A randomized placebo-controlled study in patients with a Gallium-68 DOTATATE PET/CT positive, clinically non-functioning pituitary macroadenoma (NFMA) of the effect of Lanreotide autosolution on Tumor (adenoma) size

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To investigate the efficacy of lanreotide therapy as compared to placebo in patients with NFMA and positive pituitary somatostatin receptor imaging using Gallium-68 DOTATATE PET/CT, on tumor size.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Interventional

Summary

ID

NL-OMON50502

Source
ToetsingOnline

Brief title
GALANT

Condition

- Hypothalamus and pituitary gland disorders
- Endocrine neoplasms benign

Synonym
pituitary adenoma, pituitary tumor

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ipsen Farmaceutica,Ipsen Pharmaceuticals

Intervention

Keyword: 68Ga-DOTATATE, drug therapy, pituitary adenoma, somatostatin analogue

Outcome measures

Primary outcome

* Change in cranio-caudal NFMA size

Secondary outcome

* Adverse events (AE*s)

* Change in quality of life

* Change in NFMA volume

* Time to progression (tumor growth)

Study description

Background summary

In patients with clinically non-functioning pituitary macroadenomas (NFMA), the current therapeutic approach is to substitute any hormonal deficits, and to perform transsphenoidal surgery if necessary, based on optic chiasm compression or visual field defects. In Amsterdam, approximately 40 of these patients per year undergo surgery. In the literature, remission rate after surgery is estimated to be about 44%, which is substantially lower than in other pituitary tumor types, and recurrence rate is about 11% during an average follow-up period of 5 years. The available evidence concerning treatment and follow-up of NFMA is based exclusively on small, observational studies, and there is a remarkable lack of randomized studies. Whereas medical therapy is regarded as first-line treatment in prolactinoma patients, the role for medical therapy in patients with NFMA is controversial. It has been known for some decades that

NFMA may express somatostatin receptors, as seen in surgical specimens and in vivo, using Indium-111 pentetreotide SPECT (*Octreoscan*). Based on these observations, a limited number of small studies has been conducted focusing on octreotide treatment and showing conflicting results on tumor size reduction. It is important to note that the normal anterior pituitary gland takes up Indium-111 pentetreotide as well. However, the spatial resolution of SPECT is insufficient to differentiate NFMA from normal anterior pituitary tissue. The more recent development of Gallium-68 DOTATATE PET/CT imaging in pituitary tumours shows a superior sensitivity and spatial resolution, which allows for accurate quantification of radioligand uptake within neuroendocrine tumours. Thus, somatostatin analogues may have potential in some NFMA patients, but there is a remarkable lack of randomized and controlled studies. Furthermore, it is not possible at present to predict which patients will respond to somatostatin analogues.

Study objective

To investigate the efficacy of lanreotide therapy as compared to placebo in patients with NFMA and positive pituitary somatostatin receptor imaging using Gallium-68 DOTATATE PET/CT, on tumor size.

Study design

Randomized, double-blind, placebo-controlled trial

Intervention

A Gallium-68 DOTATATE PET/CT will be performed in suitable patients after obtaining informed consent. The first 44 patients with a positive PET/CT will be randomized into two treatment groups:
Group 1 will receive monthly subcutaneous injections of lanreotide (18 months)
Group 2 will receive monthly subcutaneous injections of placebo (18 months)

Study burden and risks

Interested patients with NFMA will be invited for visit 1 at their own center (informed consent, in- and exclusion criteria, quality of life questionnaire, physical exam, venipuncture, pituitary MRI, and * if applicable * a pregnancy test). The physical exam, venipuncture and pituitary MRI are part of standard NFMA evaluation. Included patients will undergo a Gallium-68 DOTATATE PET/CT scan. For AMC based patients this scan can take place on the same day during visit 1 at the AMC; for VUmc and LUMC patients the scan will be planned on a second visit. The scan is very well tolerated and the total radiation exposure is estimated at 3.1 mSv (millisievert). The first 44 patients with a positive PET/CT will be randomized to receiving a deep subcutaneously injection of lanreotide autosolution 120 mg, or to receiving placebo injection consisting of

saline once every 4 weeks for 18 months (18 visits). The injections will either be administered at the clinical Endocine Unit of the AMC by an endocrine nurse, or at home by trained nurses from Eurocept Homecare.
Treatment with lanreotide autosolution 120 mg was shown to be safe and well-tolerated as a first-line therapy in patients with growth hormone secreting pituitary adenomas. It does carry a small risk of developing symptomatic gall stones. In ~10% of patients it may cause diarrhea, loose stools, or abdominal pain, especially after the first injection. In <10% it may cause injection site reactions.
Every 24 weeks or so a study visit takes place, consisting of a short physical examination (± 5 minutes), blood tests (8 vials via one venipuncture, total volume 36 milliliters), a quality of life questionnaire and documentation of adverse events. Pituitary MRI will be repeated after 6 months and after 18 months. Again, the physical exam, the blood tests and the MRI are part of standard NFMA care.
The total number of study visits to the hospital depends on where the injections are administered. The minimum is 4 visits for AMC patients and 5 visits for VUmc and LUMC patients, the maximum is 21 visits. During the study period, patients are not deprived of any standard therapy. The benefit is potentially reduced NFMA growth rate, which may postpone or obviate transsphenoidal surgery or radiotherapy. If this study shows a positive effect on tumor size, standard treatment of NFMA could be improved in a major way.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Clinically non-functioning pituitary macroadenoma, or post-surgical residue/recurrence ><= 10mm, with suprasellar extension

Exclusion criteria

* Optic chiasm compression and/or visual field defects
* Hypersensitivity for somatostatin or similar peptides
* Obstructive neuroendocrine gut tumor
* Symptomatic cholelithiasis
* Use of dopamine agonists in the past 6 months
* Use of somatostatin analogues in the past 6 months
* Pregnancy (plans)
* Any contraindication to perform MRI with gadolinium based contrast agent (including implanted metallic devices, impaired renal function and severe claustrophobia)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-11-2015
Enrollment:	66
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Somatuline
Generic name:	Lanreotide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	25-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	01-07-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	21-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	22-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	14-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2015-001234-22-NL
CCMO	NL52821.018.15