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

No registrations found.

Ethical review	Not applicable
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON28682

Source
Nationaal Trial Register

Brief title
CASTUS

Health condition

Primary aldosteronism

Sponsors and support

Primary sponsor: Radboudumc
Source(s) of monetary or material Support: ZonMW, PentixaPharm

Intervention

Outcome measures

Primary outcome

-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)

Secondary outcome

- To establish definitive quantitative criteria of [68Ga]Ga-PentixaFor uptake in unilateral and bilateral PA.
- In patients who receive an unilateral adrenalectomy, we compare [68Ga]Ga-PentixaFor uptake in PET/CT imaging between immunohistochemically (CYP11B2 staining) diagnosed multinodular hyperplasia and solitary adenomas.
- To assess the diagnostic accuracy of adrenal CT compared with [68Ga]Ga-PentixaFor PET/CT and AVS.
- Cost analysis of AVS versus [68Ga]Ga-PentixaFor PET/CT management
- Changes in quality of life assessed by a validated disease specific health-related Quality of Life (HRQoL) questionnaire and the Short Form health survey (SF36)(2, 3)
- To perform a safety analysis of [68Ga]-Pentixafor administration on clinical symptoms by Adverse Events outcomes.

Study description

Background summary

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.

Study objective

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

Study design

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.

Intervention

[68Ga]Ga-PentixaFor PET/CT

Contacts

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Eligibility criteria

Inclusion criteria

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

Exclusion criteria

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/1.73m^2

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-02-2022
Enrollment:	265
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Plan description
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.

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 49887
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

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

Study results