



Clinical trial results:

A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP EFFICACY AND SAFETY TRIAL OF BAPINEUZUMAB (AAB-001, ELN115727) IN SUBJECTS WITH MILD TO MODERATE ALZHEIMER DISEASE WHO ARE APOLIPOPROTEIN E 4 NON-CARRIERS.

Summary

EudraCT number	2007-005994-79
Trial protocol	ES IE GB BE DE FR FI SE IT SK PT AT NL DK
Global end of trial date	27 November 2012

Results information

Result version number	v1 (current)
This version publication date	10 June 2016
First version publication date	10 June 2016

Trial information

Trial identification

Sponsor protocol code	3133K1-3000-WW
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00667810
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 East 42nd Street,, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 800 718 1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 800 718 1021, ClinicalTrials.gov_Inquiries@pfizer.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 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 October 2012
Global end of trial reached?	Yes
Global end of trial date	27 November 2012
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective was to demonstrate an advantage of the efficacy of multiple doses of intravenous administered bapineuzumab (0.5 mg/kg or 1.0 mg/kg) compared to placebo in participants with mild to moderate Alzheimer's disease as measured by both the following:

1. The change from baseline to Week 78 for the Alzheimer's Disease assessment scale - cognitive subscale, 11-item (ADAS-Cog/11) total score;
2. The change from baseline to Week 78 for the disability assessment for dementia (DAD) total score.

The safety objective of this study was to assess the safety of multiple doses of intravenous administered bapineuzumab in participants with mild to moderate Alzheimer's Disease versus placebo, including;

- The incidence and severity of TEAEs;
- Clinically important changes in safety assessment results (including, as appropriate, vital signs, weight, clinical laboratory tests, electrocardiograms (ECGs), brain MRI scans, and physical and neurologic examinations).

Protection of trial subjects:

The study was conducted in accordance with applicable laws and regulations including, but not limited to, the International Conference on Harmonization Guideline for Good Clinical Practice (GCP) and the ethical principles that have their origins in the Declaration of Helsinki. All regulatory requirements were followed; in particular, those affording greater protection to the safety of study participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 June 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	Serbia: 8
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Mexico: 10
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	Germany: 12

Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	South Africa: 14
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Portugal: 23
Country: Number of subjects enrolled	Canada: 42
Country: Number of subjects enrolled	Chile: 48
Country: Number of subjects enrolled	France: 57
Country: Number of subjects enrolled	Spain: 91
Country: Number of subjects enrolled	United Kingdom: 93
Country: Number of subjects enrolled	Japan: 140
Country: Number of subjects enrolled	United States: 213
Worldwide total number of subjects	885
EEA total number of subjects	371

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)	275
From 65 to 84 years	566
85 years and over	44

Subject disposition

Recruitment

Recruitment details:

The study was terminated on 06 August 2012 due to lack of clinical efficacy observed in completed studies ELN115727-301 (ApoE4 non-carriers) and ELN115727-302. A total of 329 participants had completed the study up to and including Week 78 before the decision was taken to terminate the study.

Pre-assignment

Screening details:

The study originally included bapineuzumab 2.0 mg/kg dose level, which was discontinued on 02 April 2009 based on input from independent safety monitoring committee. It was estimated at the time that about 10 participants received 2.0mg/kg. These participants are not included in the efficacy analyses.

Period 1

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

Blinding implementation details:

This study was blinded to participants, investigators and sponsors. The responsibility of the unblinded dispenser had to be assigned to a person who did not participate in the evaluation of any study participant. Contact between the unblinded dispenser and study participants was to be avoided. Psychometric and global raters were to be blinded not only to treatment assignment but also to adverse events experienced by the participants.

Arms

Are arms mutually exclusive?	Yes
Arm title	Bapineuzumab 0.5 mg/kg

Arm description:

Participants received 0.5 mg/kg bapineuzumab by intravenous (IV) infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Arm type	Experimental
Investigational medicinal product name	Bapineuzumab 0.5 mg/kg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 0.5 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Arm title	Bapineuzumab 1.0 mg/kg
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Arm description:

Participants received 1.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Arm type	Experimental
Investigational medicinal product name	Bapineuzumab 1.0 mg/kg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Arm title	Bapineuzumab 2.0 mg/kg
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Arm description:

Participants received 2.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Arm type	Experimental
Investigational medicinal product name	Bapineuzumab 2.0 mg/kg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 2.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Arm title	Placebo
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Arm description:

Participants received placebo by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received placebo by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Number of subjects in period 1	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Bapineuzumab 2.0 mg/kg
Started	267	263	11
Completed	102	94	9
Not completed	165	169	2
Adverse event, serious fatal	1	1	-
Physician decision	1	1	-
Consent withdrawn by subject	14	20	1
Adverse event, non-fatal	13	13	1
Not specified	5	6	-
Discontinuation of Study by Sponsor	129	118	-
Loss of Caregiver	-	1	-
Vasogenic Edema Recurrence	-	3	-

Failed to Return	-	-	-
Lost to follow-up	1	4	-
Lack of efficacy	1	-	-
Protocol deviation	-	2	-

Number of subjects in period 1	Placebo
Started	344
Completed	124
Not completed	220
Adverse event, serious fatal	3
Physician decision	1
Consent withdrawn by subject	28
Adverse event, non-fatal	19
Not specified	5
Discontinuation of Study by Sponsor	155
Loss of Caregiver	3
Vasogenic Edema Recurrence	-
Failed to Return	2
Lost to follow-up	2
Lack of efficacy	2
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	Bapineuzumab 0.5 mg/kg
Reporting group description: Participants received 0.5 mg/kg bapineuzumab by intravenous (IV) infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.	
Reporting group title	Bapineuzumab 1.0 mg/kg
Reporting group description: Participants received 1.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.	
Reporting group title	Bapineuzumab 2.0 mg/kg
Reporting group description: Participants received 2.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.	
Reporting group title	Placebo
Reporting group description: Participants received placebo by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.	

