intErNationaL non-randomized, sIngle arm, lonG-term follow-up study of patients with uncontrolled HyperTensioN (ENLIGHTN II)

Published: 10-07-2013
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The purpose of this Clinical investigation is to further evaluate the safety and performance of the EnligHTN* Renal Denervation System in the treatment of patients with uncontrolled hypertension.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Vascular hypertensive disorders
Study type	Observational invasive

Summary

ID

NL-OMON40104

Source
ToetsingOnline

Brief title
EnligHTN II

Condition

- Vascular hypertensive disorders

Synonym
Therapy resistant Hypertension - Uncontrolled High Blood Pressure

Research involving
Human

Sponsors and support

Primary sponsor: St. Jude Medical

Source(s) of monetary or material Support: St. Jude Medical

Intervention

Keyword: BP reduction, Post market, Renal ablation, Uncontrolled hypertension

Outcome measures

Primary outcome

The primary objective is to evaluate a mean reduction in office Systolic Blood Pressure at six (6) months across all subjects post renal denervation and within sub-groups.

Secondary outcome

The secondary objectives are:

1. Safety

Acute (30 days post procedure):

* The assessment of peri-procedural events

Midterm (6 months):

* Assessment of renovascular safety as measured by new renal artery stenosis or aneurysm at the site of ablation

* Renal function change based on eGFR

Long term (2 and 5 years):

* Assessment of renovascular safety as measured by new renal artery stenosis or aneurysm at the site of ablation

* Renal function change based on eGFR

2. BP reduction

* Change in Ambulatory Blood Pressure parameters at 6 months

* Change in office Diastolic Blood Pressure at 6 months

* Percentage of subjects achieving office Systolic Blood Pressure < 140mmHg at

6 month visit

*Change in Office and Ambulatory Blood Pressure parameters at 12, 24, 36, 48,

60 months post denervation

Study description

Background summary

Hypertension or high blood pressure is a major risk factor for cardiovascular and cerebrovascular events. It is responsible for approximately one half of the coronary heart disease and two thirds of the cerebrovascular disease burdens. It is also the world*s number one attributable risk for death. The global prevalence of hypertension has been increasing. An analysis indicated that more than one quarter (nearly one billion) of the world*s adult population had hypertension in 2000. This is projected to increase to 1.56 billion affected individuals with a prevalence rate of 29% in 2025. This is a major public health challenge in both economically developing and developed countries.

Previous studies showed that drug therapy may reduce the risk of major cardiovascular events by about 20% and the risk of stroke by about 40% in patients with hypertension. However, these may not apply to all patients with hypertension. A large proportion of patients with hypertension still remains untreated or uncontrolled due to many factors. For patients with resistant hypertension despite the use of aggressive drug therapy, which includes at least 3 anti-hypertensive drugs with a diuretic being one of these drugs, blood pressure management remains uncontrolled. In the general hypertensive population, the prevalence of resistant hypertension is estimated to be about 5% to 12%. In patients with co-morbidity, such as chronic renal failure or diabetes, the prevalence of resistant hypertension is even significantly higher. Hypertension is also mainly an symptomatic disease, which could be difficult to have the patient understanding about the importance of complying and adhering to the lifelong drug therapy. Alternative approaches to control the blood pressure of these patients are urgently needed.

The kidneys represent the central homeostatic organ regulating blood pressure and blood volume. Previous experimental functional studies showed that renal

denervation could reduce the norepinephrine level of up to 95%. In various experimental models the magnitude of the hypertension has been reduced and the renal blood flow has been increased during the observation period after renal denervation.

Percutaneous catheter-based methods deliver radiofrequency (RF) energy to the renal sympathetic nerves for the ablation-induced renal denervation. This minimally invasive and more localized approach allows for possibly much shorter procedural time, shorter hospital stay and shorter recovery time, which may benefit more patients with uncontrolled hypertension.

Recent clinical studies reported significant improvement of office blood pressure measurement in patients with resistant hypertension after the catheter-based renal denervation procedure (about -20/-10 mmHg, -25/11 mmHg, -23/-11 mmHg and -32/-14 mmHg at 1, 6, 12 and 24 months respectively from baseline systolic/diastolic blood pressures).

EnligHTN-I (ARSENAL) was a feasibility study to demonstrate the safety and efficacy of the St. Jude Medical Radiofrequency Renal Denervation System in the treatment of patients with resistant hypertension. Subjects will be followed for 24 months post procedure. This clinical data shows that the average systolic / diastolic Blood Pressure between baseline and one month was -28/-10 mmHg with 78% of the patients experiencing a * 10 mmHg reduction in systolic Blood Pressure. After three months this difference was -27/-10 mmHg with 80% of the patients experiencing a * 10 mmHg reduction in systolic Blood Pressure. The mean systolic/diastolic ambulatory Blood Pressure difference between baseline and 3 months was -9.9/-5.4 mmHg. Recently the 6 month data was presented; the difference was -27/-10 mmHg and -10,3/-5,7 in systolic ambulatory Blood Pressure.

Study objective

The purpose of this Clinical investigation is to further evaluate the safety and performance of the EnligHTN* Renal Denervation System in the treatment of patients with uncontrolled hypertension.

Study design

This is a post market, prospective, multicenter, non-randomized, single arm study of the EnligHTN* Renal Denervation System. Approximately 500 subjects with uncontrolled hypertension will undergo renal artery ablation at approximately 40 investigational sites located internationally and will be followed up to five (5) years post procedure.

Study burden and risks

Having blood taken may cause some discomfort or bruising. Sometimes, the blood vessel may swell, or blood may clot in the blood vessel, or the spot from which blood is taken could become inflamed. Rarely, there could be a minor infection or bleeding. If this happens, it can be easily treated.

The renal denervation is an interventional approach, and as such carries some potential risks, which may include but are not limited to the following:
*Acute renal injury such as unintended renal tissue damage or bruising
*Injury to the renal arteries such as a tear in the lining of the artery, formation of a blood clot or narrowing of the artery
*Bleeding
*Injury to the tissues surrounding the renal arteries
*Worsening of high blood pressure
*Low blood pressure that may result in feeling light headed, faint or dizzy
*Injury at the site of catheter insertion such as:
o The formation of an abnormal connection between an artery and vein resulting in abnormal blood flow
o The formation of a blood clot
o The obstruction of a blood vessel by an air bubble, foreign object or blood clot
o Bulging of an artery due to injury to one or more of its layers
o Bruising
o Decreased blood flow and oxygen to the limb
o Damage to the nerve in the thigh
o Accumulation and seeping of cellular fluid at the insertion site
*Formation of small blood clots inside the blood vessels throughout the body (disseminated intravascular coagulation)
*Temporary very slow heart beat during the procedure
*Pain (including back pain)
*Unintended reactions to the drugs used during the procedure
*Allergic reaction due to contrast media injected during the procedure
*Infection (at the site of catheter insertion or throughout the body)
*Renal failure
*Worsening of heart failure
*Heart attack
*Stroke
*Difficulty breathing
*Death
*Blood vessels spasms (vasospasms)
*Discomfort which may lead to fainting (vasovagal episodes)

When you have a CT scan or renal artery angiogram, you will be exposed to radiation. This research study involves exposure to a small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from this study is about 25 mSv. The dose from this study is comparable to that received from several computed tomography

x-ray (CT) and nuclear medicine procedures. The benefits from the study should be weighed against the possible detrimental effects of radiation, including an increased risk of fatal cancer. In this particular study, the risk is moderate and the estimated risk of such harm is about 1 in 800. For comparison, this risk is about 200 times lower than the cancer mortality rate in the general population of about one case in every four people.

The effects of renal denervation procedure on the unborn child and on the newborn baby are not known. Because of this, it is important that study participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you may be required to undergo a pregnancy test prior to commencing the research project.

There may be other risks that are not known at this time.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Subject is * 18 years of age at time of consent
- Subject must be able and willing to provide written informed consent
- Subject must be able and willing to comply with the required follow-up schedule
- Subject has office Systolic Blood Pressure * 140 mmHg at confirmatory visit
- Subject has a daytime mean Systolic Ambulatory Blood Pressure > 135 mmHg within 90 days prior to enrollment
- Subject has established hypertension (diagnosed *12 month prior to baseline) and on a stable, guideline based drug regimen consisting of * 3 anti-hypertensive medications (must include 1 diuretic) or subject has a documented drug(s) intolerance.

Exclusion criteria

- Subject has significant renovascular abnormalities such as renal artery stenosis > 30%
- Subject has undergone prior renal angioplasty, renal denervation, indwelling renal stents, and/or abdominal aortic stent grafts
- Subject has hemodynamically significant valvular heart disease as determined by study investigator
- Subject has a life expectancy less than 12 months, as determined by the Investigator
- Subject is participating in another clinical study which has the potential to impact their hypertension management (pharmaceutical/device/homeopathic)
- Subject is pregnant, nursing, or of childbearing potential and is not using adequate contraceptive methods
- Subject has active systemic infection
- Subject has renal arteries with diameter(s) < 4 mm in diameter
- Subject has an estimated GFR <15 mL/min per 1.73 m2 using the Modification of Diet in Renal Disease (MDRD) formula
- Subject had a renal transplant or is awaiting a renal transplant

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-10-2013
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	Renal Ablation
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	10-07-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-11-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NCT01705080
CCMO	NL42560.041.13