Clinical trial results:
A Phase II, Randomized, Double-Blind,Placebo-Controlled Study to Evaluate the Efficacy and Safety of Atacicept in IgA Nephropathy

Summary

EudraCT number	2016-002262-31
Trial protocol	GB
Global end of trial date	07 February 2020

Results information

Result version number	v1 (current)
This version publication date	22 February 2021
First version publication date	22 February 2021

Trial information

Trial identification

Sponsor protocol code	MS700461-0035

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02808429
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck KGaA, Darmstadt, Germany
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Communication Centre, Merck KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com
Scientific contact	Communication Center, Merck KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2020
Global end of trial reached?	Yes
Global end of trial date	07 February 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to evaluate the safety, tolerability, dose response and efficacy of Atacicept in subjects with Immunoglobulin A (IgA) nephropathy and persistent proteinuria. The study hypothesis was that treatment with Atacicept would reduce proteinuria compared to placebo.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 1
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	16
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	16
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was to be conducted in 2 parts; Part A and Part B. However, study was terminated early as per sponsor decision due to unexpectedly slow enrollment and Part B was not initiated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo matched to Atacicept once weekly as subcutaneous (SC) injection during this study up to a maximum of 72.1 weeks.

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

Dosage and administration details:

Subjects received placebo matched to Atacicept once weekly as subcutaneous (SC) injection for 72 weeks.

Arm title	Atacicept 25 mg

Arm description:

Subjects received 25 milligrams (mg) of Atacicept once weekly as SC injection during this study up to a maximum of 73.6 weeks.

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

Dosage and administration details:

Subjects received 25 milligarms (mg) of Atacicept once weekly as SC injection for 72 weeks.

Arm title	Atacicept 75 mg

Arm description:

Subjects received 75 mg of Atacicept once weekly as SC injection during this study up to a maximum of 74.1 weeks.

Arm type	Experimental

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

Dosage and administration details:

Subjects received 75 mg of Atacicept once weekly as SC injection for 72 weeks.

Number of subjects in period 1	Placebo	Atacicept 25 mg	Atacicept 75 mg
Started	5	6	5
Completed	2	5	3
Not completed	3	1	2
Relocation	-	-	1
Lost to follow-up	1	-	-
Premature Study termination by Sponsor	2	-	1
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to Atacicept once weekly as subcutaneous (SC) injection during this study up to a maximum of 72.1 weeks.	
Reporting group title	Atacicept 25 mg
Reporting group description:	
Subjects received 25 milligrams (mg) of Atacicept once weekly as SC injection during this study up to a maximum of 73.6 weeks.	
Reporting group title	Atacicept 75 mg
Reporting group description:	
Subjects received 75 mg of Atacicept once weekly as SC injection during this study up to a maximum of 74.1 weeks.	

Reporting group values	Placebo	Atacicept 25 mg	Atacicept 75 mg
Number of subjects	5	6	5
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	46	41	43
standard deviation	± 3.1	± 16.9	± 8.7
Sex: Female, Male Units: Subjects			
Female	1	5	2
Male	4	1	3
Race (NIH/OMB) Units: Subjects			
Asian	1	1	1
White	4	5	2
Unknown or Not Reported	0	0	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	3
Not Hispanic or Latino	5	5	2
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	16		
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		

Sex: Female, Male Units: Subjects			
Female	8		
Male	8		
Race (NIH/OMB) Units: Subjects			
Asian	3		
White	11		
Unknown or Not Reported	2		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4		
Not Hispanic or Latino	12		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to Atacicept once weekly as subcutaneous (SC) injection during this study up to a maximum of 72.1 weeks.	
Reporting group title	Atacicept 25 mg
Reporting group description:	
Subjects received 25 milligrams (mg) of Atacicept once weekly as SC injection during this study up to a maximum of 73.6 weeks.	
Reporting group title	Atacicept 75 mg
Reporting group description:	
Subjects received 75 mg of Atacicept once weekly as SC injection during this study up to a maximum of 74.1 weeks.	

Primary: Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs), Adverse Event of Special Interest (AESIs), Serious TEAEs, TEAEs Leading to Discontinuation and TEAEs Leading to Death

End point title	Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs), Adverse Event of Special Interest (AESIs), Serious TEAEs, TEAEs Leading to Discontinuation and TEAEs Leading to Death[1]

End point description:

Adverse Event (AE) any untoward medical occurrence in subject administered with a study drug, which does not necessarily had a causal relationship with this treatment. Serious AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial/prolonged inpatient hospitalization; congenital anomaly/birth defect. TEAEs: AEs that developed or worsened/became serious during on-treatment period (time from the first dose of study drug up to the end of study [Week 96]). TEAEs included serious AEs and non-serous AEs. AESIs included infections, cardiac failure, cardiomyopathy/ ischemic heart disease (IHD), hypersensitivity reaction (HR), injection site reactions (ISRs) and demyelinating disorders (DD). Investigator or his /her designee assessed ISRs as local reactions. Safety population set (SAF) included all randomized subjects who received at least 1 dose of IMP and had at least one post-dose assessment.

