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

ClinicalTrials.gov ID: NCT00430495

Study Identification

Unique Protocol ID:	27298
Brief Title:	A Phase 2 Dose-finding Study of Atacicept in Subjects With Rheumatoid Arthritis (AUGUST I)
Official Title:	A Randomized, Double-blind, Placebo-controlled, Multicentre, Phase II Dose-finding Study of Atacicept Given Subcutaneously in Subjects With Rheumatoid Arthritis and Inadequate Response to TNFa Antagonist Therapy
Secondary IDs:	

Study Status

Record Verification:	January 2016
Overall Status:	Completed
Study Start:	December 2006
Primary Completion:	September 2009 [Actual]
Study Completion:	September 2009 [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: 100321 Serial Number: 000 Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 09/13/2006 Board Name: Coast IRB Board Affiliation: Coast IRB Phone: (949) 218-9969 Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This was a double-blind, placebo-controlled, parallel-arm, multicentre, prospective dose-finding trial of the safety and efficacy of atacicept in subjects with active rheumatoid arthritis who had failed a three month therapeutic trial with a tumor necrosis factor alpha (TNFa) antagonist due to lack of efficacy.
Detailed Description:	

Conditions

Conditions:	Rheumatoid Arthritis
Keywords:	atacicept arthritis

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: 256 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Atacicept 25 mg	Drug: Atacicept 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 21 weeks.
Experimental: Atacicept 75 mg	Drug: Atacicept 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 21 weeks.
Experimental: Atacicept 150 mg	Drug: Atacicept 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 21 weeks.
Placebo Comparator: Placebo	Drug: Placebo matched to atacicept Placebo matched to atacicept was administered subcutaneously twice a week for initial 4 weeks, followed by once a week for subsequent 21 weeks.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

1. Rheumatoid arthritis (RA) satisfying American College of Rheumatology (ACR) diagnostic criteria with a disease history of at least one year

2. Male or female greater than or equal to (>=)18-years of age at time of informed consent
3. Active RA as defined by:
    - >=8 swollen joints (66-joint count),
    - >=8 tender joints (68-joint count), and
    - C-reactive protein (CRP) >=10 milligram per liter (mg/L) (central laboratory) and/or erythrocyte sedimentation rate (ESR) >= to 28 millimeter per hour (mm/h)
4. Failure of at least one TNFa antagonist therapy (previously or at the time of screening) as specified in the protocol
5. Other protocol defined inclusion criteria could apply

Exclusion Criteria:

1. Any condition, including laboratory findings or findings in the medical history or pre-trial assessments, that in the opinion of the Investigator constitutes a risk or a contraindication for the subject's participation in the trial or that could interfere with the trial objectives, conduct or evaluation
2. Treatment with biologics aiming at B cell modulation such as rituximab or belimumab within 2 years before study Day 1
3. Any previous treatment with anakinra (Kineret), abatacept (Orencia) or tocilizumab within 3 months before study Day 1
4. Use of etanercept (Enbrel) within 28 days before study Day 1, or of infliximab (Remicade) or adalimumab (Humira) within 60 days before study Day 1
5. Participation in any interventional clinical trial with an unapproved investigational therapy within the 3 months before the start of this study (or within 5 half-lives of the investigated compound before study Day 1, whichever is longer)
6. 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: United States, Massachusetts
EMD Serono
Rockland, Massachusetts, United States, 02370

Canada
Merck/Serono
Canada, Canada

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	A total of 456 subjects were screened, of whom 256 were enrolled and randomized of which 254 received the trial medication and included in Intention to Treat (ITT) population.

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 21 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 21 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 21 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 21 weeks.

Overall Study

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Started	64	66	62	64
Treated	62	66	62	64
Completed	50	59	49	60
Not Completed	14	7	13	4
Adverse Event	2	3	2	0
Death	0	0	1	0
Lost to Follow-up	0	1	4	0
Protocol Violation	1	0	1	0
Disease Progression	1	1	0	0
Unspecified	8	2	5	4
Randomized but not Treated	2	0	0	0

Baseline Characteristics

Analysis Population Description

Intention-to-treat (ITT) population included all randomized participants who received at least one treatment dose.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Baseline Measures

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg	Total
Number of Participants	62	66	62	64	254
Age, Continuous [units: years] Mean (Standard Deviation)	53.1 (12.5)	53.4 (13.1)	55.3 (12.0)	53.5 (10.1)	53.8 (11.9)
Gender, Male/Female [units: participants]					
Female	51	54	53	53	211
Male	11	12	9	11	43

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Achieving American College of Rheumatology 20 Response Based on C-reactive Protein (ACR20-CRP) at Week 26
Measure Description	ACR20-CRP response is defined as greater than or equal to (>=) 20 percent (%) improvement in both tender joint counts (based on a total of 68 joints) and swollen joint counts (based on a total of 66 joints) together with >=20% improvement in at least 3 of the following 5 measures: 1) participant's assessment of pain; 2) participant's global assessment of disease activity; 3) physician's global assessment of disease activity; 4) participant's assessment of physical function; and 5) acute-phase marker (CRP).

Time Frame	Week 26
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who received at least 1 treatment dose.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	62	66	62	64
Percentage of Participants Achieving American College of Rheumatology 20 Response Based on C-reactive Protein (ACR20-CRP) at Week 26 [units: percentage of participants]	29.0	30.3	27.4	39.1

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving American College of Rheumatology 50 Response Based on CRP (ACR50-CRP) at Week 26
Measure Description	ACR50-CRP response is defined as >=50% improvement in both tender joint counts (based on a total of 68 joints) and swollen joint counts (based on a total of 66 joints) together with >=50% improvement in at least 3 of the following 5 measures: 1) participant's assessment of pain; 2) participant's global assessment of disease activity; 3) physician's global assessment of disease activity; 4) participant's assessment of physical function; and 5) acute-phase marker (CRP).
Time Frame	Week 26

Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who received at least 1 treatment dose.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	62	66	62	64
Percentage of Participants Achieving American College of Rheumatology 50 Response Based on CRP (ACR50-CRP) at Week 26 [units: percentage of participants]	6.5	13.6	11.3	10.9

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving American College of Rheumatology 70 Response Based on CRP (ACR70-CRP) at Week 26
Measure Description	ACR70-CRP response is defined as >=70% improvement in both tender joint counts (based on a total of 68 joints) and swollen joint counts (based on a total of 66 joints) together with >=70% improvement in at least 3 of the following 5 measures: 1) participant's assessment of pain; 2) participant's global assessment of disease activity; 3) physician's global assessment of disease activity; 4) participant's assessment of physical function; and 5) acute-phase marker (CRP).
Time Frame	Week 26
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who received at least 1 treatment dose.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	62	66	62	64
Percentage of Participants Achieving American College of Rheumatology 70 Response Based on CRP (ACR70-CRP) at Week 26 [units: percentage of participants]	0.0	6.1	4.8	0.0

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Disease Activity Score in 28 Joints (DAS28) Based on CRP (DAS28-CRP) of Less Than or Equal to (<=) 3.2 at Week 26
Measure Description	DAS28-CRP incorporates non-graded joint counts for tenderness and swelling based on a total of 28 joints, CRP as a marker of inflammation, and a general health assessment using a 100-millimeter (mm) visual analog scale (the participant's global assessment of disease activity). DAS28 ranges between 0 and 10 representing current disease activity. A value above 5.1 represents high disease activity, a value below 3.2 represents low disease activity, and a value below 2.6 represents remission.
Time Frame	Week 26
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who received at least 1 treatment dose.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	62	66	62	64
Percentage of Participants Achieving Disease Activity Score in 28 Joints (DAS28) Based on CRP (DAS28-CRP) of Less Than or Equal to (<=) 3.2 at Week 26 [units: percentage of participants]	9.7	10.6	9.7	12.5

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Disease Activity Score in 28 Joints (DAS28) Based on CRP (DAS28-CRP) of <=2.6 at Week 26
Measure Description	DAS28-CRP incorporates non-graded joint counts for tenderness and swelling based on a total of 28 joints, CRP as a marker of inflammation, and a general health assessment using a 100 mm visual analog scale (the participant's global assessment of disease activity). DAS28 ranges between 0 and 10 representing current disease activity. A value above 5.1 represents high disease activity, a value below 3.2 represents low disease activity, and a value below 2.6 represents remission.
Time Frame	Week 26
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who received at least 1 treatment dose.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	62	66	62	64
Percentage of Participants Achieving Disease Activity Score in 28 Joints (DAS28) Based on CRP (DAS28-CRP) of <=2.6 at Week 26 [units: percentage of participants]	1.6	6.1	4.8	4.7

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Improvement in Health Assessment Questionnaire Disability Index (HAQ-DI) of at Least 0.3 From Baseline at Week 26
Measure Description	The HAQ-DI is a participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item was scored on 4-point scale from 0 to 3: 0 = no difficulty; 1 = some difficulty; 2 = much difficulty; 3 = unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range is 0 to 3 where 0 = least difficulty and 3 = extreme difficulty. Percentage of participants achieving improvement in HAQ-DI of at least 0.3 from baseline at Week 26 was reported.
Time Frame	Week 26
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who received at least 1 treatment dose. Here, 'N' (number of participants analyzed) signifies those participants who were evaluable for this outcome measure.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	38	41	34	48
Percentage of Participants Achieving Improvement in Health Assessment Questionnaire Disability Index (HAQ-DI) of at Least 0.3 From Baseline at Week 26 [units: percentage of participants]	47.4	48.8	55.9	37.5

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Good or Moderate European League Against Rheumatism (EULAR) Response at Week 26
Measure Description	The EULAR response criteria evaluate change in DAS28 scores represented as "good response", "moderate response", or "no response" considering both the current DAS28 score and the observed improvement from baseline. Participants were considered to have "good" or "moderate" EULAR response if at the time of assessment, their DAS28 score was <=5.1 and the improvement from baseline in their DAS28 score was greater than (>) 0.6; or if at the time of assessment, their DAS28 score was >5.1 and improvement from baseline in their DAS28 score was >1.2.
Time Frame	Week 26
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who received at least 1 treatment dose.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	62	66	62	64
Percentage of Participants With Good or Moderate European League Against Rheumatism (EULAR) Response at Week 26 [units: percentage of participants]	41.9	31.8	35.5	53.1

8. Secondary Outcome Measure:

Measure Title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)
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.
Time Frame	Baseline up to Week 38
Safety Issue?	Yes

Analysis Population Description

Safety population included all randomized participants who received at least 1 treatment dose and had safety data following their first dose.

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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 weeks.

Measured Values

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
Number of Participants Analyzed	62	66	62	64
Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) [units: participants]				
AEs	41	49	42	46
SAEs	3	9	8	5

Reported Adverse Events

Time Frame	Baseline up to Week 38
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 21 weeks.
Atacicept 25 mg	Atacicept was administered subcutaneously at a dose of 25 mg twice a week for initial 4 weeks as loading dose, followed by 25 mg once a week for subsequent 21 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 21 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 21 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	3/62 (4.84%)	9/66 (13.64%)	8/62 (12.9%)	5/64 (7.81%)
Blood and lymphatic system disorders				
Anaemia [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Cardiac disorders				
Acute myocardial infarction [A] *	0/62 (0%)	0/66 (0%)	1/62 (1.61%)	0/64 (0%)
Angina pectoris [A] *	0/62 (0%)	0/66 (0%)	1/62 (1.61%)	0/64 (0%)
Cardio-respiratory arrest [A] *	0/62 (0%)	0/66 (0%)	1/62 (1.61%)	0/64 (0%)
Right ventricular failure [A] *	0/62 (0%)	0/66 (0%)	0/62 (0%)	1/64 (1.56%)
Endocrine disorders				
Basedow's disease [A] *	1/62 (1.61%)	0/66 (0%)	0/62 (0%)	0/64 (0%)
Hyperthyroidism [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Gastrointestinal disorders				
Diverticular perforation [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Inguinal hernia [A] *	0/62 (0%)	0/66 (0%)	0/62 (0%)	1/64 (1.56%)
Intestinal obstruction [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
General disorders				
Non-cardiac chest pain [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Pyrexia [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Immune system disorders				
Drug hypersensitivity [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Infections and infestations				
Bronchitis [A] *	0/62 (0%)	0/66 (0%)	0/62 (0%)	1/64 (1.56%)
Pyopneumothorax [A] *	0/62 (0%)	0/66 (0%)	0/62 (0%)	1/64 (1.56%)
Relapsing fever [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Stenotrophomonas infection [A] *	0/62 (0%)	0/66 (0%)	0/62 (0%)	1/64 (1.56%)
Injury, poisoning and procedural complications				
Femur fracture [A] *	1/62 (1.61%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Hip fracture [A] *	0/62 (0%)	0/66 (0%)	2/62 (3.23%)	0/64 (0%)
Humerus fracture [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Pelvic fracture [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Upper limb fracture [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Investigations				
Fibrin D dimer increased [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Gamma-glutamyltransferase increased [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Musculoskeletal and connective tissue disorders				
Back pain [A] *	1/62 (1.61%)	0/66 (0%)	0/62 (0%)	0/64 (0%)
Osteonecrosis [A] *	0/62 (0%)	0/66 (0%)	1/62 (1.61%)	0/64 (0%)
Rheumatoid arthritis [A] *	0/62 (0%)	2/66 (3.03%)	2/62 (3.23%)	0/64 (0%)
Nervous system disorders				
Migraine [A] *	1/62 (1.61%)	0/66 (0%)	0/62 (0%)	0/64 (0%)
Vasculitis cerebral [A] *	0/62 (0%)	0/66 (0%)	1/62 (1.61%)	0/64 (0%)

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pregnancy, puerperium and perinatal conditions				
Abortion spontaneous [A] *	0/62 (0%)	0/66 (0%)	0/62 (0%)	1/64 (1.56%)
Reproductive system and breast disorders				
Fallopian tube cyst [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	0/64 (0%)
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism [A] *	1/62 (1.61%)	0/66 (0%)	0/62 (0%)	0/64 (0%)
Skin and subcutaneous tissue disorders				
Angioedema [A] *	0/62 (0%)	0/66 (0%)	1/62 (1.61%)	0/64 (0%)
Surgical and medical procedures				
Prostatic operation [A] *	0/62 (0%)	0/66 (0%)	0/62 (0%)	1/64 (1.56%)

* 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	15/62 (24.19%)	25/66 (37.88%)	16/62 (25.81%)	26/64 (40.62%)
Blood and lymphatic system disorders				
Iron deficiency anaemia [A] *	0/62 (0%)	1/66 (1.52%)	0/62 (0%)	4/64 (6.25%)
Gastrointestinal disorders				
Constipation [A] *	1/62 (1.61%)	4/66 (6.06%)	1/62 (1.61%)	2/64 (3.12%)
Diarrhoea [A] *	1/62 (1.61%)	4/66 (6.06%)	6/62 (9.68%)	5/64 (7.81%)
Nausea [A] *	1/62 (1.61%)	5/66 (7.58%)	4/62 (6.45%)	1/64 (1.56%)
Infections and infestations				
Nasopharyngitis [A] *	1/62 (1.61%)	3/66 (4.55%)	1/62 (1.61%)	4/64 (6.25%)

	Placebo	Atacicept 25 mg	Atacicept 75 mg	Atacicept 150 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Upper respiratory tract infection [A] *	4/62 (6.45%)	3/66 (4.55%)	0/62 (0%)	8/64 (12.5%)
Urinary tract infection [A] *	3/62 (4.84%)	4/66 (6.06%)	3/62 (4.84%)	5/64 (7.81%)
Nervous system disorders				
Headache [A] *	4/62 (6.45%)	12/66 (18.18%)	5/62 (8.06%)	3/64 (4.69%)
Vascular disorders				
Hypertension [A] *	5/62 (8.06%)	3/66 (4.55%)	3/62 (4.84%)	2/64 (3.12%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.1)

Limitations and Caveats

[Not specified]

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.

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