Effect of Etripamil Nasal Spray on Ventricular Rate in Patients Experiencing Symptomatic Atrial Fibrillation

NODE-303 Atrial Fibrillation Heart Rate Analysis

Paul Dorian, MD[1]; Marco Alings, MD, PhD, FESC[2]; Benoit Coutu, MD[3]; James E. Ip, MD, FACC, FHRS[4]; Felipe A. Martinez, MTFAC, FACC, FESC[5]; Jonathan P. Piccini, MD[6]; Bruce S. Stambler, MD[7]; Nathalie Thermil, MSc[8]; Sarah Omodele, DNP, FNP[9]; Silvia Shardonofsky, MD[8]; Francis Plat, MD[8]; David B. Bharucha, MD, PhD, FACC[9]; A John Camm, MD, FRCP, FAC, FESC, FHRS[10]

1. University of Toronto; Division of Cardiology, St. Michael's Hospital, Toronto, ON, Canada. 2. Amphia Ziekenhuis, Breda, North Brabant, Netherlands. 3. Department of Medicine, University of Montréal; Cardiac Electrophysiology Department, Centre Hospitalier Universitaire de Montréal, Montreal, QC, Canada. 4. Division of Cardiology, Weill Cornell Medicine, New York, NY, USA. 5. Universidad Nacional de Córdoba; Instituto DAMIC/Fundacion Rusculleda, Córdoba, Argentina. 6. Department of Medicine, Duke University School of Medicine, Durham, NC, USA. 7. Piedmont Heart Institute, Atlanta, GA, USA. 8. Milestone Pharmaceuticals, Montreal, QC, Canada. 9. Milestone Pharmaceuticals, Charlotte, NC, USA. 10. St. George's University of London, London, England, UK.

Atrial Fibrillation with Rapid Ventricular Response (AF/RVR)

- Atrial fibrillation is often associated with symptoms related to a rapid ventricular response

- There are no available rapidly acting agents to slow ventricular rates, suitable for outpatient self-administration

- Etripamil is a novel calcium channel blocker formulated for intranasal administration ,with rapid onset of action ($T_{max} \leq 7$ min), under investigation for reentrant SVT

Comparison of PK and PD Profile of Etripamil 70 mg (N=24)
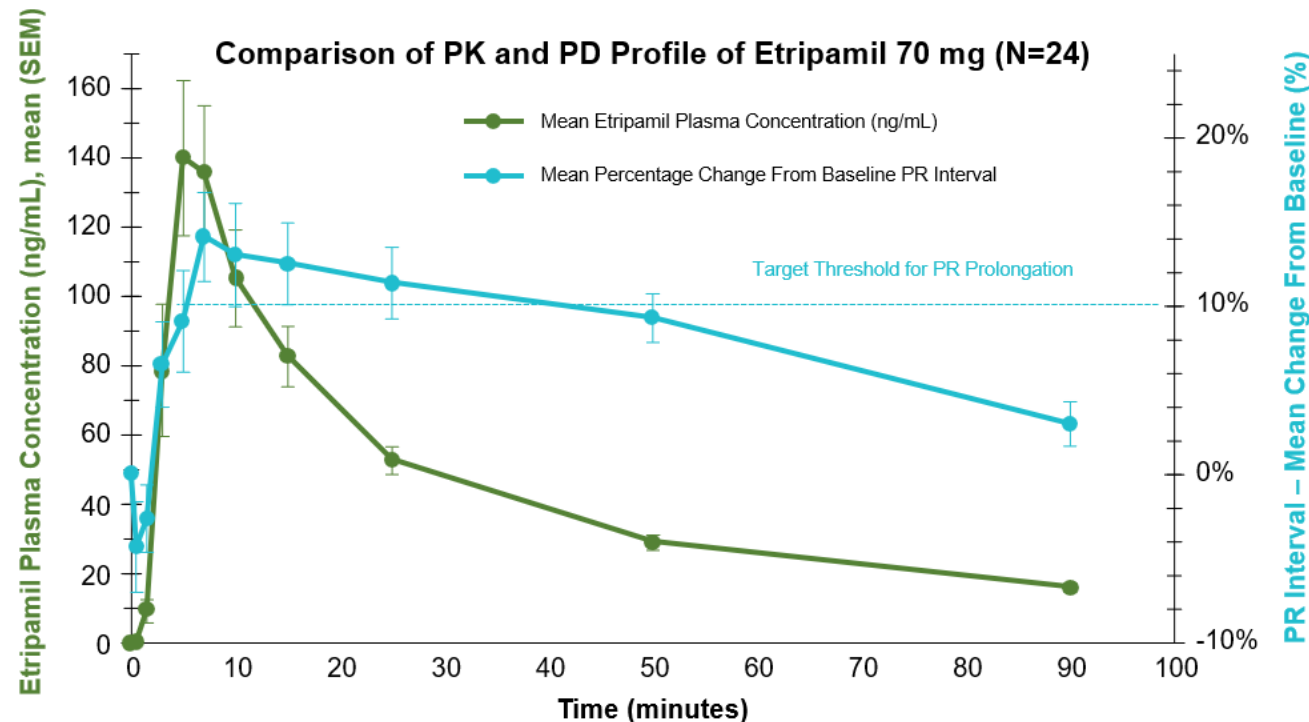
NODE-303: Open-Label, Phase 3 Trial of Etripamil for SVT

Trial Design

- Event-driven, multi-center, open-label, multi-exposure study to evaluate the safety of etripamil in patients with PSVT

- Patients perceived PSVT episodes as outpatients and self-administered etripamil nasal spray (70 mg)

- Continuous ECG data (patient applied) were acquired at the onset of symptoms for 1 hour

Current study: Ad Hoc Analysis in patients with AF

Some patients in NODE-303 experienced AF rather than PSVT; these episodes were the subject of this sub-study.

- 21 of 1024 treated perceived-PSVT episodes (n = 18 patients) were actually AF/RVR rather than PSVT based on ECG data

- Start of ECG recording was used as Time=0 for assessment of ventricular rate

PSVT = paroxysmal supraventricular tachycardia; ECG = electrocardiogram.

Results

	PATIENTS WITH AF EPISODES (n=18)
Mean age, years	56.3
Female, %	56

	BASELINE	15 MIN	30 MIN
AF ECGs used for analysis (NSR excluded)	21	20	19
Mean VR	129.7	104.6	110.7
SD	24.8	28.7	27.6
SEM	5.4	6.4	6.3
Median VR	127.0	95.5	108.0
Mean % change in VR from Baseline		-23.2	-18.4
SD		25.6	28.0
SEM		5.7	6.4
Median % change in VR from Baseline		-28.5	-22.0

	PATIENTS WITH AF EPISODES (n=18)
Patients with mild/moderate AEs* related to drug, n (%)	7 (39)
Patients with severe AEs related to drug, n (%)	0 (0)

*The most frequent AEs were nasal congestion, nasal discomfort, and rhinorrhea.

AE = adverse event; NSR = normal sinus rhythm; VR = ventricular rate.

Change in Ventricular Rate from Baseline
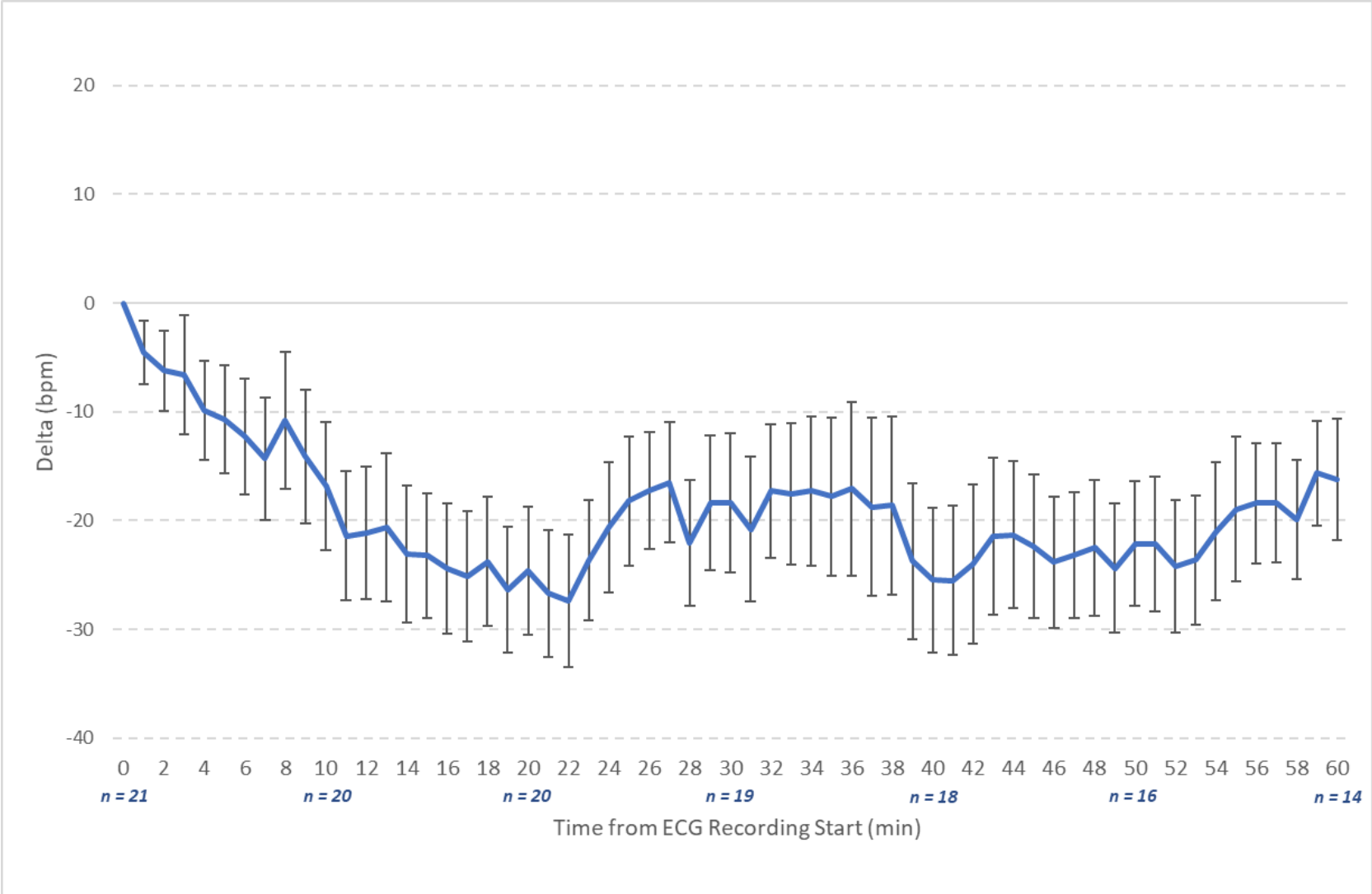
Average difference ± standard error from baseline in ventricular rate. The start of the ECG recording was used as an estimated dosing time for all episodes.

#HRS2023

Limitations

- Time of drug administration was variably related to the start of ECG recording

  - Start time of the ECG recording was used as baseline for the analysis

- Patients have a history of SVT, and may not be representative of the entire AF population

Conclusions

- In patients experiencing episodes of atrial fibrillation (AF) and a rapid ventricular response rate (RVR), self-administration of etripamil, an investigational new drug, resulted in a reduction in the ventricular rate that was sustained over 60 min

- Timing of response aligned with the known pharmacologic profile of etripamil nasal spray

- These findings warrant further study and suggest a potential role for the drug in the acute control of RVR in patients with AF