CALM-DIEM_EUR - Controlling and Lowering Blood Pressure with the MobiusHD* - Defining Efficacy Markers ;CALM-DIEM_EUR Sub-study - Studying the Effect of the MobiusHDTM on Sympathetic Activity and Baroreflex Sensitivity;CALM-DIEM_HTN-HF Sub-study - Studying the Effect of the MobiusHD® System in Hypertensive Patients with mild Chronic Heart Failure

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To evaluate the safety and performance of the MobiusHD system in subjects with resistant hypertension. Substudy HF:As above, and obtain an initial understanding of the efficacy of the MobiusHD System on cardiac performance and functional status in...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45889

Source
ToetsingOnline

Brief title
CALM-DIEM_EUR;CALM-DIEM_EUR Sub-study;CALM-DIEM_HTN-HF Sub-study

Condition

- Other condition

Synonym
Drug resistant high blood pressure, Refractory hypertension

Health condition

Resistant Hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Vascular Dynamics, Inc.
Source(s) of monetary or material Support: Vascular Dynamics Inc.

Intervention

Keyword: Carotid, Heart Failure, Hypertension, MöbiusHD

Outcome measures

Primary outcome

Efficacy Outcome - Change in the 24-hour systolic Ambulatory Blood Pressure

Measurements (ABPM) from Baseline to 90 days post implant.

Safety Outcome - 30-day major adverse clinical events (MACE) including death,

stroke, and/or myocardial infarction.

Substudy HF:

Change in cardiac function/ structure from baseline to 90 days post implant.

Secondary outcome

• Peri-procedural device-related serious events (i.e., dissection, rupture,

aneurysm)

• Incidence of serious adverse events (SAEs) and unanticipated adverse device effects (UADE) reported for the population from implantation through 3 years of follow-up.

• Change in ABPM from baseline to 6 months and 3 years,

Study description

Background summary

Background of the study.
The MobiusHD is a device developed specifically for patients with refractory hypertension. The MobiusHD device is designed to make the blood pressure sensors (baroreceptors) in the carotid artery more sensitive, increasing signals that a patient*s blood pressure is too high.
The MobiusHD device has been tested in animals. After placement of the MobiusHD device in the carotid artery of dogs, their blood pressure decreased significantly.
The MobiusHD device is tested in patients in the CALM-FIM studies (CALM-FIM_US and CALM-FIM_EUR). The CALM-FIM_EUR has completed enrollment. The purpose of this study is to measure the benefits and the safety of treatment with the MobiusHD system in research participants with refractory hypertension. The results of the study are considered very positive and the MobiusHD has been granted CE mark for the treatment of resistant hypertension. The CALM_US study is still ongoing and until now the results of that study seem to be positive for the patients. The CALM-DIEM study was kicked off as part of the post-market surveillance.

Background of the sub-study:
It is assumed that the MobiusHD device lowers blood pressure through activation of the baroreflex and thereby inhibiting the sympathetic nervous system and decreasing peripheral vascular resistance. However, there is no evidence that the MobiusHD device truly inhibits sympathetic activity through this mechanism. Therefore, to test this hypothesis, we need to assess whether MobiusHD implantation truly decreases sympathetic activity in treated patients.

Background of the sub-study HF
Hypertension is the most common cause of HF, and most patients who have developed HF have a history of hypertension. A number of clinical trials demonstrate the benefit of treating hypertension in the prevention and treatment of heart failure. Primary prevention trials demonstrate up to a 50% reduction in the incidence of heart failure in patients with hypertension who

are treated with blood pressure lowering agents. In patients with established heart failure, further decreases of blood pressure with therapy may improve the mortality, the progression of disease, hospitalizations, exacerbations, and enhance the quality of life and the functional capacity.
Based on these findings, this sub-study aims to evaluate the impact of the MobiusHD on hypertensive patients who have already developed mild to moderate heart failure. (see also page 10 of the substudy HF)

Study objective

To evaluate the safety and performance of the MobiusHD system in subjects with resistant hypertension.

Substudy HF:
As above, and obtain an initial understanding of the efficacy of the MobiusHD System on cardiac performance and functional status in hypertensive patients with mild to moderate heart failure.

Study design

This is an open-label, prospective, multicenter study. Eligible subjects with resistant hypertension who consent to study participation will be treated with the MobiusHD system, and will be followed for 3 years.

Intervention

MobiusHD implantation

Study burden and risks

The potential risk associated with this procedure should be reasonably similar to the known risks of a similar procedure called carotid angioplasty.

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

1. >= 18 years of age and <= 80 years of age;
2. Diagnosed with primary resistant hypertension;
3. Mean 24-hour systolic ABPM is >=130 mmHg following at least 30 days on a stable anti-hypertensive medication regimen (no changes in medication or dose) and no more than 7 days prior to implantation.For the sub-study:
1. Eligible for the CALM-DIEM Study and having passed all CALM-DIEM Study inclusion and exclusion criteria at CALM-DIEM Study ScreeningFor the HF sub-study:
1. Eligible for the CALM-DIEM Study and having passed all CALM-DIEM Study inclusion and exclusion criteria at CALM-DIEM Study Screening
2. Mild to moderate chronic heart failure (New York Heart Association (NYHA) Class II or III)ndefined

Exclusion criteria

1. An inability provide written informed consent.
2. Known or clinically suspected baroreflex failure or autonomic neuropathy.
3. Known significant aortoiliac or common femoral artery disease that will prohibit safe femoral access.
4. Hypertension secondary to an identifiable and treatable cause other than sleep apnea (e.g., hyperaldosteronism, renal artery stenosis, pheochromocytoma, Cushing's disease, co-arctation of the aorta, hyperparathyroidism and intracranial tumor).

5. Treatable cause of resistant hypertension including, but not limited to, improper BP measurement, volume overload and pseudotolerance (excessive sodium intake, volume retention from kidney disease, inadequate diuretic therapy), drug-induced or other causes (non-adherence, inadequate doses, inappropriate combinations, NSAIDs, COX-2 inhibitors, cocaine, amphetamines, or other drugs, sympathomimetics, oral contraceptives (confirmed cause of resistant hypertension), adrenal steroids, cyclosporine, and tacrolimus, erythropoietin , licorice (including some chewing tobacco), ephedra, ma haung, bitter orange); and excessive alcohol intake.
6. Arm circumference greater than 46 cm and/or BMI >= 45.
7. Chronic atrial fibrillation or recurrent atrial fibrillation with episode within the last twelve (12) months.
8. History of bleeding complications with dual antiplatelet therapy in the past or has known uncorrectable bleeding diathesis.
9. Current use of anticoagulation therapy, other than dual antiplatelet medications. Examples include vitamin K antagonists and novel oral anticoagulants including apixaban, rivaroxaban, dabigatran etexilate and edoxoban.
10. Peptic ulcer disease with documented active ulcer or bleeding within the last year.
11. History of allergy to contrast media that cannot be managed medically.
12. Persistent symptomatic orthostatic hypotension (>20/10 mmHg).
13. Persistent symptomatic syncope documented to be related to hypertension within the last six (6) months.
14. History of myocardial infarction or unstable angina within the past three (3) months.
15. History of cerebral vascular accident (stroke or TIA) within the past year, and NIHSS >5 or mRs >1.
16. Chronic kidney disease (GFR calculated by the Modification of Diet in Renal Disease equation < 45 ml/min).
17. Prior carotid surgery, radiation, or endovascular stent placement in either carotid region.
18. Severe valvular or structural heart disease (excluding LV hypertrophy).
19. Severe chronic obstructive pulmonary disease (requiring twenty-four-hour oxygen or oral steroids), asthma, or severe pulmonary hypertension.
20. Uncontrolled diabetes mellitus with HbA1c >= 10 %.
21. Active infection within the last month requiring antibiotics.
22. Uncontrolled co-morbid medical condition, including mental health issues, that would adversely affect participation in the trial.
23. Co-morbid condition that reduces life expectancy to less than one (1) year.
24. Planned surgery or other procedure within the next six (6) months requiring cessation of antiplatelet medications.
25. Pregnant or lactating females. For females of child-bearing potential, a positive pregnancy test within seven (7) days of the pre-randomization screening or refusal to use a medically accepted method of birth control for the duration of the trial;
26. Presence of visible atherosclerotic plaque or areas of intimal thickness

(IMT) of >1500 micron in the region of the carotid bifurcation (15 mm proximal and 15 mm distal to the ICA ostium), determined at a central core laboratory.
27. Significant obstructive vascular disease, calcification or plaque of aortic arch and great vessels by ultrasound, CTA or MRA;
28. Renal artery stenosis >50% or systolic gradient >10mmHg in borderline cases diagnosed by renal artery imaging in the last 36 months. Acceptable renal artery imaging modalities include renal duplex, magnetic resonance angiography, CT angiography, and selective or nonselective renal angiography depending on trial site diagnostic standards;
29. Internal Carotid Artery (ICA) lumen diameters <5 mm or >12.5 mm within the planned location of the implant placement via CTA or MRA. Evidence of landing zone restrictions, such as inadequate length, vessel tapering, and/or vessel curvature that would preclude safe placement of the implant;
30. Enrolled in a concurrent clinical trial or an investigational drug or device that has not yet reached its primary endpoint.
31. Unable or unwilling to fulfill the protocol follow-up requirements.
32. Subject is a prisoner or member of other vulnerable population. For the sub-study:
1. An inability to provide written informed consent for the sub-study;
2. Use of anti-hypertensive medications directly acting on the sympathetic nervous system, that
cannot be discontinued safely;
3. Uncontrolled or involuntary movements disturbing microneurography, such as tremors, fasciculations and chorea;
4. Absence or paralysis of both legs;
5. Polyneuropathy or clinical suspicion for autonomic nervous system dysfunction;
6. Known claustrophobia;
7. Metallic implants, prostheses or other foreign bodies causing potential artefacts obscuring the visibility of signals from the site of MobiusHD implantation during MRI scanning;
8. Cochlear implants, pacemakers, neurostimulators, stents or grafts at risk of malfunction due to the magnetic field;
9. Underlying conditions that prohibit a Valsalva maneuver: i.e. aortic stenosis, cardiac arrhythmia, glaucoma, and/or retinopathy.Angiographic
1. Evidence of any carotid plaque, ulceration or any stenosis on selective carotid angiography performed in orthogonal views. Luminal diameters will be assessed to exclude subjects with ICA lumen diameters < 5 mm or > 11.75 mm within the planned location of the device placement;
2. Any angiographic evidence of plaque or ulceration in the aortic arch and/or the supra aortic vasculature;
3. Inappropriate anatomy of the carotid bifurcation for deployment of the MobiusHD, including, but not limited to; tortuosity of the extracranial vessels and significant angulation of the common carotid artery bifurcation;
4. Type III arch or horizontal takeoff of the left carotid from the innominate and calcification of the carotid bulb.For the HF sub-study:
1. Patients must not have any of the following specific Heart Failure Sub-study

exclusion criteria:
• NYHA Class IV Heart Failure
• Acute pulmonary edema or unstable angina within 60 days
• On IV inotropic medication
• Receiving cardiac resynchronization therapy

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Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-06-2016
Enrollment:	39
Type:	Actual

Medical products/devices used

Generic name:	MOBIUS HD system
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	12-05-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	30-08-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-10-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-11-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-12-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-05-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-08-2017
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-11-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-03-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-06-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NCT01831895
CCMO	NL56326.100.15