Healthcare Resource Utilization After Etripamil Treatment to Terminate Paroxysmal Supraventricular Tachycardia: A Pooled Analysis of Clinical Trials

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Introduction

- Paroxysmal supraventricular tachycardia (PSVT) is a regular and rapid cardiac rhythm characterized by sporadic, sudden onset and termination.
- Many patients require medical intervention to resolve a PSVT episode, leading to a substantial burden on the healthcare system.
- Etripamil is an investigational, fast-acting, non-dihydropyridine, calcium channel blocker for the acute treatment of PSVT, formulated as a self-administered nasal spray that can be utilized by patients outside of a healthcare setting.
- The objective of this analysis is to characterize healthcare resource utilization (HCRU) incurred by patients who participated in Phase 3 trials (etripamil versus placebo or etripamil only) to terminate PSVT episodes.

Methods

- Clinical trial data that assessed additional medical interventions following etripamil/placebo administration were pooled from: (**Table 1**)
  - Three randomized double-blind studies:
    - NODE-301 Part 1
    - RAPID
    - RAPID Extension
  - Four open-label studies with etripamil treatment:
    - NODE-302
    - RAPID Open Label
    - NODE-303
- Medical interventions were defined as any actions, treatments, or drugs other than self-administration of study drug, including: 1) Any medical intervention outside the clinical trial setting, such as the oral administration of a "pill-in-pocket" at home and 2) Emergency department (ED) visits with or without the administration of oral or intravenous medication, other treatment (eg, vagal maneuvers assisted by a health practitioner or electrical cardioversion).
- In NODE-303, the use of medical intervention for a PSVT episode was recorded via the Episode Survey PRO administered during the study.

Results

- The overall conversion rate of PSVT to sinus rhythm (SR) in patients treated with etripamil across all Phase 3 clinical studies was consistent.
- In NODE-301 Part 1, there was a clear trend in the reduction of the proportion of patients seeking rescue medical intervention (eg, ED): 15% of etripamil patients and 27% of placebo patients (P=0.12; **Figure 1**).
- In RAPID, a numerically lower proportion of patients in the etripamil group sought additional medical intervention (etripamil 15.2% versus placebo 24.7%, P=0.103) and ED care (etripamil 14% versus 21%, P=0.209) versus the placebo group (**Figure 1**).
- A statistically significant relative reduction of 39% (P=0.035) in the proportion of patients going to an ED due to an episode of PSVT in the etripamil group versus placebo was observed using the pre-defined pooled dataset from NODE-301 Part 1 and RAPID pre-specified analysis.
- In the randomized trials, 370 patients (placebo, n=149; etripamil, n=221) were included in the analysis and 18.6% (69/370) sought additional medical intervention after receiving randomized treatment. This represents a 45% relative reduction favoring etripamil treatment (P=0.005; **Table 2**).
- Across the open-label studies, 14% of patients who received etripamil in NODE-303 and the RAPID open-label extension studies sought additional medical intervention; these rates were 13% in NODE-302 and 9.9% in the RAPID open-label studies (**Figure 2**).
- Specifically in NODE-303, the proportion of patients who reported seeking medical intervention was 8.3% for use of oral pills (7.7% of episodes), 14.4% for ED visits (11.9% of episodes), and 4.8% for hospital visits and admissions (3.7% of episodes).

Table 1. Description of Clinical Studies That Evaluated Healthcare Resource Utilization

Study Design	Study	Treatments	Population	Primary Objective
Multi-center, double-blind, placebo-controlled studies	NODE-301 Part 1	Test dose under medical supervision (70 mg; 200 µL total [100 µL in each nostril]) Randomized 2:1 (etripamil: placebo) Single dose (placebo, 70 mg)	• Male or female • ≥18 years of age • Electrocardiographically documented history of PSVT and a history of sustained (>20 min) episodes of PSVT	Adjudicated termination of a confirmed episode of PSVT and conversion to SR for at least 30 sec within 300 min of start of study drug dosing
	RAPID (NODE-301 Part 2)	Test dose (2 x 70 mg; 10 min apart during SR) Randomized 1:1 (etripamil: placebo) Optional repeat dose regimen: • Placebo, 70 mg • First 70-mg dose; repeated dose after 10 min if symptoms of PSVT persisted	• Male or female • ≥18 years of age • Electrocardiographically documented history of PSVT with a history of sustained episodes (patients from NODE-301 Part 1 and newly enrolled patients)	Time to an adjudicated termination of a confirmed episode of PSVT and conversion to SR for at least 30 sec within 30 min of start of study drug dosing
	RAPID Extension	See RAPID	Patients from RAPID who did not complete RAPID before the cut-off date (July 20, 2022)	See RAPID
Multi-center, open-label studies	NODE-302 (Safety)	Etripamil, 70 mg	Extension of NODE-301 Part 1 Patients randomized in NODE-301 Part 1	Adjudicated termination of a confirmed episode of PSVT (AV nodal–reentrant tachycardia or AV re-entrant tachycardia determination if possible) and conversion to SR for at least 30 sec
	RAPID Open Label	Repeat dose regimen (etripamil, 70 mg; repeated dose after 10 min if symptoms of PSVT persisted)	Patients from NODE-301 Part 1 and newly enrolled patients	See RAPID
	RAPID Extension Open Label	Repeat dose regimen (etripamil, 70 mg dose; repeated dose after 10 min if symptoms of PSVT persisted)	Patients from RAPID who did not complete RAPID before the cut-off date (July 20, 2022)	See RAPID
	NODE-303 (Safety)	Repeat dose regimen (etripamil, 70 mg; repeated dose after 10 min if symptoms of PSVT persisted)	• Male or female • ≥18 years of age • PSVT diagnosis with at least one previous episode of PSVT	Safety of self-administered etripamil

AV, atrioventricular; PSVT, paroxysmal ventricular tachycarda; SR, sinus rhythm.

Figure 1. Patients Seeking Medical Intervention (A) and Patients With Emergency Department Visits (B) in a Pre-specified Pooled Analysis

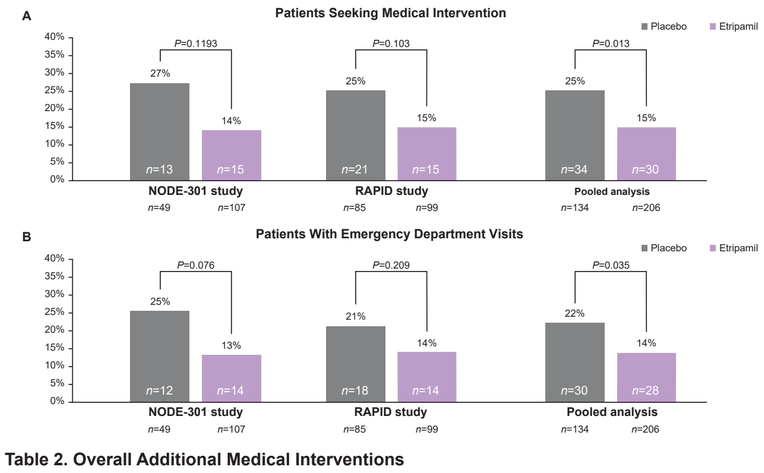
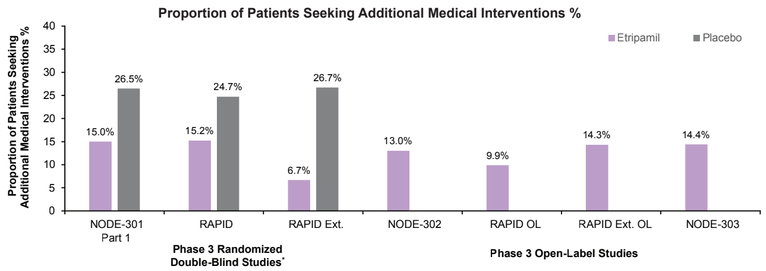


Table 2. Overall Additional Medical Interventions

	Placebo *n/N* (%)	Etripamil *n/N* (%)
Medical intervention after randomized treatment for PSVT		
Number of patients seeking additional medical intervention	38/149 (25.5)	31/221 (14.0)
P value[a]		0.005

[a]*P* value is obtained from a chi-square test. Medical Intervention is defined as a PSVT episode that was terminated due to a medical intervention other than study drug. ECG CMS data from patients with a medical intervention were examined by the independent adjudication committee based on flagged information provided by the sponsor. The time of conversion (eg, due to emergency department treatment) in these patients was noted by the expert adjudicators and was considered a conversion due to medical intervention.
CMS, cardiac monitoring system; ECG, electrocardiography; PSVT, paroxysmal supraventricular tachycardia.

Figure 2. Patients Seeking Medical Intervention Across Phase 3 Clinical Studies



*Across randomized trials, healthcare resource use was significantly lower in the etripamil arm versus the placebo arm (P=0.005). Ext, extension; OL, open label.

Conclusions

- These findings indicate that HCRU is similar across randomized and open-label studies. Fewer patients treated with etripamil needed additional medical intervention to terminate a PSVT episode when compared to placebo.
- In each individual randomized, double-blind, Phase 3 study, there is a consistent trend towards a reduction in additional medical intervention in favor of etripamil; furthermore, there is a statistically significant reduction in additional medical interventions in a pre-specified analysis of the pooled blinded, randomized Phase 3 data.
- In the open-label Phase 3 studies, the rates of etripamil-treated patients receiving additional medical intervention are consistent and similar to the low rates observed for blinded etripamil-treated patients.

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