Minimal Blood Pressure Effects of Intranasal Etripamil for PSVT

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BACKGROUND

Etripamil (CARDAMYST™), a novel intranasal calcium channel blocker (CCB), was FDA approved in December 2025 as the first and only self-administered nasal spray for adults with paroxysmal supraventricular tachycardia (PSVT) and is under investigation for atrial fibrillation with rapid ventricular rate[1]. Phase 3 PSVT trials included NODE-301 parts 1-3, NODE-302, and NODE-303 **(Table 1)** CCBs are associated with a risk of hypotension; therefore, blood pressure (BP) or symptoms of hypotension were assessed.

Table 1. Studies Evaluating the Efficacy and Safety of Etripamil for PSVT

Study	ClinicalTrials.gov ID	Phase	Design*	Dates	Location	*Ref.*
NODE-301 Part 1	NCT03464019	3	DB RCT (2:1 randomized)	06/2018 - 01/2023	U.S., Canada	*[2]*
NODE-301 Part 2, RAPID	NCT03464019	3	DB RCT (1:1 randomized)	10/2020 - 07/2022	U.S., Canada, Europe	*[3]*
RAPID (Extension)	NCT03464019	3	DB RCT (1:1 randomized)	07/2022 - 02/2023	U.S., Canada, Europe	*[4]*
RAPID (Open Label)	NCT03464019	3	Open-label	10/2020 - 07/2022	U.S., Canada, Europe	*[4]*
RAPID (Open Label Extension)	NCT03464019	3	Open-label	07/2022 - 02/2023	U.S., Canada, Europe	*[4,5]*
NODE-302	NCT03635996	3	Open-label	06/2018 - 10/2020	U.S., Canada	*[6]*
NODE-303	NCT04072835	3	Open-label	09/2019 - 01/2023	U.S., Canada, South America	*[7,8]*

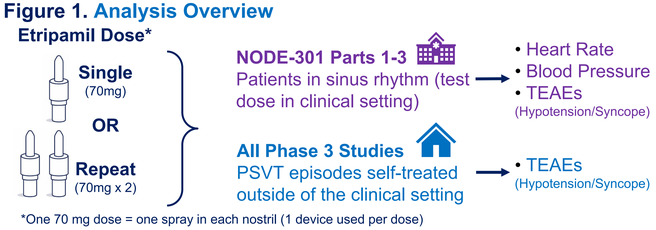
DB=double blind; RCT=randomized control trial; Ref=reference; US=United States. *1:1 and 2:1 indicates the etripamil to placebo randomization ratio in RCTs. **Note:** All studies sponsored by Milestone Pharmaceuticals, Inc.

Kaplan-Meier estimates of **conversion rates by 30 minutes** were **64%** with etripamil and 31% with placebo[3]. **Median time to conversion** was **17.2 minutes** with etripamil and 53.5 minutes with placebo[3].

METHODS

Mean heart rate (HR) and BP change from baseline was analyzed for 30-45 min post-test dose (TD) of etripamil 70mg by NODE 301 parts 1-3 patients in sinus rhythm self-administering either a single (70mg) or repeat TD (70mg x 2, 10 minutes apart) **(Figure 1).** We also report a descriptive analysis of symptoms of hypotension or syncope TEAEs across phase 3 trials conducted during PSVT episodes self-treated outside of the clinical setting **(Figure 1).**

Figure 1. Analysis Overview



*One 70 mg dose = one spray in each nostril (1 device used per dose)

PSVT=paroxysmal supraventricular tachycardia; TEAE=treatment emergent adverse event

Low incidence of hypotension and syncope with intranasal calcium channel blocker etripamil

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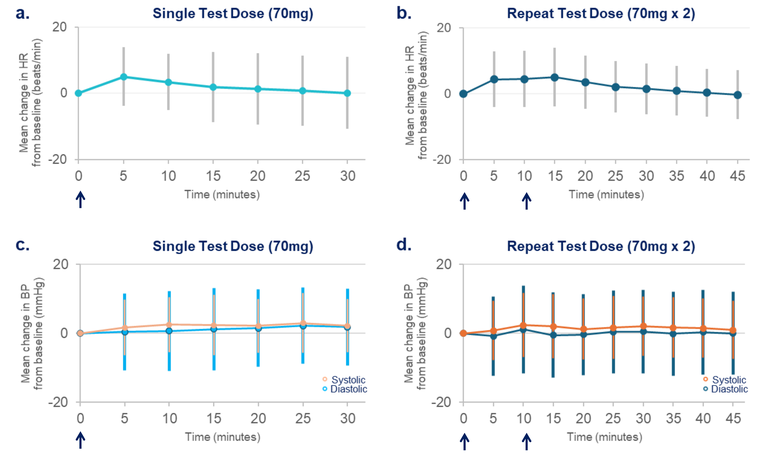
RESULTS

- Minimal changes from baseline HR and BP were observed after etripamil test dose administration **(Figure. 2).** Mean systolic BP change was 1.8 mmHg (SD 11.2) over 30 min for a single 70mg dose (N=438-440, **Figure. 2c**) and 0.0 mmHg (SD 12.0) over 45 min for repeat doses (N=709-714, **Figure. 2d**).

Figure 2. Change in Heart Rate and Blood Pressure After Etripamil Test Dose in Sinus Rhythm



Change in heart rate (HR) (a, b) and blood pressure (BP) (c, d) after etripamil nasal spray test dose. Single (a, c; 70mg, N=438-440) or Repeat (b, d; 70mg x2, N=709-714) doses were administered 10 minutes (arrow) after the first dose among newly enrolled or re-randomized patients in sinus rhythm from NODE-301 parts 1-3. **Note:** N (ranges) due to HR/BP data availability across timepoints.

- Among **1610 patients**, TEAEs of **hypotension and syncope within 24 hours were 0.4% (N=7) and 0.2% (N=4), respectively**. All events resolved without medical intervention.
- Syncope events reported before study drug administration in 2 patients were included as TEAEs; no reports of loss of consciousness from syncope were attributable to etripamil.

DISCUSSION

- Oral and intravenous CCBs carry a risk of hypotension, however minimal BP reduction after intranasal etripamil test dose in sinus rhythm was observed.
- Symptoms of hypotension were rare after self-treatment with etripamil.
- There were no episodes of syncope attributable to etripamil during outpatient, self-treatment of perceived PSVT.

LIMITATIONS

- This work is descriptive and does not include rigorous statistical analysis.
- The generation of high-quality real-world evidence (RWE) outside of clinical trial settings is needed.

CONCLUSON

- Etripamil is a safe therapy for PSVT management and can be used by patients to self-treat episodes.

REFERENCES

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DISCLOSURE INFORMATION

JEI received compensation as steering committee member for Milestone Pharmaceuticals, honoraria/speaking/consulting fees for Abbott Medical, Boston Scientific, and Medtronic Inc. NS and BSS are consultants for Milestone Pharmaceuticals. JPP received personal fees from Milestone Pharmaceuticals outside the submitted work. SS, and DBB are employees of Milestone Pharmaceuticals. AJC received compensation as a consultant for Milestone Pharmaceuticals; grants and personal fees from Acesion, Sanofi, Anthos and Johnson and Johson; personal fees from Medtronic, Boston Scientific, Menarini, and Biotronik; and support from Anthos, Sanofi, Abbott, GlaxoSmithKline, and Johnson & Johnson.