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GENERIC DRUG NAME / COMPOUND NUMBER: Bapineuzumab / AAB-001, PF-05236801, WAY-203740, ELN115727

PROTOCOL NO.: 3133K1-3002 (B2521003)

PROTOCOL TITLE: A Phase 3 Extension, Multicenter, Double-Blind, Parallel-Group, Long-Term Safety and Tolerability Trial of Bapineuzumab (AAB-001, ELN115727) in Subjects With Alzheimer Disease Who Are Apolipoprotein E ε4 Noncarriers and Participated in Study-3133K1-3000-WW or 3133K1-3000-US

Study Centers: A total of 91 study centers in 17 countries took part in the study and enrolled subjects; 25 in Japan, 13 each in France and Spain, 8 in the United Kingdom, 5 each in Australia and Poland, 3 each in Belgium, the Netherlands, and Portugal, 2 each in Chile, Finland, Italy, Slovakia, and South Africa, and 1 each in New Zealand, Sweden, and Switzerland.

Study Initiation and Final Completion Dates: 03 February 2010 to 25 October 2012. The study was terminated prematurely on 06 August 2012.

Please note that this study drug is no longer in development and is not available for prescribing.

Phase of Development: Phase 3

Study Objectives:

Primary Objective: To evaluate the long-term safety and tolerability of intravenously (IV) administered bapineuzumab in subjects with Alzheimer disease (AD).

METHODS

Study Design: This was a Phase 3 extension, multicenter, double-blind, parallel-group, long-term safety and tolerability trial of bapineuzumab in subjects with AD who were Apolipoprotein E ε4 (ApoE ε4) noncarriers and participated in the previous base study (A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Efficacy and Safety Trial of Bapineuzumab in Subjects With Mild to Moderate ad who are Apoe E4 Non-Carriers [NCT00667810]).

Subjects originally randomized to active treatment in the previous base study continued to receive treatment with bapineuzumab via IV infusion once every 13 weeks at the dose level assigned in the previous base study (ie, 0.5 mg/kg or 1.0 mg/kg).

Subjects originally randomized to placebo in the previous base study were randomized to 1 of the 2 dose levels (0.5 mg/kg or 1.0 mg/kg bapineuzumab) at a ratio of 1:1. Randomization was stratified according to Mini-Mental State Examination (MMSE) score (10-15, 16-21, 22-26, 27-30) at the Week 78 visit of the previous base study and concomitant cholinesterase inhibitor and/or memantine use (yes; no) at the Week 78 visit of the previous base study. Participation in substudies was also included in the overall randomization logic for treatment assignment, in order to manage balance within substudies for relevant factors.

Subjects who, after a vasogenic edema (VE) in the previous base study, resumed or were eligible to resume investigational product infusions, may have required a dose adjustment.

The treatment assigned in the previous base study remained blinded to investigator sites during the time the subjects were screened for the extension study and until unblinding for the previous base study. Subjects, blinded Sponsor staff, and blinded site staff remained blinded to the dose level received in this study, until completion of this study's clinical report.

The duration of subject participation was 4 years. The study flowchart for the study is presented in Table 1 and Table 2.

Table 1. Study Flowchart

First Year, Study Week (W)	Screening[a]	Day 1[b]	W6	W13	W19	W26	W32	W39	W45	W52
Visit Windows[c]		**12-16 Weeks After Last Infusion (W65 of Previous Study)**	**±7 Days**							
Informed consent	X									
Procedures										
Demography	X									
Inclusion/exclusion criteria	X									
AEs and concomitant medication	X	X	X	X	X	X	X	X	X	X
Suicidality assessment	X	X[d]	X	X	X	X	X	X	X	X
Physical and neurological examinations	X		X		X				X	
Vital signs[e, f, g]	X	X	X	X	X	X	X	X	X	X
12-lead ECG	X								X	
Blood chemistry, hematology, and urinalysis	X		X		X		X		X	
Serum anti-bapineuzumab antibody[h]	X									X
Biochemical characterization[i]		X	X	X						
ADAS-Cog, DAD	X			X		X		X		X
NPI, DS, RUD-Lite v2.4, HUI	X					X				X
MMSE	X		X		X		X		X	
Clinical brain MRI[c,,j]			X		X		X		X	
Volumetric brain MRI[k]									X	
PIB PET imaging[k, l], urine pregnancy test[m]									X	
CSF sample collection[k, n]										X
Infusion/infusion site assessment[o]		X		X		X		X		X
24 hour postinfusion phone contact		X		X		X		X		X

ADAS-Cog = alzheimer's disease assessment scale–cognitive subscale; AE = adverse event; CSF = cerebrospinal fluid; DAD = disability assessment scale for dementia; DS = dependence scale; ECG = electrocardiogram; HUI = health utilities index; MMSE = mini-mental state examination; MRI = magnetic resonance imaging; NPI = neuropsychiatric inventory; PET = positron emission tomography; PIB = [^{11}C]-Pittsburgh compound B; RUD-Lite v2.4 = resource utilization in dementia, version 2.4; W = week.

a. Screening visit for this study was the same visit as the Week 78 of the previous base study. Previous study Week 78 procedures were not repeated. In addition, informed consent was obtained for this extension study before any procedures specific to this extension study were performed. If the extension protocol was not yet initiated at a site at the Week 78 visit of the previous base study, the screening procedures specific to this study were performed at another time point prior to Day 1.

b. With Sponsor clinician physician review and approval, a subject received his first infusion between 16 and 26 weeks after Week 65 of the previous base study (last infusion). The Sponsor clinician physician requested additional screening evaluations as needed.

c. During the first year, follow-up visits (Weeks 6, 19, 32, and 45), including clinical brain MRI, were scheduled to occur 6 weeks after each infusion. These visits were scheduled relative to the actual infusion date and within the visit window (±7 days).

d. At Day 1, suicidality assessment was not mandatory if the previous base suicidality assessment (screening visit) was conducted within 7 days before Day 1.

e. Vital signs included weight at all visits.

Table 1. Study Flowchart

f. Sitting vital signs were measured at non-infusion visits.
g. Supine blood pressure and pulse were taken within 1 hour before dose administration and at 15, 30, 60 (end of infusion), and 120 minutes after the start of infusion. Temperature and respiratory rate were to be taken within 1 hour before dose administration, and at 60 (end of infusion) and 120 minutes after the start of infusion. For Day 1 and Week 13, vital signs were also to be measured 240 minutes (4 hours) after the start of infusion.
h. Blood sample for serum antibapineuzumab antibody was collected just prior to investigational product infusion.
i. Day 1 sample was collected after infusion; Week 13 sample was collected before infusion. Samples were collected at selected sites.
j. Central and local radiology review was required for all MRI scans. Both the local and central radiology reports had to be available and reviewed by the Investigator prior to each investigational product infusion.
k. Only for subjects participating in the same substudies as in the previous base study and who consented to continue in the substudies.
l. PET scans were obtained within ±14 days of the visit. The PET scan schedule could be modified locally to decrease the number of required scans to ensure compliance with local radiation safety requirements. The schedule provided in the flowchart for PIB PET scans represents the maximum number of scans that each subject may have received. Subjects in France were not allowed to participate in the PIB PET substudy.
m. Urine pregnancy test required prior to each PET scan only for female subjects aged <55 years who participated in the PET substudy.
n. CSF and associated blood samples could be collected within 4 weeks prior to the Week 52 visit.
o. The infusion site was assessed before dose administration and at 1 and 2 hours after the start of infusion for all visits and also at 4 hours for Day 1 and Week 13.

Table 2. Study Flowchart

Second, Third, and Fourth Year Study Week (W)	W65	W78	W91	W104	W117	W130	W143	W156	W169	W182	W195	W208 or Early Termination (ET)
Visit windows	±7 Days											
Procedures												
AEs and concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X
Suicidality assessment	X	X	X	X	X	X	X	X	X	X	X	X
Physical and neurological examinations		X		X		X		X		X		X
Vital signs[a]	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG				X				X				X
Blood chemistry, hematology, and urinalysis		X		X		X		X		X		X
Serum antibapineuzumab antibody[b]				X				X				X
ADAS-Cog, DAD		X		X		X		X		X		X
NPI, MMSE, DS, RUD-Lite v2.4, HUI		X		X		X		X		X		X
Clinical brain MRI[c]		X		X		X		X		X		X
Volumetric brain MRI[d]				X				X				X
PIB PET imaging[d,e] /urine pregnancy test[f]				X				X				X
CSF sample collection[d]												X
Infusion/infusion site assessment[g]	X	X	X	X	X	X	X	X	X	X	X	
24hour post-infusion phone contact	X	X	X	X	X	X	X	X	X	X	X	

ADAS-Cog = alzheimer's disease assessment scale–cognitive subscale; AE = adverse event; CSF = cerebrospinal fluid; DAD = disability assessment for dementia; DS = dependence scale; ECG = electrocardiogram; ET = early termination; HUI = health utilities index; MMSE = mini-mental state examination; MRI = magnetic resonance imaging; NPI = neuropsychiatric inventory; PET = positron emission tomography; PIB = [11C]-Pittsburgh compound B; RUD-Lite v2.4 = resource utilization in dementia, version 2.4; W = week.

a. Vital signs included weight at all visits. Supine blood pressure and pulse were taken within 1 hour before dose administration and at 15, 30, 60 (end of infusion), and 120 minutes after the start of infusion. Temperature and respiratory rate were taken within 1 hour before dose administration, 60 (end of infusion) and 120 minutes after the start of infusion. Sitting vital signs were taken at noninfusion visits (Week 208 or ET).
b. Blood sample for serum antibapineuzumab antibody was collected just prior to investigational product infusion at Week 104 and Week 156.
c. Central and local radiology review was required for all MRI scans including ET. Both the local and central radiology reports had to be available and reviewed by the Investigator prior to each investigational product infusion. Weeks 78, 104, 130, 156 and 182 MRI scans were to be scheduled ≥2 weeks prior to the visit.
d. Only for subjects participating in the same substudies as in the previous base study and who consented to continue in the substudies.
e. PET scans could be obtained within 2 weeks before or after the date of the visit. The PET scan schedule could be modified locally to decrease the number of required scans to ensure compliance with local radiation safety requirements. The schedule provided in the flowchart for PIB PET scans represents the maximum number of scans that each subject may have received. Subjects in France were not allowed to participate in the PIB PET substudy.
f. Urine pregnancy test required prior to each PET scan for female subjects aged <55 years who participated in the PET substudy.
g. Assessed infusion site before dose administration and at 1 and 2 hours after the start of infusion.

Number of Subjects (Planned and Analyzed): An estimated 1000 subjects were planned for enrollment into this study and 202 subjects were enrolled which included 39 in placebo+bapi 0.5 mg/kg, 66 in bapi 0.5 mg/kg+bapi 0.5 mg/kg, 37 in placebo+bapi 1.0 mg/kg, 56 in bapi 1.0 mg/kg+bapi 1.0 mg/kg and 4 in bapi 0.2 mg/kg+bapi 0.1 mg/kg.

Diagnosis and Main Criteria for Inclusion: Male and female subjects aged 51 years and older who had completed the previous base study and whose brain magnetic resonance imaging (MRI) scan was consistent with the diagnosis of AD. Subjects had to have MMSE ≥10 at Screening and a caregiver able to attend all clinic visits with the subject.

Exclusion Criteria: Subjects with any medical or psychiatric contraindication or clinically significant abnormality that, in the Investigator's judgment, could substantially increase the risk associated with the subject's participation in and completion of the study or could preclude the evaluation of the subject's response. Subjects with any significant brain MRI abnormality and subjects with a history of use of any investigational drugs or devices, other than bapineuzumab within the last 60 days prior to screening were also excluded from the study.

Study Treatment: Bapineuzumab 0.5 mg/kg or 1.0 mg/kg and matching placebo was administered by IV infusion approximately every 13 weeks. Investigational product was supplied in sterile, unblinded vials to be made up in 100-mL bags of 0.9% saline (site-supplied) by an unblinded drug dispenser/pharmacist at the study site. The blinded admixture was administered to the subjects by blinded study staff. The study duration was approximately 4 years (208 weeks).

Safety Endpoints:

Primary Endpoint: To evaluate the long-term safety and tolerability of IV-administered bapineuzumab in subjects with AD.

Safety Evaluations: Adverse events (AEs), serious adverse events (SAEs), brain MRI scans, vital signs, weight, ECG measurements, clinical laboratory tests, physical and neurological examinations, suicidality assessment and local reactions at infusion site. The potential treatment-emergent adverse events (TEAEs) of VE were carefully evaluated. The study was continuously monitored by an independent safety monitoring committee.

Statistical Methods:

Analysis Sets: The modified intent-to-treat (MITT) population was defined as all randomly assigned subjects who received any amount of investigational product in the previous base study and who had a Baseline for the base study and at least 1 valid postbaseline assessment of the alzheimer's disease assessment scale–cognitive subscale (ADAS-Cog) total score and disability assessment for dementia (DAD) total score in the base study or this extension study.

The extension MITT analysis population was defined as all randomly assigned subjects who received at least 1 dose of study drug in the extension study and who had a Baseline for the

extension study and at least 1 valid postbaseline assessment of the ADAS-Cog total score and DAD total score in the extension study.

The safety analysis population included all subjects who consented to participate in this extension study and received at least 1 dose of study drug in this study.

All safety analyses were conducted on the safety population. The following treatment groups were used in safety analyses:

- 0.5 mg/kg bapineuzumab + 0.5 mg/kg bapineuzumab
- 1.0 mg/kg bapineuzumab + 1.0 mg/kg bapineuzumab
- 2.0 mg/kg bapineuzumab + 1.0 mg/kg bapineuzumab
- Placebo + 0.5 mg/kg bapineuzumab
- Placebo + 1.0 mg/kg bapineuzumab

For safety analyses, the subjects were summarized according to the treatment that they actually received (during the previous base study and this extension study). In general, no formal statistical testing was performed; only summary statistics were provided, unless otherwise noted. Missing safety data were not imputed.

TEAEs were summarized by treatment group. Vital signs, ECGs, and clinical laboratory evaluations were summarized with descriptive statistics, by treatment group, at all time-points where these variables are collected. For subjects who received bapineuzumab in the previous base study, the primary Baseline value of interest for vital signs, ECGs, and laboratory evaluations was the Baseline value from the previous base study (before bapineuzumab was given). For subjects who received placebo in the previous base study, the primary Baseline value of interest was the final evaluation in the previous base study.

The treatment differences at the end of extension study were compared to those at the end of the base study, to explore whether administering bapineuzumab for an extended period would continue to provide benefit.

Similar analyses were done based on the extension portion of the study using the extension MITT analysis population, for each of the individual groupings as well as for the combined grouping, with change from the Baseline of the extension study (Baseline Ex) in the endpoint at each postbaseline visit of the extension study as the response variable. In these analyses, the MMSE score stratum in the model was the 1 to which subjects were randomized at the start of the extension (10-15, 16-21, 22-26, 27-30) rather than those to which they were randomized at the start of the base study. Similarly, cholinesterase inhibitor or memantine use stratum was the 1 measured at the start of the extension.

RESULTS

Subject Disposition and Demography: Subjects originally randomized to 2.0 mg/kg bapineuzumab were reassigned to the 1.0 mg/kg dose level after discontinuation of 2.0 mg/kg dose level in the base study and continued the 1.0 mg/kg dose in this extension study.

Table 3 presents a summary of subject disposition.

Table 3. Subject Disposition

Conclusion Status Reason	Placebo + Bapi 0.5 mg/kg	Bapi 0.5 mg/kg + Bapi 0.5 mg/kg	Placebo + Bapi 1.0 mg/kg	Bapi 1.0 mg/kg + Bapi 1.0 mg/kg	Bapi 2.0 mg/kg + Bapi 1.0 mg/kg	Total
Screened for extension study						209
Modified intent-to-treat[a]						209
Safety[b]	39	66	37	56	4	202
Extension Modified intent-to-treat[c]	38	62	33	53	4	190
Extension PET[d, e]	1	0	0	1	0	2
Extension CSF[e]	3	3	6	2	0	14
Extension vMRI[e]	17	20	10	23	1	71
Started	39	66	37	56	4	
Treated	39	66	37	56	4	
Completed	0	0	0	0	0	
Not completed	39	66	37	56	4	
Lack of efficacy	1	1	2	2	0	
Adverse event	2	5	2	6	0	
Withdrawal on subject request	1	4	3	3	2	
Physician decision	1	0	0	0	0	
Discontinuation of study by Sponsor	31	54	30	45	2	
Loss of caregiver	0	1	0	0	0	
Other	3	1	0	0	0	

Bapi = bapineuzumab; CSF = cerebrospinal fluid; N = number of subjects in treatment group; PET = positron emission tomography; vMRI = volumetric magnetic resonance imaging.
Denominators for percentages were the number of subjects randomized to treatment arms.

a. Defined as all randomly assigned subjects who received any amount of investigational product in the base study and who had a Baseline for the base study and at least one valid postbaseline assessment of the ADAS Cog total score and DAD total score in the base study or the extension study and signed informed consent in the extension study.
b. The safety population was defined as all subjects who consented to participate in the extension and received at least one dose of study drug (in the extension study).
c. Defined as all randomly assigned subjects who received at least one dose of study drug in the extension study and who had a baseline for the extension study and at least one valid postbaseline assessment of the ADAS Cog total score and DAD total score in the extension study.
d. Defined in general as those who enrolled in a given substudy in each row, in the safety population, and had a valid Baseline and at least one postbaseline measurement in the extension study.
e. Subject with a SUVr ≥1.35 at Baseline for the base study.

Table 4 presents a summary of demographic characteristics.

Table 4. Demographic Characteristics-Safety Population

	Placebo + Bapi 0.5 mg/kg	Bapi 0.5 mg/kg + Bapi 0.5 mg/kg	Placebo + Bapi 1.0 mg/kg	Bapi 1.0 mg/kg + Bapi 1.0 mg/kg	Bapi 2.0 mg/kg + Bapi 1.0 mg/kg	Total
Number of subjects	39	66	37	56	4	202
Age (years)						
Mean ± SD	68.7±9.63	71.4±8.83	68.9±9.10	70.6±9.48	71.3±10.63	70.2±9.23
<65	18	17	14	19	1	69
≥65	21	49	23	37	3	133
Gender						
Female	14	31	15	21	3	84
Male	25	35	22	35	1	118

Bapi = bapineuzumab; SD = standard deviation.

Efficacy Results: Efficacy measures were considered exploratory in this study and are not reported here due to the early discontinuation of this study.

Safety Results:

Non-Serious Adverse Events: Table 5 presents a summary of subjects reporting non-serious AEs with >5% incidence in any treatment group. In the bapineuzumab 2.0 mg/kg + 1.0 mg/kg treatment group, overall 3 subjects reported 8 TEAEs, which were all of mild intensity and none of these events was considered by the Investigator to be related to study treatment. Treatment-related TEAEs were reported by 7 (17.9%) subjects in the placebo + bapineuzumab 0.5 mg/kg group, 11 (16.7%) subjects in the bapineuzumab 0.5 mg/kg + 0.5 mg/kg group, 8 (21.6%) subjects in the placebo + bapineuzumab 1.0 mg/kg group, and 13 (23.2%) subjects in the bapineuzumab 1.0 mg/kg + 1.0 mg/kg group (Table 6).

Serious Adverse Events: The proportion of subjects reporting treatment-emergent SAEs was lowest in the placebo + bapineuzumab 1.0 mg/kg group. Treatment-emergent SAEs were reported by 6 (15.4%) subjects in the placebo + bapineuzumab 0.5 mg/kg group, 10 (15.2%) subjects in the bapineuzumab 0.5 mg/kg + 0.5 mg/kg group, 1 (2.7%) subject in the placebo + bapineuzumab 1.0 mg/kg group, and 11 (19.6%) subjects in the bapineuzumab 1.0 mg/kg + 1.0 mg/kg group. The most common treatment-emergent SAE by preferred term (PT) was subdural hematoma, reported by 3 (5.4%) subjects in the bapineuzumab 1.0 mg/kg + 1.0 mg/kg group (but by no subjects in the other treatment groups). All other treatment-emergent SAEs were reported by no more than 1 subject in any treatment group. None of the subjects in the bapineuzumab 2.0 mg/kg + 1.0 mg/kg group reported a treatment-emergent SAE.

