68Ga-NODAGA-exendin-4 PET/CT in patients with AHH - a prospective comparative evaluation of preoperative imaging

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON40821

Source
ToetsingOnline

Brief title
68Ga-NODAGA-exendin-4 PET/CT in patients with AHH

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Endocrine gland therapeutic procedures

Synonym
adult hyperinsulinemic hypoglycemia

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: europese unie in het kader van een FP7 research project (BetaCure no 602812)

Intervention

Keyword: AHH, Beta cells, Insulinoma, PET

Outcome measures

Primary outcome

Comparison of sensitivity, specificity, positive predictive value, diagnostic odds ratio and receiver operating characteristics between 68Ga-NODAGA-exendin 4 PET/CT and conventional imaging such as triple phase CT, MRI, F-18-DOPA, C-11-HTP and 68Ga-DOTATOC/DOTATATE PET/CT in adult patients with biochemically proven endogenous hyperinsulinemic hypoglycemia in the fasting state.

Secondary outcome

• Calculation of the organ- and effective dose of 68Ga-NODAGA-exendin 4

• Assessing the impact on clinical management of GLP-1R imaging

• Calculation and comparison of the interobserver variability of 68Ga-NODAGA-exendin 4 PET/CT and EUS combined with triple phase CT or MRI

• Comparison of imaging parameters (SUVmax), intraoperative findings, histology and GLP-1/sst2 receptor expression in vitro autoradiography on frozen tissue samples

Study description

Background summary

We hypothesize that we can improve the sensitivity and specificity of pre-operative imaging for the localization of insulin producing pancreatic neuroendocrine tumours (IPPNET) in patients with adult endogenous hyperinsulinemic hypoglycemia (AHH) by using a novel imaging compound which targets the glucagon-like peptide-1 receptor (GLP-1R); 68Ga-NODAGA-exendin-4

Study objective

The primary objective is to compare GLP-1R-imaging to standard imaging techniques now used in pre-operative imaging of patients with AHH. All patients will undergo the standard imaging procedures of the specific centre and in addition we will perform a 68Ga-NODAGA-exendin 4 PET/CT. The results of the GLP-1R-imaging, in respect to sensitivity, specificity and diagnostic odds ratio for location and size of the IPPNET will be compared to the standard imaging modalities.
GLP-1- and sst-2-receptor expression and autoradiography of surgical specimens will be compared to results of quantitative imaging in order to determine the interdependency of radiotracer uptake, beta cell mass and receptor expression.

Study design

Multicenter prospective imaging (phase II) study in which we will compare GLP-1R-imaging with the standard imaging protocols for pre-operative imaging in patients with AHH.

Study burden and risks

All individuals will undergo physical examination and blood sampling for standard laboratory parameters. In addition, all patients will undergo the current standard preoperative care (68Ga-DOTATOC PET/CT or 68Ga-DOTATATE PET/CT combined with conventional imaging (endoscopic ultrasound (EUS) and triple phase CT or MRI) and in some centers 18F-DOPA PET and/or 11C-5-HTP PET. At the next visit 4-7 µg 68Ga-NODAGA-Exendin-4 will be administered intravenously and scanning will be performed 1 hour after injection of the tracer. Blood pressure and blood glucose levels will be measured just before and 15, 30, 60 and 120 minutes after injection of the radiopharmaceutical. Injection of the radiolabeled tracer may result in nausea and headache as has been reported for (very high doses (10-100µg) of) Byetta® in therapy studies. In addition, a decrease of blood glucose levels (0.8 - 2.1 mmol/l have been described after injection of 8 - 14 µg 111In-DTPA-exendin-4 in patients with AHH (Christ E. et al. Lancet Diabetes Endocrinol 2013;1:115-22). Importantly, regular monitoring of glucose concentrations injection led to no serious episodes of hypoglycaemia. Therefore, no side-effects are anticipated with injection of 4-7 µg of radiolabeled exendin, although patients will be closely monitored. Furthermore, glucose infusion (10%) will be administered of needed.
The expected radiation exposure will not exceed 5,5 mSv for

68Ga-NODAGA-exendin-4 PET/CT. In relation to the expected benefit in diagnostic imaging by improving preoperative non-invasive localization of foci in AHH with higher sensitivity and specificity and the resulting impact on AHH treatment, this additional radiation exposure is acceptable. Especially in view of the expected replacement of several other imaging procedures by GLP-1R scanning in the future, the radiation burden for future AHH patients will significantly be reduced.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein-Zuid 10
Nijmegen 6500 HB
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein-Zuid 10
Nijmegen 6500 HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Biochemically proven endogenous hyperinsulinemic hypoglycemia: neuroglycopenic symptoms in the fasting state with low plasma glucose, inappropriately high serum insulin and C-peptide concentrations

• Signed informed consent
• Standard imaging not older than 8 weeks. This includes a triple-phase CT or MRI, somatostatin receptor imaging (68Ga-DOTATOC, 68Ga-DOTATATE or 111In-DTPA-octreotide SPECT/CT) and endocopic ultrasound (EUS).

Exclusion criteria

• Breast feeding
• Pregnancy or the wish to become pregnant within 6 months
• Calculated creatinine clearance below 40ml/min
• Evidence of other malignancy than insulin producing tumors in conventional imaging (suspicious liver, bone and lung lesions)
• Age < 18 years
• No signed informed consent

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-11-2015
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	68Ga-NODAGA-exendin-4
Generic name:	n.v.t

Ethics review

Approved WMO Date:	07-01-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-04-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-02-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-12-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-09-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-003167-38-NL
CCMO	NL50643.091.14