shortreport

Regione Emilia-Romagna
SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA
osservatorio regionale per l'innovazione

n. 1

Technology

Implantable device for the treatment of drug-resistant hypertension

Commercial technology name

Rheos®

Producer / supplier

CVRx, Inc., USA

Use

■ therapeutic
☐ diagnostic
☐ other .....

Category

Medical device: implantable neurotransmitter

Therapeutic or diagnostic field of application

Cardiovascular

Patients / clinical condition

- Drug-resistant hypertension
- Heart failure

Contraindications

The use is contraindicated in the patients with:

- diagnosed bilateral carotid bifurcations, located above the level of the mandible;
- baroreflex loss;
- symptomatic, uncontrolled cardiac bradyarrhythmias;
- carotid atherosclerosis > 50%, diagnosed by ultrasound or angiographic evaluation;
- ulcer lesions of the carotid artery, diagnosed by ultrasound or angiographic evaluation;
- previous surgery or radiation treatment of a carotid sinus.

Technology description

The Device Based Therapy of Hypertension (DEBuT-HT) employs a battery generator of pulses to the carotid sinuses, able to induce electrically and chronically the carotid reflection (baroreflex). When the baroreceptors are activated, they send signals to the brain, along the neural pathways, where they are interpreted as an increase in blood pressure.

The brain reacts to this perceived rise in blood pressure by sending signals to other parts of the body (heart, blood vessels and kidneys) to relax the blood vessels and inhibit the

The report

A brief presentation of a technology, providing sufficient information to decide whether to undertake a comprehensive assessment process.

The reported information derives from:

› the consultation of web materials supplied by the producer and of current national and/or regional registries

› the search of secondary studies on HTA databases and of primary studies, indexed on Medline.

! The report does not represent a definitive assessment of the technology.

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production of stress hormones. These changes are designed to reduce blood pressure and allow the heart to increase the cardiac output, while maintaining stable or reducing its workload.

The Rheos system® includes the following components:

- Rheos implantable pulse generator model 2000
- Rheos derivations for carotid sinuses
- Rheos programming system model 9000, including a computer for programming, a programming interface, an USB memory device and the programming software.

Target patients

From the literature: in the ALLHAT study (*1*) about 8% of patients received an anti-hypertensive treatment with 4 or more drugs and it has been estimated that at least 15% of them were treatment-resistant.

From the database of the pharmaceutical area of the Emilia-Romagna Region it appears that, in the year 2008, 2 695 patients received at least 3 of the following drugs, with a compliance above 75% (MPR, Medication Possession Ratio) (*a*): beta-blockers, ACE inhibitors, diuretics, calcium-channel blockers. If the Rheos technology should prove effective, 15% of these patients (about 400) could be eligible for its implantation.

Standard treatment / method

Changes in lifestyle (reduction of salt and alcohol intake, weight loss), treatment of the causes of secondary hypertension, multiple drug treatments.

Main expected benefits

Control of hypertension in patients otherwise resistant to drug therapies.

Available evidence and results

N° and type of studies

- Published between 2006-2009 (previous indexed publications have not been found):
  - ¬ 1 Horizon Scanning Technology Prioritising Summary (*2*) (where 4 case series were included, 3 of which available only as not indexed abstracts);
  - ¬ 6 publications from Pubmed:
    - * 4 case series - N. included patients: 10-21 with a max. follow up of 4 months (*3*, *4*, *5*, *6*);
    - * 2 case reports (*7*, *8*);
- The documentation produced by the supplier includes 63 publications in the form of abstracts, presentations at conferences and posters related to preclinical and clinical studies. Among the publications defined as clinical, 2 case reports and 20 case series are not included in the Horizon Scanning report (*2*) nor indexed in PubMed.
  Three of these case series relate to heart failure. These case series have a sample size between 5 and 61 patients, with the exception of a study on 170 patients (with a follow up of 2 years for 32 patients). Most of these case series are double publications or report results probably already described in other studies. Names of the authors suggest that the majority of the studies is conducted by the same researchers.

Outcomes

- EFFICACY
  The 4 case series included in the Horizon Scanning report (*2*) describe a significant and strong reduction of the blood pressure (max follow up: 2 years). Some studies show a positive effect of the device on left ventricular hypertrophy.

  The quality and quantity of studies does not allow to draw conclusions about the efficacy of the device.

- SAFETY
  Two of the three studies included in the Horizon Scanning report (*2*) refer that there were no important adverse events associated with the procedure or device. In one study (N=16) the following adverse events are reported: infection (N=1), trauma to the hypoglossal nerve (N=1); intraoperative bradycardia, spontaneously resolved (N=2); pain (N=6); wound complications (N=3); complications due to anaesthesia (N=2).

  The quality and quantity of studies does not allow to draw conclusions about the safety of the device.

Notes

The Horizon Scanning report (*2*) refers that, in each of the four case series, one of the co-authors

belonged to CVRx, the manufacturer Company.

Costs

The product is still experimental and its price has not yet been determined.

According to the manufacturer, the cost of the device could be placed between that of a basic pacemaker (€ 5 000) and that of an implantable cardioverter (€ 25 000). Costs of procedures associated with the implant, monitoring and periodic replacement should also to be added.

Presumed impact

Clinical issues

Although cardiovascular risk reduction with treatment of drug resistant hypertension is not known, there is consensus that control of hypertension leads to substantial clinical benefits (*9*).

Economic issues

The economic impact is likely to be high and variable, depending on the indications of use (implanting the device in all subjects with drug-resistant hypertension, or only on a proportion of them, e.g. according to the severity of the hypertension, the compliance of the patient to the pharmacological treatment, other risk factors and concomitant diseases).

It is still to be evaluated whether implant of the device can have an effect on patients' clinical pathways (e.g. need for subsequent hospitalisation).

Organisational issues

The application of the device requires specialised professionals.

The implant of the Rheos device requires a surgical procedure at the carotid sinuses and therefore needs to be carried out in facilities equipped with the necessary services, such as: a department of Anaesthesiology, Intensive Care and Vascular Surgery.

Ethical-social issues

Not evaluated.

Ongoing studies

5 registered studies (all sponsored by CVRx): 3 RCTs and 2 non-controlled studies (*10*).

STUDY	PATIENTS / CONDITIONS	STUDY DESIGN	PRIMARY ENDPOINTS	END OF STUDY
Rheos Pivotal trial NCT00442286	Drug-resistant hypertension (N = 300)	RCT Rheos ON vs. OFF (*b*)	» BP reduction at 6 months » Sustained response to therapy at 12 months » Adverse effects associated with the system/procedure at 30 days » Events associated with hypertension at 13 months » Severe adverse effects associated with the device at 13 months	DEC 2009
Rheos Diastolic Heart Failure trial NCT00718939	Heart failure (N = 60)	RCT Rheos ON vs. OFF (*b*)	» BP reduction at 6 months - Left ventricular mass index at 6 months » Adverse effects at 6 months	JAN 2011
Rheos HOPE4HF NCT00957073	Heart failure (N = 540)	RCT Rheos ON vs. placebo	» Cardiovascular mortality or episodes of heart failure » Complications related to the system and procedure at 6 months	DEC 2013
Device based therapy in hypertension extension trial NCT00710294	Drug-resistant hypertension (N = 50)	Non-controlled study	» Adverse effects associated with the system/procedure at 13 days	DEC 2010
Device based therapy in hypertension trial NCT00710190	Drug-resistant hypertension (N = 45)	Non-controlled study	» Safety and efficacy	DEC 2010

Authorisations

CE mark: N. 517096.

FDA authorisation: in progress, pending the completion of clinical trials.

Medical Devices Repertoire number (Italian Dept. of Health): 218347.

Diffusion / diffusion prediction

The product will be marketed in Italy starting from October 2009.

Brief summary

The technology is still experimental and results on safety and clinical efficacy are not yet available. The implant of the device involves a rather complex surgical procedure requiring high expertise for surgery and anaesthesia, and it is achievable only in appropriate facilities. Assuming that further empirical studies can document its actual clinical value, it is reasonable to hypothesize that it will be limited to that subset of hypertensive patients whose blood pressure control is demonstrated not to be restored with other interventions (i.e. to ensure better patient compliance to treatment).

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10. http://www.clinicaltrials.gov

Note

a. MPR is an index used to express the level of compliance. It is calculated as a percentage of the treatment time in which the drug was available.

b. Rheos ON indicates the device activated, while Rheos OFF indicates device deactivated.

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