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A Multicentre, Randomised, Double Blind, Placebo Controlled, Multiple Ascending Dose, Safety, Tolerability, And Amyloid-Imaging Positron Emission Tomography (PET) Trial Of AAB 001 (ELN115727) In Patients With Mild To Moderate Alzheimer's Disease (AD)

Submission date
18/11/2005

Registration date
28/11/2005

Last Edited
20/11/2012

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Nervous System Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2004-004120-12

ClinicalTrials.gov (NCT)
NCT00112073

Protocol serial number
AAB-001-202

Study information

Scientific Title

Acronym
AAB-001-202

Study objectives
1. To assess the safety and tolerability of multiple doses of AAB 001 in patients with mild to moderate Alzheimer's disease (AD)
2. To evaluate the effect of AAB 001 on brain amyloid burden in patients with mild to moderate AD

Please note that as of 05/09/2008, the anticipated end date of this trial was extended to 30th October 2009. The previous anticipated end date was 31/08/2008.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Joint UCL/UCLH Committees on the Ethics of Human Research (Committee A); Approval Date 02 June 2005; REC reference number 05/Q0505/29.

Study design
Interventional, double-blind, placebo-controlled, parallel group study

Primary study design
Interventional

Study type(s)
Not Specified

Health condition(s) or problem(s) studied
Alzheimer's Disease

Interventions
Intravenous Infusion of AAB-001 or placebo; brain PET scans; brain MRI scans.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
1. The incidence and severity of treatment-emergent adverse events (TEAEs)
2. Clinically important changes in safety assessment results (including, as appropriate, vital signs, weight, clinical laboratory tests, electrocardiograms [ECGs], MRIs, and physical and neurological exams)
3. Change from screening brain amyloid burden at weeks 24, 50, and 78 on PET, Pittsburgh Compound B (PIB) an amyloid binding agent
4. Change from screening in regional cerebral metabolic rates for glucose at week 78 on PET using fluoro-deoxyglucose (FDG)

Key secondary outcome(s))
1. The change from screening scores for the Neuropsychological Test Battery (NTB), the Alzheimer's Disease Assessment Scale - Cognitive subscale (ADAS COG), and the Disability Assessment Scale for Dementia (DAD) at weeks 11, 24, 37, 50, 63, and 78
2. The change from screening scores for the Clinical Dementia Rating Sum of Boxes (CDR-SOB), and Neuropsychiatric Inventory (NPI), at weeks 24, 50, and 78
3. The change from screening scores for the Mini-Mental State Exam (MMSE) at weeks 6, 11, 19, 24, 32, 37, 50, 78
4. The change from screening volumes for whole brain volume, brain boundary shift integral (BBSI), ventricular volume, and ventricular boundary shift integral (BSI), at weeks 6, 19, 58, and 78

Completion date
30/10/2009

Eligibility

Key inclusion criteria
1. Signed and dated written informed consent obtained from the patient and/or the patient's legally acceptable representative, if applicable, in accordance with the local regulations
2. Diagnosis of Probable Alzheimer's disease according to National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria
3. Age from 50 to 80 years, inclusive
4. Mini-Mental State Examination (MMSE) score of 18-26
5. Rosen Modified Hachinski Ischemic score <4
6. Lives at home with appropriate caregiver capable of accompanying the patient on all clinic visits, or community dwelling with caregiver capable of accompanying patient on all clinic visits and visiting with patient approximately 5 times per week for the duration of the study
7. Screening visit brain magnetic resonance imaging (MRI) scan consistent with the diagnosis of AD and determined to be of sufficient quality for brain volumetric analyses
8. Fluency in local language and evidence of adequate premorbid intellectual functioning. Patient must have adequate visual and auditory abilities to perform all aspects of the cognitive and functional assessments
9. Receiving stable doses of medications for the treatment of non-excluded medical conditions for at least 30 days prior to screening. If a patient is taking acetylcholinesterase inhibitors and/or memantine, then these medication(s) must be maintained on a stable dose regimen for at least 120 days prior to screening evaluations
10. Likely to be able to participate in all scheduled evaluations and complete all required tests
11. In the opinion of the investigator, the patient and the caregiver will be compliant and have a high probability of completing the study

12. Measurable amyloid burden on the screening PIB PET scan with PIB retention in the range expected for AD patients. Defined as 3 of the 5 target regions (anterior cingulate, posterior cingulate, frontal cortex, temporal cortex and parietal cortex) having a ratio of target region radioactivity (kBq/ml) over reference region radioactivity (cerebellar grey matter) >1.5. Patients with a previous PIB PET scan may be eligible to enter the study, subject to fulfilling the required local and/or national radiation safety exposure requirements

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
50 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Significant neurological disease other than AD that may affect cognition
2. Current presence of a clinically significant major psychiatric disorder (e.g. Major Depressive Disorder) according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), or any symptom (e.g. hallucinations), that could affect the patients ability to complete the study
3. Current clinically significant systemic illness that is likely to result in deterioration of the patients condition or affect the patient's safety during the study
4. History of clinically evident stroke or history of clinically significant carotid or vertebrobasilar stenosis or plaque
5. History of seizures, excluding febrile seizures in childhood
6. Weight greater than 120 kg (264 lbs)
7. History or evidence of any significant autoimmune disease or disorder of the immune system
8. Clinically significant infection within the last 30 days (e.g. chronic persistent or acute infection)
9. Treatment with immunosuppressive medications (e.g. systemic corticosteroids) within the last 90 days (topical and nasal corticosteroids and inhaled corticosteroids for asthma are permitted) or chemotherapeutic agents for malignancy within the last 3 years
10. Myocardial infarction within the last 2 years
11. History of cancer within the last 5 years, with the exception of basal cell carcinoma, and nonmetastatic squamous cell carcinoma of the skin
12. Other clinically significant abnormality on physical, neurological, laboratory, or electrocardiogram (ECG) examination (e.g. atrial fibrillation) that could compromise the study or be detrimental to the patient
13. Hemoglobin less than 11 g/dl
14. Smoking more than 20 cigarettes per day
15. History of alcohol or drug dependence or abuse within the last 2 years

16. Hamilton Psychiatric Rating Scale for Depression (HAM D) (17 item) score >12
17. Current use of anticonvulsants for seizures, anti-Parkinson's, anticoagulant (excluding the use of aspirin 325 mg/day or less), or narcotic medications
18. Current use of prescription or nonprescription medication for cognitive enhancement other than cholinesterase inhibitors and memantine. Current cholinesterase inhibitor and memantine use is prohibited unless the following conditions are met:
18.1. Maintained on a stable dose regimen for at least 120 days prior to screening
18.2. Patient is free of any clinically significant side effects attributable to the drug
18.3. Patient and caregiver agree that, barring unforeseen circumstances, the same regimen will be continued for the duration of the trial
19. Unless maintained on a stable dose regimen for at least 30 days prior to screening, any other medications with the potential to affect cognition other than those mentioned in #18 (including, but not limited to, anxiolytics, sedatives, hypnotics, antipsychotics, herbal, antidepressants, over-the-counter [OTC] sleeping aids, sedating anti-allergy medications, vitamin E, thyroid supplements, and vitamin B12 supplements by injection)
20. Patients who have discontinued cholinesterase inhibitors, memantine, cognitive enhancing agents, or drugs that potentially affect cognition in the 60 days prior to screening
21. Use of experimental medications for AD or any other investigational medication or device within 60 days prior to screening or within 5 half-lives of use of such a medication prior to screening, whichever is longer
22. Any prior experimental treatment with AN1792 or other experimental immunotherapeutic or vaccine for AD
23. Any known hypersensitivity to any of the excipients contained in the study drug formulation
24. Women of childbearing potential
25. Patients who have donated blood (routine blood donation) in the 90 days prior to screening
26. Presence of pacemakers, aneurysm clips, artificial heart valves, ear implants, CSF shunts, metal fragments or foreign bodies in the eyes, skin or body that would contraindicate a brain MRI scan

Date of first enrolment
31/08/2005

Date of final enrolment
30/10/2009

Locations

Countries of recruitment
United Kingdom

England

Finland

Study participating centre
Six Hills Court
Stevenage
United Kingdom
SG1 2BA

Sponsor information

Organisation
Elan Pharma Ltd (UK)

ROR
https://ror.org/035n6ph62

Funder(s)

Funder type
Industry

Funder Name
Elan Pharma Ltd (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2010		Yes	No
Results article	results	01/08/2012		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes