Analysis of Clinical Outcomes in the Node-301 Trial:

Etripamil Nasal Spray Relieves Symptoms and Reduces Emergency Room Interventions in Patients with Paroxysmal Supraventricular Tachycardia (PSVT)

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Disclosures

- ***B Stambler***: Honoraria, Consulting Fees, Contracted Grants for PIs - Milestone.
- The **NODE-301** trial and these analyses were funded by Milestone Pharmaceuticals.
- The trial was conducted and coordinated by Medpace.

Etripamil

- Novel, L-type calcium channel blocker
- Administered as a rapidly-acting nasal spray
- Being developed as a self-administered therapy to terminate AV nodal-dependent PSVT.

Phase 3 Efficacy and Safety Study of Etripamil Nasal Spray

- Rapid termination of symptomatic, sustained PSVT;
- Multi-center (US and Canada);
- Nasal spray self-administered during PSVT outside the emergency room or hospital without direct medical supervision.

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Study Design

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Objective: Superiority of etripamil over placebo in terminating PSVT events in the outpatient setting

Randomized
Etripamil:Placebo (2:1)
(N=419, 97%)

Patient dosed for suspected episode
Safety Dataset
(N=198, Etripamil=138, Placebo=60)

Test Dose
Active drug while in SR
(N=431)

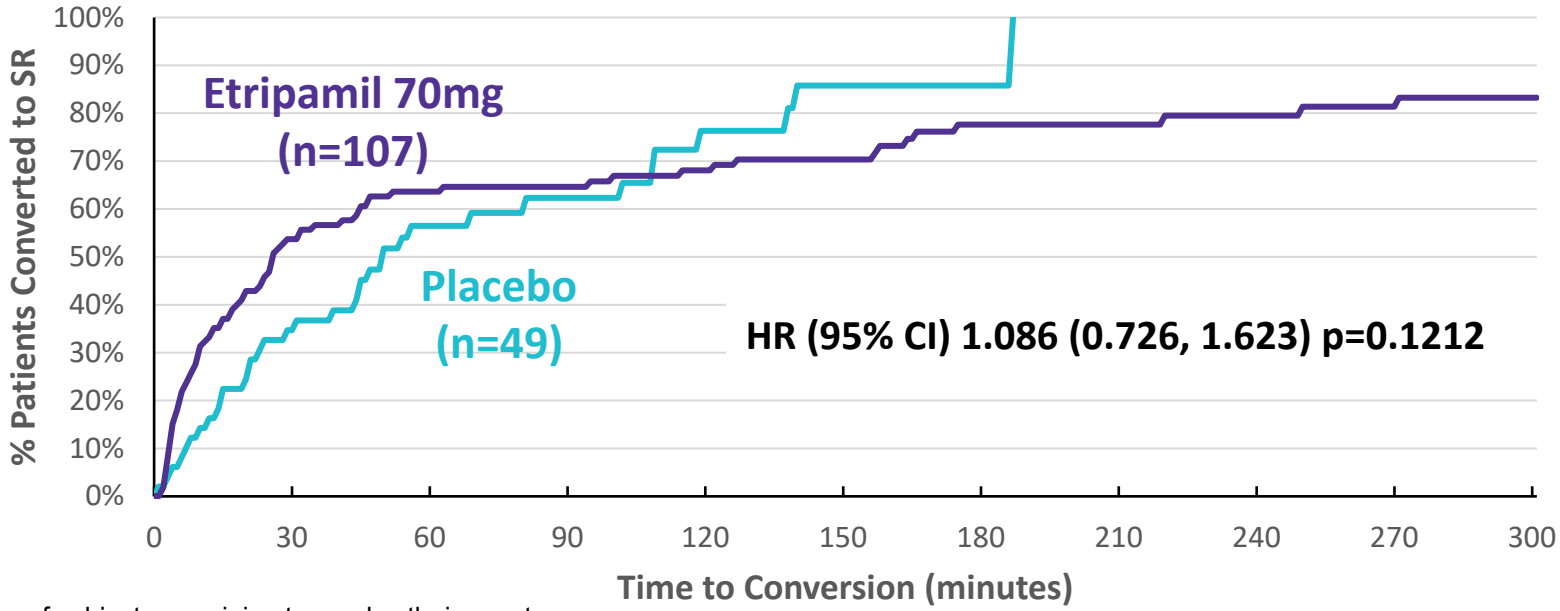
Positively-Adjudicated PSVT events
Efficacy Dataset
(N=156, Etripamil=107, Placebo=49)