Table 7 presents a summary of subjects reporting an SAE in any treatment group.

Deaths: None of the subjects died during the study.

Discontinuations: Overall, TEAEs that led to discontinuation of treatment were reported by 2 (5.1%) subjects in the placebo + bapineuzumab 0.5 mg/kg group, 5 (7.6%) subjects in the bapineuzumab 0.5 mg/kg + 0.5 mg/kg group, 2 (5.4%) subjects in the placebo + bapineuzumab 1.0 mg/kg group, and 6 (10.7%) subjects in the bapineuzumab 1.0 mg/kg

+ 1.0 mg/kg group. No TEAE (defined by PT) led to discontinuation from treatment in >1 subject per treatment group (Table 8).

Overall, TEAEs that led to discontinuation of the study were reported in 2 (5.1%) subjects in the placebo + bapineuzumab 0.5 mg/kg group, 1 (1.5%) subject in the bapineuzumab 0.5 mg/kg + 0.5 mg/kg group, 1 (2.7%) subject in the placebo + bapineuzumab 1.0 mg/kg group, and 1 (1.8%) subject in the bapineuzumab 1.0 mg/kg + 1.0 mg/kg group. No TEAE (defined by PT) led to discontinuation of the study in >1subject per treatment group (Table 9).

Table 5. Number of Subjects (%) Reporting All Causality Non-Serious Adverse Events (>5% Incidence of Subjects) in Any Treatment Group - Safety Population

System Organ Class Preferred Term	Placebo + Bapi 0.5 mg/kg		Bapi 0.5 mg/kg + Bapi 0.5 mg/kg		Placebo + Bapi 1.0 mg/kg		Bapi 1.0 mg/kg + Bapi 1.0 mg/kg		Bapi 2.0 mg/kg + Bapi 1.0 mg/kg	
	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events
Number of subjects evaluable for AEs	39		66		37		56		4	
Number of subjects with non-serious AEs	18		21		15		15		3	
Blood and lymphatic system disorders										
Anaemia	2 (5.13)	2	1 (1.52)	1	0	0	0	0	0	0
Eye disorders										
Arteriosclerotic retinopathy	0	0	0	0	0	0	0	0	1 (25.00)	1
Cataract	0	0	2 (3.03)	3	0	0	0	0	1 (25.00)	1
Gastrointestinal disorders										
Nausea	2 (5.13)	2	0	0	0	0	0	0	0	0
General disorders										
Gait disturbance	3 (7.69)	3	0	0	1 (2.70)	1	0	0	0	0
Infections and infestations										
Cystitis	0	0	0	0	0	0	1 (1.79)	1	1 (25.00)	1
Gastroenteritis	0	0	0	0	3 (8.11)	3	0	0	0	0
Nasopharyngitis	3 (7.69)	3	1 (1.52)	1	1 (2.70)	2	2 (3.57)	2	0	0
Urinary tract infection	2 (5.13)	2	7 (10.61)	7	1 (2.70)	2	0	0	0	0
Injury, poisoning and procedural complications										
Fall	0	0	3 (4.55)	6	2 (5.41)	2	3 (5.36)	3	0	0
Metabolism and nutrition disorders										
Folate deficiency	0	0	0	0	0	0	0	0	1 (25.00)	1
Hypercholesterolaemia	0	0	0	0	0	0	0	0	1 (25.00)	1
Nervous system disorders										
Cerebral microhaemorrhage	0	0	1 (1.52)	2	0	0	3 (5.36)	3	1 (25.00)	1
Cognitive disorder	1 (2.56)	1	2 (3.03)	3	2 (5.41)	2	3 (5.36)	3	0	0
Dizziness	1 (2.56)	1	4 (6.06)	4	0	0	0	0	0	0
Headache	1 (2.56)	1	1 (1.52)	1	3 (8.11)	4	2 (3.57)	2	0	0
Presyncope	0	0	1 (1.52)	1	2 (5.41)	2	0	0	0	0
Vasogenic cerebral oedema	2 (5.13)	2	2 (3.03)	2	5 (13.51)	5	3 (5.36)	3	0	0
Psychiatric disorders										
Aggression	2 (5.13)	3	0	0	0	0	0	0	0	0
Delusion	3 (7.69)	3	3 (4.55)	3	0	0	0	0	0	0

Table 5. Number of Subjects (%) Reporting All Causality Non-Serious Adverse Events (>5% Incidence of Subjects) in Any Treatment Group - Safety Population

System Organ Class Preferred Term	Placebo + Bapi 0.5 mg/kg		Bapi 0.5 mg/kg + Bapi 0.5 mg/kg		Placebo + Bapi 1.0 mg/kg		Bapi 1.0 mg/kg + Bapi 1.0 mg/kg		Bapi 2.0 mg/kg + Bapi 1.0 mg/kg	
	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events
Depression	0	0	0	0	2 (5.41)	3	0	0	0	0
Reproductive system and breast disorders										
Benign prostatic hyperplasia	0	0	0	0	1 (2.70)	1	0	0	1 (25.00)	1
Respiratory, thoracic and mediastinal disorders										
Cough	2 (5.13)	3	0	0	0	0	2 (3.57)	2	0	0
Skin and subcutaneous tissue disorders										
Rash erythematous	0	0	0	0	0	0	0	0	1 (25.00)	1

MedDRA version 15.0 coding dictionary was applied.
AEs = adverse events; Bapi = bapineuzumab; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects.

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Placebo + 0.5 mg/kg N=39 All n (%)	Placebo + 0.5 mg/kg N=39 Yes n (%)	Placebo + 0.5 mg/kg N=39 No n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 All n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 Yes n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 No n (%)	Placebo + 1.0 mg/kg N=37 All n (%)	Placebo + 1.0 mg/kg N=37 Yes n (%)	Placebo + 1.0 mg/kg N=37 No n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 All n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 Yes n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 No n (%)
Any treatment-emergent adverse event	32 (82.1)	7 (17.9)	25 (64.1)	48 (72.7)	11 (16.7)	37 (56.1)	25 (67.6)	8 (21.6)	17 (45.9)	36 (64.3)	13 (23.2)	23 (41.1)
Blood and lymphatic system disorders												
Anaemia	2 (5.1)	0	2 (5.1)	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Iron deficiency anaemia	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Leukopenia	1 (2.6)	1 (2.6)	0	0	0	0	0	0	0	0	0	0
Normochromic normocytic anaemia	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Cardiac disorders												
Atrial fibrillation	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Bradycardia	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Extrasystoles	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Myocardial infarction	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Sinus bradycardia	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Ear and labyrinth disorders												
Ear haemorrhage	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Hypoacusis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Vertigo	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Vertigo positional	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Endocrine disorders												
Hyperparathyroidism primary	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Eye disorders												
Cataract	0	0	0	2 (3.0)	0	2 (3.0)	0	0	0	0	0	0
Conjunctival haemorrhage	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	1(1.8)	0	1 (1.8)
Conjunctivitis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Conjunctivitis allergic	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Diplopia	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Dry eye	1 (2.6)	1 (2.6)	0	0	0	0	0	0	0	0	0	0
Eye inflammation	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Glaucoma	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Placebo + 0.5 mg/kg N=39			Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66			Placebo + 1.0 mg/kg N=37			Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56		
	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)
Gastrointestinal disorders												
Abdominal hernia	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Abdominal pain	0	0	0	2 (3.0)	0	2 (3.0)	0	0	0	1 (1.8)	0	1 (1.8)
Aerophagia	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Constipation	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	1 (1.8)	0	1 (1.8)
Dental caries	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Diarrhoea	1 (2.6)	0	1 (2.6)	3 (4.5)	0	3 (4.5)	0	0	0	2 (3.6)	0	2 (3.6)
Dysphagia	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Faecalith	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Flatulence	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Gastric ulcer	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Gastrooesophageal reflux disease	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Gingival bleeding	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Haemorrhoidal haemorrhage	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Haemorrhoids	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Large intestine perforation	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Large intestine polyp	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Nausea	2 (5.1)	1 (2.6)	1 (2.6)	0	0	0	0	0	0	0	0	0
Oesophagitis	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Proctalgia	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Rectal haemorrhage	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Vomiting	1 (2.6)	1 (2.6)	0	1 (1.5)	0	1 (1.5)	0	0	0	1 (1.8)	0	1 (1.8)
General disorders and administration site conditions												
Application site erythema	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Asthenia	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	1 (1.8)	1 (1.8)	0
Chest pain	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Discomfort	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Fatigue	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Gait disturbance	3 (7.7)	1 (2.6)	2 (5.1)	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Hyperthermia	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Bapineuzumab											
	Placebo + 0.5 mg/kg N=39			0.5 mg/kg + 0.5 mg/kg N=66			Placebo + 1.0 mg/kg N=37			1.0 mg/kg + 1.0 mg/kg N=56		
	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)
Influenza like illness	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Injection site reaction	0	0	0	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Irritability	0	0	0	2 (3.0)	0	2 (3.0)	1 (2.7)	0	1 (2.7)	0	0	0
Malaise	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Oedema peripheral	0	0	0	3 (4.5)	0	3 (4.5)	0	0	0	0	0	0
Pain	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Pyrexia	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	1 (1.8)	0	1 (1.8)
Spinal pain	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Hepatobiliary disorders												
Hepatic function abnormal	0	0	0	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Hepatic steatosis	0	0	0	1 (1.5)	1 (1.5)	0	0	0	0	0	0	0
Infections and infestations												
Appendicitis	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Bacterial infection	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Bronchitis	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	0	0	0	2 (3.6)	0	2 (3.6)
Cystitis	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Ear infection	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Furuncle	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Gastroenteritis	0	0	0	0	0	0	3 (8.1)	0	3 (8.1)	0	0	0
Gingivitis	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Influenza	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	0	0	0	1 (1.8)	0	1 (1.8)
Lower respiratory tract infection	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Nasopharyngitis	3 (7.7)	0	3 (7.7)	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	2 (3.6)	0	2 (3.6)
Onychomycosis	0	0	0	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	0	0	0
Oral candidiasis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Otitis externa	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Periodontitis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Pneumonia	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Pyelonephritis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	1 (1.8)	0	1 (1.8)
Respiratory tract infection	0	0	0	0	0	0	1 (2.7)	0	1	0	0	0
Rhinitis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Placebo + 0.5 mg/kg N=39			Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66			Placebo + 1.0 mg/kg N=37			Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56		
	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)
Sinusitis	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Subcutaneous abscess	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Tinea pedis	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Tooth abscess	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Upper respiratory tract infection	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	2 (3.6)	0	2 (3.6)
Urinary tract infection	2 (5.1)	0	2 (5.1)	7 (10.6)	0	7 (10.6)	1 (2.7)	0	1 (2.7)	0	0	0
Viral infection	0	0	0	1 (1.5)	1 (1.5)	0	0	0	0	0	0	0
Vulvovaginal candidiasis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Injury, poisoning and procedural complications												
Arthropod sting	0	0	0	0	0	0	0	0	0	2 (3.6)	0	2 (3.6)
Chest injury	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Chillblains	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Contusion	0	0	0	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	0	0	0
Drug dispensing error	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Fall	0	0	0	3 (4.5)	0	3 (4.5)	2 (5.4)	0	2 (5.4)	4 (7.1)	0	4 (7.1)
Femur fracture	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Hand fracture	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	1 (1.8)	0	1 (1.8)
Hip fracture	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Jaw fracture	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Ligament sprain	0	0	0	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	0	0	0
Limb injury	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Post-traumatic pain	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Rib fracture	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Scratch	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Skull fracture	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Subdural haematoma	0	0	0	0	0	0	0	0	0	3 (5.4)	1 (1.8)	2 (3.6)
Thermal burn	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Underdose	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Upper limb fracture	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Placebo + 0.5 mg/kg N=39			Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66			Placebo + 1.0 mg/kg N=37			Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56		
	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)
Wound	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Wrong drug administered	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Investigations												
Alanine aminotransferase increased	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Aspartate aminotransferase increased	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Blood creatinine increased	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Blood glucose increased	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Electrocardiogram QT prolonged	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Electrocardiogram T wave inversion	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Gamma-glutamyltransferase increased	0	0	0	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Lymphocyte count decreased	1 (2.6)	1 (2.6)	0	0	0	0	0	0	0	0	0	0
Neutrophil count decreased	1 (2.6)	1 (2.6)	0	0	0	0	0	0	0	0	0	0
Weight decreased	0	0	0	2 (3.0)	1 (1.5)	1 (1.5)	1 (2.7)	0	1 (2.7)	1 (1.8)	0	1 (1.8)
Weight increased	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Metabolism and nutrition disorders												
Decreased appetite	0	0	0	1 (1.5)	1 (1.5)	0	1 (2.7)	0	1 (2.7)	0	0	0
Dehydration	0	0	0	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	0	0	0
Diabetes mellitus	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Gout	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Hyperglycaemia	1 (2.6)	0	1 (2.6)	2 (3.0)	0	2 (3.0)	0	0	0	0	0	0
Hypoglycaemia	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Hypokalaemia	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Malnutrition	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Type 2 diabetes mellitus	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	1 (1.8)	0	1 (1.8)
Vitamin D deficiency	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Placebo + 0.5 mg/kg N=39 All n (%)	Placebo + 0.5 mg/kg N=39 Yes n (%)	Placebo + 0.5 mg/kg N=39 No n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 All n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 Yes n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 No n (%)	Placebo + 1.0 mg/kg N=37 All n (%)	Placebo + 1.0 mg/kg N=37 Yes n (%)	Placebo + 1.0 mg/kg N=37 No n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 All n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 Yes n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 No n (%)
Musculoskeletal and connective tissue disorders												
Arthralgia	1 (2.6)	0	1 (2.6)	2 (3.0)	0	2 (3.0)	1 (2.7)	0	1 (2.7)	0	0	0
Arthritis	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Back pain	0	0	0	2 (3.0)	0	2 (3.0)	1 (2.7)	0	1 (2.7)	2 (3.6)	0	2 (3.6)
Bursitis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Joint swelling	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Muscle rigidity	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Muscle spasms	0	0	0	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	0	0	0
Musculoskeletal chest pain	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Osteoarthritis	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Pain in extremity	0	0	0	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	1 (1.8)	0	1 (1.8)
Polymyalgia rheumatica	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Posture abnormal	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Rhabdomyolysis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Spinal osteoarthritis	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Tendonitis	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)												
Basal cell carcinoma	0	0	0	2 (3.0)	0	2 (3.0)	0	0	0	0	0	0
Bladder cancer	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Melanocytic naevus	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Metastatic squamous cell carcinoma	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Pancreatic neoplasm	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Nervous system disorders												
Basal ganglion degeneration	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Cerebellar infarction	0	0	0	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Cerebral infarction	0	0	0	1 (1.5)	1 (1.5)	0	0	0	0	1 (1.8)	0	1 (1.8)
Cerebral microhaemorrhage	0	0	0	1 (1.5)	1 (1.5)	0	0	0	0	3 (5.4)	3 (5.4)	0
Cerebrospinal fluid leakage	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Placebo + 0.5 mg/kg N=39			Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66			Placebo + 1.0 mg/kg N=37			Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56		
	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)
Cognitive disorder	1 (2.6)	0	1 (2.6)	2 (3.0)	1 (1.5)	1 (1.5)	2 (5.4)	0	2 (5.4)	3 (5.4)	0	3 (5.4)
Convulsion	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Dementia	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Dementia Alzheimer's type	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	0	0	0
Dizziness	1 (2.6)	1 (2.6)	0	4 (6.1)	1 (1.5)	3 (4.5)	0	0	0	0	0	0
Dysgraphia	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Dyspraxia	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Epilepsy	1 (2.6)	0	1 (2.6)	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Extensor plantar response	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Extrapyramidal disorder	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Headache	1 (2.6)	1 (2.6)	0	1 (1.5)	1 (1.5)	0	3 (8.1)	2 (5.4)	1 (2.7)	2 (3.6)	1 (1.8)	1 (1.8)
Hemianopia	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Hemiplegia	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Hypersomnia	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Ischaemic stroke	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	1 (1.8)	0	1 (1.8)
Lacunar infarction	0	0	0	0	0	0	1 (2.7)	1 (2.7)	0	0	0	0
Loss of consciousness	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Myoclonus	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Partial seizures with secondary generalisation	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Presyncope	0	0	0	1 (1.5)	0	1 (1.5)	2 (5.4)	0	2 (5.4)	0	0	0
Psychomotor hyperactivity	0	0	0	2 (3.0)	1 (1.5)	1 (1.5)	1 (2.7)	0	1 (2.7)	0	0	0
Sensory loss	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Somnolence	1 (2.6)	0	1 (2.6)	2 (3.0)	0	2 (3.0)	0	0	0	0	0	0
Subarachnoid haemorrhage	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Syncope	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
VIIth nerve paralysis	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Vasogenic cerebral oedema	3 (7.7)	3 (7.7)	0	2 (3.0)	2 (3.0)	0	6 (16.2)	6 (16.2)	0	3 (5.4)	3 (5.4)	0
Psychiatric disorders												
Abnormal behaviour	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Affective disorder	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Aggression	2 (5.1)	0	2 (5.1)	0	0	0	0	0	0	0	0	0

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Bapineuzumab											
	Placebo + 0.5 mg/kg N=39			0.5 mg/kg + 0.5 mg/kg N=66			Placebo + 1.0 mg/kg N=37			1.0 mg/kg + 1.0 mg/kg N=56		
	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)
Agitation	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	0	0	0	1 (1.8)	0	1 (1.8)
Anxiety	1 (2.6)	0	1 (2.6)	2 (3.0)	0	2 (3.0)	1 (2.7)	0	1 (2.7)	0	0	0
Apathy	0	0	0	1 (1.5)	0	1 (1.5)	1 (2.7)	1 (2.7)	0	0	0	0
Conduct disorder	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Confusional state	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Delusion	3 (7.7)	1 (2.6)	2 (5.1)	3 (4.5)	0	3 (4.5)	0	0	0	0	0	0
Depression	0	0	0	0	0	0	2 (5.4)	1 (2.7)	1 (2.7)	0	0	0
Depressive symptom	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Disorientation	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Dysthymic disorder	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Expressive language disorder	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Hallucination	1 (2.6)	0	1 (2.6)	2 (3.0)	0	2 (3.0)	0	0	0	0	0	0
Hallucination, visual	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Insomnia	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	1 (2.7)	0	1 (2.7)	1 (1.8)	0	1 (1.8)
Mania	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Poriomania	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Sleep disorder	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Stress	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Suicidal ideation	0	0	0	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Renal and urinary disorders												
Dysuria	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Haematuria	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	2 (3.6)	0	2 (3.6)
Leukocyturia	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Nephrolithiasis	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Pollakiuria	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Renal impairment	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Urinary incontinence	1 (2.6)	0	1 (2.6)	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Reproductive system and breast disorders												
Atrophic vulvovaginitis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Benign prostatic hyperplasia	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Prostatitis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Placebo + 0.5 mg/kg N=39 All n (%)	Placebo + 0.5 mg/kg N=39 Yes n (%)	Placebo + 0.5 mg/kg N=39 No n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 All n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 Yes n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 No n (%)	Placebo + 1.0 mg/kg N=37 All n (%)	Placebo + 1.0 mg/kg N=37 Yes n (%)	Placebo + 1.0 mg/kg N=37 No n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 All n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 Yes n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 No n (%)
Vulvovaginal dryness	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders												
Cough	2 (5.1)	0	2 (5.1)	0	0	0	0	0	0	2 (3.6)	0	2 (3.6)
Dyspnoea	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Epistaxis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Hiccups	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Oropharyngeal pain	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Productive cough	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Pulmonary embolism	0	0	0	1 (1.5)	1 (1.5)	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Wheezing	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Skin and subcutaneous tissue disorders												
Asteatosis	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Dermal cyst	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Dermatitis	0	0	0	1 (1.5)	1 (1.5)	0	0	0	0	0	0	0
Dermatitis allergic	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Dermatitis contact	1 (2.6)	0	1 (2.6)	0	0	0	0	0	0	0	0	0
Eczema	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Erythema multiforme	0	0	0	0	0	0	1 (2.7)	0	1 (2.7)	0	0	0
Intertrigo	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Pain of skin	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Rash	0	0	0	2 (3.0)	0	2 (3.0)	0	0	0	0	0	0
Skin exfoliation	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0
Skin fissures	1 (2.6)	1 (2.6)	0	0	0	0	0	0	0	0	0	0
Uncoded												
Uncoded	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Vascular disorders												
Deep vein thrombosis	0	0	0	1 (1.5)	1 (1.5)	0	0	0	0	0	0	0
Hypertension	0	0	0	3 (4.5)	0	3 (4.5)	0	0	0	1 (1.8)	1 (1.8)	0
Hypotension	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0

Table 6. Incidence and Relationship to Treatment of Treatment-Emergent Adverse Events - Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Bapineuzumab											
	Placebo + 0.5 mg/kg N=39			0.5 mg/kg + 0.5 mg/kg N=66			Placebo + 1.0 mg/kg N=37			1.0 mg/kg + 1.0 mg/kg N=56		
	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)	All n (%)	Yes n (%)	No n (%)
Orthostatic hypotension	0	0	0	0	0	0	0	0	0	1 (1.8)	1 (1.8)	0
Phlebitis	0	0	0	0	0	0	0	0	0	1 (1.8)	0	1 (1.8)
Varicose vein	0	0	0	1 (1.5)	0	1 (1.5)	0	0	0	0	0	0

Missing relatedness was considered as related. If an event had both relationships among same subject then related to study drug was considered.
Denominators for percentages were the number of subjects in the safety population.
MedDRA (v15.0) coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities; N = number of subjects evaluable; n = number of subjects with specified event; v = version.

Table 7. Treatment-Emergent Serious Adverse Events (all-Causalities- Safety Analysis Population)

Number (%) of Subjects With Serious Adverse Events by: System Organ Class Preferred Term	Placebo + 0.5 mg/kg N=39 n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 n (%)	Placebo + 1.0 mg/kg N=37 n (%)	1.0 mg/kg + 1.0 mg/kg N=56 n (%)	2.0 mg/kg + 1.0 mg/kg N=4 n (%)
Any treatment-emergent serious adverse event	6 (15.4)	10 (15.2)	1 (2.7)	11 (19.6)	0
Cardiac disorders	0	0	0	1 (1.8)	0
Myocardial infarction	0	0	0	1 (1.8)	0
Gastrointestinal disorders	1 (2.6)	0	0	0	0
Large intestine perforation	1 (2.6)	0	0	0	0
General disorders and administration site conditions	0	0	0	1 (1.8)	0
Chest pain	0	0	0	1 (1.8)	0
Infections and infestations	1 (2.6)	1 (1.5)	0	2 (3.6)	0
Appendicitis	1 (2.6)	0	0	0	0
Bronchitis	0	0	0	1 (1.8)	0
Pyelonephritis	0	1 (1.5)	0	1 (1.8)	0
Injury, poisoning and procedural complications	0	2 (3.0)	0	5 (8.9)	0
Chest injury	0	0	0	1 (1.8)	0
Fall	0	0	0	1 (1.8)	0
Femur fracture	0	1 (1.5)	0	0	0
Hip fracture	0	0	0	1 (1.8)	0
Skull fracture	0	1 (1.5)	0	0	0
Subdural haematoma	0	0	0	3 (5.4)	0
Musculoskeletal and connective tissue disorders	0	1 (1.5)	0	1 (1.8)	0
Polymyalgia rheumatica	0	0	0	1 (1.8)	0
Rhabdomyolysis	0	1 (1.5)	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (2.6)	1 (1.5)	0	1 (1.8)	0
Basal cell carcinoma	0	1 (1.5)	0	0	0
Bladder cancer	0	0	0	1 (1.8)	0
Metastatic squamous cell carcinoma	0	1 (1.5)	0	0	0
Pancreatic neoplasm	1 (2.6)	0	0	0	0

Table 7. Treatment-Emergent Serious Adverse Events (all-Causalities- Safety Analysis Population)

Number (%) of Subjects With Serious Adverse Events by: System Organ Class Preferred Term	Placebo + 0.5 mg/kg N=39 n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 n (%)	Placebo + 1.0 mg/kg N=37 n (%)	1.0 mg/kg + 1.0 mg/kg N=56 n (%)	2.0 mg/kg + 1.0 mg/kg N=4 n (%)
Nervous system disorders	3 (7.7)	3 (4.5)	1 (2.7)	3 (5.4)	0
Cerebellar infarction	0	0	0	1 (1.8)	0
Dementia	0	1 (1.5)	0	0	0
Epilepsy	1 (2.6)	0	0	0	0
Ischaemic stroke	0	1 (1.5)	0	1 (1.8)	0
Loss of consciousness	0	0	0	1 (1.8)	0
Partial seizures with secondary generalisation	1 (2.6)	0	0	0	0
Subarachnoid haemorrhage	0	1 (1.5)	0	0	0
Vasogenic cerebral oedema	1 (2.6)	0	1 (2.7)	0	0
Psychiatric disorders	1 (2.6)	0	0	1 (1.8)	0
Disorientation	1 (2.6)	0	0	0	0
Suicidal ideation	0	0	0	1 (1.8)	0
Respiratory, thoracic and mediastinal disorders	0	1 (1.5)	0	0	0
Pulmonary embolism	0	1 (1.5)	0	0	0
Vascular disorders	0	1 (1.5)	0	1 (1.8)	0
Deep vein thrombosis	0	1 (1.5)	0	0	0
Phlebitis	0	0	0	1 (1.8)	0

Denominators for percentages are the number of subjects in thepsafety sopulation. Subjects were counted only once per treatment in each row.
MedDRA (v15.0) coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities, n = number of available subjects; N = total number of subjects; v = version.

Table 8. Treatment-Emergent Adverse Events that led to Discontinuation of Treatment by SOC and PT Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Placebo + 0.5 mg/kg N=39 n (%)	Bapineuzumab 0.5 mg/kg + 0.5 mg/kg N=66 n (%)	Placebo + 1.0 mg/kg N=37 n (%)	Bapineuzumab 1.0 mg/kg + 1.0 mg/kg N=56 n (%)
Any treatment-emergent adverse events that led to discontinuation of treatment	2 (5.1)	5 (7.6)	2 (5.4)	6 (10.7)
Gastrointestinal disorders	1 (2.6)	0	0	0
Large intestine perforation	1 (2.6)	0	0	0
Injury, poisoning and procedural complications	0	1 (1.5)	0	1 (1.8)
Femur fracture	0	1 (1.5)	0	0
Subdural haematoma	0	0	0	1 (1.8)
Musculoskeletal and connective tissue disorders	0	0	0	1 (1.8)
Polymyalgia rheumatica	0	0	0	1 (1.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (2.6)	1 (1.5)	0	0
Metastatic squamous cell carcinoma	0	1 (1.5)	0	0
Pancreatic neoplasm	1 (2.6)	0	0	0
Nervous system disorders	1 (2.6)	1 (1.5)	2 (5.4)	3 (5.4)
Cerebellar infarction	0	0	0	1 (1.8)
Cerebral infarction	0	0	0	1 (1.8)
Dementia	0	1 (1.5)	0	0
Hemiplegia	0	0	0	1 (1.8)
Ischaemic stroke	0	0	0	1 (1.8)
Partial seizures with secondary generalisation	1 (2.6)	0	0	0
Psychomotor hyperactivity	0	0	1 (2.7)	0
Vasogenic cerebral oedema	0	0	1 (2.7)	0
Psychiatric disorders	0	0	1 (2.7)	1 (1.8)
Abnormal behaviour	0	0	1 (2.7)	0
Suicidal ideation	0	0	0	1 (1.8)
Respiratory, thoracic and mediastinal disorders	0	1 (1.5)	0	0
Pulmonary embolism	0	1 (1.5)	0	0
Vascular disorders	0	1 (1.5)	0	0
Deep vein thrombosis	0	1 (1.5)	0	0

Denominators for percentages were the number of subjects in the safety sopulation.
Subjects were counted only once per treatment in each row.
MedDRA (v15.0) coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities; SOC = system organ class; PT = preferred term; v = version.

Table 9. Treatment-Emergent Adverse Events that led to Discontinuation of Study by SOC and PT Safety Analysis Population

Adverse Events by: System Organ Class MedDRA (v15.0) Preferred Term	Bapineuzumab			
	Placebo + 0.5 mg/kg N=39 n (%)	0.5 mg/kg + 0.5 mg/kg N=66 n (%)	Placebo + 1.0 mg/kg N=37 n (%)	1.0 mg/kg + 1.0 mg/kg N=56 n (%)
Any treatment-emergent adverse events that led to discontinuation of treatment	2 (5.1)	1 (1.5)	1 (2.7)	1 (1.8)
Gastrointestinal disorders	1 (2.6)	0	0	0
Large intestine perforation	1 (2.6)	0	0	0
Injury, poisoning and procedural complications	0	1 (1.5)	0	0
Femur fracture	0	1 (1.5)	0	0
Musculoskeletal and connective tissue disorders	0	0	0	0
Polymyalgia rheumatica	0	0	0	0
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1 (2.6)	0	0	0
Pancreatic neoplasm	1 (2.6)	0	0	0
Nervous system disorders	1 (2.6)	0	0	1 (1.8)
Hemiplegia	0	0	0	1 (1.8)
Ischaemic stroke	0	0	0	1 (1.8)
Partial seizures with secondary generalisation	1 (2.6)	0	0	0
Psychiatric disorders	0	0	1 (2.7)	0
Abnormal behaviour	0	0	1 (2.7)	0

Denominators for percentages were the number of subjects in the Safety Population.
Subjects were counted only once per treatment in each row.
MedDRA (v15.0) coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities, N = number of subjects evaluable, n = number of subjects with specified event, PT = preferred term; SOC = system organ class, v = version.

Suicidality Assessments: No subject committed suicide during the study.

Vasogenic Edema: The incidence proportions for VE were higher in the placebo + bapineuzumab versus (vs) the corresponding bapineuzumab + bapineuzumab groups, ie, compared to the treatment groups receiving the same bapineuzumab dose in the extension study. Incidence proportions for VE were 7.7% vs 3.0% in the placebo + bapineuzumab 0.5 mg/kg vs bapineuzumab 0.5 mg/kg +0.5 mg/kg groups, and 16.2% vs 5.4% in the placebo + bapineuzumab 1.0 mg/kg vs bapineuzumab 1.0 mg/kg + 1.0 mg/kg groups. Intracranial hemorrhage was reported in treatment groups already receiving bapineuzumab 0.5 mg/kg or 1.0 mg/kg in the base study, but not in those treatment groups receiving placebo. Intraparenchymal hemorrhage did not occur in any treatment group and singular instances of seizures/convulsions were reported in all treatment groups except for bapineuzumab 1.0 mg/kg + 1.0 mg/kg, for which no events were reported.

Laboratory Evaluations: For base study Baseline normal to extension study minimum post baseline value: small percentages of subjects had potentially clinically important (PCI) reductions in hematocrit (1.5% to 7.7% across treatment groups), hemoglobin (3.0% to 7.7%), and lymphocyte count (0 to 5.1%). For extension study Baseline normal to extension study minimum postbaseline value: small percentages of subjects showed PCI reductions for hematocrit (0 to 7.7% of treatment groups), hemoglobin (3.0 to 7.7%), and lymphocyte count (0 to 5.1% of treatment groups). For base study Baseline normal to extension study maximum postaseline value: small percentages of subjects had PCI increases in alanine aminotransferase (ALT) (0 to 2.7% across treatment groups), aspartate aminotransferase (AST) (0 to 1.5%), gamma-glutamyl transpeptidase (GGT) (0 to 5.4%), glucose (2.7% to 7.7%), and total bilirubin (0 to 3.0%). For extension study Baseline normal to extension study maximum post baseline value: small percentages of subjects had PCI increases in ALT (0 to 2.7% across treatment groups), AST (0 to 1.5%), GGT (0 to 3.6%), glucose (2.7% to 7.7%), and total bilirubin (0 to 3.0%).

Vital Signs: Transient changes were observed in diastolic and systolic blood pressure, pulse rate, respiratory rate and weight but no clinically relevant abnormal trends were noted. Transient reductions in temperature and transient changes in weight were observed but no significant trends were noted.

ECG: No clinically relevant abnormal trends in ECG results were noted.

CONCLUSIONS:

IV infusion of bapineuzumab 0.5 mg/kg or 1.0 mg/kg every 13 weeks for up to approximately 3.5 years was generally well tolerated, with a safety and tolerability profile that was similar to that observed in previous studies of bapineuzumab. No new or unexpected safety concerns were identified.