Clinical trial results:
18F-MFBG PET imaging of the norepinephrine transporter in neural crest and neuroendocrine tumors: a phase I PET/CT study

Summary

EudraCT number	2019-003872-37
Trial protocol	BE
Global end of trial date	13 July 2022

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	S63142

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04258592
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospitals Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Christophe Deroose, University Hospitals Leuven, 0032 16343715, christophe.deroose@uzleuven.be
Scientific contact	Christophe Deroose, University Hospitals Leuven, 0032 16343715, christophe.deroose@uzleuven.be

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	15 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 July 2022
Global end of trial reached?	Yes
Global end of trial date	13 July 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Evaluate the potential of 18F-MFBG as a PET hNET imaging agent in patients with neural crest and neuroendocrine tumors

Protection of trial subjects:

Adult female participants of childbearing potential must agree to use highly effective medically accepted contraceptive methods to prevent pregnancy. Minor female participants of childbearing potential that are sexually active, may only participate if they already use highly effective contraceptive methods. A serum and urinary hCG test is performed prior to 18F-MFBG administration. Male participants should refrain from sexual activity for 90 days after injection, or otherwise use a condom to prevent pregnancy, except for vasectomized. Sperm donation or preservation is also prohibited during this 90-day interval.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	07 February 2020
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	Belgium: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	1
Adolescents (12-17 years)	0
Adults (18-64 years)	4

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were either contacted at the time when they were scheduled for 123I-MIBG imaging or they were recruited by members of the study team during their contact with the patient.

Pre-assignment

Screening details:

Patients, aged 1 year or older, with neural crest tumors (or neuroendocrine tumors) with routine clinical 123I-MIBG imaging (planar + SPECT) performed in the previous six months or scheduled within three months were enrolled.

Pre-assignment period milestones

Number of subjects started	7[1]
Number of subjects completed	6

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One patient underwent a screening visit, but withdrew consent before the actual inclusion visit and was therefore not enrolled in the trial, as defined in the study protocol.

Period 1

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

Blinding implementation details:

NA

Arms

Arm title	Patients

Arm description: -

Arm type	Experimental
Investigational medicinal product name	[18F]MFBG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

4 MBq/kg (adult participants); 2 MBq/kg (minor participants)
1 day, single dose
no treatment: diagnostic scanning

Number of subjects in period 1	Patients
Started	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)
Reporting group description:	
Neural crest tumor patients with a routine clinical 123I-MIBG imaging scintigraphy performed within 6 months prior to inclusion or scheduled within 3 months after inclusion.	

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
Children (2-11 years)	1	1	
Adults (18-64 years)	4	4	
From 65-84 years	1	1	
Gender categorical Units: Subjects			
Female	2	2	
Male	4	4	

End points

End points reporting groups

Reporting group title	Patients
Reporting group description: -	
Subject analysis set title	123I-MIBG
Subject analysis set type	Full analysis
Subject analysis set description: Routine clinical 123I-MIBG scintigraphy	
Subject analysis set title	18F-MFBG 1h p.i.
Subject analysis set type	Full analysis
Subject analysis set description: 18F-MFBG study PET scan at 1 hour post-injection (p.i.)	
Subject analysis set title	18F-MFBG 2h p.i.
Subject analysis set type	Full analysis
Subject analysis set description: 18F-MFBG study PET scan at 2 hour post-injection (p.i.)	
Subject analysis set title	18F-MFBG 3h p.i.
Subject analysis set type	Full analysis
Subject analysis set description: 18F-MFBG study PET scan at 3 hour post-injection (p.i.)	
Subject analysis set title	Adult patients
Subject analysis set type	Sub-group analysis
Subject analysis set description: Adult patients with dynamic 18F-MFBG study PET scan	
Subject analysis set title	Phaeochromocytoma patients
Subject analysis set type	Sub-group analysis
Subject analysis set description: Adult phaeochromocytoma patients with dynamic 18F-MFBG study PET scan	

Primary: Primary: Lesion detection rate

End point title	Primary: Lesion detection rate
End point description:	
End point type	Primary
End point timeframe: End of study	

End point values	123I-MIBG	18F-MFBG 1h p.i.	18F-MFBG 2h p.i.	18F-MFBG 3h p.i.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	5	5
Units: Detection rate (%)				
number (not applicable)				
Patient 1	33.8	98.7	98.7	89.6
Patient 2	86.7	100.0	100.0	100.0
Patient 3	100.0	100.0	100.0	100.0
Patient 4	57.4	100.0	.0	.0

Patient 5	50.0	100.0	75.0	75.0
Patient 6	38.2	100.0	100.0	100.0

Statistical analyses

Statistical analysis title	Lesion detection rate comparison
Comparison groups	123I-MIBG v 18F-MFBG 1h p.i.
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.043
Method	Wilcoxon (Mann-Whitney)

Secondary: Pharmacokinetics

End point title	Pharmacokinetics

End point description:

End point type	Secondary

End point timeframe:

End of study

End point values	Adult patients	Phaeochromocytoma patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	4		
Units: VT(ml/cm³)				
median (full range (min-max))	29.0 (8.4 to 144.8)	37.4 (18.0 to 144.8)		

Attachments (see zip file)	Pharmacokinetics.jpg

Statistical analyses

No statistical analyses for this end point

Secondary: Normal organ uptake (as a function of time)

End point title	Normal organ uptake (as a function of time)

End point description:

End point type	Secondary

End point timeframe:
End of study

End point values	123I-MIBG	18F-MFBG 1h p.i.	18F-MFBG 2h p.i.	18F-MFBG 3h p.i.
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	4	3	3
Units: SUVmean				
arithmetic mean (standard deviation)				
Salivary glands	2.42 (± .0)	9.19 (± 3.38)	8.38 (± 4.39)	8.31 (± 4.72)
Liver (left lobe)	3.01 (± 1.02)	6.59 (± 2.14)	4.94 (± 2.78)	4.05 (± 2.16)
Liver (right lobe)	1.87 (± 0.89)	4.22 (± 1.67)	2.96 (± 1.47)	2.47 (± 1.13)
Thyroid	2.52 (± .0)	6.56 (± 1.89)	5.29 (± 0.74)	5.07 (± 0.60)
Adrenals	2.77 (± 1.38)	4.32 (± 2.28)	4.18 (± 3.05)	4.53 (± 3.58)
Left ventricle wall	2.22 (± 1.42)	6.60 (± 4.15)	4.72 (± 3.89)	4.04 (± 3.35)
Kidneys	0.74 (± 0.29)	2.27 (± 0.75)	1.52 (± 0.29)	1.22 (± 0.47)
Pancreas	1.12 (± 0.85)	2.91 (± 2.06)	1.70 (± 1.57)	1.29 (± 1.15)
Bowel	1.02 (± 0.50)	2.40 (± 0.86)	1.78 (± 0.83)	1.55 (± 0.75)
Spleen	1.09 (± 0.86)	1.33 (± 0.61)	1.23 (± 0.73)	1.14 (± 0.85)
Muscle	0.52 (± 0.12)	0.66 (± 0.36)	0.94 (± 0.09)	0.98 (± 0.15)
Bone	0.31 (± 0.10)	0.65 (± 0.21)	0.60 (± 0.22)	0.63 (± 0.19)
Bloodpool	0.23 (± 0.10)	0.43 (± 0.11)	0.36 (± 0.10)	0.34 (± 0.14)

Statistical analyses

No statistical analyses for this end point

Secondary: 18F-MFBG lesion SUVmax as a function of time (lesion targeting and ideal time point identification)

End point title	18F-MFBG lesion SUVmax as a function of time (lesion targeting and ideal time point identification)

End point description:

End point type	Secondary

End point timeframe:
End of study

End point values	18F-MFBG 1h p.i.	18F-MFBG 2h p.i.	18F-MFBG 3h p.i.	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	5	5	
Units: SUVmax				
arithmetic mean (standard deviation)				
Bone lesions	9.1 (± 0.9)	8.2 (± 2.2)	7.7 (± 2.8)	
Lymph nodes	15.4 (± 9.1)	14.6 (± 8.5)	14.8 (± 9.8)	

Other lesions	15.8 (± 13.4)	17.3 (± 16.0)	18.0 (± 17.3)	
All lesions	19.3 (± 10.7)	20.8 (± 13.4)	21.7 (± 14.8)	

Statistical analyses

Statistical analysis title	Comparison of SUVmax of all lesions between scans
Comparison groups	18F-MFBG 1h p.i. v 18F-MFBG 2h p.i.
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.34
Method	t-test, 2-sided

Statistical analysis title	Comparison of SUVmax of all lesions between scans
Comparison groups	18F-MFBG 1h p.i. v 18F-MFBG 3h p.i.
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.34
Method	t-test, 2-sided

Statistical analysis title	Comparison of SUVmax of all lesions between scans
Comparison groups	18F-MFBG 3h p.i. v 18F-MFBG 2h p.i.
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.34
Method	t-test, 2-sided

Secondary: 18F-MFBG lesion TBR as a function of time (lesion targeting and ideal time point identification)

End point title	18F-MFBG lesion TBR as a function of time (lesion targeting and ideal time point identification)

End point description:

End point type	Secondary

End point timeframe:

End of study

End point values	18F-MFBG 1h p.i.	18F-MFBG 2h p.i.	18F-MFBG 3h p.i.	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	5	5	5	
Units: TBR (tumor-to-background ratio)				
arithmetic mean (standard deviation)				
Bone lesions	21.1 (± 1.4)	20.7 (± 7.1)	17.9 (± 7.1)	
Lymph nodes	17.1 (± 9.4)	16.8 (± 8.6)	18.4 (± 11.3)	
Other lesions	16.8 (± 14.1)	17.1 (± 14.8)	17.6 (± 14.8)	
All lesions	23.6 (± 8.4)	24.6 (± 8.5)	24.5 (± 9.0)	

Statistical analyses

Statistical analysis title	Comparison of TBR of all lesions between scans
Comparison groups	18F-MFBG 1h p.i. v 18F-MFBG 2h p.i.
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.52
Method	t-test, 2-sided

Statistical analysis title	Comparison of TBR of all lesions between scans
Comparison groups	18F-MFBG 1h p.i. v 18F-MFBG 3h p.i.
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.69
Method	t-test, 2-sided

Statistical analysis title	Comparison of TBR of all lesions between scans
Comparison groups	18F-MFBG 3h p.i. v 18F-MFBG 2h p.i.
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.98
Method	t-test, 2-sided

Secondary: Comparison of lesion SUVmax with 18F-MFBG and 123I-MIBG (lesion

targeting)	
End point title	Comparison of lesion SUVmax with 18F-MFBG and 123I-MIBG (lesion targeting)
End point description: For patients in whom a quantitative SPECT was obtained	
End point type	Secondary
End point timeframe: End of study	

End point values	123I-MIBG	18F-MFBG 1h p.i.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	4		
Units: SUVmax				
arithmetic mean (standard deviation)	15.8 (± 13.2)	22.1 (± 18.2)		

Statistical analyses

Statistical analysis title	Comparison of lesion SUVmax between tracers
Comparison groups	123I-MIBG v 18F-MFBG 1h p.i.
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.37
Method	t-test, 2-sided

Secondary: Comparison of lesion TBR with 18F-MFBG and 123I-MIBG (lesion targeting)	
End point title	Comparison of lesion TBR with 18F-MFBG and 123I-MIBG (lesion targeting)
End point description: For all patients	
End point type	Secondary
End point timeframe: End of study	

End point values	123I-MIBG	18F-MFBG 1h p.i.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: TBR (tumor-ro-background ratio)				
arithmetic mean (standard deviation)	23.7 (± 15.7)	27.2 (± 11.3)		

Statistical analyses

Statistical analysis title	Comparison of lesion TBR between tracers
Comparison groups	123I-MIBG v 18F-MFBG 1h p.i.
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.44
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Until last telephone follow-up interview of the subject	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03
Reporting groups	
Reporting group title	Patients

Reporting group description: -

Serious adverse events	Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)		
Investigations			
Neutrophil count decreased	Additional description: Grade 1		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia	Additional description: Grade 1		
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Gastrointestinal disorders			
Nausea	Additional description: Grade 1		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Metabolism and nutrition disorders			

Hypocalcaemia	Additional description: Grade 1		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyponatraemia	Additional description: Grade 1		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyperkalaemia	Additional description: Grade 1		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2020	The age of the population to be studied was changed from 18 years to 1 year or older and some flexibility was introduced in the imaging protocol for minor participants only to increase the feasibility for these patients. For adult participants the substantial amendment did not imply any changes to the study procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported