Clinical trial results:
A Phase 3, Randomized, Double-Blind Clinical Trial to Evaluate the Efficacy and Safety of Abatacept SC with Standard Treatment Compared to Standard Treatment Alone in Improving Disease Activity in Adults with Active Idiopathic Inflammatory Myopathy (IIM)

Summary

EudraCT number	2016-002269-77
Trial protocol	DE CZ SE FR IT
Global end of trial date	02 August 2022

Results information

Result version number	v2 (current)
This version publication date	01 October 2023
First version publication date	17 August 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	IM101-611

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	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	22 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective for this study is to compare the clinical efficacy of weekly abatacept in combination with standard treatment to standard treatment alone by assessing the percentage of subjects who achieve the IMACS DOI by Week 24 compared to baseline, defined as:
- An improvement of >/= 20% in 3 IMACS core measures, AND
- No more than 2 IMACS core measure scores worsen by >/= 25%, AND
- Manual Muscle Test (MMT-8) may not decrease by >/= 25%

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 participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 May 2017
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	Brazil: 24
Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Japan: 21
Country: Number of subjects enrolled	Korea, Republic of: 15
Country: Number of subjects enrolled	Mexico: 20
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United States: 48
Worldwide total number of subjects	148
EEA total number of subjects	20

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	133
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

148 were randomized and treated

Period 1

Period 1 title	Double-Blind Period (24 weeks)
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 + Standard Treatment

Arm description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

Arm title	Placebo + Standard Treatment

Arm description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo to match abatacept SC in 1 ml pre-filled syringes

Number of subjects in period 1	Abatacept + Standard Treatment	Placebo + Standard Treatment
Started	75	73
Completed	69	65
Not completed	6	8
Poor/Non-Compliance	-	1
Participant withdrew consent	1	1
Adverse event, non-fatal	-	2
Participant no longer meets study criteria	1	-
Other reasons	-	1
Lost to follow-up	1	-
Participant request to discontinue study treatment	1	1
Lack of efficacy	2	2

Period 2

Period 2 title	Open-Label (OL) Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Abatacept + Standard Treatment

Arm description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

Arm title	Placebo + Standard Treatment

Arm description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.

Arm type	Experimental

Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

Number of subjects in period 2[1]	Abatacept + Standard Treatment	Placebo + Standard Treatment
Started	69	63
Completed	65	61
Not completed	4	2
Lost to follow-up	1	-
Participants withdrew consent	-	2
Participant request to discontinue study treatment	1	-
Lack of efficacy	2	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the preceding period moved onto the next period.

Period 3

Period 3 title	Long-Term Open Label
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Abatacept + Standard Treatment

Arm description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

Arm title	Placebo + Standard Treatment

Arm description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo

to abatacept in the Open-Label and Long-Term Open Label Periods.

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Abatacept SC 125 mg in 1 ml pre-filled syringes

Number of subjects in period 3[2]	Abatacept + Standard Treatment	Placebo + Standard Treatment
Started	25	21
Completed	1	0
Not completed	24	21
Participant withdrew consent	1	-
Adverse event, non-fatal	1	2
Administrative reason by sponsor	20	17
Participant request to discontinue study treatment	1	1
Lack of efficacy	1	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants who completed the preceding period moved onto the next period.

Baseline characteristics

Reporting groups	
Reporting group title	Abatacept + Standard Treatment
Reporting group description:	
Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.	
Reporting group title	Placebo + Standard Treatment
Reporting group description:	
Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.	

Reporting group values	Abatacept + Standard Treatment	Placebo + Standard Treatment	Total
Number of subjects	75	73	148
Age Categorical Units: Participants			
16-29 years old	9	9	18
30-39 years old	8	14	22
40-49 years old	14	14	28
50-59 years old	31	19	50
>/= 60 years old	13	17	30
Age Continuous Units: Years			
arithmetic mean	49.3	48.1	
standard deviation	± 14.41	± 14.09	-
Sex: Female, Male Units: Participants			
Female	52	54	106
Male	23	19	42
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7	3	10
Not Hispanic or Latino	19	19	38
Unknown or Not Reported	49	51	100
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	3	3	6
Asian	10	6	16
Black or African American	9	8	17
White	42	42	84
Japanese	11	10	21
Other	0	3	3
Unknown	0	1	1

End points

End points reporting groups

Reporting group title	Abatacept + Standard Treatment

Reporting group description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

Reporting group title	Placebo + Standard Treatment

Reporting group description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.

Reporting group title	Abatacept + Standard Treatment

Reporting group description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

Reporting group title	Placebo + Standard Treatment

Reporting group description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.

Reporting group title	Abatacept + Standard Treatment

Reporting group description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants continue to receive abatacept in the Open-Label and Long-Term Open Label Periods.

Reporting group title	Placebo + Standard Treatment

Reporting group description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment for the first 24 weeks (6 months) during the double-blind period. Participants then switch from placebo to abatacept in the Open-Label and Long-Term Open Label Periods.

Primary: Number of Participants Achieving International Myositis Assessment and Clinical Studies Definition of Improvement (IMACS DOI) at Week 24 Without Rescue

End point title	Number of Participants Achieving International Myositis Assessment and Clinical Studies Definition of Improvement (IMACS DOI) at Week 24 Without Rescue

End point description:

The number of participants who achieve IMACS DOI (International Myositis Assessment and Clinical Studies definition of improvement) without rescue medication at week 24.

The IMACS DOI is: An improvement of >/= 20% from baseline in 3 IMACS core measures, no more than 2 IMACS core measure scores worsen by >/= 25% from baseline, and no more than 2 IMACS core measure scores worsen by >/= 25% from baseline.

IMACS core measures are: Physician Global Assessment of Disease Activity (PGA), Patient (Subject) Global Assessment of Disease Activity (SGA), Manual Muscle Test (MMT-8), Health Assessment Questionnaire-Disability Index (HAQ-DI), Muscle Enzyme levels, Myositis Disease Activity Assessment Tool (MDAAT) Extramuscular Global Activity.

End point type	Primary

End point timeframe:

From first dose to 24 weeks after first dose. (Approximately 169 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	73		
Units: Participants	42	31		

Statistical analyses

Statistical analysis title	IMACs DOI at week 24
Comparison groups	Abatacept + Standard Treatment v Placebo + Standard Treatment
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.083
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	3.5

Secondary: Mean change in Health Assessment Questionnaire-Disability Index (HAQ-DI) from baseline to Week 24

End point title	Mean change in Health Assessment Questionnaire-Disability Index (HAQ-DI) from baseline to Week 24

End point description:

The adjusted mean change from baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI). HAQ-DI is a patient-reported outcome measuring disability by asking a total of 20 questions in eight categories of function: dressing, arising, eating, walking, hygiene, reach, grip, and activities. If an aid or device is used or if help is required from another individual, then the minimum score for that section is 2. The highest component score in each category determines the score for the category and scores are averaged to give the disability index. The HAQ scale ranges from 0 (no difficulties) to 3 (unable to do).

End point type	Secondary

End point timeframe:

From first dose to 24 weeks after first dose. (Approximately 169 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	62		
Units: Score on a scale				
arithmetic mean (standard error)	-0.31 (± 0.067)	-0.20 (± 0.069)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in Muscle Endurance Using the Myositis Function Index (FI-2) from Baseline to Week 24

End point title	Mean Change in Muscle Endurance Using the Myositis Function Index (FI-2) from Baseline to Week 24

End point description:

The adjusted mean change from baseline in Myositis FI-2 scores is assessing muscle endurance impairment by testing specific muscle groups. The 3 Score average includes shoulder flexion, hip flexion, and head lift. Each muscle group is scored as the number of correctly performed repetitions with 60 maximal number of repetitions.

The total score is based on hip flexion, shoulder flexion (R/L) and neck divided by 3 (range 0-60 repetitions).

End point type	Secondary

End point timeframe:

From first dose to 24 weeks after first dose. (Approximately 169 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	58		
Units: Number of repetitions				
arithmetic mean (standard error)	4.1 (± 1.33)	1.2 (± 1.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in Myositis Disease Activity Assessment Tool (MDAAT) assessment of extra-muscular from baseline to Week 24

End point title	Mean change in Myositis Disease Activity Assessment Tool (MDAAT) assessment of extra-muscular from baseline to Week 24

End point description:

The adjusted mean change from baseline in the Myositis Disease Activity Assessment Tool (MDAAT) assessment of extra-muscular uses a 100 mm Visual Analog Scale (VAS) scale. This VAS assesses the

overall extra-muscular clinical features based upon: 1) The presence of clinical features or symptoms within the previous 4 weeks that are due to active disease. 2) The judgment that the feature is due to the myositis disease process. 3) The concept that disease activity is defined as a potentially reversible finding. 4) A clinical, functional, and laboratory assessments.

The scoring is performed by the investigator and ranges from 0 (absent extra-muscular disease activity) to 100 (maximum extra-muscular disease activity).

End point type	Secondary

End point timeframe:

From first dose to 24 weeks after first dose. (Approximately 169 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	60		
Units: Score on a scale				
arithmetic mean (standard error)	-1.56 (± 0.202)	-1.40 (± 0.208)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events (AE) in the Double-Blind Period

End point title	Number of Participants Experiencing Adverse Events (AE) in the Double-Blind Period

End point description:

The number of treated participants experiencing an adverse event. An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in participants administered a study drug and that does not necessarily have a causal relationship with the treatment.

End point type	Secondary

End point timeframe:

From first dose up to approximately 56 days post last dose date in double-blind period or first dose in open-label period. (Up to approximately 274 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	73		
Units: Participants	52	55		

Statistical analyses

No statistical analyses for this end point

Secondary: Myositis Response Criteria (MRC) Total Improvement Score From Baseline to Week 24

End point title	Myositis Response Criteria (MRC) Total Improvement Score From Baseline to Week 24

End point description:

The Myositis Response Criteria (MRC) is a continuous total improvement score from baseline (range 0-100) based on the sum of the absolute percent change in the 6 core domains (weighted) used in the IMACS DOI (International Myositis Assessment and Clinical Studies definition of improvement)

IMACS core measures are: Physician Global Assessment of Disease Activity (PGA), Patient (Subject) Global Assessment of Disease Activity (SGA), Manual Muscle Test (MMT-8), Health Assessment Questionnaire-Disability Index (HAQ-DI), Muscle Enzyme levels, Myositis Disease Activity Assessment Tool (MDAAT) Extramuscular Global Activity.

The total improvement score ranges between 0 and 100 percent corresponds to the degree of improvement, with higher scores corresponding to a greater degree of improvement (>/= 20 represents minimal improvement, a score of >/= 40 represents moderate improvement, and a score of >/= 60 represents major improvement).

End point type	Secondary

End point timeframe:

From first dose to 24 weeks after first dose. (Approximately 169 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	58		
Units: Score on a scale				
arithmetic mean (standard error)	40.83 (± 2.873)	37.22 (± 2.963)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Serious Adverse Events (SAE) in the Double-Blind Period

End point title	Number of Participants Experiencing Serious Adverse Events (SAE) in the Double-Blind Period

End point description:

The number of treated participants experiencing a Serious Adverse Event (SAE). A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event.

End point type	Secondary

End point timeframe:

From first dose up to approximately 56 days post last dose date in double-blind period or first dose in open-label period. (Up to approximately 274 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	73		
Units: Participants	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events (AE) of Special Interest in the Double-Blind Period

End point title	Number of Participants Experiencing Adverse Events (AE) of Special Interest in the Double-Blind Period

End point description:

The number of treated participants experiencing adverse events of special interest: infections, malignancies, autoimmune events, local injection site reactions, and systemic injection reactions.

End point type	Secondary

End point timeframe:

From first dose up to approximately 56 days post last dose date in double-blind period or first dose in open-label period. (Up to approximately 274 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	73		
Units: Participants				
Infections	19	31		
Malignancies	0	0		
Autoimmune Disorders	2	3		
Systemic Injection Reactions	4	5		
Local Injection Site Reactions	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Laboratory Test Abnormalities in the Double-Blind Period

End point title	Number of Participants Experiencing Laboratory Test Abnormalities in the Double-Blind Period

End point description:

The number of participants experiencing laboratory test abnormalities. Laboratory analysis was performed on the following: hematology, liver and kidney function, electrolytes, other chemistry testing (glucose, protein, cardiac), and urine chemistry. Only tests with participants experiencing abnormalities were reported.

End point type	Secondary

End point timeframe:

From first dose up to approximately 56 days post last dose date in double-blind period or first dose in open-label period. (Up to approximately 274 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	73		
Units: Participants				
LOW LEUKOCYTES	1	0		
HIGH LEUKOCYTES	2	4		
HIGH EOSINOPHILS (ABSOLUTE)	3	2		
LOW LYMPHOCYTES (ABSOLUTE)	17	14		
LOW NEUTROPHILS + BANDS (ABSOLUTE)	1	0		
HIGH ALANINE AMINOTRANSFERASE (ALT)	1	1		
HIGH ASPARTATE AMINOTRANSFERASE (AST)	0	1		
HIGH G-GLUTAMYL TRANSFERASE (GGT)	4	1		
HIGH BLOOD UREA NITROGEN	0	1		
HIGH CREATININE	3	3		
HIGH CALCIUM, TOTAL	1	0		
LOW PHOSPHORUS, INORGANIC	0	1		
HIGH PHOSPHORUS, INORGANIC	1	0		
HIGH SODIUM, SERUM	0	1		
LOW GLUCOSE, SERUM	4	3		
HIGH GLUCOSE, SERUM	8	8		
HIGH PROTEIN, TOTAL	0	1		
HIGH CREATINE KINASE (CK)	0	4		
HIGH LACTATE DEHYDROGENASE (LD)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events (AE) in the Cumulative Abatacept Period

End point title	Number of Participants Experiencing Adverse Events (AE) in the Cumulative Abatacept Period

End point description:

The number of treated participants experiencing an adverse event. An Adverse Event (AE) is defined as

any new untoward medical occurrence or worsening of a preexisting medical condition in participants administered a study drug and that does not necessarily have a causal relationship with the treatment.

End point type	Secondary

End point timeframe:

From first dose up to approximately 56 days post last dose (up to approximately 54 months)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	63		
Units: Participants	64	39		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Serious Adverse Events (SAE) in the Cumulative Abatacept Period

End point title	Number of Participants Experiencing Serious Adverse Events (SAE) in the Cumulative Abatacept Period

End point description:

The number of treated participants experiencing a Serious Adverse Event (SAE). A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or causes prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event.

End point type	Secondary

End point timeframe:

From first dose up to approximately 56 days post last dose (up to approximately 54 months)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	63		
Units: Participants	14	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events (AE) of Special Interest in the Cumulative Abatacept Period

End point title	Number of Participants Experiencing Adverse Events (AE) of Special Interest in the Cumulative Abatacept Period

End point description:

The number of treated participants experiencing adverse events of special interest: infections, malignancies, autoimmune events, local injection site reactions, and systemic injection reactions.

End point type	Secondary

End point timeframe:

From first dose up to approximately 56 days post last dose (up to approximately 54 months)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	63		
Units: Participants				
Infections and infestations	34	19		
Malignancies	0	0		
Autoimmune Disorders	5	4		
Systemic Injection Reactions	5	3		
Local Injection Site Reactions	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Laboratory Test Abnormalities in the Open-Label Period

End point title	Number of Participants Experiencing Laboratory Test Abnormalities in the Open-Label Period

End point description:

The number of participants experiencing laboratory test abnormalities. Laboratory analysis was performed on the following: hematology, liver and kidney function, electrolytes, other chemistry testing (glucose, protein, cardiac), and urine chemistry. Only tests with participants experiencing abnormalities were reported. For participants who enter the Japan open-label extension period or long-term extension period, assessments after the first dose in the open-label period and before the first dose date in the subsequent period are included. For participants who prematurely discontinue the open-label period or complete the open-label period but do not enter the Japan open-label extension period or long-term term extension period, assessments after the first dose in the open-label period and up to 56 days post last dose are included. 99999 = N/A - no participants had laboratory reports for this analyte.

End point type	Secondary

End point timeframe:

From first dose in open label period to first dose date in the subsequent period or up to 56 days post last dose (up to approximately 666 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	63		
Units: Participants				
LOW HEMOGLOBIN	0	1		
LOW LEUKOCYTES	2	1		
HIGH LEUKOCYTES	2	0		
HIGH EOSINOPHILS (ABSOLUTE)	2	0		
LOW LYMPHOCYTES (ABSOLUTE)	15	8		
HIGH LYMPHOCYTES (ABSOLUTE)	1	0		
LOW NEUTROPHILS + BANDS (ABSOLUTE)	2	0		
HIGH ALANINE AMINOTRANSFERASE (ALT)	1	0		
HIGH ALKALINE PHOSPHATASE (ALP)	0	2		
HIGH ASPARTATE AMINOTRANSFERASE (AST)	0	1		
HIGH G-GLUTAMYL TRANSFERASE (GGT)	2	1		
HIGH BLOOD UREA NITROGEN	2	1		
HIGH CREATININE	6	2		
HIGH POTASSIUM, SERUM	1	0		
LOW GLUCOSE, SERUM	1	1		
HIGH GLUCOSE, SERUM	3	3		
LOW ALBUMIN	0	1		
HIGH CREATINE KINASE (CK)	3	5		
HIGH LACTATE DEHYDROGENASE (LD)	0	1		
HIGH BLOOD, URINE Abatacept Arm-n=2	2	99999		
HIGH WBC, URINE Abatacept Arm n=1	1	99999		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Laboratory Test Abnormalities in the Long-Term Open Label Period

End point title	Number of Participants Experiencing Laboratory Test Abnormalities in the Long-Term Open Label Period

End point description:

The number of participants experiencing laboratory test abnormalities. Laboratory analysis was performed on the following: hematology, liver and kidney function, electrolytes, other chemistry testing (glucose, protein, cardiac), and urine chemistry. Only tests with participants experiencing abnormalities were reported. For participants who completed/discontinued the Long-Term Extension Period, assessments after the first dose in the Long-Term Extension Period and up to 56 days post last dose in the Long-Term Extension Period are included.

End point type	Secondary

End point timeframe:

From first dose in the Long-Term Open Label Period up to 56 days post last dose in the Long-Term Open Label Period (up to approximately 958 days)

End point values	Abatacept + Standard Treatment	Placebo + Standard Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	21		
Units: Participants				
LOW HEMOGLOBIN	1	0		
LOW LYMPHOCYTES (ABSOLUTE)	1	4		
HIGH BLOOD UREA NITROGEN	2	0		
HIGH CREATININE	2	1		
HIGH GLUCOSE, SERUM	1	0		
HIGH CREATINE KINASE (CK)	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality was assessed from participants first dose to their study completion (up to approximately 55 months) SAEs and Other AEs were assessed from first dose to 100 days following last dose (up to approximately 55 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Abatacept + Standard Treatment

Reporting group description:

Participants receive subcutaneous abatacept (125 mg weekly) in combination with standard treatment during the cumulative abatacept period.

Reporting group title	Placebo + Standard Treatment

Reporting group description:

Participants receive placebo (to match subcutaneous abatacept) in combination with standard treatment during the double-blind period.

Serious adverse events	Abatacept + Standard Treatment	Placebo + Standard Treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 138 (15.94%)	5 / 73 (6.85%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoproliferative disorder			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Influenza like illness			

subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (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			
Pulmonary fibrosis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 138 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Obsessive-compulsive disorder			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (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			
Spinal compression fracture			
subjects affected / exposed	2 / 138 (1.45%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Comminuted fracture			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	2 / 138 (1.45%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 138 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyositis			
subjects affected / exposed	2 / 138 (1.45%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 138 (0.72%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 138 (2.17%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	2 / 138 (1.45%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 138 (0.72%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 73 (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	Abatacept + Standard Treatment	Placebo + Standard Treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 138 (22.46%)	23 / 73 (31.51%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 138 (2.90%)	4 / 73 (5.48%)	
occurrences (all)	5	5	
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 138 (5.07%)	1 / 73 (1.37%)	
occurrences (all)	7	1	

Nervous system disorders Headache subjects affected / exposed occurrences (all)	8 / 138 (5.80%) 12	7 / 73 (9.59%) 7	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	7 / 138 (5.07%) 7	2 / 73 (2.74%) 2	
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 138 (2.17%) 3 9 / 138 (6.52%) 14	6 / 73 (8.22%) 6 8 / 73 (10.96%) 8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 2017	Clarifies the target population (Inclusion/Exclusion criteria), randomization stratification criteria, exploratory endpoints, study procedures and sub-studies, training requirements for site staff, the process for adjudication, the duration of samples retention for additional research and the duration of post drug follow-up.
09 May 2018	Clarifies language and allowable concomitant medication and adjusts criteria to improve subject selection.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported