Multi-Centre, Multi-National, Open Label, Safety Study of Etripamil Nasal Spray for Patients with Paroxysmal Supraventricular Tachycardia

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Primary:1. The primary objective is to evaluate the safety of self-administered etripamil nasal spray (NS) outside of the clinical settingSecondary Objectives:1. To evaluate the efficacy of self-administered etripamil NS outside of the clinical...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON50059

Source
ToetsingOnline

Brief title
Milestone NODE-303

Condition

- Cardiac arrhythmias

Synonym
heart rhythm disorder, Paroxysmal Supraventricular Tachycardia

Research involving
Human

Sponsors and support

Primary sponsor: Milestone Pharmaceuticals

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

Intervention

Keyword: Nasalspray, Paroxysmal Supraventricular Tachycardia, Selfadministration

Outcome measures

Primary outcome

The primary objective of this study is to evaluate the safety of selfadministered etripamil NS. Efficacy variables will be collected as secondary or exploratory analyses.

Safety variables will include clinical adverse events (AEs), vital signs, and arrhythmias and conduction disorders detected on surface ECG or CMS recordings.

Secondary outcome

The secondary efficacy endpoints will include:

• Frequency of additional medical intervention to treat PSVT, as measured by emergency department (ED) visits, hospital admissions, and concomitant medication use.

• Improvement in patient quality of life, as measured by the BIPQ, CAQ, SF-36 questionnaire and other surveys.

• Patient satisfaction with treatment, as measured by the Treatment Satisfaction Questionnaire for Medication (TSQM-9) and other questions.

• Termination of PSVT episodes.

The exploratory endpoints will include:

• Frequency of PSVT episodes, and use of etripamil NS for those episodes, as

captured by the PRO.

• Characteristics of patient PSVT episodes, as measured by the data collected

by the CMS.

Study description

Background summary

Etripamil, an L-type calcium channel antagonist and short-acting verapamil analog, is being developed by Milestone Pharmaceuticals Inc. (hereinafter Milestone) for the treatment of paroxysmal supraventricular tachycardia (PSVT), used in reference to both the disorder and its associated tachyarrhythmia. A relatively common disorder, PSVT is characterized by episodes of tachyarrhythmia typically with a heart rate (HR) over 100 bpm and a QRS duration of <120 msec. Etripamil is directed towards the 2 most common subtypes of PSVT, atrioventricular (AV) nodal reentrant tachycardia (AVNRT) and AV reentrant tachycardia (AVRT), together accounting for approximately 90% of PSVT cases. In both conditions, a pharmaceutical agent capable of transiently prolonging AV conduction time can result in arrhythmia termination and restoration of normal sinus rhythm (SR). Historically, intravenous (IV) verapamil has been used as an effective agent for treatment of acute episodes of PSVT. However, it has been replaced in recent years by IV adenosine, which is equally effective in terminating acute episodes of PSVT. Adenosine has the advantage of having a very short half-life, as it is rapidly metabolized during the time required to terminate an episode of PSVT. However, the short half-life of adenosine renders it ineffective when given via routes of administration other than IV. As both of these medications require the establishment of IV access, they are not appropriate for a patient self-administration paradigm in an outpatient setting.

Study objective

Primary:
1. The primary objective is to evaluate the safety of self-administered etripamil nasal spray (NS) outside of the clinical setting
Secondary Objectives:
1. To evaluate the efficacy of self-administered etripamil NS outside of the clinical setting, and

2. To evaluate the impact of etripamil NS on PSVT disease burden, and
3. To evaluate the safety and efficacy of etripamil NS when used for multiple PSVT episodes

Study design

NODE-303 is a multi-center, open label study all patients will be provided with an ambulatory Cardiac Monitoring System (CMS) to help document PSVT episodes. The CMS will be self-applied by the patient, when PSVT symptoms begin. Patients will self-administer etripamil NS if vagal maneuver is ineffective. After an episode of PSVT where drug is administered, the patient will return to the investigative site for a study visit and will be given the option to continue in NODE-303 and manage subsequent episodes of PSVT with etripamil NS up to 4 treatments with etripamil NS.

Intervention

when PSVT symptoms begin. Patients will self-administer etripamil NS if vagal maneuver is ineffective.

Study burden and risks

the burden and risk of the study mainly consist out of extra time spend in comparision to standard treatment (going to the study site and completing surveys) and side effects.
possible side effects of etripamil NS:
• Nasal congestion (stuffy nose)
• Nasal discomfort
• Eyes watering
• Rhinorrhea (runny nose)
• Sore throat
• Cough
• Sneezing
• Bleeding from the nose
• Decrease in heart rate and/or a drop in blood pressure (hypotension), with symptoms that include dizziness and fainting. In severe cases, low blood pressure can be life-threatening.
• A condition called heart block, where a naturally occurring electrical signal that controls the heartbeat is partially or completely blocked from reaching the heart*s ventricles (the 2 large chambers in the heart that collect and distribute blood from the heart to the rest of the body). In severe cases, heart block can be life-threatening.

Patients have the benefit of the possibility to self administer the study drug to stop a PSVT episode and do not need to go to a hospital directly when having

a PSVT episode.

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) Has been diagnosed with PSVT by a medical professional and reports having at least one previous episode of PSVT. For clarity, PSVT refers to episodic SVT that includes the AV node as a critical part of reentrant circuit.
2) Is of at least 18 years of age
3) Signed NODE-303 written informed consent
4) Women of child-bearing potential must be willing to use at least 1 form of contraception during the trial, and must be willing to discontinue from the study should they become or plan to become pregnant

5) Willing and able to comply with study procedures

Exclusion criteria

1) Patients with only a history of atrial arrhythmia that does not involve the atrioventricular (AV) node as part of the tachycardia circuit (e.g., atrial fibrillation, atrial flutter, intra-atrial tachycardia) are not eligible.
Patients with a history of these tachycardias who are also diagnosed with PSVT are eligible.
2) History of allergic reaction to verapamil
3) Current therapy with digoxin, or any Class I or III antiarrhythmic drug.
Patients may be eligible if these drugs are stopped at least five half-lives before the administration of etripamil NS. The only exception is amiodarone which must be stopped 30 days before enrollment.
4) History of ventricular pre-excitation, e.g., delta waves, Wolff-Parkinson-White syndrome.
5) History of a second- or third-degree AV block
6) Symptoms of congestive heart failure New York Heart Association Class II to IV
7) Significant physical or psychiatric condition including alcoholism or drug abuse, which, in the opinion of the Investigator, could jeopardize the safety of the patient, or impede the patient*s capacity to follow the study procedures
8) History of syncope due to an arrhythmic etiology at any time, or history in last 5 years of unexplained syncope
9) Is pregnant or breastfeeding
10) Previously enrolled in a clinical trial for etripamil and received study drug
11) History of ACS or stroke within 6 months of screening
12) Evidence of renal dysfunction as determined by an estimated glomerular filtration rate assessed at the Screening Visit as follows:
a) < 60mL/min/1.73m2 for patients < 60 years of age
b) < 40mL/min/1.73m2 for patients >=60 and < 70 years of age
c) < 35mL/min/1.73m2 for patients >=70 years of age

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	50
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	10-12-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-03-2020
Application type:	First submission
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	EUCTR2019-001857-13-NL
ClinicalTrials.gov	NCT04072835
CCMO	NL71299.100.19

Study results

Results posted: 13-12-2023

Summary results
Trial never started

First publication
04-08-2023