Multi-Centre, Placebo-Controlled, Phase 2 Study of Etripamil Nasal Spray (NS) for the Reduction of Ventricular Rate in Patients with Atrial Fibrillation

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

Summary

ID

NL-OMON51562

Source
ToetsingOnline

Brief title
ReVeRA-201

Condition

- Cardiac arrhythmias

Synonym
Abnormal heart rhythm, arrhythmia

Research involving
Human

Sponsors and support

Primary sponsor: Milestone Pharmaceuticals
Source(s) of monetary or material Support: Milestone Pharmaceuticals

Intervention

Keyword: Atrial fibrillation, Etripamil, Ventricular rate reduction

Outcome measures

Primary outcome

The primary objective of this study is to demonstrate the superiority of

etripamil NS over placebo in reducing ventricular rate in patients with AF.

Secondary outcome

The secondary objective is to evaluate the safety and efficacy of etripamil NS

in patients with AF.

Study description

Background summary

Etripamil an L-type calcium channel antagonist and short-acting verapamil analog, is currently being developed for the treatment of paroxysmal supraventricular tachycardia (PSVT), and other arrhythmias.
Atrial fibrillation (AF) is the most common sustained arrhythmia in humans, with an irregular and often rapid heart rate that increases the risk of stroke and heart failure. For most patients, current treatment for AF consists of anti-coagulant therapy, either warfarin or novel oral anti-coagulants to reduce the risk of blood clot embolization and stroke; those who cannot take these stronger blood thinners may be prescribed aspirin, but aspirin has only been shown to be somewhat efficacious in a very small and specific population. With regard to the abnormal heart rate that occurs during AF, there are two strategies. One strategy focuses on controlling the heart rate during AF to reduce or eliminate symptoms, while the other takes aim at terminating AF and maintaining sinus rhythm. The major unmet needs are for more efficacious and safer rhythm-control drugs as well as rate-control drugs with a faster onset of action to bring down the heart rate. Based on data from both the Phase 1 and Phase 2 studies, etripamil has demonstrated its ability to prolong conduction through the AV node, which is key to reducing the ventricular rate during AF. This makes etripamil an excellent candidate for use in controlling the ventricular rate in a subset of patients with AF.

Study objective

The primary objective of this study is to demonstrate the superiority of etripamil NS over placebo in reducing ventricular rate in patients with AF.

Study design

This is a multi-center, randomized, double-blind, placebo-controlled study to evaluate the effects of etripamil NS in patients with AF. This study includes screening procedures, treatment procedures, and a follow-up period. Patients will be randomized in a double-blind fashion to yield at least 50 evaluable patients in 2 groups of at least 25 patients each (Efficacy Population). Each patient will receive a single dose of Placebo or 70 mg etripamil intranasally. Patients will be contacted for follow-up the next day and 7 days after dosing. Total duration of participation is 1 week.

Intervention

1 Group of patients will receive a single dose of intranasal admnistration of etripamil 70 mg, while the other group will receive placebo.

Study burden and risks

The primary benefit of this study is that etripamil nasal spray may provide rapid symptom relief to patients with atrial fibrillation by decreasing the ventricular response rate.
The potential risks of study participation include those associated with exposure to etripamil and the risks of medical evaluation. AEs associated with etripamil include nasal irritation, nasal discomfort, and throat irritation. Potential adverse events which have been rare or not observed in studies to date include other cardiac arrhythmias, or AEs associated with drops in blood pressure (dizziness, headache).

Contacts

Public
Milestone Pharmaceuticals

1111 Dr. Frederik-Philips Blvd., Suite 420
Saint-Laurent QC H4M 2X6
CA
Scientific
Milestone Pharmaceuticals

1111 Dr. Frederik-Philips Blvd., Suite 420
Saint-Laurent QC H4M 2X6

CA

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Aged 18 years and over
2. Has provided written informed consent
3. Patients with episodes of paroxysmal, persistent or permanent AF, presenting with AF and a ventricular rate >=110 bpm, measured over 1 minute on an ECG
4. Patients should receive appropriate antithrombotic therapy as per Canadian Cardiovascular Society (CCS) guidelines.
a. Etripamil (a calcium channel blocker) is intended for acute rate control only. If rhythm control is desired (outside of the present protocol), anticoagulation as per CCS guidelines may start after the administration of study drug.

Exclusion criteria

1. Has evidence of atrial flutter (ECG) at presentation
2. Has a history of stroke, transient ischemic attack, or peripheral embolism within the last 3
months
3. Has received by IV route any of the following within one hour before study drug
administration: flecainide, procainamide, digoxin, beta-blocker, or calcium chanel blocker
4. Has signs and symptoms of severe congestive heart failure at presentation (e.g. tachypnea,
oxygen desaturation <90% unless due to known pulmonary disease, pulmonary rales, sign

of peripheral hypoperfusion)
5. Hemodynamic instability, with systolic blood pressure <90 mmHg or diastolic blood
pressure <60 mmHg
6. Known uncorrected severe aortic or mitral stenosis
7. Hypertrophic cardiomyopathy with outflow tract obstruction
8. Has a history of second- or third-degree atrioventricular block
9.Regular rhythm suggesting a complete AV block
10. Has a history or evidence of torsades de pointes, sick sinus syndrome, or Brugada syndrome
11. Evidence of Acute Coronary Syndrome within the last 12 months except if patient was
successfully revascularized
12. Positive pregnancy test result at screening, and females of childbearing potential who do
not agree to use adequate method of contraception for the duration of the study
13. Has evidence of any clinically significant acute or chronic condition of the nasal cavity
(e.g., rhinitis or deviated septum) which could interfere with administration of the study
drug in either or both nasal cavities
14. Has a history of sensitivity to verapamil
15. Has previously participated in a clinical study for etripamil
16. Has a history of sensitivity to any components of the investigational product.
17. Signs of alcohol or drugs intoxication at the time of presentation which, in the opinion of
the Investigator, would impact the validity of study results;
18. Is currently participating in another drug or device study, or has received an investigational
drug or device within 30 days of Screening
19. Has evidence of clinically significant cardiovascular, endocrine, gastrointestinal,
hematologic, hepatic, immunologic, neurologic, oncologic, pulmonary, psychiatric, or
renal disease or any other condition which, in the opinion of the Investigator, would
jeopardize the safety of the patient or impact the validity of study results.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-02-2023
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Etripamil
Generic name:	Etripamil

Ethics review

Approved WMO Date:	30-08-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-11-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2022-001854-49-NL
ClinicalTrials.gov	NCT04467905
CCMO	NL82019.056.22