

Very Low Efficacy of Vagal Maneuvers in Terminating Paroxysmal Supraventricular Tachycardia: Results From the NODE-301 Study

Bruce S. Stambler,^{1*} James E. Ip,² Francis Plat,³ Benoit Coutu,⁴ Blandine Mondesert,⁵ Atul Verma,⁶ Silvia Shardonofsky,³ A. John Camm⁷

¹Piedmont Heart Institute, Atlanta, GA, USA; ²Weill Cornell Medicine, NewYork-Presbyterian Hospital, New York, NY, USA; ³Milestone Pharmaceuticals, Montreal, QC, Canada; ⁴Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada; ⁵Montreal Heart Institute, Montreal, QC, Canada; ⁶Partners in Advanced Cardiac Evaluation, Cardiology Clinic, Newmarket, ON, Canada; ⁷St. George's University of London, London, UK

*Presenting author

Background

- Vagal maneuvers are often recommended to individuals with atrioventricular (AV) nodal-dependent paroxysmal supraventricular tachycardia (PSVT) as a first-line treatment for sustained episodes of AV nodal reentrant tachycardia or AV reentrant tachycardia^{1,2}
- Common vagal maneuvers include carotid sinus massage, Valsalva maneuver, modified Valsalva maneuver, and diving reflex
- Vagal maneuvers have a Class I recommendation in current Heart Rhythm Society supraventricular tachycardia guidelines largely based on clinical experience and studies conducted in the hospital or emergency department setting²⁻⁶
- However, the true success rate (ie, efficacy) of vagal maneuvers when they are attempted by patients themselves during ongoing symptomatic, sustained, AV nodal-dependent PSVT in a real-world, non-medically supervised setting remains unknown and has not been previously studied

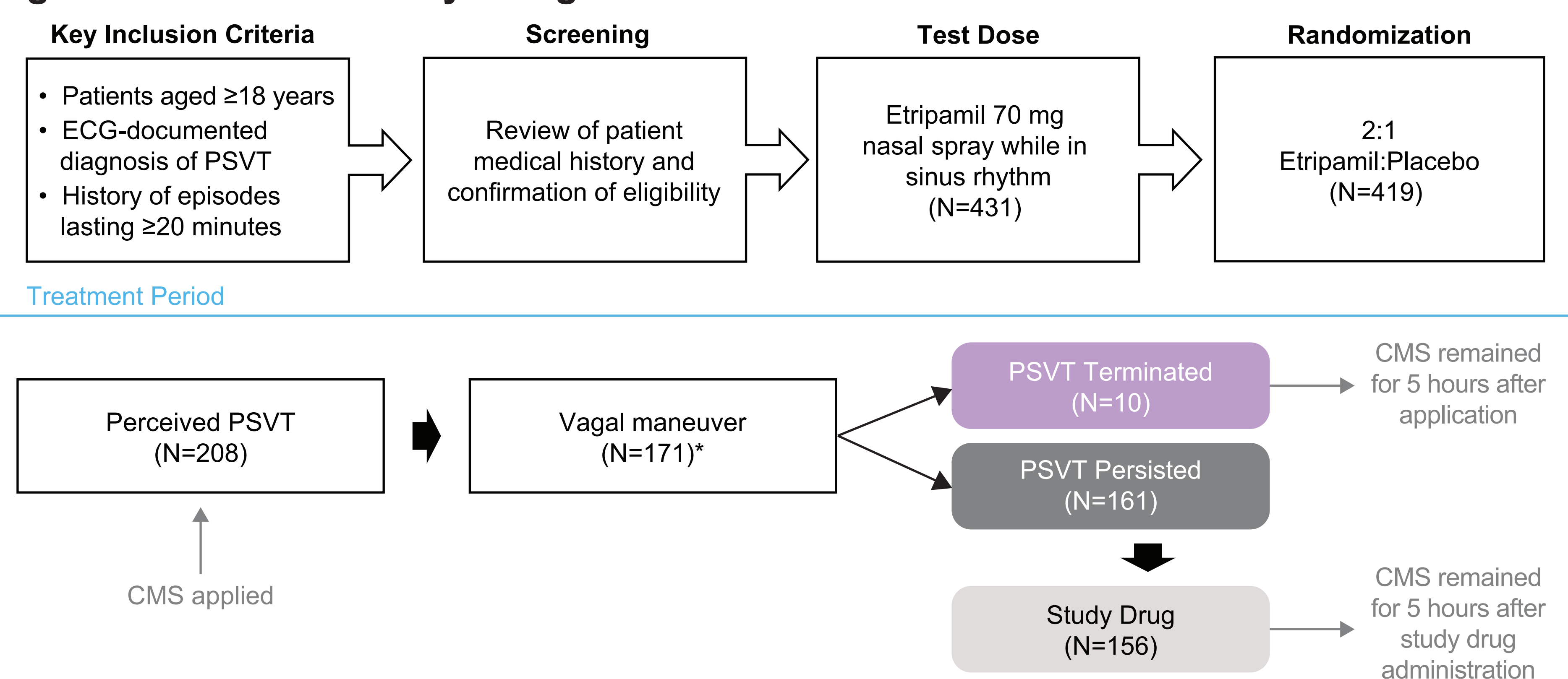
Objective

- The objective of this analysis was to determine the effectiveness of vagal maneuvers as a first-line treatment in resolving episodes of symptomatic sustained PSVT in the NODE-301 study

Methods

- NODE-301 (NCT03464019) was a randomized, double-blind, placebo-controlled, multicenter, phase 3 study evaluating the effectiveness of self-administered etripamil nasal spray for acute termination of PSVT not responsive to vagal maneuver
- Patients aged ≥18 years with a history of sustained AV nodal-dependent PSVT (≥20 minutes in duration) were trained on how to perform a vagal maneuver
- Study patients were instructed to use a vagal maneuver as their first attempt to acutely resolve a perceived PSVT event within a 5-hour monitoring period (**Figure 1**)

Figure 1. NODE-301 Study Design



*Represents number of positively adjudicated PSVT with a vagal maneuver performed. CMS, cardiac monitoring system; ECG, electrocardiogram; PSVT, paroxysmal supraventricular tachycardia.

- Consistent with a real-world environment, the type of vagal maneuver was left to the discretion of the investigator and was not documented
- Each perceived PSVT event was documented by a wearable ambulatory cardiac monitoring system that was placed on the chest when symptoms began and recorded for at least 5 hours by continuous electrocardiogram (ECG)
- Recordings were then reviewed by an independent adjudication committee that confirmed the occurrence and termination of PSVT
- Exploratory efficacy endpoints included the number of confirmed PSVT events that were successfully terminated (ie, converted to sinus rhythm) by a vagal maneuver alone
 - Endpoints were described via descriptive statistics
- If the vagal maneuver was unsuccessful in terminating the episode, patients self-administered study drug (etripamil 70 mg or placebo)

Results

- Overall, 208 (48.3%) of 431 patients in NODE-301 experienced a perceived PSVT event during the study
- 175 of these ECG-recorded events were confirmed (positively adjudicated) as AV nodal-dependent PSVT
- 164 patients performed vagal maneuvers on 171 (97.7%) of the 175 confirmed cases of PSVT
 - The baseline characteristics of these patients are reported in the **Table**

Table. Baseline Characteristics of Patients Who Performed Vagal Maneuvers for Confirmed PSVT Events

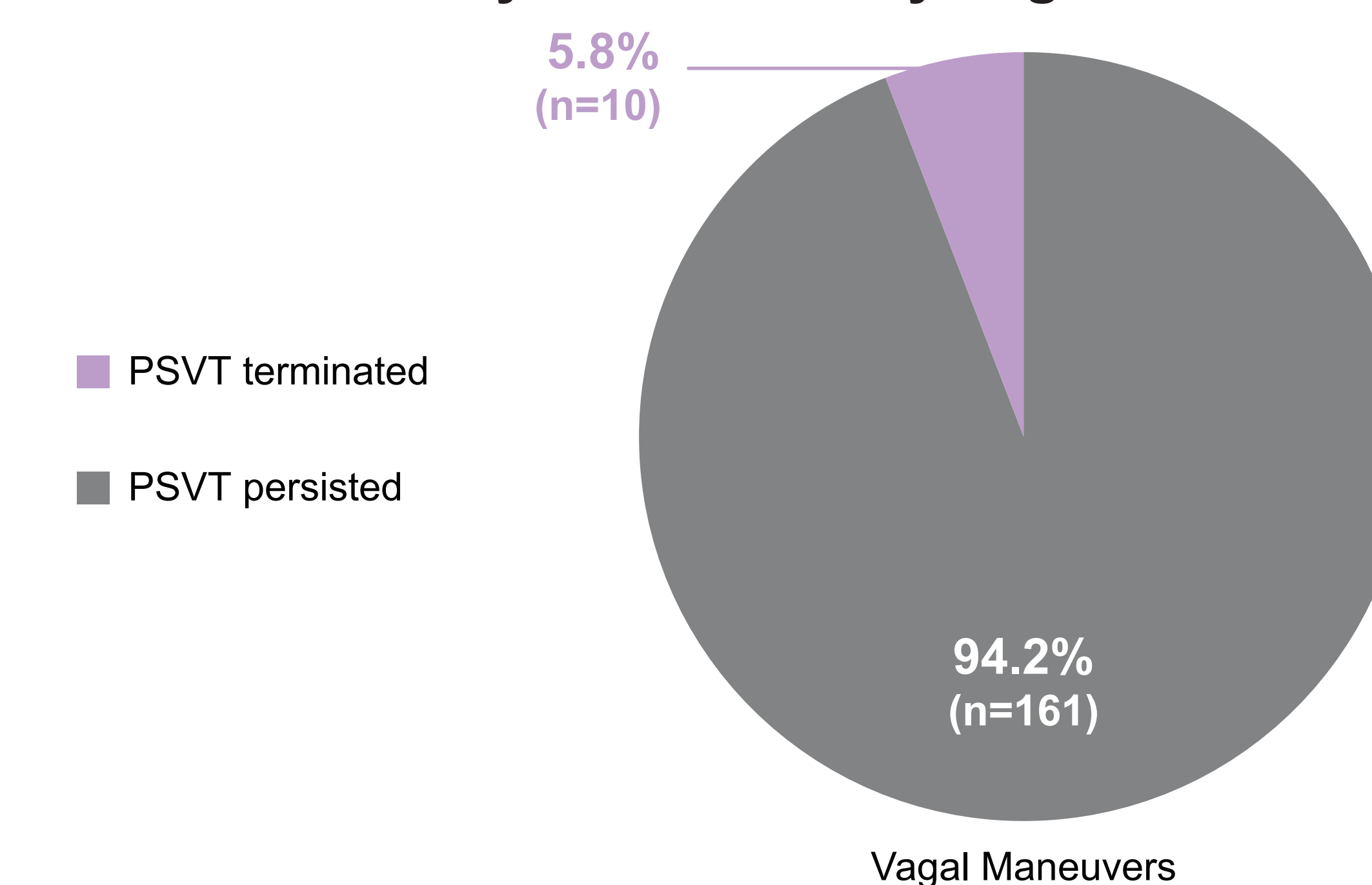
Characteristic	Overall (N=164)
Age, years	55.8 (13.5)
Female, n (%)	111 (67.7)
BMI at screening (kg/m ²)	28.6 (7.3)
Age at PSVT confirmation, years	54.9 (13.6)
PSVT duration, years	1.4 (2.4)
PSVT events in past year	8.9 (10.2)
Lifetime ED visits for PSVT events	3.0 (3.8)
Prescribed beta blocker	60 (36.6)
Prescribed calcium channel blocker	46 (28.0)
Hypertension, n (%)	56 (34.1)

Values are mean (SD) except as indicated. BMI, body mass index; ED, emergency department; PSVT, paroxysmal supraventricular tachycardia; SD, standard deviation.

- **Vagal maneuvers alone terminated only 10 (5.8%) of 171 PSVT events prior to administration of study drug (Figure 2)**

- For the remaining symptomatic PSVT episodes that persisted after vagal maneuvers, 156 were treated with study drug

Figure 2. PSVT Successfully Terminated by Vagal Maneuver



PSVT, paroxysmal supraventricular tachycardia.

Conclusions

- This is the first report on the effectiveness of vagal maneuvers in terminating ECG-adjudicated PSVT in a real-world setting
- In this study, vagal maneuvers alone were rarely successful in terminating symptomatic sustained PSVT despite patients being trained on the procedure beforehand
- A limitation of the study is that details regarding the type of vagal maneuvers performed and the number of attempts were not collected, and some patients may not have applied the CMS if PSVT was not sustained
- Patients with recurrent PSVT should be counseled about the limited effectiveness of vagal maneuvers when self-performed outside a medically supervised setting
- There remains an unmet therapeutic need for a safe and effective at-home, on-demand therapy to reliably and quickly terminate PSVT

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Disclosures

BSS, BM, and AJC are consultants for Milestone Pharmaceuticals, Inc. JEI is a steering committee member for Milestone Pharmaceuticals, Inc. FP and SS are employees of Milestone Pharmaceuticals, Inc.

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