Reporting group values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Bapineuzumab 2.0 mg/kg
Number of subjects	267	263	11
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	71.4 ± 9.38	70.8 ± 9.73	66.5 ± 7.94
Gender, Male/Female Units: Number of participants			
Female	151	150	4
Male	116	113	7

Reporting group values	Placebo	Total	
Number of subjects	344	885	
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	69.9 ± 9.76	-	
Gender, Male/Female Units: Number of participants			
Female	199	504	
Male	145	381	

End points

End points reporting groups

Reporting group title	Bapineuzumab 0.5 mg/kg
Reporting group description: Participants received 0.5 mg/kg bapineuzumab by intravenous (IV) infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.	
Reporting group title	Bapineuzumab 1.0 mg/kg
Reporting group description: Participants received 1.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.	
Reporting group title	Bapineuzumab 2.0 mg/kg
Reporting group description: Participants received 2.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.	
Reporting group title	Placebo
Reporting group description: Participants received placebo by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.	

Primary: The change from baseline in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog)/11 total score at Week 78

End point title	The change from baseline in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog)/11 total score at Week 78 ^[1]
End point description: This scale evaluates memory, language, praxis with items such as orientation, word recall, word recognition, object-identification, comprehension, completion of simple tasks. The analysis was based upon 11 item score from the items; word recall task, naming objects and fingers, following commands, constructional praxis, ideational praxis, orientation, word recognition, remembering instructions, spoken language ability, word finding difficulty in spontaneous speech, and comprehension. Scale was administered by a psychometric rater who did not have access to information of adverse events experienced. The scale ranged from 0 to 70 points, with higher score indicating a greater degree of impairment. Analysis population is modified intent-to-treat(mITT) population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score	
End point type	Primary
End point timeframe: 78 weeks	

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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Units on a scale				
least squares mean (standard error)	6.05 (± 0.71)	8.07 (± 0.73)	7.88 (± 0.64)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Change from baseline in ADAS-Cog/11 total score was analyzed using a restricted maximum likelihood (REML) based mixed model for repeated-measures (MMRM). The number of participants in each group provided approximately 90% power to detect a 2.65 point advantage at Week 78. This calculation was based on a 2-sided test with alpha set at 0.05, the use of the Hochberg procedure to control for multiplicity.	
Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.057 ^[2]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.71
upper limit	0.05

Notes:

[2] - The p-value is not adjusted for multiple comparison. The Hochberg approach is used to control for multiplicity between the two dose levels (0.5 mg/kg and 1.0 mg/kg) of bapineuzumab.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Change from baseline in ADAS-Cog/11 total score was analyzed using a REML based MMRM. The number of participants in each group provided approximately 90% power to detect a 2.65 point advantage at Week 78. This calculation was based on a 2-sided test with alpha set at 0.05, the use of the Hochberg procedure to control for multiplicity.	
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.848 ^[3]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.73
upper limit	2.1

Notes:

[3] - The p-value is not adjusted for multiple comparison. The Hochberg approach is used to control for multiplicity between the two dose levels (0.5 mg/kg and 1.0 mg/kg) of bapineuzumab.

Primary: The change from baseline in the Disability Assessment for Dementia (DAD) total score at Week 78

End point title	The change from baseline in the Disability Assessment for Dementia (DAD) total score at Week 78 ^[4]
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End point description:

The DAD is administered to the participant caregiver in the form of an interview. Scale was administered by a certified global rater who did not have access to any information of adverse events experienced. This scale assesses a participant's ability to initiate, plan, and perform activities related to hygiene, dressing, continence, eating, meal preparation, telephoning, going on an outing, finance and correspondence, medications, leisure, and housework. Each item can be scored as 1=yes, 0=no, non-applicable=NA. A total score is obtained by adding the rating for each question and converting this total score out of 100. Higher scores indicate better function. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Primary
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End point timeframe:

78 weeks

Notes:

[4] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Units on a scale				
least squares mean (standard error)	-14.58 (± 1.5)	-15.07 (± 1.55)	-16.08 (± 1.36)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Change from baseline in DAD total score was analyzed using a REML based MMRM. The number of participants in each group provided approximately 90% power to detect a 6.56 point advantage at Week 78. This calculation was based on a 2-sided test with alpha set at 0.05, the use of the Hochberg procedure to control for multiplicity.

Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.459 ^[5]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.48
upper limit	5.49

Notes:

[5] - The p-value is not adjusted for multiple comparison. The Hochberg approach is used to control for multiplicity between the two dose levels (0.5 mg/kg and 1.0 mg/kg) of bapineuzumab.

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Change from baseline in DAD total score was analyzed using a REML based MMRM. The number of participants in each group provided approximately 90% power to detect a 6.56 point advantage at Week 78. This calculation was based on a 2-sided test with alpha set at 0.05, the use of the Hochberg procedure to control for multiplicity.

Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.623 ^[6]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.04
upper limit	5.07

Notes:

[6] - The p-value is not adjusted for multiple comparison. The Hochberg approach is used to control for multiplicity between the two dose levels (0.5 mg/kg and 1.0 mg/kg) of bapineuzumab.

Secondary: The change from baseline in Brain Amyloid Burden at Week 71.

End point title	The change from baseline in Brain Amyloid Burden at Week
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End point description:

Brain amyloid burden as imaged by 11C-Pittsburgh compound B (PiB) positron emission tomography (PET). The latter is a semiquantitative measure of the extent of fibrillar amyloid in the brain. PIB PET measurements were made in cortical regions found to have the highest burden of fibrillar amyloid at autopsy in participants diagnosed as having Alzheimer's pathology, and also regions reported to have the highest average retention of PIB signal in previous PET studies enrolling participants with probable AD. This parameter reflects overall brain amyloid deposition as indexed by imaging. The change from baseline was measured as average standard uptake value ratio (SUVR) in prespecified regions of interest (ROI) assessed by PIB PET imaging in a subset of participants.

End point type	Secondary
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End point timeframe:

71 Weeks

Notes:

[7] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	11	13	
Units: Units on a scale				
least squares mean (standard error)	-0.04 (\pm 0.08)	0 (\pm 0.05)	0.02 (\pm 0.04)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
The analysis is based on the pooled bapineuzumab (with subjects in the bapineuzumab 0.5 and 1.0 mg/kg groups combined) treatment difference estimated at Week 71. The number of participants gave 90% power to detect a 0.186 unit advantage for a bapineuzumab dose group over placebo for PiB PET binding at Week 71. The calculations were based on 2-sided tests with alpha set at 0.05 and the use of the Hochberg procedure to control for multiplicity for 2 individual doses.	
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.654
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.09

Secondary: The change from baseline in phospho-tau levels in the cerebrospinal fluid (CSF) at Week 71.

End point title	The change from baseline in phospho-tau levels in the cerebrospinal fluid (CSF) at Week 71. ^[8]
End point description:	
Biomarkers CSF phospho-tau (p-tau) is an indicator of neuronal injury and neurodegeneration. An elevation in levels of tau, as well as specific p-tau species, is thought to be a marker for progressive cellular degeneration in AD. Accordingly, a reduction from baseline in levels of CSF tau in participants who received bapineuzumab compared with participants who received placebo may be indicative of a reduction in neuronal loss in participants treated with bapineuzumab.	
End point type	Secondary
End point timeframe:	
71 Weeks	

Notes:

[8] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	22	33	
Units: pg/mL				
least squares mean (standard error)	-6.62 (± 3.9)	-6.35 (± 3.73)	0.7 (± 3.03)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
The analysis is based on the pooled bapineuzumab (with participants in the bapineuzumab 0.5 and 1.0 mg/kg groups combined) treatment difference estimated at Week 71. The number of participants gave 90% power to detect a 15 ng/L advantage in p-tau for a bapineuzumab dose group over placebo at Week 71. The calculations were based on 2-sided tests with alpha set at 0.05 and the use of the Hochberg procedure to control for multiplicity for 2 individual doses.	
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.085
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-7.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.38
upper limit	1.02

Secondary: The change from baseline in brain volume at Week 71

End point title	The change from baseline in brain volume at Week 71 ^[9]
End point description:	
Brain volume was examined in a subset of participants by Magnetic Resonance Imaging Brain Boundary Shift Integral (MRI BBSI). Cerebral atrophy correlates closely with the gradual cognitive decline in AD and can be visualized by MRI. The BBSI technique involves positional matching of serial 3-dimensional MRI brain images, such that brain MRI-image volumes were first registered and then subtracted from each other. Atrophy rates would generally be expected to be lower if the underlying disease was attenuated by effective treatment.	
End point type	Secondary
End point timeframe:	
71 Weeks	
Notes:	
[9] - 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: Data for the reporting arm Placebo was not available	

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	121	153	
Units: mL/year				
least squares mean (standard error)	18.55 (\pm 0.97)	18.6 (\pm 1)	17.54 (\pm 0.86)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Change in MRI BBSI was analyzed using a REML based MMRM. The number of participants gave 90% power to detect a 5.05-cm ³ advantage for a bapineuzumab dose group over placebo on reduction in brain volume as measured by the BBSI at Week 71. The calculations were based on 2-sided tests with alpha set at 0.05 and the use of the Hochberg procedure to control for multiplicity for 2 individual doses.	
Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	275
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	3.57

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Change in MRI BBSI was analyzed using a REML based MMRM. The number of participants gave 90% power to detect a 5.05-cm ³ advantage for a bapineuzumab dose group over placebo on reduction in brain volume as measured by the BBSI at Week 71. The calculations were based on 2-sided tests with alpha set at 0.05 and the use of the Hochberg procedure to control for multiplicity for 2 individual doses.	
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.423
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.54
upper limit	3.66

Secondary: Divergence of effect on the ADAS-Cog/11 total scores from Week 39 to Week 78

End point title	Divergence of effect on the ADAS-Cog/11 total scores from Week 39 to Week 78 ^[10]
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End point description:

The MMRM estimated slope (based on linear contrasts) of the differences between bapineuzumab and placebo for the ADAS-Cog/11 total scores from Week 39 to Week 78 was presented. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

Week 39 to Week 78

Notes:

