following criteria: eGFR is normal or no <85% of the baseline value; eGFR is based on mean creatinine value from day 358 and 365. Proteinuria: UPCR<0.5 mg/mg. Urine sediment: No cellular casts. Corticosteroid dose: Daily dose must be no >10 mg prednisone or equivalent for at least 28 days prior. Subjects with >10mg/day prednisone or equivalent for non-renal disease within 28 days prior to day 365 will be imputed as CR if the following are true: Met all criteria for CR at day 337 and all criteria for CR except corticosteroid dose at day 365; Investigator confirms increase in steroid dose is not related to renal disease. Adjusted odds ratio is estimated from logistic regression model which includes treatment group, baseline ACEi/ARBs use, race and baseline UPCR as a continuous variable.

End point type	Secondary

End point timeframe:

Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[42]	203[43]		
Units: Percentage				
number (not applicable)	99999	99999		

Notes:

[42] - Study terminated, efficacy not met

[43] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in overall population in Complete Renal Response of lupus glomerulonephritis at Day 729 of the double-blind period

End point title	Percentage of participants in overall population in Complete Renal Response of lupus glomerulonephritis at Day 729 of the double-blind period

End point description:

Number of participants achieving CR was divided by total participants in that arm, expressed as a percentage. CR is defined the following criteria: eGFR is normal or no <85% of the baseline value; eGFR is based on mean creatinine value from day 358 and 365. Proteinuria: UPCR<0.5 mg/mg. Urine sediment: No cellular casts. Corticosteroid dose: Daily dose must be no >10 mg prednisone or equivalent for at least 28 days prior. Subjects with >10mg/day prednisone or equivalent for non-renal disease within 28 days prior to day 365 will be imputed as CR if the following are true: Met all criteria for CR at day 337 and all criteria for CR except corticosteroid dose at day 365; Investigator confirms increase in steroid dose is not related to renal disease. Adjusted odds ratio is estimated from logistic regression model which includes treatment group, baseline ACEi/ARBs use, race and baseline UPCR as a continuous variable.

End point type	Secondary

End point timeframe:

Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[44]	203[45]		
Units: Percentage				
number (not applicable)	99999	99999		

Notes:

[44] - Study terminated, efficacy not met

[45] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Hematology laboratory abnormalities throughout the Double Blind period

End point title	Number of participants with Marked Hematology laboratory abnormalities throughout the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value HEMOGLOBIN g/L 4.0 HB >3 G/DL DECREASE FROM PRE RX HEMATOCRIT vol 6.3 HCT <0.75X PRE RX ERYTHROCYTES x10*12 c/L 5.2 RBC <0.75X PRE RX PLATELET COUNT x10*9 c/L 5.0 PLAT <0.67X LLN OR >1.5X ULN, OR IF PRE RX<LLN THEN USE 0.5X PRE RX AND <100,000/MM3 LEUKOCYTES x10*9 c/L 6.2 WBC <0.75X LLN OR >1.25X ULN, OR IF PRE RX<LLN THEN USE <0.8X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.2X PRE RX OR <LLN EOSINOPHILS (ABSOLUTE) x10*9 c/L 8.3 EOSA IF VALUE > .750 X10*3 c/uL BASOPHILS (ABSOLUTE) x10*9 c/L 8.3 BASOA IF VALUE > 400/MM3 MONOCYTES (ABSOLUTE) x10*9 c/L 8.3 MONOA IF VALUE > 2000/MM3 LYMPHOCYTES (ABSOLUTE) x10*9 c/L 8.3 LYMPA IF VALUE < .750 X10*3 c/uL OR IF VALUE > 7.50 X10*3 c/uL N = the number of participants with at least 1 on treatment lab result for each analyte

End point type	Secondary

End point timeframe:

