SYNOPSIS

Issue Date: 03 Apr 2013

Document No.: EDMS-ERI-30263285:2.0

Name of Sponsor/Company	Janssen Alzheimer Immunotherapy
Name of Finished Product	Not available
Name of Active Ingredient(s)	Bapineuzumab (AAB-001, ELN115727)

Protocol No.: ELN115727-351

Title of Study: A Phase 3 Extension, Multicenter, Double-Blind, Long Term Safety and Tolerability Treatment Trial of Bapineuzumab (AAB-001, ELN115727) in Subjects with Alzheimer's Disease who Participated in Study ELN115727-301 or in Study ELN115727-302

National Clinical Trial No.: NCT00937352

Clinical Registry No.: ELN115727-351

Coordinating Investigator: Stephen P Salloway, MD, MS; Butler Hospital, [redacted] USA

Study Center(s): This study was conducted in Canada, Germany, and the United States. As of the data cut-off date of 02 Apr 2012, data was available from 13 sites in Canada and 173 sites in the United States.

Publication (Reference): none at the time of finalization of this CSR

Study Period: 15 Oct 2009 – 02 Apr 2012 (data cut-off date for this report)

Phase of Development: Phase 3

Objectives:

Primary Objectives and Endpoints: To evaluate the long-term safety and tolerability of intravenously (IV) administered bapineuzumab in subjects with Alzheimer's Disease (AD) as assessed by the incidence and severity of treatment-emergent adverse events (TEAEs) and clinically important changes in vital signs, weight, clinical laboratory tests, electrocardiograms (ECGs), brain magnetic resonance imaging (MRI), physical and neurological examinations, and infusion site assessments.

Secondary Efficacy Objective and Endpoints: To demonstrate the maintenance of efficacy after 6 months of bapineuzumab IV treatment by measuring the changes from parent study baseline and extension study baseline in the Alzheimer's Disease Assessment Scale – Cognitive subscale (ADAS-Cog/11) and the Disability Assessment Scale for Dementia (DAD).

Secondary Health Outcome Objective and Endpoints: To demonstrate the effect of long-term bapineuzumab IV treatment on AD-related health outcomes by measuring the changes from parent study baseline and extension study baseline over time in the Dependence Scale (DS).

Exploratory Objectives and Endpoints: To evaluate the effect of long-term bapineuzumab IV treatment on other clinical, biomarker, immunogenicity, health outcome, and pharmacogenomic measures.

Methodology: This was a multicenter, double-blind, long-term safety and tolerability study conducted in subjects who had participated in 2 Phase 3, double-blind, placebo-controlled studies (Study 301 or Study 302, referred to as the parent studies). Subjects from Study 302 were carriers of the apolipoprotein

E gene, E4 allele (*APOE*E4)* and subjects from Study 301 were noncarriers. All subjects enrolled in Study 351 were assigned to receive IV infusions of bapineuzumab, regardless of whether they had received bapineuzumab or placebo in their parent study. Infusions of bapineuzumab (0.5 or 1.0 mg/kg) occurred at 13-week intervals over the course of the study. The specific bapineuzumab dose level assignment upon entering Study 351 depended on the following criteria: (a) the subject's *APOE*E4* status (ie, carrier vs noncarrier), and (b) the treatment that the subject had most recently received in the parent study. Safety was monitored by an Independent Safety Monitoring Committee.

Studies 302 and 301 were completed in Apr 2012 and Jun 2012, respectively. The results showed that bapineuzumab IV was not clinically efficacious in subjects with mild to moderate AD. Therefore, the Sponsor decided to stop development of bapineuzumab IV for this indication and to terminate all ongoing IV studies.

This report summarizes results from Study 351 as of the cut-off date of 02 Apr 2012. The decision to present results as of that date was made before development of bapineuzumab IV for the treatment of mild to moderate AD was stopped.

The last subject's last visit in Study 351 occurred on 07 Nov 2012. Final data through that date will be presented in an addendum to this CSR.

Number of Subjects (planned and analyzed): The planned maximum enrollment for this study was the number of subjects who completed Studies 301 and 302 (N=1738). Of these, 1408 (81.0%) subjects subsequently enrolled in the extension study and met the eligibility criteria; 1390 (80.0%) subjects had received bapineuzumab in Study 351 as of 02 Apr 2012 and were included in the safety analysis population (664 carriers and 726 noncarriers). Seventy-eight of the latter subjects were originally randomized to receive bapineuzumab 2.0 mg/kg in Study 301 but were re-assigned to the 1.0 mg/kg dose. These subjects were analyzed separately in both Study 301 and Study 351. Of the remaining 648 noncarriers, 297 received placebo in the parent study and bapineuzumab in Study 351 (called the placebo→bapi group) and 351 received bapineuzumab in both studies (called the bapi→bapi group). Of the 664 carriers, 286 were in the placebo→bapi group and 378 were in the bapi→bapi group.

The primary efficacy analysis population was the parent study modified intent-to-treat (mITT) population, which included all randomized subjects who received at least 1 infusion or portion of an infusion of study drug and who had a baseline and at least 1 postbaseline assessment of the ADAS-Cog/11 total score and DAD total score in Study 301 or 302. This population included 1114 noncarriers (493 in the placebo→bapi group and 621 in the bapi→bapi group) and 1090 carriers (432 in the placebo→bapi group and 658 in the bapi→bapi group).

Diagnosis and Main Criteria for Inclusion: Subjects were eligible to enroll in Study 351 if they had completed all 6 infusions in the parent study (unless they were required to temporarily suspend study drug but continued with the required visits) and completed Visit 15/Week 78; had a brain MRI scan at Visit 14/Week 71 of the parent study; and continued to live at home or in a community with an appropriate caregiver capable of accompanying the subject on all clinic visits and visiting with the subject approximately 5 times per week for the duration of the study. Key exclusion criteria included any new medical contraindication or clinically significant abnormality that precluded continued or initiation of treatment with bapineuzumab or participation in the study; and a screening visit brain MRI scan (ie, MRI from Study 301 or 302 Visit 14/Week 71) indicative of any significant abnormality.

Test Product, Dose and Mode of Administration, Batch No.: Bapineuzumab was provided in vials that allowed for withdrawal of 54, 70, 90, or 100 mg of the active compound. It was given by IV infusion (60 ± 20 minutes) prepared in 100-mL bags containing 0.9% saline solution. The following Pfizer drug product batch numbers were used during this study: E62079, E54370, E54371, E54372, 0000056023, and 0000060439.

Reference Therapy, Dose and Mode of Administration, Batch No.: There was no placebo or other reference drug used during the study.

Duration of Treatment: The planned study duration was approximately 4 years. The study was terminated in Aug 2012 when the clinical development of bapineuzumab IV for the treatment of mild to moderate AD was stopped by the Sponsor.

Criteria for Evaluation: Efficacy and health outcome objectives and endpoints were evaluated using the ADAS-Cog/11, DAD, and Mini-Mental State Examination (MMSE) assessed at approximately 3-month intervals for the first year, then at 6-month intervals (MMSE) and 12-month intervals (ADAS and DAD); and the DS, Abbreviated Resource Utilization in Dementia, Health Utilities Index, and Neuropsychiatric Inventory assessed at approximately 6-month intervals.

Safety objectives and endpoints were assessed by monitoring adverse events (AEs), vital signs, ECG parameters, clinical laboratory tests, brain MRI scans, physical and neurological examinations, infusion site assessments, and suicidality assessments.

The following biomarker endpoints were evaluated in subsets of subjects who agreed to participate in the respective optional substudies: brain amyloid burden imaged by positron emission tomography using ^{11}C-labeled Pittsburgh Compound B (^{11}C-PiB PET); change in cerebrospinal fluid (CSF) levels of amyloid beta, total tau, and phosphorylated tau; and whole brain volume and brain boundary shift integral, ventricular volume and ventricular boundary shift integral, and hippocampal volume and hippocampal boundary shift integral measured by volumetric brain MRI (vMRI). Note that no results from the CSF substudy are presented in this report.

Statistical Methods: Results for *APOE*E4* carriers and noncarriers were analyzed separately. Results for subjects who were originally randomized to 2.0 mg/kg in Study 301 are displayed in the tables, but they were not included in the pooled treatment groups or in any statistical analyses.

Analysis of ADAS-Cog/11 Total Score, DAD Total Score, and DS Total Score: Longitudinal differences between subjects who received bapineuzumab in Study 301 or Study 302 prior to Study 351 (the "early-start" or bapi→bapi group) and those who received placebo in Study 301 or Study 302 prior to Study 351 (the "delayed-start" or placebo→bapi group) were evaluated using a mixed model for repeated measures (MMRM) to analyze the change in scores from the parent study baseline. The primary efficacy analysis population was the parent study mITT population, which included all randomized subjects who received at least 1 infusion or portion of an infusion of study drug and who had a baseline and at least 1 postbaseline assessment of the ADAS-Cog/11 total score and DAD total score in Study 301 or 302. The results were also analyzed using the efficacy analysis population, which included all subjects who received at least 1 infusion or portion of an infusion of bapineuzumab in the extension study, and who had a parent study baseline and an extension study baseline assessment of ADAS-Cog/11 total score or DAD total score.

Exploratory Analyses: Descriptive statistics were used in exploratory analyses for efficacy, health outcomes, and behavioral measures. Where appropriate, the same MMRM analysis as for the ADAS-Cog/11, DAD, and DS total scores was used for the exploratory analyses.

Safety Analyses: AEs were classified into standard terminology using the Medical Dictionary for Regulatory Activities (MedDRA) version 14.1. AEs were summarized overall by MedDRA preferred terms, by Investigator's assessment of relationship to treatment, and by maximum severity. Other safety variables (eg, vital signs, ECGs, and clinical laboratory tests) were also summarized.

RESULTS:

Study Population: Overall, 937 subjects were continuing in the study as of the data cut-off date of 02 Apr 2012. This represents 36% of the subjects randomized in the parent studies, and 72% of the safety

analysis population for Study 351. The percentage of subjects who withdrew from the extension study was similar for *APOE*E4* noncarriers (30.3%) and carriers (35.1%). The percentage was higher for noncarriers originally randomized to the bapineuzumab 2.0 mg/kg group (48.7%). The most common reasons for early termination among both noncarriers and carriers were withdrawal by subject and adverse event.

Demographic and baseline characteristics of the safety analysis population were generally similar for noncarriers and carriers and, within each cohort, for the placebo→bapi and bapi→bapi groups. Among noncarriers, the mean age at extension study baseline was 72.2 years in the placebo→bapi group (range, 52 to 90 years) and 73.6 years in the bapi→bapi group (range, 51 to 90 years). Most subjects were white (94.3% and 93.7%, respectively) and approximately half were female (49.2% and 51.9%, respectively). Among carriers, the mean age was 72.9 years in the placebo→bapi group (range, 53 to 89 years) and 72.5 years in the bapi→bapi group (range, 51 to 90 years). Most subjects were white (96.9% and 95.2%, respectively) and slightly more than half were female (58.7% and 54.2%, respectively). The percentage of subjects with mild AD (MMSE total score ≥21) at extension study baseline was higher among noncarriers (41.8% of the subjects in the placebo→bapi group and 44.4% of those in the bapi→bapi group) than carriers (32.5% and 35.4%, respectively). MMSE scores at extension study baseline ranged from 0 to 30 in both noncarriers and carriers, indicating that some subjects who had mild or moderate AD (MMSE score of 16 to 26 inclusive) upon entering the parent study had severe AD (MMSE score <16) upon entering the extension study.

Major protocol deviations were mainly due to rater deviations, missing data, and informed consent form deviations. Site [redacted] violated GCP. Therefore, data from this site was excluded from efficacy, biomarker, and health outcome analyses.

As of 02 Apr 2012, the mean extent of exposure to bapineuzumab was 1.17 years for noncarriers in the placebo→bapi group and 1.28 years for carriers in the placebo→bapi group. In the bapi→bapi groups, the mean extent of exposure was 2.74 years for noncarriers and 2.91 years for carriers.

Efficacy and Health Outcome Results: The mean changes from parent study baseline to extension Week 26 in ADAS-Cog/11, DAD, and DS total scores were similar for noncarriers and carriers. Within each cohort, there were no differences between the placebo→bapi and bapi→bapi groups based on the MMRM analysis. For ADAS-Cog/11 total score, the least-squares (LS) mean (standard error [SE]) change was 9.9 (0.60) in the placebo→bapi group and 10.0 (0.54) in the bapi→bapi group among *APOE*E4* noncarriers; the LS mean difference between the groups was 0.2 (95% confidence interval [CI]: -1.4, 1.8), p=0.823. For carriers, the LS mean (SE) change was 12.2 (0.61) in the placebo→bapi group and 11.6 (0.51) in the bapi→bapi group; the LS mean difference between the groups was -0.6 (95% CI: -2.2, 0.9), p=0.436. For DAD total score, the LS mean (SE) change was -21.8 (1.25) in the placebo→bapi group and -20.0 (1.12) in the bapi→bapi group among *APOE*E4* noncarriers; the LS mean difference between the groups was 1.8 (95% CI: -1.5, 5.1), p=0.284. For carriers, the LS mean (SE) change was -22.6 (1.29) in the placebo→bapi group and -24.4 (1.09) in the bapi→bapi group; the LS mean difference between the groups was -1.8 (95% CI: -5.1, 1.5), p=0.282. Subgroup analyses by disease severity showed no treatment differences in the efficacy endpoints for subjects with either mild or moderate AD. As noted earlier, some subjects in the "moderate AD" subgroup had severe AD when they entered Study 351.