[10] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Units/Year				
least squares mean (standard error)				
Week 39	2.59 (± 0.41)	3.41 (± 0.42)	3.37 (± 0.37)	
Week 52	3.08 (± 0.5)	4.3 (± 0.51)	4.38 (± 0.45)	
Week 65	4.56 (± 0.6)	6.46 (± 0.62)	6.02 (± 0.54)	
Week 78	6.05 (± 0.71)	8.07 (± 0.73)	7.88 (± 0.64)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Bapineuzumab 0.5 mg/kg v Placebo
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.212
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	0.76

Statistical analysis title	Statistical analysis 2
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.725
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.76
upper limit	2.52

Secondary: Divergence of effect on the DAD total scores from Week 39 to Week 78

End point title	Divergence of effect on the DAD total scores from Week 39 to Week 78 ^[11]
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End point description:

The MMRM estimated slope (based on linear contrasts) of the differences between bapineuzumab and placebo for the DAD total scores from Week 39 to Week 78 was presented. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

Week 39 to Week 78

Notes:

[11] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Units/Years				
least squares mean (standard error)				
Week 39	-7.24 (± 0.87)	-6.44 (± 0.89)	-6.31 (± 0.78)	
Week 52	-8.82 (± 1.07)	-11.09 (± 1.1)	-9.16 (± 0.96)	
Week 65	-11.57 (± 1.3)	-12.93 (± 1.35)	-12.61 (± 1.17)	
Week 78	-14.58 (± 1.5)	-15.07 (± 1.55)	-16.08 (± 1.36)	

Statistical analyses

Statistical analysis title	Statistical analysis 2
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.375
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.44
upper limit	6.46

Statistical analysis title	Statistical analysis 1
Comparison groups	Bapineuzumab 0.5 mg/kg v Placebo
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.149
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.15
upper limit	7.56

Secondary: Time to median placebo deterioration on ADAS-Cog/11 total score (European Union [EU] analysis plan)

End point title	Time to median placebo deterioration on ADAS-Cog/11 total score (European Union [EU] analysis plan) ^[12]
End point description:	
<p>The time to first median placebo deterioration (for the EU) was defined as the first time a subject experienced an increase from baseline (worsening) in ADAS Cog/11 total score greater than or equal to the median worsening observed at Week 78 in the placebo group. The Kaplan Meier estimate of the median time to first median placebo deterioration in ADAS Cog/11 total score was presented. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.</p>	
End point type	Secondary
End point timeframe:	
78 Weeks	

Notes:

[12] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Days				
median (confidence interval 95%)	546 (546 to 9999)	462 (455 to 546)	540 (462 to 546)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Logrank

Statistical analysis title	Statistical analysis 2
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.567
Method	Logrank

Secondary: Time to First Clinically Meaningful Deterioration on ADAS-Cog/11 total score (United States [US] analysis plan)

End point title	Time to First Clinically Meaningful Deterioration on ADAS-Cog/11 total score (United States [US] analysis plan) ^[13]
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End point description:

The time to first clinically meaningful deterioration (for the US) was defined as the first time a participant experienced an increase (worsening) from baseline in ADAS-Cog/11 total score of ≥ 7 . The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

78 weeks

Notes:

[13] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Days				
median (confidence interval 95%)	546 (546 to 9999)	546 (455 to 546)	546 (476 to 546)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.079
Method	Logrank

Statistical analysis title	Statistical analysis 2
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.675
Method	Logrank

Secondary: Time to median placebo deterioration on DAD total score

End point title	Time to median placebo deterioration on DAD total score ^[14]
End point description:	
The time to first median placebo deterioration (for the EU) was defined as the first time a participant experienced a decrease (worsening) in DAD total score greater than or equal to the median worsening at Week 78 in the placebo group. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.	
End point type	Secondary
End point timeframe:	
78 Weeks	

Notes:

[14] - 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.

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Days				
median (confidence interval 95%)	541 (455 to 546)	534 (372 to 9999)	463 (453 to 546)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.846
Method	Logrank

Statistical analysis title	Statistical analysis 2
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.797
Method	Logrank

Secondary: Time to First Clinically Meaningful Deterioration on DAD total score (US analysis plan)

End point title	Time to First Clinically Meaningful Deterioration on DAD total score (US analysis plan) ^[15]
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End point description:

The time to first clinically meaningful deterioration was defined as the first time a participant experienced a decrease (worsening) from baseline in DAD total score of ≥ 12 . The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

78 Weeks

Notes:

[15] - 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.

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Days				
median (confidence interval 95%)	542 (456 to 546)	539 (450 to 9999)	540 (453 to 546)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.933
Method	Logrank

Statistical analysis title	Statistical analysis 2
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.714
Method	Logrank

Secondary: Percentage of participants with worsening from baseline in ADAS-Cog/11 total score at Week 78 (European Union analysis plan)

End point title	Percentage of participants with worsening from baseline in ADAS-Cog/11 total score at Week 78 (European Union analysis plan) ^[16]
End point description:	
Percentage of participants whose increase (worsening) in ADAS-Cog/11 total score from baseline to Week 78 was at most 0, 3, 7 points. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.	
End point type	Secondary
End point timeframe:	
78 Weeks	

Notes:

[16] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Number of participants				
number (confidence interval 95%)				
Worsening of 0 points	10.6 (7.1 to 15)	8.7 (5.5 to 12.9)	7.3 (4.7 to 10.7)	
Worsening of 3 points	16.1 (11.8 to 21.2)	13.4 (9.5 to 18.3)	10.1 (7 to 13.8)	
Worsening of 7 points	23.1 (18.1 to 28.8)	19 (14.3 to 24.4)	19.2 (15.1 to 23.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with worsening from baseline in ADAS-Cog/11 total score at Week 78 (US analysis plan)

End point title	Percentage of participants with worsening from baseline in ADAS-Cog/11 total score at Week 78 (US analysis plan) ^[17]
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End point description:

Percentage of participants whose increase (worsening) from baseline to Week 78 in ADAS-Cog/11 total score is <7. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

78 Weeks

Notes:

[17] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Percentage of participants				
number (not applicable)	22.4	18.6	18.6	

Statistical analyses

Statistical analysis title	Statistical analysis 2
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.996
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.277
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of participants with worsening from baseline in DAD total score at Week 78 (European Union analysis plan)

End point title	Percentage of participants with worsening from baseline in DAD total score at Week 78 (European Union analysis plan) ^[18]
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End point description:

Percentage of participants whose decrease (worsening) from baseline to Week 78 in DAD total score was at most 0, 6, 12 points. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

78 Weeks

Notes:

[18] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Percentage of participants				
number (confidence interval 95%)				
Worsening of 0 points	10.2 (6.8 to 14.6)	11.9 (8.1 to 16.5)	9.1 (6.3 to 12.8)	
Worsening of 6 points	15.7 (11.4 to 20.7)	16.6 (12.2 to 21.8)	14.3 (10.7 to 18.6)	
Worsening of 12 points	20 (15.3 to 25.4)	22.1 (17.2 to 27.8)	19.5 (15.4 to 24.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with worsening from baseline in DAD total score at Week 78 (US analysis plan)

End point title	Percentage of participants with worsening from baseline in DAD total score at Week 78 (US analysis plan) ^[19]
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End point description:

Percentage of participants whose decrease (worsening) from baseline to Week 78 in DAD total score was <12. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

78 weeks

Notes:

[19] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Percentage of participants				
number (not applicable)	20	22.1	19.5	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.855
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 2
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.423
Method	Cochran-Mantel-Haenszel

Secondary: Change from Baseline in Dependence Scale Total Score at Week 78

End point title	Change from Baseline in Dependence Scale Total Score at Week 78 ^[20]
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End point description:

The Dependence Scale (DS) is a 13-item, caregiver-rated instrument for determining the amount of support required by a participant with AD. The DS total score ranges from 0 to 15, with higher scores indicating more need for assistance. The DS was administered as an interview to the caregiver at scheduled study visits. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

78 Weeks

Notes:

[20] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Units on a scale				
least squares mean (standard error)	1.29 (± 0.19)	1.16 (± 0.19)	1.45 (± 0.17)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Change in DS score was analyzed using a REML based MMRM.

Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.516
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.33

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Change in DS score was analyzed using a REML based MMRM.

Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
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Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.257
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.21

Secondary: Change from baseline in Clinical Dementia Rating Sum of Boxes (CDR-SOB) total score at Week 78

End point title	Change from baseline in Clinical Dementia Rating Sum of Boxes (CDR-SOB) total score at Week 78 ^[21]
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End point description:

The CDR-SOB is a global clinical staging instrument that sums 6 clinical ratings: 1) memory, 2) orientation, 3) judgment and problem solving, 4) involvement in community affairs, 5) home and hobbies, and 6) personal care based on the Clinical Dementia Rating Scale (CDR) interview. The CDR includes discussions with the participant and caregiver using a structured format. This scale had to be administered by a trained and certified global rater who did not have access to any information regarding adverse events experienced by the participant. CDR-SOB total score range is 0 (least impairment) to 18 (most impairment); a negative change from baseline indicates an improvement. The analysis population is the mITT population included all randomized participants who received at least one infusion or portion of an infusion of study drug and who had a baseline and at least one post-baseline assessment of the ADAS-Cog/11 total score and DAD total score.

End point type	Secondary
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End point timeframe:

78 Weeks

Notes:

[21] - 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: Data for the reporting arm Placebo was not available

End point values	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	255	253	328	
Units: Units on a scale				
least squares mean (standard error)	2.23 (± 0.23)	2.41 (± 0.23)	2.59 (± 0.2)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Change in CDR-SOB total score was analyzed using a REML based MMRM.

Comparison groups	Placebo v Bapineuzumab 0.5 mg/kg
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Number of subjects included in analysis	583
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.238
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.24

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Change in CDR-SOB total score was analyzed using a REML based MMRM.	
Comparison groups	Bapineuzumab 1.0 mg/kg v Placebo
Number of subjects included in analysis	581
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.564
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	0.43

Adverse events

Adverse events information

Timeframe for reporting adverse events:

4 years

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as nonserious in another participant, or one participant may have experienced both a serious and nonserious event during the study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.0
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Reporting groups

Reporting group title	Bapineuzumab 0.5 mg/kg
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Reporting group description:

Participants received 0.5 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Reporting group title	Bapineuzumab 1.0 mg/kg
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Reporting group description:

Participants received 1.0 mg/kg bapineuzumab by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Reporting group title	Placebo
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Reporting group description:

Participants received placebo by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Reporting group title	Bapineuzumab 2.0 mg/kg
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Reporting group description:

Participants received placebo by IV infusion every 13 weeks, for a total of 6 infusions over the course of the study. A final follow-up visit was performed at Week 78, 13 weeks after the last infusion.

Serious adverse events	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 267 (11.99%)	34 / 263 (12.93%)	53 / 344 (15.41%)
number of deaths (all causes)	3	1	5
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Adenocarcinoma pancreas			

subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Breast cancer			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	2 / 344 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Glioblastoma			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratoacanthoma			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			

subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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 liver			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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 lung			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	2 / 344 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic stenosis			

subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic thrombosis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Deep vein thrombosis			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery stenosis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granuloma			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Dyspnoea			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Nasal polyps			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Organising pneumonia			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Pneumothorax			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Pulmonary embolism			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			

subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aggression			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholic psychosis			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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	0 / 267 (0.00%)	1 / 263 (0.38%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			

subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impulsive behaviour			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jealous delusion			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ECG signs of myocardial ischaemia			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	1 / 267 (0.37%)	1 / 263 (0.38%)	0 / 344 (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

Fall			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	2 / 344 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Femoral neck fracture			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Femur fracture			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heat illness			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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	1 / 267 (0.37%)	1 / 263 (0.38%)	0 / 344 (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
Humerus fracture			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Joint dislocation			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Multiple injuries			

subjects affected / exposed	2 / 267 (0.75%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Skull fractured base			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Spinal compression fracture			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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 / 267 (0.00%)	1 / 263 (0.38%)	2 / 344 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			

subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Adams-Stokes syndrome			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Angina pectoris			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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	1 / 267 (0.37%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			

subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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 failure congestive			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Coronary artery disease			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Myocardial infarction			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Cerebral infarction			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral microhaemorrhage			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Convulsion			

subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 267 (0.37%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	2 / 267 (0.75%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial hypotension			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perineurial cyst			

subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Quadriparesis			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Radiculopathy			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Senile dementia			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Status epilepticus			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Subdural hygroma			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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	1 / 267 (0.37%)	1 / 263 (0.38%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasogenic cerebral oedema			
subjects affected / exposed	6 / 267 (2.25%)	12 / 263 (4.56%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	8 / 8	20 / 20	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Diarrhoea			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecal incontinence			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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

Gastritis			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Intestinal ischaemia			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Vomiting			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	2 / 344 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pruritus			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Osteoarthritis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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			
Anal abscess			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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

Clostridium difficile colitis			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Herpes zoster oticus			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Meningitis viral			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Otitis media			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Periorbital cellulitis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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 tract infection			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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
Urosepsis			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
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			
Decreased appetite			
subjects affected / exposed	1 / 267 (0.37%)	0 / 263 (0.00%)	0 / 344 (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
Dehydration			
subjects affected / exposed	0 / 267 (0.00%)	0 / 263 (0.00%)	1 / 344 (0.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypokalaemia			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (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	Bapineuzumab 2.0		
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	mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colorectal cancer			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric cancer			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glioblastoma			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Keratoacanthoma				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to central nervous system				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to liver				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to lung				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal cancer				

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aortic thrombosis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral artery stenosis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Granuloma			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nasal polyps			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Organising pneumonia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aggression			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Agitation			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcohol abuse			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcoholic psychosis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Delirium			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hallucination			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Impulsive behaviour			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jealous delusion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
ECG signs of myocardial ischaemia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver function test abnormal			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Weight decreased			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Heat illness			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaw fracture			

subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple injuries				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skull fractured base				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adams-Stokes syndrome			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral microhaemorrhage			

subjects affected / exposed	1 / 11 (9.09%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dementia Alzheimer's type				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracranial hypotension				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Perineurial cyst			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Quadriparesis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radiculopathy			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Senile dementia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subarachnoid haemorrhage			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural hygroma			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vasogenic cerebral oedema			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences causally related to treatment / all	7 / 7		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Faecal incontinence			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal ischaemia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urticaria			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal osteoarthritis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Bacteraemia				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster oticus				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis viral				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	0 / 11 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periorbital cellulitis				

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 1		
Pyelonephritis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 11 (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	Bapineuzumab 0.5 mg/kg	Bapineuzumab 1.0 mg/kg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	109 / 267 (40.82%)	123 / 263 (46.77%)	124 / 344 (36.05%)
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 267 (3.00%)	10 / 263 (3.80%)	9 / 344 (2.62%)
occurrences (all)	8	12	16
Hypotension			
subjects affected / exposed	1 / 267 (0.37%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Catheter site haematoma			
subjects affected / exposed	0 / 267 (0.00%)	1 / 263 (0.38%)	0 / 344 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	4 / 267 (1.50%)	3 / 263 (1.14%)	6 / 344 (1.74%)
occurrences (all)	4	5	6
Depression			
subjects affected / exposed	13 / 267 (4.87%)	11 / 263 (4.18%)	9 / 344 (2.62%)
occurrences (all)	25	21	24
Hallucination			
subjects affected / exposed	2 / 267 (0.75%)	2 / 263 (0.76%)	2 / 344 (0.58%)
occurrences (all)	2	2	2
Psychotic disorder			

subjects affected / exposed occurrences (all)	1 / 267 (0.37%) 1	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Investigations Blood pressure increased subjects affected / exposed occurrences (all)	5 / 267 (1.87%) 5	5 / 263 (1.90%) 9	6 / 344 (1.74%) 7
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all)	6 / 267 (2.25%) 7 18 / 267 (6.74%) 25	8 / 263 (3.04%) 10 16 / 263 (6.08%) 18	1 / 344 (0.29%) 1 18 / 344 (5.23%) 26
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	2 / 344 (0.58%) 2
Nervous system disorders Aphasia subjects affected / exposed occurrences (all) Ataxia subjects affected / exposed occurrences (all) Balance disorder subjects affected / exposed occurrences (all) Cerebral microhaemorrhage subjects affected / exposed occurrences (all) Disturbance in attention subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	1 / 267 (0.37%) 1 2 / 267 (0.75%) 2 0 / 267 (0.00%) 0 11 / 267 (4.12%) 13 0 / 267 (0.00%) 0 8 / 267 (3.00%) 8	2 / 263 (0.76%) 4 0 / 263 (0.00%) 0 1 / 263 (0.38%) 1 22 / 263 (8.37%) 41 0 / 263 (0.00%) 0 7 / 263 (2.66%) 20	2 / 344 (0.58%) 6 0 / 344 (0.00%) 0 0 / 344 (0.00%) 0 9 / 344 (2.62%) 21 0 / 344 (0.00%) 0 16 / 344 (4.65%) 17

Dizziness postural subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	1 / 344 (0.29%) 2
Exertional headache subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	17 / 267 (6.37%) 19	15 / 263 (5.70%) 36	29 / 344 (8.43%) 36
Hyporeflexia subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Mental impairment subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Paraesthesia subjects affected / exposed occurrences (all)	1 / 267 (0.37%) 1	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Parkinson's disease subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Vasogenic cerebral oedema subjects affected / exposed occurrences (all)	7 / 267 (2.62%) 16	20 / 263 (7.60%) 43	2 / 344 (0.58%) 7
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	1 / 263 (0.38%) 4	1 / 344 (0.29%) 1
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea	6 / 267 (2.25%) 16	6 / 263 (2.28%) 6	9 / 344 (2.62%) 10

subjects affected / exposed occurrences (all)	8 / 267 (3.00%) 8	7 / 263 (2.66%) 7	11 / 344 (3.20%) 15
Vomiting subjects affected / exposed occurrences (all)	9 / 267 (3.37%) 11	9 / 263 (3.42%) 11	10 / 344 (2.91%) 12
Skin and subcutaneous tissue disorders Petechiae subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	6 / 267 (2.25%) 15	5 / 263 (1.90%) 17	6 / 344 (1.74%) 9
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	1 / 267 (0.37%) 1	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	17 / 267 (6.37%) 23	18 / 263 (6.84%) 24	28 / 344 (8.14%) 44
Sinusitis subjects affected / exposed occurrences (all)	5 / 267 (1.87%) 16	3 / 263 (1.14%) 3	3 / 344 (0.87%) 5
Urinary tract infection subjects affected / exposed occurrences (all)	15 / 267 (5.62%) 17	13 / 263 (4.94%) 17	9 / 344 (2.62%) 13
Metabolism and nutrition disorders Hypophagia subjects affected / exposed occurrences (all)	0 / 267 (0.00%) 0	0 / 263 (0.00%) 0	0 / 344 (0.00%) 0

Non-serious adverse events	Bapineuzumab 2.0 mg/kg		
Total subjects affected by non-serious adverse events subjects affected / exposed	9 / 11 (81.82%)		
Vascular disorders Hypertension			

subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 9		
Hypotension subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
General disorders and administration site conditions Catheter site haematoma subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2		
Psychiatric disorders Confusional state subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Hallucination subjects affected / exposed occurrences (all) Psychotic disorder subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 3 2 / 11 (18.18%) 9 1 / 11 (9.09%) 1 1 / 11 (9.09%) 2		
Investigations Blood pressure increased subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3 1 / 11 (9.09%) 1		
Cardiac disorders Tachycardia			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Ataxia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Balance disorder			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Cerebral microhaemorrhage			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	9		
Disturbance in attention			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	5		
Dizziness postural			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Exertional headache			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	9		
Hyporeflexia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Mental impairment			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	5		

Paraesthesia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Parkinson's disease subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 5		
Vasogenic cerebral oedema subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 3 / 11 (27.27%) 3		
Skin and subcutaneous tissue disorders Petechiae subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Musculoskeletal stiffness	1 / 11 (9.09%) 5		

subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	12		
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypophagia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2008	In global protocol amendment 1, the following changes such as interim analysis was removed; all screening MRI scans to be reviewed by a central radiologist; timing of caregiver instruction was changed; NPI administration expanded to include the principal investigator, a sub-investigator, the psychometric rater (not the global rater), or the study coordinator. Thus the NPI rater need not have been blinded to AEs. Deep vein thrombosis (DVT), Pulmonary embolism (PE) and seizure/convulsion were added as new events of special circumstance.
16 April 2009	In global protocol amendment 2, the following changes such as 2.0 mg/kg dose group was discontinued as a treatment arm on 02 April 2009; intracranial hemorrhage was added as an AE of special circumstance; Evidence of subdural hematoma on the screening MRI scan was added as an exclusion criteria; Central radiology review (in addition to the local radiology review) added for all scheduled MRI scans through Week 32 inclusive. All unscheduled MRI scans required a central radiology review in addition to local review; Weight at Day 1 collected as part of vital sign data; the ICRS component of the RUD-Lite v2.4 was removed; The QOL AD to be completed by both the caregiver and the participant; the number of participants increased to include US sites; Infusion details updated; IRB/IEC and health authority approval required to resume test article administration following vasogenic edema (VE); sampling blood volumes refined for sub-studies; cholesterol and triglycerides added as laboratory test and personnel changes.
16 October 2009	In global protocol amendment 3, the following changes were included; AE of special circumstance language for cerebral hemorrhage was modified to indicate that HD was not included as an AE of special circumstance; MRI scan central reading added at Week 71; Immune complement and complex sampling removed; 18F-fluorodeoxyglucose (FDG) PET removed as a substudy; Week 78 visit defined as the screening visit for extension study 3133K1-3002; Pre-Day 1 serum and CSF bapineuzumab sampling removed for participants in the CSF sub study; Clinical experience with PiB section added to the protocol; VE section updated; "Amyloid" PET changed to "PiB" PET; PET imaging hypotheses added; Preferably obtain the Apo E genotype prior to obtaining the screening MRI if scheduling allowed; Frequency of anti bapineuzumab antibody testing decreased to collection at Day 1, Week 26 and Week 78/early withdrawal; Vital signs added at Week 71; PET scanning time and schedule clarified; Reporting of medication errors was clarified; Definition of rating scale and health outcome assessment workbooks as source documents; Resumption of test article administration following VE to occur following VE resolution; PET radiation exposure updated; ECG frequency decreased to collection at screening, Week 45 and Week 78/early withdrawal; Fluorodeoxyglucose PET was removed as a substudy to this protocol; Prior medication section modified to remove language that requires prior approval of the sponsor for irregular use of medication for non-excluded conditions.

17 February 2011	In global protocol amendment 4, the following changes were made; Duration of study increased to 6 years (72 months); Participants with hemosiderin deposit (HD) greater than 10 mm in any direction to receive no further IP infusion; reporting of potential cases of drug-induced liver injury (potential Hy's Law cases) added; Inclusion criterion 8 updated to allow native languages under certain circumstances; All study MRI scans required to be read by a local and central radiologist and the investigator to review and sign off both the local and central radiology report prior to each next test article infusion; Added central MRI reading at Weeks 45 and 78; Timing window added for collection of the post-infusion vital sign measurements, infusion site assessments and blood collection; Pre-Day 1 CSF and associated blood samples collectable at any point in the screening period; Pre-Day 1 PiB PET scan at any point in the screening period; VE section updated; Cerebral hemorrhage specified as an adverse drug reaction for bapineuzumab; Information on seizure/convulsion and venous thrombotic events (DVT and PE) added; Week 78 visit defined as the screening visit for extension study; Due to recruitment issues, participation in 1 or more substudies may have been required rather than optional; Addition of recommendation added to contact the sponsor for new medications initiated where there may have been questions regarding safety or impact on efficacy assessment; and Information regarding concomitant treatment with anticoagulants added.
20 July 2011	In global protocol amendment 5, the following changes were made; Revisions to the protocol objectives were made in accordance with regulatory/scientific advice obtained in consultation with regulatory authorities. Analyses and methods to address the additional protocol objectives were elaborated in the Statistical analysis plan. An assessment of suicidality was incorporated with associated revision to exclusion criteria; Expansion of window for scheduling PET scans at Week 45 and Week 71; Clarification of use of medications with potential to affect cognition; Infusion duration/window clarified; Investigator's responsibilities regarding local and central radiology reports clarified; Expectations for the conduct of full examinations or targeted examinations clarified; An alternative or additional exploratory PiB PET scan to be obtained from participants in the PiB PET substudy who experienced VE; Change in sponsor SAE collection policy, including sponsor requests for additional information of events reported as non-serious by the investigator and investigator recording of awareness of an SAE occurrence; Reportable dosing error definition clarified.
15 December 2011	In global protocol amendment 6, the following updates included; Definitions of AEs and SAEs updated in accordance with regulatory requirements; Safety sections updated to meet Pfizer standards; Medication errors were reportable events regardless of whether or not they were accompanied by an AE and had to be documented accordingly. Overdose no longer needed to be reported on an SAE form if not associated with a SAE; Criteria for laboratory abnormalities for further evaluation in the context of potential cases of drug-induced liver injury clarified and updated to include prothrombin time; Clarification of SAE reporting requirements added, including those in the post active reporting period and also to clarify the clock start for reportable events; Management of allergic or immune mediated reaction related to IP infusion were clarified; Storage conditions of placebo were changed; CSF volume to be collected was clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
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06 August 2012	The sponsor made the decision to terminate all ongoing bapineuzumab IV studies in participants with mild to moderate AD mainly due to the lack of clinical benefit seen in the completed bapineuzumab phase 3 studies, Study ELN115727-301 (ApoE4 allele non-carriers) and Study ELN115727-302 (ApoE4 allele carriers) conducted by Janssen Alzheimer Immunotherapy. Therefore, both 3133K1-3000-WW and 3133K1-3000-US were terminated earlier than planned. A total of 335 participants had completed the study up to and including Week 78 before the decision was taken to end the study prematurely. Participants who had not completed the final follow-up visit in either study prior to 06 August 2012 were asked to complete an early withdrawal/termination visit to perform the protocol-defined procedures.	-
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Notes:

Limitations and caveats

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

The impact of study termination, the shorter observational periods and the resulting small sample size coupled with not having enough participants with post baseline assessments for various reasons were limiting factors for data interpretation.

Notes: