Clinical trial results:
Non-inferiority study between molecular imaging of dopamine transporters obtained by the [123I]FP-CIT marker in SPECT and the [18F] LBT-999 biomarker in PET in the differential diagnosis between Parkinson’s Disease and Essential Tremor (DATTEP)

Summary

EudraCT number	2019-000247-27
Trial protocol	FR
Global end of trial date	02 August 2024

Results information

Result version number	v1 (current)
This version publication date	20 June 2026
First version publication date	20 June 2026

Trial information

Trial identification

Sponsor protocol code	ZX-2018-LBT999-DATTEP-3

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GE HealthCare
Sponsor organisation address	Pollards Wood, Nightingales Lane, Chalfont St Giles , Buckinghamshire, United Kingdom, HP8 4SP
Public contact	Victoria Haas, GE HealthCare, +33 6 29 86 53 56, victoria.haas@gehealthcare.com
Scientific contact	Victoria Haas, GE HealthCare, +33 6 29 86 53 56, victoria.haas@gehealthcare.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	20 February 2026
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate non-inferiority of [18F]LBT-999 Positron Emission Tomography (PET) imaging compared with [123I]FP-CIT Single Photon Emission Computed Tomography (SPECT) imaging in visual analysis for the differential diagnosis between subjects with typical Parkinson’s disease (PD) compared with subjects with essential tremor (ET).

Protection of trial subjects:

This study was conducted in full accordance with the Declaration of Helsinki, the Good Clinical Practice: Consolidated Guideline approved by the International Council for Harmonization (ICH), and any applicable national and local laws and regulations.
Investigators were responsible for performing the study in accordance with the protocol and ICH E6-Good Clinical Practice (GCP), for collecting, recording, and reporting the data accurately and properly. Agreement of the investigator to conduct and administer this study in accordance with the protocol was documented in separate study agreements with the Sponsor and other forms as required by national authorities in the country where the study centre was located.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2021
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: 156
Worldwide total number of subjects	156
EEA total number of subjects	156

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)	63
From 65 to 84 years	93
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 15 National Clinical Research Network for Parkinson’s Disease and Movement Disorders (NS-Park) centres in France from 01 December 2021 to 02 August 2024.

Pre-assignment

Screening details:

A total of 156 subjects provided informed consent and were screened for this study, out of which 152 were enrolled and randomised in this study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

Expert panel for image analysis were blinded in this study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Parkinson’s Disease

Arm description:

Subjects with Parkinson's disease received a single dose of investigational medicinal product (IMP) and comparator IMP on Visit 1. Subjects were then randomised to undergo [18F]LBT-999 PET imaging on Visit 1 followed by [123I]FP-CIT SPECT imaging on Visit 2 or undergo [123I]FP-CIT SPECT imaging on Visit 1 followed by [18F]LBT-999 PET imaging on Visit 2.

Arm type	Experimental
Investigational medicinal product name	GEH300022 (18F) Injection
Investigational medicinal product code	
Other name	[18F]LBT-999
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a single dose of [18F]LBT-999 at 3 megabecquerels per kilogram (MBq/kg) ±10% in a maximum volume of 10 millilitre (mL).

Investigational medicinal product name	DaTSCAN™
Investigational medicinal product code	
Other name	[123I]FP-CIT
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a single dose of [123I]FP-CIT at 185 MBq ±10% in a maximum volume of 5mL.

Arm title	Essential Tremor

Arm description:

Subjects with essential tremors received a single dose of IMP and comparator IMP on Visit 1. Subjects were then randomised to receive [18F]LBT-999 PET imaging on Visit 1 followed by [123I]FP-CIT SPECT imaging on Visit 2 or undergo [123I]FP-CIT SPECT imaging on Visit 1 followed by [18F]LBT-999 PET imaging on Visit 2.

Arm type	Experimental

Investigational medicinal product name	GEH300022 (18F) Injection
Investigational medicinal product code	
Other name	[18F]LBT-999
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a single dose of [18F]LBT-999 at 3 MBq/kg ±10% in a maximum volume of 10 mL.

Investigational medicinal product name	DaTSCAN™
Investigational medicinal product code	
Other name	[123I]FP-CIT
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a single dose of [123I]FP-CIT at 185 MBq ±10% in a maximum volume of 5mL.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Only the expert panel for image analysis were blinded in this study. Investigators, staff at the investigating centres, and the subjects taking part in the study were not blinded.

Number of subjects in period 1	Parkinson’s Disease	Essential Tremor
Started	77	79
Safety Population (SAF)	71	74
Full Analysis Set (FAS)	70	72
Completed	69	72
Not completed	8	7
Other	3	3
Adverse event	1	-
Screen failure	1	3
Withdrawal of consent	1	1
Withdrawal by subject	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Parkinson’s Disease
Reporting group description:	
Subjects with Parkinson's disease received a single dose of investigational medicinal product (IMP) and comparator IMP on Visit 1. Subjects were then randomised to undergo [18F]LBT-999 PET imaging on Visit 1 followed by [123I]FP-CIT SPECT imaging on Visit 2 or undergo [123I]FP-CIT SPECT imaging on Visit 1 followed by [18F]LBT-999 PET imaging on Visit 2.	
Reporting group title	Essential Tremor
Reporting group description:	
Subjects with essential tremors received a single dose of IMP and comparator IMP on Visit 1. Subjects were then randomised to receive [18F]LBT-999 PET imaging on Visit 1 followed by [123I]FP-CIT SPECT imaging on Visit 2 or undergo [123I]FP-CIT SPECT imaging on Visit 1 followed by [18F]LBT-999 PET imaging on Visit 2.	

Reporting group values	Parkinson’s Disease	Essential Tremor	Total
Number of subjects	77	79	156
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	40	23	63
From 65-84 years	37	56	93
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	62.5	65.9	
standard deviation	± 9.4	± 10.4	-
Gender categorical Units: Subjects			
Female	26	32	58
Male	51	47	98

End points

End points reporting groups

Reporting group title	Parkinson’s Disease

Reporting group description:

Subjects with Parkinson's disease received a single dose of investigational medicinal product (IMP) and comparator IMP on Visit 1. Subjects were then randomised to undergo [18F]LBT-999 PET imaging on Visit 1 followed by [123I]FP-CIT SPECT imaging on Visit 2 or undergo [123I]FP-CIT SPECT imaging on Visit 1 followed by [18F]LBT-999 PET imaging on Visit 2.

Reporting group title	Essential Tremor

Reporting group description:

Subjects with essential tremors received a single dose of IMP and comparator IMP on Visit 1. Subjects were then randomised to receive [18F]LBT-999 PET imaging on Visit 1 followed by [123I]FP-CIT SPECT imaging on Visit 2 or undergo [123I]FP-CIT SPECT imaging on Visit 1 followed by [18F]LBT-999 PET imaging on Visit 2.

Subject analysis set title	PET scan
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who underwent a PET scan either at Visit 1 or Visit 2.

Subject analysis set title	SPECT scan
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who underwent a SPECT scan at Visit 1 or Visit 2.

Primary: Proportion of Subjects With Parkinson’s Disease Whose Images Were Sensitive (Interpreted as Pathological)

End point title	Proportion of Subjects With Parkinson’s Disease Whose Images Were Sensitive (Interpreted as Pathological)

End point description:

Sensitivity was defined as proportion of subjects with PD whose images were interpreted as pathological. Independent blinded image evaluation of PET and SPEC images was conducted by 5 expert readers in France and Switzerland. For the initial assessment, readers were blinded to subject sex and age to prevent bias (i.e., without demographic data). In a subsequent confirmatory assessment, readers re-evaluated the images with access to subject sex, age and their original conclusion (i.e., with demographic data). In this endpoint, proportion of subjects with sensitivity, when assed with demographic data and when assessed without demographic data has been reported. Analysis was performed on the FAS, which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable. Here, 'number of subjects analysed' = subjects with evaluable data for this endpoint.

