Quantitative GLP-1 receptor imaging correlated to ex vivo distribution of In-111-exendin

Published: 07-05-2014
Last updated: 20-04-2024

The primary objective is to correlate ex vivo 111In-exendin tracer accumulation in the pancreas of patients undergoing pancreatectomy for pancreatic cancer or chronic pancreatitis to establish the relation between tracer uptake and beta cell mass in...

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

Summary

ID

NL-OMON44912

Source
ToetsingOnline

Brief title
GLP-1-ex-vivo

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Nucleaire Geneeskunde
Source(s) of monetary or material Support: europese unie in het kader van een FP7

research project (BetaImage)

Intervention

Keyword: beta cell, diabetes, radiopeptides, SPECT

Outcome measures

Primary outcome

Quantitative determination of the uptake of In-111-exendin into the pancreas in all subjects as determined by 3D SPECT imaging in order to correlate the uptake to the ex vivo distribution and accumulation of the tracer in the pancreas with the BCM.

Secondary outcome

* Validation of the 111In-exendin distribution and accumulation in the pancreas

* Determination of the uptake ratio of 111In-exendin between the endocrine and exocrine pancreas by quantitative analysis autoradiography

* Determination of the radioactivity concentration in the pancreas by quantitative analysis of SPECT images to validate of in vivo measurement of the pancreatic 111In-exendin uptake

* Validation of the correlation between BCM and 111In-exendin uptake (determined ex vivo and in vivo)

* Determination of the beta cell function of the patients by oral glucose tolerance testing and arginine stimulation testing to evaluate the relationship between BCM and beta cell function

* Determination of 111In-exendin uptake in pancreatic carcinoma and pancreatitis in order to determine if 111In-exendin can be used to discriminate between both diseases

* Identification of the cells responsible for uptake of 111In-exendin in the

duodenum and pylorus

Study description

Background summary

In order to fully characterize the highly promising innovative tracer In-111-DTPA-[K40]-Exendin 4 (In-111-exendin) in humans, we aim to correlate quantitative SPECT imaging with ex vivo tracer distribution in patients undergoing pancreatectomy for pancreatic cancer or chronic pancreatitis. We propose to combine in vivo imaging with post-pancreatectomy (micro)autoradiography, measurement of In-111-DTPA-[K40]-Exendin 4 concentrations in the pancreas using a gamma counter and morphometric determination of the actual beta cell mass. By this means, we will establish the relation between tracer uptake and beta cell mass in non-diabetic patients and T2D patients. These highly relevant data will allow us to improve the interpretation of clinical quantitative SPECT data in subsequent studies in patients with T1D and T2D. In addition, high uptake has been observed in the duodenum/pyloric area in patients in an ongoing study. At this point in time, it remains unclear which cells are responsible for this uptake. It would be of great interest to identify the GLP-1R positive cells in order to better understand the physiological actions of GLP-1 agonists.

Study objective

The primary objective is to correlate ex vivo 111In-exendin tracer accumulation in the pancreas of patients undergoing pancreatectomy for pancreatic cancer or chronic pancreatitis to establish the relation between tracer uptake and beta cell mass in non-diabetic patients and patients with diabetes.
These highly relevant data will improve the interpretation of clinical quantitative SPECT data in subsequent studies.

Study design

After recruitment of the participating individuals, all patients will undergo an enrollment check at the Department of Nuclear Medicine consisting of a medical interview and a physical examination performed by a qualified physician (in case this is not done during intake and surgical evaluation for pancreatectomy). Recent blood samples for standard laboratory checks (blood counts, electrolytes, liver enzymes, inflammation parameters) that have been taken prior to pancreatectomy, will be analyzed. Another visit is needed for an oral glucose tolerance test and an glucose-dependent arginine-stimulation test.

One day prior to pancreatectomy, In-111-exendin will be administered to all patients. We aim to include 50 patients into this study with a first interim analysis that will be accomplished after participation of the first 15 patients.
After pancreatectomy, samples for histology and autoradiography will be taken from the pancreatic head, body and tail and duodenum/pylorus if resected. Tissue samples will be fixed in formalin and autoradiography will be performed to correlate pancreatic uptake with the In-111-exendin tracer distribution ex vivo. In case patients appear to have impaired glucose tolerance without being diagnosed for diabetes earlier, patients will undergo a second oral glucose tolerance test and (in case of improved glucose tolerance) an In-111-Exendin scan after pancreatectomy.

Study burden and risks

The risk of serious side effects of the study medication is very low. Bruising may occur after venous puncture. Measures like local pressure will be taken to minimize the risk. The risk of sampling the pancreas is very low because the biopsy is taken from resected pancreatic tissue
In conclusion, the risk of adverse events during this study is very low. On the other hand, there is a very high (and increasing) incidence of diabetes mellitus (especially type 2), which can lead to serious complications including death. This study aims to establish an innovative imaging technology for the non-invasive in vivo determination of the beta cell mass. Such a technology would be an asset on our way to better understand the mechanisms involved in the development of diabetes mellitus and can lead to the development of new treatment options.
The subjects will not benefit directly from participating in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Scheduled for partial or complete pancreatectomy or complete drainage procedure in case of chronic pancreatitis, Intraductal papillary mucinous neoplasm (IPMN) or pancreatic cancer at Radboudumc

Exclusion criteria

* Resection of only small part of the pancreas without possibility to safely sample other pancreatic parts
* Breast feeding
* Pregnancy or the wish to become pregnant within 6 months
* Creatinine clearance below 40ml/min
* Liver disease defined as aspartate aminotransferase or alanine aminotransferase level of more than three times the upper limit of normal range
* Age < 18 years
previous treatment with synthetic Exendin (Exenatide, Byetta®) or Dipeptidyl-Peptidase IV inhibitors

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-11-2015
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	In-111-DTPA-[K40]-Exendin-4
Generic name:	n.v.t.

Ethics review

Approved WMO Date:	07-05-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-12-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-07-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-10-2019

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	EUCTR2013-004012-21-NL
CCMO	NL47132.091.14

Study results

Date completed:	14-06-2021
Actual enrolment:	12

Summary results
Trial ended prematurely