Two new screenings technics for the early detection of pancreatic neuroendocrine tumors in Multipele Endocrine Neoplasia type 1 (MEN1) and Von Hippel-Lindau disease (VHL).

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23812

Bron
NTR

Verkorte titel
EUS and HTP PET for PNET in MEN1 and VHL.

Aandoening

pancreatic neuroendocrine tumors in patients with MEN1 en VHL.

Ondersteuning

Primaire sponsor: dr. T.P. Links
Overige ondersteuning: Dutch Cancer Society

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Group A:
The number of new (unknown) pancreatic NET lesions in MEN1 or VHL patients with proven pancreatic involvement (anatomical, with or without biochemical neuroendocrine activity) and in MEN1 or VHL patients with proven neuroendocrine activity (biochemical, without anatomical localization) detected by EUS ± FNA and 11C-HTP PET.

Group B:
The number of new (unknown) pancreatic NET lesions in patiens with MEN1 or VHL during routine follow-up detected by EUS ± FNA and 11C-HTP PET.

Toelichting onderzoek

Achtergrond van het onderzoek

Multiple Endocrine Neoplasia type 1 (MEN1) and Von Hippel-Lindau disease (VHL) are rare autosomal dominantly inherited disorders characterized by the occurrence of various tumors. Therefore, mutation carriers undergo regular screening (yearly for VHL and three yearly for MEN1) to enable early treatment. With earlier detection of treatable tumors, e.g. renal cell carcinoma in VHL patients, survival is improving. This increases however the chance to develop other tumor types such as pancreatic neuroendocrine tumors (NET) to occur. Pancreatic NETs develop in MEN1 in 65% and in VHL in 10-20%, and is the second most frequent tumor manifestation in MEN1 patients. Pancreatic NETs are discovered in an advanced stage by serum markers (e.g. insulin, chromogranin A). Non-functioning pancreatic NETs are even more difficult to detect at early stage with currently available imaging modalities, while early detection would allow sparing curative surgery. Standard regular screening for pancreatic NETs consists of ultrasound, MRI, CT and somatostatin receptor scintigraphy (SRS). However, the sensitivity of these techniques is limited.
Two new imaging strategies have emerged. Endoscopic ultrasound (EUS) with fine needle aspiration (FNA) for cytology with an estimated sensitivity of 80% and positron emission tomography (PET) using the serotonin precursor tracer 11C-5-HTP. EUS with FNA of pancreatic lesions is still a specialized technique performed in a few Dutch centers among which is the UMCG. We recently showed that 11C-5-HTP PET imaging is superior to conventional imaging in the detection of pancreatic NETs. The UMCG is one of the three centers worldwide that have this technique available. Introduction of these two techniques will most likely improve early NET detection and will allow sparing curative surgery in these high risk individuals for pancreatic NET.
Objective: To determine the additional value of EUS + FNA and 11C-5-HTP PET scan for detection of pancreatic NET.
Study design:observational study.
Study population:

A) 40 VHL or MEN1 patients with suspicion of a pancreatic NET based on biochemical values and/or a pancreatic lesion on conventional imaging techniques (MRI, CT, SRS) and B) in 50 MEN1 or VHL patients with a negative standard follow-up (no signs of pancreatic NET biochemically and by conventional imaging techniques) will be included. Patients will be accrued from the participating centers consisting of the expert MEN1 and VHL centers in the Netherlands (UMCs Utrecht, Rotterdam, Nijmegen, Groningen).
Main study parameters/endpoints: Finding additional NET tumor sites, which can be considered as clinically relevant
To find additional sites on EUS and/or 11C-5-HTP PET in 25% of the patients with already proven pancreatic NETs – which can be considered as clinically relevant-, a number of 20 patients is necessary to reach a 5% level of significance (and a power of 80%) in McNemar's test. To find tumor localization on EUS and/or 11C-5-HTP PET in 25% of the patients with only biochemical proven pancreatic NETs - which can be considered as clinically relevant-, a number of 20 patients is necessary to reach a 5% level of significance (and a power of 80%) in McNemar's test. In total 40 patients will be included in group A.
Localization of pancreatic NETs in 10% of the individuals who are screened yearly for pancreatic NETs without biochemical and radiological evidence of disease can be considered as clinically relevant. Therefore, 50 patients should be included in group B to demonstrate a difference of 10% (p=0.05; power 80% McNemar's test).

Possible results/relevance for cancer research: Early detection allowing surgery with selective extirpation of pancreatic NET, which will most likely increase life expectancy and quality of life in these patients.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
Standard conventional imaging in patients with VHL consists of yearly abdominal US (MRI or CT on indication), whereas in patients with MEN1 standard imaging consists of a SRS combined with CT or MRI every three years according to national and international guidelines (1,3,4,34). SRS, abdominal US, MRI and CT scan will be performed in the UMCG or in one of the other UMCs. In the VHL patients on study in both groups, the conventional imaging procedures will be expanded with one extra SRS imaging out of the standard protocol. In this group of patients the SRS scan should be considered conventional imaging, but has not been routinely included in the follow-up protocol.
Standard laboratory investigation includes yearly determination of fasting plasma levels of C-peptide, chromogranin A, insulin, pancreatic polypeptide, gastrin and glucagon.
Study imaging Patients will undergo once a combined endoscopic ultrasound of the pancreas and FNA and a 11C-5-HTP PET as additional diagnostic procedures in the UMCG.

Doel van het onderzoek

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Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

1. 11C-5-HTP-PET scan;

2. Endo Ultrasonography with fine needle aspirtation;

3. Bloodsamples.

Contactpersonen

Publiek

University Medical Center Groningen
Div Endocrinology
PO Box 30 001
T.P. Links
Groningen 9700 RB

The Netherlands
+31 (0)50 3613962/+31 (0)50 3616161

Wetenschappelijk

University Medical Center Groningen
Div Endocrinology
PO Box 30 001
T.P. Links
Groningen 9700 RB
The Netherlands
+31 (0)50 3613962/+31 (0)50 3616161

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

The study populations covers two different groups:

1. Group A: MEN1 or VHL patients with signs of a pancreatic tumor (biochemically and/or on conventional imaging) will undergo regular follow-up visits to control tumor localization. These patients are eligible for inclusion providing that the time period between the available conventional imaging data and the investigational imaging procedures does not exceed 4 months;

2. Group B: MEN1 or VHL patients without signs of a pancreatic tumor (biochemically and on conventional imaging) are regularly scheduled for routine follow-up. During this routine follow-up, these patients are eligible to participate in the trial. Also, the conventional and investigational imaging procedures will be performed within a period of 4 months.

INCLUSION CRITERIA:

1. Group A:

A. Genetically proven MEN 1 or VHL, or clinically proven MEN1 or VHL also in first grade family members:

B. Signs of a pancreatic tumor biochemically and/or on conventional imaging;

C. The time period between the available conventional imaging data, biochemical markers and the investigational imaging procedures does not exceed 4 months;

D. Over 24 years of age;

E. In case of recent surgery at least a 3 months interval between surgery and EUS and 11C-HTP PET scanning;

F. Written informed consent.

2. Group B:

A. Genetically proven MEN 1 or VHL, or clinically proven MEN1 or VHL also in first grade family members;

B. No signs of a pancreatic tumor biochemically and/or on conventional imaging;

C. The time period between the available conventional imaging data, biochemical markers and the investigational imaging procedures does not exceed 4 months;

D. Over 24 years of age;

E. In case of recent surgery at least a 3 months interval between surgery and EUS and 11C-HTP PET scanning;

F. Written informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Patients with any signs of neurological or psychiatric disorders that will preclude him/her from expressing her/his own free will;

2. Pregnancy;

3. Patients not eligible for surgical intervention;

4. Patients with alcohol abusus;

5. Patients with chronic pancreatitis;

6. VHL type 2C.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm

Controle: N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-02-2009
Aantal proefpersonen:	90
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	12-02-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1588
NTR-old	NTR1668

Register	ID
Ander register	ABR METC : 23797
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten
N/A