A Phase III Prospective, Randomized, Double-Blind, Active-Controlled, Multi-Center, Superiority Study of Vernakalant Injection versus Amiodarone in Subjects with Recent Onset Atrial Fibrillation

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

Summary

ID

NL-OMON33298

Source
ToetsingOnline

Brief title
Vernakalant study

Condition

- Cardiac arrhythmias
- Cardiac therapeutic procedures

Synonym
atrial fibrillation (AF), irregular heart-rhythm

Research involving
Human

Sponsors and support

Primary sponsor: Quintiles
Source(s) of monetary or material Support: Cardiome Pharma Corp.

Intervention

Keyword: Active-Controlled, Atrial Fibrillation, Double-Blind, Vernakalant Injection

Outcome measures

Primary outcome

Efficacy assessments include assessment of conversion of AF to sinus rhythm at 90 minutes after the start of treatment and assessment of symptom relief at 90 minutes after the start of treatment. At 2 hours after the start of infusion, electrical cardioversion may be performed or rate control medication may be administered. Class I and Class III antiarrhythmics are not to be administered to the subject for 24 hours after the start of infusion. Subjects are to remain in the clinic for at least 6 hours after the start of infusion.

Secondary outcome

Subjects will attend a follow-up visit at 7 (±2) days after treatment and will receive a follow-up telephone call at 30 (±3) days for assessment of serious adverse events, concomitant medications related to serious adverse events, and recurrence of AF

Study description

Background summary

To demonstrate the superiority of vernakalant injection over amiodarone injection in the conversion of atrial fibrillation (AF) to sinus rhythm (SR).

Study objective

The primary objective of the study is to demonstrate the superiority of vernakalant injection over amiodarone injection in the conversion of atrial fibrillation (AF) to sinus rhythm (SR) within 90 minutes of the start of drug administration. The secondary objective is to compare the safety of vernakalant to amiodarone.

Study design

This is a double-blind, active-controlled, double-dummy, multi-center, randomized trial in two tratment groups.

Intervention

Vernakalant Injection: In one infusion line, subjects will receive a 10-minute infusion of 3.0 mg/kg vernakalant followed by a 15-minute observation period, followed by an additional 10-minute infusion of 2.0 mg/kg of vernakalant if required (if the subject is still in AF). To maintain blinding, a 60-minute infusion of placebo (D5W) will be administered in a second infusion line, followed by a maintenance infusion of placebo for a minimum of an additional 60 minutes. Amiodarone Injection: In one infusion line subjects will receive a 60-minute infusion of 5 mg/kg amiodarone followed by a maintenance infusion of 50 mg amiodarone over an additional 60 minutes (equivalent to approximately 15 mg/kg over 24 hrs). To maintain blinding, a 10-minute infusion of placebo (normal saline) will be administered in a second infusion line, followed by a

Study burden and risks

Safety will be assessed through the monitoring of adverse events, vital signs, continuous telemetry monitoring, 12-lead Holter monitoring, 12-lead ECGs, and laboratory tests. Vernakalant only stays in the blood for a short period of time so that the chance of undesired side-effects is minimalizedMany of the side effects of Amiodarone occur with long term use, and would not occur after receiving one dose, like will be given in this study. Amiodarone stays in the body for weeks after administration, and you may need to be careful what other drugs you take because some drugs may interact badly with the amiodarone that is still in the body.

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

1. Have symptomatic AF of 3 to 48 hours duration at baseline.
2. Be eligible for cardioversion.
3. Be 18 to 85 years of age.
4. Comprehend and sign a written informed consent form.
5. Women must not be pregnant, be non-nursing, and if pre-menopausal, must be using an effective form of birth control from time of screening until 3 months after discharge.
6. Have adequate anticoagulation therapy for cardioversion in accordance with standard of practice as recommended by ACC/AHA/ESC guidelines [1].
7. Be hemodynamically stable and have systolic blood pressure (BP) above 100 mmHg and less than 160 mmHg and diastolic BP less than 95 mmHg at screening and baseline.
8. Have a body weight between 45 and 136 kg (99 and 300 lbs). For subjects weighing >113 kg (250 lbs), the vernakalant dose should be based on a weight of 113 kg (250 lbs) and not higher.

Exclusion criteria

1. Known or suspected prolonged QT or uncorrected QT interval of >440 msec as measured

at screening on a 12-lead ECG, familial long QT syndrome, or previous torsades de pointes, ventricular fibrillation; or sustained ventricular tachycardia (VT).
2. Symptomatic bradycardia, sick sinus syndrome, or ventricular rate less than 50 beats per minute (bpm) as documented by 12-lead ECG at screening.
3. A QRS interval >140 msec.
4. Any known concurrent temporary secondary causes of AF such as alcohol intoxication, pulmonary embolism, hyperthyroidism, pneumonia, acute pericarditis, myocarditis, or hypoxemia.
5. Atrial flutter.
6. Significant valvular stenosis, hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy or constrictive pericarditis.
7. Documented previous episodes of second or third degree atrioventricular (AV) block.
8. Had a myocardial infarction (MI), acute coronary syndrome or cardiac surgery within 30 days prior to entry into the study.
9. Uncorrected electrolyte imbalance of serum potassium (K+) <3.5 mmol/L or >5.5 mmol/L or magnesium (Mg2+) below the lower limit of normal (Mg2+< 0.65 mmol/L in subjects 65 years or younger and <0.80 mmol/L in subjects 66 years or older). Both K+ and Mg2+ must be corrected prior to dosing.
10. Clinical evidence of digoxin toxicity in the opinion of the Investigator.
11. Failed electrical cardioversion during current episode of AF.
12. Received intravenous Class I or Class III antiarrhythmic drugs within 24 hours prior to dosing.
13. Received any oral Class I or Class III antiarrhythmic drugs for the purpose of conversion of AF to sinus rhythm within 24 hours prior to dosing.
14. Received amiodarone injection within 30 days prior to dosing, or oral amiodarone within 90 days prior to dosing.
15. A pacemaker.
16. Unstable congestive heart failure (CHF), Class IV CHF, or CHF requiring inotropes.
17. Serious pulmonary, hepatic, metabolic, renal, gastrointestinal, central nervous system or psychiatric disease, infection, febrile illness (oral temperature > 38.5°C), end stage disease states, or any other disease that could interfere with the conduct or validity of the study or compromise subject safety.
18. Have any evidence of an atrial thrombus.
19. Troponin (I or T) levels above the upper limit of normal.
20. Had a cerebrovascular accident within past 3 months.
21. Any other surgical or medical condition that, in the judgment of the clinical Investigator might warrant exclusion or be contraindicated for safety reasons.
22. Thyroid dysfunction, hypersensitivity to iodine, or any other condition for which amiodarone injection is contraindicated.
23. Had previous exposure to vernakalant.
24. Have known or suspected hypersensitivity to vernakalant injection or any component of its formulation, or amiodarone injection or any component of its formulation.
25. Be concurrently participating in another drug study or have received an investigational drug within 30 days prior to screening.
26. Be unable to communicate well with the Investigator and to comply with the requirements of the entire study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-09-2009
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	vernakalant injection
Generic name:	Vernakalant

Ethics review

Approved WMO Date:	05-08-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-08-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	25-09-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-09-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-10-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-11-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2007-005625-29-NL

Register	ID
CCMO	NL28796.060.09