Clinical trial results:
A study evaluating the imaging characteristics of 18F-AV-45 in patients with frontotemporal dementia compared to patients with Alzheimer's disease and normal controls

Summary

EudraCT number	2008-003597-18
Trial protocol	GB
Global end of trial date	12 January 2013

Results information

Result version number	v1 (current)
This version publication date	01 February 2016
First version publication date	26 September 2014

Trial information

Trial identification

Sponsor protocol code	18F-AV-45-010

Additional study identifiers

ISRCTN number	ISRCTN58435532
ClinicalTrials.gov id (NCT number)	NCT01890343
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Avid Radiopharmaceuticals
Sponsor organisation address	3711 Market St., Philadelphia, United States, 19104
Public contact	Clinical Operations, Avid Radiopharmaceuticals, 215 2980700,
Scientific contact	Chief Medical Officer, Avid Radiopharmaceuticals, 215 2980700,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2012
Global end of trial reached?	Yes
Global end of trial date	12 January 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To compare amyloid pathology as determined by 18F-AV-45 positron emission tomography (PET) in patients with frontal temporal dementia (FTD) vs. Alzheimer's disease (AD);
2. To expand the database of 18-F-AV-45 PET imaging in cognitively normal volunteers;
3. To expand the database of 18F-AV-45 PET imaging in AD and FTD patients to determine if 18F-AV-45 PET imaging yields the expected prevalence of AB positivity in clinically defined AD and FTD patients, based on historical autopsy data:
4. To determine the relationship between 18F-AV-45 in-vivo kinetics, cortical atrophy and metabolic impairment in FTD.

Protection of trial subjects:

Subjects who received florbetapir 18F were closely followed by means of adverse event reporting and vital signs. In the event of a study related adverse event, subjects would not have been discharged until the event had resolved or stabilized. Subjects were made aware of the planned procedures and their comfort in the scanner was mazimized to minimize the risk of any discomfort while in the PET scanner.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 July 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 34
Worldwide total number of subjects	34
EEA total number of subjects	34

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	21
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were enrolled as either cognitively normal subjects, subjects with AD or subjects with FTD.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Frontotemporal Disorder

Arm description:

Subjects with frontotemporal disorder (FTD).

florbetapir 18F: Subjects received a one-time intravenous (IV) bolus injection of 300 megabecquerels (MBq) florbetapir 18F.

18F-FDG: FTD subjects received a one-time IV bolus injection of 185 MBq of 18F-FDG.

Arm type	Experimental
Investigational medicinal product name	florbetapir (18F)
Investigational medicinal product code	18F-AV-45
Other name	Amyvid, florbetapir F 18
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a one-time intravenous (IV) bolus injection of 300 megabecquerels (MBq) florbetapir (18F).

Investigational medicinal product name	18F-FDG
Investigational medicinal product code	
Other name	FDG, fluorodeoxyglucose (18F), fludeoxyglucose (18F)
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

FTD subjects received a one-time IV bolus injection of 185 MBq of 18F-FDG.

Arm title	Cognitively Normal

Arm description:

Cognitively normal (CN) subjects.

Arm type	Experimental
Investigational medicinal product name	florbetapir (18F)
Investigational medicinal product code	18F-AV-45
Other name	Amyvid, florbetapir F 18
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a one-time intravenous (IV) bolus injection of 300 megabecquerels (MBq) florbetapir 18F.

Arm title	Alzheimer's Disease

Arm description:

Subjects with Alzheimer's disease (AD).

Arm type	Experimental
Investigational medicinal product name	florbetapir (18F)
Investigational medicinal product code	18F-AV-45
Other name	Amyvid, florbetpair F 18
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a one-time intravenous (IV) bolus injection of 300 megabecquerels (MBq) florbetapir 18F.

Number of subjects in period 1[1]	Frontotemporal Disorder	Cognitively Normal	Alzheimer's Disease
Started	8	10	10
Completed	8	10	10

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide total represents the number of subjects enrolled in the study. Six subjects dropped out of the study prior to receiving a florbetapir injection. The baseline period represents the number of subjects who received a florbetapir (18F) scan.

Baseline characteristics

Reporting groups	
Reporting group title	Frontotemporal Disorder
Reporting group description:	
Subjects with frontotemporal disorder (FTD). florbetapir 18F: Subjects received a one-time intravenous (IV) bolus injection of 300 megabecquerels (MBq) florbetapir 18F. 18F-FDG: FTD subjects received a one-time IV bolus injection of 185 MBq of 18F-FDG.	
Reporting group title	Cognitively Normal
Reporting group description:	
Cognitively normal (CN) subjects.	
Reporting group title	Alzheimer's Disease
Reporting group description:	
Subjects with Alzheimer's disease (AD).	

Reporting group values	Frontotemporal Disorder	Cognitively Normal	Alzheimer's Disease
Number of subjects	8	10	10
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	62.4	62.4	62.6
standard deviation	± 9.62	± 4.99	± 4.35
Gender categorical Units: Subjects			
Female	0	5	3
Male	8	5	7

Reporting group values	Total		
Number of subjects	28		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	8		
Male	20		

End points

End points reporting groups

Reporting group title	Frontotemporal Disorder

Reporting group description:

Subjects with frontotemporal disorder (FTD).

florbetapir 18F: Subjects received a one-time intravenous (IV) bolus injection of 300 megabecquerels (MBq) florbetapir 18F.

18F-FDG: FTD subjects received a one-time IV bolus injection of 185 MBq of 18F-FDG.

Reporting group title	Cognitively Normal

Reporting group description:

Cognitively normal (CN) subjects.

Reporting group title	Alzheimer's Disease

Reporting group description:

Subjects with Alzheimer's disease (AD).

Primary: Qualitative Amyloid Image Assessment

End point title	Qualitative Amyloid Image Assessment[1]

End point description:

Four readers blinded to all clinical information classified florbetapir Positron Emission Tomography (PET) images as either positive for amyloid or negative for amyloid. The majority read classification is presented as either positive, negative or tied.

End point type	Primary

End point timeframe:

50-60 minutes after injection

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed on this outcome measure.

End point values	Frontotemporal Disorder	Cognitively Normal	Alzheimer's Disease	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	10	10	
Units: Participants				
Positive	2	1	8	
Negative	4	8	2	
Tie	2	1	0	

Statistical analyses

No statistical analyses for this end point

Primary: Quantitative Amyloid Image Assessment

End point title	Quantitative Amyloid Image Assessment

End point description:

The effect of diagnostic group on mean total cortical grey matter florbetapir binding relative to cerbellar cortex is presented as standard uptake value ratios (SUVRs).

End point type	Primary

End point timeframe:

50-60 minutes after injection

End point values	Frontotemporal Disorder	Cognitively Normal	Alzheimer's Disease	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	10	10	
Units: SUVr				
arithmetic mean (standard deviation)				
Mean cortical SUVR	1.25 (± 0.36)	1.29 (± 0.11)	1.77 (± 0.38)	

Statistical analyses

Statistical analysis title	Effect of diagnostic group on SUVr

Statistical analysis description:

The effect of diagnostic group on mean cortical florbetapir binding relative to cerebellar cortex was determined.

Comparison groups	Frontotemporal Disorder v Alzheimer's Disease v Cognitively Normal
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.002
Method	Kruskal-wallis

Notes:

[2] - Null hypothesis is no difference between the group means.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 7 days	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Frontotemporal Disorder
Reporting group description: Subjects with frontotemporal disorder (FTD). florbetapir 18F: Subjects received a one-time intravenous (IV) bolus injection of 300 megabecquerels (MBq) florbetapir 18F. 18F-FDG: FTD subjects received a one-time IV bolus injection of 185 MBq of 18F-FDG.	
Reporting group title	Cognitively Normal
Reporting group description: Cognitively normal (CN) subjects.	
Reporting group title	Alzheimer's Disease
Reporting group description: Subjects with Alzheimer's disease (AD).	

Serious adverse events	Frontotemporal Disorder	Cognitively Normal	Alzheimer's Disease
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Frontotemporal Disorder	Cognitively Normal	Alzheimer's Disease
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 10 (0.00%)	1 / 10 (10.00%)
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported