Clinical trial results:
Multicenter study to explore the impact of florbetaben (FBB) in change of diagnosis in patients who are evaluated for AD at the CMRR, and are eligible for analysis of CSF according to HAS recommendations, and in whom lumbar puncture is contraindicated or CSF results are ambiguous.

Summary

EudraCT number	2015-002606-37
Trial protocol	FR
Global end of trial date	29 September 2016

Results information

Result version number	v1 (current)
This version publication date	24 September 2017
First version publication date	24 September 2017

Trial information

Trial identification

Sponsor protocol code	FBB-01-02-15

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02681172
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Piramal Imaging Limited
Sponsor organisation address	Langstone Technology Park, Langstone Road, Havant, United Kingdom, P09 1SA
Public contact	South West Europe Medical Affairs , Piramal Imaging Ltd, 49 30461124615, rossella.gismondi@piramal.com
Scientific contact	South West Europe Medical Affairs , Piramal Imaging Ltd, 49 30461124615, rossella.gismondi@piramal.com

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	14 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2016
Global end of trial reached?	Yes
Global end of trial date	29 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To estimate the change in diagnosis comparing pre- and post-scan outcomes in the study population

Protection of trial subjects:

The trial was conducted in accordance with GCP Guidelines, the Declaration of Helsinki and according to national law. The trial started only after regulatory and ethical approval. Recruitment only started after the protocol was signed by the investigator. Only patients with informed consent were included in the study. All necessary insurances to guarantee compensation of patients in the case of adverse reactions were in place.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 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	France: 218
Worldwide total number of subjects	218
EEA total number of subjects	218

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)	66
From 65 to 84 years	136
85 years and over	16

Subject disposition

Recruitment

Recruitment details:

Eligible patients were evaluated for AD in tertiary memory centers and had a preliminary uncertain diagnosis after a prior comprehensive workup, according to recommendations from the French Health Authority.

Pre-assignment

Screening details:

At total of 218 patients were enrolled in the study. 13 patients did not receive a florbetaben injection or did not have at least one PET/CT image available (e.g. consent withdrawn), therefore, 205 patients were included in the full analysis set and were evaluated.

Pre-assignment period milestones

Number of subjects started	218
Number of subjects completed	205

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No FBB scan available: 13

Period 1

Period 1 title	Full Analysis Set (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Full Analysis Set
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Florbetaben
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

A single dose of 300 Megabecquerel (8.1 millicurie) Neuraceq was administered per subject. The applied FBB radioactive dose was ± 20%.

Number of subjects in period 1[1]	Full Analysis Set
Started	205
Completed	205

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: At total of 218 patients were enrolled in the study. For 13 patients no amyloid PET scans were available, therefore, 205 patients were evaluated in the full analysis set.

Baseline characteristics

Reporting groups

Reporting group title	Full Analysis Set

Reporting group description: -

Reporting group values	Full Analysis Set	Total	
Number of subjects	205	205	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	62	62	
From 65-84 years	129	129	
85 years and over	14	14	
Age continuous Units: years			
arithmetic mean	70.9		
standard deviation	± 9.7	-	
Gender categorical Units: Subjects			
Female	102	102	
Male	103	103	
MMSE score Units: MMSE			
arithmetic mean	22.1		
standard deviation	± 5.1	-	

End points

End points reporting groups

Reporting group title	Full Analysis Set
Reporting group description: -	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

To determine the impact of FBB Positron Emission Tomography (PET) imaging on clinical utility parameters in the study population.

Primary: Change of Diagnosis Comparing Pre- and Post-scan Outcomes

End point title	Change of Diagnosis Comparing Pre- and Post-scan

End point description:

End point type	Primary

End point timeframe:

Visit 1 (baseline evaluation) and Visit 3 (up to 6 months later)

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: For the full analysis set (n=205), 137 of the patients had a change in diagnosis post-FBB scan. Only frequency results are reported that correspond to a change of 66.8% (137/205) with a 95% confidence interval of 59.9% - 73.2%.

End point values	Full Analysis Set			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of subjects	137			

Statistical analyses

No statistical analyses for this end point

Secondary: Improved Level of Physician Confidence in Diagnosis at Visit 3

End point title	Improved Level of Physician Confidence in Diagnosis at Visit 3

End point description:

End point type	Secondary

End point timeframe:

Visit 1 (baseline evaluation) and Visit 3 (up to 6 months later)

End point values	Full Analysis Set			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of subjects	167			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Management Plan

End point title	Change of Management Plan

End point description:

End point type	Secondary

End point timeframe:

Visit 1 (baseline evaluation) and Visit 3 (up to 3 months later)

End point values	Full Analysis Set			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of subjects	164			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Positive FBB PET Scan

End point title	Number of Subjects With Positive FBB PET Scan

End point description:

End point type	Secondary

End point timeframe:

Visit 3 (up to 6 months after baseline evaluation)

End point values	Full Analysis Set			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of subjects	132			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Negative FBB PET Scans

End point title	Number of Subjects With Negative FBB PET Scans

End point description:

End point type	Secondary

End point timeframe:

Visit 3 (up to 6 months after baseline evaluation)

End point values	Full Analysis Set			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of subjects	73			

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects With Contraindicated or Failed Lumbar Puncture

End point title	Subjects With Contraindicated or Failed Lumbar Puncture

End point description:

End point type	Secondary

End point timeframe:

Visit 1 (baseline evaluation)

End point values	Full Analysis Set			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of subjects	45			

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects With Available CSF Analysis But Results Considered as Non-contributory by the Clinician

End point title	Subjects With Available CSF Analysis But Results Considered as Non-contributory by the Clinician

End point description:

End point type	Secondary

End point timeframe:

Visit 1 (baseline evaluation)

End point values	Full Analysis Set			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of subjects	87			

Statistical analyses

No statistical analyses for this end point

Secondary: Lumbar Punctures Refused by the Patient

End point title	Lumbar Punctures Refused by the Patient

End point description:

End point type	Secondary

End point timeframe:

Visit 1 (baseline evaluation)

End point values	Full Analysis Set			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of subjects	75			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events were captured for up to 7 days after the PET scan procedure.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18

Reporting groups	
Reporting group title	Safety Analysis Set

Reporting group description: -

Serious adverse events	Safety Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 205 (0.49%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Cerebellar infarction			
subjects affected / exposed	1 / 205 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety Analysis Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 205 (10.24%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm malignant			
subjects affected / exposed	1 / 205 (0.49%)		
occurrences (all)	1		
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	1 / 205 (0.49%)		
occurrences (all)	2		
Nervous system disorders			

Cerebellar infarction subjects affected / exposed occurrences (all)	1 / 205 (0.49%) 1		
Headache subjects affected / exposed occurrences (all)	1 / 205 (0.49%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 205 (0.49%) 1		
Inflammation subjects affected / exposed occurrences (all)	1 / 205 (0.49%) 1		
Injection site haematoma subjects affected / exposed occurrences (all)	2 / 205 (0.98%) 2		
Injection site pain subjects affected / exposed occurrences (all)	4 / 205 (1.95%) 4		
Injection site paraesthesia subjects affected / exposed occurrences (all)	5 / 205 (2.44%) 5		
Eye disorders Glaucoma subjects affected / exposed occurrences (all)	1 / 205 (0.49%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	1 / 205 (0.49%) 1		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	1 / 205 (0.49%) 1		
Pruritus			

subjects affected / exposed occurrences (all) Skin ulcer subjects affected / exposed occurrences (all)	1 / 205 (0.49%) 1 1 / 205 (0.49%) 1		
Psychiatric disorders Confusional state subjects affected / exposed occurrences (all)	 1 / 205 (0.49%) 1		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	 1 / 205 (0.49%) 1		
Musculoskeletal and connective tissue disorders Polymyalgia rheumatica subjects affected / exposed occurrences (all)	 1 / 205 (0.49%) 1		
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all)	 1 / 205 (0.49%) 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

None reported