Effectiviteit en veiligheid van behandeling met cinacalcet bij patiënten met primaire hyperparathyreoïdie door een MEN-I mutatie.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23587

Source
NTR

Health condition

MEN-1
Primary Hyperparathyroidism
Primair Hyperparathyreoidie
Cinacalcet
CaSR

Sponsors and support

Primary sponsor: Leiden University Medical Center
Dutch MEN-1 Study Group
Source(s) of monetary or material Support: Leiden University Medical Center

Intervention

Outcome measures

Primary outcome

Effects of cinacalcet on clinical and biochemical parameters, including bone turnover markers.

Secondary outcome

1. Effect of cinacalcet on bone mineral density, nephrocalcinosis and nephrolithiasis;

2. Effect of cinacalcet on the development and/or growth of pituitary adenomas, insulinomas, gastrinomas and/or other pancreatic tumors;

3. Is there a loss or decrease of the CaR expression in pathological specimens obtained at surgery in patients with primary hyperparathyroidism due to a MEN-I mutation? And does this influence the response to treatment with cinacalcet?

Study description

Background summary

This study will look at the efficacy and safety of cinacalcet in patients with PHPT due to a MEN-1 mutation.

Efficacy will be evaluated on the basis of clinical and biochemical data.

Safety will be evaluated on the basis of neurocognitive function tests, biochemical data and radiological data.
Patients will be treated with cinacalcet for 1 year at a starting dose of 30 mg once daily and a maximum dose of 30 mg twice daily.

Patients will be recruited from medical centers in the Netherlands.

Study objective

Patients with MEN-1 have a high risk of developing primary hyperparathyroidism (PHPT). Surgical removal of all pathological parathyroid glands is the only approach that provides definitive cure, however, the recurrence rate in patients with a MEN-1 mutation is reported to be 50% 8-12 years after subtotal parathyroidectomy. Revision neck explorations are technically more challenging than initial surgery and associated with an up to a 3-fold increase in morbidity. The potential of non-invasive approaches such as the use of calcimimetics has been explored in patients with PHPT who cannot or will not have surgery and was found to be promising. The use of these agents would be particularly beneficial in patients with MEN-1 where recurrence and persistence of hyperparathyroidism is common after initial parathyroidectomy.

In addition to the parathyroid glands, the CaSR has also been identified in cells of the kidneys, bone, colon, thyroid, brain, pancreas and gastrinoma cells of the stomach. Stimulation of the CaSR by cinacalcet has been reported to increase urine calcium excretion and increase bone turnover, without having a significant effect on the bone mineral density. In contrast to patients with sporadic PHPT, patients with PHPT due to a MEN-1 mutation have a 33-50% chance of developing pituitary tumors, insulinomas, gastrinomas and other pancreatic tumors. The effect of cinacalcet on these associated endocrine pathologies has not been previously studied.

Study design

Primary Endpoints:

1. Specific and non-specific symptoms will be assessed using the validated Pasieka's "Parathyroid Assessment of Symptoms Score (PAS)" before and 1, 2, 3, 6 and 12 months after start of cinacalcet;

2. Global cognitive function will be assessed using a battery of neuropsychological tests before and 1, 2, 3, 6 and 12 months after start of cinacalcet;

3. Quality of life will be assessed using the SF-36 questionnaire before and 12 months after the start of cinacalcet;

4. Blood will be collected to measure for serum calcium, PTH, phosphate, creatinine, albumin, 25OH vitamin D, alkaline phosphatase, B-crosslaps, P1NP, TSH, FT4, gastrin, insulin, prolactin, testosterone, FSH and LH before and 1, 2, 3, 6 and 12 months after the start of cinacalcet;

5. Two times 24-hrs urine will be collected to measure for calcium, phosphate and creatinine (TMP/GFR) before and 1, 2, 3, 6 and 12 months after the start of cinacalcet.

Secondary Endpoints:

1. BMD will be measured using dual energy X-ray absorptiometry (DXA, Hologic QDR 4500; Waltham, MA, USA) before and 12 months after the start of cinacalcet;

2. Lateral X-rays of spine will be performed before and 12 months after the start of cinacalcet;

3. An ultrasound of the kidneys will be performed before and 12 months after the start of cinacalcet;

4. An MRI of the abdomen and the brain will be performed before and 12 months after the start of cinacalcet;

5. CaR and VDR expression on pathological parathyroid samples will be determined and DNA analysis for somatic and germline mutations of the following genes will be performed; PTH, MEN-1, HRPT2, CaSR including newly identified gene targets.

Intervention

Treatment with Cinacalcet (Primpara ®). Patients will be treated with cinacalcet for 1 year at a starting dose of 30 mg once daily and a maximum dose of 30 mg twice daily.

Contacts

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Eligibility criteria

Inclusion criteria

A diagnosis of primary hyperparathyroidism due to a genetically confirmed germline mutation in the MEN-1 gene.

Exclusion criteria

1. Sporadic primary hyperparathyroidism;

2. Autonomous hyperparathyroidism due to chronic renal failure or vitamin D deficiency;

3. Absence of genetic confirmation of a mutation in the MEN-1 gene;

4. Contraindications for MRI scanning, such as metallic fragments, pacemakers and defibrillators, nerve stimulators, intracranial clips, cochlear implants. ferromagnetic implants or claustrophobia;

5. Pregnancy.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-08-2010
Enrollment:	30
Type:	Anticipated

Ethics review

Positive opinion

Date:	21-09-2010
Application type:	First submission

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
NTR-new	NL2417
NTR-old	NTR2525
Other	METC LUMC / CCMO : P10-038 / NL30971.058.10 ;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A