Quinidine versus verapamil in short-coupled idiopathic ventricular fibrillation: An open label, randomized crossover pilot trial.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON55988

Source
ToetsingOnline

Brief title
QUEEN-IVF

Condition

- Cardiac arrhythmias

Synonym
Short-coupled idiopathic ventricular fibrillation; short-coupled torsades de pointes

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC

Source(s) of monetary or material Support: Netherlands Heart Institute

Intervention

Keyword: Short-coupled IVF

Outcome measures

Primary outcome

The primary endpoint is freedom from sustained ventricular arrhythmia, assessed

using the severity scoring system.

Secondary outcome

The secondary endpoints are:

• Time to first arrhythmic event

• Incidence of quinidine-induced torsade de pointes

• Incidence of sustained monomorphic ventricular tachycardia

• Inappropriate ICD shocks

Study description

Background summary

Short-coupled idiopathic ventricular fibrillation (IVF) is a rare syndrome and subtype of idiopathic ventricular fibrillation that is characterized by ventricular fibrillation or polymorphic ventricular tachycardia (PVT) initiated by a short-coupled premature ventricular contraction (PVC). Although patients are protected from sudden cardiac death by an implantable cardioverter-defibrillator (ICD), additional antiarrhythmic drug therapy is indispensable as recurrent ICD shocks are common and can negatively affect quality of life. Verapamil and quinidine have been suggested as effective antiarrhythmic drugs, but is it not known whether these drugs reduce the incidence of arrhythmic events. Due to the small number of patients described in the literature, arrhythmic event rates in patients treated with verapamil and quinidine are unknown, making it impossible to perform an accurate sample size calculation to design a randomized controlled trial (RCT). This pilot study will provide insight into the feasibility of a RCT and provide data

needed to determine the most appropriate design and the sample size.

Study objective

This study has been transitioned to CTIS with ID 2024-511190-30-00 check the CTIS register for the current data.

To investigate the feasibility of a definitive RCT to assess the efficacy and safety of verapamil and quinidine in patients with short-coupled IVF.

Study design

Multicenter, open-label, randomized, controlled, crossover pilot trial with blinded outcome assessment.

Intervention

Oral quinidine or oral verapamil. Patients will be randomly assigned in a 1:1 ratio to treatment A (quinidine or verapamil) for 18 months and, after a washout period of one week, patients will cross over to treatment B (verapamil or quinidine) for another 18 months.

Study burden and risks

Previous clinical studies as well as decades of clinical experience have shown that these drugs are safe and generally well-tolerated. As such, trial participants will not be exposed to new drugs with unknown risks. Additionally, the incidence of arrhythmic events is expected to decrease with initiation of the study medication. An independent data safety monitoring board will oversee trial conduct. The burden of participation in this study is low, considering the frequency and degree of invasiveness of the assessments. No physical or psychological discomfort associated with participation is expected.

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

• At least one of the following 3 principal diagnostic criteria for short-coupled VF:
1. Diagnosis of short-coupled IVF, based on any documentation (through electrocardiogram (ECG), Holter monitor, device electrogram (EGM), or telemetry) of PVT of >=3 consecutive beats or VF initiated by a PVC with a coupling interval <350 ms
2. Isolated PVCs with a coupling interval <350 ms during the index admission after SCA based on a shockable rhythm or presumed arrhythmogenic syncope
3. DPP6 haplotype carrier (also without documentation of short-coupled IVF)
• Functioning transvenous or subcutaneous ICD in place
• Sudden cardiac arrest, (near)syncope, appropriate ICD shock or nonsustained PVT documented by the ICD at least once in the past 2 years
• Genetic testing has been initiated. Results are not required to be known at the time of inclusion. In subjects who are family members of DPP6 carrying index patients, others genes than DPP6 are not required to be tested.
• Willing to undergo two assigned treatment periods with verapamil and quinidine
• Age >= 18 years

Exclusion criteria

• Pregnancy or lactation
• Current treatment with amiodarone
• Patients with a history of therapy refractory ventricular arrhythmia on an

adequate dose of verapamil or quinidine, as determined by the treating cardiologist.
• Contra-indication to quinidine or verapamil (see section 7.5)
• Significant structural heart disease (left ventricular ejection fraction <50%, suspicion or definitive diagnosis of cardiomyopathy, moderate/severe pulmonary, mitral, or aortic valve stenosis or regurgitation)
• Suspicion or definitive diagnosis of another (heritable) arrhythmia syndrome, e.g. Brugada syndrome, early repolarization syndrome or catecholaminergic polymorphic ventricular tachycardia
• Presence of a short (<350 ms) or prolonged (>480 ms) heart-rate corrected QT interval on the resting ECG at baseline
• Presence of a pathogenic or likely-pathogenic RYR2 mutation. DPP6 carrier family members are not required to be tested for RYR2 carrier status.
• Presence of ischemia-induced short-coupled ventricular arrhythmia in patient with documented coronary spasm
• Presence of pause-dependent torsade de pointes [preceding R-R interval prior to the trigger PVC >1500 ms in individuals without pacemaker/ICD or >1300 ms in individuals with pacemaker/ICD] following a stable baseline rhythm. Initiation of ventricular arrhythmia by short-long-short cycles (R-R cycles <1300 ms) with a short-coupled trigger PVC is allowed
• Significant coronary artery disease (>=50% narrowing of the diameter of the lumen of the left main coronary artery or >=70% narrowing of the diameter of the lumen of the left anterior descending coronary artery, left circumflex artery or right coronary artery)
• Reversible metabolic or pharmacological/toxicological conditions that may cause similar electrophysiological findings
• Patients who are considered electrically unstable, at physician*s discretion, due to active electrical storm or very frequent nonsustained episodes of short-coupled IVF requiring intravenous or invasive therapy
• Successful radiofrequency ablation of the PVC initiating short-coupled IVF and absence of documented (non)sustained episodes of short-coupled PVT/VF afterwards. The patient will, however, be eligible to participate in the study if >= 1 episode of short-coupled PVT/VF is documented after the ablation procedure
• Intention to perform radiofrequency ablation of the PVC initiating short-coupled IVF during the course of the study
• Serious known comorbid disease with a life expectancy of less than two years
• Ongoing medical condition that is deemed by the Principal Investigator to interfere with the conduct or assessments of the study or safety of the subject.
• Circumstances that prevent follow-up
• Is unable to take orally administered tablets
• Inability to provide informed consent

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-10-2022
Enrollment:	35
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Generic
Generic name:	Quinidine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Generic
Generic name:	Verapamil
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	25-08-2022
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	15-11-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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
EU-CTR	CTIS2024-511190-30-00
EudraCT	EUCTR2021-005688-36-NL
CCMO	NL79429.018.22