Quality-of-Life Measures With Etripamil Self-Administration for Acute Episodes of Paroxysmal Supraventricular Tachycardia in a Medically Unsupervised Setting: Patient-Reported Outcomes From NODE-303

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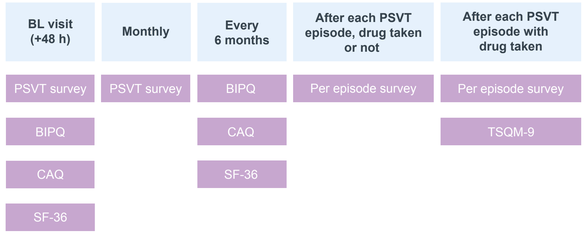
Introduction

- Etripamil nasal spray (NS) is a fast-acting, self-administered calcium channel blocker in development for the conversion of atrioventricular (AV)-nodal dependent paroxysmal supraventricular tachycardia (PSVT) in a medically unsupervised setting.[1]
- Etripamil was studied previously in NODE-301 Part 1 and RAPID to assess the safety and efficacy in patients who self-administered this treatment outside the healthcare setting.[1,2]
- In the RAPID study, evaluation of patient-reported outcomes (PROs) demonstrated significant symptomatic improvement by the Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9) Effectiveness Scale in patients who self-treated with etripamil compared to placebo.[1]
- The NODE-303 study was designed to characterise the safety of self-administered etripamil in a medically unsupervised setting for the treatment of multiple perceived episodes of PSVT (ie, in a real-world setting).[3,4]
- The data presented here are part of NODE-303 PRO instruments assessed for quality of life (QoL) over multiple etripamil-treated episodes of PSVT.

Methods

- NODE-303 was an open-label study conducted at 148 clinical study sites in the United States, Canada and Latin America from 21 June 2019 to 24 February 2023.
- Adult patients (≥18 years) were eligible for the study if they had been diagnosed with at least one episode of AV-nodal dependent PSVT prior to enrolment.
- Enrolled patients (*N*=312) who perceived PSVT symptoms applied an ambulatory electrocardiography (ECG) cardiac monitoring system (CMS), performed a pre-trained vagal manoeuvre and, if symptoms persisted, self-administered etripamil NS 70 mg.
- A study amendment allowed a repeat dose (etripamil NS 70 mg) if symptoms persisted 10 minutes after the first dose. Each patient could self-treat up to four episodes.
- PRO assessments are shown in **Figure 1**.
- Patients completed PROs at baseline (BL), monthly and per PSVT episode, which collected information on symptoms, episode characteristics, rescue medications and emergency department visits.

Figure 1. NODE-303 Questionnaires



Brief Illness Perception Questionnaire (BIPQ) assesses the cognitive and emotional representation of illness

Cardiac Anxiety Questionnaire (CAQ) measures anxiety in domains of fear, avoidance and heart-focused attention

36-Item Short Form Health Survey (SF-36) assesses QoL in domains of physical and mental health

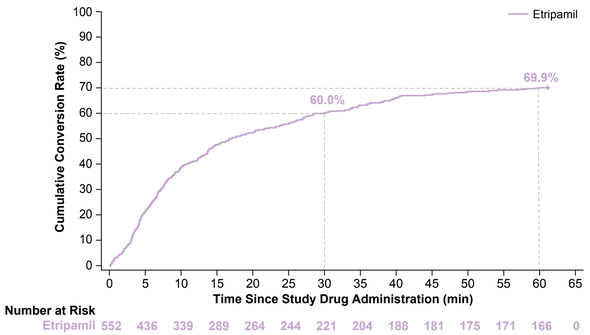
Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9)

BL survey is completed at the BL visit. Patient may complete the BIPQ, CAQ and SF-36 at the BL visit or at home within 48 hours of the BL visit. Patient will receive a reminder to complete each survey that is due 24 hours after the BL visit.
BL, baseline; PSVT, paroxysmal supraventricular tachycardia.

Results

- The rate of conversion to SR for all PSVT episodes 60 minutes post etripamil administration was 69.9% with median time to conversion 17.0 minutes (**Figure 2**).

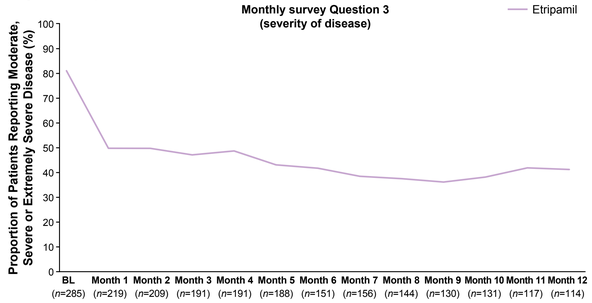
Figure 2. NODE-303 Rate of Conversion of PSVT Episodes to SR Within 60 Minutes



PSVT, paroxysmal ventricular tachycardia; SR, sinus rhythm.

- Extremely severe, severe and moderate disease severity was reported by smaller proportions of patients than at BL, though incomplete surveys at later visits may limit this analysis (**Figure 3**).

Figure 3. Overall Severity of PSVT From Monthly Survey Question 3 (Efficacy Population[a])



[a]The efficacy population is defined as the 312 patients who received study drug for an episode confirmed as PSVT based on the ECG CMS data. Patients classified overall severity as: not at all severe, minimal, mild, moderate, severe, extremely severe.
BL, baseline; CMS, cardiac monitoring system; ECG, electrocardiography; PSVT, paroxysmal supraventricular tachycardia.

Table 1. Summary of PROs to Assess QoL (Efficacy Population[a] [*N*=312])

	BL	6 Months	12 Months	24 Months
Monthly 7-question PSVT survey[b]	*n*=285	*n*=151	*n*=114	*n*=39
Overall severity, *n* (%)				
Not at all severe	2 (0.7)	43 (28.5)	29 (25.4)	9 (23.1)
Minimal	15 (5.3)	14 (9.3)	11 (9.6)	5 (12.8)
Mild	37 (13.0)	31 (20.5)	27 (23.7)	6 (15.4)
Moderate	120 (42.1)	40 (26.5)	33 (28.9)	11 (28.2)
Severe	76 (26.7)	19 (12.6)	13 (11.4)	7 (17.9)
Extremely severe	35 (12.3)	4 (2.6)	1 (0.9)	1 (2.6)
Level of anxiety over future PSVT				
Change from BL, mean (SD)	-	–0.8 (2.0)	–0.9 (2.0)	–0.7 (2.3)
Level of stress over future PSVT				
Change from BL, mean (SD)	-	–0.5 (1.8)	–0.3 (2.4)	–0.6 (2.3)
	Follow-up Visit 1	**Follow-up Visit 1**	**Follow-up Visit 1**	**Final study Visit**
Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9)[c]	*n*=208	*n*=112	*n*=71	*n*=69
Mean (SD) score, domain				
Global satisfaction	65.1 (24.2)	67.5 (26.4)	66.2 (25.1)	65.6 (29.3)
Effectiveness	63.6 (28.4)	66.6 (28.8)	60.4 (27.8)	65.1 (27.9)
Convenience	71.5 (16.4)	71.7 (18.1)	70.0 (16.7)	70.0 (17.5)

[a]The efficacy population is defined as the 312 patients who received study drug for an episode confirmed as PSVT based on the ECG CMS data. [b]For disease severity, a higher proportion of patients identifying their illness as not at all severe, minimal or mild would be considered an improvement; for levels of anxiety and stress, an improvement would be a decrease from BL. [c]Levels of global satisfaction, effectiveness and convenience ≥50 on the TSQM instrument are considered to be favourable. The TSQM-9 is composed of nine questions with responses on a scale of 1 (extremely dissatisfied) to 7 (extremely satisfied), which were converted to a 0- to 100-point score for analysis of domains.
BL, baseline; PRO, patient-reported outcome; PSVT, paroxysmal supraventricular tachycardia; QOL, quality of life.

- When participants were asked, "How would you rate your level of anxiety about experiencing a possible future SVT episode?" a mean change of <0.6 points from BL was observed at 1 month and maintained over 2 years.
- When participants were asked, "How would you rate your level of stress about experiencing a possible future SVT episode?" a mean change of <0.5 points from BL was observed at 1 month and maintained over 2 years.
- Measures of treatment satisfaction, effectiveness and convenience were consistent across multiple episodes and were at levels considered favourable for the TSQM instrument (**Table 1**).
- Rates of emergency department visits and hospital admissions across multiple treated PSVT episodes were similar to those observed in trials assessing single episodes (**Table 2**).
- No notable change was observed in the overall BIPQ score, in the total CAQ score or in the eight SF-36 dimensions.

Table 2. Healthcare Resource Utilisation for All Confirmed PSVT Episodes (Efficacy Population[a])

Category	Unique Patients	Episodes
Visits to emergency department to treat confirmed PSVT episodes, *n/N* (%)	45/312 (14.4)	54/455 (11.9)
Hospital admissions to treat confirmed PSVT episodes, *n/N* (%)	15/312 (4.8)	17/455 (3.7)

[a]The efficacy population is defined as the 312 patients who received study drug for an episode confirmed as PSVT based on the ECG CMS data. All confirmed PSVT episodes refers to those collected across all follow-up visits and with ECG CMS data confirming PSVT.
PSVT, paroxysmal supraventricular tachycardia.

Conclusions

- Etripamil self-administration was associated with patient-reported improvements in disease severity, decreased anxiety and stress over future PSVT episodes.
  - In addition, the levels of treatment satisfaction, effectiveness and convenience were considered favourable based on the PRO instrument.
- Using a symptom-prompted, self-administered treatment for PSVT could potentially improve QoL measures and reduce healthcare resource utilisation.

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