End point type	Primary

End point timeframe:

Baseline up to 96 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive summary statistics was planned for this endpoint.

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	5	
Units: percentage of subjects				
Subjects with TEAE	100	100	60	
Subjects with AESI: Cardiac failure	0	0	0	
Subjects with AESI: Ischemic heart disease	0	0	0	
Subjects with AESI: Cardiac arrhythmia	0	0	0	
Subjects with AESI: Hypersensitivity reactions	20	67	20	

Subjects with AESI: demyelinating disorders	0	0	0	
Subjects with AESI: injection site reactions	0	83	20	
Subjects with AESI: Infections	40	83	20	
Subjects with serious TEAEs	20	50	0	
Subjects with TEAEs Leading to discontinuation	0	17	0	
Subjects with TEAEs leading to death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Atacicept Concentrations

End point title	Serum Atacicept Concentrations

End point description:

Serum Atacicept Concentrations was to be performed; however; as per changed in planned analysis the endpoint related to pharmacokinetic (PK) parameters was not assessed.

End point type	Secondary

End point timeframe:

Week 0 Day 1 (pre-dose), Weeks 1, 2, 4, 8, 12, 16, 24, 40, 48, 72, Early Termination (up to Week 72) and Post-treatment (PT) Follow Up (FU) Weeks 4, 12 and 24

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: gram per liter				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[2] - No subject was analyzed because as per change in planned analysis PK endpoints were not assessed.

[3] - No subject was analyzed because as per change in planned analysis PK endpoints were not assessed.

[4] - No subject was analyzed because as per change in planned analysis PK endpoints were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Levels in Serum Immunoglobulin A (IgA)

End point title	Change from Baseline Levels in Serum Immunoglobulin A (IgA)

End point description:

The change in serum levels of IgA from baseline was reported. The safety population set (SAF) included all randomized subjects who received at least 1 dose of IMP and had at least one post-dose assessment. Here "n" = subjects who were evaluable for this endpoint at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 8, 12, 16, 20, 24, 32, 40, 48, 60, 72, Early Termination (up to Week 72) and and PT FU Weeks 4, 12 and 24

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	5	
Units: gram per liter				
arithmetic mean (standard deviation)				
Change at Week 1 (n=5,6,5)	-0.194 (± 0.3012)	-0.203 (± 0.1325)	-0.278 (± 0.1561)	
Change at Week 2 (n=5,6,5)	-0.114 (± 0.2825)	-0.280 (± 0.1108)	-0.486 (± 0.2289)	
Change at Week 4 (n=5,6,5)	-0.014 (± 0.3570)	-0.197 (± 0.1952)	-0.828 (± 0.2319)	
Change at Week 8 (n=5,5,5)	0.008 (± 0.5340)	-0.572 (± 0.2838)	-1.144 (± 0.4997)	
Change at Week 12 (n=5,5,5)	-0.030 (± 0.4011)	-0.476 (± 0.3879)	-1.146 (± 0.4226)	
Change at Week 16 (n=5,5,5)	0.044 (± 0.4869)	-0.692 (± 0.3608)	-1.296 (± 0.4237)	
Change at Week 20 (n=5,5,5)	0.218 (± 0.6157)	-0.616 (± 0.2880)	-1.430 (± 0.4635)	
Change at Week 24 (n=5,5,5)	0.212 (± 0.3140)	-0.514 (± 0.4552)	-1.424 (± 0.5226)	
Change at Week 32 (n=5,4,5)	0.180 (± 0.4924)	-0.920 (± 0.2950)	-1.468 (± 0.3851)	
Change at Week 40 (n=5,3,4)	0.112 (± 0.7745)	-0.963 (± 0.2815)	-1.388 (± 0.3212)	
Change at Week 48 (n=5,3,4)	0.526 (± 1.2935)	-0.710 (± 0.3804)	-1.375 (± 0.4680)	
Change at Week 60 (n=4,3,4)	0.233 (± 0.3676)	-0.733 (± 0.3057)	-1.283 (± 0.4308)	
Change at Week 72 (n=3,3,3)	0.307 (± 0.3650)	-0.957 (± 0.2157)	-1.240 (± 0.4491)	
Change at Early Termination (n=2,3,2)	0.420 (± 0.0849)	-0.493 (± 0.2173)	-1.835 (± 0.1344)	
Change at PT FU Week 4 (n=5,5,3)	0.300 (± 0.4757)	-0.452 (± 0.3529)	-1.223 (± 0.2515)	
Change at PT FU Week 12 (n=5,5,4)	0.622 (± 0.7436)	-0.440 (± 0.6335)	-0.668 (± 0.2843)	
Change at PT FU Week 24 (n=4,5,4)	0.563 (± 0.6716)	-0.420 (± 0.6503)	-0.370 (± 0.1160)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Levels in Serum Iimmunoglobulin G (IgG)

End point title	Change from Baseline Levels in Serum Iimmunoglobulin G (IgG)

End point description:

The change in serum levels of IgG from baseline was reported. The safety population set (SAF) included all randomized subjects who received at least 1 dose of IMP and had at least one post-dose assessment. Here "n" = subjects who were evaluable for this endpoint at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 8, 12, 16, 20, 24, 32, 40, 48, 60, 72, Early Termination (up to Week 72) and PT FU Weeks 4, 12 and 24

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	5	
Units: gram per liter				
arithmetic mean (standard deviation)				
Change at Week 1 (n=5,6,5)	-0.630 (± 0.5524)	-0.480 (± 0.4289)	-0.444 (± 0.4372)	
Change at Week 2 (n=5,6,5)	-0.362 (± 0.7146)	-0.650 (± 0.5764)	-0.898 (± 0.5507)	
Change at Week 4 (n=5,6,5)	-0.354 (± 0.7073)	-0.415 (± 0.4965)	-1.792 (± 0.8182)	
Change at Week 8 (n=5,5,5)	-0.562 (± 1.0023)	-1.128 (± 0.3574)	-2.812 (± 1.2085)	
Change at Week 12 (n=5,5,5)	-0.472 (± 0.9304)	-0.930 (± 0.7748)	-3.126 (± 0.9324)	
Change at Week 16 (n=5,5,5)	-0.608 (± 1.1858)	-1.480 (± 0.4687)	-3.360 (± 0.8546)	
Change at Week 20 (n=5,5,5)	0.016 (± 1.0781)	-1.024 (± 0.3893)	-3.684 (± 0.7597)	
Change at Week 24 (n=5,5,5)	-0.748 (± 1.0059)	-0.926 (± 0.8289)	-3.776 (± 1.0876)	
Change at Week 32 (n=5,4,5)	-0.296 (± 1.1195)	-1.055 (± 0.5701)	-3.962 (± 0.8830)	
Change at Week 40 (n=5,3,4)	0.218 (± 0.8904)	-1.363 (± 0.4895)	-3.623 (± 0.2993)	
Change at Week 48 (n=5,3,4)	0.256 (± 1.5731)	-0.600 (± 0.7654)	-3.745 (± 0.4608)	
Change at Week 60 (n=4,3,4)	0.305 (± 1.2881)	-0.743 (± 1.5627)	-3.368 (± 0.5721)	
Change at Week 72 (n=3,3,3)	-0.203 (± 1.3606)	-0.867 (± 0.7772)	-3.477 (± 0.8618)	
Change at Early Termination (n=2,3,2)	0.655 (± 0.5445)	-1.547 (± 0.5353)	-3.995 (± 0.0636)	
Change at PT FU Week 4 (n=5,5,3)	0.360 (± 1.7711)	-0.736 (± 0.7900)	-2.553 (± 0.7160)	
Change at PT FU Week 12 (n=5,5,4)	0.922 (± 1.2793)	-0.800 (± 1.4692)	-1.300 (± 0.5610)	
Change at PT FU Week 24 (n=4,5,4)	0.273 (± 0.9758)	-0.878 (± 1.0395)	0.020 (± 1.2498)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Levels in Serum Immunoglobulin M (IgM)

End point title	Change from Baseline Levels in Serum Immunoglobulin M (IgM)

End point description:

The change in serum levels of IgM from baseline was reported. The safety population set (SAF) included all randomized subjects who received at least 1 dose of IMP and had at least one post-dose assessment. Here "n" = subjects who were evaluable for this endpoint at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 4, 8, 12, 16, 20, 24, 32, 40, 48, 60, 72, Early Termination (up to Week 72) and at PT FU Weeks 4, 12 and 24

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	5	
Units: gram per liter				
arithmetic mean (standard deviation)				
Change at Week 1 (n=5,6,5)	-0.082 (± 0.0835)	-0.072 (± 0.0736)	-0.096 (± 0.0924)	
Change at Week 2 (n=5,6,5)	-0.054 (± 0.1026)	-0.140 (± 0.1906)	-0.102 (± 0.1625)	
Change at Week 4 (n=5,6,5)	-0.002 (± 0.1190)	-0.197 (± 0.2655)	-0.410 (± 0.1637)	
Change at Week 8 (n=5,5,5)	0.006 (± 0.1710)	-0.302 (± 0.3114)	-0.558 (± 0.1859)	
Change at Week 12 (n=5,5,5)	0.022 (± 0.0955)	-0.360 (± 0.3169)	-0.638 (± 0.2497)	
Change at Week 16 (n=5,5,5)	0.024 (± 0.1412)	-0.408 (± 0.3531)	-0.710 (± 0.2463)	
Change at Week 20 (n=5,5,5)	0.082 (± 0.2288)	-0.444 (± 0.3965)	-0.748 (± 0.2500)	
Change at Week 24 (n=5,5,5)	-0.016 (± 0.1390)	-0.364 (± 0.3377)	-0.774 (± 0.2517)	
Change at Week 32 (n=5,4,5)	-0.016 (± 0.1566)	-0.510 (± 0.4498)	-0.796 (± 0.2773)	
Change at Week 40 (n=5,3,4)	0.036 (± 0.1464)	-0.247 (± 0.1553)	-0.848 (± 0.2668)	
Change at Week 48 (n=5,3,4)	0.012 (± 0.1951)	-0.227 (± 0.1250)	-0.848 (± 0.2557)	
Change at Week 60 (n=4,3,4)	-0.033 (± 0.0907)	-0.297 (± 0.2495)	-0.843 (± 0.2573)	
Change at Week 72 (n=3,3,3)	-0.027 (± 0.0153)	-0.337 (± 0.2914)	-0.900 (± 0.3081)	
Change at Early Termination (n=2,3,2)	0.115 (± 0.0354)	-0.463 (± 0.1626)	-0.670 (± 0.1414)	
Change at PT FU Week 4 (n=5,5,3)	-0.048 (± 0.1941)	-0.328 (± 0.1906)	-0.667 (± 0.2259)	
Change at PT FU Week 12 (n=5,5,4)	0.058 (± 0.2281)	-0.214 (± 0.1739)	-0.465 (± 0.2319)	
Change at PT FU Week 24 (n=4,5,4)	0.020 (± 0.1687)	-0.178 (± 0.1504)	-0.340 (± 0.1896)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Galactose Deficient-IgA1 (Gd-IgA1) Levels

End point title	Change From Baseline in Serum Galactose Deficient-IgA1 (Gd-IgA1) Levels

End point description:

The change in serum Gd-IgA1 from baseline was reported. The safety population set (SAF) included all randomized subjects who received at least 1 dose of IMP and had at least one post-dose assessment. Here "n" = subjects who were evaluable for this endpoint at given time points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 12, 24, 48, 72, Early Termination (up to Week 72) and at PT FU Weeks 12 and 24

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	5	
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Change at Week 4 (n=5,6,5)	-1438 (± 598.2)	-620 (± 1580.4)	-2288 (± 730.5)	
Change at Week 12 (n=5,5,5)	-380 (± 1505.0)	-1672 (± 1459.2)	-2778 (± 1345.8)	
Change at Week 24 (n=5,5,4)	160 (± 848.8)	-1912 (± 1835.0)	-3660 (± 1940.9)	
Change at Week 48 (n=5,3,4)	1140 (± 4339.5)	-423 (± 795.1)	-2938 (± 1756.9)	
Change at Week 72 (n=3,3,3)	580 (± 2594.8)	-1327 (± 1181.4)	-3202 (± 1594.9)	
Change at Early Termination (n=2,3,2)	3520 (± 4638.6)	-2383 (± 2551.1)	-2680 (± 1258.7)	
Change at PT FU Week 12 (n=5,5,3)	1926 (± 3523.3)	-772 (± 2050.2)	-818 (± 1277.9)	
Change at PT FU Week 24 (n=3,5,2)	1673 (± 5072.9)	-1262 (± 2444.1)	-1090 (± 70.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Complement C3 and C4 Levels

End point title	Change From Baseline in Serum Complement C3 and C4 Levels

End point description:

The change in serum component C3 and C4 from baseline were reported. The safety population set (SAF) consisted of all randomized subjects who received at least 1 dose of IMP and had at least one post-dose assessment. "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category. Here, '99999' signifies that standard deviation could not be calculated as only 1 subject was analyzed for this category.

End point type	Secondary

End point timeframe:

Baseline, Week 12, 24, 48, 72, Early Termination (ET) (up to Week 72) and at PT FU Weeks 12 and 24

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	5	
Units: milligram per liter				
arithmetic mean (standard deviation)				
Complement C3: Change at Week 12 (n=5,5,5)	-60.0 (± 88.32)	80.0 (± 125.10)	122.0 (± 114.76)	
Complement C3: Change at Week 24 (n=5,5,4)	-38.0 (± 100.85)	-6.0 (± 220.64)	70.0 (± 104.24)	
Complement C3: Change at Week 48 (n=5,3,4)	82.0 (± 215.57)	63.3 (± 110.15)	162.5 (± 219.91)	
Complement C3: Change at Week 72 (n=3,3,3)	-56.7 (± 127.41)	43.3 (± 212.21)	196.7 (± 196.55)	
Complement C3: Change at ET (n=2,3,1)	-145.0 (± 190.92)	-60.0 (± 284.78)	180.0 (± 99999)	
Complement C3: Change at PT FU Week 12 (n=5,5,3)	-12.0 (± 106.16)	-96.0 (± 196.67)	170.0 (± 390.00)	
Complement C3: Change at PT FU Week 24 (n=4,5,4)	-85.0 (± 183.76)	-144.0 (± 93.97)	164.0 (± 205.45)	
Complement C4: Change at Week 12 (n=5,5,5)	-26.8 (± 25.35)	13.4 (± 9.24)	33.8 (± 44.81)	
Complement C4: Change at Week 24 (n=5,5,4)	-27.0 (± 32.26)	8.8 (± 29.66)	34.3 (± 40.20)	
Complement C4: Change at Week 48 (n=5,3,4)	-0.4 (± 20.74)	33.3 (± 18.90)	16.0 (± 27.89)	
Complement C4: Change at Week 72 (n=3,3,3)	-43.0 (± 82.46)	12.0 (± 17.35)	49.7 (± 30.02)	
Complement C4: Change at ET (n=2,3,1)	-22.0 (± 32.53)	-8.0 (± 38.57)	125.0 (± 99999)	
Complement C4: Change at PT FU Week 12 (n=5,5,3)	-12.6 (± 32.00)	-4.2 (± 9.07)	-1.3 (± 44.52)	
Complement C4: Change at PT FU Week 24 (n=4,5,4)	-37.0 (± 64.97)	-18.2 (± 30.34)	19.5 (± 18.30)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Immune Cell Subsets by Flow Cytometry Analysis

End point title	Change From Baseline in Immune Cell Subsets by Flow Cytometry Analysis

End point description:

Change from baseline in immune cell subsets included total T cells, helper T cells, cytotoxic T cells, total B cells (assay with [AW] CD45 or assay without [AWO] CD45), mature naïve B cells, memory B cells, plasma cells, plasma blasts, and natural killer (NK) cells and were reported. Analysis was performed by flow cytometry analysis. Flow Cytometry (FC) Set: all subjects in SAF set who were part of the selected sites for FC analysis and who had at least 1 sample taken for FC analysis. "Number of subjects

analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category. Here, '99999' signifies that standard deviation could not be calculated as only 1 subject was analyzed and "9999" standard deviation could not be calculated as 0 subjects was analyzed for this category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 12, 24, 48, 72, Early Termination (up to Week 72) and at PT FU Week 24

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	2	3	
Units: cells per microliter				
arithmetic mean (standard deviation)				
Cytotoxic T Cells:Change at Week 4(n=0,2,3)	9999 (± 99999)	-22.5 (± 215.67)	46.7 (± 72.57)	
Cytotoxic T Cells:Change at Week 12(n=1,1,3)	713.0 (± 99999)	-114.0 (± 99999)	75.0 (± 33.41)	
Cytotoxic T Cells:Change at Week 24(n=2,2,2)	101.5 (± 243.95)	-30.5 (± 125.16)	37.0 (± 39.60)	
CytotoxicT Cells:Change Week 48(n=2,0,2)	9.0 (± 224.86)	9999 (± 9999)	38.0 (± 42.43)	
Cytotoxic T Cells:Change Week 72(n=1,0,2)	-60.0 (± 99999)	9999 (± 9999)	-186.0 (± 289.91)	
Cytotoxic T Cells:Change at ET(n=1,0,1)	282.0 (± 99999)	9999 (± 9999)	45.0 (± 99999)	
Cytotoxic T Cells:Change at PT FU Week 24(n=1,0,0)	132.0 (± 99999)	9999 (± 9999)	99999 (± 99999)	
Helper T Cells:Change at Week 4 (n=0,2,3)	9999 (± 9999)	59.0 (± 240.42)	114.7 (± 117.05)	
Helper T Cells:Change at Week 12 (n=1,1,3)	124.0 (± 99999)	-51.0 (± 99999)	221.3 (± 85.33)	
Helper T Cells:Change at Week 24(n=2,2,2)	-79.0 (± 190.92)	134.0 (± 124.45)	85.0 (± 45.25)	
Helper T Cells:Change at Week 48(n=2,0,2)	-129.5 (± 338.70)	9999 (± 9999)	72.5 (± 86.97)	
Helper T Cells:Change at Week 72 (n=1,0,2)	-170.0 (± 99999)	9999 (± 9999)	-312.5 (± 427.80)	
Helper T Cells:Change at ET(n=1,0,1)	81.0 (± 99999)	9999 (± 9999)	348.0 (± 99999)	
Helper T Cells:Change at PT FU Week 24(n=1, 0,0)	90.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	
Mature naive B Cells:Change at Week 4(n=0,2,3)	9999 (± 9999)	-76.5 (± 12.02)	-17.0 (± 78.31)	
Mature B Cells: Change Week 12(n=1,1,3)	137.0 (± 99999)	-106.0 (± 99999)	-14.7 (± 94.07)	
Mature B Cells: Change Week 24(n=2,2,2)	1.0 (± 42.43)	-117.5 (± 51.62)	-87.5 (± 109.60)	
Mature B Cells: Change Week 48(n=2,0,2)	21.5 (± 74.25)	9999 (± 9999)	-91.0 (± 107.48)	
Mature B Cells: Change Week 72(n=1,0,1)	-24.0 (± 99999)	9999 (± 9999)	-32.0 (± 99999)	
Mature B Cells: Change at ET (n=1,0,1)	36.0 (± 99999)	9999 (± 9999)	-1.0 (± 99999)	
Mature BCells ChangePTFU Week24(n=1,0,0)	8.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	
Memory B Cells:Change at Week 4(n=0,1,2)	9999 (± 9999)	8.0 (± 99999)	14.5 (± 2.12)	

Memory B Cells:Change at Week 12(n=1,0,2)	5.0 (± 99999)	9999 (± 9999)	34.0 (± 0.00)	
Memory B Cells: Change at Week 24(n=2,1,2)	-1.5 (± 7.78)	13.0 (± 99999)	5.5 (± 21.92)	
Memory B Cells: Change at Week 48(n=2,0,2)	-1.0 (± 4.24)	9999 (± 9999)	5.0 (± 16.97)	
Memory B Cells: Change at Week 72(n=1,0,1)	-6.0 (± 99999)	9999 (± 9999)	8.0 (± 99999)	
Memory B Cells:Change at ET(n=1,0,0)	-3.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	
MemoryBCells:Change PTFU Week24(n=1,0,0)	6.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	
NK Cells: Change at Week 4(n=0,2,3)	9999 (± 9999)	19.0 (± 227.69)	88.3 (± 30.62)	
NK Cells:Change at Week 12(n=1,1,3)	43.0 (± 99999)	-105.0 (± 99999)	74.0 (± 89.94)	
NK Cells:Change at Week 24(n=2,2,2)	44.5 (± 20.51)	-34.5 (± 112.43)	37.5 (± 58.69)	
NK Cells: Change at Week 48 (n=2,0,2)	20.5 (± 16.26)	9999 (± 9999)	39.0 (± 48.08)	
NK Cells: Change at Week 72 (n=1,0,1)	130.0 (± 99999)	9999 (± 9999)	104.0 (± 99999)	
NK Cells: Change at ET (n=1,0,1)	54.0 (± 99999)	9999 (± 9999)	12.0 (± 99999)	
NKCells:Change at PT FU Week 24(n=1,0,0)	81.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	
Plasma Blasts:Change at Week 4 (n=0,1,2)	9999 (± 9999)	0.10 (± 99999)	-0.05 (± 0.071)	
Plasma Blasts:Change at Week12 (n=1,0,2)	-0.10 (± 99999)	9999 (± 9999)	0.55 (± 0.212)	
Plasma Blasts:Change at Week24 (n=2,1,2)	0.05 (± 0.071)	-0.30 (± 99999)	0.10 (± 0.283)	
Plasma Blasts:Change at Week48 (n=2,0,2)	1.40 (± 1.414)	9999 (± 9999)	0.15 (± 0.212)	
Plasma Blasts:Change at Week72 (n=1,0,1)	-0.10 (± 99999)	9999 (± 9999)	0.40 (± 99999)	
Plasma Blasts:Change at ET (n= 1,0,0)	0.80 (± 99999)	9999 (± 9999)	9999 (± 9999)	
Plasma Blasts:Change PTFUWeek24(n=1,0,0)	3.40 (± 99999)	9999 (± 9999)	9999 (± 9999)	
Plasma Cells: Change at Week 4 (n=0,1,2)	9999 (± 9999)	0.10 (± 99999)	0.00 (± 0.141)	
Plasma Cells: Change at Week 12 (n= 1,0,2)	-0.10 (± 99999)	9999 (± 9999)	0.15 (± 0.212)	
Plasma Cells: Change at Week 24 (n=2,1,2)	0.05 (± 0.071)	-0.10 (± 99999)	0.00 (± 0.000)	
Plasma Cells: Change at Week 48 (n=2,0,2)	0.30 (± 0.283)	9999 (± 9999)	0.00 (± 0.000)	
Plasma Cells: Change at Week 72 (n=1,0,1)	0.00 (± 99999)	9999 (± 9999)	0.20 (± 99999)	
Plasma Cells: Change at ET (n=1,0,0)	0.20 (± 99999)	9999 (± 9999)	9999 (± 9999)	
Plasma Cells Change PTFU Week24(n=1,0,0)	0.10 (± 99999)	9999 (± 9999)	9999 (± 9999)	
AWCD45: Change at Week 4 (n=0,2,3)	9999 (± 9999)	-50.0 (± 36.77)	37.3 (± 64.39)	
AWCD45:Change at Week 12 (n=1,1,3)	154.0 (± 99999)	-105.0 (± 99999)	108.7 (± 88.90)	
AWCD45:Change at Week 24 (n=2,2,2)	-0.5 (± 57.28)	-78.0 (± 131.52)	-32.5 (± 116.67)	
AWCD45:Change at Week 48 (n=2,0,2)	20.0 (± 91.92)	9999 (± 9999)	-27.5 (± 115.26)	
AWCD45::Change at Week 72 (n=1,0,1)	-31.0 (± 99999)	9999 (± 9999)	2.0 (± 99999)	
AWCD45:Change at ET (n=1,0,1)	43.0 (± 99999)	9999 (± 9999)	71.0 (± 99999)	

AWCD45:Change at PT FU Week 24 (n=1,0,0)	27.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	
AWOCD45: Change at Week 4 (n=0,2,3)	9999 (± 9999)	-33.0 (± 104.65)	41.0 (± 40.60)	
AWOCD45: Change at Week 12 (n=1,1,3)	16.0 (± 99999)	-137.0 (± 99999)	52.0 (± 65.09)	
AWOCD45:Change at Week 24 (n=2,2,2)	-11.0 (± 53.74)	-96.5 (± 135.06)	-40.5 (± 88.39)	
AWOCD45:Change at Week 48 (n= 2,0,2)	9.0 (± 113.14)	9999 (± 9999)	-52.5 (± 81.32)	
AWOCD45: Change at Week 72 (n=1,0,1)	-38.0 (± 99999)	9999 (± 9999)	-78.0 (± 99999)	
AWOCD45:Change at Week ET (n=1,0,1)	23.0 (± 99999)	9999 (± 9999)	48.0 (± 99999)	
AWOCD45: Change at PTFU Week24(n=1,0,0)	-36.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	
Total T Cells: Change at Week 4 (n=0,2,3)	9999 (± 9999)	40.0 (± 466.69)	169.0 (± 189.71)	
Total T Cells: Change at Week 12 (n=1,1,3)	861.0 (± 99999)	-165.0 (± 99999)	314.7 (± 50.54)	
Total T Cells: Change at Week 24 (n=2,2,2)	18.5 (± 419.31)	111.0 (± 260.22)	130.0 (± 2.83)	
Total T Cells: Change at Week 48 (n=2,0,2)	-116.5 (± 564.98)	9999 (± 9999)	113.5 (± 140.71)	
Total T Cells: Change at Week 72 (n=1,0,2)	-227.0 (± 99999)	9999 (± 9999)	-529.5 (± 767.21)	
Total T Cells: Change at Week ET (n=1,0,1)	350.0 (± 99999)	9999 (± 9999)	393.0 (± 99999)	
Total T Cells:Change PT FU Week 24 (n=1,0,0)	220.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Urinary IgG, IgA, and IgM levels

End point title	Change From Baseline in Urinary IgG, IgA, and IgM levels

End point description:

Urinary IgG, IgA and IgM levels to be measured by Immuno-Electrophoresis. As per changed in planned analysis the outcome measure related to Urinary Immunoglobulins was not assessed.

End point type	Secondary

End point timeframe:

Baseline (Day1), Weeks 24, 48 and Early Termination (up to Week 72)

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: gram per liter				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[5] - As per changes in planned analysis the endpoint related to Urinary Immunoglobulins was not assessed.

[6] - As per changes in planned analysis the endpoint related to Urinary Immunoglobulins was not assessed.

[7] - As per changes in planned analysis the endpoint related to Urinary Immunoglobulins was not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Positive Anti-Drug Antibody (ADA)

End point title	Percentage of Subjects With Positive Anti-Drug Antibody (ADA)

End point description:

Percentage of subjects with positive ADA were reported. The safety population set (SAF) included all randomized subjects who received at least 1 dose of IMP and had at least one post-dose assessment.

End point type	Secondary

End point timeframe:

Baseline up to safety follow-up (96 weeks)

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	5	
Units: percentage of subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Significant Abnormalities in Laboratory Assessments

End point title	Percentage of Subjects with Clinical Significant Abnormalities in Laboratory Assessments

End point description:

Laboratory investigation included hematology, biochemistry, urinalysis and Urine sediment analysis. Clinical significance was to be decided by the investigator. As per changed in planned analysis the endpoint related to clinically significant abnormalities laboratory assessments was not assessed.

End point type	Secondary

End point timeframe:

Baseline up to safety follow-up (96 weeks)

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Percentage of Subjects				
number (not applicable)				

Notes:

[8] - As per changes in planned analysis the endpoint laboratory assessments was not assessed.

[9] - As per changes in planned analysis the endpoint laboratory assessments was not assessed.

[10] - As per changes in planned analysis the endpoint laboratory assessments was not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Significant Abnormalities in Vital Signs

End point title	Percentage of Subjects with Clinical Significant Abnormalities in Vital Signs

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, pulse rate, weight and height. The systolic and diastolic blood pressure and pulse rate was measured after the subjects have in a rested at least 3 minutes in seated position. Clinical significance was to be decided by the investigator. As per changed in planned analysis the endpoint related to clinically significant abnormalities vital signs was not assessed.

End point type	Secondary

End point timeframe:

Baseline up to safety follow-up (96 weeks)

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: Percentage of subjects				
number (not applicable)				

Notes:

[11] - As per changes in planned analysis the endpoint related to vital signs was not assessed.

[12] - As per changes in planned analysis the endpoint related to vital signs was not assessed.

[13] - As per changes in planned analysis the endpoint related to vital signs was not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Significant Abnormalities in 12-Lead Electrocardiograms (ECGs)

End point title	Percentage of Subjects With Clinical Significant Abnormalities in 12-Lead Electrocardiograms (ECGs)

End point description:

12-lead ECG were recorded after the subjects have rested for at least 15 minutes in supine position. Clinically significance was decided by the investigator. The percentages of subjects with clinically significant abnormalities in 12-lead ECG were reported. The safety population set (SAF) included all randomized subjects who received at least 1 dose of IMP and had at least one post-dose assessment.

End point type	Secondary

End point timeframe:

Baselien up to safety follow-up (96 weeks)

End point values	Placebo	Atacicept 25 mg	Atacicept 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	6	5	
Units: percentage of subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to safety follow up period (96 weeks)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matched to Atacicept once weekly as subcutaneous (SC) injection for 72 weeks.	
Reporting group title	Atacicept 25 mg
Reporting group description:	
Subjects received 25 milligrams (mg) of Atacicept once weekly as SC injection for 72 weeks.	
Reporting group title	Atacicept 75 mg
Reporting group description:	
Subjects received 75 mg of Atacicept once weekly as SC injection for 72 weeks.	

Serious adverse events	Placebo	Atacicept 25 mg	Atacicept 75 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	3 / 6 (50.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian adenoma			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder haemorrhage			

subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Atacicept 25 mg	Atacicept 75 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	6 / 6 (100.00%)	3 / 5 (60.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 5 (0.00%)	4 / 6 (66.67%)	1 / 5 (20.00%)
occurrences (all)	0	4	1
Injection site bruising			
subjects affected / exposed	0 / 5 (0.00%)	3 / 6 (50.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Injection site pruritus			

subjects affected / exposed	0 / 5 (0.00%)	3 / 6 (50.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Injection site reaction			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	0	1	2
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injection site induration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injection site inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Allergy to chemicals			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Dysphonia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Cervical radiculopathy			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Head discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Paratracheal lymphadenopathy			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	2 / 5 (40.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Abdominal tenderness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haematochezia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rash erythematous			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin mass			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			

Arthropathy			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Synovial cyst			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	3 / 6 (50.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Gastroenteritis viral			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Herpes simplex			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection bacterial			

subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Diabetes mellitus			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2016	A staggered enrollment design had been added so that the IDMC can review interim 12 week cumulative safety data in the placebo and lower dose atacicept arms. Upon approval and Sponsor review, subjects were enrolled into the high-dose (150 mg) atacicept arm; subjects were randomized to all 4 arms.
20 October 2016	Primary and Secondary objectives were updated. Exclusion criteria was updated.
15 September 2017	Reordered the objectives since they were not key secondary objectives. Adverse Events of the primary endpoint were not repeated as secondary endpoint.
27 November 2018	Removed mention of needle gauge. Included and provided a description of an interim analysis to inform the Sponsor decision with regards to Part A of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was prematurely terminated due to poor enrollment and Part B was not conducted as per Sponsor decision. This decision was not related to any safety or efficacy findings regarding Atacicept.

Notes: