Clinical trial results:
A prospective triple-arm, monocentric, phase-II explorative study on evaluation of diagnostic efficacy of the PET tracer (18F)-florbetaben (Neuraceq®) in patients with cardiac amyloidosis - FLORAMICAR 2

Summary

EudraCT number	2017-001660-38
Trial protocol	IT
Global end of trial date	31 July 2020

Results information

Result version number	v1 (current)
This version publication date	19 November 2021
First version publication date	19 November 2021
Summary attachment (see zip file)	Floramicar 2 trial report results (j.jcmg.2020.05.031.pdf)

Trial information

Trial identification

Sponsor protocol code	FLORAMICAR2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	FONDAZIONE TOSCANA 'GABRIELE MONASTERIO'
Sponsor organisation address	VIA TRESTE, PISA, Italy,
Public contact	U.O.C. Farmaceutica Ospedaliera, Fondazione Toscana Gabriele Monasterio, +39 0585493507, farmacisti@ftgm.it
Scientific contact	U.O.C. Farmaceutica Ospedaliera, Fondazione Toscana Gabriele Monasterio, +39 0585493507, farmacisti@ftgm.it

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	31 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the specificity of the tracer [18F]-Florbetaben for amyloid deposits in patients with cardiac amyloidosis AL and ATTR by comparison with a control group represented by patients with left-ventricular non-infiltrative hypertrophic cardiomyopathy.

Protection of trial subjects:

The study protocol conformed to the 1975 Declaration of Helsinki and was approved by the institutional ethics committee and by the Agenzia Italiana del Farmaco committee (EudraCT number: 2017- 001660-38); all patients provided written informed consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2017
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: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	40
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients <20 years of age and those with coronary artery disease, chronic liver diseases, and severe renal failure (estimated glomerular filtration rate <30 ml/min/1.73 m2) were excluded.

Pre-assignment

Screening details:

Forty patients with biopsy-proven diagnoses of CA (20 ALs and 20 ATTRs) and 20 patients referred to our tertiary center with the initial clinical suspicion of CA and then diagnosed with non-CA conditions were prospectively enrolled and underwent PET/CT with [18F]-florbetaben.

Period 1

Period 1 title	[18F]-Florbetaben PET/CT (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	AL CA

Arm description:

20 patients with biopsy-proven diagnoses of AL CA

Arm type	Experimental
Investigational medicinal product name	florbetaben
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

infusion of 300 MBq/ml of [18F]-Florbetaben
followed by a saline flush of 10 ml (1 ml/s);

Arm title	ATTRs CA

Arm description:

20 patients with biopsy-proven diagnoses of ATTRs CA

Arm type	Experimental
Investigational medicinal product name	florbetaben
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

infusion of 300 MBq/ml of [18F]-Florbetaben
followed by a saline flush of 10 ml (1 ml/s);

Arm title	No-CA

Arm description:

20 patients referred to our tertiary center with the initial clinical suspicion of CA and then diagnosed with non-CA conditions

Arm type	Experimental

Investigational medicinal product name	florbetaben
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

infusion of 300 MBq/ml of [18F]-Florbetaben
followed by a saline flush of 10 ml (1 ml/s);

Number of subjects in period 1	AL CA	ATTRs CA	No-CA
Started	20	20	20
Completed	20	20	20

Baseline characteristics

Reporting groups

Reporting group title	[18F]-Florbetaben PET/CT

Reporting group description: -

Reporting group values	[18F]-Florbetaben PET/CT	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
18-85	60	60	
Gender categorical Units: Subjects			
Female	17	17	
Male	43	43	

Subject analysis sets

Subject analysis set title	Results
Subject analysis set type	Full analysis

Subject analysis set description:

CLINICAL CHARACTERISTICS. Clinical characteristics and echocardiographic features of the subjects are summarized in Table 1. Representative histological patterns are shown in Figure 1. Patients with ATTR, compared with those with AL and non-CA, were older and presented with higher left atrial volume and left ventricular mass index (23.5 4.5 ml/m2; p ¼ 0.003 vs.
non-CA; and 129 39 g/m2; p ¼ 0.003 vs. non-CA, respectively). Furthermore, whereas patients with CA presented with worse diastolic dysfunction, no difference could be observed in terms of left ventricular systolic function when patients with CA were
compared with patients with non-CA.
CARDIAC PET/CT CHARACTERISTICS. Static images qualitative analysis. A total of 240 static cardiac scans (4 scans per patient: early; intermediate; late; and delayed) were evaluated by 2 independent observers. Images indicated a significant radiotracer myocardial uptake in 121 of 240 scans (50%).

Reporting group values	Results		
Number of subjects	60		
Age categorical Units: Subjects			
18-85	60		
Gender categorical Units: Subjects			
Female	17		
Male	43		

End points

End points reporting groups

Reporting group title	AL CA
Reporting group description:	
20 patients with biopsy-proven diagnoses of AL CA	

Reporting group title	ATTRs CA
Reporting group description:	
20 patients with biopsy-proven diagnoses of ATTRs CA	

Reporting group title	No-CA
Reporting group description:	
20 patients referred to our tertiary center with the initial clinical suspicion of CA and then diagnosed with non-CA conditions	

Subject analysis set title	Results
Subject analysis set type	Full analysis
Subject analysis set description:	
CLINICAL CHARACTERISTICS. Clinical characteristics and echocardiographic features of the subjects are summarized in Table 1. Representative histological patterns are shown in Figure 1. Patients with ATTR, compared with those with AL and non-CA, were older and presented with higher left atrial volume and left ventricular mass index (23.5 4.5 ml/m2; p ¼ 0.003 vs. non-CA; and 129 39 g/m2; p ¼ 0.003 vs. non-CA, respectively). Furthermore, whereas patients with CA presented with worse diastolic dysfunction, no difference could be observed in terms of left ventricular systolic function when patients with CA were compared with patients with non-CA. CARDIAC PET/CT CHARACTERISTICS. Static images qualitative analysis. A total of 240 static cardiac scans (4 scans per patient: early; intermediate; late; and delayed) were evaluated by 2 independent observers. Images indicated a significant radiotracer myocardial uptake in 121 of 240 scans (50%).	

Primary: This study aimed to test the diagnostic value of [18F]–florbetaben positron emission tomography (PET) in patients with suspicion of CA.

End point title	This study aimed to test the diagnostic value of [18F]–florbetaben positron emission tomography (PET) in patients with suspicion of CA.
End point description:	
A significant difference in retention index (RI) among patients with AL (red) and those with either ATTR (green) or non-CA (blue) is found within the 20- to 60-min period of observation. No significant difference was found between ATTR and non-CA RI during the whole dynamic acquisition.	
End point type	Primary
End point timeframe:	
only one acquisition	

End point values	AL CA	ATTRs CA	No-CA	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	20	20	
Units: SUVmean values				
number (not applicable)	4.70	1.45	1.60	

Attachments (see zip file)	j.jcmg.2020.05.031.pdf

Statistical analyses

Statistical analysis title	results
Comparison groups	ATTRs CA v AL CA v No-CA
Number of subjects included in analysis	60
Analysis specification	Post-hoc
Analysis type	non-inferiority[1]
P-value	< 0.001
Method	Chi-squared

Notes:

[1] - Normal distribution was assessed by the Kolmogorov-Smirnov test; continuous variables with normal distribution were presented as mean SD, whereas those with non-normal distribution were presented as median (interquartile
range [IQR]); and categorical variables were shown as percentages. Differences among groups were tested by 1-way analysis of variance on ranks (Kruskal-Wallis H test) or by chi-square test, as appropriate.

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: all study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	all patients
Reporting group description: -	

Serious adverse events	all patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	all patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)		

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 SAE OR AE REGISTERED DURING THE STUDY

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

na

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32771577