Clinical trial results:
[18F] FE-PE2I PET/CT study of Dopamine Transporters in Early Parkinsonian disease.

Summary

EudraCT number	2015-003045-26
Trial protocol	SE
Global end of trial date	11 June 2020

Results information

Result version number	v1 (current)
This version publication date	03 June 2021
First version publication date	03 June 2021

Trial information

Trial identification

Sponsor protocol code	Pearl-PD

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Umeå University Hospital, Umeå Sweden
Sponsor organisation address	NA, umeå, Sweden, 901 85
Public contact	Susanna Jakobson Mo, Dept of Radiology, Umeå University Hospital, Umeå Sweden, 46 90785 31 79, susanna.jakobson.mo@umu.se
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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	11 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 June 2020
Global end of trial reached?	Yes
Global end of trial date	11 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the diagnostic potential of [18F] FE PE2I PET in early stage untreated parkinsonian disease
To "head-to-head" compare the diagnostic accuracy of the index test (with [18F] FE PE2I PET / CT) with the reference test (123I-FP-Cit, DaTSCAN ™ SPECT/CT) in newly onset idiopathic parkinsonism

Protection of trial subjects:

All participants in the study gave their written and oral informed consent prior to inclusion. All imaging procedures were conducted by healthcare professionals at the hospital, and except for imaging with the index radiopharmaceuticval, all imaging procedures were conducted according to clinical routine practices. This study was approved my the regional Ethics Committee and the local radiation safety committee and the Swedish Medical Products Agency. Patients participating in this study were otherwise treated and followed up according to clinical routine. Collected data was pseudoized before statistical analysis.

Background therapy:

All patients and healthy subjects did a brain MRI.

Evidence for comparator: -

Actual start date of recruitment	25 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 77
Worldwide total number of subjects	77
EEA total number of subjects	77

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)	15
From 65 to 84 years	62
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study patients were recruited consecutively at first admission to the dept. of Neurology at Umeå University Hospital for newly onset idiopathic parkinsonism. Healthy controls were recruited via announcements in the local newspaper.

Pre-assignment

Screening details:

A first screening of patients' eligibility according to inclusion and exclusion criteria were made from the letter of referral, then a second screening was done by neurological assessment. Healthy controls were interviewed briefly by a phone call and if eligible, were then invited and asessed physically by a neurologist.

Period 1

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

Blinding implementation details:

The study is single-blind, as for image data analysis and evaluation takes place without knowledge of the study participant's clinical diagnosis or clinical condition or results of other imaging diagnostics or laboratory diagnostics.

Arms

Are arms mutually exclusive?	Yes
Arm title	Patients

Arm description:

Patients with recent onset of idiopathic parkinsonism

Arm type	Experimental
Investigational medicinal product name	[18F] FE PE2I PET
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

200 MBq at weight 70 kg (2.86 MBq / kg). If the weight is less than 70 kg, the dose is reduced in proportion to the weight.

Arm title	Healthy controls

Arm description:

Reference group

Arm type	Experimental
Investigational medicinal product name	[18F] FE PE2I PET
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

200 MBq at weight 70 kg (2.86 MBq / kg). If the weight is less than 70 kg, the dose is reduced in proportion to the weight.

Investigational medicinal product name	DaTSCAN™
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

185 MBq which gives an effective radiation dose of 4.4 mSv

Arm title	Healty control dosimetry

Arm description: -

Arm type	Experimental
Investigational medicinal product name	[18F] FE PE2I PET
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

200 MBq at weight 70 kg (2.86 MBq / kg). If the weight is less than 70 kg, the dose is reduced in proportion to the weight.

Number of subjects in period 1	Patients	Healthy controls	Healty control dosimetry
Started	35	37	5
Completed	32	36	5
Not completed	3	1	0
Consent withdrawn by subject	1	1	-
Procedure complication before study drug	1	-	-
Patient deceased due to cancer. Not AE in study.	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	77	77	
Age categorical Units: Subjects			
Adults (18-64 years)	15	15	
From 65-84 years	62	62	
Gender categorical Units: Subjects			
Female	35	35	
Male	42	42	

End points

End points reporting groups

Reporting group title	Patients
Reporting group description: Patients with recent onset of idiopathic parkinsonism	
Reporting group title	Healthy controls
Reporting group description: Reference group	
Reporting group title	Healty control dosimetry
Reporting group description: -	

Primary: Sensitivity, specificity and predictive value of PET / CT with 18F FE PE2I in the striatum and extrastriatalt in the brain

End point title	Sensitivity, specificity and predictive value of PET / CT with 18F FE PE2I in the striatum and extrastriatalt in the brain[1]
End point description: -Sensitivity, specificity and predictive value of PET / CT with 18F FE PE2I in the striatum and extrastriatalt in the brain -Statistical difference in the sensitivity and specificity of PET / CT with 18F FE PE2I (Index test) compared to SPECT / CT imaging with 123I-FPCit (reference test)	
End point type	Primary
End point timeframe: Two years after the imaging, when the clinical diagnosis is reassessed.	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint are not assessed for arm Dosimetry.

End point values	Patients	Healthy controls		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30		
Units: Numbers				
number (not applicable)	32	30		

Statistical analyses

Statistical analysis title	Statistical differences between groups
Statistical analysis description: Statistical differences between groups are analyzed by t-test and ANOVA or equivalent non-parametric tests depending on the type of data and group sizes. Relationship analyzes are performed with Pearson's correlation analysis or equivalent and regression models. Roc-analysis was used for calculation of predictive values.	
Comparison groups	Patients v Healthy controls

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 2015-12-04--2018-07-02	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	5.0
Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 74 (0.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 74 (16.22%)		
Injury, poisoning and procedural complications			
Discomfort and neck pain lying on the hard bunk in the PET-camera			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
Passing palpitations after drug administration			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
Diffuse aching in the body caused by lying in the PET camera			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
Cold hands	Additional description: Cold hands		

subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
Discomfort of mask	Additional description: The moulded mask squeezed over face		
subjects affected / exposed	2 / 74 (2.70%)		
occurrences (all)	2		
Passing numbness in right arm during scan	Additional description: Passing numbness in right arm during scan		
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
Pain in neck and occiput after scanning			
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
General disorders and administration site conditions			
Passing pricking sensation in the temple and tearing eye	Additional description: Passing pricking sensation in the temple and tearing eye		
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
Sensation of tiredness and diffuse "haziness" during the day after scanning	Additional description: Sensation of tiredness and diffuse "haziness" during the day after scanning		
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
Cough	Additional description: Fit of coughing during scan		
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhea	Additional description: Diarrhea the day after administration of 18F FE-PE2I. This was due to a known adverse reaction related to another medication		
subjects affected / exposed	1 / 74 (1.35%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2016	1. Change of the number of included healthy controls from 20 to 30, permitting additional recruitment of healthy controls. 2. In the original protocol version, an interim analysis was planned for evaluation of the correlation between regional cerebral flow measured with dynamic 18F FE-PE2I-PET (index test) compared to the reference test with 15O H2O-PET only using data from the first included subjects. With the amendment, theprotocol stated that this analysis should be done including all participants after competion.
11 October 2017	1. Prolongation of the inclusion period with 12 months 2. Change of procedure for perfusion imaging with 15O H2O-PET 3. Adjustment in the text pertaining interim analyses, permitting reporting of scientifically important findings after finalizing the baseline imaging period

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/29348315

http://www.ncbi.nlm.nih.gov/pubmed/30443684