AdreView* Myocardial Imaging for Risk Evaluation * A multicentre trial to guide ICD implantation in NYHA class II & III heart failure patients with 25% * LVEF * 35%. ADMIRE-ICD

Published: 11-02-2016
Last updated: 19-04-2024

To demonstrate the efficacy of AdreView* imaging for appropriately guiding the decision of ICD implantation in a population of New York Heart Association (NYHA) class II and III Heart Failure (HF) patients with 25% * left ventricular ejection...

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

Summary

ID

NL-OMON44945

Source
ToetsingOnline

Brief title
ADMIRE-ICD

Condition

- Heart failures

Synonym
heart failure, New York Heart Association class II or class III heart failure patients

Research involving
Human

Sponsors and support

Primary sponsor: GE Healthcare AS
Source(s) of monetary or material Support: GE Healthcare

Intervention

Keyword: AdreView, Heart Failure, ICD implantation, Radiopharmaceutical

Outcome measures

Primary outcome

The primary endpoint will be all-cause mortality.

Secondary outcome

* A composite of the rate of hospitalisation and death related to major complications of device implantation (i.e., need for thoracotomy, pericardiocentesis, or vascular surgery) and a composite of the rate of complications of long-term device therapy (i.e., infection not leading to hospitalisation, lead and/or generator removal/replacement, inappropriate shocks, explantation). (AdreView* Low-risk group vs SoC H/M *1.6)

* Cardiac death (composed of SCD, death due to cardiac arrhythmia, death due to HF, and death due to other cardiovascular causes).

* The rate of hospitalisation for cardiovascular cause.

* The rate of all-cause hospitalisation.

* A composite of the occurrence of resuscitated life-threatening ventricular tachycardia, unstable ventricular tachy-arrhythmias, SCD and resuscitated cardiac arrest.

Study description

Background summary

Many people in North America (U.S. & Canada) and Europe suffer from heart failure (HF). Chronic HF has been shown to have a serious impact on people*s day-to-day life and reduce life expectancy. Drug and medical device based treatments are recommended in order to improve survival and the treatment method selected is dependent on the severity of HF. While both types of treatment improve symptoms and survival, current international guidelines recommend the implantation of a device called an *implantable cardioverter defibrillator* (ICD) device in patients with mild or moderate HF and a heart blood-pumping efficiency that is * 35%. In this situation, the ICD device shocks the heart if there is any significant change in the heart*s beating rhythm. These electrical shocks are designed to restore the heart*s normal beating rhythm.
Currently, only about half of the patients who meet the criteria for an ICD device actually receive one. Also, some patients that do receive an ICD device do not benefit from the device but still have the increased risks that are associated with the introduction of devices into the body. These risks include infections from the implanting procedure, inappropriate device activation (meaning the device delivers shocks when it is not needed), device failure, and the need for device replacement every few years.
The latest research suggests that an ICD device may not be suitable for all patients with mild to moderate HF and a heart blood-pumping efficiency that is between 25% and 35%. An AdreView* heart function scan could be used to identify patients who have a high- or low-risk of a fatal event in the next 1 to 2 years. This additional information may make it possible to take a more accurate decision about who would and who would not benefit from an ICD device implantation.
To investigate whether the results of an AdreView* scan can help to predict who is most likely to benefit from ICD implantation, the ADMIRE-ICD study aims to recruit around 2,000 patients in North America (U.S. & Canada) and Europe, image their heart function (using an AdreView* heart function scan), and follow their condition. Approximately 42 subjects will be expected to be included in The Netherlands
The main purpose of this study will be to see if knowing how well the heart functions (using an AdreView* heart function scan) can help doctors to identify patients with a heart blood-pumping efficiency of between 25% and 35% who are more likely to benefit from having an ICD device implanted.
All patients involved in this study will receive an AdreView* heart function scan. This heart function scan uses a radioactive imaging drug, AdreView*, a product that is already approved in North America and several European countries, including the Netherlands, for heart function imaging and the diagnosis of other diseases (eg cancer). Patients will receive the approved recommended dose for adults (10 mCi [370 MBq]) that will be injected into the

bloodstream through a vein.

Study objective

To demonstrate the efficacy of AdreView* imaging for appropriately guiding the decision of ICD implantation in a population of New York Heart Association (NYHA) class II and III Heart Failure (HF) patients with 25% * left ventricular ejection fraction (LVEF) * 35%. This will be achieved by comparing allcause mortality observed in the AdreView*-guided therapy group to that observed in patients receiving the Standard of Care (SoC; defined as the medical care as recommended by internationally accepted HF guidelines), in whom no clinical decision will be made based upon AdreView* scan results.

Study design

This is an event-driven Phase IIIb, multicentre, randomised, clinical study to demonstrate the efficacy of AdreView* imaging for appropriately guiding the decision of ICD implantation, in NYHA class II and III HF patients with 25% * LVEF * 35%, and in particular, for identifying patients who are at low risk for SCD and who would not benefit, or may suffer harm, from implantation of an ICD device.

Intervention

Investigational Medicinal Product (IMP):
After randomisation to either the AdreView* group or the SoC group, all patients will receive an intravenous injection of 10 mCi (370 MBq) of AdreView*. A ± 10% tolerance of the nominal dose will be allowed, thus yielding an acceptable dose range of 9 to 11 mCi (333 to 407 MBq) in accordance with the Package Insert/Summary of Product Characteristics/Investigator*s Brochure (IB). AdreView* will be administered in a volume of 5 mL (diluted using 0.9% sodium chloride as needed) and injected as a slow infusion over 1 to 2 minutes followed by 10 mL of saline flush injected over a maximum of 5 seconds. Patients being allocated to the AdreView* low-risk group will receive a second injection of AdreView* and planar/SPECT imaging 2 years after the first one. If any of these patients voluntarily withdraw prior to completion of the study they will be offered this second AdreView* scan prior to withdrawal being effective.
Comparator:
No comparator imaging modality(ies) will be used. The main comparator will be medical SoC (defined as the medical care as recommended by internationally accepted HF guidelines).
Duration of Study:
This will be an event-driven study. A 6-year study (including 4 years accrual of patients and mean observational time per patient of 2.75 to 3 years) is anticipated as being sufficient for accrual of endpoints. Patients will be

enrolled and followed up until 247 primary endpoint events have occurred in the study. A recommendation from the DSMB may lead to an early termination of the study as defined in the DSMB

Study burden and risks

Patients considered to be at low risk by AdreView* imaging (i.e., those with a planar image H/M ratio *1.6) will not receive an ICD, thus avoiding the exposure to complications; however they may face the risk that a potentially beneficial ICD implantation is withheld. GE Healthcare-sponsored study reports used for regulatory submissions (MBG311, MBG312 and MBG313; reports available upon request) have consistently showed a significant difference in all-cause and cardiac mortality between the high and the low risk groups in favour of the latter.
These patients will also receive the standard guideline-directed medical therapy needed for their condition, including all the necessary follow-up visits and tests deemed necessary by the physician in charge. In addition, these patients will undergo a second AdreView* H/M ratio determination 2 years after the first one in order to assess if their risk level has increased and ICD implantation is warranted. Moreover and as described in the protocol, the DSMB will regularly assess all safety aspects of the study.
Patients randomised to the SoC group will be treated in accordance to guidelines including having an ICD implanted, and therefore should then face the same risks and benefits as those managed according to guidelines in the regular clinical setting.

Contacts

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NO

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

(1) Patients *18 years of age at the time dated informed consent is obtained.
(2) Female patients must be pre-menarchal, surgically sterile (had a documented bilateral oophorectomy and/or documented hysterectomy), postmenopausal (cessation of menses for more than 1 year), non-lactating, or, if of childbearing potential, a serum or urine pregnancy test with the results known prior to AdreView* (Iobenguane I123 Injection) administration) is negative.
(3) Patients willing and able to comply with all study procedures and a signed and dated informed consent is obtained before any study-procedure is carried out.
(4) Heart failure NYHA class II or III for symptoms, patients with ischemic or non-ischemic heart disease, eligible for ICD implantation as per each site*s standard of practice.
(5) Non-ischemic dilated cardiomyopathy or ischemic heart disease of at least 3 months duration receiving guideline-directed optimal medical therapy.
(6) 25% * LVEF * 35%, performed within 3 months before or at time of enrolment, as measured by radionuclide ventriculography, or electrocardiogram [ECG]-gated SPECT myocardial perfusion imaging [MPI], or magnetic resonance imaging [MR], computed tomography [CT], or 3D or 2D echocardiography [Simpson*s or multidisc method or equivalent only, M-mode echocardiography is not accepted].
In case LVEF measurement is performed within 3 months before enrolment, measurement should be performed at least 40 days after a hospitalisation for HF or acute coronary syndrome (including myocardial infarction), and to be valid, method of measurement should be in accordance with the protocol and the imaging exam should be made available to the Sponsor in digital format.
In case several valid LVEF measurements are available, the closest to enrolment will be used for inclusion determination.
(7) Clinically stable HF in the medical judgment of the investigator (i.e., no significant changes in medication, no worsening of symptoms, no unscheduled visits to the doctor*s office) for the past 30 days and no hospitalisation for HF or acute coronary syndrome (including myocardial infarction) in the past 40 days.

(8) Reasonable expectation of meaningful survival for at least 1 year.

Exclusion criteria

(1) Patients with existing ICD or patient having an indication of ICD implantation for secondary prevention of SCD.
(2) Hospitalisation for HF or for acute coronary syndrome in the previous 40 days.
(3) Patients where a cardiac resynchronisation therapy (CRT) is planned or indicated
(4) Other indication for placement of device (sustained ventricular tachycardia, resuscitated sudden death, need for atrioventricular pacing).
(5) NYHA class I or class IV symptoms at the time of study entry.
(6) American College of Cardiology-American Heart Association (ACC-AHA) class III or class IV (unstable) angina.
(7) Patient with chronic renal insufficiency defined as serum creatinine * 3 mg/dl (or * 265.2 *mol/L).
(8) Known or suspected hypersensitivity/allergy to Iobenguane or to any of the excipients in AdreView* (Iobenguane I123 Injection).
(9) Patient who is pregnant or plans to become pregnant within 2 weeks after AdreView* (Iobenguane I123 Injection) administration.
(10) Patient who has used any medication in the 2 weeks before AdreView* (Iobenguane I123 Injection) that could interfere with the test: e.g., but not limited to amitriptyline or derivatives, imipramine or derivatives, other antidepressants or drugs known or suspected to inhibit the norepinephrine transporter, antihypertensives that deplete norepinephrine stores or inhibit reuptake, sympathomimetic amines or cocaine.
(11) Patients that have a medical condition that could interfere with the AdreView* test (e.g., but not limited to left ventricular assist device, or prior heart transplant).
(12) Patients who participated in a clinical study involving a drug or device within 30 days prior to study entry and patients participating in any other clinical study.
(13) Patients having serious non-cardiac medical condition associated with significant elevation of plasma catecholamines, including pheochromocytoma.
(14) Patients with a clinical diagnosis of (or being treated for) Parkinson*s disease or Multiple System Atrophy.
(15) The patient has participated in a research study using ionizing radiation in the previous 12 months.
(16) Patients previously randomised in this study.

Study design

Design

Study phase: 3

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-01-2017
Enrollment:	42
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AdreView
Generic name:	Iobenguane I123

Ethics review

Approved WMO Date:	11-02-2016
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	03-05-2016
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-08-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-08-2016

Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	14-10-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	07-11-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	08-11-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-11-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	23-02-2017
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-09-2017
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-12-2017
Application type:	Amendment
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
EudraCT	EUCTR2015-001464-19-NL
Other	HC6-24-C185975
CCMO	NL53920.058.15