AdreView Myocardial Imaging for Risk Evaluation- A Multicentre Trial to Guide ICD Implantation in NYHA II&III HF

Patients with 30≤LVEF≤35 (ADMIRE-ICD)

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Rationale

All patients with a reduced LVEF may not benefit from an implantable cardiac defibrillator (ICD)1,2,3:
- About one-third of the total study population in MADIT II was classified as “low-risk” and had a 2-year mortality of only 8%, receiving no benefit from an ICD4.
- Patients with an LVEF between 30-35% may not benefit from an ICD5.
- An ICD will prevent about two deaths per year for every 100 devices implanted in patients with mild HF (NYHA II).  
AdreView (labeledenguane 123I injection) imaging was FDA-approved in 2013 for scintigraphic assessment of myocardial sympathetic innervation and may be useful in selecting patients with HF who are at low-risk for SCD. AdreView may be used to identify patients with lower 1/2 years mortality who will benefit from a second ICD, which may reduce the risk for SCD.

The aim of ADMIRE ICD is to demonstrate the efficacy of AdreViewTM imaging for guiding the decision of (ICD) implantation.

The H/M cut-off of 1.6 is based upon published results in AdreView-HF and AdreView-HFx studies, where AdreView uptake was prospectively validated to discriminate between patients at high and low risk of mortality at 1 and 2 years.

Ethical Considerations

Besides withholding ICD for patients with an LVEF 30-35% and H/M ≥1.6, patients will be managed according to standard of care. Physicians can manage changes in the clinical status as needed. An independent Data Safety Monitoring Board (DSMB) will oversee all safety aspects of the study. Monitoring will be performed on an ongoing basis to detect any possible safety imbalance between groups to act upon accordingly. Efficacy events will be adjudicated by an independent committee.

Trial Design

Primary Endpoint: All-cause mortality
Key Secondary Endpoint: Rate of hospitalization and death related to major complications of ICD implantation and a composite of rate of complications of long-term device therapy between low risk groups and between all patients in AdreView™ vs SOC groups.
- Cardiac death (SCD), death due to cardiac arrhythmias, death due to HF, and death due to other cardiovascular causes.
- Rate of all-cause hospitalization for CV cause.
- A composite of the occurrence of resuscitated life-threatening ventricular tachycardia, unstable ventricular tachy-arrhythmias, SCD and resuscitated cardiac arrest.
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Inclusion criteria: Ischaemic and non-ischaemic stable HF
30≤LVEF<35% (by any method accepted M-mode echocardiography); NYHA classes II and III

Exclusion criteria: Existing ICD Secondary prevention of SCD
Unstable angina
Chronic renal insufficiency (creatinine 2mg/dl)
Medication known or suspected to inhibit mIBG uptake or reuptake, or to deplete NE stores.
Heart transplant

Randomization: R: 1:1

Follow-up: H/M: Heart to mediastinum ratio
R: Randomisation
SCD: Sudden cardiac death

ICD implanted

ICD not implanted

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Trial details

Sample size: 2216 patients in 130 sites in North America and EU
Event driven: Efficacy analysis when 247 primary events are accrued

Data Safety Monitoring Board: Monitors safety, oversees conduct of the trial, recommends changes to ensure favourable risk-benefit ratio

Clinical Events Adjudication Committee: Independently adjudicates efficacy

References

Efficacy analysis when 247 primary events are accrued

Sponsor/Financial Support

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