# 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<br>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<br>Units: years | | | |
| arithmetic mean | 67.7 | | |
| standard deviation | ± 6.52 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 8 | 8 | |
| Male | 13 | 13 | |
| Race<br>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<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 21 | 21 | |
| Highest Level of Education<br>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<br>Units: Subjects | | | |
| Never | 3 | 3 | |
| Not Current User | 2 | 2 | |
| Occasional | 6 | 6 | |
| Moderate | 10 | 10 | |
| Frequent | 0 | 0 | |
| Smoking History<br>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:<br>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:<br>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