End point type	Primary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	70		
Units: proportion of subjects				
number (confidence interval 95%)				
Without Demographic Data	0.943 (0.868 to 0.982)	1.000 (0.958 to 1.000)		
With Demographic Data	0.943 (0.868 to 0.982)	1.000 (0.958 to 1.000)		

Statistical analyses

Statistical analysis title	PET vs SPECT (Without Demographic Data)
Comparison groups	PET scan v SPECT scan
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0148
Method	Restricted maximum likelihood estimation
Parameter estimate	Difference Observed
Point estimate	-0.057
Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	-0.141

Statistical analysis title	PET vs SPECT (With Demographic Data)
Comparison groups	PET scan v SPECT scan
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0148
Method	Restricted maximum likelihood estimation
Parameter estimate	Difference Observed
Point estimate	-0.057
Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	-0.141

Primary: Proportion of Subjects With Essential Tremor Whose Images Were Specific (Interpreted as Normal)

End point title	Proportion of Subjects With Essential Tremor Whose Images Were Specific (Interpreted as Normal)

End point description:

Specificity was defined as proportion of subjects with ET whose images were interpreted as normal. Independent blinded image evaluation of PET and SPEC images was conducted by 5 expert readers in France. For the initial assessment, readers were blinded to subject sex and age to prevent bias (i.e., without demographic data). In a subsequent confirmatory assessment, readers re-evaluated the images with access to subject sex, age and their original conclusion (i.e., with demographic data). In this endpoint, proportion of subjects with specificity, when assed with demographic data and when assessed without demographic data has been reported. Analysis was performed on the FAS, which included all

subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable. Here, 'number of subjects analysed' = subjects with evaluable data for this endpoint.

End point type	Primary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	70		
Units: proportion of subjects				
number (confidence interval 95%)				
Without Demographic Data	1.000 (0.959 to 1.000)	0.625 (0.509 to 0.731)		
With Demographic Data	1.000 (0.959 to 1.000)	0.611 (0.495 to 0.718)		

Statistical analyses

Statistical analysis title	PET vs SPECT (Without Demographic Data)
Comparison groups	PET scan v SPECT scan
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Restricted maximum likelihood estimation
Parameter estimate	Difference Observed
Point estimate	0.375
Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	0.221

Statistical analysis title	PET vs SPECT (With Demographic Data)
Comparison groups	PET scan v SPECT scan
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	Restricted maximum likelihood estimation
Parameter estimate	Difference Observed
Point estimate	0.389

Confidence interval	
level	Other: 97.5 %
sides	1-sided
lower limit	0.233

Secondary: Threshold of Specific Binding Ratio (SBR) and Putaminal Index

End point title	Threshold of Specific Binding Ratio (SBR) and Putaminal Index

End point description:

Putaminal Index is a measure specific to DaTsoft-3D. It accounts for the minimum uptake in the left/right posterior putamina, striatal contrast and participant age. The discrimination thresholds for the SBR between the right and left putamen, right and left posterior part of the putamen and the putaminal index (Parkinson index), determined using the minimum SBR values are reported. Threshold with Wald-type 2-sided 95% confidence interval (delta method approximation) was determined by maximum correct classification rate and maximum Younden index. Analysis was performed on the FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint. Threshold of the minimum value of the binding potential between right and left putamen, threshold of the minimum value of the binding potential between right and left posterior of putamen and threshold of the Putaminal Index (Parkinson Index) is reported for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Day 53

End point values	PET scan			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: Ratio				
number (confidence interval 95%)				
Right and left putamen	2.33 (1.98 to 2.68)			
Right and left posterior part of putamen	1.71 (1.21 to 2.21)			
Putaminal Index (Parkinson Index)	0.88 (0.16 to 1.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subject Comfort as Assessed Using a Visual Analog Scale (VAS)

End point title	Subject Comfort as Assessed Using a Visual Analog Scale (VAS)

End point description:

Subject comfort was measured using a VAS for each type of scan ([18F]LBT-999 PET or [123I]FP-CIT SPECT). VAS scale ranged from 0 to 10, where 0 signifies very uncomfortable to 10 being very comfortable. Analysis was performed on FAS population which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable. Here, 'number of subjects analysed' = subjects in the FAS population without whole-body dosimetry participation.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	132	132		
Units: score on a scale				
arithmetic mean (standard deviation)	8.9 (± 1.5)	8.4 (± 1.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Diagnostic Confidence as Assessed Using Image Quality

End point title	Diagnostic Confidence as Assessed Using Image Quality

End point description:

Diagnostic confidence in the interpretation of radiopharmaceutical IMP binding for the caudate nuclei and putamen of each subject for each type of scan ([18F]LBT-999 PET or [123I]FP-CIT SPECT) was reported. This confidence was assessed for each reviewer using criteria scales for image quality and interpretation confidence. Image quality was assessed as "Not Readable" (artifacts, low contrast, low signal level or poor focus seriously compromise image interpretation) , "Readable but sub-optimal" (artifacts or suboptimal signal to noise ratio may somewhat reduce confidence of interpretation) and "Readable" (artifacts, if evident, present no obstacle to interpretation). Analysis was performed on the FAS, which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable. The data reported applies for analyses conducted both with and without demographic data.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: subjects				
Reader 1: Not Readable	0	2		
Reader 1: Readable but Sub-Optimal	9	89		
Reader 1: Readable	133	51		
Reader 2: Not Readable	0	0		
Reader 2: Readable but Sub-Optimal	3	21		
Reader 2: Readable	139	121		
Reader 3: Not Readable	0	0		
Reader 3: Readable but Sub-Optimal	0	34		
Reader 3: Readable	142	108		
Reader 4: Not Readable	0	8		
Reader 4: Readable but Sub-Optimal	0	62		

Reader 4: Readable	142	72		
Reader 5: Not Readable	0	0		
Reader 5: Readable but Sub-Optimal	0	30		
Reader 5: Readable	142	112		

Statistical analyses

No statistical analyses for this end point

Secondary: Diagnostic Confidence as Assessed Using Interpretation Confidence

End point title	Diagnostic Confidence as Assessed Using Interpretation Confidence

End point description:

Diagnostic confidence in the interpretation of radiopharmaceutical IMP binding for the caudate nuclei and putamen of each subject for each type of scan ([18F]LBT-999 PET or [123I]FP-CIT SPECT) was reported. This confidence was assessed for each reviewer using criteria scales for image quality and interpretation confidence. In this endpoint, interpretation confidence, when assed with demographic data and when assessed without demographic data has been reported. Interpretation confidence was assessed as "Low" (no or limited capacity to assess the normal or abnormal), "Moderate" (normality or abnormality can be likely established) and "Strong" (normality or abnormality can be well established). Analysis was performed on the FAS, which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: subjects				
Reader 1-Without Demo data: Low	0	4		
Reader 1-Without Demo data: Moderate	8	53		
Reader 1-Without Demo data: Strong	134	83		
Reader 2-Without Demo data: Low	12	24		
Reader 2-Without Demo data: Moderate	24	32		
Reader 2-Without Demo data: Strong	106	86		
Reader 3-Without Demo data: Low	0	3		
Reader 3-Without Demo data: Moderate	7	37		
Reader 3-Without Demo data: Strong	135	102		
Reader 4-Without Demo data: Low	1	31		
Reader 4-Without Demo data: Moderate	1	49		
Reader 4-Without Demo data: Strong	140	54		
Reader 5-Without Demo data: Low	1	4		
Reader 5-Without Demo data: Moderate	3	33		
Reader 5-Without Demo data: Strong	138	105		
Reader 1-With Demo data: Low	1	4		
Reader 1-With Demo data: Moderate	5	42		
Reader 1-With Demo data: Strong	136	94		

Reader 2-With Demo data: Low	6	20		
Reader 2-With Demo data: Moderate	21	31		
Reader 2-With Demo data: Strong	115	91		
Reader 3-With Demo data: Low	0	3		
Reader 3-With Demo data: Moderate	7	37		
Reader 3-With Demo data: Strong	135	102		
Reader 4-With Demo data: Low	1	29		
Reader 4-With Demo data: Moderate	1	49		
Reader 4-With Demo data: Strong	140	56		
Reader 5-With Demo data: Low	1	8		
Reader 5-With Demo data: Moderate	3	30		
Reader 5-With Demo data: Strong	138	104		

Statistical analyses

No statistical analyses for this end point

Secondary: Sensitivity and Specificity of Diagnosis by the Specific Binding Ratio of Different Brain Areas

End point title	Sensitivity and Specificity of Diagnosis by the Specific Binding Ratio of Different Brain Areas

End point description:

The quantitative performance of [18F]LBT-999 PET and [123I]FP-CIT SPECT was evaluated by the sensitivity and specificity of each imaging method for classifying images as normal (consistent with ET) or pathological (consistent with PD), based on the discrimination thresholds for the SBR determined for the putamen, posterior part of the putamen and putaminal index (Parkinson index). Analysis was performed on the FAS, which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable. Here, "n" = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: ratio				
number (confidence interval 95%)				
Putamen: Sensitivity (n=70,70)	0.829 (0.727 to 0.904)	0.929 (0.849 to 0.973)		
Putamen: Specificity (n=72,72)	0.944 (0.871 to 0.982)	0.972 (0.911 to 0.995)		
Posterior Part of Putamen: Sensitivity (n=70,70)	0.900 (0.812 to 0.955)	0.943 (0.868 to 0.982)		
Posterior Part of Putamen: Specificity (n=72,72)	1.000 (0.959 to 1.000)	0.986 (0.933 to 0.999)		
Putaminal Index: Sensitivity (n=70,70)	0.871 (0.777 to 0.935)	0.943 (0.868 to 0.982)		
Putaminal Index: Specificity (n=72,72)	1.000 (0.959 to 1.000)	0.986 (0.933 to 0.999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Coefficient of Variation (CV) of the Specific binding ratio

End point title	Coefficient of Variation (CV) of the Specific binding ratio

End point description:

The CV of the SBR measurements (putamen and posterior part of the putamen) and putaminal index (Parkinson index) for both [18F]LBT-999 PET and [123I]FP-CIT SPECT was utilised as a measure of precision. The CV was calculated as the ratio between standard deviation (SD) and the mean. Analysis was performed on the FAS, which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: ratio				
number (not applicable)				
Putamen	52.5	66.5		
Posterior Part of the Putamen	73.7	85.5		
Putaminal Index (Parkinson Index)	88.3	98.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With any Adverse Events (AE), Treatment-emergent AE (TEAE), Serious TEAE and Severe TEAE

End point title	Number of Subjects With any Adverse Events (AE), Treatment-emergent AE (TEAE), Serious TEAE and Severe TEAE

End point description:

An AE was defined as any harmful occurrence in a person who was the subject of research involving humans, whether or not the occurrence was related to the research or to the product to which the research related. TEAE was defined as any AE that occurred during treatment which was absent before treatment, or worsened compared to the pre-treatment state. An SAE was defined as any AE that: resulted in death; was life-threatening; required inpatient hospitalisation or prolongation of existing hospitalisation; resulted in persistent or long-lasting disability or incapacity; was a congenital anomaly or malformation; was another significant medical event. Severe TEAE was an event that prevented normal everyday activities. Analysis was performed on SAF. The SAF included all subjects who signed an informed consent form, were randomised and had at least 1 scan performed.