Documented diagnosis of PSVT with a history of episodes lasting ≥ 20 minutes

PSVT = Paroxysmal Supraventricular Tachycardia; SR = Sinus Rhythm;

NODE-301 Primary Endpoint – Time to Conversion

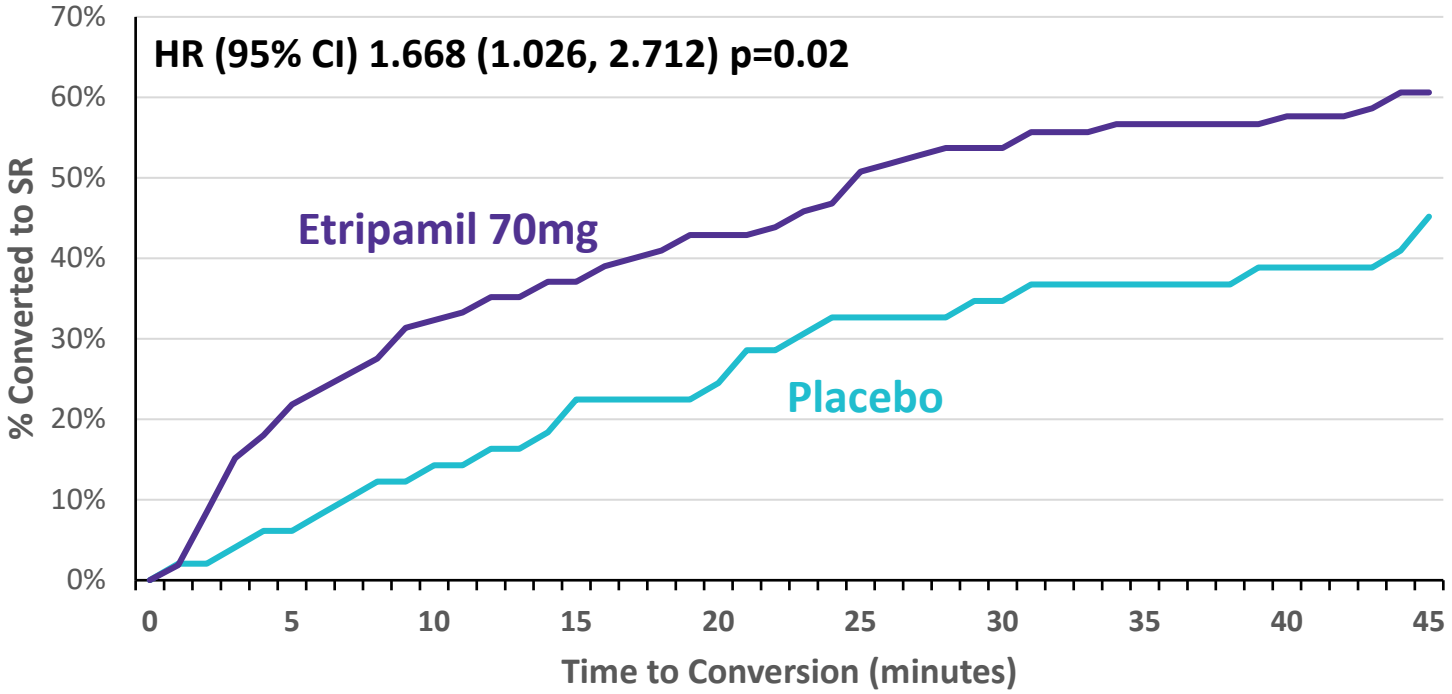
Kaplan-Meier analysis of time to conversion of positively-adjudicated PSVT episodes over 5 hours



Number of subjects remaining to resolve their event

Placebo	49	32	18	12	5	1	1	0			
Etripamil	107	47	36	31	28	22	15	13	11	9	3

NODE-301 Efficacy – Time to Conversion over 45 Minutes



Objectives

- **To compare efficacy of etripamil with placebo regarding the following prospectively-defined, key secondary clinical endpoints:**
  - **relief of specific PSVT-related symptoms;**
  - **patient-reported satisfaction with treatment;**
  - **need for emergency room (ER) medical interventions;**
  - **need for additional rescue medical therapy.**

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Demographics

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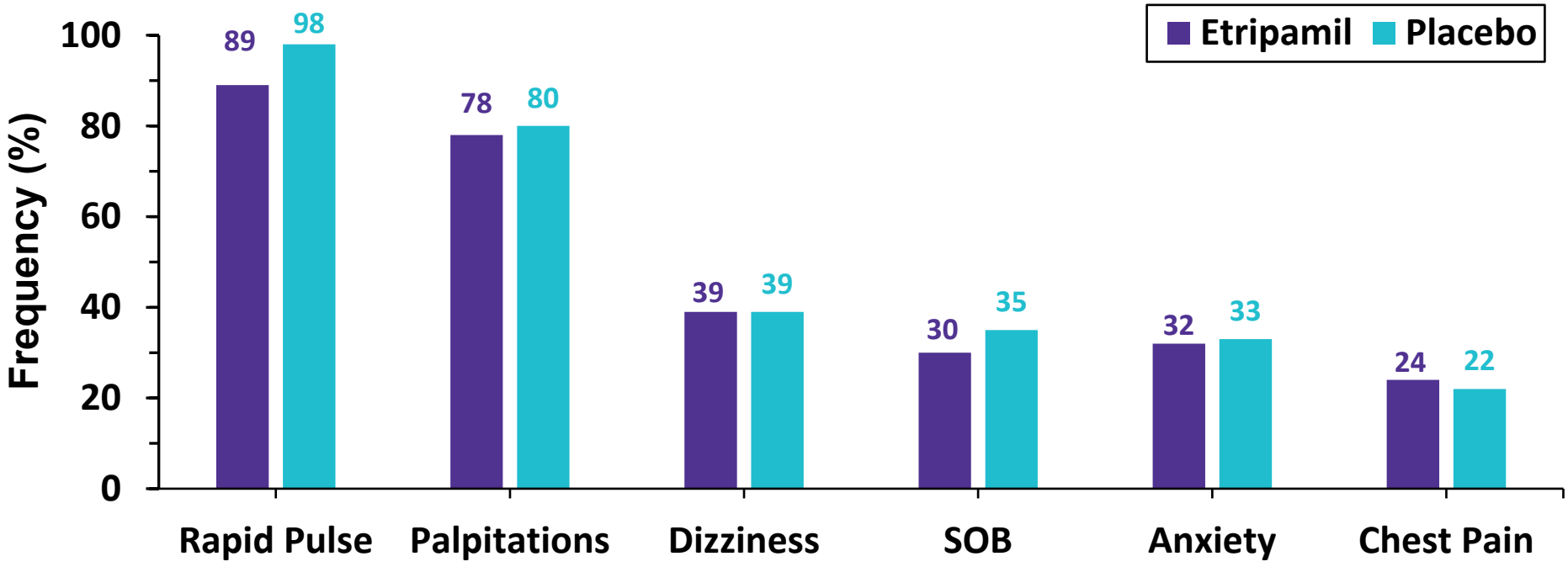
	Efficacy Population	
	Etripamil (N=107)	**Placebo** (N=49)
Age, years	56.9	54.3
Gender		
Female, n (%)	73 (68.2)	33 (67.3)
Male, n (%)	34 (31.8)	16 (32.7)
PSVT Duration, yrs	1.5	1.3
# PSVT in past yr	7.4	11.3
Lifetime ER visits	2.7	3.4

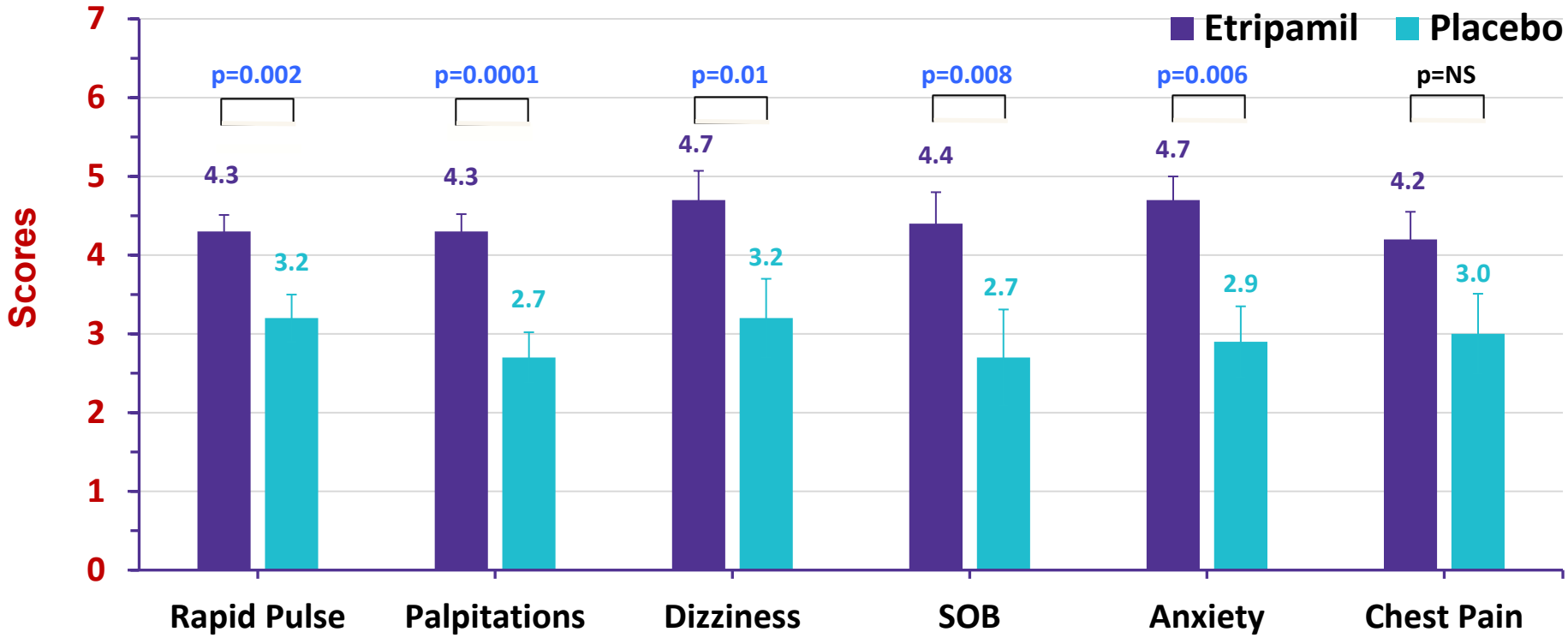
ER = emergency room

Specific PSVT Symptoms



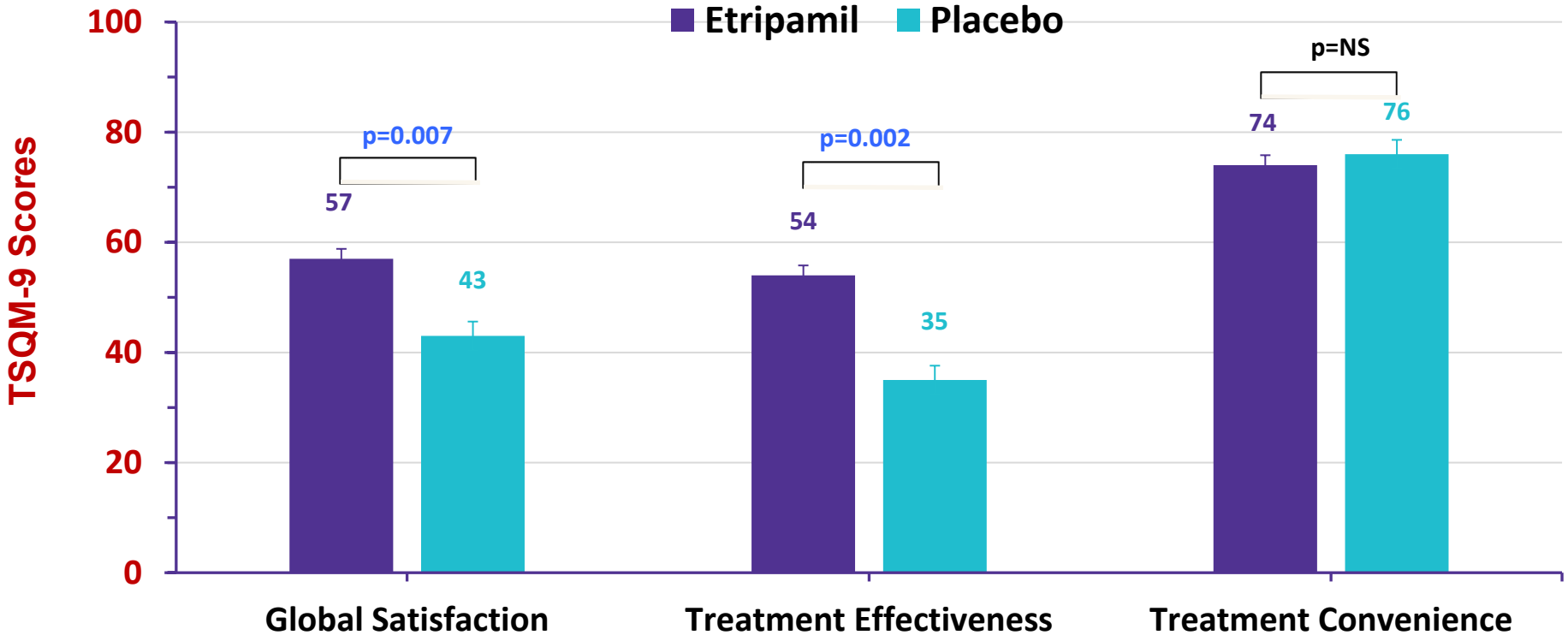
SOB = shortness of breath

Relief of PSVT Symptoms



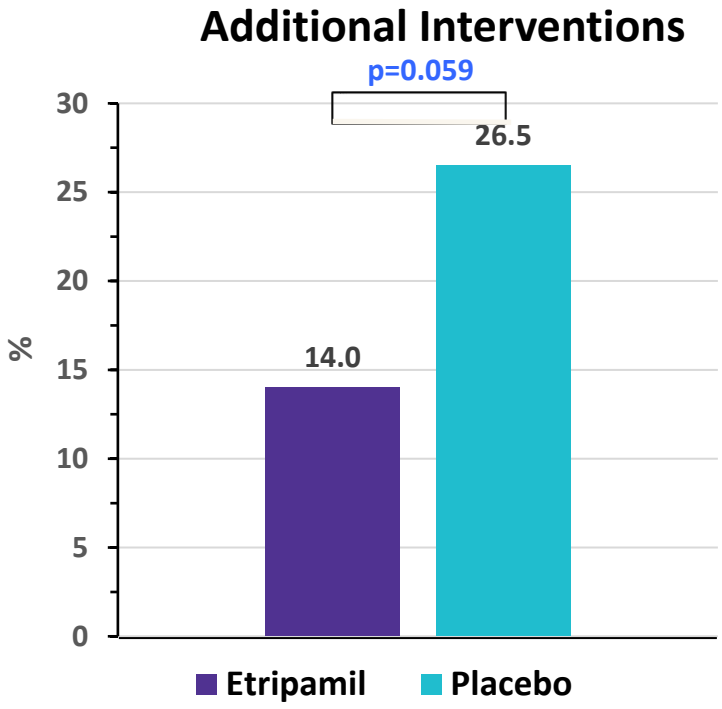
Scores: 1 = extremely dissatisfied; 2 = very dissatisfied; 3 = dissatisfied;
4 = somewhat satisfied; 5 = satisfied; 6 = very satisfied; 7 = extremely satisfied.

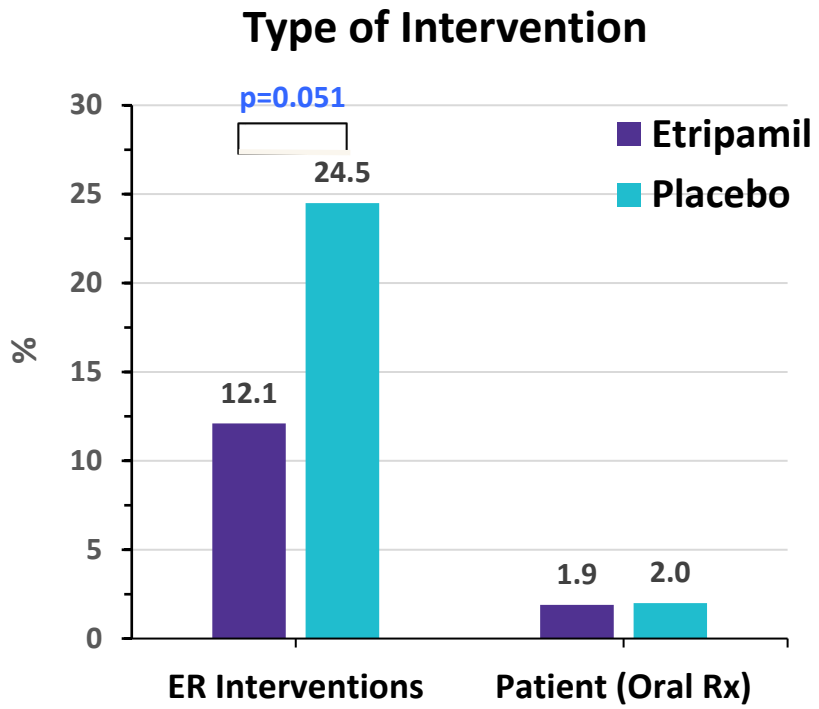
Patient-Reported Satisfaction with Study Medication (TSQM-9®)



TSQM-9: 9-Item Treatment Satisfaction Questionnaire for Medication (Scores: 0-100).

Rescue Medical Interventions Sought for PSVT

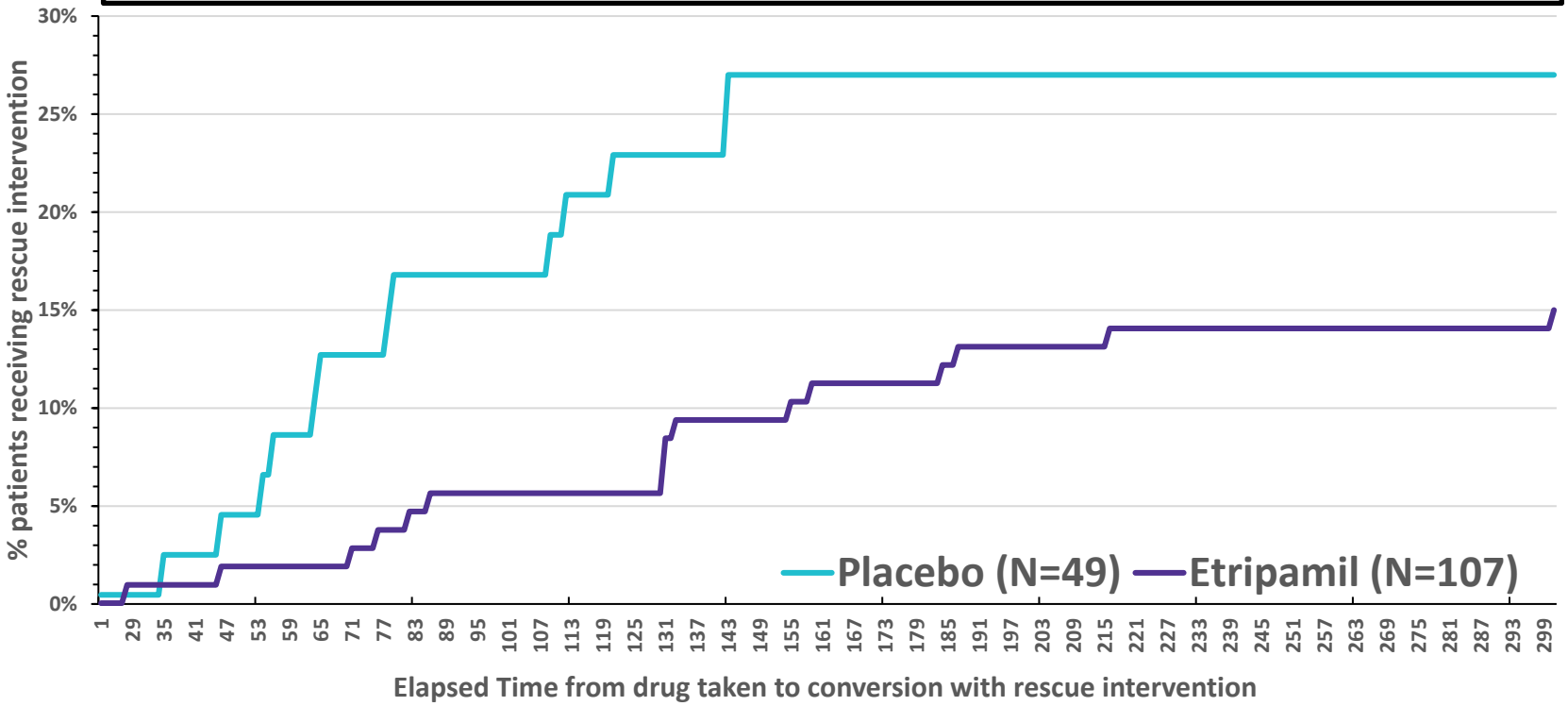




ER Interventions (n=25): IV adenosine n=20; IV adenosine + oral verapamil n=1; IV procainamide n=1; IV diltiazem n=2; vagal-maneuver n=1.
Patient Self-Administered Rescue Medications (n=3): oral beta-blocker n=2; verapamil n=1.

Rescue Medical Medications by Time

- Time to ER intervention occurred later in the etripamil vs. placebo group*
  - 116±14 vs. 79±10 minutes, p<0.05



* Recommended not earlier than 20 minutes after study drug administration

Summary

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- Etripamil significantly improved PSVT-related symptoms.
- Satisfaction and effectiveness of at-home, nasal spray therapy for PSVT were higher for etripamil than placebo.
- Etripamil tended to reduce need for emergency room medical interventions for PSVT.
- These data support continued development of etripamil nasal spray for acute treatment of PSVT.