RESEARCH LETTER

Self-Administered Etripamil and Emergency Department Visits in Supraventricular Tachycardia: A Secondary Analysis of a Randomized Clinical Trial

Paroxysmal supraventricular tachycardia (PSVT) includes a range of heart-rhythm disorders with sudden onset of elevated heart rates, often requiring medical intervention for termination. Oral treatments for PSVT often lack effectiveness and are associated with adverse effects.[1] Etripamil is a fast-acting, self-administered, intranasal calcium channel blocker (CCB) in development to acutely treat atrioventricular-nodal-dependent PSVT. The NODE-301 phase 3 trial consisted of part 1 and part 2 (RAPID). The efficacy of etripamil in terminating PSVT was evaluated in patients outside the hospital.[2,3] NODE-301 part 1 and RAPID were not individually powered to detect a difference in the rate of emergency department (ED) visits after treatment. Prespecified pooled analysis was performed to evaluate the rate of ED care after treatment in the combined cohort.[4]

Supplemental content

Methods | NODE-301 part 1 and RAPID (NCT03464019) were event-driven, randomized, double-blind, placebo-controlled studies evaluating the efficacy and safety of etripamil, 70 mg, in patients experiencing PSVT at home. Primary trial results have been published.[2,3] WIRB-Copernicus Group approved this study. Written informed consent was obtained from all participants. We followed the CONSORT reporting guideline.

In part 1, patients were randomly assigned to etripamil, 70 mg, or placebo. In RAPID, repeat dose of etripamil, 70 mg, was administered 10 minutes after the first dose if symptoms persisted. Patients were instructed to seek medical care if symptoms did not resolve 30 minutes after study drug administration. A blinded committee adjudicated electrocardiogram recordings to confirm if atrioventricular-nodal-dependent PSVT episodes had occurred and terminated after drug administration. The number of patients seeking emergency care within 24 hours of treatment was collected. χ^2 Tests were performed on pooled data to assess statistical significance between the placebo and etripamil cohorts.

Two-sided $P < .05$ indicated statistical significance. Data analysis was performed between August and December 2022 using SAS 9.4 (SAS Institute).

Results | Vagal maneuvers were attempted by 370 patients during PSVT episodes before drug administration; only 17 patients (4.6%) had PSVT termination. The pooled cohort comprised 340 patients (237 females [69.7%]; mean [SD] age, 54.7 [13.2] years), of whom 206 received etripamil and 134 received placebo. The mean (SD) number of past-year PSVT episodes was 8.1 (12.9) (**Table**).

One hundred nineteen patients (57.8%) had PSVT termination within 30 minutes of using etripamil compared with 43 (32.1%) using placebo ($P < .001$). Thirty-four patients (25.4%) assigned to placebo and 30 (14.6%) assigned to etripamil received additional intervention (oral or intravenous medications) ($P = .01$). Furthermore, 28 of 206 etripamil recipients (13.6%) required an ED visit for ongoing PSVT vs 30 of 134 placebo recipients (22.4%), demonstrating an 8.8% absolute risk reduction and a 39% relative risk (RR) reduction (RR, 0.61; 95% CI, 0.38-0.97; $P = .04$) (**Figure**). The most common adverse events were localized to the nasal administration site. No serious adverse events were associated with etripamil.

Discussion | The PSVT prevalence in the US is estimated to be 1 in 300 patients.[5] PSVT is associated with significant health care resource use, including ED visits and health care expenditures.[6] Therefore, managing patients in the outpatient setting, when feasible, may be more efficient. Patients with PSVT often try vagal

Table. Patient Characteristics

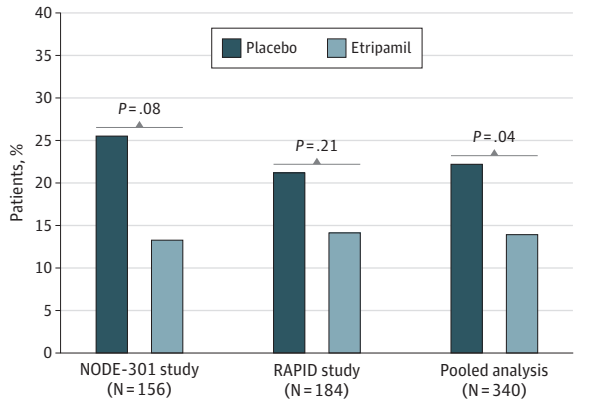
Characteristics	Patients, No. (%)		
	NODE-301 Part 1 (n = 156)[a]	RAPID Part 2 (n = 184)[b]	Pooled analysis (N = 340)
Age, mean (SD), y	56.1 (13.8)	53.5 (12.6)	54.7 (13.2)
Sex			
Female	106 (67.9)	131 (71.2)	237 (69.7)
Male	50 (32.1)	53 (28.8)	103 (30.3)
PSVT episodes in past year, mean (SD)	8.6 (9.9)	7.7 (15.0)	8.1 (12.9)
Self-administered placebo	49 (31.4)	85 (46.2)	134 (39.4)
Episode terminated within 30 min	17/49 (34.7)	26/85 (30.6)	43/134 (32.1)
Self-administered etripamil	107 (68.6)	99 (53.8)[a]	206 (60.6)[a]
Episode terminated within 30 min	56/107 (52.3)	63/99 (63.6)	119/206 (57.8)

Abbreviations: NODE, Efficacy and Safety of Intranasal MSP-2017 (Etripamil) for the Conversion of PSVT to Sinus Rhythm; PSVT, paroxysmal supraventricular tachycardia.

[a] Single-dose regimen of etripamil nasal spray (1 × 70 mg) was self-administered.

[b] Optional repeat-dose regimen of etripamil nasal spray (2 × 70 mg) was self-administered if symptoms persisted 10 minutes after the first dose. A total of 66.3% of patients eligible for etripamil and 79.2% of patients eligible for placebo self-administered a repeat dose of study drug when given the option.

Figure. Patients Who Visited the Emergency Department Within 24 Hours of Treatment



Part 1 of the NODE-301 trial included 49 patients in the placebo group and 107 in the etripamil group. The RAPID trial included 85 patients in the placebo group and 99 in the etripamil group. The pooled analysis included 134 patients in the placebo group and 206 in the etripamil group.

maneuvers as a first-line intervention; however, the pooled analysis found that this intervention was effective in only 4.6% of patients when performed without clinician assistance, although the data may not fully reflect its success rate in the broader SVT population. Oral medications, such as β-blockers and CCBs, have limited and delayed effectiveness in terminating acute PSVT episodes and have associated safety concerns.[1] Self-administered etripamil was nearly twice as likely as placebo to terminate a PSVT episode within 30 minutes. In this pooled analysis, the number of episodes needed to treat with self-administered etripamil to prevent 1 ED visit was 12. Self-administered, outpatient-based treatment for PSVT could contribute to reduced ED visits and cost and complexity of care.

Limitations include pooling the studies for statistical power. Future analyses of etripamil's implications for ED visits would broaden the applicability of results.

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