Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter, Phase II Study to Evaluate the Impact of MABT5102A on Brain Amyloid Load and Related Biomarkers in Patients With Mild to Moderate Alzheimer's Disease

Summary

EudraCT number	2010-022598-32
Trial protocol	ES
Global end of trial date	17 April 2014

Results information

Result version number	v2 (current)
This version publication date	19 May 2016
First version publication date	07 August 2015
Version creation reason	• Correction of full data set Review and re-release of record required as a result of EudraCT database failure.

Trial information

Trial identification

Sponsor protocol code	ABE4955g

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01397578
WHO universal trial number (UTN)	-
Other trial identifiers	GN00762: ABE4955g, BLAZE: ABE4955g

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline , F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline , F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.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	31 May 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 May 2011
Global end of trial reached?	Yes
Global end of trial date	17 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess amyloid burden via 18F-florbetapir (18F-AV-45) positron emission tomography (PET) in subjects with mild to moderate Alzheimer's Disease and to evaluate whether treatment with MABT5102A/Crenezumab (a monoclonal antibody to beta-amyloid [Abeta]) over 68 weeks results in a change in amyloid burden after dosing.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United States: 85
Worldwide total number of subjects	91
EEA total number of subjects	6

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)	24
From 65 to 84 years	67
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening involved examination and determination of baseline clinical variables, including diagnosis of probable Alzheimer's Disease according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Subcutaneous Injection Crenezumab

Arm description:

300 mg of crenezumab administered as subcutaneous injections (SC) every two weeks (q2wk) over 68 weeks.

Arm type	Experimental
Investigational medicinal product name	Crenezumab
Investigational medicinal product code	MABT5102A
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg of crenezumab administered as two 1-mL subcutaneous (SC) injections every two weeks (q2wk)

Arm title	Subcutaneous Injection Placebo

Arm description:

Matching placebo administered as subcutaneous (SC) injections every two weeks (q2wk) over 68 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo administered as two 1-mL subcutaneous (SC) injections every two weeks (q2wk).

Arm title	Intravenous Infusion Crenezumab

Arm description:

15 mg/kg crenezumab administered by intravenous (IV) infusion every 4 weeks (q4wk) over 68 weeks.

Arm type	Experimental

Investigational medicinal product name	Crenezumab
Investigational medicinal product code	MABT5102A
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 mg/kg crenezumab administered by intravenous (IV) infusion every 4 weeks (q4wk)

Arm title	Intravenous Infusion Placebo

Arm description:

Matching placebo administered by intravenous (IV) infusion every 4 weeks (q4wk) over 68 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Matching placebo administered by intravenous (IV) infusion every 4 weeks (q4wk)

Number of subjects in period 1	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab
Started	26	13	36
Completed	5	0	1
Not completed	21	13	35
Consent withdrawn by subject	2	3	8
Adverse event, non-fatal	1	-	1
Death	-	-	2
Not specified	-	-	3
To Open-Label Extension GN28525	18	10	21

Number of subjects in period 1	Intravenous Infusion Placebo
Started	16
Completed	1
Not completed	15
Consent withdrawn by subject	3
Adverse event, non-fatal	3
Death	-
Not specified	1
To Open-Label Extension GN28525	8

Baseline characteristics

Reporting groups	
Reporting group title	Subcutaneous Injection Crenezumab
Reporting group description:	
300 mg of crenezumab administered as subcutaneous injections (SC) every two weeks (q2wk) over 68 weeks.	
Reporting group title	Subcutaneous Injection Placebo
Reporting group description:	
Matching placebo administered as subcutaneous (SC) injections every two weeks (q2wk) over 68 weeks.	
Reporting group title	Intravenous Infusion Crenezumab
Reporting group description:	
15 mg/kg crenezumab administered by intravenous (IV) infusion every 4 weeks (q4wk) over 68 weeks.	
Reporting group title	Intravenous Infusion Placebo
Reporting group description:	
Matching placebo administered by intravenous (IV) infusion every 4 weeks (q4wk) over 68 weeks.	

Reporting group values	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab
Number of subjects	26	13	36
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	11	4	6
From 65-84 years	15	9	30
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	66.7	68.9	71.6
standard deviation	± 9.5	± 8.3	± 7.1
Gender categorical Units: Subjects			
Female	14	8	24
Male	12	5	12

Reporting group values	Intravenous Infusion Placebo	Total	
Number of subjects	16	91	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	24	
From 65-84 years	13	67	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	69.4		
standard deviation	± 7.7	-	
Gender categorical			
Units: Subjects			
Female	6	52	
Male	10	39	

End points

End points reporting groups

Reporting group title	Subcutaneous Injection Crenezumab
Reporting group description:	
300 mg of crenezumab administered as subcutaneous injections (SC) every two weeks (q2wk) over 68 weeks.	
Reporting group title	Subcutaneous Injection Placebo
Reporting group description:	
Matching placebo administered as subcutaneous (SC) injections every two weeks (q2wk) over 68 weeks.	
Reporting group title	Intravenous Infusion Crenezumab
Reporting group description:	
15 mg/kg crenezumab administered by intravenous (IV) infusion every 4 weeks (q4wk) over 68 weeks.	
Reporting group title	Intravenous Infusion Placebo
Reporting group description:	
Matching placebo administered by intravenous (IV) infusion every 4 weeks (q4wk) over 68 weeks.	

Primary: Change in Brain Amyloid Load

End point title	Change in Brain Amyloid Load
End point description:	
Change in brain amyloid load measured as change in standardised uptake value ratio (SUVR) from baseline to week 69 and assessed by florbetapir positron emission tomography (PET) imaging.	
End point type	Primary
End point timeframe:	
Baseline to week 69	

End point values	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab	Intravenous Infusion Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	10	21	10
Units: Standardised uptake value ratio				
least squares mean (standard error)	-0.029 (± 0.038)	-0.018 (± 0.059)	-0.02 (± 0.03)	-0.071 (± 0.043)

Statistical analyses

Statistical analysis title	Mean Difference Subcutaneous Groups MMRM
Statistical analysis description:	
Least-square mean difference between least-square means of crenezumab and placebo in subcutaneous administration groups according to Mixed Model Repeated Measures (MMRM) analysis.	
Comparison groups	Subcutaneous Injection Placebo v Subcutaneous Injection Crenezumab

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.878
Method	MMRM

Statistical analysis title	Mean Difference Intravenous Groups

Statistical analysis description:

Least-square mean difference between least-square means of crenezumab and placebo in intravenous administration groups according to Mixed Model Repeated Measures (MMRM) analysis.

Comparison groups	Intravenous Infusion Crenezumab v Intravenous Infusion Placebo
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.338
Method	MMRM

Secondary: Change in cerebrospinal fluid (CSF) concentration of Abeta42

End point title	Change in cerebrospinal fluid (CSF) concentration of Abeta42

End point description:

Change in cerebrospinal fluid (CSF) concentration of Abeta42, a biomarkers relevant to Alzheimer's disease, from baseline to week 69.

End point type	Secondary

End point timeframe:

Baseline to week 69

End point values	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab	Intravenous Infusion Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	10	17	8
Units: pg/mL				
least squares mean (standard error)	74.9 (± 19.62)	-52.11 (± 27.91)	7.86 (± 19.71)	-86.65 (± 30.09)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in cerebrospinal fluid (CSF) concentration of total Tau

End point title	Change in cerebrospinal fluid (CSF) concentration of total Tau

End point description:

Change in cerebrospinal fluid (CSF) concentration of total Tau, a biomarkers relevant to Alzheimer's disease, from baseline to week 69.

End point type	Secondary

End point timeframe:

Baseline to week 69

End point values	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab	Intravenous Infusion Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	10	17	7
Units: pg/mL				
least squares mean (standard error)	59.15 (± 39.01)	-22.92 (± 56.2)	-46.15 (± 36.85)	-43.02 (± 60.79)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in cerebrospinal fluid (CSF) concentration of p-Tau

End point title	Change in cerebrospinal fluid (CSF) concentration of p-Tau

End point description:

Change in cerebrospinal fluid (CSF) concentration of p-Tau, a biomarkers relevant to Alzheimer's disease, from baseline to week 69

End point type	Secondary

End point timeframe:

Baseline to week 69

End point values	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab	Intravenous Infusion Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	10	17	7
Units: pg/mL				
least squares mean (standard error)	1.56 (± 3.02)	-6.4 (± 4.35)	-7.2 (± 2.77)	-6.23 (± 4.61)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in brain metabolism

End point title	Change in brain metabolism

End point description:

Change in brain metabolism as measured by standardised uptake value ratio (SUVR) from baseline to week 69 and assessed by 18F-fluorodeoxyglucose positron emission tomography (FDG PET) imaging.

End point type	Secondary

End point timeframe:

Baseline to week 69

End point values	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab	Intravenous Infusion Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	10	21	10
Units: Standardised uptake value ratio				
least squares mean (standard error)	-0.032 (± 0.012)	-0.04 (± 0.018)	-0.063 (± 0.019)	-0.036 (± 0.027)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAS Cog) score

End point title	Change in Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAS Cog) score

End point description:

Change in Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAS-Cog) scores from baseline to week 73.