For DS total score, the LS mean (SE) change was 1.8 (0.14) in the placebo→bapi group and 1.9 (0.13) in the bapi→bapi group among *APOE*E4* noncarriers; the LS mean difference between the groups was 0.1 (95% CI: -0.3, 0.5), p=0.633. For carriers, the LS mean (SE) change was 2.1 (0.15) in the placebo→bapi group and 2.3 (0.13) in the bapi→bapi group; the LS mean difference between the groups was 0.2 (95% CI: -0.2, 0.6), p=0.388.

The results of the ^{11}C-PiB PET and vMRI substudies, and of other efficacy and health outcome measures, were similar for noncarriers and carriers. Within each cohort, there were no statistically significant differences between the placebo→bapi group and the bapi→bapi group.

Safety Results: Infusion of bapineuzumab 0.5 or 1.0 mg/kg every 13 weeks for up to 4 years was generally well tolerated. Overviews of TEAEs that occurred in the parent and extension studies as of 02 Apr 2012 are provided in Table S-1 for *APOE*E4* noncarriers and Table S-2 for *APOE*E4* carriers. The percentages of subjects with TEAEs, treatment-emergent serious AEs (SAEs) related to study drug, TEAEs leading to early termination from the study, TEAEs related to study drug leading to early termination, and TEAEs leading to death were similar for noncarriers and carriers. The percentages of subjects with TEAEs related to study drug and with treatment-emergent SAEs were higher for carriers than noncarriers. Within each cohort, the overall TEAE profile was similar for the placebo→bapi and bapi→bapi groups. Among the noncarriers, the percentages of subjects with treatment-emergent SAEs, treatment-emergent SAEs related to study drug, TEAEs leading to early termination from the study, and TEAEs related to study drug leading to early termination were higher in the group originally randomized to 2.0 mg/kg than in the other dose groups.

The TEAE profile in subjects with mild AD (MMSE ≥21) was consistent with that in the overall safety analysis population and with that in subjects with moderate AD (MMSE <21).

Table S-1 Treatment-Emergent Adverse Events Overview (Parent and Extension Studies) for *APOE*E4* Noncarriers (Safety Analysis Population)

	Study 301→351 (Individual Bapineuzumab Doses)					Pooled Doses	
	Pbo→ Bapi 0.5 mg/kg (N=148) n (%)	Bapi 0.5→0.5 mg/kg (N=181) n (%)	Pbo→ Bapi 1.0 mg/kg (N=149) n (%)	Bapi 1.0→1.0 mg/kg (N=170) n (%)	Bapi 2.0(1.0) →1.0 mg/kg (N=78) n (%)	Pbo→Bapi (N=297) n (%)	Bapi→Bapi (N=351) n (%)
Subjects Who Died in the Study	5 (3.4)	3 (1.7)	2 (1.3)	3 (1.8)	3 (3.8)	7 (2.4)	6 (1.7)
Treatment-Emergent AEs	144 (97.3)	176 (97.2)	144 (96.6)	161 (94.7)	75 (96.2)	288 (97.0)	337 (96.0)
Treatment-Emergent AEs Related to Study Drug	50 (33.8)	52 (28.7)	43 (28.9)	54 (31.8)	24 (30.8)	93 (31.3)	106 (30.2)
Treatment-Emergent Serious AEs	45 (30.4)	54 (29.8)	43 (28.9)	49 (28.8)	38 (48.7)	88 (29.6)	103 (29.3)
Treatment-Emergent Serious AEs Related to Study Drug	5 (3.4)	5 (2.8)	4 (2.7)	10 (5.9)	6 (7.7)	9 (3.0)	15 (4.3)
Early Termination From Study Due to							
Treatment-Emergent AEs	18 (12.2)	13 (7.2)	13 (8.7)	14 (8.2)	13 (16.7)	31 (10.4)	27 (7.7)
Treatment-Emergent AEs Related to Study Drug	2 (1.4)	5 (2.8)	5 (3.4)	3 (1.8)	5 (6.4)	7 (2.4)	8 (2.3)

Notes:
1. Bapi = Bapineuzumab; Pbo = Placebo.
2. Subjects in Study 301 who were originally randomized to 2.0 mg/kg were reassigned to the 1.0 mg/kg dose in that study, and continued the 1.0 mg/kg dose in Study 351. These subjects are not included in the Bapi 1.0 → 1.0 mg/kg or Bapi → Bapi group.
3. Each AE was classified by the investigator as "Related" or "Not Related" on the CRF and that classification is used for this table. AEs with missing relatedness are counted as "Related".
4. Counts and percentages are based on the number of subjects with AEs (not events).
5. An AE is regarded as treatment-emergent if it started during or after the first infusion of study drug and prior to or on the date of last dose + 137 days.
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Source: Table 15.3.1.1.1.1-t

Table S-2 Treatment-Emergent Adverse Events Overview (Parent and Extension Studies) for *APOE*E4* Carriers (Safety Analysis Population)

	Study 302→351	
	Pbo→ Bapi 0.5 mg/kg (N=286) n (%)	Bapi 0.5→0.5 mg/kg (N=378) n (%)
Subjects Who Died in the Study	12 (4.2)	11 (2.9)
Treatment-Emergent AEs	275 (96.2)	373 (98.7)
Treatment-Emergent AEs Related to Study Drug	113 (39.5)	139 (36.8)
Treatment-Emergent Serious AEs	95 (33.2)	135 (35.7)
Treatment-Emergent Serious AEs Related to Study Drug	10 (3.5)	13 (3.4)
Early Termination From Study Due to		
Treatment-Emergent AEs	34 (11.9)	39 (10.3)
Treatment-Emergent AEs Related to Study Drug	10 (3.5)	15 (4.0)

Notes:
1. Bapi = Bapineuzumab; Pbo = Placebo.
2. Each AE was classified by the investigator as "Related" or "Not Related" on the CRF and that classification is used for this table. AEs with missing relatedness are counted as "Related".
3. Counts and percentages are based on the number of subjects with AEs (not events).
4. An AE is regarded as treatment-emergent if it started during or after the first infusion of study drug and prior to or on the date of last dose + 137 days.
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Source: Table 15.3.1.1.1.10-t

The most common (≥10%) TEAEs in noncarriers were fall (22.2% of the subjects in the placebo→bapi group vs 22.5% of those in the bapi→bapi group), urinary tract infection (18.5% vs 16.5%), depression (18.5% vs 12.0%), headache (15.5% vs 16.0%), anxiety (14.1% vs 11.7%), agitation (12.8% vs 12.3%), hypertension (12.8% vs 9.7%), back pain (12.1% vs 9.4%), diarrhea (11.8% vs 12.3%), dizziness (11.4% vs 10.3%), upper respiratory tract infection (10.1% vs 9.7%), and cough (10.8% vs 8.8%). The most common TEAEs in carriers were fall (22.7% vs 26.5%), urinary tract infection (21.7% vs 16.1%), headache (18.9% vs 17.7%), agitation (16.1% vs 14.6%), depression (16.1% vs 16.1%), diarrhea (15.0% vs 15.3%), anxiety (14.3% vs 15.3%), vomiting (14.3% vs 8.2%), vasogenic cerebral edema (12.2% vs 11.9%), hypertension (12.9% vs 8.2%), upper respiratory tract infection (10.1% vs 13.0%), dizziness (10.5% vs 12.4%), nausea (11.2% vs 11.6%), nasopharyngitis (9.4% vs 11.4%), and back pain (10.1% vs 9.5%).

Extension-onset AEs occurred in 81.1% of *APOE*E4* noncarriers in the placebo→bapi group and 76.4% of those in the bapi→bapi group. The most common event was fall (10.4% and 11.1%, respectively). No other event occurred in ≥10% of the subjects in either group. Extension-onset AEs occurred in 83.3% of the subjects originally randomized to receive the 2.0 mg/kg dose, with fall occurring in 12.8% of the subjects. In *APOE*E4* carriers, extension-onset AEs occurred in 88.8% of the subjects in the placebo→bapi group and 84.9% of those in the bapi→bapi group. The most common (≥10% of the subjects in either group) events were fall (10.8% in the placebo→bapi group vs 14.3% in the bapi→bapi group), urinary tract infection (11.5% vs 11.1%), agitation (11.5% vs 9.3%), and vasogenic cerebral edema (11.9% vs 5.0%), hereafter referred to as amyloid-related imaging abnormalities, edema and effusion (ARIA-E [VE]).

Thus, one notable difference between noncarriers and carriers was in the incidence proportion of ARIA-E [VE], which occurred in higher percentages of carriers than noncarriers, both during the parent + extension studies (carriers: 12.2% of those in the placebo→bapi group vs. 11.9% of those in the bapi→bapi group; noncarriers: 5.4% vs. 6.0%, respectively), and during the extension study only

(carriers: 11.9% vs. 5.0%; noncarriers: 5.4% vs. 0.9%). All ARIA-E (VE) cases were mild or moderate (except in 1 carrier in the placebo→bapi group with severe ARIA-E [VE]), most were asymptomatic (88.2% for noncarriers and 84.9% for carriers), and most resolved without sequelae (100% for noncarriers and 92.5% for carriers). ARIA-E (VE) was not listed as the cause of death for any subject. Extension-onset AEs related to ARIA-E (VE) occurred in 25.0% of noncarriers in the placebo→bapi group with ARIA-E (VE) and 0% of noncarriers in the bapi→bapi group, and in 20.6% and 5.3%, respectively, of carriers. The most common AE was cerebral microhemorrhage (4 carriers in the placebo→bapi group).

The mean (standard deviation [SD]) duration of resolved and unresolved ARIA-E (VE) cases was 127.9 days (97.81 days) for *APOE*E4* noncarriers in the placebo→bapi group and 192.7 days (168.17 days) for those in the bapi→bapi group. For *APOE*E4* carriers, the mean (SD) duration was 123.2 days (108.31 days) and 93.7 days (77.79 days), respectively. Note that, because this study was ongoing as of the 02 Apr 2012 cut-off date for this report, the duration of some unresolved events was imputed to 365 days in accordance with the Statistical Analysis Plan.

At extension baseline, the percentage of subjects with HDs <10 mm was 10.1% in the placebo→bapi group and 14.5% in the bapi→bapi group in *APOE*E4* noncarriers and 10.5% and 15.9%, respectively, in carriers. In both noncarriers and carriers who first received bapineuzumab in the extension study (ie, the placebo→bapi group), all cases of ARIA-E (VE) that occurred during the extension study, and most cases of HD, began after the 1st, 2nd, or 3rd bapineuzumab infusion.

The incidence proportion of seizures/convulsion was higher in carriers who had received bapineuzumab in both the parent and extension studies than in other groups. There were no noteworthy differences between *APOE*E4* noncarriers and carriers, or between the placebo→bapi and bapi→bapi groups within each cohort, in the incidence proportions of other Events of Special Circumstance, ie, intracranial hemorrhage or deep vein thrombosis/ pulmonary embolism.

Changes from parent study baseline in laboratory parameters were generally small and not considered clinically relevant. There were no notable differences between *APOE*E4* noncarriers and carriers, or between the placebo→bapi and bapi→bapi groups within each cohort, in the incidence of subjects with potentially clinically important laboratory values. Likewise, there were no notable differences in vital signs or ECGs. There were no anti-bapineuzumab antibodies detected in any serum samples, suggesting low immunogenic potential of bapineuzumab.

STUDY LIMITATIONS: Although parent study blinding was maintained in Study 351, both subjects and site personnel knew that all subjects received bapineuzumab in the extension study. Also, there may have been differences in study completion rates between treatment groups in the parent studies, resulting in imbalances between the placebo→bapi and bapi→bapi groups analyzed in Study 351.

CONCLUSION(S): Infusion of bapineuzumab 0.5 or 1.0 mg/kg IV every 13 weeks for up to 4 years was generally well tolerated in subjects who had mild or moderate AD at the start of the parent studies. A clinically relevant increase in ARIA-E (VE) in *APOE*E4* carriers was the only notable safety finding related to bapineuzumab treatment. In the double-blind, placebo-controlled parent studies (Studies 301 and 302), bapineuzumab was not clinically efficacious. When subjects from those studies received bapineuzumab 0.5 or 1.0 mg/kg IV in the long-term extension Study 351, similar deterioration of cognition and function occurred in the placebo→bapi and bapi→bapi groups. The results were similar for *APOE*E4* noncarriers and carriers. There were no statistically significant differences between those who received bapineuzumab in both the parent and extension studies and those who first received bapineuzumab in the extension study.

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