



Clinical trial results: Validating in vivo quantification of tau with [18F]AV-1451 PET Summary

EudraCT number	2015-004230-10
Trial protocol	NL
Global end of trial date	08 November 2018

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021
Summary attachment (see zip file)	Published paper (Timmers_2019_JCBFM_test_retest_AV1451_published.pdf)

Trial information

Trial identification

Sponsor protocol code	15-14
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VU University Medical Center
Sponsor organisation address	De Boellelaan 1117, Amsterdam, Netherlands, 1081 HV
Public contact	Dept of Radiology Nuclear Medicine, VU University Medical Center, 0031 204441948, t.timmers@vumc.nl
Scientific contact	Dept of Radiology Nuclear Medicine, VU University Medical Center, 0031 204441948, t.timmers@vumc.nl

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	30 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 November 2018
Global end of trial reached?	Yes
Global end of trial date	08 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To validate the previously defined simplified tracer kinetic model to quantify specific binding of [18F]AV-1451

Protection of trial subjects:

No trial specific measures were put in place. Regular procedures regarding scanning and puncture procedures were in place.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 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: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	6
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All AD patients will be recruited from the memory clinic of the VUmc Alzheimer Center Amsterdam. Annually, the Alzheimer Center receives 600 new patients.

Control subjects will be recruited through advertisements in newspapers and by means of flyers.

Pre-assignment

Screening details:

Inclusion criteria included:

Amyloid positive MCI or AD patients over the age of 50, with a MMSE above 17, able to tolerate scanning procedures. Or 50+ CN subjects able to tolerate scanning procedures

Period 1

Period 1 title	test
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Overall study
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Arm description:

NA

Arm type	18F-AV1451 scan
Investigational medicinal product name	[18F]AV1451
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

240 MBq via intravenous injection

Number of subjects in period 1	Overall study
Started	14
Completed	14

Period 2

Period 2 title	retest
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Overall study
Arm description: -	
Arm type	overall study
Investigational medicinal product name	[18F]AV1451
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

240 MBq via intravenous injection

Number of subjects in period 2	Overall study
Started	14
Completed	14

Baseline characteristics

Reporting groups

Reporting group title | test

Reporting group description:

8 MCI/AD subjects and 6 CN controls were recruited and scanned with [¹⁸F]AV1451

Reporting group values	test	Total	
Number of subjects	14	14	
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			
66,5 (51-81)			
Units: years			
median	66.5		
full range (min-max)	51 to 81	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	7	7	

End points

End points reporting groups

Reporting group title	Overall study
Reporting group description: NA	
Reporting group title	Overall study
Reporting group description: -	

Primary: test-retest variability of the previously defined simplified tracer kinetic model to quantify specific binding of [¹⁸F]AV-1451

End point title	test-retest variability of the previously defined simplified tracer kinetic model to quantify specific binding of [¹⁸ F]AV-1451
End point description: For all methods and across ROIs, TRT repeatability ranged from (median (IQR)) 0.84% (0.68–2.15) to 6.84% (2.99–11.50). TRT repeatability was good for all reference methods used, although semi-quantitative models (i.e. SUVr) performed marginally worse than quantitative models, for instance TRT repeatability of RPM: 1.98% (0.78–3.58) vs. SUVr _{80–100} : 3.05% (1.28–5.52), $p < 0.001$. The count for RPM method is provided, given that that is the most used method.	
End point type	Primary
End point timeframe: Test-retest repeatability	

End point values	Overall study	Overall study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: percentages	2	2		

Statistical analyses

Statistical analysis title	Main statistics
Statistical analysis description: TRT repeatability (%) was defined as $\frac{j_{\text{retest}} - \text{test}_j}{(\text{average}(\text{test}_{\text{pretest}}))100}$. For RPM and STRM2, TRT repeatability was assessed using BPND _{p1} , corresponding to DVR, in order to directly compare values to RLogan and SUVr methods. To compare TRT repeatability per reference region method (RLogan, RPM, SRTM2, SUVr for 3 time intervals) and to compare TRT repeatability per tau-specific region (MTL, LTL and global ROI), we used Kruskal–Wallis tests and post-hoc Mann–Whitney U testing with B	
Comparison groups	Overall study v Overall study

Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05 ^[1]
Method	Kruskal-wallis

Notes:

[1] - With Bonferroni correction

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

All adverse events, which occur 48 hours after administration of the radioactive tracer, and are reported spontaneously by the subject or observed by the investigator or his staff will be recorded.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	VUmc/CRB
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Dictionary version	1
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Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No no-serious adverse events were reported during the study

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2018	Wijzigingen in het studieprotocol: tijdens de screening wordt geen ECG en geen lab verricht, er wordt geen arterieel bloed meer afgenomen, ook patiënten met MCI op basis van de ziekte van Alzheimer worden geïncludeerd. Wijzigingen in de informatiebrief en het IC: aanpassingen voor de proefpersoon zoals boven beschreven, en vrouwen mogen tot 24u na de PET scan niet zwanger worden. Voor mannen gelden geen restricties.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31575335>