The "Radiance II" Pivotal Study - A Study of the ReCor Medical Paradise System in Stage II Hypertension

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The objective of the RADIANCE II Pivotal study is to demonstrate the effectiveness and safety of the Paradise System in subjects with Stage 2 hypertension on 0-2 medications at the time of consent. Prior to randomization, subjects will be…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Vascular hypertensive disorders
Study type	Interventional

Summary

ID

NL-OMON55721

Source
ToetsingOnline

Brief title
The *Radiance II* Pivotal Study

Condition

- Vascular hypertensive disorders

Synonym
hypertension - high blood pressure

Research involving
Human

Sponsors and support

Primary sponsor: ReCor Medical B.V.
Source(s) of monetary or material Support: ReCor Medical BV

Intervention

Keyword: Reduction ambulatory blood pressure, Renal denervation, Therapeutic ultrasound energy, Uncontrolled hypertension

Outcome measures

Primary outcome

The Primary Efficacy endpoint is a reduction in average daytime ambulatory

systolic BP from baseline to 2 months post procedure.

Secondary outcome

The statistical analysis of the Secondary Efficacy Endpoints will follow the

methodology of the Primary Efficacy Endpoint:

• Reduction in average 24-hr ambulatory systolic BP at 2 months post procedure.

• Reduction in average office systolic BP at 2 months post procedure

• Reduction in average home systolic BP at 2 months post procedure

• Reduction in average daytime ambulatory diastolic BP at 2 months post

procedure

• Reduction in average 24-hr ambulatory diastolic BP at 2 months post procedure

• Reduction in average office diastolic BP at 2 months post procedure

• Reduction in average home diastolic BP at 2 months post procedure

The primary safety endpoint is the 30 day post randomization incidence of Major

Adverse Events (MAE), a patient level composite of the incidence of the

following events:

• All-cause mortality

• New onset (acute) end-stage renal disease (eGFR< 15 mL/min/m2 or need for

renal replacement therapy)

• Significant embolic event resulting in end-organ damage (e.g., kidney/bowel infarct, lower extremity ulceration or gangrene, or doubling of serum

• creatinine)

• Renal artery perforation requiring an invasive intervention

• Renal artery dissection requiring an invasive intervention

• Major vascular complications (e.g, clinically significant groin hematoma, arteriovenous fistula, pseudoaneurysm) requiring surgical repair, interventional procedure, thrombin injection, or blood transfusion (requiring more than 2 units of packed red blood cells within any 24-hr period during the first 7 days post randomization)

• Hospitalization for hypertensive or hypotensive crisis

• Hospitalization for major cardiovascular- or hemodynamic- related events (e.g. HF; MI; Stroke)

• New onset Stroke

• New onset Myocardial Infarction

or,

• New renal artery stenosis >70%, confirmed by angiography within 6 months of randomization

Study description

Background summary

The ReCor Medical Paradise® Renal Denervation System (Paradise System) is a catheter-based system that delivers ultrasound energy to thermally ablate and

disrupt the renal efferent and afferent sympathetic nerves while sparing the renal arterial wall. The goal of renal nerve ablation is to achieve a reduction in sympathetic over-activity with the resultant effect of reducing systemic arterial blood pressure (BP), and mitigating resultant end organ damage.

Study objective

The objective of the RADIANCE II Pivotal study is to demonstrate the effectiveness and safety of the Paradise System in subjects with Stage 2 hypertension on 0-2 medications at the time of consent. Prior to randomization, subjects will be hypertensive in the absence of hypertension medication

Study design

RADIANCE II is a randomized, double-blind, sham-controlled, single cohort study designed to demonstrate the effectiveness and safety of the Paradise Renal Denervation System in hypertensive subjects.

Intervention

Subjects with hypertension (average seated office BP >= 140/90 mmHg and < 180/120 mmHg will undergo a 4-week washout period of drug discontinuation. Drug discontinuation will occur in accordance with accepted, institutional guidelines for the subjects* current medication. Subjects currently not taking any antihypertensive medication with an average seated office BP >= 140/90 mmHg and < 180/120 mmHg will undergo a 4-week run-in period.

After 4 weeks of drug discontinuation or run-in, all subjects will undergo a second office BP check. Assuming that the subject has not met the safety escape criteria during the washout/run-in period, they will undergo a 24-hr ambulatory BP (ABP) measurement. Subjects whose daytime ABP remains >= 135/85 mmHg and <170/105 mmHg, will undergo a baseline renal Computed Tomography Angiography (CTA) or Magnetic Resonance Angiography (MRA) to rule out renal abnormalities, renal artery pathology and/or significant renal artery stenosis, and to confirm anatomical eligibility if a cross-sectional imaging study (either CTA or MRA) is not already available that has been performed within one year prior to consent. Subjects with suitable renal artery anatomy on CTA/MRA will undergo a renal angiogram procedure. Subjects whose renal anatomy is re-confirmed as suitable will then be randomized to renal denervation or blinded control (*sham*).*

*For those subjects randomized to blinded control, the renal angiogram will be considered the sham
procedure

Study burden and risks

Since all subjects that are included in the RADIANCE-HTN Study have been diagnosed with hypertension, all patients may benefit from the close evaluation of their hypertension via frequent office follow-ups, medication review and home and 24-hr ambulatory blood pressure measurements. All subjects may also benefit from having diagnostic non-invasive and invasive evaluation of their renal anatomy in the event of previously undiagnosed renal abnormalities or stenosis. These benefits may help to balance any additional burden caused by having to come monthly to the hospital for the purpose of the study for the first 6 months.

The renal denervation procedure is a standard interventional cardiology procedure that can be performed quickly with minimal injury to non-target tissues. Ablation of nerves can be painful however the procedure is tolerable with appropriate analgesic medication. For patients that are treated, there is a potential that they may have their elevated blood pressure decreased without the need for additional antihypertensive medications or indeed with a concomitant reduction in antihypertensive medications. Over the long term, such a reduction in blood pressure may result in a decreased risk of cardiovascular events including stroke, that are associated with prolonged hypertension. The procedure risks are limited to short-term pain, and standard angioplasty catheter related risks. For sham patients, the risks related to the procedure are limited to those related to a renal angiogram procedure which can be reduced further by appropriate use of appropriate guide catheters, anticoagulation protocols taking into consideration the risk to the patient and analgesia.

Before treatment:
Questions about healthcare
Questions about possible changes in medication intake
2x office bloodpressure
24-hour ambulatory BP
2X physical examination
12-lead ECG
withdrawal HTN medication
blood and urine samples
urine analysis for detection of blood pressure medications
CTA/MRA (if needed)
Pregnancy test (if applicable)

During procedure day: sedation and pain relief medication per hospital protocol, catheterization, angiogram, renal denervation both kidneys

Discharge; Blood pressure measurement (if required), Questions about possible changes in medication intake, pain perception, blinding index

Visits and procedures during study (na 1, 2, 3, 4, 5, 6 en 12) months
• BP measurement

• Review and discuss home BP measurements
• Physical examinations
• Questions about healthcare
• Questions about possible changes in medication intake

Additional assessments done during visits at 2, 6 en 12 months:
* 24-hour ambulatory BP
* ECG
* Blood and urine samples
* Urine analysis for detection of blood pressure medications
* Questions about healthcare
* Questions about possible changes in medication intake
* Questions about patient idea whether is treated or not (not at 12 months)
* CTA / MRA after 6 and 12 months (at 12 months, only for the renal denervation group)

Visits and procedures during study after 24, 36, 48 en 60 months:
* BP measurement
* Physical examinations
* Questions about healthcare

There are possible risks associated with the general renal denervation procedure as well as risks specifically associated with use of the Paradise catheter system. These include but are not limited to:
Pain
Arrhythmias (bradycardia or tachycardia)
Cardiopulmonary arrest
Embolism
Allergy to contrast
Renal insufficiency/renal failure
Hematoma/pseudo aneurysm
Hypertension or hypotension
Infection
Fever
Renal artery stenosis/dissection/perforation/spasm
Nephrectomy
Arterio-venous or enteric fistula
Hematuria
Exposure to radiation
Cerebrovascular events including Stroke and TIA
There are also potential risks associated with the use of antihypertensive medication including allergy or intolerance.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Appropriately signed and dated informed consent
• Documented history of hypertension
• Previously or currently prescribed antihypertensive therapy
• Average seated office BP >= 140/90 mmHg <180/120 mmHg at Screening Visit (V0) while stable for at least 4 weeks on 0-2 anti-hypertensive medications of different classes
• Able and willing to comply with all study procedures
Subjects who meet the following criteria will be considered eligible for randomization:
• Documented daytime ABP >= 135/85 mmHg and < 170/105 mmHg at Baseline Visit (V1) after 4-week washout/run-in period
• Suitable renal anatomy compatible with the renal denervation procedure, documented by renal CTA or MRA of good quality performed within one year prior

to consent (a CTA or MRA will be obtained in patients without a recent (<=1 year) cross-sectional renal imaging) and confirmed by renal angiogram in subjects that continue to procedure

Exclusion criteria

• Renal artery anatomy on either side, ineligible for treatment including:
o Main renal artery diameter < 3 mm or > 8 mm
o Main renal treatable artery length < 20 mm (may include proximal branching)
o A single functioning kidney
o Presence of abnormal kidney tumors
o Renal artery with aneurysm
o Pre-existing renal stent or history of renal artery angioplasty
o Pre-existing aortic stent or history of aortic aneurysm
o Prior renal denervation procedure
o Fibromuscular disease of the renal arteries
o Presence of renal artery stenosis of any origin >= 30%
o Accessory arteries with diameter >=2mm <3.5 mm or > 8 mm
• Known, uncorrected causes of secondary hypertension other than sleep apnea
• Any history of cerebrovascular event (e.g. stroke, transient ischemic event, cerebrovascular accident)
• Any history of severe cardiovascular event (e.g. myocardial infarction, CABG, acute heart failure requiring hospitalization (NYHA III-IV)
• Documented confirmed episode(s) of stable or unstable angina
• Documented repeat (>1) hospitalization for hypertensive crisis within the prior 12 months and/or any hospitalization for hypertensive crisis within three (3) months prior to consent
• Prescribed to any standard antihypertensive of cardiovascular medication (e.g. beta blockers) for other chronic conditions (e.g. ischemic heart disease) such that discontinuation might pose serious risk to health in the opinion of the Investigator

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-07-2021
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Catheter based system that delivers ultrasound energy
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	29-01-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-07-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-01-2022
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
ClinicalTrials.gov	NCT03614260
CCMO	NL67166.078.19