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# Amyloid imaging in Alzheimer's disease, frontotemporal dementia and healthy volunteers

**Submission date**
18/06/2009

**Recruitment status**
No longer recruiting

**Registration date**
04/08/2009

**Overall study status**
Completed

**Last Edited**
25/05/2016

**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

**Protocol serial number**
18F-AV-45-010

## Study information

**Scientific Title**
A study evaluating the imaging characteristics of florpiramine F 18 (18F-AV-45) in patients with frontotemporal dementia compared to patients with Alzheimer's disease and normal controls

## Study objectives
1. To evaluate the cerebral uptake of florpiramine F 18 as measured by positron emission tomography (PET) imaging in frontotemporal dementia (FTD) in comparison to cognitively normal volunteers and patients with Alzheimer's disease (AD)
2. To compare amyloid pathology as determined by florpiramine F 18 PET in patients with FTD versus AD
3. To expand the database of florpiramine F 18 PET imaging in cognitively normal volunteers to refine the definition of a negative scan
4. To expand the database of florpiramine F 18 PET imaging in AD and FTD patients to determine if florpiramine F 18 PET imaging yields the expected prevalence of Aß positivity in clinically defined AD and FTD patients, based on historical autopsy data
5. To determine the relation between florpiramine F 18 in-vivo kinetics, cortical atrophy, and metabolic impairment in FTD

Please note that as of 04/02/2013, the anticipated end date for this study was updated from 31 /03/2010 to 31/03/2013

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Newcastle & North Tyneside 2 Research Ethics Committee approved on the 20th March 2009 (ref: 08/H0907/158)

## Study design
Phase II single centre diagnostic open-label non-randomised study

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Frontotemporal dementia and Alzheimer's disease

## Interventions
A single administration of florpiramine F 18 (18F-AV-45) injection for intravenous use followed by a 60 minute continuous list-mode brain PET imaging started at the time of injection. A follow-up phone call to the patients (or the caregiver as appropriate) will be conducted approximately 7 days after final imaging session.

## Intervention Type
Drug

## Phase
Phase II

## Drug/device/biological/vaccine name(s)
Florpiramine F 18 (18F-AV-45)

### Primary outcome(s)
1. Evaluation of FDG PET imaging (FDG patients only)
2. Evaluation of amyloid imaging (FDG and AD patients)

Florpiramine F 18 images will be evaluated qualitatively and quantitatively. Images will be visually examined and will be classified as Aß+ (amyloid positive, AD-like) or Aß- (amyloid negative, not AD). Images will be evaluated quantitatively and qualitatively. Parametric statistics will be used to compare the SUV/SUVR in the various brain regions for patients with AD, patients with FTD and cognitively healthy volunteers to evaluate the hypothesis that cortical to cerebellar SUVR will be higher in target regions of patients with AD than in FTD patients. The primary analysis will contrast (t-test) precuneus to cerebellar SUVR in patients with AD versus patients with FTD. Finally the blinded reader interpretation (with and without sequential unblinding) will be compared to the clinical diagnosis for subjects with AD, FTD, and cognitively healthy volunteers.

### Key secondary outcome(s))
No secondary outcome measures

### Completion date
31/03/2013

## Eligibility

### Key inclusion criteria
Subjects who meet all of the following criteria are eligible to enrol in the arm of this trial reserved for patients with probable AD:
1. Male or female patients, at least 50 years of age, with probable AD according to the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS)/Alzheimer's Disease and Related Disorders Association (ADRDA) criteria
2. Patients with mild/moderate dementia as evidenced by a Mini-Mental State Examination (MMSE) score ranging from 10 to 24, boundaries included, at screening
3. Patients whose history of cognitive decline has been gradual in onset and progressive over a period of at least 6 months. Evidence should be present indicating sustained memory deterioration in an otherwise cognitively normal patient, plus additional impairment in another cognitive function such as: orientation, judgment and problem solving, or functioning in personal care.
4. Patients who live with or have regular visits from a responsible caregiver willing to provide information about the patient
5. Patients who give informed consent by signing a UK Multicentre Research Ethics Committee (MREC) approved informed consent prior to any study procedures. If the patient is incapable of giving informed consent, the caregiver may consent on behalf of the patient (the patient must still confirm assent). The consent procedure will be performed in accordance with the Mental Capacity Act 2005.

Subjects who meet all of the following criteria are eligible to enrol in the arm of this trial reserved for patients with FTD:
1. Males or females at least 45 years of age
2. Meet the consensus criteria for frontotemporal lobar degeneration and have mild to moderate disease severity. Clinical and neuropsychological criteria will be applied and will include only patients with the clinical phenotypes of behavioural-dysexecutive FTD. Clinical and neuropsychological features are obligatory, while patients can also be included if structural

imaging findings are supportive of the diagnosis or neutral (not suggesting an alternative diagnosis). Functional imaging findings will not be considered prior to patient inclusion.
3. Have a caregiver who can report on their mental status and Activities of Daily Living (ADL)
4. Patients who give informed consent by signing a UK Multicentre Research Ethics Committee (MREC) approved informed consent prior to any study procedures. If the patient is incapable of giving informed consent, the caregiver may consent on behalf of the patient (the patient must still confirm assent). The consent procedure will be performed in accordance with the Mental Capacity Act 2005.

Subjects who meet all of the following criteria are eligible to enrol in this trial as normal healthy volunteers:
1. Healthy male or female at least 45 years of age, with no evidence of significant cognitive impairment by history and psychometric testing
2. MMSE greater than or equal to 29, and are cognitively normal by informant report and on the psychometric test battery at screening
3. Volunteers who give informed consent by signing a UK Main Research Ethics Committee (MREC) approved informed consent prior to any study procedures

## Participant type(s)
Healthy volunteer

## Healthy volunteers allowed
No

## Age group
Adult

## Sex
All

## Key exclusion criteria
1. Neurodegenerative disorders other than AD or FTD as appropriate, including, but not limited to Parkinson's disease, Huntington's disease, Down's syndrome, Creutzfeldt-Jacob disease, normal pressure hydrocephalus, and progressive supranuclear palsy
2. Have now or have had a diagnosis of other dementing/neurodegenerative disease (e.g. Parkinson's disease, dementia with Lewy bodies, Lewy body variant AD, etc.)
3. Have now or have had a diagnosis of mixed dementia
4. Cognitive impairment or significant residual findings on magnetic resonance imaging (MRI) resulting from:
4.1. Acute cerebral trauma or post-traumatic brain injury, subdural haematoma, or injuries secondary to chronic trauma (e.g., sequella from boxing)
4.2. Hypoxic cerebral damage regardless of aetiology; e.g., cognitive or neurological deficits resulting from cardiac arrest or cardiac surgery, anaesthesia, or severe self-poisoning episode, secondary to severe hypovolaemia (orthostatic hypotension should not lead to exclusion)
4.3. Vitamin deficiency states documented by medical history such as folate, vitamin B12 and other B complex deficiencies; e.g., thiamine deficiency in Korsakoff's syndrome (patients taking regular B12 and folate are not necessarily excluded)
4.4. Cerebral infection including abscess, syphilis, meningitis, encephalitis or acquired immune deficiency syndrome (AIDS)
4.5. Primary or metastatic cerebral neoplasia
4.6. Significant endocrine or metabolic disease; e.g., thyroid, parathyroid, or pituitary disease,

Cushing's syndrome, or severe renal failure
4.7. Mental retardation
Before enrolling a patient with past or current history of any of the above conditions, the investigator must contact the sponsor to discuss whether the condition could have contributed to the cognitive impairment.
5. Clinically significant infarct or possible multi-infarct dementia as defined by the NINCDS criteria, including:
5.1. A history of a significant cerebrovascular event resulting in a physical or neurological deficit that may confound the assessment of the patient's intellectual function
5.2. Multiple focal signs on neurologic examination indicative of multiple ischaemic episodes
5.3. One or more of the following findings on a MRI scan:
5.3.1. Multiple (two or more) infarcts or white matter lacunes
5.3.2. A single large infarct or a strategically placed infarct in the angular gyrus, the thalamus, the basal forebrain, the posterior cerebral artery (PCA), or anterior cerebral artery (ACA) territory
5.3.3. Extensive periventricular white matter disease. Leukoaraiosis (periventricular white matter, low attenuation) should be distinguished from multiple infarctions. Leukoaraiosis is common in normal individuals and patients with AD. White matter deterioration should not result in exclusion unless it is abnormal and widespread, e.g., Binswanger's disease.
6. Any evidence on screening MRI, computed tomography (CT), or other biomarker studies that suggests an alternate aetiology (other than probable AD in patients with AD, FTD in patients with clinically defined FTD) for cognitive deficit; or in the case of cognitively normal controls any evidence on screening MRI, CT, or other biomarker studies that suggests the presence of AD, FTD or other significant neuropathology.
7. Current clinically significant psychiatric disease, as judged by Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria, particularly current major depression or schizophrenia. Patients with dementia who are experiencing behavioural disturbances that may require treatment with psychotropic medications may be entered only after discussion and with the approval of the sponsor. The investigator and sponsor should carefully consider whether subjects with behavioural dysfunction will be able to complete the imaging session.
8. History of epilepsy or convulsions, except for febrile convulsions during childhood
9. Clinically significant hepatic, renal, pulmonary, metabolic, or endocrine disturbances
10. Current clinically significant cardiovascular disease. Clinically significant cardiovascular disease usually includes one or more of the following:
10.1. Cardiac surgery or myocardial infarction within the last 6 months
10.2. Unstable angina
10.3. Coronary artery disease that required an increase in medication within the last 3 months
10.4. Decompensated congestive heart failure
10.5. Significant cardiac arrhythmia or conduction disturbance, particularly those resulting in atrial or ventricular fibrillation, or causing syncope, near syncope, or other alterations in mental status
10.6. Severe mitral or aortic valvular disease
10.7. Uncontrolled high blood pressure
10.8. Congenital heart disease
10.9. Clinically significant abnormal result on electrocardiogram (ECG), including but not limited to QTc greater than 450 msec
Before enrolling a patient with any of the above conditions, the investigator must contact the sponsor.
11. History of drug or alcohol abuse within the past year, or prior prolonged history of abuse
12. Clinically significant infectious disease, including AIDS or human immunodeficiency virus (HIV) infection or previous positive test for any form of hepatitis
13. Women of childbearing potential who are not permanently surgically sterile, or are not

refraining from sexual activity while not using adequate contraception. Women must not be pregnant (negative serum beta-human chorionic gonadotrophin [beta-hCG] at the time of screening and negative urine beta-hCG on the day of imaging) or lactating at screening, must avoid becoming pregnant, and must agree to use adequate contraceptive methods for 30 days prior to and 30 days after administration of florpiramine F 18. Specifically, to participate in this study, sexually active females must be either two or more years post-menopausal or permanently surgically sterilised, or must be using two forms of highly effective contraception from the following list:
13.1. Established use of oral, injected or implanted hormonal methods of contraception for at least three months prior to the start of the screening visit
13.2. Placement of an intrauterine device (IUD) or intrauterine system (IUS) at least two months prior to the start of the screening visit
13.3. Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository
13.4. Male sterilisation (with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate)
14. Patients who, in the opinion of the investigator, are otherwise unsuitable for a study of this type
15. History of severe drug allergy or hypersensitivity
16. Patients who had received an investigational medication within the last 30 days or who have participated in a clinical trial with any experimental medication in the last 30 days. Additionally, the time between the last dose of the previous experimental medication and enrollment (completion of screening assessments) must be at least equal to 5 times the terminal half-life of the previous experimental medication. Patients who have ever participated in an experimental study with an amyloid targeting therapy (e.g., immunotherapy, secretase inhibitor) may not be enrolled unless it can be demonstrated that the patient received only placebo in the course of the trial.
17. Patients with current clinically significant medical comorbidities, as indicated by history, physical exam, ECG (including but not limited to QTc greater than 450 msec) or laboratory evaluations, that might pose a potential safety risk, interfere with the absorption or metabolism of the study medication, or limit interpretation of the trial results. These include but are not limited to clinically significant hepatic, renal, pulmonary, metabolic or endocrine disease, cancer, HIV infection and AIDS.
18. Have had a radiopharmaceutical imaging or treatment procedure within 7 days of the day of imaging, other than as defined in this protocol

### Date of first enrolment
22/06/2009

### Date of final enrolment
31/03/2013

## Locations

### Countries of recruitment
United Kingdom

England

**Study participating centre**
**Wolfson Molecular Imaging Centre**
Manchester
United Kingdom
M20 3LJ

# Sponsor information

**Organisation**
Avid Radiopharmaceuticals Inc.

**ROR**
https://ror.org/01qat3289

# Funder(s)

**Funder type**
Industry

**Funder Name**
Avid Radiopharmaceuticals Inc.

# 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: | 01/03/2015 | | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |