# CXCR4-directed [68Ga]Ga-PentixaFor vs AVS performance in a diagnoStic randomized Trial Ultimately comparing hypertenSion outcome in primary aldosteronism (CASTUS trial)

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[68Ga]Ga-PentixaFor PET/CT is non-inferior to adrenal vein sampling in subtyping in patients with primary aldosteronism

| | |
|---|---|
| **Ethische beoordeling** | Niet van toepassing |
| **Status** | Werving gestart |
| **Type aandoening** | - |
| **Onderzoekstype** | Observationeel onderzoek, zonder invasieve metingen |

## Samenvatting

### ID

NL-OMON28682

**Bron**
NTR

**Verkorte titel**
CASTUS

**Aandoening**

Primary aldosteronism

### Ondersteuning

**Primaire sponsor:** Radboudumc
**Overige ondersteuning:** ZonMW, PentixaPharm

### Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

-To assess the concordance between [68Ga]Ga-PentixaFor PET/CT and AVS for identification and/or lateralization of APAs in patients with PA. (Step 1)
-To assess the quantity of antihypertensive medication after 1 year of follow-up needed to normalize blood pressure in patients who have been managed for PA according to either AVS or [68Ga]Ga-PentixaFor PET/CT. (Step 2)

# Toelichting onderzoek

### Achtergrond van het onderzoek

Rationale:
Primary aldosteronism (PA) is the most frequent form of secondary hypertension. Correct diagnosis and targeted treatment of PA are essential because of high vascular morbidity associated with PA as compared to essential hypertension with comparable blood pressure levels. PA is usually caused by either a unilateral aldosterone-producing adenoma (APA) or by bilateral adrenal hyperplasia (BAH). Distinction between APA and BAH is critical since the former may be cured by adrenalectomy, and the latter necessitates life-long medical therapy with mineralocorticoid receptor antagonists (MRA). The distinction between unilateral and bilateral PA can be made by adrenal vein sampling (AVS), as recommended by The Endocrine Society 2016 guideline (1). Since AVS is invasive, not widely available, dependent on skilled radiologists and costly, there is a need for an accurate, non-invasive functional imaging modality. Based on clinical data obtained in retrospective studies so far, it appears that a potentially suitable imaging modality for this purpose is [68Ga]Ga-PentixaFor PET/CT. We propose to perform an two-step trial, in which the first step consists of a prospective feasibility study of [68Ga]Ga-PentixaFor PET/CT scanning. When the concordance of [68Ga]Ga-PentixaFor PET/CT and AVS appears to be >50%, we will continue to the second step: a prospective, randomized diagnostic study comparing outcomes of AVS-based and [68Ga]Ga-PentixaFor PET/CT based management of patients with primary aldosteronism.

Study design:
Two-step design in which step one is a two-center, single arm and open label study, followed, conditionally on the results of step one, by a two-center, prospective, two-armed, diagnostic randomized controlled trial.
Study population: Patients with primary aldosteronism, confirmed by an intravenous salt-loading test, >18 years old (according to the Endocrine Society guidelines)(1).
Intervention: In the first step patients will undergo AVS and a CT scan. Subsequently, in these patients a Ga-68-pentixafor PET/CT will be performed. Lateralization (based on [68Ga]Ga-PentixaFor uptake criteria) will be compared with lateralization results of the AVS. Based on the results of the adrenal vein sampling, patients will undergo unilateral adrenalectomy or MRA therapy (standard of care). When the concordance of [68Ga]Ga-PentixaFor PET/CT and

AVS >50%, we will start with the randomized controlled trial (RCT).
In step 2 patients will be randomized to undergo either [68Ga]Ga-PentixaFor PET/CT or AVS. The result of these tests will determine the course of action: adrenalectomy for APA or MRA therapy for bilateral hyperplasia.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
The extra burden of participation in the first step consists of a tracer injection and a PET/CT scan. The risks associated with a peptide injection in the microdose range are low. Adverse reactions have not been observed. Effective radiation dose of 150 +/- 50 MBq [68Ga]Ga-PentixaFor will be approximately 2.3 mSv, which is an acceptable dose.

**Doel van het onderzoek**

[68Ga]Ga-PentixaFor PET/CT is non-inferior to adrenal vein sampling in subtyping in patients with primary aldosteronism

**Onderzoeksopzet**

Step 1: The diagnosis of unilateral or bilateral disease will be based on AVS and CT scan. Subsequently, in these patients a [68Ga]Ga-PentixaFor PET/CT will be performed. . The [68Ga]Ga-PentixaFor PET/CT images will be interpreted by a clinician, blinded for the AVS and CT results, with extensive experience in radiolabeled imaging.

Step 2: Each subject will be randomly assigned to one of the diagnostic methods. Based on AVS or [68Ga]Ga-PentixaFor PET/CT results, patients with a unilateral cause of PA will receive surgery and patients with a bilateral cause of PA will receive antihypertensive medication. Both diagnostic methods will be compared by measuring the daily defined doses of antihypertensive medication from both groups after one year follow- up starting after the diagnosis has been given. Management of antihypertensive medication will be compared between groups in terms of daily defined doses.

**Onderzoeksproduct en/of interventie**

[68Ga]Ga-PentixaFor PET/CT

# Contactpersonen

## Publiek

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### Wetenschappelijk

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## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• The patient has a diagnosis of primary aldosteronism, confirmed by an elevated aldosterone/rennin ratio (ARR) and an intravenous salt-loading test (according to the Endocrine Society guidelines)(1)
• Age over 18 years at time of consent
• Signed informed consent

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in this study:

• Refusal by the patients to undergo AVS, [68Ga]Ga-PentixaFor PET/CT, CT, or adrenalectomy
• Suspicion of familial hyperaldosteronism type 1 (FH-1) or type 3 (FH-3)
• Suspicion of adrenocortical carcinoma
• Severe comorbidity potentially interfering with treatment or health-related quality of life
• Requirement of medication interfering with the study protocol
• Any medical condition present that in the opinion of the investigator will affect patients' clinical status.
• Pregnancy or lactation
• Estimated glomerular filtration rate (eGFR) < 40 ml/min/1.73m²

## Onderzoeksopzet

## Opzet

| | |
|---|---|
| Type: | Observationeel onderzoek, zonder invasieve metingen |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Open / niet geblindeerd |
| Controle: | N.v.t. / onbekend |

## Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestart |
| (Verwachte) startdatum: | 07-02-2022 |
| Aantal proefpersonen: | 265 |
| Type: | Verwachte startdatum |

## Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Ja

**Toelichting**
Deintendified participant data will be available after the article publication. Data will be shared with researchers who provide a methodologically sound proposal. To gain access, requestors will need to sign a data access agreement.

# Ethische beoordeling

Niet van toepassing

| | |
|---|---|
| Soort: | Niet van toepassing |

# Registraties

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 49887
Bron: ToetsingOnline
Titel:

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

| Register | ID |
|---|---|
| NTR-new | NL9625 |
| CCMO | NL78206.091.21 |
| OMON | NL-OMON49887 |

# Resultaten