Day 1 to Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[46]	203[47]		
Units: participants				
HEMOGLOBIN, low	99999	99999		
HEMOGLOBIN, high	99999	99999		
HEMATOCRIT, low	99999	99999		
HEMATOCRIT, high	99999	99999		
ERYTHROCYTES, low	99999	99999		
ERYTHROCYTES, high	99999	99999		
PLATELET COUNT, low	99999	99999		
PLATELET COUNT, high	99999	99999		
LEUKOCYTES, low	99999	99999		
LEUKOCYTES, high	99999	99999		
EOSINOPHILS (ABSOLUTE), low	99999	99999		
EOSINOPHILS (ABSOLUTE), high	99999	99999		
BASOPHILS (ABSOLUTE), low	99999	99999		
BASOPHILS (ABSOLUTE), high	99999	99999		
MONOCYTES (ABSOLUTE), low	99999	99999		

MONOCYTES (ABSOLUTE), high	99999	99999		
LYMPHOCYTES (ABSOLUTE), low	99999	99999		
LYMPHOCYTES (ABSOLUTE), high	99999	99999		

Notes:

[46] - Study terminated, efficacy not met

[47] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Liver and Kidney Function Laboratory Abnormalities throughout the Double Blind period

End point title	Number of participants with Marked Liver and Kidney Function Laboratory Abnormalities throughout the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value ALKALINE PHOSPHATASE (ALP) U/L 5.0 ALP >2X ULN, OR IF PRE RX>ULN THEN USE >3X PRE RX ASPARTATE AMINOTRANSFERASE (AST) U/L 5.0 AST >3X ULN, OR IF PRE RX>ULN THEN USE >4X PRE RX ALANINE AMINOTRANSFERASE (ALT) U/L 5.0 ALT >3X ULN, OR IF PRE RX>ULN THEN USE >4X PRE RX G-GLUTAMYL TRANSFERASE (GGT) U/L 5.0 GGT >2X ULN, OR IF PRE RX>ULN THEN USE >3X PRE RX BILIRUBIN, TOTAL umol/L 5.1 TBILI >2X ULN, OR IF PRE RX>ULN THEN USE >4X PRE RX BILIRUBIN, DIRECT umol/L 5.1 DBILI >1.5X ULN, OR IF PRE RX>ULN THEN USE >2X PRE RX BLOOD UREA NITROGEN mmol/L 5.1 BUN >2X PRE RX CREATININE umol/L 5.0 CREAT >1.5X PRE RX N = the number of participants with at least 1 on treatment lab result for each analyte

End point type	Secondary

End point timeframe:

Day 1 to Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[48]	203[49]		
Units: participants				
ALKALINE PHOSPHATASE (ALP), low	99999	99999		
ALKALINE PHOSPHATASE (ALP), high	99999	99999		
ASPARTATE AMINOTRANSFERASE (AST), low	99999	99999		
ASPARTATE AMINOTRANSFERASE (AST), high	99999	99999		
ALANINE AMINOTRANSFERASE (ALT), low	99999	99999		
ALANINE AMINOTRANSFERASE (ALT), high	99999	99999		
G-GLUTAMYL TRANSFERASE (GGT), low	99999	99999		
G-GLUTAMYL TRANSFERASE (GGT), high	99999	99999		
BILIRUBIN, TOTAL, low	99999	99999		
BILIRUBIN, TOTAL, high	99999	99999		
BILIRUBIN, DIRECT, low	99999	99999		
BILIRUBIN, DIRECT, high	99999	99999		
BLOOD UREA NITROGEN, low	99999	99999		
BLOOD UREA NITROGEN, high	99999	99999		
CREATININE, low	99999	99999		

CREATININE, high	99999	99999		

Notes:

[48] - Study terminated, efficacy not met

[49] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Electrolyte Laboratory Abnormalities throughout the Double Blind period

End point title	Number of participants with Marked Electrolyte Laboratory Abnormalities throughout the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value SODIUM, SERUM mmol/L 4.0 NA <0.95X LLN OR >1.05X ULN, OR IF PRE RX<LLN THEN USE <0.95X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.05X PRE RX OR <LLN POTASSIUM, SERUM mmol/L 4.1 K <0.9X LLN OR >1.1X ULN, OR IF PRE RX<LLN THEN USE <0.9X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.1X PRE RX OR <LLN CHLORIDE, SERUM mmol/L 5.0 CL <0.9X LLN OR >1.1X ULN, OR IF PRE RX<LLN THEN USE <0.9X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.1X PRE RX OR <LLN N = the number of participants with at least 1 on treatment lab result for each analyte

End point type	Secondary

End point timeframe:

Day 1 to Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[50]	203[51]		
Units: participants				
SODIUM, SERUM, low	99999	99999		
SODIUM, SERUM, high	99999	99999		
POTASSIUM, SERUM, low	99999	99999		
POTASSIUM, SERUM, high	99999	99999		
CHLORIDE, SERUM, low	99999	99999		
CHLORIDE, SERUM, high	99999	99999		
CALCIUM, TOTAL, low	99999	99999		
CALCIUM, TOTAL, high	99999	99999		
PHOSPHORUS, INORGANIC, low	99999	99999		
PHOSPHORUS, INORGANIC, high	99999	99999		

Notes:

[50] - Study terminated, efficacy not met

[51] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Marked Urinalysis Laboratory Abnormalities throughout the Double Blind period

End point title	Number of participants with Marked Urinalysis Laboratory Abnormalities throughout the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value PROTEIN, URINE Unknown UPRO IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4 GLUCOSE, URINE N/A UGLU IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4 BLOOD, URINE N/A UBLD IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4 RBC, URINE hpf 5.0 URBC IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4 WBC, URINE hpf 5.0 UWBC IF MISSING PRE THEN USE >=2, OR IF VALUE >=4, OR IF PRE RX =0 OR 0.5 THEN USE >=2, OR IF PRE RX =1 THEN USE >=3, OR IF PRE RX =2 OR 3 THEN USE >=4

End point type	Secondary

End point timeframe:

Day 1 to Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[52]	203[53]		
Units: participants				
PROTEIN, URINE, low	99999	99999		
PROTEIN, URINE, high	99999	99999		
GLUCOSE, URINE, low	99999	99999		
GLUCOSE, URINE, high	99999	99999		
BLOOD, URINE, low	99999	99999		
BLOOD, URINE, high	99999	99999		
Red blood cells (RBC), URINE, low	99999	99999		
Red blood cells (RBC), URINE, high	99999	99999		
White blood cells (WBC), URINE, low	99999	99999		
White blood cells (WBC), URINE, high	99999	99999		

Notes:

[52] - Study terminated, efficacy not met

[53] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with other Marked Chemistry Laboratory Abnormalities throughout the Double Blind period

End point title	Number of participants with other Marked Chemistry Laboratory Abnormalities throughout the Double Blind period

End point description:

LLN= Lower limit of normals ULN= Upper limit of normals Pre RX = Baseline value CALCIUM, TOTAL mmol/L 5.2 CA <0.8X LLN OR >1.2X ULN, OR IF PRE RX<LLN THEN USE <0.75X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE >1.25X PRE RX OR <LLN PHOSPHORUS, INORGANIC mmol/L 5.2 PHOS <0.75X LLN OR >1.25X ULN, OR IF PRE RX<LLN THEN USE <0.67X PRE RX OR >ULN GLUCOSE, SERUM mmol/L 4.1 GLUC <65 mg/dL, OR >220 mg/dL PROTEIN, TOTAL g/L 5.0 TPRO <0.9X LLN OR >1.1X ULN, OR IF PRE RX<LLN THEN USE 0.9X PRE RX OR >ULN, OR IF PRE RX>ULN THEN USE 1.1X PRE RX OR <LLN ALBUMIN g/L 3.0 ALB <0.9X LLN, OR IF PRE RX<LLN THEN USE <0.75X PRE RX CHOLESTEROL, TOTAL (TC) mmol/L 5.2 CHOL >2X PRE R N = the number of participants with at least 1 on treatment lab result for each analyte

End point type	Secondary

End point timeframe:

Day 1 to Day 729

End point values	Abatacept IV	Placebo IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202[54]	203[55]		
Units: participants				
GLUCOSE, SERUM, low	99999	99999		
GLUCOSE, SERUM, high	99999	99999		
PROTEIN, TOTAL, low	99999	99999		
PROTEIN, TOTAL, high	99999	99999		
ALBUMIN, low	99999	99999		
ALBUMIN, high	99999	99999		

Notes:

[54] - Study terminated, efficacy not met

[55] - Study terminated, efficacy not met

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Day 1 up to 56 days post last dose (assessed up to May 2018, approximately 66 months)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	Placebo IV
Reporting group description: Placebo IV	
Reporting group title	Abatacept IV
Reporting group description: Abatacept IV	

Serious adverse events	Placebo IV	Abatacept IV	
Total subjects affected by serious adverse events			
subjects affected / exposed	63 / 203 (31.03%)	64 / 202 (31.68%)	
number of deaths (all causes)	7	7	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypergammaglobulinaemia benign monoclonal			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of conjunctiva			

subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelofibrosis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Naevus lipomatosus cutaneous superficialis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seborrhoeic keratosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vasculitis			

subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 203 (0.00%)	3 / 202 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	3 / 203 (1.48%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Oedema peripheral			
subjects affected / exposed	1 / 203 (0.49%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Serositis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
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 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	2 / 203 (0.99%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenomyosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 203 (0.49%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			

subjects affected / exposed	2 / 203 (0.99%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 203 (0.00%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	2 / 2	
Pleuritic pain			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychogenic seizure			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance-Induced psychotic disorder			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gamma-Glutamyltransferase increased			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 203 (0.49%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			

subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Lupus myocarditis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			

subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 203 (0.00%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic intracranial hypertension			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus encephalitis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory loss			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (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	3 / 203 (1.48%)	3 / 202 (1.49%)	
occurrences causally related to treatment / all	2 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of chronic disease			

subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histiocytosis haematophagic			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 203 (0.99%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain upper			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	2 / 203 (0.99%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Intussusception			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal cyst			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 203 (0.99%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Azotaemia			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus nephritis			
subjects affected / exposed	3 / 203 (1.48%)	4 / 202 (1.98%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal failure			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			

subjects affected / exposed	2 / 203 (0.99%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	5 / 203 (2.46%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	2 / 203 (0.99%)	4 / 202 (1.98%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	1 / 203 (0.49%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated tuberculosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	0 / 203 (0.00%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 203 (0.99%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital herpes			
subjects affected / exposed	0 / 203 (0.00%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	5 / 203 (2.46%)	5 / 202 (2.48%)	
occurrences causally related to treatment / all	3 / 5	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Lung infection			
subjects affected / exposed	0 / 203 (0.00%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			

subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 203 (0.00%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 203 (2.96%)	17 / 202 (8.42%)	
occurrences causally related to treatment / all	2 / 6	13 / 17	
deaths causally related to treatment / all	0 / 1	3 / 3	
Pyelonephritis			
subjects affected / exposed	2 / 203 (0.99%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonella bacteraemia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 203 (0.49%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	1 / 203 (0.49%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Sinusitis			
subjects affected / exposed	1 / 203 (0.49%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxoplasmosis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous pleurisy			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 203 (0.49%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	4 / 203 (1.97%)	2 / 202 (0.99%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspergillus infection			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella zoster virus infection			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval abscess			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 202 (0.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 202 (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	Placebo IV	Abatacept IV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	183 / 203 (90.15%)	167 / 202 (82.67%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 203 (6.40%)	7 / 202 (3.47%)	
occurrences (all)	14	7	
Hypotension			
subjects affected / exposed	13 / 203 (6.40%)	5 / 202 (2.48%)	
occurrences (all)	14	6	
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 203 (2.96%)	12 / 202 (5.94%)	
occurrences (all)	7	13	
Headache			
subjects affected / exposed	23 / 203 (11.33%)	26 / 202 (12.87%)	
occurrences (all)	61	35	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	25 / 203 (12.32%)	22 / 202 (10.89%)	
occurrences (all)	28	25	
General disorders and administration			

site conditions			
Oedema peripheral			
subjects affected / exposed	14 / 203 (6.90%)	17 / 202 (8.42%)	
occurrences (all)	17	19	
Pyrexia			
subjects affected / exposed	13 / 203 (6.40%)	9 / 202 (4.46%)	
occurrences (all)	15	10	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	15 / 203 (7.39%)	9 / 202 (4.46%)	
occurrences (all)	16	10	
Diarrhoea			
subjects affected / exposed	51 / 203 (25.12%)	49 / 202 (24.26%)	
occurrences (all)	64	85	
Nausea			
subjects affected / exposed	17 / 203 (8.37%)	16 / 202 (7.92%)	
occurrences (all)	25	21	
Vomiting			
subjects affected / exposed	7 / 203 (3.45%)	13 / 202 (6.44%)	
occurrences (all)	8	17	
Dental caries			
subjects affected / exposed	4 / 203 (1.97%)	11 / 202 (5.45%)	
occurrences (all)	7	13	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	27 / 203 (13.30%)	26 / 202 (12.87%)	
occurrences (all)	34	32	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	11 / 203 (5.42%)	13 / 202 (6.44%)	
occurrences (all)	14	17	
Rash			
subjects affected / exposed	20 / 203 (9.85%)	14 / 202 (6.93%)	
occurrences (all)	26	18	
Psychiatric disorders			

Insomnia			
subjects affected / exposed	20 / 203 (9.85%)	15 / 202 (7.43%)	
occurrences (all)	20	16	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	20 / 203 (9.85%)	24 / 202 (11.88%)	
occurrences (all)	25	29	
Back pain			
subjects affected / exposed	19 / 203 (9.36%)	12 / 202 (5.94%)	
occurrences (all)	23	13	
Osteonecrosis			
subjects affected / exposed	11 / 203 (5.42%)	2 / 202 (0.99%)	
occurrences (all)	13	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	27 / 203 (13.30%)	21 / 202 (10.40%)	
occurrences (all)	35	24	
Conjunctivitis			
subjects affected / exposed	16 / 203 (7.88%)	15 / 202 (7.43%)	
occurrences (all)	17	17	
Gastroenteritis			
subjects affected / exposed	17 / 203 (8.37%)	13 / 202 (6.44%)	
occurrences (all)	18	17	
Herpes zoster			
subjects affected / exposed	18 / 203 (8.87%)	21 / 202 (10.40%)	
occurrences (all)	19	22	
Influenza			
subjects affected / exposed	11 / 203 (5.42%)	14 / 202 (6.93%)	
occurrences (all)	15	17	
Nasopharyngitis			
subjects affected / exposed	46 / 203 (22.66%)	45 / 202 (22.28%)	
occurrences (all)	104	79	
Pharyngitis			
subjects affected / exposed	26 / 203 (12.81%)	21 / 202 (10.40%)	
occurrences (all)	35	30	
Upper respiratory tract infection			

subjects affected / exposed	44 / 203 (21.67%)	43 / 202 (21.29%)	
occurrences (all)	88	85	
Urinary tract infection			
subjects affected / exposed	42 / 203 (20.69%)	46 / 202 (22.77%)	
occurrences (all)	70	77	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 June 2014	The primary purpose of this amendment is to revise and clarify the eligibility criteria and study assessments, clarify dosing of background medications, provide updated references and appendices and clarify protocol language to ensure consistency within the protocol.
27 March 2015	The primary purpose of this amendment is to identify key secondary objectives and to add a 52 week long-term extension to expand the observations of the effects of continued treatment with mycophenolic mofetil (MMF) with or without abatacept on the maintenance of renal response in subjects after 2 years of treatment of active Class III or Class IV lupus nephritis (LN). During this period, adjustment to treatment will be allowed including reduction of the MMF dose and switching from IV abatacept to subcutaneous (SC) abatacept.
06 April 2016	The main purpose of this amendment is to provide a mechanism for supply of study drug (MMF and abatacept/placebo) for study subjects who continue to derive benefit by extending the study past the Long-Term Extension (LTE).
19 April 2017	Provides clarification on the duration of Group C (MPE) and procedures to be performed during the MPE; updates Appendix 5 with the correct version of SF-36 used in the study; updates the Medical Monitor contact information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 May 2018	This study was terminated prematurely by the sponsor after the primary analysis failed to show a statistical significant treatment difference in the primary endpoint, and analyses of secondary and other efficacy endpoints failed to demonstrate clinically meaningful differences between the abatacept and placebo groups.	-

Notes:

Limitations and caveats

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

Study terminated early after review of Year 1 data. At unblinding most participants had completed Year 2 and many entered LTE. Only Year 2/LTE data captured within blind was analyzed. Some post-Year 1 outcomes not calculated due to early termination.

Notes: