C-LBCT01 Session: Late-Breaking Clinical Trials I

Thursday, May 11, 2017
8 - 9:30 a.m.

CHAIRS:

Jeanne E. Poole, MD, FHRS, CCDS. *University of Washington, Seattle, WA*

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C-LBCT01-01

THE S-ICD POST-MARKET APPROVAL STUDY

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Introduction: The subcutaneous ICD (S-ICD) was developed to reduce short and long term complications associated with transvenous ICD leads. Early studies in the US and Europe were enriched with younger patients with less left ventricular systolic dysfunction and fewer comorbidities than transvenous ICD subjects, making comparisons between systems difficult. Following FDA approval in 2013 a prospective registry of the S-ICD was undertaken, which is the largest study of this device to date.
Methods: Pre-implantation patients were enrolled if they met criteria for ICD, passed at least one vector in ECG screening and had a life expectancy > 1 year. Implant technique, programming and conversion testing were performed using the standard of care of investigational centers. Results were analyzed with descriptive statistics, Kaplan Meier time to event analysis, and multivariate logistic regression.
Application: The study included 1637 patients implanted with an S-ICD at 86 US centers. The majority of patients were treated for primary prevention with LV dysfunction (EF≤35%), and 13.4% were on dialysis. Patient demographics and comorbidities are shown in the Table. ECG screening was successful in at least one, two, or three vectors in 100%, 93.8%, and 51.4%, respectively. Multivariate analysis yielded no clinical predictors of number of vectors passed. The system was implanted with two incision technique in 52.2% of patients and under general anesthesia in 64.1%. Repositioning occurred in 2.8% of patients during initial implant and in 0.7% during 30-day follow-up. Conversion of induced VT/VF was successful in 98.7%, with first shock conversion achieved in 95.6%. The 30-day complication-free rate was 96.2% including an infection rate of 1.2%. Predictors of complications included female gender and diabetes.
Next Steps/Future: Contemporary US patients implanted with an S-ICD are younger with more end state renal failure but otherwise have similar co-morbidities and clinical characteristics as transvenous ICD patients. Implantation success is high and short term complication rates are acceptable. At the time of presentation, mean follow-up will be 2 years; follow-up will continue to 5 years for all patients.

Demographics and Comorbidities				
Demographics			**Diagnosed Conditions**	
Age (years)	53.2±15.0		Heart Failure	74.0%
Male	68.6%		Hypertension	61.6%
Caucasian	60.2%		Diabetes	33.6%
African American	28.2%		Hemodialysis	13.4%
Height (in)	68.1 ± 4.2		Channelopathies	5.1%
Weight (lb)	197.2 ± 53.5			
BMI	29.8 ± 7.6		**Medications**	
Creatinine (mg/d L)	2.0 ± 3.2		Beta-Blockers	85.0%
EF	32.0 ± 14.6%		ACE / ARB	57.3%
EF ≤35%	75.4%		Diuretics	50.1%
Indication			Anticoagulants	25.9%
Primary Prevention	76.7%			
Secondary Prevention	23.3%		**Procedure History**	
Cardiac Disease History			PCI	27.5%
Myocardial Infarction	33.2%		CABG or Valve Surgery	20.6%
Cardiac Arrest	15.4%		Pacemaker	2.7%
Endocarditis / Bacteremia	6.7%		Previous ICD	12.9%

C-LBCT01-02

INTRANASAL ETRIPAMIL FOR CONVERSION OF PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA (PSVT). NODE-1 TRIAL

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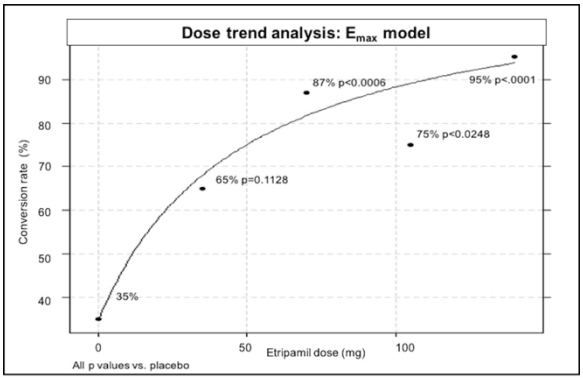
ter, MN, University of Kansas Medical Center, Kansas City, KS, Baylor St-Luke's Hospital, Houston, TX, Mayo Clinic at Jacksonville, Jacksonville, FL, Mercy General Hospital, Sacramento, CA

Introduction: PSVT termination may require acute IV administration of adenosine, calcium channel blockers, or beta-blockers to restore sinus rhythm. Etripamil is a rapid onset of action, short-acting L-type calcium channel blocker designed for intranasal administration. Etripamil is being developed as a self-administered therapy to terminate PSVT outside of the emergency room or hospital.
Methods: NODE-1 is a Phase 2, multicentre, randomized, parallel-group, double-blind, placebo-controlled study designed to evaluate the efficacy of different doses of etripamil in terminating PSVT during an EP study. Following induced 5 minute-sustained AVRT or AVNRT, one dose of 35 mg, 70 mg, 105 mg, 140 mg of etripamil, or placebo was administered to the patient according to randomization. The primary endpoint was the termination rate of PSVT within 15 minutes of study drug administration. Conversion rates for each etripamil dose were compared to placebo by Fisher's exact test. Secondary endpoints included time to conversion, dose-related trend in efficacy and side effects. Clinicaltrial.gov ID: NCT02296190.
Application: A total of 104 subjects were randomized and received the study drug. Conversion rates were 65%, 87%, 75%, and 95% for the etripamil 35 (n=20), 70 (n=23), 105 (n=20), and 140 mg (n=21) groups respectively, compared to 35% in the placebo group (n=20); differences vs. placebo were statistically significant ($p<0.05$) for all but the 35 mg dose. The mean time to conversion (SD) in patients who converted ranged from 2.60 (1.92) to 3.37 (2.12) min in the etripamil groups. The Emax, i.e., asymptotic model best fitted the dose-response (see figure). The most common adverse event was nasal congestion (up to 45%) with etripamil vs. none with placebo. Transient Mobitz 1, second-degree AV block was observed in one patient (140 mg). A transient reduction in blood pressure was observed at the two highest doses, two cases of hypotension were reported as adverse events.
Next Steps/Future: Etripamil showed high efficacy and was well tolerated without major adverse effects. The next step of the development will test etripamil in a "real world" situation of patient self-administration to terminate PSVT.



C-LBCT01-03

LONG DETECTION PROGRAMMING IN SINGLE CHAMBER DEFIBRILLATORS REDUCES UNNECESSARY THERAPIES AND MORTALITY: THE ADVANCEIII TRIAL.

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Introduction: Programming strategies may reduce unnecessary implantable cardioverter defibrillator (ICD) shocks and their adverse effects but to date have been described only for dual chamber ICDs. We aimed to evaluate the effects of programming a long detection in single chamber (VVI) ICDs in the multicenter prospective ADVANCEIII trial.
Methods: 545 subjects (85% male, atrial fibrillation (AF) 25%, LVEF 31%, ischemic etiology 68%, secondary prevention indications 32%) receiving VVI ICDs were randomized to Long Detection (30/40 intervals) or Standard Programming (18/24) based on device type, AF history and indication. In both arms, anti-tachycardia pacing (ATP) therapy during charging was programmed for episodes with cycle length 320-200 ms and shock only for cycle length <200 ms; wavelet and stability functions enabled. Therapies delivered were compared using a negative binomial regression model.
Applications: 267 patients were randomized to long detection and 278 to control group. Median follow up was 12 months. 112 therapies (shocks and ATP) occurred in long detection vs 257 in the control arm, ie a 48% reduction with 30/40 (95%CI: 0.36-0.76, p=0.002). In the long detection vs control, overall shocks were reduced by 40% (48 vs 24, 95%CI: 0.38-0.94, p=0.026) and appropriate shocks by 51% (34 vs 74, 95%CI: 0.26-0.94, p=0.033). Syncopes did not differ between arms but survival improved in the long detection (Fig.1).
Next Steps/Future: Among patients implanted with VVI ICDs programming long detection significantly reduced appropriate therapies, shocks and all-cause mortality.