# 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<br>Units: Subjects | | | |
| Children (2-11 years) | 1 | 1 | |
| Adults (18-64 years) | 4 | 4 | |
| From 65-84 years | 1 | 1 | |
| Gender categorical<br>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:<br>For patients in whom a quantitative SPECT was obtained | |
| End point type | Secondary |
| End point timeframe:<br>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:<br>For all patients | |
| End point type | Secondary |
| End point timeframe:<br>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