Analysis of Healthcare Resource Utilization in the NODE-303 Trial to Terminate Paroxysmal Supraventricular Tachycardia Episodes

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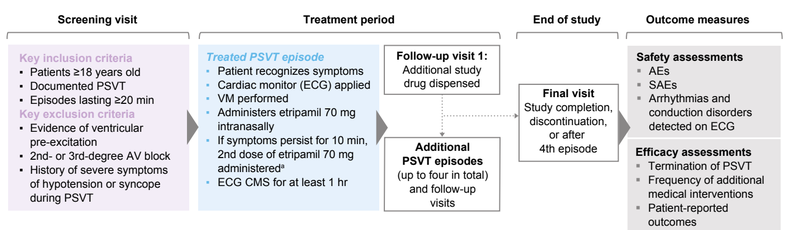
Introduction

- Paroxysmal supraventricular tachycardia (PSVT) is an episodic, often reentrant arrhythmia that creates a substantial burden on the healthcare system, with many patients requiring treatment in a clinical setting.[1]
- PSVT is associated with significant healthcare resource utilization (HCRU), including emergency department (ED) visits and healthcare costs.[2]
- Etripamil is a novel, fast-acting, non-dihydropyridine calcium channel blocker currently under investigation for intranasal self-administration to terminate episodes of PSVT.[3]
- Etripamil was studied previously in NODE-301 Part 1 and RAPID to assess its safety and efficacy in patients who self-administered this treatment outside the healthcare setting.[3,4]
- The NODE-303 trial was designed with broad inclusion criteria to assess the safety and efficacy of etripamil for multiple PSVT episodes in a real-word setting with an option of a repeat-dose regimen.[5]
- The objective of the present analysis is to characterize HCRU among patients in the NODE-303 study.

Methods

- NODE-303 was an event-driven, multi-center, open-label, single-arm, Phase 3 study conducted at 148 clinical study sites in the United States, Canada, and Latin America from June 21, 2019, to February 24, 2023.

Figure 1. NODE-303 Study Design



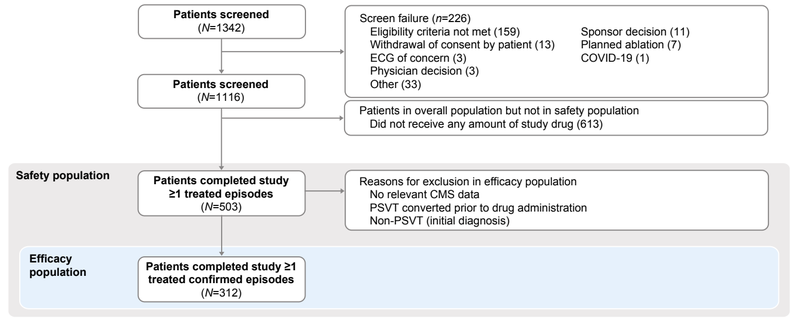
[a]Approximately 21 months after the study started, the protocol was amended to allow a repeat 70-mg dose to be self-administered if symptoms persisted 10 minutes following the first dose.

AE, adverse event; AF, atrial fibrillation; AFL, atrial flutter; AV, atrioventricular; CMS, cardiac monitoring system; ECG, electrocardiography; PSVT, paroxysmal supraventricular tachycardia; SAE, serious adverse event; SR, sinus rhythm; VM, vagal maneuver.

- Adult patients (≥18 years) diagnosed with at least 1 episode of atrioventricular-nodal–dependent PSVT were eligible for the study (**Figure 1**).
- Patients initiated an electrocardiography (ECG) cardiac monitoring system (CMS) as soon as the first symptoms of a PSVT episode were perceived, which continued for 60 minutes after etripamil administration.
- Treatment comprised of a vagal maneuver followed by a single 70-mg dose of etripamil administered in two 100-µL nasal sprays, one in each nostril.
- A repeat dose of etripamil could be self-administered if symptoms did not resolve after 10 minutes following the first dose (protocol amendment 21 months post study start).
- If the symptoms of PSVT did not resolve within 20 minutes after study drug administration, the patient could seek appropriate medical care as needed.
- Descriptive statistics were used to characterize HCRU, including ED visits, hospital admissions, and medical interventions (defined as patients who received oral or intravenous [IV] treatment following study drug administration).

Results

Figure 2. Patient Disposition



CMS, cardiac monitoring system; ECG, electrocardiography; PSVT, paroxysmal supraventricular tachycardia.

- Of the 1116 enrolled patients, 503 (45.1%) patients self-administered etripamil to treat perceived PSVT episodes (safety population; **Figure 2**).
  - 428 (85.1%) patients administered a single dose of etripamil (70 mg) for an episode and 75 (14.9%) patients administered a repeat dose.
- Of the 503 patients, 312 had PSVT episodes that were confirmed by medical review of the ECG CMS data (efficacy population).
- On average, patients were on study for 436 days.

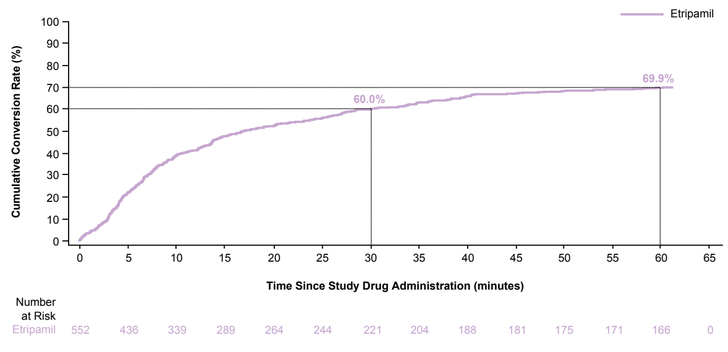
Table 1. Demographics and Baseline Characteristics

Category	Safety Population[a] Etripamil (*N*=503)	Efficacy Population Etripamil (*N*=312)
Age, years, mean (SD)	54.9 (13.6)	55.1 (12.8)
Sex, *n* (%)		55.8 (13.5)
Female	344 (68.4)	210 (67.3)
Male	159 (31.6)	102 (32.7)
Region, *n* (%)		
North America	353 (70.2)	219 (70.2)
South America	150 (29.8)	93 (29.8)
Age at first PSVT diagnosis, years, mean (SD)	47.7 (16.8)	47.1 (16.3)
Time since first PSVT diagnosis, years, mean (SD)	7.0 (9.2)	7.5 (9.3)
Mean number of PSVT episodes in past year, *n* (%)	9.8 (17.6)	6.9 (12.0)
Mean number of patient-reported ED visits for PSVT since diagnosis, *n* (%)	3.9 (5.7)	4.3 (6.4)
Patients with concomitant medications of interest, *n* (%)[b]		
β-blocker or calcium channel blocker	355 (70.6)	208 (66.7)
β-blocker only[c]	238 (47.3)	129 (41.3)
Calcium channel blocker only[d]	68 (13.5)	49 (15.7)
β-blocker and calcium channel blocker	49 (9.7)	30 (9.6)
NDHP calcium channel blocker (verapamil, diltiazem)	92 (18.3)	67 (21.5)

[a]Safety population included patients who self-administered study drug for at least one episode of perceived PSVT; the efficacy population included patients who received study drug for an event confirmed as PSVT by medical review of the ECG CMS data. [b]Drugs acting on the atrioventricular node that were started at any time and were taken at any time after the date of informed consent until the end of the follow-up period. [c]β-blocker only category does not include calcium channel blockers. [d]Calcium channel blocker only category does not include β-blockers.
CMS, cardiac monitoring system; ECG, electrocardiography; ED, emergency department; NDHP, non-dihydropyridine; PSVT, paroxysmal supraventricular tachycardia; SD, standard deviation.

- Mean (SD) age of the efficacy population was 55.1 (12.8) years, and 67.3% (210/312) of the patients were female (**Table 1**).

Figure 3. Kaplan-Meier Analyses of Confirmed PSVT to SR Conversion at 60 Minutes by Episode (Efficacy Population)[a]



[a]Efficacy population includes patients who received study drug for an event confirmed as PSVT by medical review of the ECG CMS data.
CMS, cardiac monitoring system; ECG, electrocardiography; PSVT, paroxysmal supraventricular tachycardia; SR, sinus rhythm.

- 69.9% (386/552) of episodes converted to sinus rhythm (SR) within 60 minutes of etripamil administration with the median time to conversion of 17.0 minutes (**Figure 3**).
- In the safety population, 428 (85.1%) patients administered a single dose of etripamil (70 mg) for an episode and 75 (14.9%) patients administered a repeat dose.

Table 2. Medical Interventions to Treat Confirmed PSVT Episodes

Category	Unique Patients[a]	Episodes[b]
Number of administrations of additional oral pills (eg, pill-in-pocket) to treat patient-reported, treated, and confirmed PSVT episodes in all visits		
n/*N* (%)	26/312 (8.3)	35/455 (7.7)
Number of visits to ED to treat patient-reported, treated, and confirmed PSVT episodes in all visits		
n/*N* (%)	45/312 (14.4)	54/455 (11.9)
Number of hospital visits and admissions to treat patient-reported, adjudicated, treated, and confirmed PSVT episodes in all visits		
n/*N* (%)	15/312 (4.8)	17/455 (3.7)

[a]Percentage was calculated using the number of patients in the efficacy population as the denominator.
[b]Percentage was calculated using the number of episodes reported by patients in the efficacy population as the denominator. ED, emergency department; PSVT, paroxysmal supraventricular tachycardia.

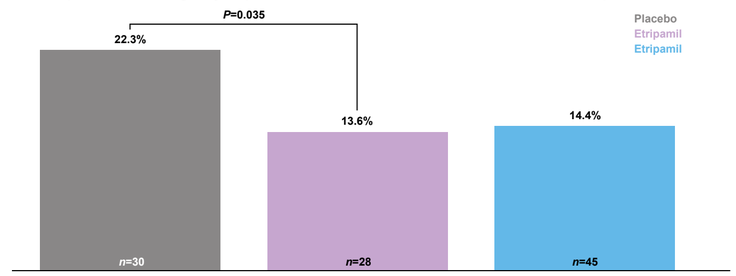
- 14.4% (45/312) of patients reported an ED visit to resolve their PSVT episode (**Table 2**).
- 54 episodes in 45 patients required a visit to the ED to treat an episode of confirmed PSVT, ~89% of which were treated with an IV medication.

Table 3. Patient-Reported Efficacy of Pill-in-Pocket Medication

	Confirmed PSVT Episodes (*N*=35)
Which best describes how well the pill worked in stopping your episode?	
The episode stopped immediately (<1 min) after taking the pill	0
The episode stopped 1–2 min after taking the pill	1 (2.9)
The episode stopped 2–5 min after taking the pill	0
The episode stopped 5–10 min after taking the pill	1 (2.9)
The episode stopped 10–20 min after taking the pill	4 (11.4)

- 35 episodes in 26 patients were treated with pill-in-pocket medication; only 6 (17.1%) were reported to terminate an episode within 20 minutes (**Table 3**).

Figure 4. Comparison of Emergency Department Visits Across Phase 3 Randomized and Open-Label Trials



[a]Data were pooled from NODE-301 Part 1 and RAPID trials. OL, open label.

- The rate at which patients visited the ED was comparable between the etripamil arm in randomized trials (13.6%; NODE-301 Part 1 and RAPID) and the open-label NODE-303 trial (14.4%; **Figure 4**).

Conclusions

- Only a small minority of patients sought additional medical intervention or ED visits to resolve their PSVT episodes after open-label etripamil treatment in NODE-303.
- The frequency of ED visits was comparable between this open-label trial and the etripamil arms of randomized Phase 3 studies, and substantially lower than in the placebo arms of randomized trials.
- Pill-in-pocket data need to be interpreted with caution. For example, oral verapamil is known not to have a peak pharmacokinetic effect until 1–2 hours after dosing, and a peak pharmacodynamic effect not until approximately 2 hours.[6]
- Etripamil may reduce ED visits for patients who are able to self-treat their PSVT episodes.

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