ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 04/15/2016

ClinicalTrials.gov ID: NCT00642902

Study Identification

Unique Protocol ID:	28063
Brief Title:	A Phase 2 Study of Atacicept in Subjects With Relapsing Multiple Sclerosis (ATAMS)
Official Title:	A Four-Arm Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase II Study to Evaluate the Safety, Tolerability and Efficacy as Assessed by Frequent MRI Measures of 3 Doses of Atacicept Monotherapy in Subjects With Relapsing Multiple Sclerosis (RMS) Over a 36 Week Treatment Course
Secondary IDs:	

Study Status

Record Verification:	April 2016
Overall Status:	Terminated
Study Start:	April 2008
Primary Completion:	September 2009 [Actual]
Study Completion:	September 2009 [Actual]

Sponsor/Collaborators

Sponsor:	EMD Serono
Responsible Party:	Sponsor
Collaborators:	

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: 100795 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: October 2007 Board Name: Coast IRB Board Affiliation: Coast IRB Phone: 1- 719 325 8400 Email: info@coastirb.com
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	To evaluate the safety and tolerability of atacicept and to explore if atacicept reduces central nervous system inflammation in subjects with relapsing multiple sclerosis (RMS) as assessed by frequent magnetic resonance imaging (MRI). This study is randomised. Study medication is administered via subcutaneous (under the skin) injections.
Detailed Description:	

Conditions

Conditions:	Relapsing Multiple Sclerosis
Keywords:	Relapsing Multiple Sclerosis Atacicept

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment

Number of Arms: 4

Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 255 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Atacicept 25 mg	Drug: Atacicept Atacicept will be administered subcutaneously at a dose of 25 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 32 weeks.
Experimental: Atacicept 75 mg	Drug: Atacicept Atacicept will be administered subcutaneously at a dose of 75 mg twice a week for initial 4 weeks as loading dose, followed by 75 mg once a week for subsequent 32 weeks.
Experimental: Atacicept 150 mg	Drug: Atacicept Atacicept will be administered subcutaneously at a dose of 150 mg twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.
Placebo Comparator: Placebo	Drug: Placebo matched to atacicept Placebo matched to atacicept will be administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 60 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Diagnosis of RMS (as per McDonald criteria, 2005) Other protocol-defined inclusion criteria could apply.

Exclusion Criteria:

- Have primary progressive multiple sclerosis (MS)
- Have secondary progressive MS without superimposed relapses
- Relevant cardiac, hepatic and renal diseases as specified in the protocol
- Pretreatment with immunosuppressants and immunomodulating drugs as specified in the protocol
- Clinical significant abnormalities in blood cell counts and immunoglobulin levels as specified in the protocol
- Clinical significant acute or chronic infections as specified in the protocol Other protocol-defined exclusion criteria could apply.

Contacts/Locations

Study Officials: Medical Responsible
Study Director
EMD Serono, an affiliate of Merck KGaA Darmstadt, Germany

Locations: Canada
Research Site
Ontario, Canada

Switzerland
Research Site
Basel, Switzerland

Austria
Research Site
Innsbruck, Austria

Belgium
Research Site
Diepenbeek, Belgium

Lebanon
Research Site
Beyrouth, Lebanon

Czech Republic
Research Site
Hradec Kralove, Czech Republic

Spain
Research Site
Madrid, Spain

United Kingdom

Research Site
Sheffield, United Kingdom

Netherlands
Research Site
Rotterdam, Netherlands

Sweden
Research Site
Stockholm, Sweden

Germany
Research Site
Dusseldorf, Germany

Australia
Research Site
Woodville, Australia

Lithuania
Research Site
Kaunas, Lithuania

Russian Federation
Research Site
Moscow, Russian Federation

Ukraine
Research Site
Kyiv, Ukraine

United States, Arizona
Research Site
Phoenix, Arizona, United States

United States, Michigan
Research Site
East Lansing, Michigan, United States

United States, Ohio
Research Site
Cleveland, Ohio, United States

United States, Tennessee
Research Site
Nashville, Tennessee, United States

United States, Pennsylvania
Philadelphia, Pennsylvania, United States

United States, Illinois
Research Site
Northbrook, Illinois, United States

Canada, Ontario
Research Site
Ottawa, Ontario, Canada

Canada, Alberta
Research Site
Calgary, Alberta, Canada

Belgium
Research Site
Sijsele, Belgium

Czech Republic
Research Site
Olomouc, Czech Republic

Spain
Research Site
Barcelona, Spain

United Kingdom
Research Site
London, United Kingdom

Research Site
Stoke on Trent, United Kingdom

Netherlands
Research Site
Nieuwegein, Netherlands

Research Site
Breda, Netherlands

Germany
Research Site
Bochum, Germany

Australia

Research Site
New Lambton, Australia

Research Site
Fitzroy, Australia

Russian Federation
Research Site
Vladimir, Russian Federation

Research Site
Samara, Russian Federation

Research Site
Yaroslavl, Russian Federation

Research Site
Ekaterinburg, Russian Federation

Ukraine
Research Site
Odessa, Ukraine

Research Site
Uzhgorod, Ukraine

Research Site
Kharkiv, Ukraine

Russian Federation
Research Site
Novosibirsk, Russian Federation

Research Site
Saint Petersburg, Russian Federation

France
Research Site
Saint-Herblain, France

Research Site
Caen, France

United States, New Hampshire
Research Site
Dartmouth, New Hampshire, United States

Spain
Research Site
Malaga, Spain

Czech Republic
Research Site
Brno, Czech Republic

Australia
Research Site
Box Hill, Australia

Russian Federation
Research Site
Dnipropetrovsk, Russian Federation

Lebanon
Research Site
Beirut, Lebanon

United States, Georgia
Research Site
Atlanta, Georgia, United States

References

Citations:

Links: URL: http://www.mslifelines.com
Description Related Info

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Placebo	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.

	Description
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 32 weeks.
Atacicept 75 mg	Atacicept was administered subcutaneously at a dose of 75 mg twice a week for initial 4 weeks as loading dose, followed by 75 mg once a week for subsequent 32 weeks.
Atacicept 150 mg	Atacicept was administered subcutaneously at a dose of 150 mg twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.

Overall Study

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Started	63	63	64	65
Treated	63	63	63	65
Completed	23	21	21	25
Not Completed	40	42	43	40
Adverse Event	0	1	3	1
Lost to Follow-up	1	1	0	0
Lack of Efficacy	0	3	3	0
Death	1	0	0	0
Premature termination of clinical trial	37	32	35	35
Randomized, but not treated	0	0	1	0
Unspecified	1	5	1	4

Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) population included all randomized participants.

Reporting Groups

	Description
Placebo	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 32 weeks.

	Description
Atacicept 75 mg	Atacicept was administered subcutaneously at a dose of 75 mg twice a week for initial 4 weeks as loading dose, followed by 75 mg once a week for subsequent 32 weeks.
Atacicept 150 mg	Atacicept was administered subcutaneously at a dose of 150 mg twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.

Baseline Measures

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg	Total
Number of Participants	63	63	64	65	255
Age, Continuous [units: years] Mean (Standard Deviation)	37.7 (10.5)	37.5 (8.5)	38.0 (10.1)	37.5 (10.5)	37.7 (9.9)
Gender, Male/Female [units: participants]					
Female	45	34	44	46	169
Male	18	29	20	19	86

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Mean Number of Time Constant 1 (T1) Gadolinium (Gd)-Enhancing Lesions Per Participant Per Scan
Measure Description	Analysis of T1 Gd-enhancing lesions was done using magnetic resonance imaging (MRI) scans. Only post-baseline scans were included in the calculation of this endpoint (excluding the Study Day 1 scan which had been conducted before first dosing).
Time Frame	Weeks 12 to 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants.

Reporting Groups

	Description
Placebo	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 32 weeks.

	Description
Atacicept 75 mg	Atacicept was administered subcutaneously at a dose of 75 mg twice a week for initial 4 weeks as loading dose, followed by 75 mg once a week for subsequent 32 weeks.
Atacicept 150 mg	Atacicept was administered subcutaneously at a dose of 150 mg twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	63	63	64	65
Mean Number of Time Constant 1 (T1) Gadolinium (Gd)-Enhancing Lesions Per Participant Per Scan [units: lesions/participant/scan] Mean (95% Confidence Interval)	3.07 (1.40 to 6.77)	2.26 (0.97 to 5.27)	2.30 (1.08 to 4.92)	2.49 (1.18 to 5.27)

2. Secondary Outcome Measure:

Measure Title	Number of New T1 Gd-enhancing Lesions Per Participant
Measure Description	Analysis of new T1 Gd-enhancing lesions was done using MRI scans.
Time Frame	Weeks 12, 24, 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. 'n' signifies participants who were evaluable for this measure at given time points for each group, respectively.

Reporting Groups

	Description
Placebo	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 32 weeks.
Atacicept 75 mg	Atacicept was administered subcutaneously at a dose of 75 mg twice a week for initial 4 weeks as loading dose, followed by 75 mg once a week for subsequent 32 weeks.
Atacicept 150 mg	Atacicept was administered subcutaneously at a dose of 150 mg twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	63	63	64	65
Number of New T1 Gd-enhancing Lesions Per Participant [units: lesions/participant] Mean (Standard Deviation)				
Week 12 (n=55, 45, 50, 55)	2.55 (7.95)	2.71 (7.67)	3.20 (6.41)	2.96 (6.58)
Week 24 (n=41, 34, 37, 41)	0.83 (1.70)	1.50 (2.79)	1.54 (2.96)	1.54 (2.94)
Week 36 (n=23, 22, 24, 26)	0.43 (0.90)	1.68 (5.09)	1.38 (1.93)	0.54 (1.07)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Free From Relapses
Measure Description	A relapse was defined as the fulfillment of all the following criteria: a) neurological abnormality, either newly appearing or re-appearing, with abnormality specified by both i) neurological abnormality separated by at least 30 days from onset of a preceding clinical event, and ii) neurological abnormality lasting for at least 24 hours; b) absence of fever or known infection (fever with temperature [axillary, orally, or intrauricular] greater than (>) 37.5 degrees Celsius or 99.5 degrees Fahrenheit); and c) objective neurological impairment, correlating with the participant's reported symptoms, defined as either i) increase in at least 1 of the functional systems of the Expanded Disability Status Scale (EDSS), or ii) increase of the total EDSS score. Percentage of participants free from relapses during 36-week treatment period was reported.
Time Frame	Baseline up to Week 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants.

Reporting Groups

	Description
Placebo	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 32 weeks.
Atacicept 75 mg	Atacicept was administered subcutaneously at a dose of 75 mg twice a week for initial 4 weeks as loading dose, followed by 75 mg once a week for subsequent 32 weeks.

	Description
Atacicept 150 mg	Atacicept was administered subcutaneously at a dose of 150 mg twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	63	63	64	65
Percentage of Participants Free From Relapses [units: percentage of participants]	81.0	69.8	71.9	61.5

4. Secondary Outcome Measure:

Measure Title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs
Measure Description	An AE was defined as any new untoward medical occurrences/worsening of pre-existing medical condition without regard to possibility of causal relationship. An SAE was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/ birth defect. Treatment-emergent are events between first dose of study drug up to 12 weeks after the last dose of the study drug that were absent before treatment or that worsened relative to pretreatment state. Number of subjects with TEAEs included subjects with both non serious and serious TEAEs.
Time Frame	From the first dose of study drug administration up to 12 weeks after the last dose of the study drug
Safety Issue?	Yes

Analysis Population Description

Safety population included all participants who received at least 1 dose of treatment (either active or placebo).

Reporting Groups

	Description
Placebo	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 32 weeks.
Atacicept 75 mg	Atacicept was administered subcutaneously at a dose of 75 mg twice a week for initial 4 weeks as loading dose, followed by 75 mg once a week for subsequent 32 weeks.
Atacicept 150 mg	Atacicept was administered subcutaneously at a dose of 150 mg twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	63	63	63	65
Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs [units: participants]				
TEAEs	46	40	39	52
Serious TEAEs	1	3	3	1

Reported Adverse Events

Time Frame	From the first dose of study drug administration up to 12 weeks after the last dose of the study drug
Additional Description	[Not specified]

Reporting Groups

	Description
Placebo	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 32 weeks.
Atacicept 75 mg	Atacicept was administered subcutaneously at a dose of 75 mg twice a week for initial 4 weeks as loading dose, followed by 75 mg once a week for subsequent 32 weeks.
Atacicept 150 mg	Atacicept was administered subcutaneously at a dose of 150 mg twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.

Serious Adverse Events

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/63 (1.59%)	3/63 (4.76%)	3/63 (4.76%)	1/65 (1.54%)
Cardiac disorders				
Myocardial infarction [A] *	1/63 (1.59%)	0/63 (0%)	0/63 (0%)	0/65 (0%)

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Endocrine disorders				
Hypothyroidism [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
General disorders				
Asthenia [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Infections and infestations				
Lung abscess [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Otitis media acute [A] *	0/63 (0%)	0/63 (0%)	0/63 (0%)	1/65 (1.54%)
Pneumonia [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Pyothorax [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Injury, poisoning and procedural complications				
Hip fracture [A] *	0/63 (0%)	1/63 (1.59%)	0/63 (0%)	0/65 (0%)
Humerus fracture [A] *	0/63 (0%)	1/63 (1.59%)	0/63 (0%)	0/65 (0%)
Investigations				
Body temperature decreased [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Parathyroid tumour benign [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Psychiatric disorders				
Acute psychosis [A] *	0/63 (0%)	1/63 (1.59%)	0/63 (0%)	0/65 (0%)
Anxiety [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Respiratory, thoracic and mediastinal disorders				
Bronchopleural fistula [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Pleurisy [A] *	0/63 (0%)	0/63 (0%)	1/63 (1.59%)	0/65 (0%)
Pneumothorax [A] *	0/63 (0%)	0/63 (0%)	2/63 (3.17%)	0/65 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (11.1)

Other Adverse Events

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

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	33/63 (52.38%)	30/63 (47.62%)	34/63 (53.97%)	44/65 (67.69%)
Gastrointestinal disorders				
Diarrhoea [A] *	1/63 (1.59%)	1/63 (1.59%)	3/63 (4.76%)	5/65 (7.69%)
Nausea [A] *	2/63 (3.17%)	3/63 (4.76%)	1/63 (1.59%)	4/65 (6.15%)
General disorders				
Fatigue [A] *	0/63 (0%)	1/63 (1.59%)	3/63 (4.76%)	4/65 (6.15%)
Injection site pain [A] *	2/63 (3.17%)	2/63 (3.17%)	0/63 (0%)	4/65 (6.15%)
Injection site reaction [A] *	8/63 (12.7%)	19/63 (30.16%)	24/63 (38.1%)	32/65 (49.23%)
Infections and infestations				
Bronchitis [A] *	1/63 (1.59%)	2/63 (3.17%)	1/63 (1.59%)	5/65 (7.69%)
Influenza [A] *	5/63 (7.94%)	1/63 (1.59%)	1/63 (1.59%)	2/65 (3.08%)
Nasopharyngitis [A] *	6/63 (9.52%)	4/63 (6.35%)	7/63 (11.11%)	13/65 (20%)
Upper respiratory tract infection [A] *	3/63 (4.76%)	1/63 (1.59%)	4/63 (6.35%)	8/65 (12.31%)
Urinary tract infection [A] *	3/63 (4.76%)	4/63 (6.35%)	7/63 (11.11%)	3/65 (4.62%)
Musculoskeletal and connective tissue disorders				
Back pain [A] *	4/63 (6.35%)	0/63 (0%)	3/63 (4.76%)	3/65 (4.62%)
Pain in extremity [A] *	4/63 (6.35%)	3/63 (4.76%)	1/63 (1.59%)	1/65 (1.54%)
Nervous system disorders				
Headache [A] *	11/63 (17.46%)	8/63 (12.7%)	3/63 (4.76%)	6/65 (9.23%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (11.1)

Limitations and Caveats

Sponsor voluntarily decided to prematurely terminate this trial due to an increase in multiple sclerosis (MS) disease activity observed in atacicept arms as compared to placebo during a routine independent data monitoring committee (IDMC) review.

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.

Prior to publishing results, Institution and Principal Investigator (PI) must first provide Sponsor with a copy of proposed publication for review at least 30 days prior to submission. If Institution and PI do not agree to modification, they shall so notify Sponsor and postpone submission for additional 60 days to allow Sponsor to seek legal remedies or file patent applications. There is a need for coordinated approach to any publication of results from sites for any multi-site study.

Results Point of Contact:

Name/Official Title: Merck KGaA Communication Center
Organization: Merck Serono, a division of Merck KGaA
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