Cardiac Contractility Modulation (CCM) Therapy in Subjects with Medically Refractory Heart Failure: A Randomized Efficacy Study (*IMPULSE-HF*)

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Ethical review	Approved WMO
Status	Pending
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON42472

Source
ToetsingOnline

Brief title
IMPULSE-HF

Condition

- Heart failures

Synonym
heart failure, wea

Research involving
Human

Sponsors and support

Primary sponsor: Impulse Dynamics Inc.

Source(s) of monetary or material Support: Impulse Dynamics Germany GmbH

Intervention

Keyword: Cardiac Contractility Modulation (CCM), Ejection Fraction 25 - 45%, Heart Failure, NYHA II-III

Outcome measures

Primary outcome

Primarv endpoint:

Comparison between the groups of change in V02 max from baseline to 24 weeks of follow-up.

VO2max will be evaluated by cardiopulmonary stress test (CPX), in a double assessment (i.e., tests will be repeated twice at each study follow-up - the two evaluations can be up to 2 weeks apart).

Secondary outcome

Secondarv endpoints:

Efficacv Comparison between the groups of:

* Change in quality of life as measure by Minnesota Living With Heart Failure Questionnaire (MLWHFQ), from baseline to 24 weeks.

* Change in NYHA class, from baseline to 24 weeks

* Change in V02max from baseline to 24 weeks for each of the following subgroups separately: Baseline EF <35% , baseline EF >35%

Other endpoints - exoloratory: Change in SHFM and MAGGIC survival prediction model scores from baseline to 6 month of follow-up.

Safetv endpoints:

Comparison between the groups of:

* All-cause mortality

* Cardiovascular mortality

* Time to first event - cardiovascular related (death, LVAD, urgent heart

transplant or unplanned heart failure hospitalization)

* Time to first event - all cause (death or unplanned hospitalization)

Study description

Background summary

The OPTIMIZER* System is CE marked, compliant with all relevant regulations and standards and is commercial (not investigational) in countries that accept the CE Mark. This study will collect efficacy data in a randomized controlled setting, including NYHA class II and III Heart Failure population with baseline ejection fraction of 25% to 45%. There is previous evidence related to the beneficial effect of CCM in patients with baseline ejection fraction of <35%. While patients with EF between 35% and 45% were not prospectively studied in the original clinical study initially conducted to support CE Marking of the OPTIMIZER System, recently available data from a randomized study that included such patients show CCM to be safe and effective in this group of patients as well. Furthermore, the literature supports that this population has very similar clinical characteristics, in practice are treated with nearly the same medications, and have similar underlying mechanisms of disease compared to patients with EF <35%. CCM has been successfully used also in patients with EF greater than 35% in routine use and in the FIX-HF-5 study. Since the system is CE marked and since the population includes patients meeting the approved indication as well as population that has shown to benefit from CCM (EF 35%-45%), the risk involved in performing such a clinical investigation seems acceptable.

Study objective

The study is designed to substantiate the efficacy of CCM in the heart failure population with ejection fraction ranging between 25 and 45%. The study is designed in an adaptive manner to ensure proper statistical significance and

power of the primary efficacy evaluation.

Study design

The study is a prospective, multi-center, randomized study comparing CCM plus optimal medical therapy (OMT) (Treatment Group) to OMT alone (Control Group) over a 6 month period.
The total number of patients enrolled and randomized at up to about 20 sites will be 100 (50 in the treatment group and 50 in the control group). The number of patients may be adjusted to no more than 200, after interim analysis of V02 data from about 50 cases.

Intervention

Subjects undergoing implantation of an OPTIMIZER pulse generator and associated leads will be prepared for device implantation according to the procedure of the institution. After access to the subclavian or cephalic vein, an atrial lead will be placed transvenously into the right atrium for sensing atrial activity. Two additional leads will be placed transvenously into the right ventricle for sensing ventricular activity and delivering CCM signals. The preferred lead arrangement is for one RV lead to be placed in the anterior septal groove and the other in the posterior groove approximately half way between the base and apex. The second most preferred lead arrangement would be for both leads to be positioned in the anterior or posterior septal groove with a Separation of at least ~2 cm.

Study burden and risks

Potential risks associated with heart failure and interventional cardiac procedures:
The results of clinical studies suggest that there are no significant risks to subjects directly related to application of CCM signals. However, there are recognized risks associated with the heart failure state itself, with interventional cardiac procedures in heart failure patients and potentially with the use of the OPTIMIZER System. These risks are described in section 3 (page 14-17) of the study protocol.
As a result of participation in the study, patients are asked to perform two standard cardiopulmonary stress tests each at baseline and at 24 weeks. The cardiopulmonary stress test is non-invasive, typically only lasts about 10 minutes and is widely used in clinical practice and in heart failure research. Therefore, while the performance of 4 tests in 6 month is typically more than routinely done in standard practice, it presents minimal risk to patients.
The therapy is provided by a CE marked device, and has been demonstrated to be safe while providing clinical benefit to the patient. The potential risks are balanced by the potential benefits which significantly outweigh any potential

negative consequences that could still arise, despite the mitigations applied

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

a) Baseline ejection fraction * 25% and *45% (as assessed by the site)
b) NYHA class II or III despite receiving optimal medical therapy for heart failure, stable for at least 30 days based on patient*s medical records (chronic, not transient, heart failure)
c) Baseline VO2,max * 9 and * 18.5 ml O2/Kg/min

Exclusion criteria

a) Potentially correctible cause of HF (valvular, congenital, or untreated ischemic heart disease)
b) Clinically significant angina pectoris
c) Hospitalization for HF requiring the use of inotropic support within 30 days of enrollment
d) PR interval greater than 375 ms
e) Permanent or long-standing persistent atrial fibrillation/flutter, or cardioversion within 30 days of enrollment.
f) Exercise tolerance limited by condition other than heart failure (e.g., angina, COPD, peripheral vascular disease, orthopedic or rheumatologic conditions) or unable to perform baseline stress testing
g) Scheduled for a CABG or a PTCA procedure, or CABG procedure within 90 days or a PTCA procedure within 30 days of enrollment.
h) Biventricular pacing system, or indication for Biventricular pacing system
i) Myocardial infarction within 90 days of enrollment.
j) Mechanical tricuspid or aortic valves.
k) Ventricular assist device
l) Prior heart transplant
m) Pregnant or planning to become pregnant during the study
n) Age below 18
o) Subject participating in another study, unrelated to CCM, at the same time (or within 30 days prior to enrollment to this study)
p) Subjects on dialysis

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2015
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Generic name:	Optimizer IVs System
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	05-04-2016
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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
CCMO	NL53739.058.15