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

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

Samenvatting

ID

NL-OMON23587

Bron
NTR

Aandoening

MEN-1
Primary Hyperparathyroidism
Primair Hyperparathyreoidie
Cinacalcet
CaSR

Ondersteuning

Primaire sponsor: Leiden University Medical Center
Dutch MEN-1 Study Group
Overige ondersteuning: Leiden University Medical Center

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

Postbus 9600
J.E. Witteveen
Leids Universitair Medisch Centrum, Department of Endocrinology and Metabolic disorders
Leiden 2300 RC
The Netherlands
+31 (0)71 5262646

Wetenschappelijk

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J.E. Witteveen
Leids Universitair Medisch Centrum, Department of Endocrinology and Metabolic disorders
Leiden 2300 RC
The Netherlands
+31 (0)71 5262646

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	26-08-2010
Aantal proefpersonen:	30
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	21-09-2010
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	NL2417
NTR-old	NTR2525
Ander register	METC LUMC / CCMO : P10-038 / NL30971.058.10 ;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A