Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter, Phase II Study to Evaluate the Efficacy and Safety of Crenezumab (MABT5102A) in Patients with Mild to Moderate Alzheimer's Disease

Summary

EudraCT number	2010-021926-37
Trial protocol	GB DE ES
Global end of trial date	18 February 2014

Results information

Result version number	v1 (current)
This version publication date	22 April 2016
First version publication date	07 August 2015

Trial information

Trial identification

Sponsor protocol code	ABE4869g

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01343966
WHO universal trial number (UTN)	-
Other trial identifiers	Abby: ABE4869g, GN00761: ABE4869g

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	18 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 February 2014
Global end of trial reached?	Yes
Global end of trial date	18 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives for this trial were to evaluate the efficacy of crenezumab (MABT5102A) compared with placebo, when administered over 68 weeks to patients with mild to moderate Alzheimer's Disease (AD), in inhibiting disease progression using the Alzheimer’s Disease Assessment Scale Cognitive Subscale (ADAS-Cog [12-item]) and the Clinical Dementia Rating, Sum-of-Boxes (CDR-SOB); and to evaluate the safety and tolerability of MABT5102A compared with placebo when administered over 68 weeks to patients with mild to moderate AD.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 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	Spain: 19
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Canada: 99
Country: Number of subjects enrolled	United Kingdom: 37
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	United States: 232
Worldwide total number of subjects	444
EEA total number of subjects	113

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)	78
From 65 to 84 years	366
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 AD 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 trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Subcutaneous injection crenezumab

Arm description: -

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 crenezumab administered by subcutaneous injection every two weeks

Arm title	Subcutaneous injection placebo

Arm description: -

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:

Placebo solution administered by subcutaneous injection every two weeks

Arm title	Intravenous infusion crenezumab

Arm description: -

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 drip use

Dosage and administration details:

15 mg/kg crenezumab administered by intravenous infusion every 4 weeks

Arm title	Intravenous infusion placebo

Arm description: -	
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 drip use

Dosage and administration details:

Placebo administered by intravenous infusion every 4 weeks

Arm title	Intravenous infusion crenezumab (safety run-in)
Arm description: -	
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 drip use

Dosage and administration details:

15 mg/kg crenezumab administered by intravenous infusion every 4 weeks

Number of subjects in period 1	Subcutaneous injection crenezumab	Subcutaneous injection placebo	Intravenous infusion crenezumab
Started	122	62	165
Completed	88	45	126
Not completed	34	17	39
Adverse event, serious fatal	-	-	1
Physician decision	1	-	2
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	2	3	5
Other	10	1	6
Withdrawal by participant	16	11	22
Non-compliance with study drug	-	-	1
Lost to follow-up	1	1	2
Protocol deviation	2	1	-
Noncompliance	2	-	-

Number of subjects in period 1	Intravenous infusion placebo	Intravenous infusion crenezumab (safety run-in)
Started	82	13
Completed	62	11
Not completed	20	2
Adverse event, serious fatal	-	-
Physician decision	1	-

Consent withdrawn by subject	-	1
Adverse event, non-fatal	3	-
Other	6	1
Withdrawal by participant	7	-
Non-compliance with study drug	-	-
Lost to follow-up	2	-
Protocol deviation	1	-
Noncompliance	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Subcutaneous injection crenezumab
Reporting group description: -	
Reporting group title	Subcutaneous injection placebo
Reporting group description: -	
Reporting group title	Intravenous infusion crenezumab
Reporting group description: -	
Reporting group title	Intravenous infusion placebo
Reporting group description: -	
Reporting group title	Intravenous infusion crenezumab (safety run-in)
Reporting group description: -	

Reporting group values	Subcutaneous injection crenezumab	Subcutaneous injection placebo	Intravenous infusion crenezumab
Number of subjects	122	62	165
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	71.2	70.3	70.9
standard deviation	± 6.3	± 7.2	± 6.8
Gender categorical Units: Subjects			
Female	66	30	84
Male	56	32	81

Reporting group values	Intravenous infusion placebo	Intravenous infusion crenezumab (safety run-in)	Total
Number of subjects	82	13	444
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	69.9	71.5	
standard deviation	± 7.2	± 6.5	-
Gender categorical			
Units: Subjects			
Female	46	8	234
Male	36	5	210

End points

End points reporting groups

Reporting group title	Subcutaneous injection crenezumab
Reporting group description: -	
Reporting group title	Subcutaneous injection placebo
Reporting group description: -	
Reporting group title	Intravenous infusion crenezumab
Reporting group description: -	
Reporting group title	Intravenous infusion placebo
Reporting group description: -	
Reporting group title	Intravenous infusion crenezumab (safety run-in)
Reporting group description: -	
Subject analysis set title	Mild subgroup subcutaneous injection crenezumab
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Mild Alzheimer's Disease as defined by Mini-Mental State Examination score 20-26: subcutaneous injection crenezumab	
Subject analysis set title	Mild subgroup subcutaneous injection Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Mild Alzheimer's Disease as defined by Mini-Mental State Examination 20-26: subcutaneous injection placebo	
Subject analysis set title	Mild subgroup intravenous infusion crenezumab
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Mild Alzheimer's Disease as defined by Mini-Mental State Examination score 20-26: intravenous injection crenezumab	
Subject analysis set title	Mild subgroup intravenous infusion placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Mild Alzheimer's Disease as defined by Mini-Mental State Examination 20-26: intravenous injection placebo	

Primary: 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[1]
End point description:	
End point type	Primary
End point timeframe:	
Baseline to week 73	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is a subgroup analysis.

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	88	45	122	64
Units: Score				
least squares mean (standard error)	7.81 (± 0.81)	7.85 (± 1.13)	8.79 (± 0.79)	10.56 (± 1.09)

End point values	Mild subgroup subcutaneous injection crenezumab	Mild subgroup subcutaneous injection Placebo	Mild subgroup intravenous infusion crenezumab	Mild subgroup intravenous infusion placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	62	31	93	47
Units: Score				
least squares mean (standard error)	5.96 (± 0.97)	5.97 (± 1.36)	7.18 (± 0.85)	9.43 (± 1.2)

Statistical analyses

Statistical analysis title	Mean difference in MITT1 population

Statistical analysis description:

Least square means (standard error [SE]) for difference between intravenous infusion (IV) of placebo and crenezumab in Mild Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 20-26. MITT1: all mild IV cohort participants.

Comparison groups	Mild subgroup intravenous infusion crenezumab v Mild subgroup intravenous infusion placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.128
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	2.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.66
upper limit	5.15
Variability estimate	Standard error of the mean
Dispersion value	1.47

Statistical analysis title	Mean difference in MITT2 population

Statistical analysis description:

Least square means (standard error [SE]) for difference between subcutaneous injection (SC) of placebo and crenezumab in Mild Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 20-26. MITT2: all mild SC cohort participants.

Comparison groups	Mild subgroup subcutaneous injection crenezumab v Mild

	subgroup subcutaneous injection Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.995
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.33
upper limit	3.35
Variability estimate	Standard error of the mean
Dispersion value	1.67

Statistical analysis title	Mean difference in MITT3 population
Statistical analysis description:	
Least square means (standard error [SE]) for difference between intravenous infusion (IV) of placebo and crenezumab in Mild-to-Moderate (M2M) Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 18-26. MITT3: all IV cohort participants.	
Comparison groups	Intravenous infusion crenezumab v Intravenous infusion placebo
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	4.44
Variability estimate	Standard error of the mean
Dispersion value	1.35

Statistical analysis title	Mean difference in MITT4 population
Statistical analysis description:	
Least square means (standard error [SE]) for difference between subcutaneous injection (SC) of placebo and crenezumab in Mild-to-Moderate (M2M) Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 18-26. MITT1: all SC cohort participants.	
Comparison groups	Subcutaneous injection crenezumab v Subcutaneous injection placebo

Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.977
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.73
upper limit	2.81
Variability estimate	Standard error of the mean
Dispersion value	1.4

Primary: Change in Clinical Dementia Rating, Sum of Boxes (CDR-SOB) Score

End point title	Change in Clinical Dementia Rating, Sum of Boxes (CDR-SOB) Score[2]

End point description:

End point type	Primary

End point timeframe:

Baseline to week 73

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is a subgroup analysis.

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	88	47	126	67
Units: Score				
least squares mean (standard error)	2.01 (± 0.26)	2.7 (± 0.36)	2.49 (± 0.25)	2.57 (± 0.35)

End point values	Mild subgroup subcutaneous injection crenezumab	Mild subgroup subcutaneous injection Placebo	Mild subgroup intravenous infusion crenezumab	Mild subgroup intravenous infusion placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	62	33	96	48
Units: Score				
least squares mean (standard error)	1.47 (± 0.31)	2.18 (± 0.43)	2.21 (± 0.28)	2.18 (± 0.4)

Statistical analyses

Statistical analysis title	Mean difference in MITT1 population

Statistical analysis description:

Least square means (standard error [SE]) for difference between intravenous infusion (IV) of placebo and crenezumab in Mild Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 20-26. MITT1: all mild IV cohort participants.

Comparison groups	Mild subgroup intravenous infusion placebo v Mild subgroup intravenous infusion crenezumab
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.964
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.96
Variability estimate	Standard error of the mean
Dispersion value	0.49

Statistical analysis title	Mean difference in MITT2 population

Statistical analysis description:

Least square means (standard error [SE]) for difference between subcutaneous injection (SC) of placebo and crenezumab in Mild Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 20-26. MITT2: all mild SC cohort participants.

Comparison groups	Mild subgroup subcutaneous injection Placebo v Mild subgroup subcutaneous injection crenezumab
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.181
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	1.75
Variability estimate	Standard error of the mean
Dispersion value	0.53

Statistical analysis title	Mean difference in MITT3 population

Statistical analysis description:

Least square means (standard error [SE]) for difference between intravenous infusion (IV) of placebo

and crenezumab in Mild-to-Moderate (M2M) Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 18-26. MITT3: all IV cohort participants.

Comparison groups	Intravenous infusion crenezumab v Intravenous infusion placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.853
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	0.92
Variability estimate	Standard error of the mean
Dispersion value	0.43

Statistical analysis title	Mean difference in MITT4 population

Statistical analysis description:

Least square means (standard error [SE]) for difference between subcutaneous injection (SC) of placebo and crenezumab in Mild-to-Moderate (M2M) Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 18-26. MITT4: all mild SC cohort participants.

Comparison groups	Subcutaneous injection crenezumab v Subcutaneous injection placebo
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.128
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	1.57
Variability estimate	Standard error of the mean
Dispersion value	0.45

Secondary: Change in Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL) Score

End point title	Change in Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL) Score[3]

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 73

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This is a subgroup analysis.

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	88	47	125	68
Units: Score				
least squares mean (standard error)	-7.02 (± 1.13)	-8.43 (± 1.54)	-9.55 (± 1.06)	-9.04 (± 1.44)

End point values	Mild subgroup subcutaneous injection crenezumab	Mild subgroup subcutaneous injection Placebo	Mild subgroup intravenous infusion crenezumab	Mild subgroup intravenous infusion placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	63	33	95	48
Units: Score				
least squares mean (standard error)	-5.04 (± 1.25)	-7.82 (± 1.73)	-8.14 (± 1.12)	-5.96 (± 1.57)

Statistical analyses

Statistical analysis title	Mean difference in MITT1 population

Statistical analysis description:

Least square means (standard error [SE]) for difference between intravenous infusion (IV) of placebo and crenezumab in Mild Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 20-26. MITT1: all mild IV cohort participants.

Comparison groups	Mild subgroup intravenous infusion crenezumab v Mild subgroup intravenous infusion placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.64
upper limit	6
Variability estimate	Standard error of the mean
Dispersion value	1.93

Statistical analysis title	Mean difference in MITT2 population
Statistical analysis description:	
Least square means (standard error [SE]) for difference between subcutaneous injection (SC) of placebo and crenezumab in Mild Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 20-26. MITT1: all mild SC cohort participants.	
Comparison groups	Mild subgroup subcutaneous injection Placebo v Mild subgroup subcutaneous injection crenezumab
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.196
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	-2.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.02
upper limit	1.46
Variability estimate	Standard error of the mean
Dispersion value	2.14

Statistical analysis title	Mean difference in MITT3 population
Statistical analysis description:	
Least square means (standard error [SE]) for difference between intravenous infusion (IV) of placebo and crenezumab in Mild-to-Moderate (M2M) Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 18-26. MITT3: all IV cohort participants.	
Comparison groups	Intravenous infusion crenezumab v Intravenous infusion placebo
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.775
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.02
upper limit	4.04
Variability estimate	Standard error of the mean
Dispersion value	1.79

	Mean difference in MITT4 population

Statistical analysis title	

Statistical analysis description:

Least square means (standard error [SE]) for difference between subcutaneous injection (SC) of placebo and crenezumab in Mild-to-Moderate (M2M) Alzheimer's Disease (AD): Mini Mental State Examination (MMSE) 18-26. MITT4: all mild SC cohort participants.

Comparison groups	Subcutaneous injection crenezumab v Subcutaneous injection placebo
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.461
Method	MMRM
Parameter estimate	Mean difference (final values)
Point estimate	-1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	2.37
Variability estimate	Standard error of the mean
Dispersion value	1.91

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 84 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Subcutaneous injection crenezumab
Reporting group description: -	
Reporting group title	Subcutaneous injection placebo
Reporting group description: -	
Reporting group title	Intravenous infusion crenezumab
Reporting group description: -	
Reporting group title	Intravenous infusion placebo
Reporting group description: -	
Reporting group title	Intravenous infusion crenezumab (safety run-in)
Reporting group description: -	

Serious adverse events	Subcutaneous injection crenezumab	Subcutaneous injection placebo	Intravenous infusion crenezumab
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 122 (13.11%)	6 / 62 (9.68%)	32 / 165 (19.39%)
number of deaths (all causes)	2	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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 cell carcinoma			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (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
Transitional cell carcinoma			

subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non−cardiac chest pain			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug interaction			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Hernia obstructive			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Pneumonia aspiration			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Respiratory failure			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Respiratory paralysis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Suicidal ideation			
subjects affected / exposed	1 / 122 (0.82%)	1 / 62 (1.61%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adjustment disorder			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			

subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	0 / 165 (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
Confusional state			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Delirium			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	0 / 165 (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
Homicidal ideation			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	0 / 165 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 122 (0.82%)	2 / 62 (3.23%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	0 / 165 (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
Femoral neck fracture			

subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture displacement			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (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
Humerus fracture			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Meniscus injury			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	0 / 165 (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
Road traffic accident			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (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
Subdural haematoma			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			

subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia alzheimer’s type			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral microhaemorrhage			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (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
Paraesthesia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Presyncope			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
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 hygroma			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (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
Gastrointestinal disorders			

Dysphagia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal hernia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Diverticular perforation			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Rectal haemorrhage			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Spigelian hernia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Umbilical hernia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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 failure			

subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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			
Muscular weakness			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	2 / 165 (1.21%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	4 / 165 (2.42%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diverticulitis			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (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
Cellulitis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Gastroenteritis			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lower respiratory tract infection			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (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
Pilonidal cyst			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	0 / 165 (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
Rectal abscess			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	0 / 165 (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
Sinusitis			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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
Hyponatraemia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (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

Serious adverse events	Intravenous infusion placebo	Intravenous infusion crenezumab (safety run-in)	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 82 (13.41%)	1 / 13 (7.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non−cardiac chest pain			

subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug interaction			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia obstructive			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory paralysis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Mental status changes			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adjustment disorder			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Homicidal ideation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			

subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			

subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia alzheimer’s type			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral microhaemorrhage			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural hygroma			

subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Spigelian hernia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 82 (2.44%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			

subjects affected / exposed	3 / 82 (3.66%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	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	99 / 122 (81.15%)	54 / 62 (87.10%)	119 / 165 (72.12%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	1 / 122 (0.82%)	4 / 62 (6.45%)	1 / 165 (0.61%)
occurrences (all)	1	4	1
Basal cell carcinoma			
subjects affected / exposed	1 / 122 (0.82%)	1 / 62 (1.61%)	4 / 165 (2.42%)
occurrences (all)	1	1	4
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 122 (1.64%)	4 / 62 (6.45%)	3 / 165 (1.82%)
occurrences (all)	2	6	3
Hot flush			