End point type	Secondary

End point timeframe:

Baseline to week 73

End point values	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab	Intravenous Infusion Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	13	29	15
Units: Score				
least squares mean (standard error)	6.76 (± 1.54)	5.91 (± 2.15)	4.8 (± 1.56)	6.8 (± 2.21)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From randomization to end of study at week 84	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Subcutaneous Injection Crenezumab
Reporting group description: 300 mg of crenezumab administered as subcutaneous injections (SC) every two weeks (q2wk) for 69 weeks.	
Reporting group title	Subcutaneous Injection Placebo
Reporting group description: Matching placebo administered as subcutaneous (SC) injections every two weeks (q2wk) for 69 weeks.	
Reporting group title	Intravenous Infusion Crenezumab
Reporting group description: 15 mg/kg crenezumab administered by intravenous (IV) infusion every 4 weeks (q4wk) for 69 weeks.	
Reporting group title	Intravenous Infusion Placebo
Reporting group description: Matching placebo administered by intravenous (IV) infusion every 4 weeks (q4wk) for 69 weeks.	

Serious adverse events	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 26 (11.54%)	1 / 13 (7.69%)	6 / 36 (16.67%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (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
Encephalopathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	0 / 36 (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
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	0 / 36 (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
Infections and infestations			
Pneumonia necrotising			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	0 / 36 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (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

Serious adverse events	Intravenous Infusion Placebo		

Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to bone			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lacunar infarction			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia necrotising			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Subcutaneous Injection Crenezumab	Subcutaneous Injection Placebo	Intravenous Infusion Crenezumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 26 (100.00%)	13 / 13 (100.00%)	32 / 36 (88.89%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	1 / 36 (2.78%)
occurrences (all)	3	1	2
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	9
Haematoma			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Hypotension			
subjects affected / exposed	0 / 26 (0.00%)	2 / 13 (15.38%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			

Facial pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	3 / 26 (11.54%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	5	0	1
Fatigue			
subjects affected / exposed	1 / 26 (3.85%)	2 / 13 (15.38%)	2 / 36 (5.56%)
occurrences (all)	1	2	2
Infusion site extravasation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	4 / 36 (11.11%)
occurrences (all)	0	0	5
Malaise			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	4	0	0
Chest pain			
subjects affected / exposed	2 / 26 (7.69%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	2	1	0
Infusion site erythema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Injection site extravasation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Injection site swelling			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Seasonal allergy			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 26 (0.00%)	2 / 13 (15.38%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Asthma			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	9 / 26 (34.62%)	0 / 13 (0.00%)	3 / 36 (8.33%)
occurrences (all)	9	0	4
Depression			
subjects affected / exposed	5 / 26 (19.23%)	2 / 13 (15.38%)	2 / 36 (5.56%)
occurrences (all)	5	2	2
Agitation			
subjects affected / exposed	4 / 26 (15.38%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	5	0	2
Insomnia			
subjects affected / exposed	3 / 26 (11.54%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	3	1	0
Hallucination			

subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Mental status changes			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Hallucination, visual			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Polydipsia psychogenic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Rapid eye movements sleep abnormal			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Weight increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Liver function test abnormal			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			

subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	2
Post lumbar puncture syndrome			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Procedural pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Arthropod bite			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Bone contusion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Burns second degree			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Laceration			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Mouth injury			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pubis fracture			

subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Wrist fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 26 (7.69%)	1 / 13 (7.69%)	2 / 36 (5.56%)
occurrences (all)	2	10	5
Dizziness			
subjects affected / exposed	4 / 26 (15.38%)	3 / 13 (23.08%)	2 / 36 (5.56%)
occurrences (all)	4	7	2
Cerebral microhaemorrhage			
subjects affected / exposed	3 / 26 (11.54%)	0 / 13 (0.00%)	4 / 36 (11.11%)
occurrences (all)	3	0	5
Dementia Alzheimer's type			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	3 / 36 (8.33%)
occurrences (all)	1	0	3
Hypoaesthesia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 13 (15.38%)	0 / 36 (0.00%)
occurrences (all)	0	4	0
Dementia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Myoclonus			

subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Occipital neuralgia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Superficial siderosis of central nervous system			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Lymphopenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Chalazion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	3 / 26 (11.54%)	1 / 13 (7.69%)	1 / 36 (2.78%)
occurrences (all)	3	2	1
Diarrhoea			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	1	2	0
Vomiting			
subjects affected / exposed	2 / 26 (7.69%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	2	1	0
Abdominal pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Lichen planus			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Papule			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	1 / 26 (3.85%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Chromaturia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 26 (19.23%)	2 / 13 (15.38%)	5 / 36 (13.89%)
occurrences (all)	7	3	5
Arthralgia			
subjects affected / exposed	3 / 26 (11.54%)	1 / 13 (7.69%)	2 / 36 (5.56%)
occurrences (all)	3	1	3
Pain in extremity			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	1 / 36 (2.78%)
occurrences (all)	1	1	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	6 / 36 (16.67%)
occurrences (all)	1	1	8
Nasopharyngitis			
subjects affected / exposed	4 / 26 (15.38%)	4 / 13 (30.77%)	1 / 36 (2.78%)
occurrences (all)	6	5	1
Upper respiratory tract infection			
subjects affected / exposed	7 / 26 (26.92%)	0 / 13 (0.00%)	4 / 36 (11.11%)
occurrences (all)	8	0	5

Bronchitis			
subjects affected / exposed	2 / 26 (7.69%)	1 / 13 (7.69%)	1 / 36 (2.78%)
occurrences (all)	2	1	1
Gastroenteritis viral			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	1
Abscess oral			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 26 (7.69%)	0 / 13 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Hypokalaemia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Diabetes mellitus			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			

subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Lactic acidosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Metabolic acidosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 13 (7.69%)	0 / 36 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Intravenous Infusion Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 16 (93.75%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	7		
Injection site erythema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

Infusion site extravasation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Malaise subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Chest pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Infusion site erythema subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 3		
Injection site extravasation subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Injection site swelling subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Asthenia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Oropharyngeal pain			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Asthma			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Agitation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hallucination			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Mental status changes			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hallucination, visual			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Panic attack			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Polydipsia psychogenic			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rapid eye movements sleep abnormal			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Liver function test abnormal			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Neutrophil count increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

Arthropod bite			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Bone contusion			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Burns second degree			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Mouth injury			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pubis fracture			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Wrist fracture			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Ventricular extrasystoles			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 5		
Dizziness subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Cerebral microhaemorrhage subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Dementia Alzheimer's type subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Dementia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Lethargy subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Myoclonus subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Occipital neuralgia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Superficial siderosis of central nervous system subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Syncope subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Leukocytosis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Lymphopenia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Eye disorders Chalazion subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Dry eye subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Vomiting subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0		
Faeces discoloured			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Ingrowing nail			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Lichen planus			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Papule			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rosacea			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Pollakiuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Chromaturia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Arthralgia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	8		
Nasopharyngitis			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Abscess oral			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Diverticulitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Localised infection			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Diabetes mellitus			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypercholesterolaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Lactic acidosis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Metabolic acidosis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2011	Increased flexibility in the timing of the first lumbar puncture for cerebrospinal fluid (CSF) sample collection. Change in fasting requirements for laboratory assessments: no fasting requirements for blood sample collection, except for screening.
20 August 2012	Amendment of eligibility criteria, which would allow subjects to roll over to an open-label extension study. A requirement for additional safety assessments at 8- and 12-weeks was added for those subjects, who discontinue prematurely from the study. Allow nurse practitioners and equivalently qualified personnel (under applicable law) to review and sign-off on the Mini-Mental State Examination (MMSE) and the Columbia-Suicide Severity Scale (C-SSRS) before the subject is discharged. Allow collection of PK samples 60−90 minutes post infusion. To clarify that start or discontinuation of an approved Alzheimer's Disease (AD) treatment or dose changes of approved AD treatments during the study are in principle not permitted. Crenezumab has been introduced as an alternative name for MABT5012A.
04 January 2013	The included and excluded concomitant medications at screening and throughout the duration of the study were clarified: soporifics are allowed if administered at a stable dose prior to randomization and throughout the study, opiates and opioids are prohibited if administered chronically; intermittent use of soporifics, opiates, opioids and benzodiazepines is allowed except 5 half-lives prior to neurocognitive assessment. The protocol has been updated to reflect the correct weight to use for intravenous (IV) dose calculations, specifically, that the subject’s screening weight (reference weight) will be used at each visit, unless the current weight has changed (increase or decrease) by >= 10% from the screening weight (or the last reference weight used). If this occurs, the current weight will become the reference weight for subsequent dosing.
04 June 2013	The interim analysis plan was modified to synchronize more closely with the companion trial (Study ABE4869g/GN00761): two interim analyses will be conducted: one after all subjects in both the subcutaneous (SC) and intravenous (IV) cohorts have completed the week 49 assessment and another after all subjects in the SC cohort have completed the week 73 assessment. Restriction on analysis of cognitive endpoints if Alzheimer’s disease (AD) medications were changed while subjects are on study, was eliminated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported