A Phase 3 Extension, Multicenter, Long-term Safety and Tolerability Trial of Bapineuzumab (AAB-001, ELN115727) in Subjects With Alzheimer Disease Who Are Apolipoprotein E Îµ4 Carriers and Participated in Study 3133K1-3001-WW

Published: 24-12-2010
Last updated: 04-05-2024

Primary objectives: To evaluate the long-term safety and tolerability of IV administered bapineuzumab in subjects with AD.Secundary objectives:To explore the long-term efficacy of IV administered bapineuzumab in subjects with AD, using the following...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Dementia and amnestic conditions
Study type	Interventional

Summary

ID

NL-OMON38076

Source
ToetsingOnline

Brief title
AAB-001 long-term safety and tolerabiltiy in Apolipoprotein E *4 carriers.

Condition

- Dementia and amnestic conditions

Synonym
Alzheimers disease

Research involving

Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pfizer bv

Intervention

Keyword: AAB-001, Apolipoprotein E 4 carriers, Bapineuzumab, Passive immunization Alzheimer

Outcome measures

Primary outcome

Health Outcomes Endpoints. To explore effect on health outcomes of long-term

treatment of IV administered bapineuzumab in subjects with AD, using the

following scales:

* Dependence Scale (DS)

* Resource Utilization in Dementia, version 2.4 (RUD Lite v2.4)

* Health Utilities Index) (HUI)

Immunogenicity. To explore the effect on immunogenicity of long-term treatment

with IV administered bapineuzumab in subjects with AD, using the following

scales:

* Serum anti-bapineuzumab antibody levels.

* In a subset of subjects, CSF anti-bapineuzumab antibody levels.

Pharmacokinetics: To determine clearance characteristics of bapineuzumab

product isoforms bapineuzumab in sera of a subset of subjects with AD, using

biochemical characterization with immunoaffinity chromatography.

Secondary outcome

* Alzheimer*s Disease Assessment Scale - Cognitive Subscale (ADAS-Cog)

* Disability Assessment Scale for Dementia (DAD)

* Mini Mental State Examination (MMSE)

* Neuropsychiatric Inventory (NPI)

Study description

Background summary

Preclinical experiments in platelet-derived growth factor promoter (PDAPP) transgenic mice suggest that passive immunization with anti-amyloid-beta protein (A*) antibodies would be efficacious in reducing or halting the progression of Alzheimer disease (AD) pathology in humans. Bapineuzumab (formerly referred to as AAB-001 or ELN115727) is a humanized monoclonal antibody proposed for the treatment of AD by passive immunization. The first-in-humans single ascending dose study, 3133K1-100-US, tested 3 doses of bapineuzumab (0.5, 1.5, and 5.0 mg/kg). While this was a single dose study designed to assess safety, tolerability, and pharmacokinetics (PK) of bapineuzumab, there was a trend in the exploratory efficacy measure of Mini-Mental State Examination (MMSE) scores. Further information on bapineuzumab from unblinded sponsor review of the interim data from the phase 2 studies, AAB-001-201 and AAB-001-202, was a key factor in the rationale for the doses selected in the phase 3 program commenced in December 2007 and which is still ongoing. The phase 3 program includes four studies: 2 studies in ApoE4 noncarriers (Wyeth study 3133K1-3000, and Elan study ELN115727-301); and 2 studies in ApoE4 carriers (Wyeth 3133K1-3001 and Elan ELN115727-302). The 3133K1-3000 noncarrier study is comprised of 2 protocols: 3133K1-3000-US and 3133K1-3000-WW. Similarly, the 3133K1-3001 study is comprised of 2 protocols: 3133K1-3001-US and 3133K1-3001-WW.

The present extension protocol 3133K1-3003-WW and the extension protocol 3133K1-3003-US propose to further investigate the long-term safety and tolerability of intravenous (IV) administered bapineuzumab in subjects with AD who participated in the 3133K1 3001 WW protocol and in the 3133K1-3001-US protocol. The *US and *WW protocols are separated for administrative reasons and are not intended to be analyzed as independent studies.

Across completed and ongoing trials to date, over 1500 subjects have been treated with bapineuzumab. A review of data from ongoing and completed studies is available in the investigator brochure (IB).

While generally well tolerated, bapineuzumab has been associated with vasogenic edema in the brain in some subjects. The doses of bapineuzumab in the above phase 3 studies and to be assessed in this phase 3 extension protocol have been selected based on a careful analysis of the risk of vasogenic edema in carriers and noncarriers of the apolipoprotein E *4 allele (ApoE4). Ongoing experience with bapineuzumab suggests that vasogenic edema is more likely to occur at doses of bapineuzumab that are greater than 0.5 mg/kg. Further, experience to date suggests that subjects who carry the ApoE4 genotype (subjects with 1 or 2 copies of the ApoE *4 allele) have a higher risk of vasogenic edema than noncarriers at doses * 1.0 mg/kg.

Current data suggest that a dose of 0.5 mg/kg for carriers may be safely administered without excessive risk of vasogenic edema.

Study objective

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

Secundary objectives:
To explore the long-term efficacy of IV administered bapineuzumab in subjects with AD, using the following scales:
* Alzheimer*s Disease Assessment Scale - Cognitive Subscale (ADAS-Cog)
* Disability Assessment Scale for Dementia (DAD)
* Mini Mental State Examination (MMSE)
* Neuropsychiatric Inventory (NPI)

Study design

This is a multicenter, long-term extension to protocol 3133K1-3001-WW. The subjects will all receive
0.5 mg/kg bapineuzumab via IV infusion once every 13 weeks, whether they had been randomized to receive bapineuzumab or placebo in protocol 3133K1-3001-WW.

Intervention

Bapineuzumab 0.5 mg/kg will be administered by IV infusion approximately every 13 weeks. Investigational product will be supplied in sterile vials to be made up in 100 mL bags of 0.9% saline (site supplied) by a drug dispenser/pharmacist at the study site. The admixture shall be administered to the subjects by

qualified study staff.

Study burden and risks

See protocol flow chart on pages 26 through 29.

Contacts

Public
Pfizer

Rivium Westlaan 142
Capelle aan de Ijssel 2909 LD
NL
Scientific
Pfizer

Rivium Westlaan 142
Capelle aan de Ijssel 2909 LD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Subject has completed all 6 infusions planned in protocol 3133K1-3001; or, if the subject was required to temporarily suspend investigational product (e.g., because of VE), he/she continued with required visits, has completed all study visits through the Week 78 visit and his/her current status indicates that he/she resumed or is eligible to resume

investigational product.
NOTE: Subjects who developed VE during study 3133K1-3001 may be considered for study 3133K1-3003 participation if the abnormality is resolved and the subject met criteria to resume investigational product. Medical monitor approval is required prior to enrrollment.
2. Brain MRI scan from Week 71 of study 3133K1-3001 is available for local radiology and central radiology evaluation and remains consistent with the diagnosis of AD.
3. MMSE score *10 at screening (Week 78 of 3133K1-3001).
4. Continues to live at home or community dwelling with appropriate caregiver capable of accompanying the subject on all clinic visits and visiting with the subject at least 5 days per week, on average for the duration of the study.
5. In the opinion of the principal investigator, the subject and the caregiver will be compliant, and likely to participate in all scheduled evaluations.

Exclusion criteria

1. Any medical or psychiatric contraindication or clinically significant abnormality on physical, neurological, laboratory, vital signs, or electrocardiogram (ECG) examination (e.g., atrial fibrillation) that, in the investigator*s judgment, will 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.
2. Brain MRI scan from study 3133K1-3001 Week 71 visit, indicative of any significant abnormality, including but not limited to multiple microhemorrhages (2 or more), history or evidence of a single prior hemorrhage > 1 cm3, multiple lacunar infarct (2 or more) or evidence of a single prior infarct > 1 cm3, evidence of a cerebral contusion, encephalomalacia, aneurysms, vascular malformations, subdural hematoma, or space occupying lesions (e.g., arachnoid cysts or brain tumors such as meningioma).
3. Use of any investigational drugs or devices, other than bapineuzumab, within the last 60 days prior to screening.
4. Current use of herbal preparations containing ginkgo biloba or use of anticoagulants.
NOTE: Platelet anti-aggregants (e.g., aspirin 325 mg/day or less, clopidogrel bisulfate, or dipyridamole for indications other than stroke) are allowed.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-07-2011
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bapineuzumab
Generic name:	Bapineuzumab

Ethics review

Approved WMO Date:	24-12-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-04-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-07-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-09-2011
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-08-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-015080-13-NL
ClinicalTrials.gov	NCT00998764
CCMO	NL33927.029.10