Consistency and Predictiveness of Conversion Among Multiple Episodes of Paroxysmal Supraventricular Tachycardia (PSVT) Treated With Etripamil: Outcomes From the NODE-303 Trial

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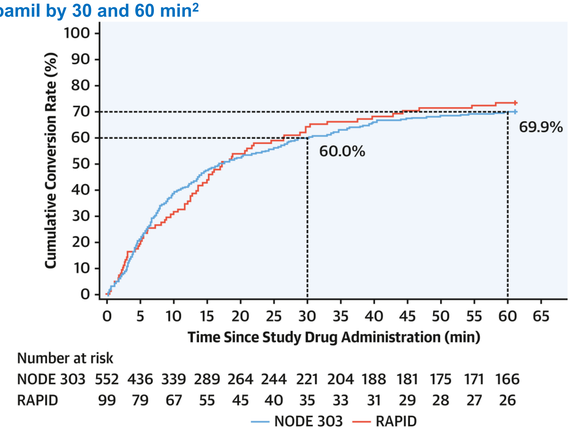
INTRODUCTION

- 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]
- In a prior open-label study, NODE-302, the safety and efficacy of single-dose etripamil was evaluated in patients who received a pre-treatment test dose and whose PSVT was treated for up to 11 episodes.[1]
- 109/181 (60.2%) of PSVT episodes converted to sinus rhythm (SR) with self-administered etripamil within 30 minutes (min); 75.1% within 60 min.[1]
- Among patients in whom PSVT was successfully terminated with etripamil during their first episode, 21 of 26 (81%) also had successful termination of PSVT with etripamil during their second episode.[1]
- NODE-303 did not require a test dose prior to treatment and allowed a repeat 70-mg dose if symptoms persisted 10 minutes after the first dose.*[2]
- The cumulative PSVT conversion rate with etripamil by 30 and 60 min from the NODE-303 and RAPID (a prior randomized control trial) studies has been previously published **(Figure).** [2]

FIGURE: NODE-303 and RAPID trial cumulative PSVT conversion rate with etripamil by 30 and 60 min[2]



Conversion of PSVT to sinus rhythm with **etripamil treatment** was **consistent across multiple episodes** and conversion in earlier episodes was **predictive** of conversion in subsequent episodes.

These data support the potential efficacy of **self-administered etripamil nasal spray** to **treat recurrent PSVT episodes without prior test dosing.**

Please scan the QR code for the NODE-303 study publication, or email jei9008@med.cornell.edu for additional information.

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METHODS

- NODE-303 was an open-label study conducted at 148 clinical study sites in the United States, Canada, and Latin America from June 21, 2019, to February 24, 2023 .[2]
- NODE-303 was designed to evaluate the safety and efficacy of etripamil across multiple episodes of PSVT; it was determined that sufficient data could be obtained by evaluating up to 4 episodes.
- To be included, patients (≥18 years of age) needed to be diagnosed with at least one episode of AV nodal–dependent PSVT prior to enrollment.
- When enrolled patients perceived PSVT symptoms, an electrocardiography (ECG) cardiac monitoring system (CMS) was self-initiated, and a pre-trained vagal maneuver was performed; if symptoms persisted, patients self-administered etripamil NS 70 mg.
- No etripamil test dosing occurred prior to first use.
- According to a protocol amendment, a repeat dose of etripamil NS 70 mg could be self-administered 10 min after the first dose. Up to four episodes could be self-treated during the study.
- Safety was assessed through adverse events, clinical data, and ECG CMS recordings.

RESULTS

TABLE. Predictiveness of conversion of PSVT at 60 min between episodes[a]

	Conversion on Next Episode[b]	No Conversion on Next Episode
Conversion on first episode, *n/N* (%)	87/108 (80.6)	21/108 (19.4)
No conversion on first episode, *n/N* (%)	24/43 (55.8)	19/43 (44.2)
Chi-square = 9.6681; *P*= 0.0019		
Conversion on second episode, *n/N* (%)	38/53 (71.7)	15/53 (28.3)
No conversion on second episode, *n/N* (%)	3/18 (16.7)	15/18 (83.3)
Chi-square = 16.6772; *P*< 0.0001		
Conversion on third episode, *n/N* (%)	8/11 (72.7)	3/11 (27.3)
No conversion on third episode, *n/N* (%)	6/7 (85.7)	1/7 (14.3)
Chi-square = 0.4174; *P*= 0.5180		

[a]Patients treating ≥1 episode (Efficacy Population), N=312. [b]Conversion by 60 min was assessed by adjudication of ECG data. Abbreviations: ECG, electrocardiography; PSVT, paroxysmal supraventricular tachycardia.

- Among patients who treated at least two episodes (*n*=151), 108 successfully converted PSVT to SR with etripamil by 60 min in the first episode; of these patients, 87 (80.6%) converted PSVT with etripamil during their second episode (*P*=0.0019) **(Table)**.
- A consistent pattern was observed between later episodes **(Table)**.
- Of patients who treated a fourth episode, 17 of 18 (94.4%) had converted to SR within 60 min during at least one of the prior three episodes.
- An unsuccessful conversion to SR with etripamil during an earlier episode was not predictive of subsequent lack of conversion **(Table)**.
- Among 43 patients who did not successfully convert to SR during their first episode, over half of them (24/43 [55.8%]) still successfully converted PSVT to SR during their etripamil-treated episode **(Table)**.
- This work is limited by the small sample size, specifically in the study groups without successful conversion to SR.
- Future real-world investigation of etripamil would aid in the understanding of conversion across multiple PSVT episodes.

DISCLOSURE INFORMATION

JEI received compensation as a steering committee member for Milestone Pharmaceuticals; and received honoraria/speaking/consulting fees from Abbott Medical, Boston Scientific, and Medtronic Inc. **BC**, **DH**, **JAU JHI**, **PN**, **MLP**, **FR**, **NS**, **NT** declare no conflicts of interest. **SSears** received compensation from Abbott and Medtronic as a consultant; received speaker compensation from Biotronik, Medtronic, and Zoll; serves as a consultant for Thryv Therapeutics, Tenaya, and Milestone Pharmaceuticals. **BS** serves as a consultant for Milestone Pharmaceuticals. **SS**, **DBB** are employees of Milestone Pharmaceuticals. **AJC** has received grants and personal fees from Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, DaiichiSankyo, and Pfizer; personal fees from Biotronik, Boston Scientific, Medtronic, and Menarini; and support from Abbott, Anthos, GlaxoSmithKline, Johnson and Johnson, and Sanofi.

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2. Ip JE, et al. *J Am Coll Cardiol*. 2024;83:2032-2034.

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*The protocol was amended after 21 months to allow a repeat 70-mg dose if symptoms persisted 10 minutes after the first dose.