Clinical trial results:
Evaluation of 18F-AV-1451 kinetic modeling in patients in Alzheimer's disease and healthy controls

Summary

EudraCT number	2014-003047-35
Trial protocol	NL
Global end of trial date	28 April 2017

Results information

Result version number	v1 (current)
This version publication date	12 May 2018
First version publication date	12 May 2018

Trial information

Trial identification

Sponsor protocol code	18F-AV-1451-A10

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., 7th Floor, Philadelphia, United States, 19104
Public contact	Stephen Truocchio, Avid Radiopharmaceuticals, Inc., 1 2152980700,
Scientific contact	Michael Pontecorvo, Avid Radiopharmaceuticals, Inc., 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	28 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 April 2017
Global end of trial reached?	Yes
Global end of trial date	28 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate tracer kinetic models for the purpose of quantifying specific binding of 18F-AV-1451 in cross sectional and longitudinal applications and to evaluate simplified methods for quantitation of 18F-AV-1451 uptake.

Protection of trial subjects:

Subjects who received flortaucipir F 18 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	05 January 2015
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	Netherlands: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	7
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

One subject was enrolled in the study but withdrew consent prior to receiving flortaucipir.

Period 1

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

Arms

Arm title	All Subjects

Arm description: -

Arm type	Experimental
Investigational medicinal product name	flortaucipir 18F
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

240 Mbq IV Injection. Dynamic Scan 0-60 and 80-130 min post injection. Arterial blood withdrawn continuously 0-60 min post injection. Manual blood camples taken at 5, 10, 15, 20, 40, 60, 80, 105, and 130 min post injection. No more than 500cc of blood was withdrawn during the PET session.

Number of subjects in period 1[1]	All Subjects
Started	21
Completed	17
Not completed	4
Physician decision	3
Consent withdrawn by subject	1

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: One subject was enrolled in the study but withdrew consent prior to receiving flortaucipir.

Baseline characteristics

Reporting groups

Reporting group title	All Subjects

Reporting group description: -

Reporting group values	All Subjects	Total	
Number of subjects	21	21	
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	67.7		
standard deviation	± 6.52	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	13	13	
Race Units: Subjects			
Asian	0	0	
Black or African American	1	1	
Caucasian	19	19	
Native American/Alaskan Native	0	0	
Native Hawaiian or Pacific Islander	0	0	
Other	1	1	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	21	21	
Highest Level of Education Units: Subjects			
Elementary School	0	0	
Middle School	0	0	
High School	7	7	
College/University	11	11	
Post Graduate School	3	3	
Other	0	0	

Alcohol History Units: Subjects			
Never	3	3	
Not Current User	2	2	
Occasional	6	6	
Moderate	10	10	
Frequent	0	0	
Smoking History Units: Subjects			
Never	7	7	
Not Current User	11	11	
Occasional	0	0	
Moderate	2	2	
Frequent	1	1	
MMSE			
Mini-Mental State Examination			
Units: Points			
arithmetic mean	26.2		
standard deviation	± 3.79	-	

End points

End points reporting groups

Reporting group title	All Subjects

Reporting group description: -

Primary: Kinetic Modeling

End point title	Kinetic Modeling[1]

End point description:

BPND (2TC DVR-1) values, and SUVr-1 values from 3 timepoints using multiple target areas with both PERSI and cere-crus as reference region were compared by a regression analysis. SUVr from scans acquired 80-100 min post dose, using the PERSI reference region provided the best approximation (r2, goodness of fit) to the BPND (2TC DVR-1) values. For this timepoint/reference region the slope of the regression line approached 1 and the intercept approached zero and the SUVr-1 value explained more than 90% of variance in BPND values. In contrast SUVr values from later timepoints or SUVr values using cere-crus reference region tended to explain less variance and tended to slightly overestimate BPND.

SUVR = Standard Uptake Value Ratio
BPND = Binding Potential
2TC = Two Tissue Compartment Model
DVR = Distribution Volume Ration
PERSI = Parametric Estimate of Reference Signal Intensity
cere-crus = Cerebellum-crus, a gray matter region of cerebellum

End point type	Primary

End point timeframe:

40-60, 80-100, and 110-130 minutes postinjection

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: There was no formal hypothesis to be tested in this study.

End point values	All Subjects			
Subject group type	Reporting group			
Number of subjects analysed	20[2]			
Units: Goodness of Fit (r2)				
number (not applicable)				
40-60 min (PERSI)	0.8022			
80-100 min (PERSI)	0.9064			
110-130 min (PERSI)	0.8509			
40-60 min (cere-crus)	0.7575			
80-100 min (cere-crus)	0.8969			
110-130 min (cere-crus)	0.8218			

Notes:

[2] - One subject did not complete the PET scan due to excessive and repeated movement.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Within 48 hours of flortaucipir injection.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	Safety Population
Reporting group description: All subjects who received flortaucipir F 18.	

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Gastrointestinal disorders			
Change of bowel habit			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2016	Arterial blood draw is now required for all study subjects. In a previous amendment, there was the possibility that the arterial blood draw could be dropped for cohort 2 (baseline scan only) subjects after analyzing the data from cohort 1 subjects (baseline and 1 year scan). Additionally, If brain MRI has been performed more than 6 months (AD) or 12 months (HV) before baseline imaging, brain MRI will be repeated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported