ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 03/11/2016

ClinicalTrials.gov ID: NCT00624338

Study Identification

Unique Protocol ID:	27646
Brief Title:	Atacicept Phase 2/3 in Generalized Systemic Lupus Erythematosus (APRIL-SLE)
Official Title:	A Randomised, Double-blind, Placebo Controlled, Multicentre Prospective Dose-finding Phase II/III Study With Atacicept Given Subcutaneously to Subjects Having Recently Experienced a Flare of Systemic Lupus Erythematosus (SLE)
Secondary IDs:	

Study Status

Record Verification:	March 2016
Overall Status:	Completed
Study Start:	January 2008
Primary Completion:	April 2012 [Actual]
Study Completion:	October 2012 [Actual]

Sponsor/Collaborators

Sponsor:	EMD Serono
Responsible Party:	Sponsor
Collaborators:	Merck KGaA

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes

	Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 11584 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 20-Nov-07 Board Name: Coast Institutional Review Board Board Affiliation: U.S. Institutional Review Board Phone: 719-325-8817 Email: srego@coastirb.com
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This study is to evaluate the efficacy and safety of atacicept compared to placebo in preventing new flares in subjects with systemic lupus erythematosus (SLE) and to confirm the optimal dose of atacicept for treatment of subjects with SLE and gain information on the effect of atacicept on markers specific to its mechanism of action (MoA) and their correlation to disease activity/progression. Study medication will be administered through subcutaneous (under the skin) injections, beginning with twice weekly injections for the first 4 weeks, followed by once weekly doses for 48 weeks. Following the last treatment, a safety follow-up period of 24 weeks will be conducted.
Detailed Description:	

Conditions

Conditions:	Lupus Erythematosus, Systemic
Keywords:	Atacicept 75 and 150 mg Placebo

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2/Phase 3

Intervention Model:	Parallel Assignment
Number of Arms:	3
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	461 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Atacicept 75 mg	Drug: Atacicept 75 mg 75 milligram (mg) atacicept injection will be administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Experimental: Atacicept 150 mg	Drug: Atacicept 150 mg 150 mg atacicept injection will be administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo Comparator: Placebo	Placebo Comparator Placebo matched to atacicept injection will be administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	16 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Male or female 16 years of age or older

- Disease history of at least six months meeting at least 4 out of the 11 American College of Rheumatology (ACR) criteria for SLE
- Active SLE with at least one British Isles Lupus Assessment Group (BILAG) flare A or B at screening requiring a change in the dose of corticosteroids
- Positive antinuclear antibody (ANA) or anti-double-stranded deoxyribonucleic acid (dsDNA) at screening
- Female subjects must be willing to avoid pregnancy by using an adequate method of contraception for 4 weeks prior to Study Day 1, during the trial and 24 weeks after the last dose of study medication
- Other protocol defined inclusion criteria could apply

Exclusion Criteria:

- Active moderate to severe glomerulonephritis (kidney impairment) as defined in the protocol
- Active central nervous system SLE deemed to be severe/progressive and/or associated with significant cognitive impairment leading to inability to provide informed consent and/or comply with the protocol
- Previous treatment with rituximab, abatacept, or belimumab
- History of demyelinating disease such as multiple sclerosis (MS) or optic neuritis
- Other protocol defined exclusion criteria could apply

Contacts/Locations

Study Officials: Medical Responsible
Study Director
Merck KGaA, Darmstadt, Germany

Locations: United States, Massachusetts
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Austria
Research Site
Wein, Austria

Australia
Research Site
Sunshine Coast, Queensland, Australia

Research Site
Woodville S.A., Australia

Lebanon
Research Site
Beirut, Lebanon

Lithuania
Research Site

Vilnius, Lithuania

United Kingdom
Research Site
London, United Kingdom

Netherlands
Research Site
Amsterdam, Netherlands

South Africa
Research Site
Durban, South Africa

Philippines
Research Site
Davao, Philippines

Russian Federation
Research Site
Kemerovo, Russian Federation

Malaysia
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Research Site
Split, Croatia

