



## Clinical trial results:

### Evaluation of Florbetapir (18F) in Subjects Participating in the IRCCS-FBF Protocol

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

#### Summary

EudraCT number	2012-003079-20
Trial protocol	IT
Global end of trial date	24 December 2014

#### Results information

Result version number	v1 (current)
This version publication date	30 March 2016
First version publication date	30 March 2016

#### Trial information

##### Trial identification

Sponsor protocol code	18F-AV-45-C02
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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, Inc., 1 215-298-0700,
Scientific contact	Chief Medical Officer, Avid Radiopharmaceuticals, Inc., 1 215-298-0700,

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	24 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 December 2014
Global end of trial reached?	Yes
Global end of trial date	24 December 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to expand the database of florbetapir (18F) safety and amyloid binding as measured by PET imaging in patients complaining of cognitive disturbances and in cognitively normal volunteers.

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	07 August 2013
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	Italy: 267
Worldwide total number of subjects	267
EEA total number of subjects	267

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)	49
From 65 to 84 years	214
85 years and over	4

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects had already met inclusion and exclusion criteria for the main protocol "Clinical assessment and follow-up of a naturalistic population of patients enrolled in an amyloid imaging program in Memory Clinics in Brescia, Italy".

### 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
<b>Arm title</b>	Alzheimer's Disease

Arm description: -

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 370 megabecquerels (MBq) florbetapir (18F).

<b>Arm title</b>	Mild Cognitive Impairment
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Arm description: -

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 370 megabecquerels (MBq) florbetapir (18F).

<b>Arm title</b>	Other Dementia Disorders
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Arm description: -

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 370 megabecquerels (MBq) florbetapir (18F).

<b>Arm title</b>	Cognitively Normal
Arm description: -	
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 370 megabecquerels (MBq) florbetapir (18F).

<b>Number of subjects in period 1</b>	Alzheimer's Disease	Mild Cognitive Impairment	Other Dementia Disorders
Started	61	135	43
Completed	61	135	43

<b>Number of subjects in period 1</b>	Cognitively Normal
Started	28
Completed	28

## Baseline characteristics

### Reporting groups

Reporting group title	Alzheimer's Disease
Reporting group description: -	
Reporting group title	Mild Cognitive Impairment
Reporting group description: -	
Reporting group title	Other Dementia Disorders
Reporting group description: -	
Reporting group title	Cognitively Normal
Reporting group description: -	

Reporting group values	Alzheimer's Disease	Mild Cognitive Impairment	Other Dementia Disorders
Number of subjects	61	135	43
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	71.6	71.1	70
standard deviation	± 7.8	± 6.7	± 7.2
Gender categorical Units: Subjects			
Female	36	67	22
Male	25	68	21

Reporting group values	Cognitively Normal	Total	
Number of subjects	28	267	
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		0 0 0 0 0 0 0	

85 years and over		0	
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Age continuous			
Units: years			
arithmetic mean	68.4		
standard deviation	± 6.8	-	
Gender categorical			
Units: Subjects			
Female	19	144	
Male	9	123	

## End points

### End points reporting groups

Reporting group title	Alzheimer's Disease
Reporting group description: -	
Reporting group title	Mild Cognitive Impairment
Reporting group description: -	
Reporting group title	Other Dementia Disorders
Reporting group description: -	
Reporting group title	Cognitively Normal
Reporting group description: -	

### Primary: Qualitative Assessment of Images

End point title	Qualitative Assessment of Images
End point description:	The results of qualitative assessment of images were reported as either A $\beta$ positive (A $\beta$ +) or A $\beta$ negative (A $\beta$ -). Visual evaluation of images was performed locally by trained radiologists or nuclear medicine specialists who were blinded to the subject's diagnosis.
End point type	Primary
End point timeframe:	50-60 minutes after injection

End point values	Alzheimer's Disease	Mild Cognitive Impairment	Other Dementia Disorders	Cognitively Normal
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	135	43	28
Units: Percentage of Subjects				
number (confidence interval 95%)				
A $\beta$ +	68.9 (56.4 to 79.1)	60 (51.6 to 67.9)	53.5 (38.9 to 67.5)	17.9 (7.9 to 35.6)
A $\beta$ -	31.1 (20.9 to 43.6)	40 (32.1 to 48.4)	46.5 (32.5 to 61.1)	82.1 (64.4 to 92.1)

### Statistical analyses

Statistical analysis title	AD vs. CN
Comparison groups	Alzheimer's Disease v Cognitively Normal
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Chi-squared

<b>Statistical analysis title</b>	MCI vs. CN
Comparison groups	Mild Cognitive Impairment v Cognitively Normal
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Chi-squared

<b>Statistical analysis title</b>	ODD vs. CN
Comparison groups	Other Dementia Disorders v Cognitively Normal
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0031
Method	Chi-squared

### Primary: Quantitative Assessment of Images

End point title	Quantitative Assessment of Images
End point description: Global cortical standard uptake value ratio (SUVR) across diagnostic groups. Quantitative evaluation of images was performed by Avid Radiopharmaceuticals.	
End point type	Primary
End point timeframe: 50-60 minutes after injection	

End point values	Alzheimer's Disease	Mild Cognitive Impairment	Other Dementia Disorders	Cognitively Normal
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	135	43	28
Units: SUVR				
arithmetic mean (standard deviation)				
Global Cortical SUVR	1.195 (± 0.241)	1.141 (± 0.209)	1.065 (± 0.221)	1.003 (± 0.146)

### Statistical analyses



<b>Statistical analysis title</b>	CN vs. Impaired
Comparison groups	Alzheimer's Disease v Mild Cognitive Impairment v Other Dementia Disorders v Cognitively Normal
Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0003
Method	ANOVA

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

48 hours post-injection

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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### Reporting groups

Reporting group title	Alzheimer's Disease
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Reporting group description: -

Reporting group title	Mild Cognitive Impairment
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Reporting group description: -

Reporting group title	Other Dementia Disorders
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Reporting group description: -

Reporting group title	Cognitively Normal
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Reporting group description: -

Serious adverse events	Alzheimer's Disease	Mild Cognitive Impairment	Other Dementia Disorders
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 61 (0.00%)	0 / 135 (0.00%)	0 / 43 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Cognitively Normal		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Alzheimer's Disease	Mild Cognitive Impairment	Other Dementia Disorders
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 61 (6.56%)	10 / 135 (7.41%)	1 / 43 (2.33%)
Vascular disorders			

Hot flush subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0	0 / 135 (0.00%) 0	0 / 43 (0.00%) 0
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0	0 / 135 (0.00%) 0	0 / 43 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)  Paraesthesia subjects affected / exposed occurrences (all)	2 / 61 (3.28%) 2  0 / 61 (0.00%) 0	8 / 135 (5.93%) 8  1 / 135 (0.74%) 1	1 / 43 (2.33%) 1  0 / 43 (0.00%) 0
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 61 (0.00%) 0	0 / 135 (0.00%) 0	0 / 43 (0.00%) 0
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Nausea subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1  1 / 61 (1.64%) 1  1 / 61 (1.64%) 1  0 / 61 (0.00%) 0	1 / 135 (0.74%) 1  0 / 135 (0.00%) 0  1 / 135 (0.74%) 1  2 / 135 (1.48%) 2	0 / 43 (0.00%) 0  0 / 43 (0.00%) 0  0 / 43 (0.00%) 0  0 / 43 (0.00%) 0
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1	0 / 135 (0.00%) 0	0 / 43 (0.00%) 0

<b>Non-serious adverse events</b>	Cognitively Normal		
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Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 28 (7.14%)		
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)  Paraesthesia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0  0 / 28 (0.00%) 0		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Nausea subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0  0 / 28 (0.00%) 0  0 / 28 (0.00%) 0  0 / 28 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
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## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2013	At the request of the regulatory authority, an explicit definition of radiation dose limits for healthy volunteers and actual exposure information was added to the protocol.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported