



Clinical trial results:

Florbetapir F 18 (18F-AV-45) Amyloid PET Imaging in Focal Dementia Syndromes

Summary

EudraCT number	2010-023852-10
Trial protocol	GB
Global end of trial date	19 July 2013

Results information

Result version number	v1 (current)
This version publication date	01 February 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	18F-AV-45-020
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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, 1 2152980700,
Scientific contact	Chief Medical Officer, Avid Radiopharmaceuticals, 1 2152980700,

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	19 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 July 2013
Global end of trial reached?	Yes
Global end of trial date	19 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To use florbetapir (18F) to investigate the pathological underpinning of the neuropsychologically distinct variants of primary progressive aphasia (PPA); and to compare patterns of florbetapir (18F) uptake between these patients and those with posterior cortical Alzheimer's disease (PCA-AD) and age-matched controls.
2. To use 18F-fluoro-2-deoxy-D-glucose (FDG) PET imaging to assess the patterns of focal hypometabolism occurring in these disorders.

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 maximized to minimize the risk of any discomfort while in the PET scanner.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2012
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: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	13

From 65 to 84 years	10
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 PPA

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	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	Posterior Cortical Alzheimer's Disease
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Arm description:

Subjects with posterior cortical Alzheimer's disease (PCA-AD).

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	Primary Progressive Aphasia
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Arm description:

Subjects with primary progressive aphasia (PPA). Efficacy endpoints for this arm will be reported as subgroup analyses by syndromic group.

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).

Number of subjects in period 1^[1]	Cognitively Normal	Posterior Cortical Alzheimer's Disease	Primary Progressive Aphasia
Started	5	5	12
Completed	5	5	12

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. One subject elected to leave the study prior to receiving florbetapir (18F). The baseline period represents the number of subjects who received a florbetapir (18F) scan.

Baseline characteristics

Reporting groups

Reporting group title	Cognitively Normal
Reporting group description: Cognitively normal (CN) subjects.	
Reporting group title	Posterior Cortical Alzheimer's Disease
Reporting group description: Subjects with posterior cortical Alzheimer's disease (PCA-AD).	
Reporting group title	Primary Progressive Aphasia
Reporting group description: Subjects with primary progressive aphasia (PPA). Efficacy endpoints for this arm will be reported as subgroup analyses by syndromic group.	

Reporting group values	Cognitively Normal	Posterior Cortical Alzheimer's Disease	Primary Progressive Aphasia
Number of subjects	5	5	12
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	63.2	58.8	66.5
standard deviation	± 6.34	± 2.17	± 6.84
Gender categorical Units: Subjects			
Female	3	2	6
Male	2	3	6

Reporting group values	Total		
Number of subjects	22		
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)	0 0 0 0 0 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	11		
Male	11		

End points

End points reporting groups

Reporting group title	Cognitively Normal
Reporting group description: Cognitively normal (CN) subjects.	
Reporting group title	Posterior Cortical Alzheimer's Disease
Reporting group description: Subjects with posterior cortical Alzheimer's disease (PCA-AD).	
Reporting group title	Primary Progressive Aphasia
Reporting group description: Subjects with primary progressive aphasia (PPA). Efficacy endpoints for this arm will be reported as subgroup analyses by syndromic group.	
Subject analysis set title	Logopenic Progressive Aphasia
Subject analysis set type	Sub-group analysis
Subject analysis set description: PPA syndromic group Logopenic Progressive Aphasia (LPA).	
Subject analysis set title	Progressive Nonfluent Aphasia
Subject analysis set type	Sub-group analysis
Subject analysis set description: PPA syndromic group Progressive Nonfluent Aphasia (PNFA).	
Subject analysis set title	Semantic Dementia
Subject analysis set type	Sub-group analysis
Subject analysis set description: PPA syndromic group Semantic Dementia (SD).	

Primary: Qualitative Image Assessment

End point title	Qualitative Image Assessment ^{[1][2]}
End point description: A blinded visual assessment was performed by three independent, experienced nuclear medicine clinicians for both florbetapir (18F) images (AB+/AB-) and FDG images (FDG abnormal/FDG normal).	
End point type	Primary
End point timeframe: Florbetapir (18F) PET imaging 50-60 minutes after injection. FDG PET Imaging 30-60 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.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The PPA arm is composed of 3 subgroups: LPA, PNFA, and SD. The efficacy data for the PPA arm is presented in the subgroup analysis for this end point.

End point values	Cognitively Normal	Posterior Cortical Alzheimer's Disease	Logopenic Progressive Aphasia	Progressive Nonfluent Aphasia
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	5	5	3	4
Units: Participants				
AB+	0	5	3	1
AB-	5	0	0	3

FDG abnormal	0	5	3	3
FDG normal	5	0	0	1

End point values	Semantic Dementia			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: Participants				
AB+	0			
AB-	5			
FDG abnormal	5			
FDG normal	0			

Statistical analyses

No statistical analyses for this end point

Primary: Quantitative Image Assessment

End point title Quantitative Image Assessment^{[3][4]}

End point description:

SUVr was calculated using a whole cerebellum reference region with no partial volume correction.

End point type Primary

End point timeframe:

Florbetapir (18F) PET imaging 50-60 minutes after injection. FDG PET Imaging 30-60 minutes after injection.

Notes:

[3] - 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.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The PPA arm is composed of 3 subgroups: LPA, PNFA, and SD. The efficacy data for the PPA arm is presented in the subgroup analysis for this end point.

End point values	Cognitively Normal	Posterior Cortical Alzheimer's Disease	Logopenic Progressive Aphasia	Progressive Nonfluent Aphasia
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	5	5	3	4
Units: SUVr				
arithmetic mean (standard deviation)				
Florbetapir (18F)	1.02 (± 0.05)	1.48 (± 0.11)	1.47 (± 0.1)	1.12 (± 0.1)
FDG	1.19 (± 0.08)	0.95 (± 0.02)	0.98 (± 0.06)	1.07 (± 0.13)

End point values	Semantic Dementia			
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Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: SUVr				
arithmetic mean (standard deviation)				
Florbetapir (18F)	0.98 (± 0.04)			
FDG	1.09 (± 0.07)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

48 hours

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Cognitively Normal
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Reporting group description:

Cognitively normal (CN) subjects.

Reporting group title	Posterior Cortical Alzheimer's Disease
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Reporting group description:

Subjects with posterior cortical Alzheimer's disease (PCA-AD).

Reporting group title	Primary Progressive Aphasia
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Reporting group description:

Subjects with primary progressive aphasia (PPA).

Serious adverse events	Cognitively Normal	Posterior Cortical Alzheimer's Disease	Primary Progressive Aphasia
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	Cognitively Normal	Posterior Cortical Alzheimer's Disease	Primary Progressive Aphasia
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
General disorders and administration site conditions			
Injection site irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study is limited by a small sample size at a single recruiting center.

Notes: