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A study comparing the safety and effects of a new compound, ACI-35 with placebo in patients with mild to moderate Alzheimer's disease

Submission date	Recruitment status	[ ] Prospectively registered
13/10/2015	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
04/11/2015	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
04/11/2015	Mental and Behavioural Disorders	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Alzheimer's disease (AD) is the most common cause of dementia, creating problems with memory, thinking and behaviour (cognitive function). It is a growing problem worldwide, affecting millions of people over the age of 60. Current treatments focus on improving symptoms, such as memory loss, however very few treatments are able to slow stop or stop the disease from progressing (getting worse). The exact cause of AD is unknown, however many scientists believe that it is related to the protein tau. This protein is important for making sure the nerve cells in our brains function properly. In AD, this protein causes important fibres within the nerve cells to 'tangle', gradually destroying them. ACI-35 is a vaccine which has been designed to produce antibodies against the tangled tau proteins, to prevent their build-up and potentially prevent progression of the disease. The aim of this study is to test the safety of this vaccine and the level of antibodies it produces in the body when it is given in different doses.

Who can participate?
Adults aged between 60 and 85 with mild to moderate Alzheimer's disease.

What does the study involve?
Participants are randomly allocated into groups who receive either a low, medium or high dose of ACI-35 or a placebo (inactive medication). This medication is given as an injection 2, 3 or 5 times over a 6 month period. Participants are also given a booster injection after 6 or 16 months. Participants in all groups are regularly assessed at clinic visits in order to test the levels of antibodies in their blood.

What are the possible benefits and risks of participating?
A potential benefit is that the vaccine may help to slow the progression of Alzheimer's disease. Risks of participating include possible side-effects of the medication.

Where is the study run from?
One hospital in Turku (Finland) and hospitals in Bath, Liverpool, Edinburgh and London (UK).

When is the study starting and how long is it expected to run for?
July 2013 to June 2017

Who is funding the study?
1. AC Immune SA (Switzerland)
2. Janssen Pharmaceuticals, Inc. (UK)

Who is the main contact?
1. Ms Eva Schier (Public)
2. Mr Julian Gray (Scientific)

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2013-000803-18

Protocol serial number
ACI-35-1201

Study information

Scientific Title
A phase Ib multicenter, double-blind, randomized, placebo-controlled study of the safety, tolerability and immunogenicity of ACI-35 in patients with mild to moderate Alzheimer's disease

Acronym
ACI-35

Study objectives
The purpose of this study is to investigate the safety and effects on the body of a new vaccine named ACI35 in treating Alzheimer's disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. National Committee on Medical Research Ethics Tukija, 31/10/2013, ref: 161/06.00.01/2013
2. NRES Committee South Central - Berkshire B, 18/03/2015, ref: 15/SC/0079

Study design
Phase Ib multi-centre double-blind randomized placebo-controlled study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Participants are randomly allocated to one of four groups using a secure interactive web based randomisation system.

Group 1: Receive a low dose of ACI-35 on a stable dosing regime of 5 administrations over a 6 month period
Group 2: Receive a medium dose of ACI-35 on a stable dosing regime of either 3 or 5 administrations over a 6 month period
Group 3: Receive a high dose of ACI-35 on a stable dosing regime of either 2 or 3 administrations over a 6 month period
Group 4: Receive a placebo on a stable dosing regime of either 2, 3 or 5 administrations over a 6 month period

In each group, this will be followed by a late booster injection about 6 months or 16 months after the initial dosing period. This will be followed by a treatment free safety follow up period of 6 months.

Intervention Type
Other

Primary outcome(s)
1. Adverse events are measured by recording vital signs and completing a physical and neurological examination at each clinic visit
2. Routine haematology and biochemistry in blood and urine is measured at baseline and periodically every second or four weeks in the initial 3 months of treatment, then every 3 months until the end of the study
3. Five MRI and ECG measurements are taken during the entire study duration. Two lumbar punctures for cerebrospinal fluid (CSF) drawing are done at baseline and after one year of treatment.
4. Immunogenicity (antibody titre response against pTau) is measured using blood samples drawn at each visit and measured at specific interim analyses, after 6 and 12 months of treatment, as well as after the safety follow-up period is completed

Key secondary outcome(s))
1. Antibody titre response is measured using blood samples which are drawn at each visit and measured at specific interim analyses, after 6 and 12 months of treatment, as well as after the safety follow-up period is completed
2. Biomarkers are measured using blood samples drawn at baseline and periodically every second or four weeks in the initial 3 months of treatment, then every 3 months until the end of the study. The biomarkers will be measured at specific interim analyses, after 6 and 12 months of treatment, as well as after the safety follow-up period is completed
3. Cognitive and Clinical Effects are measured using ADAS-cog, MMSE, Trail Making Test and Fluency Tests and the Clinical Global Impression of Change Disability Assessment in Dementia and Neuropsychiatric Inventory Scale at baseline, 14, 26, 50 and 60 weeks

Completion date
30/06/2017

Eligibility

Key inclusion criteria
1. Probable AD according to NINCDS-ADRDA criteria
2. Age equal to or over 60 and equal to or less than 85 years
3. Mini-Mental Status Examination (MMSE) 18 – 28 points at screening
4. Patient must be receiving a stable dose of acetylcholinesterase inhibitors for at least 3 months prior to screening
5. Patient cared for by a reliable spouse or other live-in caregiver who gives written consent to assist with clinical assessments and report safety issues
6. Patient who in the opinion of the investigator are able to understand and sign written informed consent, and to comply with all study procedures
(Note that consent must be obtained prior to conducting any trial-related procedures)
7. Women must be post-menopausal for at least one year and/or surgically sterilized
8. Female partner of male patients who are not postmenopausal or surgically sterilized must use reliable contraceptive measures e.g. double barrier contraception or hormonal contraception

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Key exclusion criteria
1. MRI scan at screening which shows an alternative cause other than AD for the dementia, e.g. space occupying lesions, hydrocephalus, significant vascular disease
2. Any medical conditions other than AD which may confound the assessment of cognition performance, e.g. Parkinson's disease, Lewy Body Dementia, vascular dementia
3. Any medical conditions (e.g. uncontrolled epilepsy, uncontrolled hypertension) which would hamper safety assessments and/or alter the ability to complete the study
4. Significant hearing or visual impairment or other issues judged relevant by the investigator preventing to comply with the protocol and to perform the outcome measures
5. Patient receiving any anticoagulant drug, or aspirin at doses greater than 100 mg daily
6. Patient receiving memantine
7. Use of tricyclic antidepressants, neuroleptics, systemic corticosteroids, immune modifying drugs including cyclosporine and mycophenolate
8. History of hemorrhagic stroke
9. History of non-hemorrhagic stroke or myocardial infarction within one year before screening
10. History of major depression, bipolar disorders, schizophrenia or other major psychiatric disorder according to DSM-5
11. History of sustained behavioural disturbances secondary to Alzheimer's disease such as hallucinations, delusions, agitation or nocturnal behavioural disturbances
12. History of inflammatory neurology disorders including meningoencephalitis
13. History of autoimmune disease with potential for CNS involvement
14. History of cancer other than localized skin cancer within the past 5 years before screening
15. Vascular dementia according to NINDS-AIREN criteria
16. Severe infections or a major surgical operation within 3 months prior to screening
17. History of chronic or recurrent infectious or inflammatory conditions such as recurrent urinary tract infections which could hamper interpretation of safety
18. Abuse of drug or alcohol within the past five years
19. Clinically significant abnormal vital signs (including sustained sitting blood pressure greater than 160/90 mm Hg)
20. Clinically significant arrhythmias or other abnormalities on ECG at screening. (Minor abnormalities documented as clinically insignificant by the investigator will be allowed)
21. Clinically significant abnormalities of clinical haematology or biochemistry including, but not limited to, elevations greater than 1.5 times the upper limit of normal of SGOT, SGPT, or creatinine at screening
22. Elevated prothrombin or partial thromboplastin time at screening
23. Positive syphilis serology, Hepatitis B or C at screening
24. Vitamin B12 or folate deficiency or hypothyroidism unless on replacement therapy for at least 3 months prior screening
25. Any vaccine received within the past 2 months before screening, including influenza vaccine which if indicated must be given at least 8 weeks prior to screening
26. Previously received AD immune therapeutic agents or vaccines
27. Previously received Tau immune therapeutic agents or vaccines or investigational agents targeting Tau pathology
28. Patient anticipated to receive any vaccination other than influenza vaccine during the study
29. MRI examination cannot be done for any reason, including metal implants contraindicated

for MRI studies and claustrophobia
30. Patient who has donated blood or blood products during the 30 days prior to screening or who plan to donate blood while participating in the study or within four weeks after completion of the study.

Date of first enrolment
01/12/2013

Date of final enrolment
30/12/2015

Locations

Countries of recruitment
United Kingdom

England

Scotland

Finland

Study participating centre
Clinical Research Services Turku, CRST
Itäinen Pitkäkatu 4 B, 3rd floor
Turku
Finland
FI-20014

Study participating centre
Research Institute for the Care of Older People (RICE)
The RICE Centre
Building 8
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Study participating centre
Royal Liverpool University Hospital (LRUH)
Prescot Street
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Study participating centre
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Study participating centre
Royal Infirmary of Edinburgh
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51 Little France Crescent
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Sponsor information

Organisation
AC Immune SA

ROR
https://ror.org/00e8cky09

Funder(s)

Funder type
Industry

Funder Name
AC Immune SA

Funder Name
Janssen Pharmaceuticals, Inc.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No