Research Site
Zagreb, Croatia

Czech Republic
Research Site
Prague, Czech Republic

France
Research Site
Lille, France

Germany
Research Site
Berlin, Germany

India
Research Site
Secunderabad, Andhra Pradesh, India

Israel
Research Site
Haifa, Israel

Research Site
Tel Aviv, Israel

Lithuania
Research Site
Kaunas, Lithuania

Philippines
Research Site

Las Pinas, Philippines

Research Site
Manila, Philippines

Russian Federation
Research Site
Petrozavodsk, Russian Federation

Research Site
St Petersburg, Russian Federation

South Africa
Research Site
Panorama, Western Cape, South Africa

Research Site
Stellenbosch, Western Cape, South Africa

Research Site
Pinelands, South Africa

Research Site
Parlow, Western Cape, South Africa

Korea, Republic of
Research Site
Gyeonggi-do, Korea, Republic of

Research Site
Seoul, Korea, Republic of

Switzerland
Research Site
St. Gallen, Switzerland

Spain
Research Site
Malaga, Spain

Taiwan
Research Site
Taichung, Taiwan

United Kingdom
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Manchester, United Kingdom

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Kyiv, Ukraine

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Bordeaux Pessac, France

Research Site
Paris, France

Research Site
Strasbourg, France

Germany
Research Site

Erlangen, Germany

Research Site
Heidelberg, Germany

Research Site
Herne, Germany

Malaysia
Research Site
Perak, Malaysia

Research Site
Seremban, Malaysia

Mexico
Research Site
Guadalajara Jalisco, Mexico

Research Site
Tijuana, BC, Mexico

Netherlands
Research Site
Maastricht, Netherlands

Poland
Research Site
Bialystok, Poland

Research Site
Krakow, Poland

Research Site
Torun, Poland

Research Site
Warsawa, Poland

Serbia
Research Site
Belgrade, Serbia

Research Site
Niska Banja, Serbia

Philippines
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Iloilo, Philippines

Russian Federation
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Yaroslavl, Russian Federation

Research Site
Ryazan, Russian Federation

Spain
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Cordoba, Argentina

Research Site

Quilmes, Argentina

Israel
Research Site
Petah-Tikva, Israel

Latvia
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Russian Federation
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Saratov, Russian Federation

Research Site
Tula, Russian Federation

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Germany
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Hanover, Germany

Research Site
Munster, Germany

Israel
Research Site
Jerasalem, Israel

Netherlands
Research Site
Leiden, Netherlands

Taiwan
Research Site

Taoyuan, Taiwan

Ukraine
Research Site
Ternopil, Ukraine

Research Site
Vinnytsya, Ukraine

Argentina
Research Site
San Juan, Argentina

France
Research Site
Toulouse, France

South Africa
Research Site
Cape Town, South Africa

Poland
Research Site
Lublin, Poland

Research Site
Szczecin, Poland

Research Site
Gdańsk, Poland

United States, New York
Research Site
New York, New York, United States

United States, California
Research Site
San Diego, California, United States

United States, Ohio
Research Site
Cincinnati, Ohio, United States

United States, Idaho
Research Site
Boise, Idaho, United States

United States, Florida
Research Site
Jacksonville, Florida, United States

United States, Texas
Research Site
Temple, Texas, United States

Australia
Research Site
Cairns, Australia

Germany
Research Site
Munchen, Germany

Philippines
Research Site
Angeles City, Pampanga, Philippines

Serbia
Research Site
Novi Beograd, Serbia

Greece
Research Site
Thessaloniki, Greece

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Atacicept 75 mg	75 milligram (mg) atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Atacicept 150 mg	150 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo	Placebo matched to atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Overall Study

	Atacicept 75 mg	Atacicept 150 mg	Placebo
Started	159	145	157
Treated	157	144	154
Completed	112	62	111
Not Completed	47	83	46
Adverse Event	14	14	18
Lost to Follow-up	1	0	0
Lack of Efficacy	11	3	14
Protocol Violation	3	3	2
Death	0	2	0
Immunoglobulin less than 3gram per liter	1	0	0
Termination of 150 mg group by Sponsor	0	55	0
Unspecified	15	5	9
Randomized but not treated	2	1	3

Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) population included all the randomized participants, regardless of whether they received treatment.

Reporting Groups

	Description
Atacicept 75 mg	75 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Atacicept 150 mg	150 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo	Placebo matched to atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Baseline Measures

	Atacicept 75 mg	Atacicept 150 mg	Placebo	Total
Number of Participants	159	145	157	461
Age, Continuous [units: years] Mean (Standard Deviation)	39.1 (12.0)	39.0 (12.8)	39.0 (12.1)	39.0 (12.2)
Gender, Male/Female [units: participants]				
Female	148	134	148	430
Male	11	11	9	31

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Experiencing a New Flare as Defined by British Isles Lupus Assessment Group (BILAG) Score A or B
Measure Description	A flare was defined as having an adjudicated BILAG A or B score in any of the 8 organ systems during treatment, or imputed for participants who had premature treatment discontinuation. Discontinuations due to sponsor termination of the atacicept 150 mg group were not imputed as flares in this analysis. The BILAG disease activity index evaluates systemic lupus erythematosus (SLE) activity in 8 organ systems, using a separate alphabetic score (A to E) assigned to each organ system defined as follows. BILAG A: Disease sufficiently active requiring disease-modifying treatment (prednisone greater than 20 mg daily or immunosuppressants); BILAG B: Disease less active than in “A”, mild reversible problems requiring only symptomatic therapy such as antimalarials, non-steroidal anti-inflammatory drugs (NSAIDs), or prednisone less than 20 mg day; BILAG C: Stable mild disease; BILAG D: System previously affected but now inactive; BILAG E: System never involved.
Time Frame	From screening up to Week 52
Safety Issue?	No

Analysis Population Description

Modified intent-to-treat (MITT) population included all the randomized participants who received study treatment.

Reporting Groups

	Description
Atacicept 75 mg	75 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Atacicept 150 mg	150 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo	Placebo matched to atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Measured Values

	Atacicept 75 mg	Atacicept 150 mg	Placebo
Number of Participants Analyzed	157	144	154
Percentage of Participants Experiencing a New Flare as Defined by British Isles Lupus Assessment Group (BILAG) Score A or B [units: percentage of participants]	57.32	36.11	53.25

Statistical Analysis 1 for Percentage of Participants Experiencing a New Flare as Defined by British Isles Lupus Assessment Group (BILAG) Score A or B

Statistical Analysis Overview	Comparison Groups	Atacicept 75 mg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.518
	Comments	Odds ratios were calculated from a logistic regression model adjusted for race and disease severity reported at screening.
	Method	Regression, Logistic
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Odds Ratio (OR)

	Estimated Value	1.160
	Confidence Interval	(2-Sided) 95% 0.74 to 1.82
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Percentage of Participants Experiencing a New Flare as Defined by British Isles Lupus Assessment Group (BILAG) Score A or B

Statistical Analysis Overview	Comparison Groups	Atacicept 150 mg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.003
	Comments	Odds ratios were calculated from a logistic regression model adjusted for race and disease severity reported at screening.
	Method	Regression, Logistic
	Comments	Atacicept 150 mg arm was discontinued prematurely. The analysis of 150 mg was considered post-hoc.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	0.490
	Confidence Interval	(2-Sided) 95% 0.31 to 0.78
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Time to First New Flare as Defined by BILAG Score A or B

Measure Description	A flare was defined as having an adjudicated BILAG A or B score in any of the 8 organ systems during treatment. Analysis was right-censored at Week 52. The hazard ratios and 95% confidence intervals were obtained from the Cox proportional hazards model. The 25th Percentile of time to new flare was reported using Kaplan-Meier estimates (Median was not reached). The BILAG disease activity index evaluates SLE activity in 8 organ systems, using a separate alphabetic score (A to E) assigned to each organ system defined as follows. BILAG A: Disease sufficiently active requiring disease-modifying treatment (prednisone greater than 20 mg daily or immunosuppressants); BILAG B: Disease less active than in "A", mild reversible problems requiring only symptomatic therapy such as antimalarials, NSAIDs, or prednisone less than 20 mg day; BILAG C: Stable mild disease; BILAG D: System previously affected but now inactive; BILAG E: System never involved.
Time Frame	From screening up to Week 52
Safety Issue?	No

Analysis Population Description

MITT population included all the randomized participants who received study treatment

Reporting Groups

	Description
Atacicept 75 mg	75 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Atacicept 150 mg	150 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo	Placebo matched to atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Measured Values

	Atacicept 75 mg	Atacicept 150 mg	Placebo
Number of Participants Analyzed	157	144	154
Time to First New Flare as Defined by BILAG Score A or B [units: days] Number (95% Confidence Interval)	143 (112 to 226)	310 (169 to NA) [1]	142 (87 to 197)

[1] Upper limit of confidence interval was not estimable as insufficient participants reached the event at the final time point for assessment.

Statistical Analysis 1 for Time to First New Flare as Defined by BILAG Score A or B

Statistical Analysis Overview	Comparison Groups	Atacicept 75 mg, Placebo
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.929
	Comments	Cox proportional hazards model was performed to calculate hazard ratios and adjusted for race and disease severity at time of screening.
	Method	Regression, Cox
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.984
	Confidence Interval	(2-Sided) 95% 0.69 to 1.40
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Time to First New Flare as Defined by BILAG Score A or B

Statistical Analysis Overview	Comparison Groups	Atacicept 150 mg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.009
	Comments	Cox proportional hazards model was performed to calculate hazard ratios and adjusted for race and disease severity at time of screening.
	Method	Regression, Cox
	Comments	Atacicept 150 mg arm was discontinued prematurely. The analysis of 150 mg was considered post-hoc.

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.562
	Confidence Interval	(2-Sided) 95% 0.36 to 0.87

	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Experiencing a New Flare as Defined by BILAG Score A or B During Initial 24 Weeks
Measure Description	A flare was defined as having an adjudicated BILAG A or B score in any of the 8 organ systems during treatment, or imputed for participants who had premature treatment discontinuation. The BILAG disease activity index evaluates SLE activity in 8 organ systems, using a separate alphabetic score (A to E) assigned to each organ system defined as follows. BILAG A: Disease sufficiently active requiring disease-modifying treatment (prednisone greater than 20 mg daily or immunosuppressants); BILAG B: Disease less active than in “A”, mild reversible problems requiring only symptomatic therapy such as antimalarials, NSAIDs, or prednisone less than 20 mg day; BILAG C: Stable mild disease; BILAG D: System previously affected but now inactive; BILAG E: System never involved.
Time Frame	From screening up to Week 24
Safety Issue?	No

Analysis Population Description

MITT population included all the randomized participants who received study treatment.

Reporting Groups

	Description
Atacicept 75 mg	75 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Atacicept 150 mg	150 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo	Placebo matched to atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Measured Values

	Atacicept 75 mg	Atacicept 150 mg	Placebo
Number of Participants Analyzed	157	144	154
Percentage of Participants Experiencing a New Flare as Defined by BILAG Score A or B During Initial 24 Weeks [units: percentage of participants]	40.13	28.47	35.06

Statistical Analysis 1 for Percentage of Participants Experiencing a New Flare as Defined by BILAG Score A or B During Initial 24 Weeks

Statistical Analysis Overview	Comparison Groups	Atacicept 75 mg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.412
	Comments	Odds ratios were calculated from a logistic regression model, adjusted for race and disease severity reported at screening.
	Method	Regression, Logistic
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.215
	Confidence Interval	(2-Sided) 95% 0.76 to 1.94
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Percentage of Participants Experiencing a New Flare as Defined by BILAG Score A or B During Initial 24 Weeks

Statistical Analysis Overview	Comparison Groups	Atacicept 150 mg, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.198
	Comments	Odds ratios were calculated from a logistic regression model, adjusted for race and disease severity reported at screening.
	Method	Regression, Logistic
	Comments	Atacicept 150 mg arm was discontinued prematurely. The analysis of 150 mg was considered post-hoc.
Method of Estimation	Estimation Parameter	Odds Ratio (OR)

	Estimated Value	0.722
	Confidence Interval	(2-Sided) 95% 0.44 to 1.19
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants Within Ordinal Response Categories for British Isles Lupus Assessment Group (BILAG) Flares
Measure Description	Ordinal response categories have been defined as: 1) No BILAG A, no BILAG B, and completed treatment, 2) No BILAG A, at least 1 BILAG B during treatment period, and 3) At least 1 BILAG A during treatment period. The BILAG disease activity index evaluates SLE activity in 8 organ systems, using a separate alphabetic score (A to E) assigned to each organ system defined as follows. BILAG A: Disease sufficiently active requiring disease-modifying treatment (prednisone greater than 20 mg daily or immunosuppressants); BILAG B: Disease less active than in "A", mild reversible problems requiring only symptomatic therapy such as antimalarials, NSAIDs, or prednisone less than 20 mg day; BILAG C: Stable mild disease; BILAG D: System previously affected but now inactive; BILAG E: System never involved.
Time Frame	Week 52
Safety Issue?	No

Analysis Population Description

MITT population included all the randomized participants who received study treatment. 'N' (number of participants analyzed) signifies participants who were evaluable for this measure.

Reporting Groups

	Description
Atacicept 75 mg	75 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Atacicept 150 mg	150 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo	Placebo matched to atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Measured Values

	Atacicept 75 mg	Atacicept 150 mg	Placebo
Number of Participants Analyzed	128	76	136

	Atacicept 75 mg	Atacicept 150 mg	Placebo
Percentage of Participants Within Ordinal Response Categories for British Isles Lupus Assessment Group (BILAG) Flares [units: percentage of participants]			
No BILAG A, no BILAG B, and completed treatment	52.3	60.5	52.9
No BILAG A, at least 1 BILAG B in treatment period	39.8	28.9	38.2
At least 1 BILAG A in treatment period	7.8	10.5	8.8

5. Secondary Outcome Measure:

Measure Title	Mean Cumulative Corticosteroid Dose
Measure Description	
Time Frame	Randomization up to Week 52
Safety Issue?	No

Analysis Population Description

MITT population included all the randomized participants who received study treatment.

Reporting Groups

	Description
Atacicept 75 mg	75 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Atacicept 150 mg	150 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo	Placebo matched to atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Measured Values

	Atacicept 75 mg	Atacicept 150 mg	Placebo
Number of Participants Analyzed	157	144	154
Mean Cumulative Corticosteroid Dose [units: mg] Mean (Standard Deviation)	2456.79 (1029.87)	2018.87 (1062.61)	2624.02 (812.44)

Reported Adverse Events

Time Frame	Baseline up to 76 weeks (end of follow-up of the study)
Additional Description	An adverse event (AE) is defined as any untoward medical occurrence in the form of signs, symptoms, abnormal laboratory findings, or diseases that emerges or worsens relative to Baseline during a clinical study with an investigational medicinal product (IMP), regardless of causal relationship and even if no IMP has been administered.

Reporting Groups

	Description
Atacicept 75 mg	75 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Atacicept 150 mg	150 mg atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.
Placebo	Placebo matched to atacicept injection was administered subcutaneously twice weekly during initial loading period for 4 weeks followed by once weekly during maintenance period for subsequent 48 weeks.

Serious Adverse Events

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	30/157 (19.11%)	23/144 (15.97%)	27/154 (17.53%)
Blood and lymphatic system disorders			
Anaemia [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Cardiac disorders			
Acute myocardial infarction [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Angina pectoris [A] *	1/157 (0.64%)	0/144 (0%)	1/154 (0.65%)
Atrial flutter [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Coronary artery disease [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Myocardial infarction [A] *	1/157 (0.64%)	0/144 (0%)	2/154 (1.3%)

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pericardial effusion [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Ear and labyrinth disorders			
Vertigo [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Eye disorders			
Vision blurred [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Gastrointestinal disorders			
Diarrhoea [A] *	2/157 (1.27%)	0/144 (0%)	0/154 (0%)
Dysphagia [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Gastrointestinal disorder [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Nausea [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Pancreatitis [A] *	1/157 (0.64%)	1/144 (0.69%)	0/154 (0%)
Pancreatitis acute [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Periproctitis [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Peritonitis [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Vasculitis gastrointestinal [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Vomiting [A] *	1/157 (0.64%)	0/144 (0%)	1/154 (0.65%)
General disorders			
Asthenia [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Injection site reaction [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Malaise [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Hepatobiliary disorders			
Autoimmune hepatitis [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Cholecystitis [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Cholecystitis acute [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Cholelithiasis [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Hepatitis [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Immune system disorders			
Anaphylactic shock [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Drug hypersensitivity [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Serum sickness [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Infections and infestations			
Abscess limb [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Appendicitis [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Arthritis bacterial [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Bronchitis [A] *	2/157 (1.27%)	0/144 (0%)	0/154 (0%)
Bronchopneumonia [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Cellulitis [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Diarrhoea infectious [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Escherichia urinary tract infection [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Gastroenteritis [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Gastroenteritis viral [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Herpes zoster [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Influenza [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Kidney infection [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Leptospirosis [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Lobar pneumonia [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Meningitis tuberculous [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Mycetoma mycotic [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Oral candidiasis [A] *	0/157 (0%)	1/144 (0.69%)	1/154 (0.65%)
Otitis media acute [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Pelvic inflammatory disease [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Pneumonia [A] *	5/157 (3.18%)	3/144 (2.08%)	2/154 (1.3%)
Pyelonephritis acute [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Salpingitis [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Sepsis [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Septic shock [A] *	0/157 (0%)	0/144 (0%)	2/154 (1.3%)
Upper respiratory tract infection [A] *	2/157 (1.27%)	2/144 (1.39%)	0/154 (0%)
Urinary tract infection [A] *	1/157 (0.64%)	0/144 (0%)	2/154 (1.3%)
Urosepsis [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Viral upper respiratory tract infection [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Injury, poisoning and procedural complications			
Ankle fracture [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Chillblains [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Fractured sacrum [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Humerus fracture [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Joint dislocation [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Laceration [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Ligament rupture [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Lumbar vertebral fracture [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Multiple fractures [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Road traffic accident [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Spinal fracture [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Thermal burn [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Investigations			
Biopsy cervix [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Hepatic enzyme increased [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
International normalised ratio increased [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Metabolism and nutrition disorders			
Hypokalaemia [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Hyponatraemia [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Muscle tightness [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Muscular weakness [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Osteochondrosis [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Polymyositis [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Systemic lupus erythematosus [A] *	0/157 (0%)	0/144 (0%)	2/154 (1.3%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of thyroid gland [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Cervix carcinoma stage 0 [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Fibroadenoma of breast [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Glioblastoma [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Uterine leiomyoma [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Nervous system disorders			
Cerebral infarction [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Dizziness [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Epilepsy [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Headache [A] *	0/157 (0%)	0/144 (0%)	2/154 (1.3%)
Hemiparesis [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Neuropsychiatric lupus [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Transient ischaemic attack [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Pregnancy, puerperium and perinatal conditions			
Abortion missed [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Intra-uterine death [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Psychiatric disorders			
Affect lability [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Anxiety [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Renal and urinary disorders			
Lupus nephritis [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Renal failure acute [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Reproductive system and breast disorders			
Cervical dysplasia [A] *	0/157 (0%)	0/144 (0%)	2/154 (1.3%)
Endometrial hyperplasia [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Uterine haemorrhage [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Uterine polyp [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Dyspnoea [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Haemoptysis [A] *	0/157 (0%)	1/144 (0.69%)	0/154 (0%)
Laryngeal oedema [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Pulmonary alveolar haemorrhage [A] *	0/157 (0%)	2/144 (1.39%)	0/154 (0%)
Skin and subcutaneous tissue disorders			
Skin disorder [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Social circumstances			
Social stay hospitalisation [A] *	1/157 (0.64%)	0/144 (0%)	1/154 (0.65%)
Surgical and medical procedures			
Hip arthroplasty [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)
Vascular disorders			
Deep vein thrombosis [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Hypertension [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Peripheral ischaemia [A] *	0/157 (0%)	0/144 (0%)	1/154 (0.65%)
Vasculitis [A] *	1/157 (0.64%)	0/144 (0%)	0/154 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 14.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	129/157 (82.17%)	120/144 (83.33%)	118/154 (76.62%)
Gastrointestinal disorders			
Abdominal pain upper [A] *	8/157 (5.1%)	3/144 (2.08%)	3/154 (1.95%)
Diarrhoea [A] *	9/157 (5.73%)	5/144 (3.47%)	13/154 (8.44%)
Nausea [A] *	11/157 (7.01%)	7/144 (4.86%)	6/154 (3.9%)
General disorders			
Injection site erythema [A] *	10/157 (6.37%)	16/144 (11.11%)	0/154 (0%)
Injection site pruritus [A] *	4/157 (2.55%)	10/144 (6.94%)	0/154 (0%)
Injection site reaction [A] *	16/157 (10.19%)	22/144 (15.28%)	3/154 (1.95%)
Pyrexia [A] *	8/157 (5.1%)	5/144 (3.47%)	4/154 (2.6%)
Infections and infestations			
Bronchitis [A] *	12/157 (7.64%)	12/144 (8.33%)	6/154 (3.9%)
Influenza [A] *	4/157 (2.55%)	6/144 (4.17%)	9/154 (5.84%)
Nasopharyngitis [A] *	21/157 (13.38%)	16/144 (11.11%)	11/154 (7.14%)
Sinusitis [A] *	8/157 (5.1%)	4/144 (2.78%)	10/154 (6.49%)
Upper respiratory tract infection [A] *	24/157 (15.29%)	27/144 (18.75%)	24/154 (15.58%)
Urinary tract infection [A] *	22/157 (14.01%)	23/144 (15.97%)	17/154 (11.04%)
Musculoskeletal and connective tissue disorders			
Back pain [A] *	14/157 (8.92%)	5/144 (3.47%)	8/154 (5.19%)
Nervous system disorders			
Headache [A] *	31/157 (19.75%)	17/144 (11.81%)	23/154 (14.94%)
Respiratory, thoracic and mediastinal disorders			

	Atacicept 75 mg	Atacicept 150 mg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Cough [A] *	10/157 (6.37%)	7/144 (4.86%)	8/154 (5.19%)
Vascular disorders			
Hypertension [A] *	8/157 (5.1%)	5/144 (3.47%)	8/154 (5.19%)
Hypotension [A] *	3/157 (1.91%)	1/144 (0.69%)	8/154 (5.19%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 14.0

Limitations and Caveats

Atacicept 150 mg group was discontinued on 2 February 2011 based on the recommendation from the Independent Data Monitoring Committee.

More Information

Certain Agreements:

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

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

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