End point type	Secondary

End point timeframe:

Baseline up to Day 53

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	144	145		
Units: subjects				
Any AE	7	5		
TEAE	7	5		
Serious TEAE	0	0		
Severe TEAE	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With any Adverse AE, TEAE, Serious TEAE and Severe TEAE

End point title	Percentage of Subjects With any Adverse AE, TEAE, Serious TEAE and Severe TEAE

End point description:

An AE was defined as any harmful occurrence in a person who was the subject of research involving humans, whether or not the occurrence was related to the research or to the product to which the research related. TEAE was defined as any AE that occurred during treatment which was absent before treatment, or worsened compared to the pre-treatment state. An SAE was defined as any AE that: resulted in death; was life-threatening; required inpatient hospitalisation or prolongation of existing hospitalisation; resulted in persistent or long-lasting disability or incapacity; was a congenital anomaly or malformation; was another significant medical event. Severe TEAE was an event that prevented normal everyday activities. Analysis was performed on SAF. The SAF included all subjects who signed an informed consent form, were randomised and had at least 1 scan performed.

End point type	Secondary

End point timeframe:

Baseline up to Day 53

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: percentage of subjects				
number (not applicable)				
Any AE	7.6	4.9		
TEAE	7.6	4.9		
Serious TEAE	0	0		
Severe TEAE	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Subject Dosimetry by Organ after PET Scan

End point title	Subject Dosimetry by Organ after PET Scan

End point description:

Internal radiation dosimetry measurements (absorbed organ dose and effective dose) for [18F]LBT-999 PET were summarised by organ for subjects who took part in the whole-body dosimetry. Analysis was performed on randomised population (RAN), which included all subjects who signed an informed consent form and were randomised. Here, 'number of subjects analysed' = subjects with available data for this endpoint. Absorbed dose data (per unit administered activity) was reported for brain, heart, kidney, liver, lungs and red bone marrow, and effective dose was reported for the whole body. Unit of measure for "Effective dose - Whole Body" category is millisieverts per megabecquerel (mSv/MBq).

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: milligray by megabecquerel (mGy/MBq)				
arithmetic mean (standard deviation)				
Absorbed Dose - Brain	0.0143 (± 0.0018)			
Absorbed Dose - Heart	0.0174 (± 0.0022)			
Absorbed Dose - Kidney	0.0210 (± 0.0028)			
Absorbed Dose - Liver	0.0147 (± 0.0016)			
Absorbed Dose - Lungs	0.0185 (± 0.0019)			
Absorbed Dose - Red Bone Marrow	0.0241 (± 0.0034)			
Effective Dose - Whole-Body	0.0178 (± 0.0028)			

Statistical analyses

No statistical analyses for this end point

Secondary: Caregiver Dosimetry Equivalent Doses to Skin and Tissues

End point title	Caregiver Dosimetry Equivalent Doses to Skin and Tissues

End point description:

The dosimetry equivalent doses to the skin and tissue of caregivers are presented by scan type and task (preparation and injection). Two dosimetry values were collected: the personal dose equivalent at a depth of 0.07 millimetre (mm) (Hp (0.07)) (operational dose for individual monitoring to assess the dose to skin, hands and feet) and the personal dose equivalent at a depth of 10 mm (Hp (10)) (operational dose for individual monitoring to assess the effective dose). Analysis was performed on RAN, which included all subjects who signed an informed consent form and were randomised. Here, 'number of subjects analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: mGy/MBq				
arithmetic mean (standard deviation)				
Operational: Hp (0.07) - Preparation (n=24,24)	0.1281 (± 0.1063)	0.0278 (± 0.0314)		
Operational: Hp (0.07) - Injection (n=23,24)	0.0804 (± 0.0669)	0.0745 (± 0.0661)		
Operational: Hp (10) - Preparation (n=24,24)	0.1191 (± 0.1078)	0.0243 (± 0.0265)		
Operational: Hp (10) - Injection (n=23,24)	0.0586 (± 0.0510)	0.0514 (± 0.0422)		
Extremity: Hp (0.07) - Preparation (n=23,22)	139.9 (± 67.0)	21.4 (± 19.3)		
Extremity: Hp (0.07) - Injection (n=13,22)	25.2 (± 5.3)	7.2 (± 4.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation Coefficient between Total Score of MDS-UPDRS Part III and Specific Binding Ratio and Parkinson Index

End point title	Correlation Coefficient between Total Score of MDS-UPDRS Part III and Specific Binding Ratio and Parkinson Index

End point description:

Correlation coefficients between total motor Movement Disorder Society – Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III score and the minimum value of the SBR between the right and left putamen, the minimum value of the SBR between the right and left posterior part of the putamen and putaminal index (Parkinson Index) are reported for PD participants in this endpoint. The correlation coefficient and its 95% CI between MDS-UPDRS Part III motor score and SBR were calculated for each scan type. The two CIs were obtained and then compared. Analysis was performed on the FAS, which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	69		
Units: Spearman correlation coefficient				
number (confidence interval 95%)				
Putamen	-0.276 (-0.482 to -0.042)	-0.133 (-0.359 to 0.107)		
Posterior Part of the Putamen	-0.116 (-0.343 to 0.124)	-0.09 (-0.32 to 0.149)		
Putaminal Index (Parkinson Index)	-0.102 (-0.331 to 0.138)	-0.093 (-0.323 to 0.147)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Whose Images Were Correctly Diagnosed

End point title	Number of Subjects Whose Images Were Correctly Diagnosed

End point description:

The accuracy of each imaging method for classifying images as normal (consistent with ET) or pathological (consistent with PD) was determined based on blinded visual interpretations performed by 5 independent nuclear medicine reviewers (majority read). For the initial assessment, readers were blinded to subject sex and age to prevent bias (i.e., without demographic data). In a subsequent confirmatory assessment, readers re-evaluated the images with access to subject sex, age and their original conclusion (i.e., with demographic data). Analysis was performed on the FAS, which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: subjects				
Without Demographic Data	138	115		
With Demographic Data	138	114		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Whose Images Were Correctly Diagnosed

End point title	Percentage of Subjects Whose Images Were Correctly Diagnosed

End point description:

The accuracy of each imaging method for classifying images as normal (consistent with ET) or pathological (consistent with PD) was determined based on blinded visual interpretations performed by 5 independent nuclear medicine reviewers (majority read). For the initial assessment, readers were blinded to subject sex and age to prevent bias (i.e., without demographic data). In a subsequent confirmatory assessment, readers re-evaluated the images with access to subject sex, age and their original conclusion (i.e., with demographic data). Analysis was performed on the FAS, which included all subjects who signed informed consent form with both [18F]LBT-999 PET and [123I]FP-CIT SPECT scans performed and interpretable.

End point type	Secondary

End point timeframe:

At Visit 1 (anytime between Day 7 and Day 45) and Visit 2 (anytime between Day 14 and Day 52)

End point values	PET scan	SPECT scan		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	142	142		
Units: percentage of subjects				
number (confidence interval 95%)				
Without Demographic Da	0.972 (0.933 to 0.991)	0.810 (0.739 to 0.868)		
With Demographic Data	0.972 (0.933 to 0.991)	0.803 (0.731 to 0.862)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 53

Adverse event reporting additional description:

Reported adverse events (AE) are treatment emergent adverse events (TEAEs). Analysis was performed on SAF. The SAF included all subjects who signed an informed consent form, were randomised and had at least 1 scan performed.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Parkinson’s Disease

Reporting group description:

Subjects with Parkinson's disease received a single dose of IMP and comparator IMP on Visit 1. Subjects were then randomised to undergo [18F]LBT-999 PET imaging on Visit 1 followed by [123I]FP-CIT SPECT imaging on Visit 2 or undergo [123I]FP-CIT SPECT imaging on Visit 1 followed by [18F]LBT-999 PET imaging on Visit 2.