subjects affected / exposed	1 / 122 (0.82%)	2 / 62 (3.23%)	3 / 165 (1.82%)
occurrences (all)	1	3	3
Phlebitis			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	4 / 122 (3.28%)	7 / 62 (11.29%)	2 / 165 (1.21%)
occurrences (all)	10	36	2
Fatigue			
subjects affected / exposed	10 / 122 (8.20%)	5 / 62 (8.06%)	9 / 165 (5.45%)
occurrences (all)	13	6	11
Oedema peripheral			
subjects affected / exposed	2 / 122 (1.64%)	4 / 62 (6.45%)	1 / 165 (0.61%)
occurrences (all)	2	4	1
Influenza like illness			
subjects affected / exposed	1 / 122 (0.82%)	1 / 62 (1.61%)	1 / 165 (0.61%)
occurrences (all)	1	1	1
Oedema			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	1 / 165 (0.61%)
occurrences (all)	0	1	1
Feeling cold			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 122 (8.20%)	2 / 62 (3.23%)	7 / 165 (4.24%)
occurrences (all)	11	3	7
Rhinorrhoea			
subjects affected / exposed	3 / 122 (2.46%)	1 / 62 (1.61%)	0 / 165 (0.00%)
occurrences (all)	3	1	0
Psychiatric disorders			

Agitation			
subjects affected / exposed	10 / 122 (8.20%)	3 / 62 (4.84%)	11 / 165 (6.67%)
occurrences (all)	11	25	11
Anxiety			
subjects affected / exposed	11 / 122 (9.02%)	6 / 62 (9.68%)	11 / 165 (6.67%)
occurrences (all)	11	6	11
Confusional state			
subjects affected / exposed	8 / 122 (6.56%)	3 / 62 (4.84%)	8 / 165 (4.85%)
occurrences (all)	9	3	9
Depression			
subjects affected / exposed	4 / 122 (3.28%)	5 / 62 (8.06%)	8 / 165 (4.85%)
occurrences (all)	4	5	9
Insomnia			
subjects affected / exposed	0 / 122 (0.00%)	4 / 62 (6.45%)	8 / 165 (4.85%)
occurrences (all)	0	4	9
Investigations			
Weight decreased			
subjects affected / exposed	5 / 122 (4.10%)	1 / 62 (1.61%)	6 / 165 (3.64%)
occurrences (all)	5	1	6
Weight increased			
subjects affected / exposed	4 / 122 (3.28%)	5 / 62 (8.06%)	6 / 165 (3.64%)
occurrences (all)	4	6	6
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	18 / 122 (14.75%)	4 / 62 (6.45%)	13 / 165 (7.88%)
occurrences (all)	30	6	18
Contusion			
subjects affected / exposed	11 / 122 (9.02%)	2 / 62 (3.23%)	10 / 165 (6.06%)
occurrences (all)	17	2	12
Laceration			
subjects affected / exposed	8 / 122 (6.56%)	2 / 62 (3.23%)	5 / 165 (3.03%)
occurrences (all)	12	2	5
Muscle strain			
subjects affected / exposed	7 / 122 (5.74%)	0 / 62 (0.00%)	4 / 165 (2.42%)
occurrences (all)	8	0	4
Excoriation			

subjects affected / exposed	4 / 122 (3.28%)	2 / 62 (3.23%)	1 / 165 (0.61%)
occurrences (all)	4	2	1
Procedural pain			
subjects affected / exposed	2 / 122 (1.64%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences (all)	2	0	1
Bone contusion			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences (all)	1	0	1
Hand fracture			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences (all)	0	0	1
Corneal abrasion			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Cerebral microhaemorrhage			
subjects affected / exposed	15 / 122 (12.30%)	10 / 62 (16.13%)	12 / 165 (7.27%)
occurrences (all)	21	12	13
Headache			
subjects affected / exposed	15 / 122 (12.30%)	3 / 62 (4.84%)	15 / 165 (9.09%)
occurrences (all)	19	5	22
Dizziness			
subjects affected / exposed	12 / 122 (9.84%)	6 / 62 (9.68%)	10 / 165 (6.06%)
occurrences (all)	16	7	12
Hyperreflexia			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	1 / 165 (0.61%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	4 / 165 (2.42%)
occurrences (all)	0	2	5
Eye disorders			
Cataract			
subjects affected / exposed	1 / 122 (0.82%)	3 / 62 (4.84%)	3 / 165 (1.82%)
occurrences (all)	2	3	3
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	15 / 122 (12.30%)	7 / 62 (11.29%)	12 / 165 (7.27%)
occurrences (all)	18	11	16
Nausea			
subjects affected / exposed	7 / 122 (5.74%)	5 / 62 (8.06%)	13 / 165 (7.88%)
occurrences (all)	12	5	14
Vomiting			
subjects affected / exposed	6 / 122 (4.92%)	3 / 62 (4.84%)	10 / 165 (6.06%)
occurrences (all)	6	4	12
Dental caries			
subjects affected / exposed	1 / 122 (0.82%)	1 / 62 (1.61%)	0 / 165 (0.00%)
occurrences (all)	1	1	0
Gastritis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	5 / 122 (4.10%)	5 / 62 (8.06%)	2 / 165 (1.21%)
occurrences (all)	11	8	4
Hyperhidrosis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 62 (1.61%)	2 / 165 (1.21%)
occurrences (all)	0	1	2
Actinic keratosis			
subjects affected / exposed	1 / 122 (0.82%)	2 / 62 (3.23%)	1 / 165 (0.61%)
occurrences (all)	1	2	1
Rash pruritic			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	3 / 165 (1.82%)
occurrences (all)	0	0	3
Glycosuria			

subjects affected / exposed	0 / 122 (0.00%)	0 / 62 (0.00%)	0 / 165 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 122 (4.92%)	7 / 62 (11.29%)	9 / 165 (5.45%)
occurrences (all)	7	9	11
Arthralgia			
subjects affected / exposed	9 / 122 (7.38%)	5 / 62 (8.06%)	10 / 165 (6.06%)
occurrences (all)	9	5	10
Pain in extremity			
subjects affected / exposed	2 / 122 (1.64%)	5 / 62 (8.06%)	4 / 165 (2.42%)
occurrences (all)	2	7	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	21 / 122 (17.21%)	6 / 62 (9.68%)	13 / 165 (7.88%)
occurrences (all)	28	6	20
Urinary tract infection			
subjects affected / exposed	16 / 122 (13.11%)	6 / 62 (9.68%)	17 / 165 (10.30%)
occurrences (all)	19	8	20
Upper respiratory tract infection			
subjects affected / exposed	16 / 122 (13.11%)	10 / 62 (16.13%)	7 / 165 (4.24%)
occurrences (all)	18	11	9
Bronchitis			
subjects affected / exposed	3 / 122 (2.46%)	2 / 62 (3.23%)	5 / 165 (3.03%)
occurrences (all)	4	2	6
Pneumonia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	3 / 165 (1.82%)
occurrences (all)	1	0	3
Diverticulitis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 62 (0.00%)	0 / 165 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 122 (0.82%)	1 / 62 (1.61%)	1 / 165 (0.61%)
occurrences (all)	1	1	1

Non-serious adverse events	Intravenous infusion placebo	Intravenous infusion crenezumab (safety run-in)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 82 (68.29%)	11 / 13 (84.62%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	2 / 82 (2.44%)	0 / 13 (0.00%)	
occurrences (all)	3	0	
Basal cell carcinoma			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	2	
Hot flush			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Phlebitis			
subjects affected / exposed	1 / 82 (1.22%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	4 / 82 (4.88%)	0 / 13 (0.00%)	
occurrences (all)	4	0	
Oedema peripheral			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			

subjects affected / exposed	1 / 82 (1.22%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Oedema			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Feeling cold			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 82 (3.66%)	1 / 13 (7.69%)	
occurrences (all)	3	1	
Rhinorrhoea			
subjects affected / exposed	3 / 82 (3.66%)	1 / 13 (7.69%)	
occurrences (all)	3	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 82 (2.44%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Anxiety			
subjects affected / exposed	5 / 82 (6.10%)	0 / 13 (0.00%)	
occurrences (all)	7	0	
Confusional state			
subjects affected / exposed	3 / 82 (3.66%)	0 / 13 (0.00%)	
occurrences (all)	3	0	
Depression			
subjects affected / exposed	5 / 82 (6.10%)	0 / 13 (0.00%)	
occurrences (all)	5	0	
Insomnia			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Investigations			
Weight decreased			
subjects affected / exposed	7 / 82 (8.54%)	0 / 13 (0.00%)	
occurrences (all)	8	0	
Weight increased			

subjects affected / exposed	2 / 82 (2.44%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 82 (6.10%)	1 / 13 (7.69%)	
occurrences (all)	6	1	
Contusion			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Laceration			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Muscle strain			
subjects affected / exposed	0 / 82 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Excoriation			
subjects affected / exposed	2 / 82 (2.44%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Procedural pain			
subjects affected / exposed	0 / 82 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Bone contusion			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Hand fracture			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Corneal abrasion			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Cerebral microhaemorrhage			
subjects affected / exposed	9 / 82 (10.98%)	0 / 13 (0.00%)	
occurrences (all)	13	0	
Headache			

subjects affected / exposed	7 / 82 (8.54%)	1 / 13 (7.69%)	
occurrences (all)	7	3	
Dizziness			
subjects affected / exposed	5 / 82 (6.10%)	1 / 13 (7.69%)	
occurrences (all)	5	1	
Hyperreflexia			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 82 (1.22%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 82 (2.44%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 82 (8.54%)	1 / 13 (7.69%)	
occurrences (all)	10	1	
Nausea			
subjects affected / exposed	6 / 82 (7.32%)	0 / 13 (0.00%)	
occurrences (all)	7	0	
Vomiting			
subjects affected / exposed	5 / 82 (6.10%)	0 / 13 (0.00%)	
occurrences (all)	5	0	
Dental caries			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Mouth ulceration			
subjects affected / exposed	1 / 82 (1.22%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			

Erythema			
subjects affected / exposed	3 / 82 (3.66%)	0 / 13 (0.00%)	
occurrences (all)	7	0	
Hyperhidrosis			
subjects affected / exposed	2 / 82 (2.44%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Actinic keratosis			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Rash pruritic			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Glycosuria			
subjects affected / exposed	0 / 82 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 82 (6.10%)	0 / 13 (0.00%)	
occurrences (all)	5	0	
Arthralgia			
subjects affected / exposed	2 / 82 (2.44%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	1 / 82 (1.22%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 82 (9.76%)	1 / 13 (7.69%)	
occurrences (all)	16	1	
Urinary tract infection			
subjects affected / exposed	10 / 82 (12.20%)	0 / 13 (0.00%)	
occurrences (all)	11	0	

Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 82 (4.88%) 4	1 / 13 (7.69%) 1	
Bronchitis subjects affected / exposed occurrences (all)	1 / 82 (1.22%) 1	1 / 13 (7.69%) 1	
Pneumonia subjects affected / exposed occurrences (all)	0 / 82 (0.00%) 0	1 / 13 (7.69%) 1	
Diverticulitis subjects affected / exposed occurrences (all)	0 / 82 (0.00%) 0	1 / 13 (7.69%) 1	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	4 / 82 (4.88%) 4	1 / 13 (7.69%) 1	

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 CSF sample collection. Change in fasting requirements for laboratory assessments.
20 August 2012	Eligibility criteria which would allow patients to roll over to an open-label extension study. A requirement for additional safety assessments 8- and 12-weeks after ET assessments was added for those patients who discontinue prematurely from the study. To allow nurse practitioners and equivalently qualified personnel (under applicable law) to review and sign-off on the MMSE and the C-SSRS before the patient is discharged. To allow collection of PK samples 60−90 minutes post infusion.
04 January 2013	For concomitant medications, intermittent use of benzodiazepines was changed to restrict use within 5 half-lives prior to neurocognitive assessment to ensure complete pharmacological washout.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported