ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 01/19/2016

ClinicalTrials.gov ID: NCT00624468

Study Identification

Unique Protocol ID:	28156
Brief Title:	Atacicept in Subjects With Optic Neuritis
Official Title:	A Two-arm, Randomized, Double-blind, Placebo-controlled, Multicenter Phase II Study to Evaluate Safety and Tolerability and to Explore the Neuroprotective Effect of Atacicept as Assessed by Optical Coherence Tomography (OCT) in Subjects With Optic Neuritis (ON) as Clinically Isolated Syndrome (CIS) Over a 36-week Treatment Course
Secondary IDs:	

Study Status

Record Verification:	January 2016
Overall Status:	Terminated
Study Start:	June 2008
Primary Completion:	September 2009 [Actual]
Study Completion:	January 2011 [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: 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: 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:	This study was intended to evaluate the efficacy, safety and tolerability of atacicept compared to placebo and to explore the neuroprotective effect of atacicept as assessed by OCT in subjects with ON as CIS. The study was randomized. Study medication was administered via subcutaneous (under the skin) injections.
Detailed Description:	

Conditions

Conditions:	Optic Neuritis
Keywords:	atacicept neuritis

Study Design

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

Number of Arms: 2

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

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 34 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Atacicept	Drug: Atacicept Atacicept will be administered subcutaneously at a dose of 150 milligram (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 unilateral symptomatic optic neuritis as first clinical manifestation within 28 days between onset of symptoms and study Day 1
- Other protocol defined inclusion criteria could apply

Exclusion Criteria:

- Pre treatment with immunosuppressants and immunomodulating drugs
- Relevant cardiac, hepatic and renal diseases
- Clinical significant abnormalities in blood cell counts and immunoglobulin levels
- Clinical significant acute or chronic infections

• Other protocol defined exclusion criteria could apply

Contacts/Locations

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

Locations: Canada, Quebec
Research Site
Montreal, Quebec, Canada

Canada, Ontario
Research Site
Ottawa, Ontario, Canada

Canada, British Columbia
Research Site
Vancouver, British Columbia, Canada

Lebanon
Research Site
Beyrouth, Lebanon

Spain
Research Site
Barcelona, Spain

Research Site
Sevilla, Spain

Czech Republic
Research Site
Hradec Kralove, Czech Republic

Germany
Research Site
Munich, Germany

Switzerland
Research Site
Lausanne, Switzerland

United Kingdom

Research Site
London, United Kingdom

Research Site
Sheffield, United Kingdom

United States, Colorado
Research Site
Aurora, Colorado, United States

United States, Vermont
Research Site
Burlington, Vermont, United States

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

United States, Connecticut
Research Site
Fairfield, Connecticut, United States

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

United States, Pennsylvania
Research Site
Philadelphia, Pennsylvania, United States

Lebanon
Research Site
Dbayeh, Lebanon

Germany
Research Site
Freiburg, Germany

Czech Republic
Research Site
Olomouc, Czech Republic

Germany
Research Site
Tübingen, Germany

Research Site
Würzburg, Germany

United States, Alabama
Research Site
Birmingham, Alabama, United States

United States, Texas
Research Site
Houston, Texas, United States

Australia, Victoria
Research Site
Parkville, Victoria, Australia

Belgium
Research Site
Bruxelles, Belgium

France
Research Site
Paris, France

Spain
Research Site
Valencia, Spain

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	Atacicept was administered subcutaneously at a dose of 150 milligram (mg) twice a week for initial 4 weeks as loading dose, followed by 150 mg once a week for subsequent 32 weeks.
Placebo: SFU Period	Subjects who received placebo matched to atacicept in double-blind period were included in safety follow-up (SFU) period (60 weeks) following premature termination of the trial.
Atacicept: SFU Period	Subjects who received atacicept in double-blind period were included in SFU period (60 weeks) following premature termination of the trial.

Double-blind Period

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
Started	17	17	0	0
Completed	3	4	0	0
Not Completed	14	13	0	0
Early Termination Initiated by Sponsor	13	12	0	0
Withdrew Prematurely	1	1	0	0

Safety Follow-up (SFU) Period

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
Started	0	0	13	14
Completed	0	0	11	11
Not Completed	0	0	2	3
Lost to Follow-up	0	0	1	2
Unspecified	0	0	1	1

Baseline Characteristics

Analysis Population Description

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

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	Atacicept was administered subcutaneously at a dose of 150 milligram (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: Double-blind Period	Atacicept: Double-blind Period	Total
Number of Participants	17	17	34
Age, Continuous [units: years] Mean (Standard Deviation)	32.3 (7.1)	30.6 (10.2)	31.4 (8.7)
Gender, Male/Female [units: participants]			
Female	14	13	27
Male	3	4	7

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Retinal Nerve Fiber Layer (RNFL) Thickness in the Affected Eye at Last Observed Value (LOV)
Measure Description	The RNFL thickness was measured for 12 sectors (every 30 degrees) per eye in triplicate by optical coherence tomography (OCT) measurements and were then averaged over 12 sectors. The change in RNFL thickness at LOV visit was calculated as RNFL thickness at LOV minus RNFL thickness at baseline.
Time Frame	Baseline, LOV (Week 48)
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	17	17
Change From Baseline in Retinal Nerve Fiber Layer (RNFL) Thickness in the Affected Eye at Last Observed Value (LOV) [units: micrometer] Mean (Standard Deviation)		
Baseline (n = 17, 17)	103.893 (17.271)	104.170 (8.832)
Change at LOV (n = 16, 15)	-17.317 (15.158)	-8.636 (10.056)

2. Secondary Outcome Measure:

Measure Title	Difference in Retinal Nerve Fibre Layer (RNFL) Thickness Between the Affected Eye and Fellow Eye
Measure Description	The RNFL thickness was measured for 12 sectors (every 30 degrees) per eye in triplicate by optical coherence tomography (OCT) measurements and was then averaged over 12 sectors. Difference was calculated as RNFL thickness in affected eye minus RNFL thickness in fellow eye.
Time Frame	Weeks 12, 24 and 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "N" (number of participants analyzed) signifies those participants who were evaluable for this outcome measure and "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	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: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	13	13
Difference in Retinal Nerve Fibre Layer (RNFL) Thickness Between the Affected Eye and Fellow Eye [units: micrometer] Mean (Standard Error)		
Change at Week 12 (n = 13, 13)	-14 (4)	-7.9 (1.5)
Change at Week 24 (n = 4, 5)	-7 (6.9)	-10.6 (3.7)
Change at Week 36 (n = 3, 4)	-7.5 (8.8)	-9.4 (6.6)

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Retinal Nerve Fiber Layer (RNFL) Thickness in the Affected Eye at Weeks 12 and 24
Measure Description	The RNFL thickness was measured for 12 sectors (every 30 degrees) per eye in triplicate by OCT measurements and was then averaged over 12 sectors. The change in RNFL thickness at Weeks 12 and 24 was calculated as RNFL thickness at Weeks 12 and 24 minus RNFL thickness at baseline, respectively.
Time Frame	Baseline, Weeks 12 and 24
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "N" (number of participants analyzed) signifies those participants who were evaluable for this outcome measure and "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	13	13
Change From Baseline in Retinal Nerve Fiber Layer (RNFL) Thickness in the Affected Eye at Weeks 12 and 24 [units: micrometer] Mean (Standard Deviation)		
Baseline (n=17, 17)	103.893 (17.271)	104.170 (8.832)
Change at Week 12 (n = 13, 13)	-17.036 (13.919)	-9.356 (9.532)
Change at Week 24 (n = 4, 5)	-17.815 (16.505)	-11.234 (14.230)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Macular Thickness at 3 Millimeter (mm) Around Fovea in the Affected Eye at Weeks 12, 24 and 36
Measure Description	The change in macular thickness at 3 mm around fovea in the affected eye at Weeks 12, 24 and 36 was calculated as macular thickness at 3 mm in the affected eye at Weeks 12, 24 and 36 minus macular thickness at 3 mm in the affected eye at baseline, respectively.
Time Frame	Baseline, Weeks 12, 24 and 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	17	17

	Placebo: Double-blind Period	Atacicept: Double-blind Period
Change From Baseline in Macular Thickness at 3 Millimeter (mm) Around Fovea in the Affected Eye at Weeks 12, 24 and 36 [units: micrometer] Mean (Standard Deviation)		
Baseline (n = 17, 17)	1054.4 (76.5)	1070.6 (72.7)
Change at Week 12 (n = 13, 13)	-29.3 (34.4)	-34.0 (21.8)
Change at Week 24 (n = 4, 5)	-72.5 (47.0)	-50.4 (47.7)
Change at Week 36 (n = 3, 4)	-32.7 (30.7)	-40.0 (51.3)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in Macular Thickness at 6 Millimeter (mm) Around Fovea in the Affected Eye at Weeks 12, 24 and 36
Measure Description	The change in macular thickness at 6 mm around fovea in the affected eye at Weeks 12, 24 and 36 was calculated as macular thickness at 6 mm in the affected eye at Weeks 12, 24 and 36 minus macular thickness at 6 mm in the affected eye at baseline, respectively.
Time Frame	Baseline, Weeks 12, 24 and 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	17	17

	Placebo: Double-blind Period	Atacicept: Double-blind Period
Change From Baseline in Macular Thickness at 6 Millimeter (mm) Around Fovea in the Affected Eye at Weeks 12, 24 and 36 [units: micrometer] Mean (Standard Deviation)		
Baseline (n = 17, 17)	954.4 (57.4)	947.5 (61.3)
Change at Week 12 (n = 13, 13)	-36.1 (28.4)	-32.8 (25.2)
Change at Week 24 (n = 4, 5)	-63.8 (32.7)	-46.2 (36.5)
Change at Week 36 (n = 3, 4)	-33.3 (33.7)	-34.8 (46.0)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Macular Volume in the Affected Eye at Weeks 12, 24 and 36
Measure Description	The change in macular volume in the affected eye at Weeks 12, 24 and 36 was calculated as macular volume in the affected eye at Weeks 12, 24 and 36 minus macular volume in the affected eye at baseline, respectively.
Time Frame	Baseline, Weeks 12, 24 and 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	17	17
Change From Baseline in Macular Volume in the Affected Eye at Weeks 12, 24 and 36 [units: cubic micrometer]		

	Placebo: Double-blind Period	Atacicept: Double-blind Period
Mean (Standard Deviation)		
Baseline (n = 17, 17)	6.8865 (0.4199)	6.8794 (0.4372)
Change at Week 12 (n = 13, 13)	-0.2389 (0.1991)	-0.2301 (0.1612)
Change at Week 24 (n = 4, 5)	-0.4630 (0.2466)	-0.3292 (0.2674)
Change at Week 36 (n = 3, 4)	-0.2353 (0.2253)	-0.2533 (0.3205)

7. Secondary Outcome Measure:

Measure Title	Low-Contrast Letter Acuity: Total Number of Letters Correctly Identified
Measure Description	Low-contrast letter acuity was measured by using the Sloan Charts at 1.25 fraction (%) and 2.5%. Sloan letters are a set of optotypes used to test visual acuity. Total number of letters correctly identified in the affected and fellow eye were reported. The possible Sloan Chart range is 0 to 70. More the number of letters identified, better is the visual acuity.
Time Frame	Weeks 12, 24 and 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "N" (number of participants analyzed) signifies those participants who were evaluable for this outcome measure and "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	15	14
Low-Contrast Letter Acuity: Total Number of Letters Correctly Identified [units: letters] Mean (Standard Deviation)		

	Placebo: Double-blind Period	Atacicept: Double-blind Period
Sloan chart 1.25%, affected eye: Week 12 (n=15,14)	14.7 (14.7)	15.7 (19.0)
Sloan chart 1.25%, affected eye: Week 24 (n = 5,5)	16.2 (13.6)	13.4 (18.4)
Sloan chart 1.25%, affected eye: Week 36 (n = 3,4)	24.7 (8.1)	9.8 (18.8)
Sloan chart 2.5%, affected eye: Week 12 (n=15, 14)	25.6 (16.7)	22.1 (19.5)
Sloan chart 2.5%, affected eye: Week 24 (n = 5, 5)	26.8 (15.2)	21.4 (19.3)
Sloan chart 2.5%, affected eye: Week 36 (n = 3, 4)	38.7 (4.7)	20.3 (18.7)
Sloan chart 1.25%, fellow eye: Week 12 (n=15,14)	25.7 (13.1)	25.9 (16.5)
Sloan chart 1.25%, fellow eye: Week 24 (n = 5,5)	22.2 (16.1)	24.6 (18.4)
Sloan chart 1.25%, fellow eye: Week 36 (n = 3,4)	35.3 (4.2)	19.8 (20.6)
Sloan chart 2.5%, fellow eye: Week 12 (n=15, 14)	35.3 (13.4)	36.4 (12.7)
Sloan chart 2.5%, fellow eye: Week 24 (n = 5, 5)	33.6 (18.2)	35.8 (15.4)
Sloan chart 2.5%, fellow eye: Week 36 (n = 3, 4)	45.7 (4.5)	32.5 (19.1)

8. Secondary Outcome Measure:

Measure Title	Contrast Sensitivity: Total Number of Letters Correctly Identified
Measure Description	Contrast Sensitivity was measured using the Pelli-Robson Charts. Pelli-Robson chart is used for clinical measurement of contrast sensitivity and determines the contrast required to read large letters of a fixed size. Total number of letters correctly identified in the affected and fellow eye were reported. The total possible range is 0 to 48. More the number of letters identified, better is the contrast sensitivity.
Time Frame	Weeks 12, 24 and 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "N" (number of participants analyzed) signifies those participants who were evaluable for this outcome measure and "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	15	14
Contrast Sensitivity: Total Number of Letters Correctly Identified [units: letters] Mean (Standard Deviation)		
Affected eye: Week 12 (n = 15, 14)	35.4 (5.9)	32.4 (8.8)
Affected eye: Week 24 (n = 5, 5)	34.2 (6.9)	33.0 (4.7)
Affected eye: Week 36 (n = 3, 3)	37.0 (5.3)	34.7 (3.2)
Fellow eye: Week 12 (n = 15, 14)	38.3 (4.1)	37.6 (3.3)
Fellow eye: Week 24 (n = 5, 5)	36.2 (9.4)	37.4 (2.4)
Fellow eye: Week 36 (n = 3, 3)	39.7 (4.0)	40.0 (1.0)

9. Secondary Outcome Measure:

Measure Title	Contrast Sensitivity: Score Line
Measure Description	Contrast sensitivity was measured using the Pelli-Robson charts with letters arranged in groups of 3. Pelli-Robson chart is used for clinical measurement of contrast sensitivity and determines the contrast required to read large letters of a fixed size. The possible score line range is 0 (visual disability) to 16 (normal contrast sensitivity).
Time Frame	Weeks 12, 24 and 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants. Here, "N" (number of participants analyzed) signifies those participants who were evaluable for this outcome measure and "n" signifies those participants who were evaluable for the specified category.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	15	14
Contrast Sensitivity: Score Line [units: units on a scale] Mean (Standard Deviation)		
Affected eye: Week 12 (n = 15, 14)	12.1 (1.5)	10.9 (2.9)
Affected eye: Week 24 (n = 5, 5)	11.4 (2.6)	11.2 (1.6)
Affected eye: Week 36 (n = 3, 3)	12.3 (2.1)	11.7 (1.5)
Fellow eye: Week 12 (n = 15, 14)	12.9 (1.5)	12.7 (1.1)
Fellow eye: Week 24 (n = 5, 5)	11.8 (3.3)	12.4 (0.5)
Fellow eye: Week 36 (n = 3, 3)	13.3 (1.2)	13.3 (0.6)

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants Converting to Clinically Definite Multiple Sclerosis (CDMS) Second Clinical Attack
Measure Description	Conversion to CDMS was defined as experiencing a second clinical attack meeting all of 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 intraauricularly] greater than 37.5 degree Celsius/99.5 degree Fahrenheit); (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 Score (EDSS), or (ii) Increase of the total EDSS score. EDSS assesses disability in 8 functional systems and total score ranges from 0 (normal) to 10 (death due to MS). Percentage of participants converting to CDMS (second clinical attack) was reported.
Time Frame	From baseline (Study Day 1) up to Week 36
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants.

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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: Double-blind Period	Atacicept: Double-blind Period
Number of Participants Analyzed	17	17
Percentage of Participants Converting to Clinically Definite Multiple Sclerosis (CDMS) Second Clinical Attack [units: percentage of participants]	17.6	35.3

Reported Adverse Events

Time Frame	Baseline up to Week 48
Additional Description	ITT population of the double-blind period included all randomized subjects according to their randomized treatment. SFU period population included all randomized participants of double-blind period who participated in the 60-week SFU (N=13,14 for Placebo and Atacicept arms respectively).

Reporting Groups

	Description
Placebo: Double-blind Period	Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 32 weeks.
Atacicept: Double-blind Period	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.
Placebo: SFU Period	Participants who received placebo matched to atacicept in double-blind period were included in SFU period (60 weeks) following premature termination of the trial.

	Description
Atacicept: SFU Period	Participants who received atacicept in double-blind period were included in SFU period (60 weeks) following premature termination of the trial.

Serious Adverse Events

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	2/14 (14.29%)
General disorders				
Pyrexia [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Infections and infestations				
Bacterial pyelonephritis [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Nervous system disorders				
Multiple sclerosis [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Myelitis [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Myelitis transverse [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Skin and subcutaneous tissue disorders				
Blister [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

Other Adverse Events

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

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	14/17 (82.35%)	16/17 (94.12%)	6/13 (46.15%)	10/14 (71.43%)
Blood and lymphatic system disorders				
Anaemia of pregnancy [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Lymphadenopathy [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Lymphopenia [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Cardiac disorders				
Bundle branch block right [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Ventricular arrhythmia [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Ear and labyrinth disorders				
Ear pain [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Vertigo [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Eye disorders				
Asthenopia [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Eye haemorrhage [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Eye pain [A] *	0/17 (0%)	2/17 (11.76%)	0/13 (0%)	1/14 (7.14%)
Photopsia [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Uhthoff's phenomenon [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Visual acuity reduced [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Vitreous floaters [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Gastrointestinal disorders				
Abdominal pain [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Abdominal pain upper [A] *	0/17 (0%)	2/17 (11.76%)	0/13 (0%)	1/14 (7.14%)
Aerophagia [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Constipation [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	1/14 (7.14%)
Diarrhoea [A] *	3/17 (17.65%)	2/17 (11.76%)	0/13 (0%)	0/14 (0%)

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Dyspepsia [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Faecal incontinence [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Nausea [A] *	1/17 (5.88%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Tongue disorder [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Vomiting [A] *	2/17 (11.76%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Vomiting in pregnancy [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
General disorders				
Asthenia [A] *	2/17 (11.76%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Chest discomfort [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Chest pain [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Fatigue [A] *	3/17 (17.65%)	3/17 (17.65%)	0/13 (0%)	0/14 (0%)
Influenza like illness [A] *	0/17 (0%)	0/17 (0%)	3/13 (23.08%)	2/14 (14.29%)
Injection site erythema [A] *	1/17 (5.88%)	2/17 (11.76%)	0/13 (0%)	0/14 (0%)
Injection site haematoma [A] *	1/17 (5.88%)	3/17 (17.65%)	0/13 (0%)	0/14 (0%)
Injection site pain [A] *	0/17 (0%)	2/17 (11.76%)	0/13 (0%)	0/14 (0%)
Injection site pruritus [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Injection site reaction [A] *	3/17 (17.65%)	11/17 (64.71%)	1/13 (7.69%)	2/14 (14.29%)
Injection site swelling [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Non-cardiac chest pain [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Pain [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Pyrexia [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Immune system disorders				

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Drug hypersensitivity [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Food allergy [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Hypersensitivity [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Infections and infestations				
Cystitis [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Ear infection [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Gastroenteritis viral [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Influenza [A] *	0/17 (0%)	2/17 (11.76%)	0/13 (0%)	0/14 (0%)
Nasopharyngitis [A] *	2/17 (11.76%)	1/17 (5.88%)	0/13 (0%)	2/14 (14.29%)
Rash pustular [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	1/14 (7.14%)
Sinusitis [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	1/14 (7.14%)
Syphilis [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Upper respiratory tract infection [A] *	1/17 (5.88%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Urinary tract infection [A] *	1/17 (5.88%)	1/17 (5.88%)	0/13 (0%)	1/14 (7.14%)
Viral pharyngitis [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Injury, poisoning and procedural complications				
Arthropod bite [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Arthropod sting [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Bone fissure [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Concussion [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Muscle strain [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Road traffic accident [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Investigations				
Alanine aminotransferase increased [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Blood glucose increased [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Liver function test abnormal [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Weight increased [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Metabolism and nutrition disorders				
Decreased appetite [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Musculoskeletal and connective tissue disorders				
Arthralgia [A] *	1/17 (5.88%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Back pain [A] *	2/17 (11.76%)	1/17 (5.88%)	1/13 (7.69%)	0/14 (0%)
Bursitis [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	1/14 (7.14%)
Muscle spasms [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Musculoskeletal pain [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Musculoskeletal stiffness [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Myalgia [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	1/14 (7.14%)
Neck pain [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Pain in extremity [A] *	1/17 (5.88%)	2/17 (11.76%)	0/13 (0%)	1/14 (7.14%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Lipoma [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Skin papilloma [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Nervous system disorders				
Balance disorder [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Carpal tunnel syndrome [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Dizziness [A] *	4/17 (23.53%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Headache [A] *	3/17 (17.65%)	4/17 (23.53%)	0/13 (0%)	2/14 (14.29%)
Hypoaesthesia [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	1/14 (7.14%)
Migraine [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Muscle contractions involuntary [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Optic neuritis [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Paraesthesia [A] *	1/17 (5.88%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Syncope [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Psychiatric disorders				
Anxiety [A] *	1/17 (5.88%)	1/17 (5.88%)	0/13 (0%)	2/14 (14.29%)
Depression [A] *	4/17 (23.53%)	2/17 (11.76%)	0/13 (0%)	1/14 (7.14%)
Insomnia [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Renal and urinary disorders				
Pollakiuria [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Stress urinary incontinence [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Urinary incontinence [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Reproductive system and breast disorders				
Dysmenorrhoea [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Galactorrhoea [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Ovarian cyst [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Respiratory, thoracic and mediastinal disorders				

	Placebo: Double-blind Period	Atacicept: Double-blind Period	Placebo: SFU Period	Atacicept: SFU Period
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Cough [A] *	0/17 (0%)	1/17 (5.88%)	2/13 (15.38%)	0/14 (0%)
Dysphonia [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Dyspnoea [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Nasal congestion [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Oropharyngeal pain [A] *	1/17 (5.88%)	2/17 (11.76%)	0/13 (0%)	1/14 (7.14%)
Pulmonary congestion [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Tracheal pain [A] *	1/17 (5.88%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Skin and subcutaneous tissue disorders				
Eczema [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)
Pruritus allergic [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Rash [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Rosacea [A] *	0/17 (0%)	0/17 (0%)	1/13 (7.69%)	0/14 (0%)
Urticaria [A] *	0/17 (0%)	1/17 (5.88%)	0/13 (0%)	0/14 (0%)
Vascular disorders				
Hypertension [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	2/14 (14.29%)
Hypertensive crisis [A] *	0/17 (0%)	0/17 (0%)	0/13 (0%)	1/14 (7.14%)
Hypotension [A] *	1/17 (5.88%)	0/17 (0%)	0/13 (0%)	0/14 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

Limitations and Caveats

The Sponsor voluntarily terminated this trial after observing increased Multiple Sclerosis (MS) disease activity in trial 28063 (ATAMS).

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 Healthcare, a business of Merck KGaA, Darmstadt, Germany
Phone: +49-6151-72-5200
Email: service@merckgroup.com