Reporting group title	Essential Tremor

Reporting group description:

Subjects with essential tremors received a single dose of IMP and comparator IMP on Visit 1. Subjects were then randomised to undergo [18F]LBT-999 PET imaging on Visit 1 followed by [123I]FP-CIT SPECT imaging on Visit 2 or undergo [123I]FP-CIT SPECT imaging on Visit 1 followed by [18F]LBT-999 PET imaging on Visit 2.

Serious adverse events	Parkinson’s Disease	Essential Tremor	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 71 (0.00%)	0 / 74 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Parkinson’s Disease	Essential Tremor	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 71 (11.27%)	3 / 74 (4.05%)	
Surgical and medical procedures			
Dental operation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	4 / 71 (5.63%)	2 / 74 (2.70%)	
occurrences (all)	4	2	
Taste disorder			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Injection site paraesthesia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	
occurrences (all)	2	0	
Dry mouth			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 74 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2021	Protocol was amended to implement the following changes: • Addition of an IMP manufacturing site in Toulouse. • Change of principal investigator in Marseille. • Change of a member on the monitoring committee.
10 February 2022	Protocol was amended to implement the following changes: • Addition of 2 participating sites. • Update of the list of investigators. • Addition of a secondary objective and an associated endpoint for the MDS-UPDRS Part III scale. • Addition of a non-inclusion criterion. • Addition of the Tremor Research Group Essential Tremor Rating Assessment Scale. • Addition of the Temperament and Character Inventory (TCI) questionnaire. • Addition of an exploratory secondary objective and an exploratory associated endpoint for the TCI. • Further details were provided for vital signs data collection. The following update was made to text in the protocol: The subject's vital signs (blood pressure, heart rate, respiratory rate, body temperature) are measured after approximately 3 to 5 minutes in the supine position,10 minutes ±5 minutes before injection and 25 minutes ±5 minutes after injection.
09 June 2022	Protocol was amended to implement the following changes: • Change of a member of the safety committee. • Addition of an investigational medicinal product manufacturing site in Orsay. • Exploratory objective/endpoint updated to ancillary objective.
19 September 2022	Protocol was amended to implement the following changes: • Addition of investigating centre. • Change of principal investigator for Centre Eugene Marquis (Nuclear Medicine Department).
02 December 2022	Protocol was amended to implement the following changes: • Change of a member of the Safety Committee. • Addition of an investigating centre. • Removal of annexes and creation of independent documents. • Clarification of the number of subjects for image reviews. • Addition of co-investigators.
21 April 2023	Protocol was amended to implement the following changes: • Increase in the total number of subjects to be included. • Modification of statistical analysis for the co-primary endpoints. • Clarification of secondary evaluation criteria. • Addition of a composite secondary objective. • Clarification of 2 eligibility criteria. • Addition of an LBT manufacturing centre in Strasbourg. • Addition of 3 investigating centres in Lyon, Strasbourg and Dijon. • Addition of 2 new co-investigators at the Bordeaux centre. • Removal of 1 co-investigator at the Rennes centre. • Modification of statistical analyses for secondary evaluation criteria. • Clarification of the analysis of the ancillary study. • Clarification of the quantification method. • Accuracy of the visit window for study data tabulation model (STDM). • Other minor changes to the text of the protocol.

11 October 2023	Protocol was amended to implement the following changes: • Addition of 1 investigating site (Avicenne Hospital Centre). • Extension of study duration (recruitment period and end of study). • Investigator list update.
17 April 2024	Protocol was amended to implement the following changes: • Modification of inclusion criteria. • Modification of main investigator. • Updated study project team.
21 June 2024	Protocol was amended to implement the following changes: • Change of study sponsor from Zionexa to GE HealthCare Limited.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported